APPLICATION OF ION EXCHANGE RESINS AS TABLET DISINTEGRANTS

By

Miss Nistakan Pattarakan

A Thesis Submitted in Partial Fulfillment of the Requirements for the Degree
Master of Pharmacy
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การประยุกต์ใช้เรซินแลกเปลี่ยนอิออนเป็นสารช่วยแตกตัวในยาเม็ด

โดย
นางสาวนิษฐกานต์ ภัทรกานต์

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาเภสัชศาสตรมหาบัณฑิต
สาขาวิชาเทคโนโลยีเภสัชกรรม
บัณฑิตวิทยาลัย มหาวิทยาลัยศิลปากร
ปีการศึกษา 2554

The Graduate School, Silpakorn University has approved and accredited the Thesis title of "Application of ion exchange resins as tablet disintegrants" submitted by Miss Nistakan Pattarakan as a partial fulfillment of the requirements for the degree of Master of Pharmacy in Pharmaceutical Technology.

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51353203 : MAJOR : PHARMACEUTICAL TECHNOLOGY
KEY WORD : ION EXCHANGE RESIN / DISINTEGRATION / DEXTROMETHORPHAN / DICLOFENAC
NISTAKAN PATTARAKAN : APPLICATION OF ION EXCHANGE RESINS AS TABLET DISINTEGRANTS. THESIS ADVISORS : ASST. PROF. PRASERT AKKARAMONGKOLPORN, Ph.D., AND ASSOC. PROF. PRANEET OPANASOPIT. 191 pp.

The purpose of this study was to investigate various ion exchange resins as disintegrant for tablet formulation. Ten types of ion exchange resins, Amberlite® IRP64, Amberlite® IRP69, Dowex® 88, Dowex® retardion, Dowex® 50Wx2-200, Dowex® 50Wx4-200, Dowex® 50Wx8-200, Dowex® 1x2-200, Dowex® 1x4-200 and Dowex® 1x8-200 were investigated. Sodium starch glycolate (SSG), which is commonly used as superdisintegrant, was chosen as positive control. In this work, all tablet formulations with and without model drugs (dextromethorphan hydrobromide, DMP and diclofenac sodium, DCN) were prepared by direct compression, and then their physical properties, i.e. hardness, thickness, diameter, friability including disintegration time of tablets and their dissolution were evaluated. Among the resins, Amberlite® IRP64, Amberlite® IRP69 and Dowex® 1x2-200 provided the tablets with sufficient hardness, suitable friability and short disintegration time. According to swelling study, the disintegrating effect of the resins might be attributed to couple mechanisms of their swelling and wicking (capillary) properties. These three resins were chosen as disintegrant for further study on the factors affecting the physical properties such as the amount of resin, compression pressure and type of diluent. The results showed that the hardness decreased with an increase of the amount of resin as disintegrant. Consequently, the excess amount of resin might cause poor stability of tablets due to higher friability. In addition, an increase in hardness resulted from an increase in compression pressure. This contributed to the longer disintegration time. Nonetheless, the higher compression pressure had no an influence on the tablets containing Dowex® 1x2-200. Type of diluents (dibasic calcium phosphate, DCP, spray dried lactose, SDL, microcrystalline cellulose, MCC and spray dried rice starch, SDRS) also had an effect on the disintegrant properties of these resins. MCC provided the highest hardness, whereas the hardness of SDRS and SDL tablets were higher than that of DCP tablet. However, the disintegration time of these tablets differed from each other depending on type of resins. When prepared as tablet formulations of DMP and DCN, freely and poorly water soluble model drugs respectively, the physical properties of resultant tablets using Amberlite® IRP64 and Dowex® 1x2-200 as disintegrants were comparable to those using SSG. In the case of DMP, the disintegration time of these tablets was ranked as follows; Amberlite® IRP64 (25.92 ± 1.73 sec) > SSG (16.25 ± 0.45 sec) > Dowex® 1x2-200 (8.00 ± 1.04 sec). The rapid released rate of DMP was found in all formulations. The fastest release rate was observed in tablet containing Dowex®1x2-200. In addition, the released amount of DMP from tablets containing Amberlite® IRP64 was obviously lower than others. As with DCN, the hardness and disintegration times of tablets containing the three resins were ranked in agreement with DMP. However, the extent of drug released from tablets containing Dowex® 1x2-200 was considerably lower than that of tablets containing SSG and Amberlite® IRP64. In addition, the release profile between DMP and DCN were highly different. As expect, the cumulative release and rate of freely water soluble drug, DMP, was higher than that of poor water soluble drug, DCN. These results demonstrated that the dissolution of drug from the tablets containing those resins dramatically depended on the type of resins and solubility of drugs. Finally, it could be concluded that ion exchange resins, if appropriately selected, could be a new disintegrant alternatively usable in tablet formulation.

Program of Pharmaceutical Technology Graduate School, Silpakorn University

Student's signature ..... Academic Year 2011

Thesis Advisors' signature 1. ..... 2. .....

51353203 : สาขาวิชาเทคโนโลยีเภสัชกรรม
คำสำคัญ : เรซินแลกเปลี่ยนอิออน / การแตกตัว / เด็กซ์โตรเมโทรฟาน / ไดโคลฟีแนค

นิษฐกานต์ ภัทรกานต์ : การประยุกต์ใช้เรซินแลกเปลี่ยนอิออนเป็นสารช่วยแตกตัวในยาเม็ด. อาจารย์ที่ปรึกษาวิทยานิพนธ์ : ภก.รศ.ดร.ประเสริฐ อัครมงคลพร และ ภญ.รศ.ดร.ปราณีต โอปณะโสภิต. 191 หน้า.

การวิจัยนี้เป็นการศึกษาผลของเรซินแลกเปลี่ยนอิออนชนิดต่างๆ ต่อประสิทธิภาพการเป็นสารช่วยแตกตัวของยาเม็ด เรซินแลกเปลี่ยนอิออนที่ใช้ศึกษา 10 ชนิด ได้แก่ แอมเบอร์ไลท์ไอาร์พี 64 แอมเบอร์ไลท์ไอาร์พี 69 โดเว็กซ์ 88 โดเว็กซ์ รีทาร์ดอิออน โดเว็กซ์ 50Wx2-200 โดเว็กซ์ 50Wx4-200 โดเว็กซ์ 50Wx8-200 โดเว็กซ์ 1x2-200 โดเว็กซ์ 1x4-200 และโดเว็กซ์ 1x8-200 โดยเปรียบเทียบกับตำรับยาเม็ดที่ใส่โซเดียมสตาร์ชไกลโคเลตซึ่งจัดเป็นสารช่วยแตกตัวชนิดยิ่งยวดที่มีขายในท้องตลาด ยาเม็ดทุกตำรับที่มีและไม่มีตัวยาสำคัญเตรียมโดยวิธีตอกตรง และทำการประเมินคุณสมบัติทางกายภาพของทุกสูตรตำรับ ได้แก่ ความแข็ง ความหนา เส้นผ่าศูนย์กลาง ความกร่อน ระยะเวลาในการแตกตัว และการละลายยา จากผลการทดลองพบว่า ยาเม็ดที่ประกอบด้วยแอมเบอร์ไลท์ไอาร์พี 64 แอมเบอร์ไลท์ไอาร์พี 69 และโดเว็กซ์ 1x2-200 มีความแข็งที่ดี ความกร่อนที่เหมาะสม และระยะเวลาในการแตกตัวสั้น จากผลการศึกษาคุณสมบัติการพองตัวของเรซิน พบว่าคุณสมบัติการเป็นสารช่วยแตกตัวของเรซินอาจเป็นผลร่วมกันจากกลไกการพองตัวและการดูดน้ำเข้าสู่รูขนาดเล็กที่เชื่อมต่อกันของของเรซิน ดังนั้นเรซินทั้ง 3 ชนิดจึงได้รับการคัดเลือกเพื่อนำมาศึกษาผลของปัจจัยต่างๆ ได้แก่ ปริมาณของเรซิน แรงตอก และชนิดของสารเพิ่มปริมาณที่มีผลต่อการเป็นสารช่วยแตกตัว ผลการศึกษาพบว่า ความแข็งของยาเม็ดลดลงเมื่อเพิ่มปริมาณเรซิน ซึ่งส่งผลต่อความคงตัวของยาเม็ด ส่วนการเพิ่มแรงตอกจะทำให้ยาเม็ดมีความแข็งเพิ่มมากขึ้น ทำให้ระยะเวลาในการแตกตัวของยาเม็ดนานขึ้น แต่อย่างไรก็ตามแรงตอกไม่มีผลต่อความแข็งและระยะเวลาในการแตกตัวของยาเม็ดที่มีโดเว็กซ์ 1x2-200 ส่วนชนิดของสารเพิ่มปริมาณใช้ 4 ชนิด ได้แก่ ไดเบสิคแคลเซียมฟอสเฟต (DCP) สเปรย์ดราย แลคโตส (SDL) ไมโครคริสตัลไลน์เซลลูโลส (MCC) และสเปรย์ดรายไรซ์สตาร์ท (SDRS) ผลการทดลองพบว่า MCC ทำให้ยาเม็ดมีความแข็งมากที่สุดในขณะที่ยาเม็ดที่เตรียมจาก SDRS และ SDL มีความแข็งมากกว่า DCP นอกจากนี้ระยะเวลาในการแตกตัวของยาเม็ดจะขึ้นกับชนิดของเรซิน จากการศึกษาตำรับยาเม็ดเดกซ์โทรเมทอร์แฟนไฮโดรโบรไมด์ (DMP) ตัวแทนยาละลายน้ำดี และไดโคลฟีแนค โซเดียม (DCN) ตัวแทนยาละลายน้ำน้อย พบว่า ระยะเวลาในการแตกตัวของตำรับยาเม็ด DMP เป็นดังนี้ แอมเบอร์ไลท์ไอาร์พี 64 (25.92 ± 1.73 วินาที) > SSG (16.25 ± 0.45 วินาที) > โดเว็กซ์ 1x2-200 (8.00 ± 1.04 วินาที) และทั้ง 3 สูตรตำรับยังคงให้อัตราการปลดปล่อยยาที่เร็ว โดยยาเม็ดที่มีโดเว็กซ์ 1x2-200 จะมีอัตราการปลดปล่อยยาที่เร็วที่สุด ส่วนปริมาณยาที่ปลดปล่อยออกมาจากตำรับที่มีแอมเบอร์ไลท์ไอาร์พี 64 จะมีค่าต่ำกว่าตำรับอื่นๆ สำหรับผลการศึกษาตำรับยา DCN พบว่าความแข็งและระยะเวลาในการแตกตัวมีความสอดคล้องกับตำรับยา DMP แต่อย่างไรก็ตาม ปริมาณยาที่ปลดปล่อยออกมาจากตำรับที่ใช้โดเว็กซ์ 1x2-200 จะมีค่าต่ำกว่าจากตำรับที่ใช้แอมเบอร์ไลท์ไอาร์พี 64 และ SSG เป็นสารช่วยแตกตัว นอกจากนี้จากผลการทดลองแสดงให้เห็นว่ารูปแบบการปลดปล่อยยาทั้ง 2 ชนิดมีความแตกต่างกันอย่างมาก โดยปริมาณยาและอัตราเร็วในการปลดปล่อยยาที่ละลายน้ำดีจะมีค่าสูงกว่ายาที่ละลายน้ำไม่ดี จากผลการทดลองชี้ให้เห็นว่าชนิดของเรซินแลกเปลี่ยนอิออนและค่าการละลายของตัวยาสำคัญมีความสำคัญต่อการละลายของยาจากยาเม็ดที่ใช้เรซินเป็นสารช่วยแตกตัว ในการวิจัยนี้สรุปได้ว่าชนิดของเรซินที่เหมาะสมสามารถนำมาใช้เป็นสารช่วยแตกตัวในตำรับยาเม็ดได้ซึ่งเป็นอีกทางเลือกหนึ่งเพื่อพัฒนาการผลิตยาเม็ด

สาขาวิชาเทคโนโลยีเภสัชกรรม บัณฑิตวิทยาลัย มหาวิทยาลัยศิลปากร

ลายมือชื่อนักศึกษา ..... ปีการศึกษา 2554

ลายมือชื่ออาจารย์ที่ปรึกษาวิทยานิพนธ์ 1. ..... 2. .....

ACKNOWLEDGEMENTS

This thesis would not have been successful without the cordially support from the kind people around me, to only some of whom it is possible to give particular mention here.

Above all, I would like to thank my thesis advisor, Assoc. Prof. Dr. Prasert Akkaramongkolporn and Assoc. Prof. Dr. Praneet Opanasopit for their invaluable advices, positive encouragement, patience and kindness.

I also would like to thank for every teachers and staffs in Faculty of Pharmacy, Silpakorn University for giving me useful knowledge and generous supports. I also would like to pass my wholehearted thanks to all my friends and members of the Pharmaceutical Development of Green Innovation Group (PDGIG) who spent their time making my thesis successful. I am very appreciated with you all.

I would like to give my special thanks to Pharmatech Co., Ltd. for financial and instrumental support throughout my study.

Indispensably, I am extremely grateful to my parents for all their love and encouragements during my study.

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LIST OF ABBREVIATIONS

%w/w	percent weight by weight
°C	degree Celsius
μg	microgram(s)
μL	microliter(s)
μm	micrometer(s)
AVG	average
cm	centimeter(s)
cm^2	square centimeter(s)
e.g.	exemplī grātiā (Latin); for example
et al.	and others
etc.	et cetera (Latin); and other things/ and so forth
g	gram(s)
h	hour(s)
kg	kilogram(s)
L	liter(s)
mg	milligram(s)
min	minute(s)
mL	milliliter(s)
mm	millimeter(s)
MW	molecular weight
nm	nanometer(s)
PBS	phosphate buffer solution
pH	potentia hydrogenii (Latin); power of hydrogen
rpm	revolutions per minute
SD	standard error

CHAPTER I

INTRODUCTION

1. Statement and significance of the research problem

Solid pharmaceutical dosage forms are the most popular dosage forms especially, tablet formulation. Good tablet formulation should provide appropriate hardness with low friability, rapid disintegration and hence dissolution of drug. For most drugs, the rapid disintegration and dissolution result in high level of bioavailability to patients after oral administration. However, the development and formulation are always challenged with major problems of unaccepted physical properties, particularly disintegration time and dissolution of tablet. To overcome these problems, tablet formulations have to use another excipient, namely disintegrant or superdisintegrant. The use of disintegrant contributes to rapid disintegration of tablet and efficient drug dissolution, which results in an increase in the amount of drug attached to gastrointestinal tract. Consequently, rapid absorption of the drug into the body is obtained. The mechanisms of action of disintegrant comprise swelling action, porosity and capillary action (wicking) and deformation. The first mechanism, swelling action, the disintegrant can swell after contact with water. Consequently, the adhesive force between other excipients in the formulation is broken, resulting in tablet disintegration. The second mechanism, porosity and capillary action, the disintegrant particles with low cohesiveness and compressibility themselves can enhance porosity and provide these pathways into the tablet. Upon contact with water, liquid is drawn up or “wicked” into these pathways through capillary action and therefore ruptures the inter-particulate bonds, causing the tablet to break apart. The last mechanism is deformation. It is the process in which disintegrant tries to return to its original condition or after contact with water (Mohanachandran,

Sindhumol, and Kiran, 2011: 105-107, Rudnic and Rhodes, 1982: 88-89). It is found that the disintegration time depends on quantity and type of disintegrant in the tablet formulation. The use of higher concentration will reduce the disintegration time of tablet. However, the disintegrant should be used in the formulation with an appropriate concentration (Zhao and Augsburger, 2005: E637). The most popular disintegrants are cellulose and its derivatives e.g. microcrystalline cellulose, cross-linked microcrystalline cellulose, starch and modified starch e.g. corn starch, sodium starch glycolate etc. (Mohanachandran, Sindhumol, and Kiran, 2011: 105-107, Ferrero et al., 1997: 11-12). The mechanisms of action of croscarmellose sodium (Ac-di-sol®) are wicking due to fibrous structure and swelling with minimal gelling and small expansion. On the contrary, microcrystalline cellulose (Avicel® pH101) can swell but cannot expand. Starch and modified starch have a great affinity for water and can swell under aqueous condition by itself resulting in the rupture of the tablet matrix. Considering the properties of other pharmaceutical excipients, it is found that some excipients could be used as tablet disintegrant if they exhibit one or more mechanisms as mentioned above.

Ion exchange resin (IER), which has swelling and non-adhesive properties, is one of the excipients that can be used as tablet disintegrant. IER are water insoluble cross-linked polymers. They consist of two main components, water insoluble polymer matrix and ion exchangeable group. The type of ion exchangeable group will determine the sort of IER, anion exchange resin or cation exchange resin. In addition, the type of ion exchangeable group will represent its ion exchange capacity. Table 1 shows the type of IER which are classified by type of ion exchangeable group. Generally, water insoluble polymer matrix comprises either styrene or methacrylic acid and divinylbenzene molecule. Each of polymer chain is contacted to another chain at the position of divinylbenzene molecule to form three-dimension structure. Because the extent of divinylbenzene has a significant effect on degree of cross-linking of IER, therefore degree of cross-linking is represented as the percentage of divinylbenzene in polymer chain. Degree of cross-linking plays an important role in the drug released rate. Furthermore, it has an impact on the porosity of resin. The lower degree of cross-linking has the higher porosity. Although, there are many types

of commercially available ion exchange resins, the main purpose of the use is to water and chemical purification instead of pharmaceutical applications. From time to time, there are only few types of ion exchange resins approved by US FDA, e.g. Amberlite® IRP64, Amberlite® IRP88, Duolite® 143 (Amin, Prabhu, and Wadhwani, 2009: 117-119, Bele and Derle, 2011: 2).

Table 1 Type of ion exchange resin

Type of resin	Ion exchangeable group		Counterion
Cation exchange resin			
Strong cation exchange resin	$-SO_3^-$	Sulfonic group	Cation
Weak cation exchange resin	$-COO^-$	Carboxylic group	Cation
Anion exchange resin			
Strong anion exchange resin	$-N^+(R)_3$	Quaternary ammonium group	Anion
Weak anion exchange resin	$-NH_2$	Primary amine group	Anion
	$=NH$	Secondary amine group	Anion
	$\equiv N$	Tertiary amine group	Anion

* Singh, I. et al. (2007). "Ion exchange resins: Drug delivery and therapeutic applications." **J Pharm Sci** 32 (June 9): 92.

For drug delivery application, an ionized drug (usually in solution) can freely exchange with an ion exchangeable group to form a complex, known as resinate. The drugs can be attached to the resin as long as they confront with other ions normally found in gastrointestinal tract. After passing ion exchange process, the drug returns to free form and thereafter it diffuses through polymer matrix, while the water insoluble unabsorbed resin will be secreted via feces (Anand, Kandarapu, and Garg, 2001: 905). Besides drug delivery application, IER can be used as

therapeutically active ingredients in order to treat hyperkalemia or cholesteremia (Elder, 2005: 583) and can be used in the field of taste masking (Puttewar et al., 2010: 229, Anand, Kandarapu, and Garg, 2001: 911), or improvement of drug stability (Singh et al., 2007: 95). Interestingly, IER can be used as tablet disintegrant due to its swelling and non-adhesive properties. However, there is only one cationic resin, i.e. poly(methacrylic acid-co-divinylbenzene) among many types of IER produced to markets, which is commercially claimed as tablet disintegrant (Amin, Prabhu, and Wadhwani, 2009: 117-119, U.S., Rohm and Hass company, 2006: 6). From these reasons, the objective of this study is to evaluate a variety of ion exchange resins as tablet disintegrant. The principal properties of resins are examined in order to describe the main mechanism of action of resin as disintegrant. Furthermore, factors affecting on the efficiency of IER based disintegrants are evaluated. Finally, tablet formulations using resin as disintegrant of model drugs e.g. dextromethorphan hydrobromide and diclofenac sodium are determined. It is expected that the information obtained from this study will provide the possibility and efficiency of other resins for use as a new disintegrant.

2. Objective of this research

2.1 To evaluate the efficacy of various ion exchange resins used as tablet disintegrant.

2.2 To evaluate the physicochemical properties and main mechanism of action of ion exchange resins used as disintegrant.

2.3 To study factors affecting on the efficacy of ion exchange resins used as tablet disintegrant.

2.4 To determine the possibility of ion exchange resins as usable disintegrant in tablet formulations of model drugs.

3. The research hypothesis

3.1 Ion exchange resins can be used as tablet disintegrant.

3.2 The physicochemical properties of ion exchange resin, such as particle size, swelling behavior, type of ion exchangeable group etc., can be used to explain the mechanism of action and efficacy of ion exchange resins as tablet disintegrant.

3.3 Efficacy of ion exchange resins as tablet disintegrant is affected by tabletting factors e.g. compression pressure, amount of resin and type of fillers.

3.4 Tablet formulations using ion exchange resins as disintegrant of both freely and poorly water soluble drug are successfully prepared.

CHAPTER II

LITERATURE REVIEW

1. Solid oral dosage forms

Oral administration is the most popular route due to ease of ingestion, pain avoidance, versatility (to accommodate various types of drug candidates) and most importantly, patient compliance. Moreover, solid oral delivery systems do not require sterile conditions and are less expensive to manufacture (Sastry, Nyshadham, and Fix, 2000: 138). Common pharmaceutical solid dosage forms are pill, tablet, capsule, specialty tablet such as buccal tablet, sublingual tablet, fast-disintegrating tablet or fast-dissolving tablet, powder, and granule.

2. Tablet formulation

A tablet is a pharmaceutical solid dosage form. It comprises of a mixture of active substances and excipients, usually in powder form, pressed or compacted from a powder into a solid dose. The advantages of tablet formulations provide manufacturer including simplicity to manufacturing process, economical preparations, convenience in packaging, shipping and dispensing. Additionally, the tablet formulations also provide the benefits for patient such as accuracy of dosage, compactness and portability, blandness of taste and ease of administration. Tablet formulation consists of 2 main components, active pharmaceutical ingredients (API) and excipients. Excipients can be classified according to their functions in the finished tablets. Namely, they help to impart satisfactory for manufacturing process and compression characteristics to the formulations.

Moreover, they help to give desirably physical characteristics to the finished tablets such as in the case of chewable tablet, flavors and sweetening agents are used to enhance patient compliant and in the case of controlled release tablet, polymer or wax is used to retard the release of drug. The various types of excipients are shown as follow:

2.1 Diluent/Filler

Diluent, an inert substance, is used to increase the bulk in order to make the practical size of tablet for compression. The examples of diluents are dibasic calcium phosphate (Emcompress®), calcium sulphate, spray dried lactose (Tablettose®), microcrystalline cellulose (Avicel®), kaolin, mannitol, sodium chloride, dry starch and powdered sugar. Certain diluents, such as mannitol, lactose, sorbitol, sucrose, when present in sufficient quantity, can impart properties to some compressed tablets that permit disintegration in the mouth by chewing. Diluents used as excipients for direct compression formulas have been subjected to give tablets flowability and compressibility.

2.2 Disintegrant

Disintegrants are used to facilitate the disintegration of tablet after administration by breaking up the tablet into small pieces. Consequently, the dissolution of drug will occur effectively and the increase in surface area of disintegrated tablet will promote the bioavailability of drug as well. The examples of disintegrants are starch i.e., tapioca starch, rice starch, corn starch), modified starch i.e., sodium starch glycolate, cellulose and its derivatives, croscarmelose, crospovidone and ion exchange resin.

2.3 Lubricant

Lubricants in tablet formulation are used to avoid adhesion of the powder mixture of tablet to the surface of the dies and punches, reduce inter-particulate friction, facilitate the ejection of the tablets from the die cavity and may improve the flowability of the tablet granulation as well. The examples of lubricants commonly

used in tablet formulation are talc, magnesium stearate, calcium stearate and stearic acid. Most lubricants are used in concentrations less than 1% except for talc. When used alone, talc may require concentrations as high as 5%.

2.4 Binder

Binder is used to impart cohesive qualities to the powder mixture to ensure that the tablet remains intact after compression. In addition, it improves the free-flowing qualities by preparing the powder mixture in form of granule which has the desired hardness and suitable particle size. The types of binder can be divided into 3 groups, sugars (sucrose, glucose, dextrose, and lactose), natural and synthetic gums (acacia, sodium alginate, carboxymethylcellulose, methylcellulose, polyvinyl pyrrolidone, veegum), and starch and modified starch. The amount of binder used in the formulation has a considerable influence on the characteristics of the compressed tablets. If the excessive amount of binder is used, the tablet will not disintegrate easily and probably attach to the punch and die during manufacturing process.

2.5 Anti-adherant

Anti-adherants, e.g. colloidal silica are used to reduce stickiness and adhesion of the tablet granulation or powder to the faces of the punches or to the die walls.

2.6 Glidant

Glidant, e.g. talcum is used to promote the flow of the tablet granulation or powder mixture by reducing friction among particles.

2.7 Other excipients

Sweeteners, e.g. mannitol, saccharin, aspartame or flavoring agents are used to enhance the taste of tablet.

Pigments including dye and lake are also used to make the tablets visually attractive and elegant. Moreover, colors also provide the user product identification**.**

3. Tablet preparation method

There are 3 methods for producing tablets;

3.1 Direct compression

For tablets in which the drug itself constitutes a major portion of the total tablet weight, it is necessary that the physical characteristics of drug required for the formulation to be compressed directly. Direct compression for tablets containing 25% or less of drug substances can be frequently used by formulating with a suitable diluent which acts as a carrier or vehicle for the drug. The common diluents are used in direct compression such as dicalcium phosphate dihydrate, tricalcium phosphate, calcium sulfate, anhydrous lactose, spray-dried lactose, pre-gelatinized starch, compressible sugar, mannitol and microcrystalline cellulose. These vehicles are odorless, tasteless and non-hygroscopic. Additionally, it has no inherent lubricating or disintegrating properties and therefore other additives must be added to prepare a satisfactory formulation.

3.2 Wet granulation

Wet granulation is a process of using a liquid binder to lightly agglomerate the powder mixture. The amount of liquid has to be properly controlled, as over-wetting will cause the granules to be too hard and under-wetting will cause them to be too soft and friable. Wet granulation is the most widely used and most general method. This can be due to the greater probability that the granulation process will meet all the physical requirements for the compression of good tablets. However, the disadvantages of this method are the number of separate steps involved, as well as the time and labor necessary to carry out the procedure, especially on a large scale.

3.3 Dry granulation

Dry granulation processes create granules by light compaction of the powder blend under low pressures. The compacts so-formed are broken up gently to produce granules (agglomerates). This process is often used when the product to be granulated is sensitive to moisture and heat. Dry granulation can be conducted on a

tablet press using slugging tooling or on a roll press called a roller compactor. Dry granulation equipment offers a wide range of pressures to attain proper densification and granule formation. Dry granulation is simpler than wet granulation, therefore the cost is reduced. However, dry granulation often produces a higher percentage of fine granules, which can compromise the quality or create yield problems for the tablet. Dry granulation requires drugs or excipients with cohesive properties, and a 'dry binder' may need to be added to the formulation to facilitate the formation of granules.

4. Disintegrants in tablet formulation

The important role of disintegrant in tablet formulation is to facilitate the breakup or disintegration of tablet or capsule content into smaller particles that dissolve more rapidly than in the absence of disintegrant. The main mechanism of disintegrant is to oppose the efficiency of the tablet binder and the physical forces that act under tablet compression. In the last decade, the term of ‘superdisintegrant’ becomes more popular in pharmaceutical solid dosage form because it has many advantages over conventional disintegrant such as low used level, typically 1-10 % by weight relative to the total weight of the dosage unit, providing the safer and giving an effective drug delivery with patient's compliance. Some details of superdisintegrants and their properties can be summarized in Table 2.

4.1 Sodium carboxymethylcellulose

Croscarmellose sodium is described as a cross-linked polymer of carboxymethylcellulose. The basic chemical structure of sodium carboxymethylcellulose is shown in Fig. 1.

Besides the differences between the starch and cellulose polymer backbones, there are two differences between the synthetic processes used to modify the polymer. Namely, the degree of substitution of croscarmellose sodium is higher than that of SSG and the mechanism of crosslinking is different.

Table 2 The examples of superdisintegrants and their properties

Superdisintegrants	**Commercially available grades**	**Mechanism of action**	**Special comment**
Crosslinked cellulose	Croscarmellose® Ac-Di-Sol®, Nymce ZSX® Primellose®, Solutab®, Vivasol®, L-HPC.	- Swells 4-8 folds in < 10 seconds - Both swelling and wicking	- Swells in two dimensions - Direct compression or granulation starch free
Crosslinked PVP	Crosspovidon M®, Kollidon®, Polyplasdone®	- Swells very little and returns to original size after compression but act by capillary action	- Water insoluble and spongy in nature so get porous tablet
Crosslinked starch	Explotab®, Primogel®	- Swells 7-12 folds in < 30 seconds	- Swells in three dimensions and high level serve as sustain release matrix
Crosslinked alginic acid	Alginic acid NF	- Rapid swelling in aqueous medium or wicking action.	- Promote disintegration in both dry and wet granulation

* Mohanachandran, P.S, P.G Sindhumol, and T.S Kiran. (2011). "Superdisintegrants: An overview." **Int J Pharm Sci Rev Res** 6, 1: 108.

The substitution is performed using Williamson's ether synthesis to give the sodium salt of carboxymethylcellulose. A key difference from the chemistry of sodium starch glycolate is that some of the carboxymethyl groups themselves are used to cross-link the cellulose chains, the process being accomplished by dehydration.

Thus the cross-links are carboxyl ester links rather than phosphate ester links as in Primojel® (Mohanachandran, Sindhumol, and Kiran, 2011: 107).

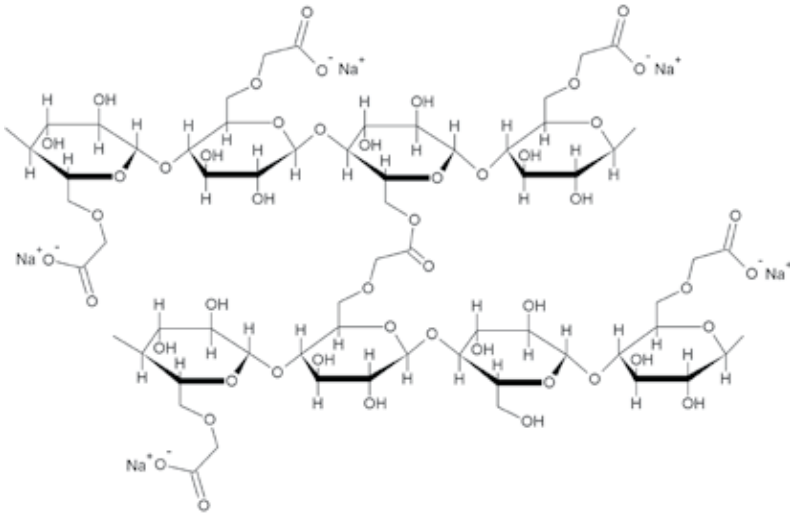

Fig. 1 Basic structure of sodium carboxymethylcellulose.

* Mohanachandran, P.S, P.G Sindhumol, and T.S Kiran. (2011). "Superdisintegrants: An overview." **Int J Pharm Sci Rev Res** 6, 1: 107.

K.A. Khan and C.T. Rhodes revealed that calcium phosphate dibasic dihydrate containing 10% w/w sodium carboxymethylcellulose, showed considerably more expansion in their thickness than in their diameter upon exposure with 100% relative humidity. This was probably due to the elastic behavior of sodium carboxymethylcellulose resulting in the expansion in the axis where compression was applied (K.A. Khan and C.T. Rhodes 1975: 447). There was the report which carried out functional comparison of three superdisintegrants, i.e. Ac-di-sol® (croscarmellose sodium), Primojel® (sodium starch glycolate) and Polyplasdone® XL (crospovidone NF). The tablets containing either 1% or 2% Ac-di-sol® disintegrated more rapidly into more or less uniform fine particles while tablets containing the other superdisintegrants disintegrated much more slowly into more or less uniform coarser particles. Moreover, the dissolution of aspirin tablets containing either 1% or 2% Ac-di-sol® was much higher than that of Primojel® or Polyplasdone® XL. This is due to the fact that the fiber-like nature of Ac-di-sol® can act as a hydrophilic channel to facilitate water uptake into the tablet matrix and help increase the total water contact

area with drug (Zhao and Augsburger, 2005: E635-E640). The study of Bussemer et al. revealed that the swelling behavior of Ac-di-sol® depended on the ionic strength and the pH of the medium due to a competition for free water and the acidic nature of this polymer (Bussemer, Peppas, and Bodmeier, 2003: 261). In addition, it is known that the poor disintegration properties due to its adhesiveness in the hydrated state (K.A. Khan and C.T. Rhodes, 1975: 447).

4.2 Starch and modified starches

4.2.1 Corn starch and potato starch

Corn and potato starch in form of powder are well-known for the most popular disintegrant. Starch has a great affinity for water and can swell under aqueous condition by itself resulting in the rupture of the tablet matrix.

4.2.2 Sodium carboxymethyl starch (Sodium starch glycolate: SSG)

Sodium starch glycolate (SSG) is manufactured by chemical modification of starch, i.e. carboxymethylation to enhance hydrophilicity and cross-linking to reduce solubility (Shah and Augsburger, 2002: 345). Consequently, it is practically insoluble in water. It consists of oval or spherical granules, 30-100 μm in diameter. It is recommended to use in tablets prepared by either direct compression or wet granulation process. The recommended concentration in a formulation is 2-8% w/w and the optimum concentration is about 4% w/w. The basic chemical structure and the morphology of SSG are shown in Fig. 2 and Fig. 3.

According to Khan and Rhodes, there has been no attempt to define the complete mechanism of action of SSG. The main reason for the effectiveness of SSG might be due to its high water uptake resulting in the relatively rapid water absorption. Consequently, the tablets containing SSG showed marked swelling and expansion properties. Moreover, this mechanism of SSG was similar to that of cationic exchange resin. SSG possesses desirable properties which are readily dispersible in water resulting from its hydrophilicity. The spherical particles can

facilitate the dispersion in a tablet systems, thus improving 'wicking mechanism' (if this mechanism is operative) and allowing penetration of water into the tablet interior (Khan and Rhodes, 1975: 447).

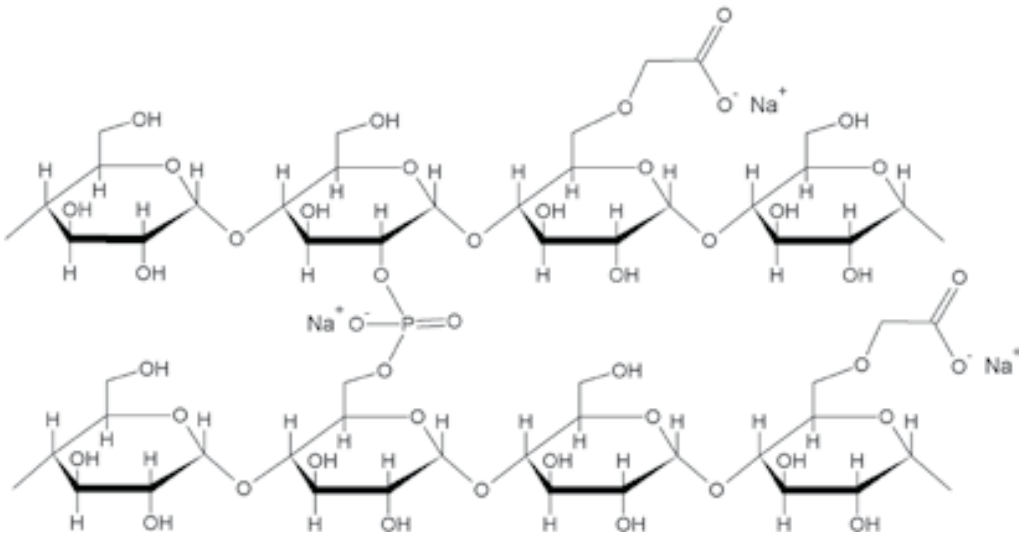

Fig. 2 Basic structure of sodium starch glycolate.

Mohanachandran, P.S, P.G Sindhumol, and T.S Kiran. (2011). "Superdisintegrants: An overview." **Int J Pharm Sci Rev Res** 6, 1: 107.

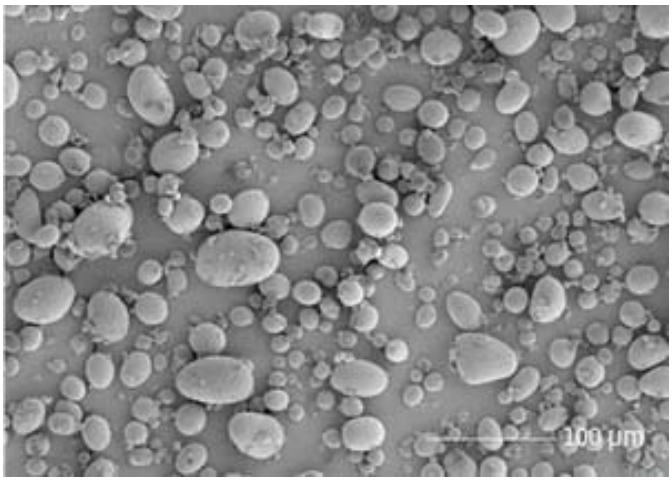

Fig. 3 Scanning electron micrograph of sodium starch glycolate (Primojel®).

*Primojel®. Accessed 31 Jan 2012. Available from http://www. dfepharma.com.

4.3 Cross-linked polyvinylpyrrolidone (Crospovidone)

Polyplasdone® is synthetic, insoluble and non-ionic cross-linked homopolymer of N-vinyl-2 pyrrolidone. Polyplasdone® provides rapid disintegration, even at low use levels (2-5% w/w). It can be used in both wet and dry granulation process by adding it during intra-granular or extra-granular process or both. Moreover, it can be used in direct compression process due to its highly compressible properties. The mechanism of action of crospovidone as superdisintegrants is a combination of swelling and wicking. When examined under a scanning electron microscope, crospovidone particles appear granular and highly porous. This unique, porous particle morphology facilitates wicking of liquid into the tablet and particles in order to generate rapid disintegration. Due to its high cross-linked density, crospovidone swells rapidly in water without gelling. In contrast to sodium starch glycolate and croscarmellose sodium, crospovidone superdisintegrants exhibit virtually no tendency toward gel formation, even at high use levels (Mohanachandran, Sindhumol, and Kiran, 2011: 106-107). Fig. 4 and Fig. 5 show scanning electron micrograph of Polyplasdone® XL and Polyplasdone® XL-10. These images demonstrate that both Polyplasdone® XL and Polyplasdone® XL-10 are porous and granular. These specific characteristic help enhance wicking of liquid into the particle.

Polyplasdone® is reported to exhibit a high capacity to retain deformation during post-compression. After wetting, the rapid swelling of tablets containing Polyplasdone® may be attributed to the recovery of deformation. However, Polyplasdone® concentrations have an effect on the disintegration behavior of tablet. At the lower concentration, the tablets tend to separate axially into upper and lower sections while the higher concentration, the tablets disintegrate further into large irregularly shaped fragments (Zhao and Augsburger, 2005: E635-E640).

4.4 Ion exchange resin (IER)

Cation exchange resin, i.e. Amberlite®IRP 88 is well-known for using as effective disintegrant in a variety of tablet systems. As compared to the other disintegrants, SSG, sodium carboxymethylcellulose and starch, Amberlite® IRP 88

showed the highest water sorption followed by SSG, sodium carboxymethylcellulose and starch. In the similar way, Amberlite® IRP 88 also exhibited the highest decrease in apparent density when it was incorporated in the tablets containing 10% w/w calcium phosphate dibasic dihydrate.

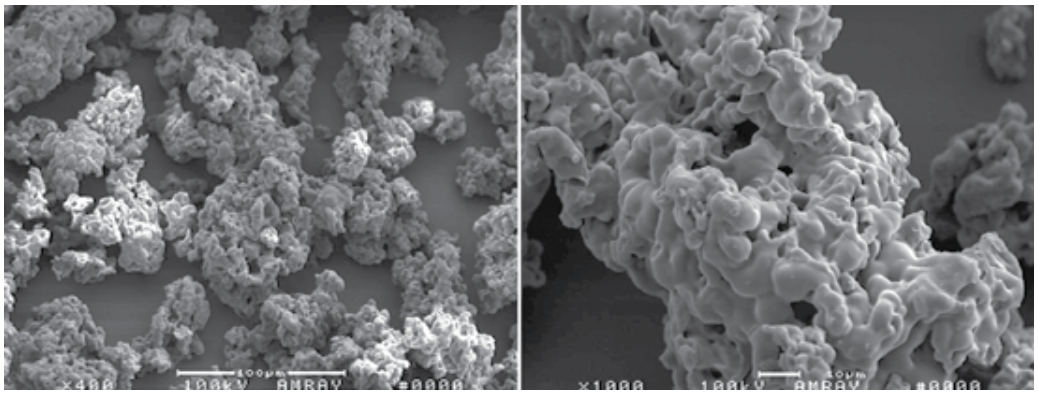

Fig. 4 Scanning electron micrograph of Polyplasdone® XL.

*Polyplasdone® superdisintegrants Product Overview. Accessed 31 Jan 2012. Available from http://www.ispcorp.com.

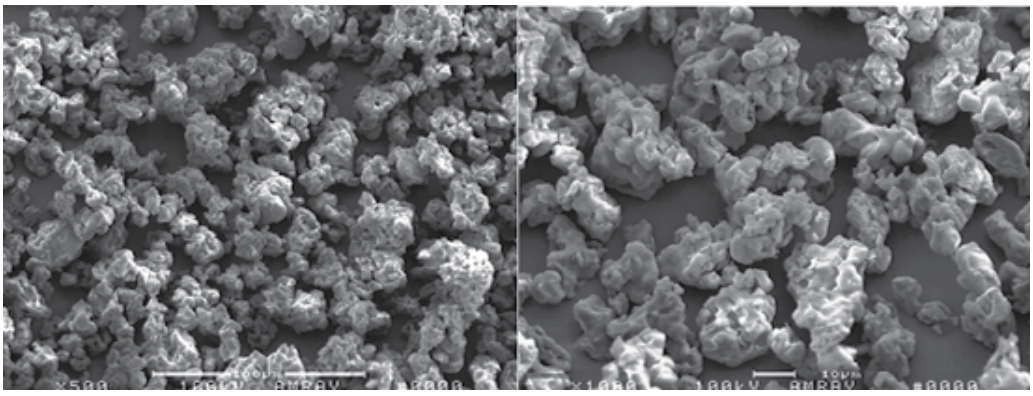

Fig. 5 Scanning electron micrograph of Polyplasdone® XL-10.

*Polyplasdone® superdisintegrants Product Overview. Accessed 31 Jan 2012. Available from http://www.ispcorp.com.

The main reason for the effectiveness of cation exchange resin is its high and rapid water uptake resulting in marked swelling and expansion properties.

Additionally, the tablets containing cation exchange resin showed a considerable increase in disintegration time and a marked reduction in its strength after storage. These results could be demonstrated that the mechanism of disintegrant which possesses higher affinity for water e.g. Amberlite® IRP 88 is swelling because the resin has lost some of their absorption and swelling ability. Kun and Kunin described hydration of the cation exchange resin as a two-step process; the hydration of the gel phase or the microreticular phase and the filling of macroreticular pore with water, either by capillary condensation or hydraulically. The other advantageous property of cation exchange resin for supporting the disintegration of tablet is that non-adhesiveness of cation exchange resin. Like starch, the concentration of cation exchange resin in the formulation should be a minimum effective concentration in order that some of the concentrations are required to form an effective capillary system (Khan and Rhodes, 1975: 447-451).

However, there was another proposed mechanism which was quite different from above. Namely, mechanism of tablet disintegration of polacrilin potassium or Amberlite® IRP 88 prefers wicking (capillary action) to swelling. The data obtained from their experiments showed that the settling volumes were found to be in the following rank order; distilled water (pH 7.0) > simulated salivary fluid or SSF (pH 6.8) > HCl (0.1 M pH 1.1). Moreover, the tablets showed minimum disintegration time in HCl (0.1 M) followed by SSF and distilled water. It could be indicated that the swelling behavior of disintegrants has no an effect on the disintegration time of tablets. If swelling capacity of disintegrant had an impact on the disintegration time of tablets, disintegrants immerged in distilled water would have been shown the shorter disintegration time (Bele and Derle, 2011: 1-7).

Amberlite® IRP69 is a strongly cationic exchange resin commercially produced in plate-like particles. When the resin was immerged in aqueous solutions, the resin hydrates and swells considerably due to the hydrophilicity and dissociation of the sodium sulfonate salts. The important property of resin is that low compressibility causing resin to exhibit poor adhesive attraction between resins itself as well as resin and other components. The incorporated resin in HPMC matrices can

promote the matrix hydration. However, the drug release from these matrices with the resin was lower than that without resin. This could be due to ion exchange mechanism which occurs within these matrices (Akkaramongkolporn et al., 2008: 899-908).

More details of IER used as superdisintegrant will be described below (in the section of pharmaceutical applications of IER).

4.5 Cross-linked alginic acid

It is insoluble in water and disintegrates by swelling or wicking action. It is a hydrophilic colloidal substance, which has high sorption capacity. It is also available as salts of sodium and potassium.

4.6 Xanthan gum

Xanthan Gum derived from Xanthomonas campestris is official in USP with high hydrophilicity and low gelling tendency. It has low water solubility and extensive swelling properties for faster disintegration.

4.7 Calcium silicate

It is a highly porous, lightweight superdisintegrant, which acts by wicking action.

5. Mechanism of action of tablet disintegrant

The mechanism of action of tablet disintegrant consists of 3 main principles; swelling, wicking (porosity and capillary action) and deformation. The most disintegrants usually belong to one or more mechanisms in order to achieve an effective disintegration.

5.1 Swelling

Some of the disintegrants, i.e. starch, SSG, IER, can swell after contact with water. Consequently, the adhesive force between other excipients in the formulation is broken, resulting in tablet disintegration.

5.2 Porosity and capillary action (wicking)

The disintegrant particles with low cohesiveness and compressibility themselves, i.e. ion exchange resin, calcium silicate, can enhance porosity and provide these pathways into the tablet. Upon contact with water, liquid is drawn up or "wicked" into these pathways through capillary action and therefore rupture the inter-particulate bonds, causing the tablet to break apart.

5.3 Deformation

Some of the disintegrants, i.e. starch are deformed under pressure and they return to their original shape when the pressure is removed. Moreover, with the compression forces involved in tablet preparation process, these starches are believed that they can be deformed more permanently and carried 'energy rich'. Thereafter this energy will be releasing after contact with water.

6. Ion exchange resins (IER)

IER were first invented over 60 years ago and were developed predominantly by Rohm and Haas and Dow chemical company (Elder, 2005: 575). IER are water insoluble cross-linked polymers containing a salt-forming group at repeating positions on the polymer chain. It can be used to overcome various pharmaceutical formulation problems including bitter taste, poor stability and poor dissolution of the drugs. Moreover, it can be used as superdisintegrants in tablet formulations because it has the great swelling properties. In addition, it can complex with various types of ionized drug causing the drug to form resinate which can be used to modify the release of drug (Singh et. al, 2007: 91).

6.1 Chemical properties of IER

IER consists of two main components, polymer matrix and ion exchangeable group. Polymer matrix is formed in three-dimension cross-linked copolymer, which has the particle size as large as the particle size of resin. This causes the resin do not dissolve in both water and organic solvent. Cross-linked copolymer is obtained from polymerization of monomer such as phenol-formaldehyde copolymer, styrene-divinylbenzene copolymer (styrene-DVB), acrylic acid-divinylbenzene copolymer, methacrylic acid-divinylbenzene copolymer etc. Additionally, ethylenediamine-epichlorohydrin, methylimidazole-epichlorohydrin and allylamine-co-N, N-diallyl-1, 3-diamino-2-hydroxypropane are found in specific resin. Ion exchangeable groups are the sort of functional groups which is ionizable. They can be divided into 2 groups, cation exchange resin and anion exchange resin. Ion exchangeable groups will be attached to cross-linked copolymer via covalent bond. These groups can dissociate to either anion or cation, which is called 'fixed ion'. The fixed ion can interact with counterion in the environment via electrostatic attraction. Namely, if the fixed ion is anion, it can interact with cation. On the other hand, if the fixed ion is cation, it can interact with anion. In addition, such counterion can exchange with other counterions in the environment.

6.2 Classification of IER

A general classification of IER is given in Fig. 6.

6.2.1 Cation exchange resin

Cation exchange resin is the resin containing functional group which can ionize itself in the environment in order to provide cross-linked copolymer exhibiting anionic behavior. Under the solution containing cationic molecules, such resin will interact with other cations and hence promote ion exchangeable process. Generally, the cation exchange resins are prepared by the copolymerization of styrene and divinyl benzene. Thereafter, sulfonic acid groups ($-SO_3H$) will be introduced into most of the benzene rings. The cation exchange resin can be divided into 3 groups in

accordance with the different-dissociating ability and the different-ion exchanging capacity.

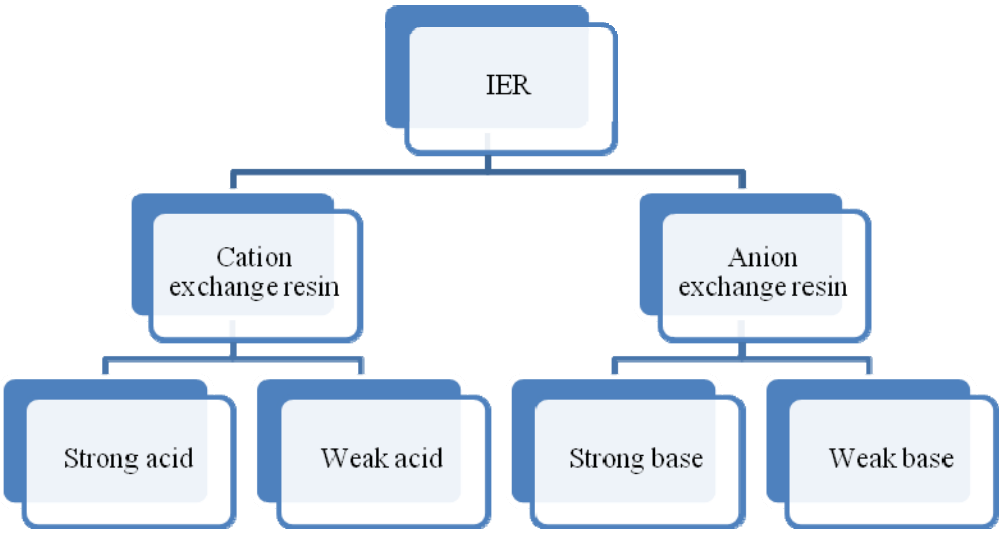

Fig. 6 Classification of IER.

* Singh, I. et al. (2007). "Ion exchange resins: Drug delivery and therapeutic applications." **J Pharm Sci** 32 (June 9): 91.

6.2.1.1 Strong acid cation exchange resin

The main ion exchangeable group of these resins is sulfonic acid group ($-SO_3H$). Additionally, the resins can be prepared in form of salt, such as Na^+, in order to use for water softening purpose. The resins can be highly ionized in both the acid ($-SO_3H$) and salt ($-SO_3Na$) form. The hydrogen and sodium forms of strong acid resins are highly dissociated and the exchangeable Na^+ and H^+ are readily available for exchange over the entire pH range. Consequently, the exchange capacity of strong acid resins is independent of the solution pH. After ion exchangeable process, the resin can be converted back to the H^+ form by contact with a strong acid solution or it can be converted back to the Na^+ form by contact with a sodium chloride solution.

6.2.1.2 Weak acid cation exchange resin

The main ion exchangeable group of these resins is carboxylic acid group (-COOH). These resins are weakly dissociated. The degree of dissociation of a weak acid resin is strongly influenced by the pH of solution. A typical weak acid resin has limited capacity below a pH of 6.0.

6.2.1.3 Bifunctional cation exchange resin

The ion exchangeable groups of these resins are composed of strong acid, i.e. sulfonic acid and weak acid, i.e. carboxylic acid.

6.2.2 Anion exchange resin

In contrast, anion exchange resin is the resin containing functional group, i.e. quaternary ammonium or amine group which can ionize itself in the environment in order to provide cross-linked copolymer exhibiting cationic behavior. Generally, the anion exchange resins are first prepared by the chlormethylating the benzene rings of styrene-divinyl benzene copolymer to attach CH_2Cl groups. Thereafter, tertiary amines such as triethylamine will be reacted with attached CH_2Cl groups. The anion exchange resin can be divided into 3 groups;

6.2.2.1 Strong base anion exchange resin

The main ion exchangeable group of these resins is quaternary ammonium group, which can be divided into 2 groups, trimethylammonium ($-N^+(CH_3)_3$) and dimethylethanolammonium ($-N^+(CH_3)_2C_2H_4OH$). The resins contained trimethylammonium are stronger than that of dimethylethanolammonium. Like strong acid resins, strong base resins are highly ionized (or protonated) and can be used over the entire pH range.

6.2.2.2 Weak base anion exchange resin

The main ion exchangeable groups of these resins are secondary amine ($-NHCH_3$) and tertiary amine ($-N(CH_3)_2$). Weak base resins are like weak acid resins in that the degree of ionization is strongly influenced by pH of

solution. Consequently, weak base resins exhibit minimum exchange capacity above a pH of 7.0.

6.2.2.3 Bifunctional anion exchange resin

The ion exchangeable groups of these resins are composed of strong base, i.e. quaternary ammonium and weak base, i.e. secondary or tertiary amine.

6.3 Physical properties of IER

IER are spherical beads of approximately 0.5–1.2 mm in diameter. The color of IER is not only opaque yellow but also transparency. The constitution of each spherical particle of IER is similar to that of a homogeneous gel. The shrinkage or expansion of the spherical volume is based on the ionic environment in which the IER are presented (Anand, Kandarapu, and Garg, 2001: 906).

6.3.1 Shape of IER

The difference between shapes of commercially available IER depends on the manufacturing process. Spherical shape obtained from oil-in-water emulsion polymerization process. In contrast, plate-like or not circular structure could be obtained from assimilation process of originally circular IER (Akkaramongkolporn, 2552: 17). The difference of shape of resin is shown in Fig. 7.

6.3.2 Particle size of IER

Particle sizes of commercially available IER are ranging form 100 to 1500 μm. Because of swelling properties of ion exchange resins, their particle sizes can be measured into 2 ways, as the resin is either dry or wet. However, the medium which resin emerged has an important effect on the swelling of the resin. It could be suggested that the measurement of particle size of resin should announce the type of used medium (Akkaramongkolporn, 2009: 17-19).

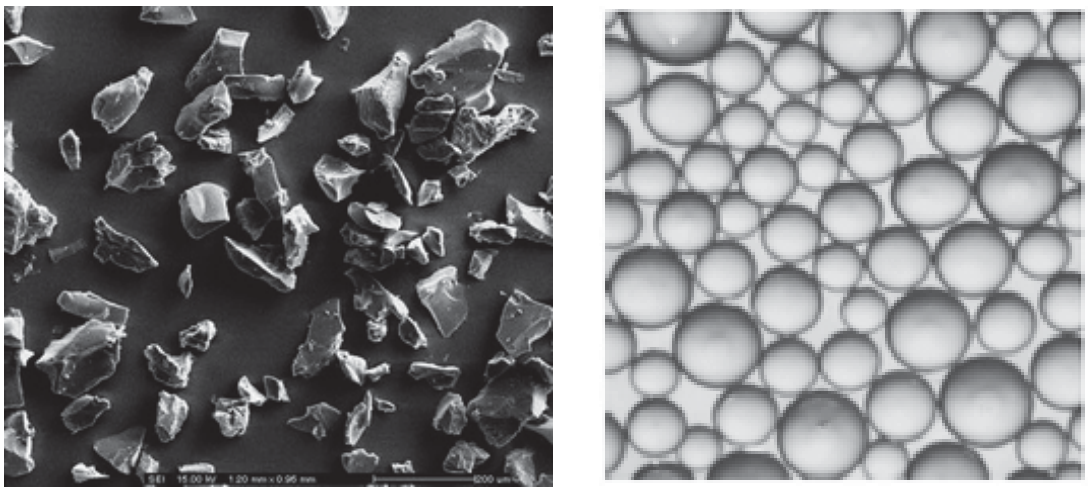

Fig. 7 Scanning electron micrograph represents plate-like structure of Amberlite® IRP 69 (left image) and spherical structure of Dowex® 50W x 8 (right image).

*Akkaramongkolporn et al., 2008: 900, Dowex® Fine Mesh Spherical Ion Exchange Resins For Fine Chemical and Pharmaceutical Column Separations. Accessed 31 January 2012. Available from http://www.dow.com.

6.3.3 Degree of cross-linking

Degree of cross-linking of resin is an important physical property because it contributes to other physical properties of resin such as swelling, density, pore size including exchange rate of counterion. A low degree of cross-linking of the resin will facilitate the exchange of large ions, but it will cause volume changes of resin.

6.3.4 Swelling properties

Upon contact with water, counterion, which is attached to fixed ion, will ionize. As a result, counterion will surround resin as long as ion exchangeable process will occur. Such counterion belongs to higher osmotic pressure compared to water and thus water can be induced into the resin matrix. The increase in the amount of water contributes to the extension of cross-linked copolymer simultaneously. Consequently, the resin is continuously swollen with larger particles.

While the resin is swelling, the resistance force of cross-linked copolymer to the swelling is synchronized. Degree of cross-linking has an important effect on the swelling ratio. The higher degree of cross-linking, the swelling of resin will decrease. This is due to the higher the resistance force of cross-linked copolymer.

6.3.5 Resin density

Generally, the resin density can be divided into 2 types; bulk density (tapped density) and true density. The density of any resin in its dry or swollen from depends upon resin type (gel resin or macroporous resin), degree of cross-linking and type of cross-linking polymer and ionic form. Degree of cross-linking increases, resin density is increased. The density of resin which has styrene-divinylbenzene cross-linked copolymer is higher than that of resin which has acrylic-divinylbenzene cross-linked copolymer. The density of gel resin is higher than that of macroporous resin. The more atomic weight of counterion, the more resin density is found (C.E. Harland, 1994: 84).

6.3.6 Solubility

IER is insoluble in water and all organic solvents.

6.4 Pharmaceutical applications of ion exchange resins (IER)

Applications of IER in drug delivery research became prominent in the 1950s when Amberlite® IRC-50 was used in the successful purification of streptomycin. Over the six decades, IER has been used as pharmaceutical active ingredients, inactive ingredients (excipients such as disintegrant), tasted masking of bitter tasting drugs, controlled and extended release of drugs and drug stabilization (Elder, 2005: 575).

6.4.1 IER as pharmaceutical active ingredients

6.4.1.1 Reduction of sodium in blood circulation

Weak acid cation exchange resin, i.e. Amberlite® IRP64, Amberlite® IRP88, has been used in the treatment of hypertension and cardiac odema (Elder, 2005: 583).

6.4.1.2 Treatment of hyperkalemia

Strong cation exchange resin in form of either sodium salt (Na^+) or calcium salt (Ca^{2+}) can absorb potassium (K^+) in gastrointestinal tract by ion exchanging process resulting in the formation of complex which is not absorbed into blood circulation. As a result, the potassium level in the blood is reduced. The products available for commercial are Kayexalate® (Sodium form) and Kalimate® (calcium form) (Elder, 2005: 583, Akkaramongkolporn, 2009: 33).

6.4.1.3 Treatment of cholesteremia

Colestyramine and colestipol are strong basic anion exchange resins in the chloride form. These resins adsorb bile salts from the gastrointestinal tract, leading to increased metabolism of cholesterol to replenish normal levels of these bile salts, which in turn results in significant reduction of serum cholesterol levels. There are USP monographs for colestyramine resin, colestyramine for oral suspension, colestipol hydrochloride and colestipol hydrochloride for oral suspension (Elder, 2005: 583, Akkaramongkolporn, 2009: 33).

6.4.2 IER used as tablet disintegrant

In the presence of water, IER incorporated in tablet can swell rapidly resulting in the disintegration process of tablet. There are many advantages of IER over conventional disintegrant such as swell on getting hydrated but do not dissolve or have an adhesive tendency, can be used in lower concentration (0.2%-5.0%), facilitate the compression phase by conferring greater hardness to the tablets

and work equally efficiently with hydrophilic and hydrophobic formulation, especially with the later where the conventional disintegrant is not effective.

Poly (potassium methacrylate-co-divinyl benzene) copolymer (Amberlite® IRP 88) is associated with the diffusional mechanism in disintegration process as a strongly swelling material. In accordance with the data obtained from Rohm and Hass, Amberlite® IRP 88 is an effective tablet disintegrant due to its extremely large swelling capacity in aqueous solutions. Additionally, it can be used effectively at 1%-2% (weight) of a solid dosage formulation (Pappas and Colombo, 1989: 249, Rohm and Haas, Dow chemical company).

Cross-linked polyacrylic with carboxylic acid functionality, COO-, (Indion® 414), in standard ionic from of K^+, shows good swelling index compared to conventional disintegrant (sodium starch glycolate, crosspovidone and crosscarmellose sodium). The good swelling properties result from its high water uptake capacity. Furthermore, it is a high molecular weight polymer, therefore it is not absorbed by the human tissues and totally safe for human consumption. Additionally, it can be successfully incorporated in each type of mouth dissolving tablets which has individual therapeutic agent such as roxithromycin (a macrolide anti-biotic), dicyclomine hydrochloride (an anti-spasmotic agent), montelukast sodium (an oral anti-asthmatic agent) (Amin, Prabhu, and Wadhwani, 2006: 117-118, Mohanachandran, sindhumol, and kiran, 2011: 108).

6.4.3 Taste masking of bitter-tasting drug by IER

Taste masking of the drug employing IER has been proved to be safe and effective method for formulation of various dosage forms. Doxylamine succinate, bitter cationic drug, can absorb onto Indion 234, the weak cationic ion exchange resin contains carboxylic acid functional group, to form the complex which is not bitter. The drug attached to the oppositely charged resin substrate through weak ionic bond could not be easily dissociated under salivary pH conditions. Consequently, patients will not pay the attention to the bitterness of drug (Puttewar,

2010: 229). There are some formulations developed for taste masking purpose which are shown in Table 3.

Table 3 Taste masking of bitter-tasting drug by IER

Drug	Type of IER
Spiramycin	Amberlite® IRP64M
Dextromethorphan HBr	Amberlite® IRP64
Paroxine	Amberlite® IRP88
Ranitidine	Amberlite® IRP64, 69, 88
Dimenhydrinate	Amberlite® IRP64

*U.S., Rohm and Haas Research Laboratories.

6.4.4 Controlled and sustained release of drug

IER plays an important role in the development of controlled or sustained release systems because of its better drug-retaining properties and prevention of dose dumping. The polymeric and ionic properties of IER provide the drug release more uniformLy compared to simple matrices. Resinate, a complex between drug in ionic form and appropriate IER, is the simplest form of controlled or sustained release delivery systems. Furthermore, microencapsulated or coated resinate is the modified resinates which provides the slower release rate compared to the simple resinate (Anand, Kandarapu, and Garg, 2001: 905, 908). The use of Dowex® 1x2, anionic exchange resin in the chloride form, with a flexibly coating material such as Eudragit® RS30D would be a feasible way to prepare a prolonged released type microcapsules containing diclofenac sodium over 24 h (Ichikawa et al., 2000: 67). More examples of drug delivery systems using IER are shown in Table 4.

Table 4 Drug delivery systems using IER

Type of system	IER	Drug
Resinate	Amberlite® IL-120	Metoclopramide
Resinate	Amberlite® and Dowex®	Propranolol
Resinate	Resicat® ABM Na-042	Codeine
Microencapsulated resinate	Dowex® 1x2, 1x4, 1x8	Theophylline
Microencapsulated resinate	Indion® 244	Bromhexine
Microencapsulated resinate	Dowex® 50Wx4	Terbutaline
Microencapsulated resinate	Dowex® 1x2	Diclofenac sodium
Cellulose acetate butyrate coated resinate	Amberlite® CG 50 R, Amberlite® CG 120 R	Diphenhydramine HCl, Chlorpheniramine HCl, Pseudoephedrine HCl

* Anand, Vikas, Raghupathi Kandarapu, and Sanjay Garg. (2001). "Ion-exchange resins: Carrying drug delivery forward." **DDT** 6, 17: 909.

7. Model drugs used in this study

7.1 Cationic model drug

Dextromethorphan hydrobromide monohydrate (DMP) is used as cationic model drug in this study. It is an antitussive (cough suppressant) drug. DMP is available in various dosage forms in the market, e.g. syrup, tablet, spray and lozenge forms. The chemical formula and molecular weight of DMP are $C_{18}H_{25}NO.HBr.H_2O$ and 370.32, respectively. The chemical structure of DMP is shown in Fig 8.

In its pure form, DMP occurs as a white powder with an odorless. The solubility of DMP in water is 1.5 g/100 mL at 25°C, 1 in 10 of ethanol, practically insoluble in ether and freely soluble in chloroform. The pH of 1% solution is between 5.2 and 6.5 (Promethazine hydrochloride and dextromethorphan hydrobromide.

Accessed 15 March 2012. Available from http://www.dailymedplus.com /monograph., US pharmacopoeia 30-NF 25, 2007: 1905).

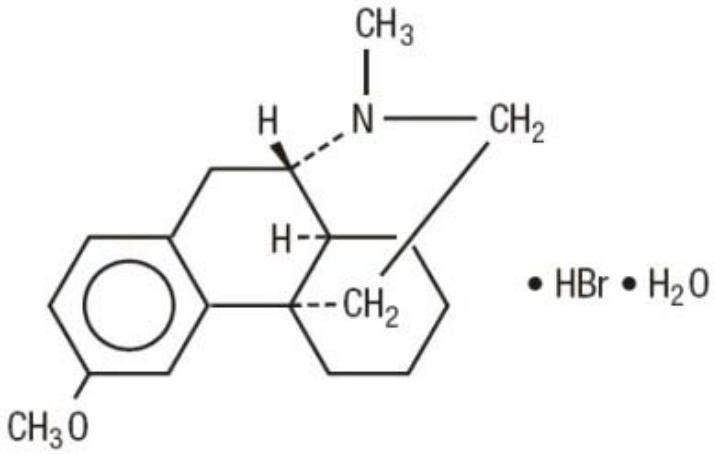

Fig. 8 Chemical structure of dextromethorphan hydrobromide monohydrate.

*Promethazine hydrochloride and dextromethorphan hydrobromide. Accessed 15 March 2012. Available from http://www.dailymedplus.com/monograph.

7.2 Anionic model drug

Diclofenac sodium (DCN) is used as anionic model drug in this study. It is a non-steroidal anti-inflammatory drug (NSAID) taken to reduce inflammation and as an analgesic reducing pain in some conditions. It is available in various dosage forms in the market, e.g. tablet formulations (25 and 50 mg), fast-disintegrating oral formulations (25 and 50 mg), powder for oral solution (50 mg), slow- and controlled-release forms (75, 100 or 150 mg), suppositories (50 and 100 mg), and injectable forms (50 and 75 mg). The chemical formula and molecular weight of DCN are $C_{14}H_{10}Cl_2NNaO_2$ and 318.13, respectively. The chemical structure of DCN is shown in Fig. 9. DCN is poorly soluble in water and acidic pH (1-3) but is rapidly soluble in alkaline pH (5-8). The pH of 1% solution is between 7.0 and 8.5 (Manjunatha, Ramana, and Satyanarayana, 2007: 385, US pharmacopoeia 30-NF 25, 2007:1922).

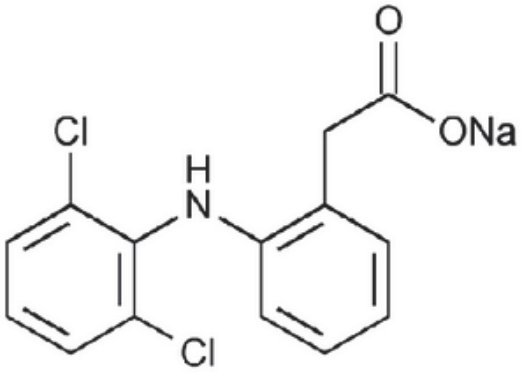

Fig. 9 Chemical structure of diclofenac sodium.

*US pharmacopoeia 30-NF 25, 2007: 1922.

CHAPTER III

MATERIALS AND METHODS

1. Materials

1.1 Dextromethorphan hydrobromide (DMP)

1.2 Diclofenac sodium (DCN)

1.3 Amberlite® IRP 64 (Sigma Chemical Co., USA)

1.4 Amberlite® IRP 69 (Sigma Chemical Co., USA)

1.5 Dowex® 88 (Dow Chemical Company, USA)

1.6 Dowex® retardion (Dow Chemical Company, USA)

1.7 Dowex 50Wx2-200 (Dow Chemical Company, USA)

1.8 Dowex 50Wx4-200 (Dow Chemical Company, USA)

1.9 Dowex 50Wx8-200 (Dow Chemical Company, USA)

1.10 Dowex 1x2-200 (Dow Chemical Company, USA)

1.11 Dowex 1x4-200 (Dow Chemical Company, USA)

1.12 Dowex 1x8-200 (Dow Chemical Company, USA)

1.13 Sodium starch glycolate (SSG, Explotab®)

1.14 Dibasic calcium phosphate (DCP)

1.15 Spray dried lactose (SDL)

1.16 Spray dried rice starch (SDRS)

1.17 Microcrystalline cellulose (MCC)

1.18 Magnesium stearate

1.19 Dextromethorphan hydrobromide STD

1.20 Diclofenac sodium STD

1.21 Potassium dihydrogen orthophosphate (Potassium phosphate, monobasic)

1.22 Diclofenac sodium STD

1.23 Sodium hydroxide

1.24 Hydrochloric acid

2. Equipments

2.1 Analytical balance

2.2 Hydraulic hand press machine (Specac, P/N 15011/25011, UK)

2.3 Friability tester (Erweka, Model TA120, Germany)

2.4 Tablet hardness tester (Erweka, Model TBH 225TD, Germany)

2.5Disintegration testing apparatus (Sotax DT3, Sotax AG CH-4008 BASEL, Switzerland)

2.6 Dissolution apparatus, Paddle, Apparatus II (Pharma Test, Hainburg, Germany)

2.7 Microscope (Dino-Lite Digital Microscope)

2.8 pH meter (Sartorius, PP-15, Germany)

2.9 High pressure liquid chromatography; HPLC (Shimadzu, Japan)

2.9.1 System controller; Model SCL-10 Avp

2.9.2 UV-Vis detector; Model SPD-10 Avp

2.9.3 Liquid chromatograph; Model LC-10 ATvp

2.10 15 mL, 50 mL centrifuge tubes-sterile (Biologix research company)

2.11 1.5 mL Microcentrifuge tubes

3. Methods

3.1 Characterization of ion exchange resin

3.1.1 Swelling property

3.1.1.1 Swelling ratio by v/v

Before starting the experiment, 1 g of dried IER was added into 10 mL cylinder. The cylinder was then tapped until a constant volume was

achieved. The initial volume was recorded. After that, 10 mL of distilled water was added into the cylinder and the dried IER was allowed to swell in distilled water. At specified time, the changed volume was recorded. The swelling ratio of each type of IER was calculated as follow;

$$\%\ Swelling\ ratio\ (v/v) = \frac{V_{final} - V_{initial}}{V_{initial}} \times 100$$

Where $V_{initial}$ and V_{final} were the initial volume of dried resin and the final volume of swollen resin, respectively.

3.1.1.2 Swelling ratio by w/w

Before starting the experiment, 200-400 mg of dried IER was added into 1.5 mL microcentrifuge tube. The initial weight was recorded. Then, 1 g of distilled water was added into the microcentrifuge tube and the dried IER was allowed to swell in the distilled water. After that the microcentrifuge tube was centrifuged at 2,000 rpm for 3 min and the supernatant was then removed. The swollen IER was weighed and recorded as the final weight. The swelling ratio of each type of IER was calculated as follow;

$$\%\ Swelling\ ratio\ (w/w) = \frac{W_{final} - W_{initial}}{W_{initial}} \times 100$$

Where $W_{initial}$ and W_{final} were the initial weight of dried resins and the final weight of swollen resins, respectively.

3.1.2 Particle size

The particle size of IER was measured by using microscope as described in BP Pharmacopeia. The diameter of IER was measured in accordance with Martin's diameter.

3.2 Screening study of IER as tablet disintegrant

The formulations and compositions of tablet are presented in Table 5. All formulations were constantly composed of 5% disintegrant or IER, 1% lubricant and

94% diluent. The used disintegrant was either SSG (as reference disintegrant) or IER, i.e. Amberlite® IRP64, Amberlite® IRP69, Dowex® 88, Dowex® retardion, Dowex® 50Wx2-200, Dowex® 50Wx4-200, Dowex® 50Wx8-200, Dowex® 1x2-200, Dowex® 1x4-200 and Dowex® 1x8-200. Magnesium stearate and DCP were used as lubricant and diluent, respectively.

Before starting the experiments, all compositions were dried in a 60°C hot air oven for 2 h. The DCP and SSG or IER were blended for 3 min. Magnesium stearate was added into the mixture and blended for 2 min. 500 mg of the final mixture was compressed on a plane-face single punch with 9.3 mm of diameter at fixed pressure, 4.5 tons for 20 sec, using a hydraulic hand press machine. The produced tablets were evaluated for thickness, diameter, hardness, friability and disintegration.

3.3 Factors affecting the properties of tablets using resin as disintegrant

The preliminary study, three types of IER which provided the tablets with the desirable properties, i.e. the shortest disintegration time, the highest hardness and the lowest friability were selected for this purpose. These resins have the possibility to be used as the tablet disintegrant.

3.3.1 Amount of IER

The mixtures of each type of IER with various quantities, i.e. 2.5%, 5.0%, 7.5%, 10% w/w and DCP (q.s. to 99 % w/w) were blended for 3 min. After that, 1% w/w of magnesium stearate was added to the mixtures and blended for 2 min. Then, 500 mg of the final mixtures was compressed at 4.5 tons for 20 sec using a hydraulic hand press machine. The properties of produced tablets were evaluated and compared to those containing SSG as the disintegrant.

Table 5 Formulations and compositions (% w/w) of tablet containing IER

Formulations	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**
SSG	5	-	-	-	-	-	-	-	-	-	-
Amberlite® IRP64	-	5	-	-	-	-	-	-	-	-	-
Amberlite® IRP69	-	-	5	-	-	-	-	-	-	-	-
Dowex® 88	-	-	-	5	-	-	-	-	-	-	-
Dowex® retardion	-	-	-	-	5	-	-	-	-	-	-
Dowex® 50Wx2-200	-	-	-	-	-	5	-	-	-	-	-
Dowex® 50Wx4-200	-	-	-	-	-	-	5	-	-	-	-
Dowex® 50Wx8-200	-	-	-	-	-	-	-	5	-	-	-
Dowex® 1x2-200	-	-	-	-	-	-	-	-	5	-	-
Dowex® 1x4-200	-	-	-	-	-	-	-	-	-	5	-
Dowex® 1x8-200	-	-	-	-	-	-	-	-	-	-	5
Magnesium stearate	1	1	1	1	1	1	1	1	1	1	1
DCP q.s.to 100 %	100	100	100	100	100	100	100	100	100	100	100

3.3.2 Compression pressure

The mixtures of 5 % w/w each IER and 94 % w/w DCP were blended for 3 min. After that, 1% (w/w) of magnesium stearate was added into the mixtures and blended for 2 min. Then, 500 mg of the final mixtures was compressed at various pressures, i.e. 0.5, 1.5, 3.0, 4.5 tons for 20 sec by using a hydraulic hand press machine. The properties of produced tablets were evaluated and compared to those containing SSG as disintegrant.

3.3.3 Type of diluent

The mixtures of 5 % w/w each IER and 94 % w/w either DCP, spray dried lactose (SDL), microcrystalline cellulose (MCC) or spray dried rice starch (SDRS) were blended for 3 min. After that, 1% w/w of magnesium stearate was added into the mixtures and blended for 2 min. Then, 500 mg of the final mixtures was compressed at 4.5 tons for 20 sec by using a hydraulic hand press machine. The properties of produced tablets were evaluated and compared to those containing SSG as disintegrant.

3.4 Tablet formulations using IER as disintegrant

In this study, dextromethorphan hydrobromide (DMP) and diclofenac sodium (DCN) were chosen as representatives of cationic and anionic model drug, respectively. The tablet formulations of either DMP or DCN are shown in Table 6 and 7, respectively, which were prepared by the procedure described above. Briefly, the mixtures of 5 % w/w each type of IER and DCP (q.s. to 100 % w/w) were blended for 3 min. After that the model drug, 15 % w/w DMP or 25% w/w DCN, was added into the mixtures and blended for 3 min. Finally, 1 % w/w of magnesium stearate was added into the mixtures and blended for 2 min. To make tablets, 500 mg of the final mixtures was compressed at 4.5 tons for 20 sec by using a hydraulic hand press machine. The properties including the dissolution test of obtained tablet formulations were evaluated and compared to those containing SSG as disintegrant.

3.5 Characterization of tablet properties

3.5.1 Hardness, diameter and thickness

The hardness, diameter and thickness of ten tablets from each formulation were characterized by using a multifunctional tablet tester.

Table 6 Formulations and compositions (% w/w) of tablet containing DMP with IER as tablet disintegrant

Formulations	**1**	**2**	**3**
DMP	15	15	15
SSG	5	-	-
Amberlite® IRP64	-	5	-
Dowex® 1x2-200	-	-	5
Magnesium stearate	1	1	1
DCP q.s.to 100 %	100	100	100

Table 7 Formulations and compositions (% w/w) of tablet containing DCN with IER as tablet disintegrant

Formulations	**1**	**2**	**3**
DCN	25	25	25
SSG	5	-	-
Amberlite® IRP64	-	5	-
Dowex® 1x2-200	-	-	5
Magnesium stearate	1	1	1
DCP q.s.to 100 %	100	100	100

3.5.2 Friability

Tested tablets were carefully cleaned from fines prior to testing. Thirteen tablets corresponding as near as possible to 6.5 g were weighed accurately

and placed in a friabilator. The tablets were rotated at 25 rpm for 4 min. After that the tablets were cleaned from fines and weighed again. The percentage of tablet friability was calculated using following equation;

$$\%\ Friability = \frac{W_{initial} - W_{final}}{W_{initial}} \times 100$$

Where $W_{initial}$ and W_{final} were the initial and final weights of tablets, respectively.

3.5.3 Disintegration test

The disintegration time was measured using a USP disintegration testing apparatus. Six tablets were placed in a basket-rack assembly at the start of each test. The medium used for this test was deionized water maintained at 37±1°C throughout testing. The disintegration time, defined as the point at which tablets disintegrated and passed through the assembly, was recorded.

3.5.4 Dissolution test

Dissolution studies were examined according to the method described in USP 30, using apparatus 2 (paddle) with 50 rpm of paddle rotation. According to the pharmacopeia, 900 mL of pH 5.8 and 6.8 PBS was used as dissolution media for the tablets containing DMP and DCN, respectively, maintained at 37°C±0.5. Filtered samples were collected at specified times (5, 10, 15, 30, 60, 120 min) and was determined for amounts of dissolved drug by HPLC method. The testing was conducted with six tablets of each formulation.

3.6 HPLC condition

3.6.1 Determination of DMP

Drug analysis was determined on a HPLC with UV detection at a wavelength of 280 nm. The column used for the analysis was a 4.6 mm x 250 mm ACE5 C18-AR. The mobile phase contained 0.007 M docusate sodium and 0.007 M ammonium nitrate in a mixture of acetonitrile and water (70:30), which was finally

adjusted to pH 3.4 with glacial acid. Samples were filtered by 0.2 μm nylon filters and then 20 μL of samples was injected. All tests were performed at 30°C and the retention time of DMP was 7 min.

3.6.2 Determination of DCN

Drug analysis was determined on a HPLC with UV detection at a wavelength of 254 nm. The column used for the analysis was a 4.6 mm x 250 mm ACE5 C18-AR. The mobile phase contained a filtered and degassed mixture of methanol and pH 2.5 PBS (700:300). Samples were filtered by 0.2 μm nylon filters and then 20 μL of samples was injected. All tests were performed at 30°C and the retention time of DCN was 21 min.

CHAPTER IV

RESULTS AND DISCUSSION

1. Characteristics of various IER used as tablet disintegrant

1.1 Structural property

Ten types of IER, Amberlite® IRP64, Amberlite® IRP69, Dowex® 88, Dowex® retardion, Dowex® 50Wx2-200, Dowex® 50Wx4-200, Dowex® 50Wx8-200, Dowex® 1x2-200, Dowex® 1x4-200 and Dowex® 1x8-200 were investigated in terms of the tablet disintegrated efficacy. Sodium starch glycolate (SSG) was chosen as the positive control. The structural property of IER used in this study is shown in Table 8 and chemical structure of Amberlite® IRP64, Amberlite® IRP69, Dowex® 88 are shown in Fig. 10 – 12, respectively. Furthermore, a simplified chemical structure of SSG is illustrated in Fig. 13.

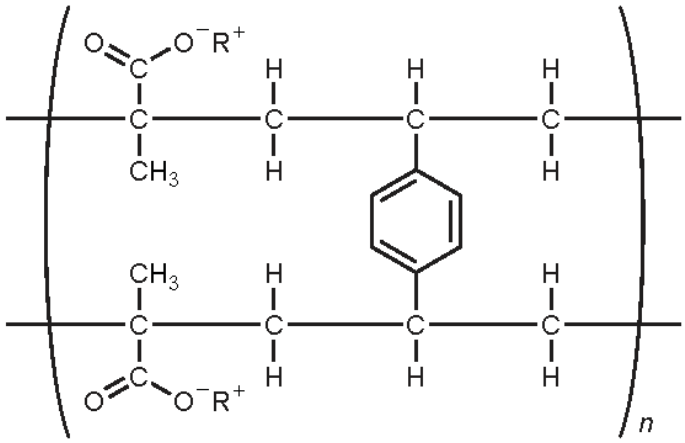

Fig. 10 Chemical structure of Amberlite® IRP64.

* Elder, David P. (2005). "Pharmaceutical applications of ion-exchange resins." **J Chem Educ** 82, 4: 575-587.

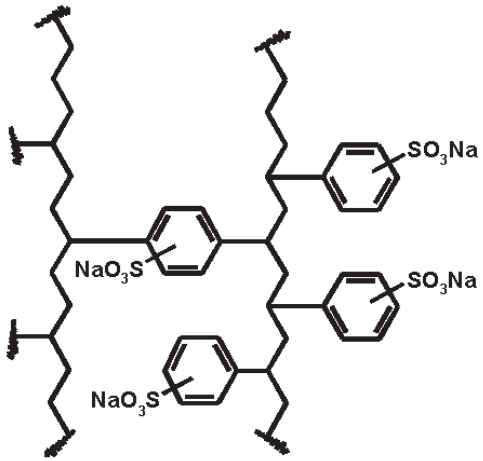

Fig. 11 Chemical structure of Amberlite® IRP69.

* Zeiss, Daniel, Marita Wagner, and Annette Bauer-Brandl. (2009). "Characterisation of the ion exchange reaction between propranolol-H+ or K+ with Amberlite™ IRP 69 resin by both, isothermal titration calorimetry and (flame) photometric equilibrium analysis." **The Open Drug Delivery Journal** 3 (January 12): 15.

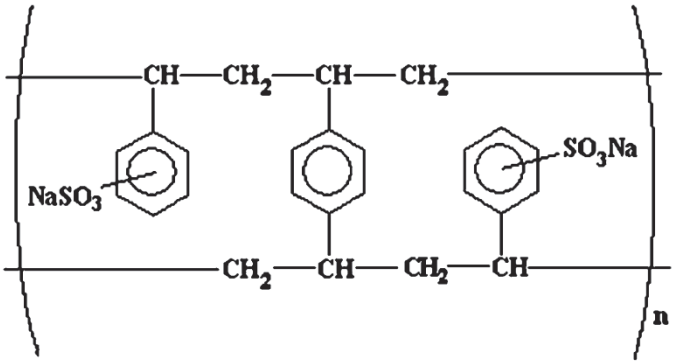

Fig. 12 Chemical structure of Dowex® 88.

* Akkaramongkolporn, Prasert et al. (2010). "Comparison between the effect of strongly and weakly cationic exchange resins on matrix physical properties and the

controlled release of diphenhydramine hydrochloride from matrices." **AAPS Pharm Sci Tech** 11, 3: 1106.

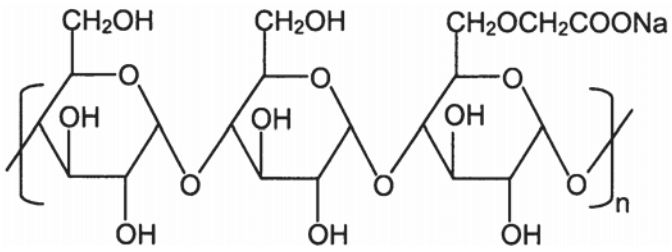

Fig. 13 Chemical structure of SSG.

* Edge, S. et al. (2002). "Chemical characterisation of sodium starch glycolate particles." **Int J Pharm** 240 (March 18): 69.

Table 8 Structural property of various types of IER

Resin	Resin type	Matrix type	Ion exchangeable group
Amberlite® IRP64	Cationic	Methacrylic acid-DVB	Carboxylic group
Amberlite® IRP69	Cationic	Styrene-DVB	Sulfonic group
Dowex® 88	Cationic	Styrene-DVB	Sulfonic group
Dowex® retardion	Amphoteric	Styrene-DVB	Carboxylic and quaternary ammonium group
Dowex® 50Wx2-200	Cationic	Styrene-DVB	Sulfonic group
Dowex® 50Wx4-200	Cationic	Styrene-DVB	Sulfonic group
Dowex® 50Wx8-200	Cationic	Styrene-DVB	Sulfonic group
Dowex® 1x2-200	Anionic	Styrene-DVB	Quaternary ammonium group
Dowex® 1x4-200	Anionic	Styrene-DVB	Quaternary ammonium group
Dowex® 1x8-200	Anionic	Styrene-DVB	Quaternary ammonium group

1.2 Swelling power

The swelling power measured by gravimetric method (% w/w) and volumetric method (% v/v) of dried IER are shown in Fig. 14 and Fig. 15, respectively. To clarify the results, both volume and weight swelling of the resins were also graphically compared as depicted in Fig. 16. SSG exhibited the remarkable swelling properties over the others. Nevertheless, all tested IER also demonstrated the ability for swelling which was different from each other as follows.

In case of Dowex®, when compared between Dowex® 50Wx2-200 and Dowex® 1x2-200, the same degree of cross-linking, both volume and weight swelling of Dowex® 50Wx2-200 was much higher than that of Dowex® 1x2-200. This could be suggested that the strong acid IER could swell effectively compared to weak base IER. Furthermore, the reduction of swelling capacity was found with an increase of degree of cross-linking. The increased cross-linking caused the difficulty for expansion of and hence water uptake into the copolymer network, thus resulting in the decreased swelling capacity.

For Amberlite®, the weight swelling of Amberlite® IRP64 (231.91 ± 2.24) was higher than that of Amberlite® IRP69 (167.18 ± 5.36). However, these results did not correlate with those obtained from volumetric method. Namely, the swelling capacity of Amberlite® IRP64 (32.11 ± 4.67) was lower than that of Amberlite® IRP69 (50.6 ± 11.34). This phenomenon was also in agreement with Dowex® 88 (macroporous resin) and Dowex® retardion (gel resin). For volumetric method, Dowex® 88 could not exhibit the swelling property whereas Dowex® retardion gave the high percentage of swelling power (38.47 ± 7.75). In contrast, Dowex® 88 exhibited high swelling property when measured by gravimetric method (158.87 ± 7.75) which was higher than that of Dowex® retardion (127.04 ± 3.99). These results might indicate that the weight and volume swelling was governed by different mechanisms. The volume swelling mainly resulted from an increase in particle size whereas the weight swelling mainly resulted from the water uptake without a need of change in the resin volume or size (wicking or capillary property) (Akkaramongkolporn et al., 2010: 1111).

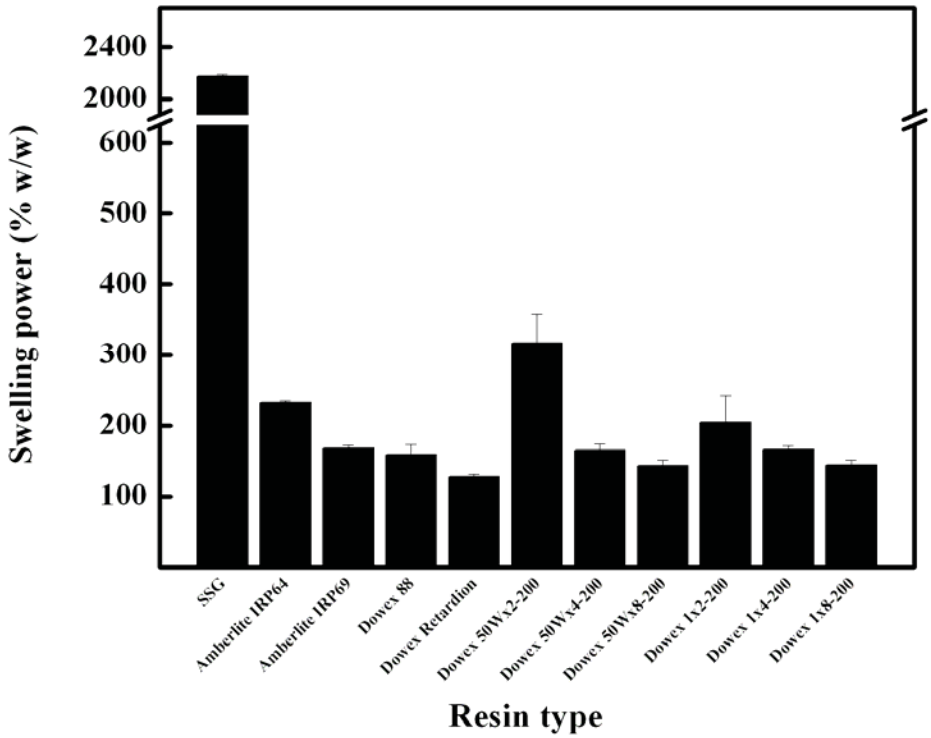

Fig. 14 Weight swelling (% w/w) of various dried IER.

From literature, Amberlite® IRP64 and Dowex® 88 are classified as macroporous resin while Amberlite® IRP69 and Dowex® retardion are classified as gel resin. Based on the above swelling results, it could be concluded that the macroporous resins i.e. Amberlite® IRP64 and Dowex® 88 might swell mainly via the wicking or capillary rather swelling action, and vice versa for the gel resins i.e. Amberlite® IRP69 and Dowex® retardion. As a results, it could be suggested that the swelling power of each resin was obviously different, which resulted from the differences in several characteristics among the resins, i.e. degree of cross-linking, resin and matrix type, ion exchangeable group, particle size, shape, moisture content etc. Existing ability for swelling postulated that IER could be served as disintegrant. The disintegrating effect of the resins might be originated by either or couple mechanisms of the swelling and wicking (capillary) properties. Further, it could be projected that the resin with high percentage of both volume swelling and weight swelling might possess the better disintegrant properties compared to the resin with either high volume swelling or high weight swelling.

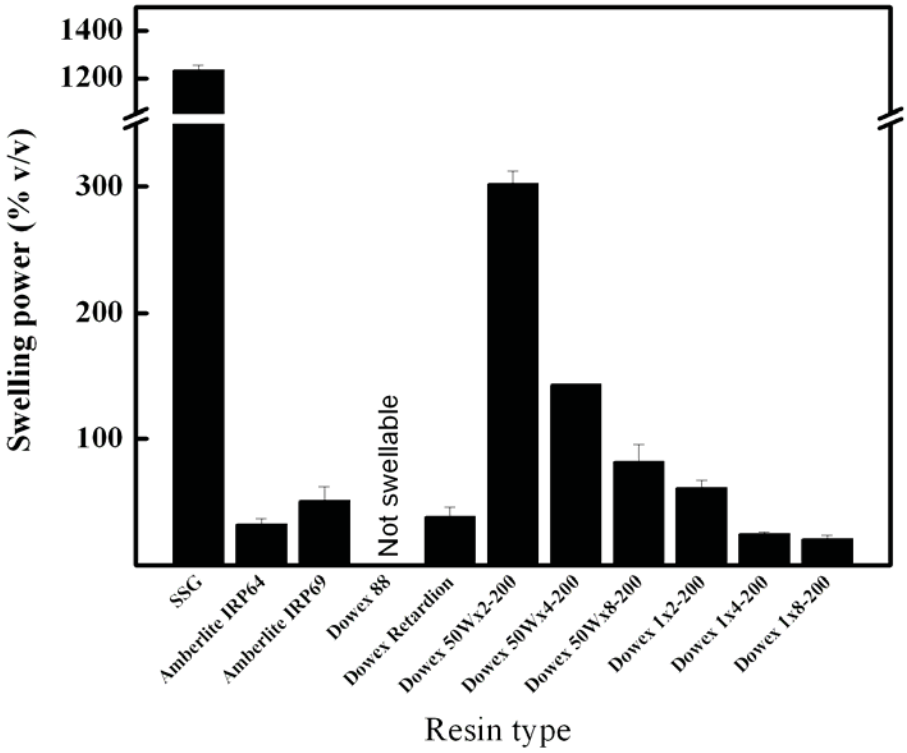

Fig. 15 Volume swelling (% v/v) of various types of dried IER.

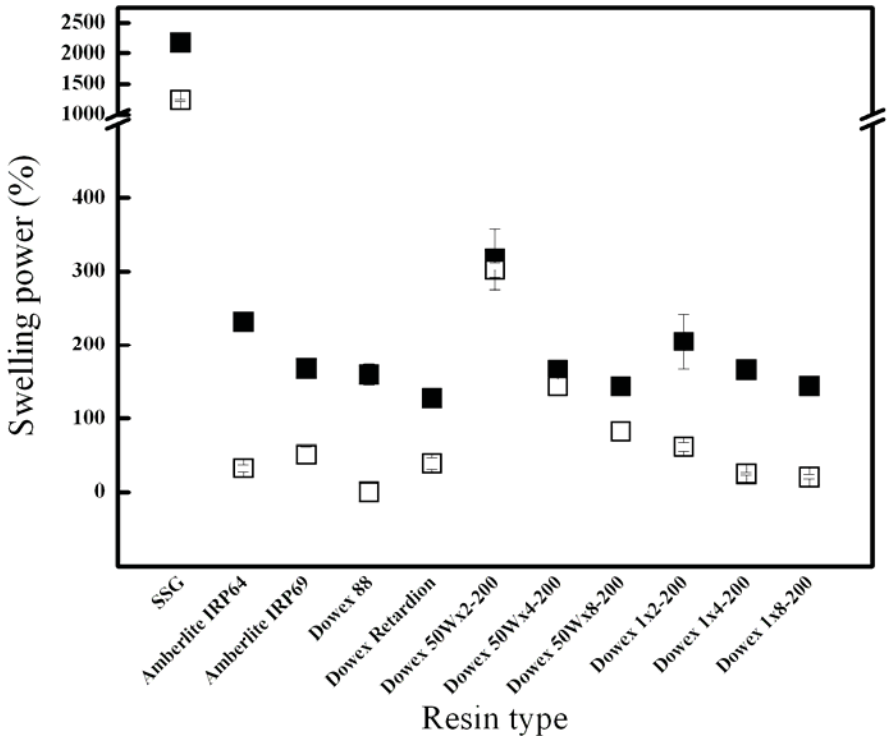

Fig. 16 Weight (■) versus volume swelling (□) of IER.

1.3 Particle size

The particle size of Dowex® 50Wx2 and Dowex® 1x2 was measured by using microscope while the particle size of SSG, Amberlite® IRP64, Amberlite® IRP69 and Dowex® 88 were measured by a particle analyzer. The particle sizes of IER are shown in Fig. 17.

From Fig. 17, the particle size of Amberlite® IRP64, Amberlite® IRP69 and Dowex® 88 were less than 80 μm whereas the particle size of the others were higher than 150 μm. The smallest particle was found in Dowex® 88 (44.06 ± 1.92) whereas Dowex® retardion was the largest (399.00 ± 12.17). In this finding, moreover, it was found that the particle size has no effect on the swelling power of IER as depicted in Fig. 18 and Fig. 19. The results demonstrated that the largest particle do

not have to possess the highest swelling capacity. The good example for explanation is Dowex® retardion, which is relatively low in both weight and volume swelling.

The particle size of IER which is suitable for use in pharmaceutical application is approximately 25-150 μm (U.S., Rohm and Hass company). In the field of tablet formulation, the excipients should have small enough in order not to cause the mixture separation during compression process. However, the resin has to meet the other requirements such as good swelling properties, good stability and excellence in disintegrant properties etc.

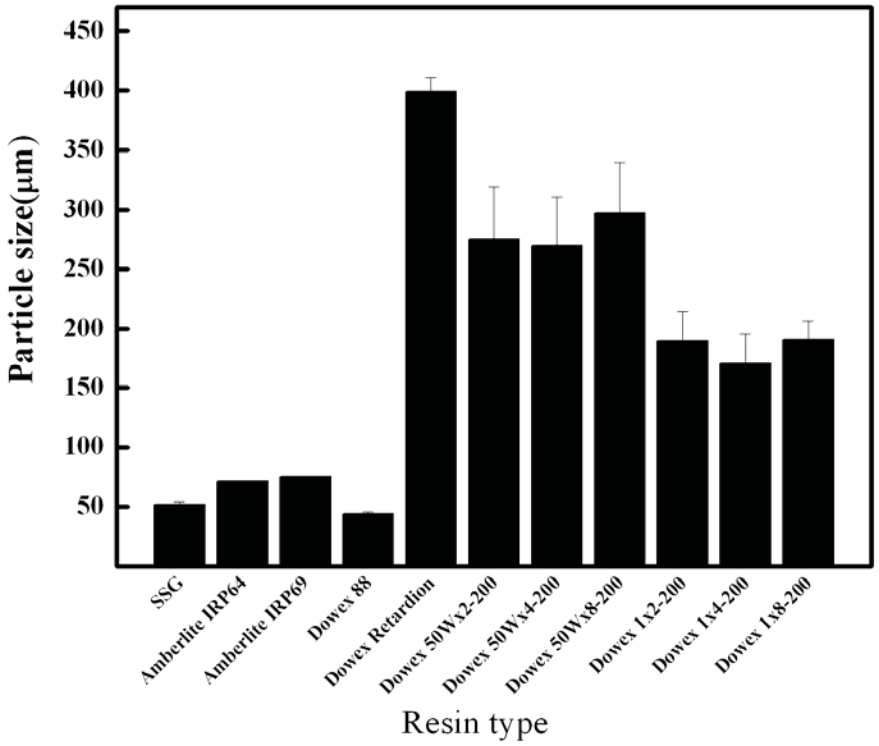

Fig. 17 Particle size of various dried IER.

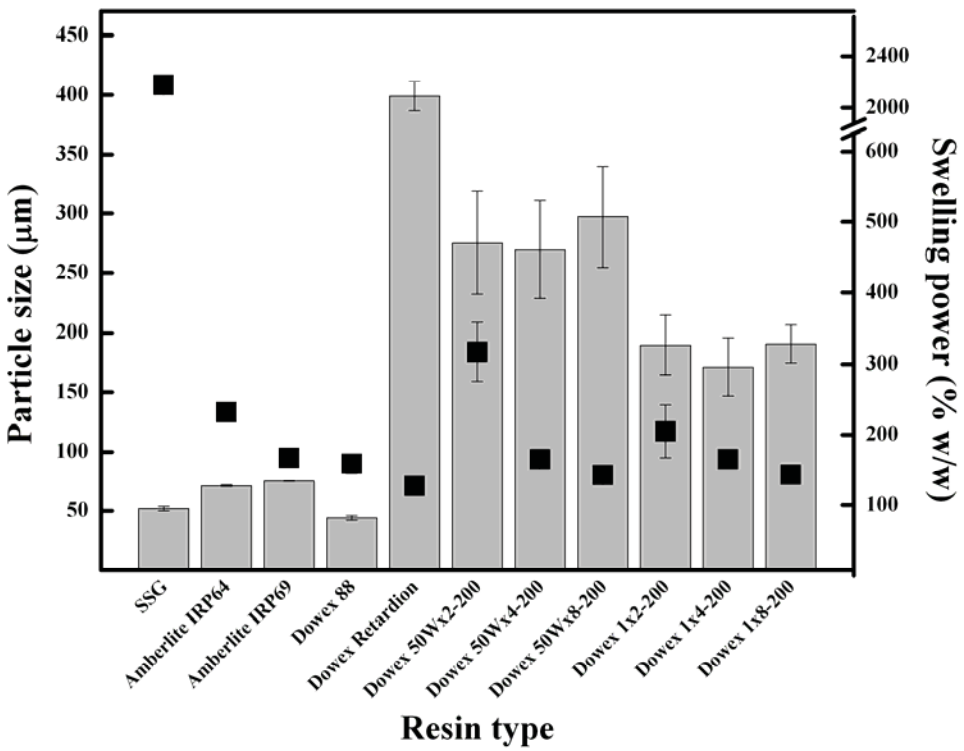

Fig. 18 Effect of particle size on swelling capacity (% w/w) of IER.

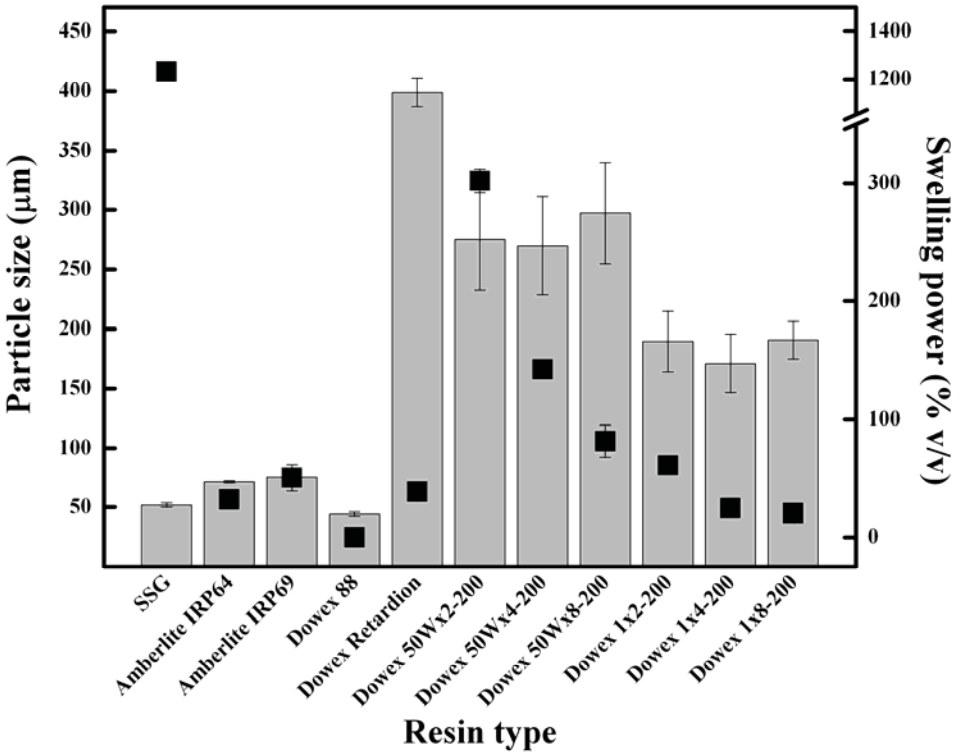

Fig. 19 Effect of particle size on swelling capacity (% v/v) of IER.

2. Screening study of DCP tablets using various IER as the disintegrant

In this study, dibasic calcium phosphate (DCP) was chosen as the excipient for direct compression because of its very low equilibrium moisture content (2.5%). Furthermore, DCP contained tablets were easier to handle after having absorbed moisture than the other were, such as those prepared from lactose (K.A. Khan and C.T. Rhodes, 1975: 447).

All tablet formulations were constantly composed of 95% DCP and 5% of sodium starch glycolate (SSG) or various types of IER. The used compression pressure was fixed at 4.5 tons and thereafter the physical properties of tablets including disintegration were immediately evaluated. The physical properties of tablets including disintegration time are shown in Table 9. To clarify the efficacy of IER used as the disintegrant, the disintegration time is depicted in Fig. 20.

DCP tablet without resin did not disintegrate within 30 min. This could be due to the lack of disintegrant in the formulation. The result was in accordance with the results reported by Peppas, and Colombo. The tablet containing calcium diphosphate without any resin exhibited minimal swelling (12%) compared to tablet containing disintegrant, either SSG or Amberlite® IRP88 (Peppas and Colombo, 1989: 249).

The results demonstrated that the disintegration time of tablets containing Amberlite® IRP64 (64.08 ± 10.76) is similar to that of SSG (60.00 ± 11.34) (reference disintegrant). Furthermore, their hardness and friability are similar to that of SSG. Although, the tablets containing Amberlite® IRP69 possesses the shorter disintegration time (29.08 ± 7.05) compared to Amberlite® IRP64, the hardness is lower and the friability is higher than the tablets containing Amberlite® IRP64. This could be due to the lower compressibility of Amberlite® IRP69 compared to Amberlite® IRP64 (Akkaramongkolporn et al., 2010: 1108). As a result, both Amberlite® IRP64 and Amberlite® IRP69 were selected in order to study in the further experiments.

Table 9 Physical properties of tablet containing various types of IER

Resin type	Hardness (N)	Thickness (mm)	Diameter (mm)	Disintegration time (sec)	Friability (%)
No disintegrant	276.8 ± 13.51	3.21 ± 0.03	9.56 ± 0.02	> 30 min	0.7698
SSG	185.8 ± 35.36	3.34 ± 0.05	9.69 ± 0.09	60.00 ± 11.34	0.8991
Amberlite® IRP 64	158.9 ± 8.97	3.55 ± 0.04	9.59 ± 0.02	64.08 ± 10.76	0.7880
Amberlite® IRP 69	75.9 ± 4.12	3.48 ± 0.10	9.63 ± 0.02	29.08 ± 7.05	1.9656
Dowex® 88	80.5 ± 4.53	3.54 ± 0.03	9.66 ± 0.01	115.90 ± 13.78	100.00
Dowex® Retardion	57.8 ± 6.86	3.81 ± 0.07	9.59 ± 0.02	> 30 min	100.00
Dowex® 50Wx2-200	33.3 ± 4.85	3.23 ± 0.02	9.61 ± 0.01	27.92 ± 3.29	4.7692
Dowex® 50Wx4-200	26.8 ± 3.58	3.28 ± 0.03	9.63 ± 0.02	8.58 ± 2.50	1.9417
Dowex® 50Wx8-200	16.1 ± 2.28	3.53 ± 0.03	9.62 ± 0.01	> 30 min	8.4158
Dowex® 1x2-200	107.2 ± 10.53	3.70 ± 0.04	9.56 ± 0.01	15.42 ± 2.97	1.9072
Dowex® 1x4-200	71.2 ± 13.85	4.01 ± 0.11	9.60 ± 0.03	25.00 ± 5.22	3.9809
Dowex® 1x8-200	69.6 ± 14.14	4.03 ± 0.12	9.56 ± 0.02	> 30 min	9.8598

The disintegration time of tablet containing Dowex® 88 was quite longer than the others. This result correlated well with the swelling power of these resins. It was not swellable when measured by volumetric method. The tablet containing Dowex® retardion cannot disintegrate within 30 min. This could be due to its particle. Consequently, the tablet cannot break apart properly. In addition, both Dowex® 88 and Dowex® retardion showed low compressibility. The tablet containing both of them exhibited the lower hardness with the highest friability. Therefore, they were not suitable for use as tablet disintegrant.

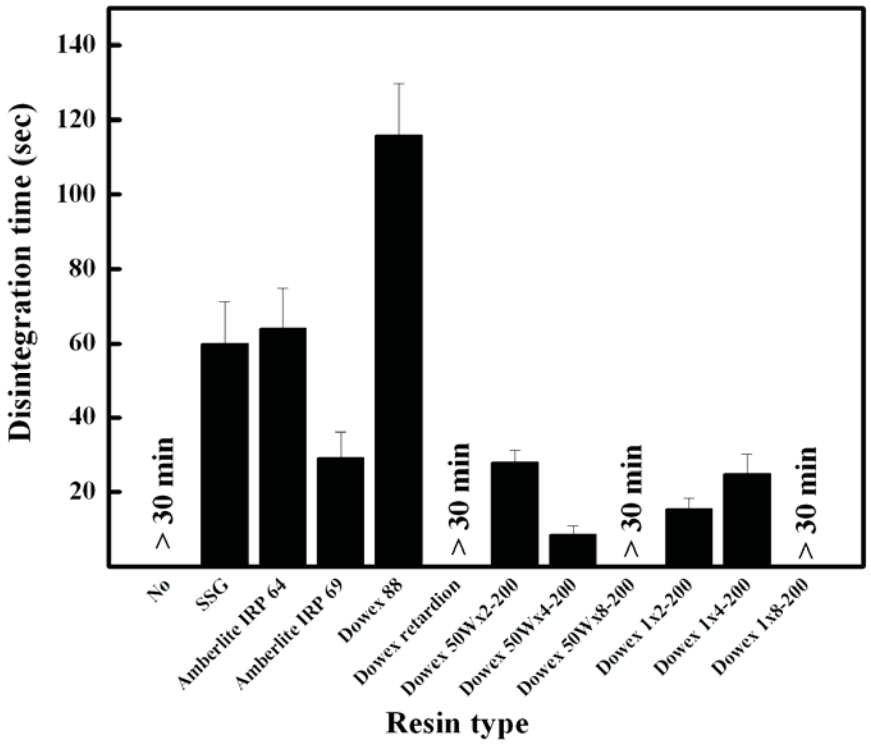

Fig. 20 Disintegration time of tablet containing various types of IER.

Considering the disintegration time of tablets containing Dowex® 50W and Dowex® 1x2, it was found that the disintegration time of these tablets was relatively short, except for Dowex® 50Wx8-200 and Dowex® 1x8-200. This could be due to their high degree of cross-linking giving the low volume swelling power. Nonetheless, tablets containing either Dowex® 50Wx2-200, Dowex® 50Wx4-200 or Dowex® 1x4-200 exhibited the low hardness with high friability indicating that they carried the poorly compressible properties.

A good release profile of drug can be obtained by selecting suitable degree of cross-linking and particle size of resin (Pongjanyakul et al., 2005: 100). These factors have an important effect on swelling power of resin and disintegration time of tablets. As a result, Amberlite® IRP64, Amberlite® IRP69 and Dowex® 1x2-200 were chosen for testing in the further experiments because these resins contributed to the tablets which possessed the good performances such as shorter disintegration time,

suitable hardness and friability. Factors affecting the physical properties such as the amount of resin, compression pressure and type of diluent were evaluated.

3. Factors affecting the properties of tablets using resin as disintegrant

3.1 Amount of IER

The mixtures of DCP and IER, i.e. Amberlite® IRP64, Amberlite® IRP69 and Dowex® 1x2-200 with various amounts (2.5%, 5.0%, 7.5% and 10% w/w) were evaluated their physical properties by using SSG as reference disintegrant. The physical properties of these tablets are shown in Table 10.

To clarify the results, the hardness was plotted against the amount of resin and shown in Fig. 21. The hardness decreased with an increase of the amount of disintegrant (Thaned et al. 2005: 194, Akkaramongkolporn et al., 2010: 1107, Khan, and Rhodes, 1975: 166). Interestingly, the reduction of hardness in tablets containing Amberlite ® IRP64 was similar to that of tablets containing SSG. On the other hand, the hardness of tablets containing Amberlite ® IRP69 and Dowex® 1x2-200 reduced dramatically. These results could be indicated that both of them have poor compressibility. These results were in accordance with the results reported by Akkaramongkolporn et al., Amberlite® IRP64 had higher compressibility than Amberlite® IRP69 (Akkaramongkolporn et al., 2010: 1108). It could be implied that the compressibility of resin relate to its chemical structure. Methacrylic acid-divinylbenzene copolymer, Amberlite® IRP64, might be inherently more compressible than styrene-divinylbenzene copolymer, Amberlite® IRP69 and Dowex® 1x2-200 (Akkaramongkolporn et al., 2010: 1108). Moreover, Thaned et al. reported that Amberlite® IRP69 caused the reduction in the hardness of dextromethorphan resinate tablet (Thaned et al. 2005: 194).

The friability increased with an increase of the amount of resin, except for SSG (Fig. 22). Although the friability of tablets containing Amberlite® IRP64 increased slightly in which the amount of resin was 10%, the friability in the lower concentrations were quite constant and similar to those of tablet containing SSG.

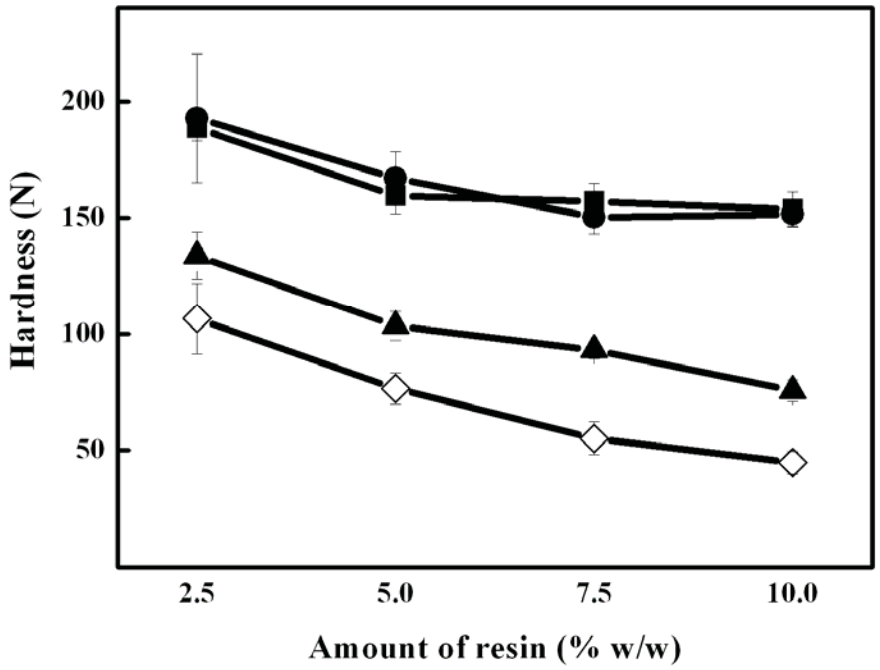

Fig. 21 Hardness of tablets with various amounts of SSG (■), Amberlite® IRP64 (●), Amberlite® IRP69 (◇) and Dowex® 1x2-200 (▲).

The disintegration time of all DCP tablets decreased with an increase of the amount of resin. These results were in accordance with the results obtained from the tablets containing Amberlite® IRP88 (U.S., Rohm and Hass company). In case of Amberlite® IRP64, 2.5% of resin was not sufficient for breaking of tablet. Consequently, the tablet disintegration was not occurred properly.

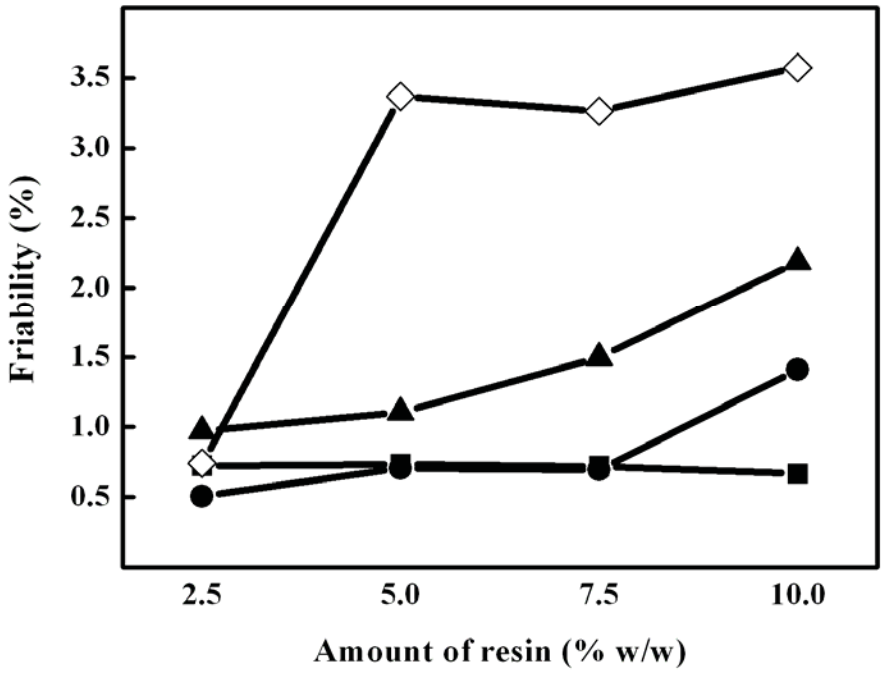

Fig. 22 Friability of tablets with various amounts of SSG (■), Amberlite® IRP64 (●), Amberlite® IRP69 (◇) and Dowex® 1x2-200 (▲).

Table 10 Physical properties of DCP tablet containing various amounts of IER

Resin	Amount of resin (% w/w)	Hardness (N)	Thickness (mm)	Diameter (mm)	Disintegration time (sec)	Friability (%)
SSG	2.5	188.70 ± 5.36	3.19 ± 0.01	9.61 ± 0.01	101.00 ± 9.19	0.7235
	5.0	159.50 ± 7.69	3.25 ± 0.02	9.60 ± 0.01	60.00 ± 11.34	0.7328
	7.5	157.10 ± 7.78	3.34 ± 0.02	9.59 ± 0.01	46.75 ± 5.96	0.7187
	10.0	153.70 ± 7.53	3.39 ± 0.02	9.59 ± 0.01	47.50 ± 6.97	0.6663
Amberlite® IRP64	2.5	192.80 ± 27.57	3.34 ± 0.03	9.59 ± 0.03	> 30 min	0.5058
	5.0	167.10 ± 11.30	3.47 ± 0.03	9.60 ± 0.01	64.08 ± 19.76	0.7062
	7.5	150.30 ± 7.10	3.55 ± 0.04	9.61 ± 0.01	21.58 ± 3.60	0.6946
	10.0	151.70 ± 5.21	3.60 ± 0.02	9.59 ± 0.01	17.92 ± 2.50	1.4123
Amberlite® IRP69	2.5	106.00 ± 16.05	3.45 ± 0.04	9.61 ± 0.01	28.58 ± 9.12	0.7418
	5.0	76.50 ± 6.65	3.49 ± 0.03	9.63 ± 0.01	15.42 ± 5.85	3.3679
	7.5	55.17 ± 7.15	3.59 ± 0.02	9.66 ± 0.01	13.27 ± 3.44	3.2647
	10.0	44.75 ± 4.86	3.70 ± 0.02	9.66 ± 0.01	15.58 ± 4.50	3.5758
Dowex® 1x2-200	2.5	133.83 ± 10.23	3.51 ± 0.03	9.61 ± 0.01	146.92 ± 11.75	0.9716
	5.0	103.42 ± 6.27	3.71 ± 0.03	9.58 ± 0.01	15.42 ± 2.97	1.1076
	7.5	93.08 ± 3.58	3.88 ± 0.02	9.59 ± 0.01	12.50 ± 1.57	1.4965
	10.0	75.58 ± 4.68	3.97 ± 0.05	9.59 ± 0.01	10.00 ± 0.00	2.1865

3.2 Compression pressure

The mixtures of DCP and 5% w/w of IER (Amberlite® IRP64 and Dowex® 1x2-200) were compressed at various pressures, i.e. 0.5, 1.5, 3.0, 4.5 tons for 20 sec by using a hydraulic hand press machine. The physical properties of produced tablets were evaluated and compared to those containing sodium starch glycolate (SSG) as the reference disintegrant. The physical properties of these tablets are shown in Table 11.

The effect of compression pressure on hardness of tablet is shown in Fig. 23. The hardness of tablet containing SSG and Amberlite® IRP64 proportionately increase with an increase of compression pressure, while the hardness of tablet containing Dowex® 1x2-200 reached a constant level at a compression pressure of 3 tons. This could be suggested that an increase of hardness is obviously parameter which can be related quite directly to the compression pressure used (Riippia et al., 1998: 340, Sunada, and Bi, 2002: 195).

The effect of compression pressure on friability of tablet is shown in Fig. 24. The friability of tablet decreased with an increase of compression pressure. This could be suggested that when the compression pressure increase, the particle deform plastically and the tablet become harder and less friable (Riippia et al., 1998: 340). Minimum friability was obtained at the compression force of 4.5 tons and the friability values were under 1% ,except for Dowex® 1x2-200, which can be regarded as desirable (Riippia et al., 1998: 340).

It is commonly known that the disintegration time of tablets increases with an increase of compression pressure (Riippia et al., 1998: 340, Sunada, and Bi, 2002: 195, Khan, and Rhodes, 1975: 166). The disintegration time of tablet containing SSG and Amberlite® IRP64 increased with an increase in compression pressure. However, tablet containing Dowex® 1x2-200 exhibited the opposite results (Table 11).

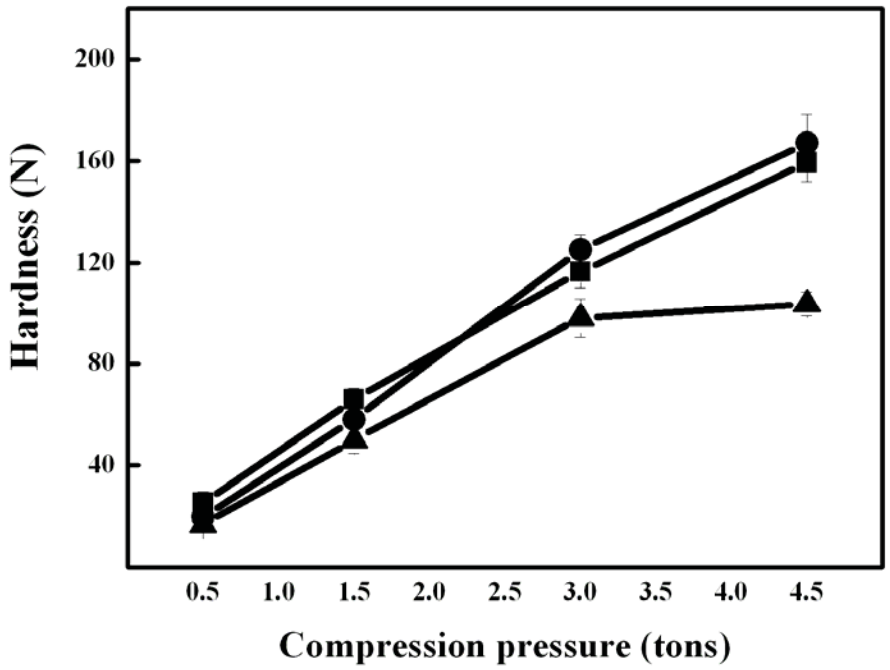

Fig. 23 Hardness of tablet containing SSG (■), Amberlite® IRP64 (●) and Dowex® 1x2-200 (▲) compressed with various compression pressures.

The results obtained from tablet containing SSG and Amberlite® IRP64 could be explained that an increase in compression pressure contributed to a decrease in tablet porosity (Peppas and Colombo, 1989: 249, Khan, and Rhodes, 1975: 166). Consequently, water penetration into tablets would slow down resulting in slower disintegration time. These results were in accordance with the data reported by Sunada and Bi and Riippia et al. With the increase in compression pressure from 100 to 2000 N, the tensile strength and disintegration time of lactose tablet increased (Sunada, and Bi, 2002: 195). Additionally, the disintegration time of tablet containing Amberlite® IRP88 used as disintegrant increased with an increase of compression pressure (Riippia et al., 1998: 340). On the contrary, the disintegration time of tablet containing Dowex® 1x2-200 decreases corresponding to an increase in compression pressure.

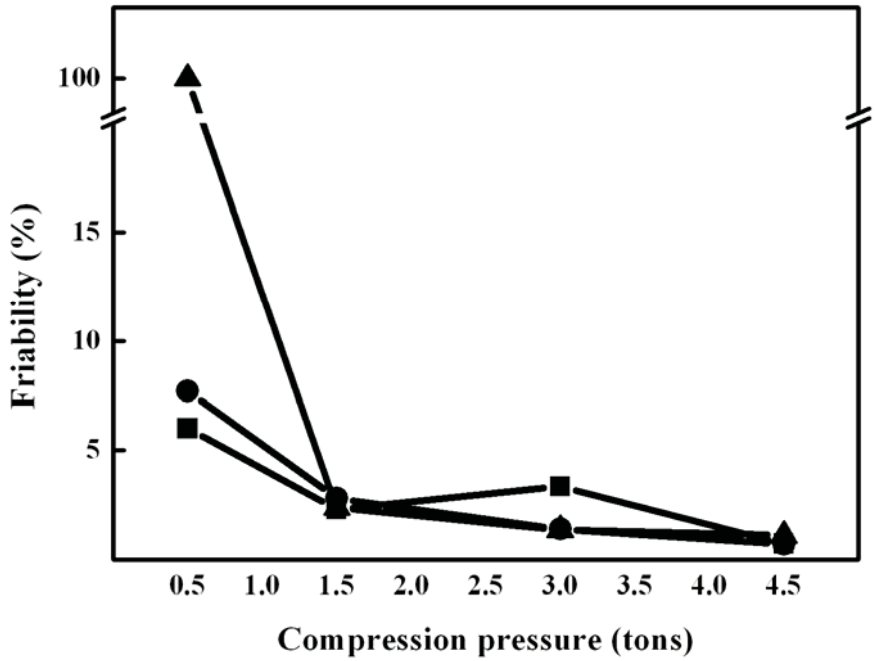

Fig. 24 Friability of tablet containing SSG (■), Amberlite® IRP64 (●) and Dowex® 1x2-200 (▲) compressed with various compression pressures.

These results could be explained that compression pressure and particle size are interrelated effect on the number of contact points between the powder particles. The higher compression pressure and smaller particle size, the more number of contact points should be obtained, resulting in the longer disintegration time (Sunada, and Bi, 2002: 195, Akkaramongkolporn et al., 2008: 901).

From literature review, both SSG and Amberlite® IRP64 belong to an irregular shape as shown in Fig. 25 and Fig. 26, respectively. Furthermore, the data obtained from this study demonstrated that both of them have a small size (approximately 51.85 ± 1.88 μm and 71.37 ± 0.73, respectively). Therefore, a more number of contact points in tablets containing SSG and Amberlite® IRP64 should be obtained. Accordingly, the disintegration time of tablets containing SSG and Amberlite® IRP64 increased corresponding to an increase in compression pressure (Sunada, and Bi, 2002: 195).

Table 11 Physical properties of DCP tablet containing 5% w/w of IER with various compression pressures (tons)

Resin	Compression pressure (Tons)	Hardness (N)	Thickness (mm)	Diameter (mm)	Disintegration time (sec)	Friability (%)
DCP without resin	0.5	18.30 ± 3.50	3.80 ± 0.02	9.60 ± 0.01	> 30 min	9.2888
	1.5	50.00 ± 6.24	3.73 ± 0.48	9.58 ± 0.01	> 30 min	2.8947
	3.0	104.80 ± 4.34	3.24 ± 0.02	9.60 ± 0.02	> 30 min	1.3513
	4.5	271.85 ± 17.58	3.23 ± 0.04	9.59 ± 0.02	> 30 min	0.7698
SSG	0.5	25.20 ± 4.39	3.86 ± 0.14	9.58 ± 0.02	12.00 ± 0.85	6.0125
	1.5	66.00 ± 4.24	3.60 ± 0.02	9.59 ± 0.02	19.50 ± 0.52	2.2970
	3.0	116.50 ± 6.40	3.47 ± 0.04	9.56 ± 0.02	32.33 ± 1.50	3.3486
	4.5	159.50 ± 7.69	3.25 ± 0.02	9.60 ± 0.01	60.00 ± 11.34	0.7328
Amberlite® IRP64	0.5	19.70 ± 2.67	4.22 ± 0.05	9.61 ± 0.01	23.17 ± 2.72	7.704
	1.5	58.00 ± 5.35	3.81 ± 0.07	9.62 ± 0.02	19.83 ± 2.21	2.8034
	3.0	125.00 ± 6.06	3.54 ± 0.02	9.63 ± 0.01	27.17 ± 5.24	1.4032
	4.5	167.10 ± 11.30	3.47 ± 0.03	9.60 ± 0.01	52.08 ± 6.27	0.7062
Dowex® 1x2-200	0.5	16.70 ± 1.57	4.11 ± 0.02	9.59 ± 0.01	26.83 ± 1.11	100.00
	1.5	50.00 ± 5.44	3.79 ± 0.02	9.58 ± 0.01	8.50 ± 0.52	2.3719
	3.0	98.00 ± 7.76	3.64 ± 0.04	9.32 ± 0.01	7.50 ± 0.52	1.3627
	4.5	103.60 ± 4.84	3.69 ± 0.04	9.58 ± 0.01	6.00 ± 0.00	1.1076

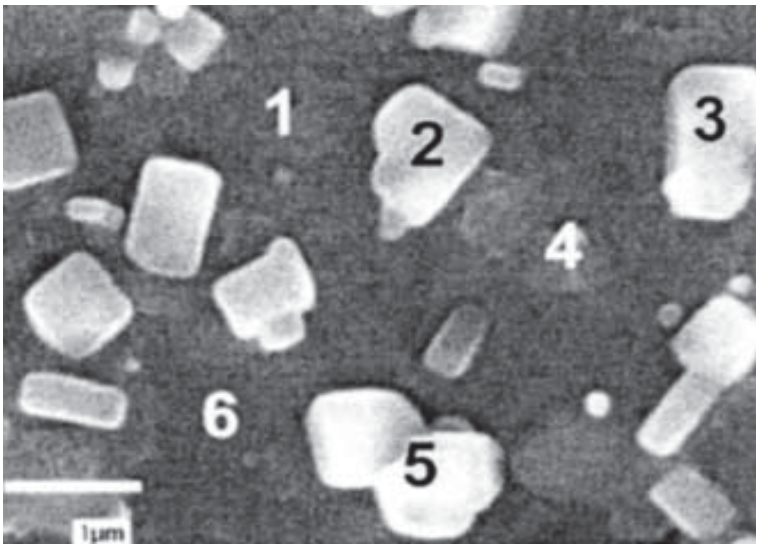

Fig. 25 SSG (Explotab®) image obtained by SEM.

* Edge, S. et al. (2002). "Chemical characterisation of sodium starch glycolate particles." **Int J Pharm** 240 (March 18): 70

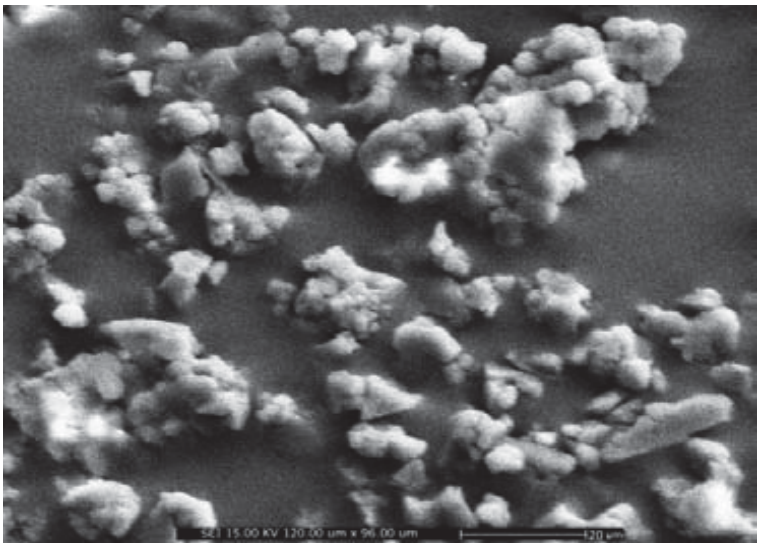

Fig. 26 Amberlite® IRP64 image obtained by SEM.

*Akkaramongkolporn, Prasert, Tanasait Ngawhirunpat, and Praneet Opanasopit. (2012). "Evaluating polarcrilex resin as direct compression filler for theophylline tablets." **Int J Pharm** 4, 1: 478-481.

Fig. 27 Dowex® 1x2-200 image obtained by microscope.

Dowex® 1x2-200 is spherical with the larger particle size (189.60 ± 25.16 μm in diameter) (Fig. 27). Therefore, there is a few number of contact points in tablets containing Dowex® 1x2-200. Moreover, Dowex® 1x2-200 might have a poor compressibility. Consequently, the number of porosity was decreased. It could be confirmed by the results obtained from the studies of the effect of compression pressure and the effect of concentration of disintegrant. The compression pressure increased, the hardness of tablets containing Dowex® 1x2-200 reached a plateau. Moreover, the hardness reduced dramatically with an increase in the amount of Dowex® 1x2-200 (Khan, and Rhodes, 1975: 167).

It should be noted that compression pressure has a slight effect on the disintegration time of tablets containing Dowex® 1x2-200. On the other hand, compression pressure has a great effect on the disintegration time of tablets containing SSG and Amberlite® IRP64. The results were in agreement with the results obtained from the studies of Khan, and Rhodes (Khan, and Rhodes, 1975: 167). In addition, the compression pressure has an important effect on hardness and friability of tablet containing SSG, Amberlite® IRP64 and Dowex® 1x2-200. Furthermore, these results could be confirmed by the results obtained from the tablets containing 2% w/w of IER (Fig. 28 – Fig. 30).

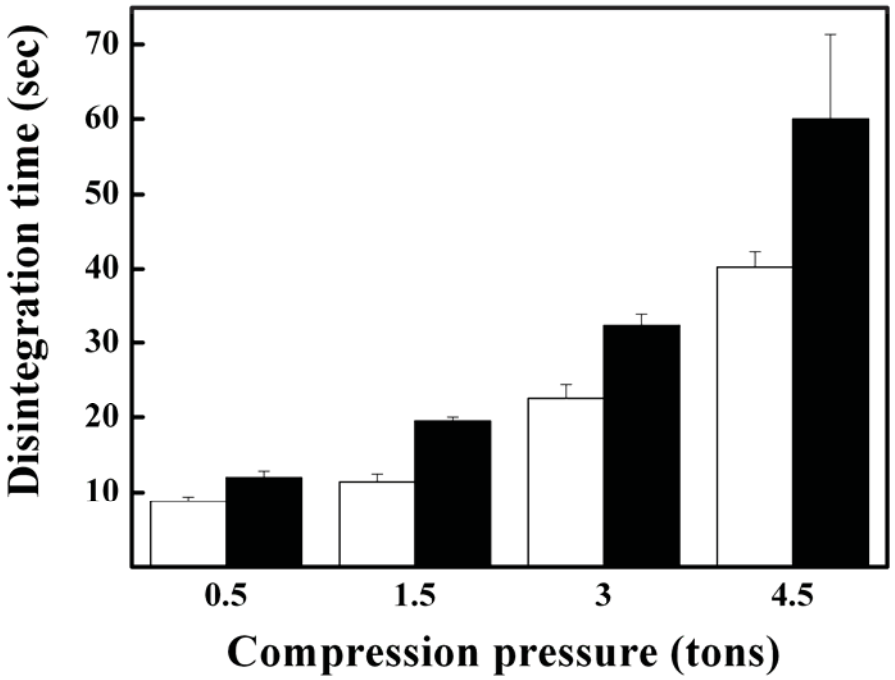

Fig. 28 Disintegration time of tablet containing 2% (white bar) and 5% w/w of SSG (black bar) compressed with various compression pressures.

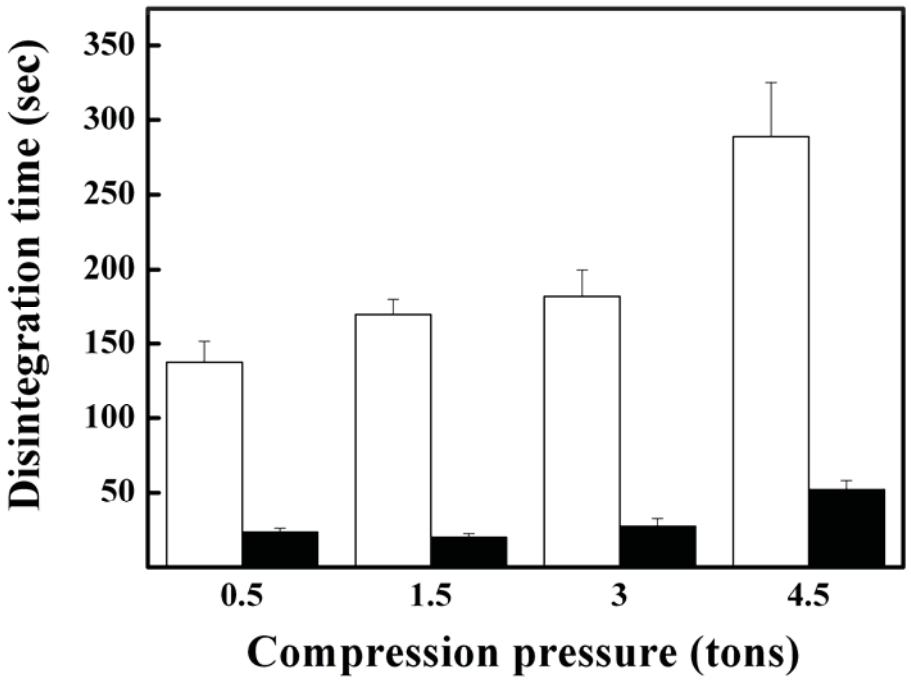

Fig. 29 Disintegration time of tablet containing 2% (white bar) and 5% w/w of Amberlite® IRP64 (black bar) compressed with various compression pressures.

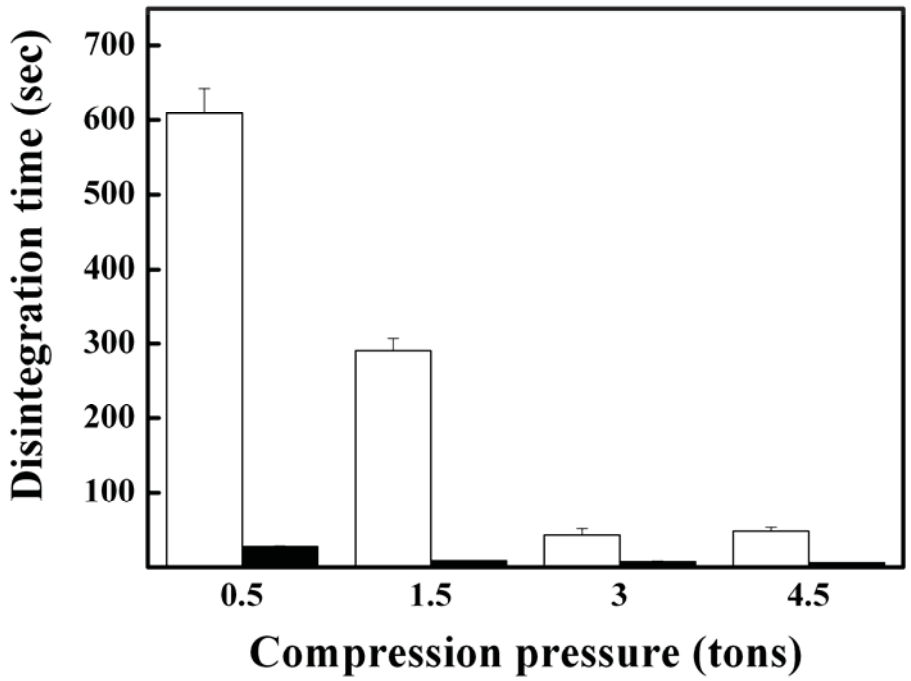

Fig. 30 Disintegration time of tablet containing 2% (white bar) and 5% w/w of Dowex® 1x2-200 (black bar) compressed with various compression pressures.

3.3 Type of diluents

The mixtures of each IER and either dibasic calcium phosphate (DCP), spray dried lactose (SDL), microcrystalline cellulose (MCC) or spray dried rice starch (SDRS) were compressed. The physical properties of these tablets were then evaluated. Table 12 shows the physical properties and disintegration time of these tablets.

The hardness of tablets containing MCC could not be evaluated by equipment used in this study because the hardness was too high. However, these results can be demonstrated that the hardness of tablets containing MCC was much higher than that of using DCP, SDL and SDRS. These results are in agreement with Thaned et al. The hardness of dextromethorphan resinate tablets using MCC was higher than that of using SDRS and DCP (Thaned et al. 2005: 194).

Table 12 Physical properties of tablet containing 5% w/w of IER with various types of diluents

Diluent	Resin type	Hardness (N)	Thickness (mm)	Diameter (mm)	Disintegration time (sec)	Friability (%)
DCP	Without resin	276.80 ± 13.51	3.21 ± 0.03	9.56 ± 0.02	> 30 min	0.7698
	SSG	159.50 ± 7.69	3.34 ± 0.05	9.60 ± 0.02	60.00 ± 11.34	0.7328
	Amberlite® IRP64	167.10 ± 11.30	3.55 ± 0.04	9.59 ± 0.02	64.08 ± 19.76	0.7062
	Amberlite® IRP69	75.90 ± 4.12	3.48 ± 0.10	9.63 ± 0.02	15.42 ± 5.85	2.3679
	Dowex® 1x2-200	103.50 ± 4.60	3.70 ± 0.04	9.56 ± 0.01	15.42 ± 2.97	1.1076
SDL	Without resin	265.00 ± 61.47	4.80 ± 0.03	9.62 ± 0.00	561.67 ± 119.38	100.00
	SSG	390.00 ± 32.32	4.76 ± 0.01	9.60 ± 0.01	504.92 ± 113.93	0.2231
	Amberlite® IRP64	369.00 ± 14.85	4.84 ± 0.01	9.61 ± 0.01	1004.58 ± 101.90	0.2923
	Amberlite® IRP69	200.70 ± 11.81	5.02 ± 0.03	9.61 ± 0.01	8.92 ± 0.79	0.9552
	Dowex® 1x2-200	262.20 ± 11.27	5.01 ± 0.03	9.60 ± 0.01	24.58 ± 4.44	0.6517
MCC	Without resin	N/A	4.99 ± 0.02	9.57 ± 0.00	> 30 min	0.0503
	SSG	N/A	4.96 ± 0.02	9.57 ± 0.01	196.42 ± 7.88	0.0000
	Amberlite® IRP64	N/A	5.06 ± 0.02	9.59 ± 0.01	2030.00 ± 368.75	0.0000
	Amberlite® IRP69	N/A	5.02 ± 0.01	9.59 ± 0.00	123.67 ± 22.57	0.0000
	Dowex® 1x2-200	N/A	5.06 ± 0.01	9.57 ± 0.01	161.92 ± 16.63	0.0000
SDRS	Without resin	145.00 ± 21.75	5.63 ± 0.04	9.73 ± 0.03	184.17 ± 26.01	100.00
	SSG	271.50 ± 24.14	5.42 ± 0.02	9.56 ± 0.02	251.00 ± 16.12	0.0520
	Amberlite® IRP64	311.50 ± 27.56	5.47 ± 0.02	9.56 ± 0.01	218.17 ± 13.66	0.0702
	Amberlite® IRP69	182.00 ± 33.13	5.54 ± 0.04	9.65 ± 0.03	170.00 ± 30.75	0.1707
	Dowex® 1x2-200	173.90 ± 37.07	5.67 ± 0.07	9.67 ± 0.04	143.67 ± 27.82	0.3127

Types of diluents in the tablet also have an effect on the disintegration time. In case of tablets containing Amberlite® IRP69 as disintegrant, the disintegration time of DCP (15.42 ± 5.85) and SDL (8.92 ± 0.79) tablets were shorter than that of MCC (123.67 ± 22.57) and SDRS (170.00 ± 30.75) tablets. The similar results were found in tablets containing Dowex® 1x2-200. The disintegration time of DCP (15.42 ± 2.97) and SDL (24.58 ± 4.44) tablets were shorter than that of MCC (161.92 ± 16.63) and SDRS (143.67 ± 27.82) tablets.

These results could be explained that a longer disintegration time of SDRS tablet could result from a gel-forming matrix upon contact with water (Thaned et al. 2005: 195). For MCC tablets, although they provided the highest hardness, the disintegration time of them were not different from that of SDRS tablets. This could be due to the disintegration properties of MCC (Thaned et al. 2005: 195). However, the results obtained from the tablet containing Amberlite® IRP64 could not be clearly explained. Lactose is water soluble diluent without swelling properties therefore it can rapidly dissolve upon contact with water, resulting in the lower disintegration time compared to MCC and SDRS tablets. It should be noted that the most important factor for disintegration of lactose tablet is tablet porosity, which is occurred after dissolving (Sunada, and Bi, 2002: 195, Zhao and Augsburger, 2005: E121).

3. Tablet formulations containing selected IER as the disintegrant

3.1 Physical properties of tablet formulations

Dextromethorphan hydrobromide **(**DMP) and diclofenac sodium (DCN) were used as a freely and a poorly water soluble model drug, respectively.

The selection of type of diluents and other excipients including disintegrant as well as condition during compression process should be carefully addressed. Physical properties and the performance of tablet formulation including release profile might be changed by different type of diluents (Vaidya, and Avachat, 2011: 375). From the previous results (Table 12), among diluents tested in this study (DCP, MCC, SDL and SDRS), DCP was selected to use as diluents in both of the

drug formulations. This is due to DCP tablets possesses good physical properties, i.e. short disintegration time and low friability. Nonetheless the disintegration time of SDL tablets was shorter than that of DCP. SDL has a high hygroscopicity which might effect on the stability of tablets and also making it complicated and difficult to storage. In case of MCC, although the tablets have a low friability, they disintegrate slowly regarding an unsuitable hardness.

Amberlite® IRP64 (weak cation exchange resin) and Dowex® 1x2-200 (strong anion exchange resin) were selected to use as tablet disintegrant. Amberlite® IRP64 has a higher compressibility compared to Amberlite® IRP69 and Dowex® 1x2-200 so that acts as a good tablet disintegrant providing the shortest disintegration time with appropriate friability. Besides, the amount of resin used in formulation must be thoroughly considered.

The previous results demonstrated that the higher amount of disintegrant, the shorter disintregration time was obtained. However, the more amount of disintegrant caused the lower hardness and higher friability (Table 10). Tablets formulations with 2.5% w/w of disintegrant, i.e. SSG, Amberlite® IRP69 and Dowex® 1x2-200, can disintegrate slowly while the tablets containing Amberlite® IRP64 cannot disintegrate within 30 min. The disintegration time of tablets containing SSG, Amberlite® IRP69 and Dowex® 1x2-200 were 101.00 ± 11.21, 28.58 ± 9.12 and 146.92 ± 11.75, respectively. When using 5% w/w of disintegrant, the tablets can disintegrate more rapidly. The disintegration time of tablets containing SSG, Amberlite® IRP64, Amberlite® IRP69 and Dowex® 1x2-200 were 60.00 ± 11.34, 64.08 ± 19.76, 15.42 ± 5.85 and 15.42 ± 2.97, respectively. Whereas the amount of disintegrant was increased from 5.0 to 10% w/w, the disintegration time of all formulation were not different. Therefore, the optimum amount of disintegrant was fixed at 5% w/w.

On the contrary, the higher compression pressure, the higher hardness and lower friability were found (Table 11). Furthermore, the disintegration time increased dramatically with an increase of compression pressure, except for Dowex® 1x2-200. All tablets exhibited the suitable disintegration time. Nevertheless, the tablets

compressed by the pressure below 4.5 tons demonstrated the undesirable friability. As a result, the tablet formulations with either DMP or DCN were compressed at 4.5 tons which is the highest compression pressure.

3.2 Dextromethorphan hydrobromide tablets

The physical properties and disintegration time of DMP tablets are shown in Table 13. Although DMP was used only 3% w/w tablets, hardness of tablets decreased obviously when compared to DCP tablets without drug. The hardness reduced from 167.10 ± 11.30 to 115.60 ± 7.31 for tablets containing Amberlite® IRP64 and from 103.50 ± 4.60 to 79.70 ± 10.10 for tablets containing Dowex® 1x2-200. These results might be due to drug in the formulations may change the compressibility of diluents used in this study. Moreover, DMP caused the increase in friability of tablets according the lower hardness.

In addition, the thickness of DMP tablet containing Dowex® 1x2-200 was higher than that of SSG and Amberlite® IRP64. This could be due to the low compressibility of Dowex® 1x2-200. Additionally, Dowex® 1x2-200 reduced hardness and increased friability dramatically resulting in poor stability. However, the positive effect of Dowex® 1x2-200 on disintegration time is the reduction of inter-particulate bond of tablets resulting in the rapid disintegration.

From the results, the increasing order of the disintegration was tablet containing Amberlite® IRP64 (25.92 ± 1.73), tablet containing SSG (16.25 ± 0.45) and tablet containing Dowex® 1x2-200 (8.00 ± 1.04). These results could be due to the hardness of tablet. The softer tablets which were tablets containing Dowex® 1x2-200 have the larger pores and greater tortuosity. These made the water penetration rapidly, leading to tablets disintegrate fast.

Table 13 Physical properties and disintegration time of DMP tablets

Disintegrant	Hardness (N)	Thickness (mm)	Diameter (mm)	Disintegration time (sec)	Friability (%)
SSG	144.70 ± 14.28	3.46 ± 0.02	9.62 ± 0.03	16.25 ± 0.45	1.5785
Amberlite® IRP64	115.60 ± 7.31	3.57 ± 0.02	9.63 ± 0.04	25.92 ± 1.73	1.9331
Dowex® 1x2-200	79.70 ± 10.10	3.73 ± 0.02	9.60 ± 0.01	8.00 ± 1.04	3.1331

From Fig. 31, the results demonstrated that the rapid released rate of DMP was found in all formulations. Moreover, the fastest release rate was found in tablet containing Dowex® 1x2-200. Additionally, the extent of drug released was similar to that of tablets containing SSG but the rate was faster. These results could be explained that a greater disintegration rate allowed the drug to be released faster due to an increase in surface area exposed to dissolution medium (Akkaramongkolporn et al., 2010: 1111). Whereas, tablets containing Amberlite® IRP64 were harder, causing the slower released rate (Akkaramongkolporn et al., 2010: 1112).

In addition, the released amount of DMP from tablets containing Amberlite® IRP64 was obviously lower than others. In dissolution medium (pH 5.8 PBS), the released DMP would protonize to a positive form (A dissociation constant value (pKa) of DMP is 8.3) (Milenkova et al., 2003: 34). Therefore, this could be indicated that Amberlite® IRP64, which was a cationic exchange resin containing carboxylic acid ion exchangeable group, was able to bind the released DMP in the dissolution medium via exchange process as follows. (Akkaramongkolporn et al., 2010: 1112).

$$\text{Resin-COO}^- \text{H}^+ + \text{DMP}^+ \rightleftharpoons \text{Resin-COO}^- \text{DMP}^+ + \text{H}^+$$

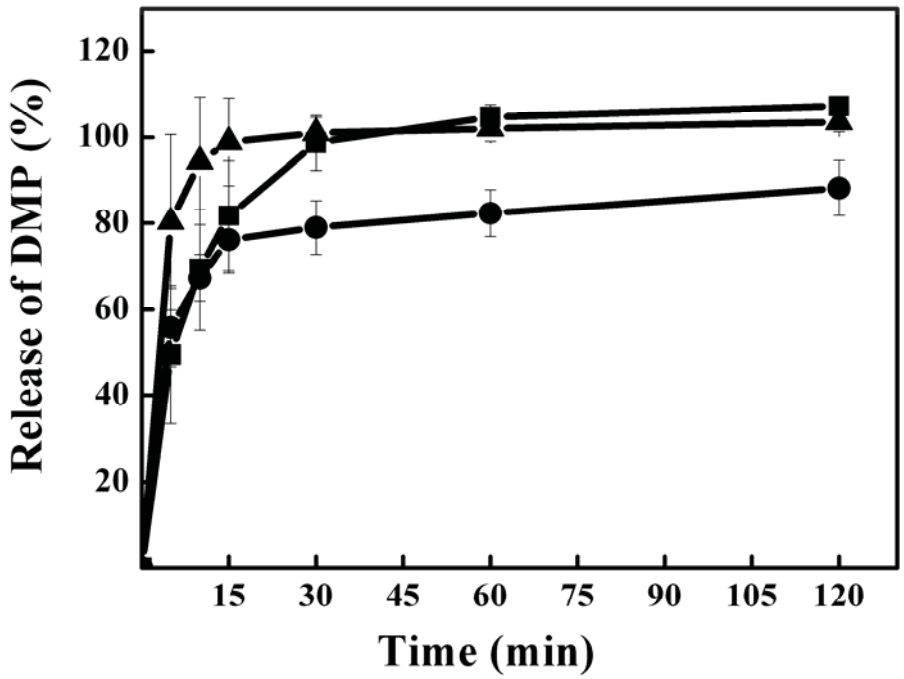

Fig. 31 Cumulative release of DMP from tablets containing various types of disintegrant; SSG (■), Amberlite® IRP64 (●) and Dowex® 1x2-200 (▲).

3.3 Diclofenac sodium tablets

The physical properties and disintegration time of DCN tablets are shown in Table 14. Likewise, the physical properties of DMP tablets which is shown in Table 13, the hardness of DCN tablets was decreased depending on type of disintegrant and the thickness can be ordered as followed; tablets containing SSG > Amberlite® IRP64 > Dowex® 1x2-200.

Although DCN was used only 5% w/w tablets, hardness of tablets decreased obviously when compared to DCP tablets without drug. Namely, the hardness reduced from 167.10 ± 11.30 to 98.20 ± 9.99 for tablets containing Amberlite® IRP64 and from 103.50 ± 4.60 to 72.40 ± 5.32 for tablets containing Dowex® 1x2-200. These results might be due to drug in the formulations may change

the compressibility of diluents used in this study. Moreover, DCN caused the increase in friability of tablets resulting from the lower hardness.

As with DCN, the hardness and disintegration times of tablets containing the three resins were ranked in agreement with DMP. However, from Fig. 32, it demonstrated that the extent of drug released from tablets containing Dowex® 1x2-200 was considerably lower than that of tablets containing SSG and Amberlite® IRP64. In dissolution medium (pH 6.8 PBS), the released DCN would dissociate to a negative form (A dissociation constant value (pKa) of DCN is 4.0) (Diclofenac Sodium (diclofenac sodium) Tablet, Delayed Release [Sandoz Inc.]. Accessed 11 May 2012. Available from http://dailymed.nlm.nih.gov/dailymed/archives/fdaDrugInfo.cfm?archiveid=3007). Therefore, this could be indicated that Dowex® 1x2-200, which was an anionic exchange resin containing quaternary ammonium ion exchangeable group, was able to bind the released DCN in the dissolution medium via exchange process as follows. (Akkaramongkolporn et al., 2010: 1112).

$$\text{Resin-}(N(CH_3)_3^+)\,Cl^- + DCN^- \rightleftharpoons \text{Resin-}(N(CH_3)_3^+)DCN^- + Cl^-$$

In addition, the release profile between DMP and DCN were highly different. As expect, the cumulative release and rate of freely water soluble drug, DMP, was higher than that of poorly water soluble drug, DCN. This could be indicated that the drug release was also depended on the solubility of formulated drug.

Table 14 Physical properties and disintegration time of DCN tablets

Disintegrant	Hardness (N)	Thickness (mm)	Diameter (mm)	Disintegration time (sec)	Friability (%)
SSG	122.90 ± 2.02	3.15 ± 0.01	9.57 ± 0.02	15.50 ± 0.52	1.4668
Amberlite® IRP64	98.20 ± 9.99	3.24 ± 0.04	9.50 ± 0.02	26.00 ± 1.04	1.8053
Dowex® 1x2-200	72.40 ± 5.32	3.39 ± 0.02	9.57 ± 0.03	10.00 ± 1.60	2.9945

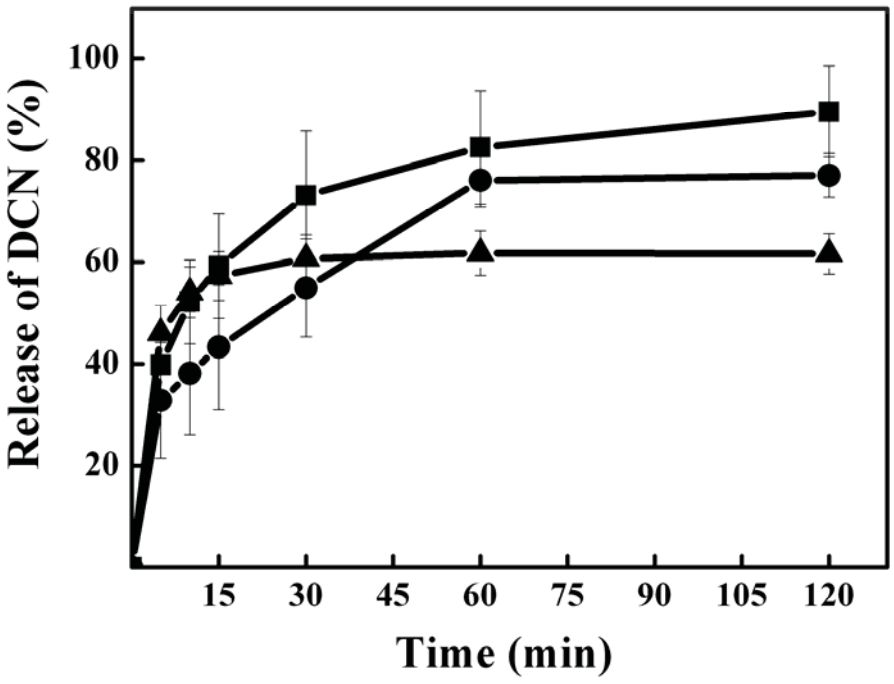

Fig. 32 Cumulative released of DCN from tablets containing various types of disintegrant; SSG (■), Amberlite® IRP64 (●) and Dowex® 1x2-200 (▲).

CHAPTER V

CONCLUSIONS

Solid pharmaceutical dosage forms are the most popular dosage forms especially, tablet formulation. Good tablet formulation should provide appropriate hardness with low friability, rapid disintegration and hence dissolution of drug. The purpose of this study was to investigate various ion exchange resins (IER) as disintegrant for tablet formulation. Sodium starch glycolate (SSG), which is commonly used as superdisintegrant in fast dissolving tablets, was chosen as positive control. In this study, all tablets with and without model drugs were prepared by direct compression, and then their physical properties, i.e. hardness, thickness, diameter and friability including disintegration time of tablets were evaluated. The results of this study could be concluded as follow:

1. Characteristics of various IER used as tablet disintegrant

1.1 Swelling power

Ten IER, Amberlite® IRP64, Amberlite® IRP69, Dowex® 88, Dowex® retardion, Dowex® 50Wx2-200, Dowex® 50Wx4-200, Dowex® 50Wx8-200, Dowex® 1x2-200, Dowex® 1x4-200 and Dowex® 1x8-200 were investigated for use as tablet disintegrant. All resins exhibited water uptake ability by increasing weight swelling or volume swelling or both. These results could be indicated that the volume swelling represents an increase in particle size whereas the weight swelling represents the amount of water which is absorbed by the resin without a need of change in volume or size (wicking or capillary property of resin). Therefore, the disintegrating effect of the resins might be governed by either or couple mechanisms of their swelling and wicking (capillary) properties.

1.2 Particle size

The particle size of Amberlite® IRP64, Amberlite® IRP69 and Dowex® 88 were less than 80 μm whereas the particle size of the others were higher than 150 μm. The smallest particle was found in Dowex® 88 (44.06 ± 1.92 μm) whereas Dowex® retardion was the largest (399.00 ± 12.17μm).

2. Screening study of DCP tablets using various IER as disintegrant

Thickness of tablet containing various types of IER was significantly different, depending on compressibility of those resins. IER with good compressibility contributed the tablets with lower thickness. The disintegration time of each tablet was mostly different due to the efficacy of IER as tablet disintegrant. The disintegration time were ordered as followed; Dowex® 88 (115.90 ± 13.78 sec) > Amberlite® IRP64 (64.08 ± 10.76 sec) > SSG (60.00 ± 11.34 sec) > Amberlite® IRP69 (29.08 ± 7.05 sec) > Dowex® 50Wx2-200 (27.92 ± 3.29 sec) > Dowex® 1x4-200 (25.00 ± 5.22 sec) > Dowex® 1x2-200 (15.42 ± 2.97 sec) > Dowex® 50Wx4-200 (8.58 ± 2.50 sec). As a result, Amberlite® IRP64, Amberlite® IRP69 and Dowex® 1x2-200 were chosen for testing in the next experiments because these resins contributed to the tablets which possessed the good performances such as shorter disintegration time, suitable hardness and friability.

3. Factors affecting the properties of tablets using resin as disintegrant

3.1 Amount of IER

Amberlite® IRP64, Amberlite® IRP69 and Dowex® 1x2-200 with various amounts (2.5%, 5.0%, 7.5% and 10% w/w) were evaluated. An increase in the amount of disintegrant caused thickness increased and hardness decreased. This might facilitate the tablet disintegration. However, the excess amount of resin might cause poor stability of tablets due to higher friability.

3.2 Compression pressure

5% w/w of IER (Amberlite® IRP64 and Dowex® 1x2-200) was compressed at various pressures (0.5, 1.5, 3.0, 4.5 tons). The lower thickness was found in tablets compressed by the higher compression pressure. In addition, an increase in hardness resulted from an increase in compression pressure. This contributed to the longer disintegration time. Nonetheless, the higher compression pressure had no an influence on the tablets containing Dowex® 1x2-200.

3.3 Type of diluents

Four types of diluents (dibasic calcium phosphate (DCP), spray dried lactose (SDL), microcrystalline cellulose (MCC) and spray dried rice starch (SDRS) were selected. DCP provided the lowest thickness, whereas SDRS gave the highest thickness. Additionally, MCC provided the highest hardness, whereas the hardness of SDRS and SDL tablets were higher than that of DCP tablet. In addition, type of diluents also had an effect on the disintegrant properties of these resins. The disintegration time of these tablets differed from each other depending on type of resin.

4. Tablet formulations containing selected IER as disintegrant

Physical properties of tablets containing dextromethorphan hydrobromide (DMP) and diclofenac sodium (DCN) were evaluated in order to study the possibility of resin disintegrant (Amberlite® IRP64 and Dowex® 1x2-200) in such formulations. Hardness of DMP tablets can be ranked as follow; SSG > Amberlite® IRP64 > Dowex® 1x2-200 and the disintegration time can be ranked as followed; Amberlite® IRP64 > SSG > Dowex® 1x2-200. From the results, the hardness might not have a proportionate effect on disintegration time. SSG exhibited the shorter disintegration time compared to Amberlite® IRP64. As with DCN, the hardness and disintegration times of tablets containing three disintegrants were ranked in agreement with DMP. In addition, both drugs released rapidly from all formulations and the cumulative drug

released of DMP and DCN was approximately 80%-100% and 60%-80%, respectively. The results revealed that the type of resin and solubility of drug had an influence on the drug release from the tablets containing those resins. Finally, it could be indicated that IER, if appropriately selected, could be a new disintegrant alternatively usable in tablet formulation.

The results demonstrated that all resins exhibited water uptake ability by increasing weight swelling or volume swelling or both. Nevertheless, the reduction of swelling capacity was found with an increase of degree of cross-linking. Nevertheless, the data obtained from different method were not equal. These results could be indicated that the volume swelling represents an increase in particle size whereas the weight swelling represents the amount of water which is absorbed by the resin without a change in volume or size (wicking or capillary property of resin). As a results, it could be suggested that the swelling power of each resin was obviously different, which resulted from the differences in several characteristics among the resins, i.e. degree of cross-linking, resin and matrix type, ion exchangeable group, particle size, shape, moisture content etc. Moreover, the disintegrating effect of the resins might be governed by couple mechanisms of their swelling and wicking (capillary) properties.

Among the resins, Amberlite® IRP64 and Dowex® 1x2-200 provided the tablets with sufficient hardness and suitable friability. The disintegration time of tablets containing these resins were approximately 60 and 30 sec, respectively, which were similar to those of SSG. These could be suggested that both of them had the better compressibility and efficacy as tablet disintegrant compared to the other.

Factors affecting the efficacy of Amberlite® IRP64 and Dowex® 1x2-200 used as disintegrant were amount of resin, compression pressure and type of diluents. The results showed that the hardness decreased with an increase of the amount of disintegrant. This might facilitate the tablet disintegration. However, the excess amount of resin might cause poor stability of tablets due to higher friability. In addition, an increase in hardness resulted from an increase in compression pressure. This contributed to the longer disintegration time. Nonetheless, the higher

compression pressure had no an influence on the tablets containing Dowex® 1x2-200. Type of diluents also had an effect on the disintegrant properties of these resins. MCC provided the highest hardness, whereas the hardness of SDRS and SDL tablets were higher than that of SSG tablet. However, the disintegration time of these tablets differed from each other depending on type of resin.

The release profiles of dextromethorphan hydrobromide (DMP), a freely water soluble model drug, and diclofenac sodium (DCN), a poorly water soluble model drug were evaluated. Both of drug released rapidly from all formulations and the cumulative drug released of DMP and DCN were approximately 80%-100% and 60%-80%, respectively. The results showed that the solubility of drug and type of resin influence on the drug released from the tablets containing those resins. Finally, it could be indicated that ion exchange resins could be a new disintegrant alternatively usable in tablet formulation.

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APPENDIX

APPENDIX A

Characterization

1. Characterization of IER

Table 15 Swelling power (% v/v) of Amberlite® IRP64

Time (h)	Swelling power (% v/v)				
	1	2	3	AVG	SD
0.017	29.41	29.41	37.50	32.11	4.67
0.083	29.41	29.41	37.50	32.11	4.67
0.167	29.41	29.41	37.50	32.11	4.67
0.5	29.41	29.41	37.50	32.11	4.67
1	29.41	29.41	37.50	32.11	4.67
2	41.18	47.06	43.75	44.00	2.95
8	47.06	58.82	43.75	49.88	7.92
24	52.94	70.59	50.00	57.84	11.14
48	52.94	64.71	50.00	55.88	7.78
96	52.94	64.71	50.00	55.88	7.78
168	82.35	88.24	87.50	86.03	3.21

Table 16 Swelling power (% v/v) of Amberlite® IRP69

Time (h)	Swelling power (% v/v)				
	1	2	3	AVG	SD
0.017	57.14	37.50	57.14	50.60	11.34
0.083	57.14	37.50	57.14	50.60	11.34
0.167	57.14	37.50	57.14	50.60	11.34
0.5	57.14	37.50	57.14	50.60	11.34
1	57.14	37.50	57.14	50.60	11.34
2	71.43	62.50	71.43	68.45	5.15
8	71.43	62.50	71.43	68.45	5.15
24	71.43	62.50	71.43	68.45	5.15
48	71.43	56.25	71.43	66.37	8.76
96	71.43	56.25	71.43	66.37	8.76
168	57.14	50.00	71.43	59.52	10.91

Table 17 Swelling power (% v/v) of Dowex® 88

Time (h)	Swelling power (% v/v)				
	1	2	3	AVG	SD
0.017	-3.57	-3.57	-3.57	-3.57	0.00
0.083	-3.57	-3.57	-3.57	-3.57	0.00
0.167	-3.57	-3.57	-3.57	-3.57	0.00
0.5	1.79	7.14	12.50	7.14	5.36
1	12.50	12.50	17.86	14.29	3.09
2	23.21	17.86	17.86	19.64	3.09
8	7.14	17.86	23.21	16.07	8.18
24	23.21	23.21	17.86	21.43	3.09
48	23.21	17.86	17.86	19.64	3.09
96	17.86	17.86	17.86	17.86	0.00
168	17.86	17.86	17.86	17.86	0.00

Table 18 Swelling power (% v/v) of Dowex® Retardion

Time (h)	Swelling power (% v/v)				
	1	2	3	AVG	SD
0.017	31.25	46.67	37.50	38.47	7.75
0.083	31.25	46.67	37.50	38.47	7.75
0.167	31.25	46.67	37.50	38.47	7.75
0.5	37.50	40.00	37.50	38.33	1.44
1	37.50	40.00	37.50	38.33	1.44
2	37.50	40.00	37.50	38.33	1.44
8	37.50	40.00	37.50	38.33	1.44
24	37.50	46.67	37.50	40.56	5.29
48	37.50	46.67	37.50	40.56	5.29
96	37.50	46.67	37.50	40.56	5.29
168	37.50	46.67	37.50	40.56	5.29

Table 19 Swelling power (% v/v) of Dowex® 50Wx2-200

Time (h)	Swelling power (% v/v)				
	1	2	3	AVG	SD
0.017	300.00	300.00	300.00	300.00	0.00
0.083	313.33	293.33	300.00	302.22	10.18
0.167	306.67	286.67	300.00	297.78	10.18
0.5	300.00	286.67	300.00	295.56	7.70
1	300.00	286.67	300.00	295.56	7.70
2	300.00	286.67	300.00	295.56	7.70
8	300.00	286.67	300.00	295.56	7.70
24	300.00	286.67	300.00	295.56	7.70
48	300.00	286.67	300.00	295.56	7.70
96	300.00	286.67	300.00	295.56	7.70
168	300.00	286.67	300.00	295.56	7.70

Table 20 Swelling power (% v/v) of Dowex® 50Wx4-200

Time (h)	Swelling power (% v/v)				
	1	2	3	Avg.	SD
0.017	142.86	142.86	142.86	142.86	0.00
0.083	142.86	142.86	142.86	142.86	0.00
0.167	142.86	142.86	142.86	142.86	0.00
0.5	142.86	142.86	142.86	142.86	0.00
1	142.86	142.86	142.86	142.86	0.00
2	142.86	142.86	142.86	142.86	0.00
8	142.86	142.86	142.86	142.86	0.00
24	142.86	142.86	142.86	142.86	0.00
48	142.86	142.86	142.86	142.86	0.00
96	142.86	142.86	142.86	142.86	0.00
168	142.86	142.86	142.86	142.86	0.00

Table 21 Swelling power (% v/v) of Dowex® 50Wx8-200

Time (h)	Swelling power (% v/v)				
	1	2	3	AVG	SD
0.017	83.33	67.44	94.59	81.79	13.64
0.083	83.33	67.44	94.59	81.79	13.64
0.167	83.33	67.44	94.59	81.79	13.64
0.5	83.33	67.44	94.59	81.79	13.64
1	83.33	67.44	94.59	81.79	13.64
2	83.33	74.42	94.59	84.12	10.11
8	83.33	67.44	94.59	81.79	13.64
24	83.33	67.44	94.59	81.79	13.64
48	91.67	74.42	94.59	86.89	10.90
96	91.67	74.42	94.59	86.89	10.90
168	91.67	74.42	94.59	86.89	10.90

Table 22 Swelling power (% v/v) of Dowex® 1x2-200

Time (h)	Swelling power (% v/v)				
	1	2	3	AVG	SD
0.017	54.84	59.68	41.18	51.90	9.59
0.083	64.52	64.52	54.41	61.15	5.83
0.167	64.52	64.52	54.41	61.15	5.83
0.5	64.52	64.52	54.41	61.15	5.83
1	64.52	64.52	54.41	61.15	5.83
2	64.52	64.52	54.41	61.15	5.83
8	64.52	64.52	54.41	61.15	5.83
24	64.52	64.52	54.41	61.15	5.83
48	64.52	64.52	54.41	61.15	5.83
96	64.52	64.52	54.41	61.15	5.83
168	64.52	64.52	54.41	61.15	5.83

Table 23 Swelling power (% v/v) of Dowex® 1x4-200

Time (h)	Swelling power (% v/v)				
	1	2	3	AVG	SD
0.017	24.14	17.86	21.05	21.02	3.14
0.083	24.14	23.21	26.32	24.56	1.59
0.167	24.14	28.57	26.32	26.34	2.22
0.5	24.14	28.57	26.32	26.34	2.22
1	24.14	28.57	26.32	26.34	2.22
2	24.14	28.57	26.32	26.34	2.22
8	24.14	28.57	26.32	26.34	2.22
24	24.14	28.57	26.32	26.34	2.22
48	24.14	28.57	26.32	26.34	2.22
96	24.14	28.57	26.32	26.34	2.22
168	24.14	28.57	26.32	26.34	2.22

Table 24 Swelling power (% v/v) of Dowex® 1x8-200

Time (h)	Swelling power (% v/v)				
	1	2	3	AVG	SD
0.017	11.11	20.00	20.00	17.04	5.13
0.083	16.67	22.22	22.22	20.37	3.21
0.167	16.67	22.22	22.22	20.37	3.21
0.5	16.67	22.22	22.22	20.37	3.21
1	16.67	22.22	22.22	20.37	3.21
2	16.67	22.22	22.22	20.37	3.21
8	16.67	22.22	22.22	20.37	3.21
24	16.67	22.22	22.22	20.37	3.21
48	16.67	22.22	22.22	20.37	3.21
96	16.67	22.22	22.22	20.37	3.21
168	16.67	22.22	22.22	20.37	3.21

Table 25 Swelling power (% w/w) of IER

Type of resin	Swelling power (% w/w)				
	1	2	3	AVG	SD
Sodium starch glycolate	2186	2182	2162	2176.90	13.05
Amberlite® IRP64	232	234	230	231.91	2.24
Amberlite® IRP69	170	171	161	167.18	5.36
Dowex® 88	156	146	174	158.87	14.16
Dowex® Retardion	127	123	131	127.04	3.99
Dowex® 50Wx2-200	341	269	341	316.76	41.60
Dowex® 50Wx4-200	159	161	175	165.13	8.92
Dowex® 50Wx8-200	139	152	137	142.73	8.30
Dowex® 1x2-200	175	247	192	204.56	37.36
Dowex® 1x4-200	159	168	169	165.37	5.78
Dowex® 1x8-200	136	144	151	143.48	7.62

Table 26 Particle size of Dowex® 50Wx2-200 (n=200)

No.	Size (μm)	No.	Size (μm)	No.	Size (μm)	No.	Size (μm)	No.	Size (μm)	No.	Size (μm)	No.	Size (μm)	No.	Size (μm)
1	179.07	**26**	220.79	**51**	239.73	**76**	262.66	**101**	280.51	**126**	296.69	**151**	310.88	**176**	325.59
2	179.57	**27**	221.84	**52**	240.19	**77**	263.24	**102**	280.74	**127**	296.75	**152**	311.46	**177**	327.74
3	180.96	**28**	223.12	**53**	240.32	**78**	263.43	**103**	281.12	**128**	297.28	**153**	311.49	**178**	329.33
4	184.06	**29**	223.85	**54**	241.13	**79**	264.76	**104**	281.15	**129**	298.37	**154**	311.88	**179**	329.33
5	194.85	**30**	223.89	**55**	241.53	**80**	265.64	**105**	281.88	**130**	299.87	**155**	311.88	**180**	329.50
6	197.08	**31**	226.08	**56**	241.82	**81**	266.14	**106**	282.39	**131**	300.16	**156**	312.28	**181**	331.37
7	198.24	**32**	229.22	**57**	242.07	**82**	266.88	**107**	282.48	**132**	300.24	**157**	312.81	**182**	332.93
8	198.47	**33**	229.35	**58**	244.14	**83**	267.05	**108**	282.62	**133**	300.66	**158**	313.11	**183**	332.96
9	199.49	**34**	229.47	**59**	245.27	**84**	267.70	**109**	283.09	**134**	300.81	**159**	314.00	**184**	333.78
10	201.40	**35**	230.75	**60**	245.96	**85**	270.32	**110**	286.02	**135**	302.26	**160**	314.11	**185**	334.27
11	202.22	**36**	230.88	**61**	248.23	**86**	270.64	**111**	286.88	**136**	302.85	**161**	314.70	**186**	334.29
12	204.95	**37**	231.42	**62**	248.47	**87**	271.79	**112**	287.45	**137**	303.42	**162**	315.01	**187**	334.32
13	205.21	**38**	231.60	**63**	249.95	**88**	273.96	**113**	287.45	**138**	303.93	**163**	315.38	**188**	334.51
14	206.17	**39**	233.54	**64**	252.04	**89**	273.99	**114**	289.02	**139**	304.81	**164**	315.71	**189**	336.51
15	206.43	**40**	233.93	**65**	252.25	**90**	274.25	**115**	290.73	**140**	305.05	**165**	315.86	**190**	340.30
16	207.66	**41**	233.98	**66**	253.30	**91**	274.69	**116**	291.80	**141**	305.22	**166**	316.23	**191**	340.90
17	207.68	**42**	235.30	**67**	254.16	**92**	274.78	**117**	293.26	**142**	305.46	**167**	316.78	**192**	341.44
18	208.19	**43**	235.47	**68**	255.96	**93**	275.23	**118**	294.35	**143**	306.29	**168**	317.90	**193**	343.09
19	208.30	**44**	237.50	**69**	256.80	**94**	275.52	**119**	294.57	**144**	307.23	**169**	319.54	**194**	343.34
20	214.94	**45**	237.76	**70**	257.36	**95**	276.32	**120**	295.32	**145**	307.42	**170**	320.52	**195**	344.24
21	215.92	**46**	238.18	**71**	257.42	**96**	277.11	**121**	295.94	**146**	308.38	**171**	320.52	**196**	348.59
22	216.69	**47**	238.94	**72**	258.20	**97**	277.28	**122**	295.95	**147**	309.12	**172**	320.80	**197**	349.49
23	217.74	**48**	239.31	**73**	258.38	**98**	277.46	**123**	296.27	**148**	309.67	**173**	324.10	**198**	357.57
24	218.70	**49**	239.57	**74**	261.28	**99**	278.97	**124**	296.52	**149**	310.09	**174**	324.23	**199**	359.44
25	220.72	**50**	239.59	**75**	261.54	**100**	279.23	**125**	296.62	**150**	310.49	**175**	324.98	**200**	359.68

Table 27 Particle size of Dowex® 50Wx4-200 (n=200)

No.	Size (µm)	No.	Size (µm)	No.	Size (µm)	No.	Size (µm)	No.	Size (µm)	No.	Size (µm)	No.	Size (µm)	No.	Size (µm)
1	194.96	**26**	217.44	**51**	234.41	**76**	250.01	**101**	270.77	**126**	289.33	**151**	306.74	**176**	320.79
2	195.55	**27**	219.58	**52**	234.74	**77**	250.54	**102**	272.74	**127**	289.38	**152**	307.06	**177**	321.50
3	198.04	**28**	220.55	**53**	235.25	**78**	251.15	**103**	272.91	**128**	289.56	**153**	307.06	**178**	324.17
4	201.91	**29**	221.26	**54**	236.17	**79**	251.48	**104**	274.96	**129**	290.30	**154**	307.09	**179**	325.68
5	202.53	**30**	222.94	**55**	237.16	**80**	251.83	**105**	275.11	**130**	290.48	**155**	308.07	**180**	326.31
6	203.28	**31**	223.31	**56**	238.01	**81**	252.14	**106**	275.27	**131**	290.55	**156**	308.56	**181**	326.44
7	203.50	**32**	224.67	**57**	238.01	**82**	253.21	**107**	277.14	**132**	290.58	**157**	308.61	**182**	326.75
8	204.56	**33**	224.79	**58**	238.17	**83**	255.16	**108**	277.91	**133**	290.94	**158**	309.55	**183**	326.75
9	205.78	**34**	226.18	**59**	238.24	**84**	255.94	**109**	278.08	**134**	293.86	**159**	309.72	**184**	328.68
10	206.94	**35**	226.68	**60**	239.43	**85**	256.08	**110**	278.98	**135**	294.39	**160**	310.05	**185**	330.51
11	207.07	**36**	226.98	**61**	240.16	**86**	256.08	**111**	279.78	**136**	294.45	**161**	310.27	**186**	331.87
12	207.79	**37**	227.71	**62**	240.83	**87**	259.14	**112**	280.39	**137**	294.77	**162**	310.60	**187**	332.30
13	208.30	**38**	227.80	**63**	240.89	**88**	259.14	**113**	281.24	**138**	295.78	**163**	310.69	**188**	332.86
14	209.27	**39**	227.88	**64**	242.58	**89**	260.68	**114**	281.94	**139**	295.98	**164**	310.92	**189**	333.28
15	211.67	**40**	228.24	**65**	242.84	**90**	261.06	**115**	283.40	**140**	296.33	**165**	313.50	**190**	335.15
16	211.72	**41**	229.20	**66**	242.89	**91**	261.27	**116**	283.95	**141**	296.85	**166**	314.14	**191**	335.44
17	212.08	**42**	229.28	**67**	242.99	**92**	261.47	**117**	284.62	**142**	297.52	**167**	314.14	**192**	335.81
18	213.03	**43**	229.58	**68**	243.32	**93**	261.60	**118**	285.04	**143**	298.15	**168**	315.09	**193**	336.89
19	213.71	**44**	231.46	**69**	243.61	**94**	261.85	**119**	285.87	**144**	299.35	**169**	316.42	**194**	337.14
20	215.32	**45**	231.51	**70**	244.37	**95**	262.17	**120**	285.98	**145**	300.36	**170**	317.20	**195**	338.00
21	215.84	**46**	231.67	**71**	245.65	**96**	263.35	**121**	286.10	**146**	304.14	**171**	317.74	**196**	340.11
22	215.88	**47**	232.46	**72**	246.67	**97**	263.78	**122**	286.44	**147**	304.21	**172**	317.91	**197**	342.94
23	216.15	**48**	232.71	**73**	249.07	**98**	264.14	**123**	287.10	**148**	304.32	**173**	318.09	**198**	350.23
24	216.58	**49**	233.24	**74**	249.85	**99**	265.51	**124**	287.12	**149**	306.50	**174**	319.47	**199**	351.25
25	216.72	**50**	233.65	**75**	249.94	**100**	267.42	**125**	287.83	**150**	306.57	**175**	320.23	**200**	355.26

Table 28 Particle size of Dowex® 50Wx8-200 (n=200)

No.	Size (μm)	No.	Size (μm)	No.	Size (μm)	No.	Size (μm)	No.	Size (μm)	No.	Size (μm)	No.	Size (μm)	No.	Size (μm)
1	211.65	**26**	250.38	**51**	267.02	**76**	285.85	**101**	296.24	**126**	306.74	**151**	326.03	**176**	346.16
2	212.23	**27**	251.02	**52**	267.51	**77**	285.85	**102**	296.34	**127**	306.77	**152**	328.97	**177**	349.05
3	213.62	**28**	252.74	**53**	267.79	**78**	285.98	**103**	296.40	**128**	307.76	**153**	329.68	**178**	350.81
4	213.70	**29**	252.90	**54**	268.54	**79**	286.69	**104**	296.88	**129**	308.71	**154**	329.76	**179**	352.27
5	217.44	**30**	253.70	**55**	268.70	**80**	286.71	**105**	297.25	**130**	308.96	**155**	331.08	**180**	354.07
6	218.42	**31**	253.70	**56**	269.00	**81**	286.77	**106**	297.51	**131**	309.65	**156**	331.31	**181**	357.18
7	220.98	**32**	254.12	**57**	269.99	**82**	286.86	**107**	298.20	**132**	309.72	**157**	332.09	**182**	357.30
8	222.09	**33**	254.40	**58**	270.19	**83**	287.16	**108**	298.30	**133**	310.38	**158**	332.23	**183**	359.40
9	222.38	**34**	255.14	**59**	270.48	**84**	287.38	**109**	298.74	**134**	310.76	**159**	332.38	**184**	361.75
10	225.12	**35**	255.24	**60**	272.45	**85**	287.45	**110**	298.87	**135**	311.94	**160**	333.42	**185**	364.02
11	226.08	**36**	255.95	**61**	274.64	**86**	288.24	**111**	299.95	**136**	312.34	**161**	334.91	**186**	364.33
12	230.50	**37**	259.18	**62**	275.61	**87**	288.80	**112**	300.16	**137**	313.03	**162**	335.90	**187**	365.67
13	230.74	**38**	259.86	**63**	276.06	**88**	288.85	**113**	301.02	**138**	313.13	**163**	336.05	**188**	366.71
14	231.23	**39**	260.13	**64**	276.49	**89**	289.89	**114**	301.09	**139**	313.78	**164**	337.07	**189**	368.51
15	236.02	**40**	260.14	**65**	276.64	**90**	290.14	**115**	302.27	**140**	314.04	**165**	337.48	**190**	372.80
16	236.57	**41**	261.28	**66**	277.76	**91**	290.76	**116**	302.32	**141**	314.64	**166**	338.12	**191**	373.54
17	236.86	**42**	261.45	**67**	278.05	**92**	291.66	**117**	302.48	**142**	314.71	**167**	338.22	**192**	375.89
18	241.54	**43**	262.23	**68**	279.59	**93**	292.00	**118**	303.19	**143**	315.50	**168**	340.42	**193**	377.37
19	241.68	**44**	263.00	**69**	281.23	**94**	292.58	**119**	303.40	**144**	319.33	**169**	341.10	**194**	379.39
20	242.35	**45**	263.50	**70**	281.38	**95**	292.88	**120**	303.96	**145**	319.87	**170**	341.28	**195**	380.42
21	243.94	**46**	264.01	**71**	281.44	**96**	294.19	**121**	304.17	**146**	323.63	**171**	342.83	**196**	387.14
22	246.23	**47**	264.28	**72**	282.19	**97**	294.55	**122**	304.96	**147**	324.38	**172**	343.43	**197**	389.06
23	246.49	**48**	264.43	**73**	282.56	**98**	295.10	**123**	306.04	**148**	324.40	**173**	343.97	**198**	391.62
24	246.95	**49**	265.28	**74**	283.97	**99**	295.98	**124**	306.36	**149**	325.70	**174**	345.09	**199**	420.10
25	248.66	**50**	266.09	**75**	284.99	**100**	295.98	**125**	306.61	**150**	325.91	**175**	345.51	**200**	423.86

Table 29 Particle size of Dowex® retardion (n=200)

No.	Size (μm)	No.	Size (μm)	No.	Size (μm)	No.	Size (μm)	No.	Size (μm)	No.	Size (μm)	No.	Size (μm)	No.	Size (μm)
1	354.16	**26**	384.54	**51**	391.96	**76**	397.26	**101**	401.35	**126**	403.47	**151**	408.23	**176**	412.48
2	362.38	**27**	385.96	**52**	392.11	**77**	397.37	**102**	401.59	**127**	403.70	**152**	408.26	**177**	412.66
3	364.02	**28**	386.01	**53**	392.14	**78**	397.55	**103**	401.64	**128**	403.77	**153**	408.56	**178**	412.73
4	368.76	**29**	386.39	**54**	392.26	**79**	397.60	**104**	401.65	**129**	403.78	**154**	408.79	**179**	412.77
5	369.24	**30**	386.59	**55**	392.62	**80**	397.72	**105**	401.74	**130**	403.83	**155**	408.85	**180**	412.99
6	370.12	**31**	386.98	**56**	392.97	**81**	398.09	**106**	401.84	**131**	403.98	**156**	408.85	**181**	413.38
7	372.97	**32**	387.01	**57**	392.99	**82**	398.42	**107**	401.93	**132**	403.98	**157**	409.20	**182**	413.53
8	373.09	**33**	387.17	**58**	393.09	**83**	398.50	**108**	402.04	**133**	404.07	**158**	409.33	**183**	413.84
9	375.50	**34**	387.37	**59**	393.30	**84**	398.73	**109**	402.06	**134**	404.13	**159**	409.35	**184**	413.88
10	375.70	**35**	387.40	**60**	393.60	**85**	398.82	**110**	402.51	**135**	404.33	**160**	409.76	**185**	414.03
11	377.16	**36**	387.75	**61**	394.07	**86**	399.01	**111**	402.55	**136**	404.47	**161**	409.99	**186**	414.36
12	377.68	**37**	387.90	**62**	394.26	**87**	399.03	**112**	402.58	**137**	404.48	**162**	410.06	**187**	415.12
13	378.16	**38**	388.07	**63**	394.50	**88**	399.20	**113**	402.61	**138**	405.07	**163**	410.18	**188**	415.41
14	378.33	**39**	388.32	**64**	394.50	**89**	399.35	**114**	402.82	**139**	405.17	**164**	410.37	**189**	415.89
15	378.52	**40**	388.55	**65**	394.52	**90**	399.42	**115**	402.92	**140**	405.17	**165**	410.43	**190**	416.51
16	381.84	**41**	389.16	**66**	394.57	**91**	399.90	**116**	402.93	**141**	406.31	**166**	410.43	**191**	416.71
17	382.03	**42**	389.24	**67**	394.87	**92**	400.01	**117**	402.94	**142**	406.67	**167**	410.54	**192**	417.09
18	382.91	**43**	390.18	**68**	394.89	**93**	400.13	**118**	403.03	**143**	406.67	**168**	410.61	**193**	417.09
19	382.97	**44**	390.22	**69**	394.93	**94**	400.18	**119**	403.16	**144**	406.70	**169**	410.95	**194**	417.74
20	383.25	**45**	390.87	**70**	395.20	**95**	400.41	**120**	403.16	**145**	406.97	**170**	411.01	**195**	417.94
21	383.52	**46**	390.90	**71**	395.48	**96**	400.46	**121**	403.27	**146**	407.09	**171**	411.71	**196**	418.40
22	384.04	**47**	391.41	**72**	395.70	**97**	400.52	**122**	403.31	**147**	407.17	**172**	411.72	**197**	418.74
23	384.14	**48**	391.72	**73**	396.10	**98**	400.58	**123**	403.42	**148**	407.49	**173**	411.88	**198**	419.23
24	384.28	**49**	391.75	**74**	396.40	**99**	400.70	**124**	403.43	**149**	407.56	**174**	412.02	**199**	419.75
25	384.36	**50**	391.87	**75**	396.85	**100**	401.17	**125**	403.47	**150**	408.23	**175**	412.09	**200**	420.31

Table 30 Particle size of Dowex® 1x2-200 (n=200)

No.	Size (µm)	No.	Size (µm)	No.	Size (µm)	No.	Size (µm)	No.	Size (µm)	No.	Size (µm)	No.	Size (µm)	No.	Size (µm)
1	126.50	**26**	153.85	**51**	174.00	**76**	188.13	**101**	195.95	**126**	203.42	**151**	205.39	**176**	216.67
2	128.21	**27**	153.85	**52**	174.36	**77**	188.13	**102**	195.95	**127**	204.04	**152**	205.39	**177**	216.67
3	129.91	**28**	153.85	**53**	174.36	**78**	188.13	**103**	195.95	**128**	204.04	**153**	205.39	**178**	216.67
4	131.62	**29**	154.16	**54**	174.36	**79**	188.13	**104**	195.95	**129**	204.04	**154**	205.39	**179**	216.67
5	136.75	**30**	154.16	**55**	176.07	**80**	191.45	**105**	195.95	**130**	204.04	**155**	206.44	**180**	216.67
6	136.75	**31**	157.26	**56**	176.07	**81**	191.45	**106**	195.95	**131**	204.04	**156**	206.44	**181**	216.67
7	138.46	**32**	157.26	**57**	176.11	**82**	191.45	**107**	195.95	**132**	204.04	**157**	206.44	**182**	216.67
8	140.17	**33**	157.26	**58**	176.11	**83**	191.45	**108**	196.58	**133**	204.04	**158**	206.44	**183**	216.67
9	140.17	**34**	158.97	**59**	176.11	**84**	192.83	**109**	196.58	**134**	204.04	**159**	206.44	**184**	218.80
10	141.88	**35**	160.68	**60**	184.62	**85**	192.83	**110**	196.58	**135**	204.04	**160**	206.44	**185**	218.80
11	143.59	**36**	162.39	**61**	184.62	**86**	192.83	**111**	196.58	**136**	204.04	**161**	206.44	**186**	220.51
12	143.60	**37**	162.39	**62**	184.62	**87**	192.83	**112**	200.08	**137**	204.04	**162**	206.44	**187**	220.51
13	145.30	**38**	162.39	**63**	184.62	**88**	192.83	**113**	200.08	**138**	204.04	**163**	206.44	**188**	222.22
14	147.01	**39**	162.39	**64**	186.32	**89**	192.83	**114**	200.08	**139**	205.13	**164**	206.44	**189**	226.13
15	148.72	**40**	162.39	**65**	186.32	**90**	192.83	**115**	200.08	**140**	205.13	**165**	206.44	**190**	226.13
16	148.72	**41**	162.39	**66**	186.32	**91**	192.83	**116**	200.08	**141**	205.13	**166**	206.44	**191**	226.13
17	148.72	**42**	164.10	**67**	188.03	**92**	192.83	**117**	200.08	**142**	205.13	**167**	208.55	**192**	227.02
18	148.72	**43**	164.10	**68**	188.13	**93**	192.83	**118**	200.08	**143**	205.39	**168**	208.55	**193**	227.02
19	148.72	**44**	165.81	**69**	188.13	**94**	192.83	**119**	200.08	**144**	205.39	**169**	208.55	**194**	227.35
20	150.43	**45**	165.81	**70**	188.13	**95**	192.83	**120**	200.08	**145**	205.39	**170**	208.55	**195**	230.78
21	152.14	**46**	169.23	**71**	188.13	**96**	195.95	**121**	200.08	**146**	205.39	**171**	210.26	**196**	242.74
22	152.14	**47**	169.23	**72**	188.13	**97**	195.95	**122**	200.08	**147**	205.39	**172**	216.67	**197**	227.35
23	153.85	**48**	169.23	**73**	188.13	**98**	195.95	**123**	200.08	**148**	205.39	**173**	216.67	**198**	230.78
24	153.85	**49**	170.94	**74**	188.13	**99**	195.95	**124**	203.42	**149**	205.39	**174**	216.67	**199**	242.74
25	153.85	**50**	174.00	**75**	188.13	**100**	195.95	**125**	203.42	**150**	205.39	**175**	216.67	**200**	242.74

Table 31 Particle size of Dowex® 1x4-200 (n=200)

No.	Size (µm)	No.	Size (µm)	No.	Size (µm)	No.	Size (µm)	No.	Size (µm)	No.	Size (µm)	No.	Size (µm)	No.	Size (µm)
1	126.75	**26**	144.69	**51**	155.64	**76**	161.31	**101**	167.92	**126**	172.89	**151**	186.32	**176**	203.92
2	128.31	**27**	144.91	**52**	155.87	**77**	161.92	**102**	168.23	**127**	173.11	**152**	186.51	**177**	205.13
3	129.73	**28**	145.13	**53**	156.16	**78**	161.99	**103**	168.23	**128**	173.56	**153**	187.33	**178**	205.84
4	131.03	**29**	145.39	**54**	156.26	**79**	162.39	**104**	168.23	**129**	173.96	**154**	187.45	**179**	206.05
5	131.62	**30**	146.05	**55**	156.76	**80**	162.39	**105**	169.20	**130**	174.36	**155**	188.03	**180**	207.58
6	133.34	**31**	148.72	**56**	157.31	**81**	162.39	**106**	169.24	**131**	174.37	**156**	188.66	**181**	207.61
7	133.34	**32**	148.73	**57**	157.39	**82**	162.43	**107**	169.24	**132**	174.43	**157**	189.01	**182**	208.55
8	135.04	**33**	149.93	**58**	157.88	**83**	162.99	**108**	169.29	**133**	175.19	**158**	189.32	**183**	213.52
9	135.14	**34**	150.43	**59**	158.38	**84**	163.68	**109**	169.50	**134**	176.20	**159**	189.74	**184**	218.06
10	135.14	**35**	150.43	**60**	158.39	**85**	163.76	**110**	170.32	**135**	176.49	**160**	189.77	**185**	218.08
11	135.17	**36**	150.93	**61**	158.39	**86**	164.10	**111**	170.47	**136**	176.49	**161**	190.51	**186**	218.57
12	135.22	**37**	150.98	**62**	158.39	**87**	164.10	**112**	170.47	**137**	176.49	**162**	190.67	**187**	218.57
13	135.57	**38**	152.14	**63**	158.61	**88**	164.11	**113**	170.62	**138**	176.49	**163**	190.67	**188**	218.57
14	136.75	**39**	152.38	**64**	158.97	**89**	164.36	**114**	170.87	**139**	178.18	**164**	192.28	**189**	220.27
15	136.85	**40**	152.47	**65**	158.97	**90**	164.54	**115**	170.97	**140**	178.47	**165**	192.55	**190**	222.37
16	138.47	**41**	152.99	**66**	158.97	**91**	164.55	**116**	171.25	**141**	178.54	**166**	193.16	**191**	222.84
17	139.64	**42**	153.51	**67**	158.97	**92**	164.67	**117**	171.49	**142**	178.84	**167**	193.46	**192**	223.70
18	139.73	**43**	153.93	**68**	158.98	**93**	164.68	**118**	171.69	**143**	181.27	**168**	193.65	**193**	224.72
19	140.17	**44**	154.49	**69**	159.06	**94**	165.61	**119**	171.69	**144**	181.59	**169**	194.94	**194**	224.72
20	140.89	**45**	154.58	**70**	159.37	**95**	165.82	**120**	171.79	**145**	181.63	**170**	195.35	**195**	224.72
21	141.30	**46**	154.66	**71**	159.56	**96**	165.84	**121**	171.79	**146**	182.77	**171**	195.77	**196**	227.61
22	141.92	**47**	154.91	**72**	159.79	**97**	166.27	**122**	171.97	**147**	182.91	**172**	198.08	**197**	228.75
23	143.60	**48**	155.56	**73**	160.25	**98**	166.52	**123**	172.01	**148**	182.91	**173**	199.33	**198**	229.25
24	143.79	**49**	155.56	**74**	160.37	**99**	167.08	**124**	172.85	**149**	184.62	**174**	200.01	**199**	229.54
25	144.41	**50**	155.59	**75**	161.03	**100**	167.71	**125**	172.89	**150**	185.89	**175**	201.71	**200**	249.73

Table 32 Particle size of Dowex® 1x8-200 (n=200)

No.	Size (μm)	No.	Size (μm)	No.	Size (μm)	No.	Size (μm)	No.	Size (μm)	No.	Size (μm)	No.	Size (μm)	No.	Size (μm)
1	160.68	**26**	175.87	**51**	179.49	**76**	183.73	**101**	186.98	**126**	193.62	**151**	199.68	**176**	209.55
2	163.36	**27**	175.94	**52**	179.50	**77**	183.73	**102**	187.27	**127**	194.39	**152**	199.70	**177**	209.60
3	164.14	**28**	175.99	**53**	179.65	**78**	183.79	**103**	187.29	**128**	194.39	**153**	200.58	**178**	210.44
4	165.07	**29**	176.07	**54**	179.69	**79**	183.87	**104**	187.33	**129**	194.62	**154**	200.66	**179**	211.10
5	165.81	**30**	176.20	**55**	180.07	**80**	184.25	**105**	187.65	**130**	194.68	**155**	200.66	**180**	211.99
6	167.04	**31**	176.23	**56**	180.07	**81**	184.34	**106**	188.27	**131**	194.90	**156**	200.78	**181**	212.52
7	167.56	**32**	176.28	**57**	180.30	**82**	184.39	**107**	188.58	**132**	194.98	**157**	201.08	**182**	212.88
8	168.22	**33**	176.62	**58**	180.43	**83**	184.44	**108**	188.69	**133**	195.06	**158**	201.10	**183**	213.68
9	169.23	**34**	177.07	**59**	180.60	**84**	184.44	**109**	189.06	**134**	195.18	**159**	201.74	**184**	214.90
10	169.71	**35**	177.47	**60**	180.88	**85**	184.46	**110**	189.38	**135**	195.28	**160**	202.45	**185**	215.38
11	169.85	**36**	177.69	**61**	181.24	**86**	184.62	**111**	189.64	**136**	195.35	**161**	203.12	**186**	216.29
12	170.30	**37**	177.78	**62**	181.33	**87**	184.65	**112**	189.64	**137**	195.62	**162**	203.42	**187**	216.39
13	170.95	**38**	177.79	**63**	181.71	**88**	184.94	**113**	189.71	**138**	196.28	**163**	203.56	**188**	216.79
14	171.15	**39**	177.81	**64**	181.82	**89**	185.26	**114**	190.63	**139**	196.28	**164**	203.58	**189**	219.61
15	171.46	**40**	177.86	**65**	181.94	**90**	185.41	**115**	190.99	**140**	196.85	**165**	204.16	**190**	219.74
16	171.79	**41**	177.91	**66**	182.46	**91**	185.41	**116**	190.99	**141**	196.87	**166**	204.31	**191**	220.94
17	172.65	**42**	178.07	**67**	182.55	**92**	185.70	**117**	191.96	**142**	197.23	**167**	204.63	**192**	221.60
18	172.68	**43**	178.18	**68**	182.61	**93**	185.82	**118**	191.96	**143**	197.47	**168**	205.31	**193**	222.42
19	173.32	**44**	178.18	**69**	182.62	**94**	186.16	**119**	191.96	**144**	197.95	**169**	207.04	**194**	226.11
20	174.37	**45**	178.25	**70**	182.84	**95**	186.32	**120**	192.07	**145**	198.15	**170**	207.85	**195**	226.62
21	174.49	**46**	178.54	**71**	182.94	**96**	186.39	**121**	192.10	**146**	198.29	**171**	207.86	**196**	230.49
22	174.90	**47**	178.84	**72**	183.03	**97**	186.40	**122**	192.22	**147**	198.36	**172**	208.22	**197**	231.03
23	174.94	**48**	178.96	**73**	183.23	**98**	186.54	**123**	192.98	**148**	198.45	**173**	208.70	**198**	239.54
24	175.14	**49**	179.15	**74**	183.25	**99**	186.57	**124**	192.99	**149**	198.76	**174**	208.74	**199**	242.57
25	175.87	**50**	179.38	**75**	183.30	**100**	186.83	**125**	193.46	**150**	198.97	**175**	209.25	**200**	246.30

2. Physical properties of DCP tablets containing IER

Table 33 Hardness of tablets containing various types of IER

	Placebo	SSG	Amberlite® IRP64	Amberlite® IRP69	Dowex® 88	Dowex® retardion	Dowex® 50x2-200	Dowex® 50x4-200	Dowex® 50x8-200	Dowex® 1x2-200	Dowex® 1x4-200	Dowex® 1x8-200
1	270.00	176.00	154.00	77.00	82.00	66.00	30.00	22.00	17.00	97.00	50.00	68.00
2	275.00	222.00	168.00	76.00	84.00	56.00	27.00	25.00	19.00	103.00	75.00	68.00
3	287.00	222.00	160.00	68.00	71.00	49.00	31.00	23.00	17.00	91.00	68.00	95.00
4	248.00	234.00	151.00	80.00	82.00	52.00	31.00	31.00	17.00	125.00	91.00	88.00
5	280.00	165.00	160.00	78.00	78.00	59.00	33.00	31.00	16.00	101.00	94.00	56.00
6	286.00	163.00	161.00	83.00	86.00	59.00	30.00	29.00	17.00	107.00	72.00	69.00
7	298.00	209.00	139.00	75.00	78.00	68.00	34.00	24.00	15.00	120.00	56.00	54.00
8	276.00	191.00	168.00	72.00	79.00	64.00	35.00	28.00	14.00	113.00	76.00	81.00
9	267.00	146.00	167.00	75.00	79.00	48.00	38.00	24.00	18.00	102.00	67.00	60.00
10	281.00	130.00	161.00	75.00	86.00	57.00	44.00	31.00	11.00	113.00	63.00	57.00
AVG	276.80	185.80	158.90	75.90	80.50	57.80	33.30	26.80	16.10	107.20	71.20	69.60
SD	13.51	35.36	8.97	4.12	4.53	6.86	4.85	3.58	2.28	10.53	13.85	14.14

Table 34 Diameter of tablets containing various types of IER

	Placebo	SSG	Amberlite® IRP 64	Amberlite® IRP 69	Dowex® 88	Dowex® retardion	Dowex® 50x2-200	Dowex® 50x4-200	Dowex® 50x8-200	Dowex® 1x2-200	Dowex® 1x4-200	Dowex® 1x8-200
1	9.53	9.60	9.60	9.61	9.64	9.58	9.62	9.63	9.62	9.54	9.64	9.57
2	9.56	9.60	9.60	9.63	9.66	9.59	9.59	9.64	9.62	9.55	9.58	9.58
3	9.54	9.57	9.61	9.64	9.66	9.60	9.62	9.64	9.60	9.56	9.57	9.58
4	9.54	9.61	9.58	9.60	9.66	9.57	9.59	9.61	9.63	9.56	9.58	9.56
5	9.57	9.62	9.59	9.65	9.67	9.61	9.60	9.62	9.62	9.58	9.56	9.55
6	9.56	9.60	9.59	9.64	9.63	9.61	9.62	9.61	9.63	9.58	9.62	9.53
7	9.56	9.60	9.62	9.64	9.68	9.60	9.62	9.64	9.62	9.57	9.58	9.56
8	9.58	9.61	9.56	9.63	9.67	9.57	9.62	9.63	9.62	9.57	9.60	9.56
9	9.57	9.58	9.59	9.63	9.67	9.58	9.63	9.64	9.60	9.57	9.61	9.58
10	9.56	9.58	9.60	9.62	9.66	9.57	9.60	9.60	9.62	9.56	9.63	9.57
AVG	9.56	9.60	9.59	9.63	9.66	9.59	9.61	9.63	9.62	9.56	9.60	9.56
SD	0.02	0.02	0.02	0.02	0.01	0.02	0.01	0.02	0.01	0.01	0.03	0.02

Table 35 Thickness of tablets containing various types of IER

	Placebo	SSG	Amberlite® IRP 64	Amberlite® IRP 69	Dowex® 88	Dowex® retardion	Dowex® 50x2-200	Dowex® 50x4-200	Dowex® 50x8-200	Dowex® 1x2-200	Dowex® 1x4-200	Dowex® 1x8-200
1	3.24	3.38	3.54	3.51	3.51	3.81	3.25	3.29	3.48	3.74	4.07	4.08
2	3.22	3.33	3.49	3.50	3.56	3.72	3.25	3.26	3.50	3.69	3.95	4.02
3	3.15	3.25	3.60	3.47	3.57	3.81	3.24	3.30	3.53	3.73	4.14	3.92
4	3.16	3.35	3.57	3.23	3.56	3.82	3.25	3.24	3.58	3.63	3.82	3.92
5	3.21	3.29	3.53	3.63	3.55	3.82	3.21	3.27	3.54	3.74	3.96	4.20
6	3.25	3.35	3.57	3.55	3.55	3.76	3.25	3.22	3.54	3.67	3.96	4.07
7	3.19	3.31	3.57	3.53	3.51	3.75	3.22	3.30	3.50	3.67	4.18	4.04
8	3.24	3.30	3.55	3.49	3.50	3.80	3.26	3.26	3.56	3.69	3.95	3.98
9	3.20	3.44	3.51	3.48	3.54	3.86	3.23	3.30	3.53	3.73	4.14	3.84
10	3.23	3.35	3.60	3.43	3.51	3.99	3.18	3.33	3.55	3.69	3.96	4.20
AVG	3.21	3.34	3.55	3.48	3.54	3.81	3.23	3.28	3.53	3.70	4.01	4.03
SD	0.03	0.05	0.04	0.10	0.03	0.07	0.02	0.03	0.03	0.04	0.11	0.12

Table 36 Friability of tablet containing various types of IER

Placebo	SSG	Amberlite® IRP 64	Amberlite® IRP 69	Dowex® 88	Dowex® retardion	Dowex® 50x2-200	Dowex® 50x4-200	Dowex® 50x8-200	Dowex® 1x2-200	Dowex® 1x4-200	Dowex® 1x8-200
0.7700	0.8990	0.7880	1.9660	100.00	100.00	4.7690	1.9420	8.4160	1.9070	3.9810	9.8600

Table 37 Disintegration time (min) of tablet containing various types of IER

	Placebo	SSG	Amberlite® IRP 64	Amberlite® IRP 69	Dowex® 88	Dowex® retardion	Dowex® 50x2-200	Dowex® 50x4-200	Dowex® 50x8-200	Dowex® 1x2-200	Dowex® 1x4-200	Dowex® 1x8-200
1	> 3 h	4.44	7.00	0.33	> 3 h	> 3 h	0.30	0.05	N/A	0.10	0.20	42
2	> 3 h	6.16	4.32	0.30	> 3 h	> 3 h	0.30	0.08	N/A	0.24	0.20	65
3	> 3 h	6.03	6.19	0.27	> 3 h	> 3 h	0.30	0.10	N/A	0.34	0.20	75
4	> 3 h	4.13	5.12	0.37	> 3 h	> 3 h	0.27	0.05	N/A	0.40	0.20	80
5	> 3 h	5.01	6.47	0.33	> 3 h	> 3 h	0.28	0.07	N/A	0.40	0.20	90
6	> 3 h	6.58	7.00	0.42	> 3 h	> 3 h	0.30	0.08	N/A	0.40	0.20	90
7	> 3 h	3.48	8.00	0.17	> 3 h	> 3 h	0.23	0.13	N/A	0.29	0.30	120
8	> 3 h	6.24	5.25	0.20	> 3 h	> 3 h	0.20	0.12	N/A	0.34	0.30	90
9	> 3 h	4.12	8.00	0.25	> 3 h	> 3 h	0.30	0.10	N/A	0.34	0.30	100
10	> 3 h	6.4	5.25	0.25	> 3 h	> 3 h	0.30	0.08	N/A	0.34	0.30	98
11	> 3 h	4.32	7.00	0.27	> 3 h	> 3 h	0.30	0.07	N/A	0.35	0.30	120
12	> 3 h	7.31	7.00	0.33	> 3 h	> 3 h	0.27	0.10	N/A	0.35	0.30	110
AVG	N/A	5.35	6.38	0.29	N/A	N/A	0.28	0.09	N/A	0.32	0.25	90.00
SD	N/A	1.24	1.18	0.07	N/A	N/A	0.03	0.03	N/A	0.08	0.05	22.60

APPENDIX B

Factors affecting disintegration properties of IER

1. Effect of amount of IER

Table 38 Physical properties of tablets containing SSG

% w/w	Physical properties	1	2	3	4	5	6	7	8	9	10	11	12	AVG	SD
2.5	**Hardness (mm)**	185.00	194.00	199.00	192.00	185.00	186.00	192.00	188.00	184.00	182.00	-	-	**188.70**	**5.36**
	Thickness (mm)	3.20	3.17	3.21	3.19	3.19	3.19	3.18	3.19	3.19	3.18	-	-	**3.19**	**0.01**
	Diameter (mm)	9.61	9.61	9.61	9.61	9.60	9.61	9.61	9.59	9.60	9.61	-	-	**9.61**	**0.01**
	Disintegration time (sec)	98	104	105	106	109	113	78	93	98	98	105	107	**101.00**	**9.19**
	Friability (%)	0.7235													
5.0	**Hardness (mm)**	155.00	159.00	148.00	163.00	170.00	165.00	149.00	167.00	165.00	154.00	-	-	**159.50**	**7.69**
	Thickness (mm)	3.25	3.26	3.24	3.26	3.23	3.26	3.24	3.23	3.23	3.28	-	-	**3.25**	**0.02**
	Diameter (mm)	9.60	9.60	9.61	9.60	9.60	9.61	9.58	9.58	9.60	9.59	-	-	**9.60**	**0.01**
	Disintegration time (sec)	41	43	48	57	60	68	58	62	65	69	72	77	**60.00**	**11.34**
	Friability (%)	0.7328													
7.5	**Hardness (mm)**	152.00	165.00	165.00	150.00	170.00	149.00	162.00	150.00	151.00	157.00	-	-	**157.10**	**7.78**
	Thickness (mm)	3.34	3.32	3.38	3.30	3.34	3.33	3.34	3.35	3.33	3.36	-	-	**3.34**	**0.02**
	Diameter (mm)	9.60	9.60	9.60	9.60	9.60	9.60	9.60	9.57	9.60	9.57	-	-	**9.59**	**0.01**
	Disintegration time (sec)	39	43	45	48	55	59	41	42	43	46	49	51	**46.75**	**5.96**
	Friability (%)	0.7187													
10.0	**Hardness (mm)**	161.00	154.00	142.00	156.00	160.00	151.00	149.00	142.00	162.00	160.00	-	-	**153.70**	**7.53**
	Thickness (mm)	3.39	3.42	3.40	3.40	3.35	3.40	3.39	3.38	3.41	3.38	-	-	**3.39**	**0.02**
	Diameter (mm)	9.58	9.59	9.59	9.59	9.60	9.59	9.60	9.59	9.60	9.56	-	-	**9.59**	**0.01**
	Disintegration time (sec)	41	42	45	54	57	61	40	45	46	47	40	52	**47.50**	**6.97**
	Friability (%)	0.6663													

Table 39 Physical properties of tablets containing Amberlite® IRP64

% w/w	Physical properties	1	2	3	4	5	6	7	8	9	10	11	12	AVG	SD
2.5	**Hardness (mm)**	222.00	182.00	157.00	195.00	173.00	153.00	213.00	190.00	238.00	205.00	-	-	**192.80**	**27.57**
	Thickness (mm)	3.36	3.33	3.38	3.34	3.36	3.32	3.32	3.35	3.28	3.35	-	-	**3.34**	**0.03**
	Diameter (mm)	9.58	9.63	9.65	9.57	9.55	9.58	9.59	9.55	9.58	9.60	-	-	**9.59**	**0.03**
	Disintegration time (sec)	> 30 min													
	Friability (%)	0.5058													
5.0	**Hardness (mm)**	154.00	161.00	161.00	186.00	176.00	154.00	174.00	179.00	169.00	157.00	-	-	**167.10**	**11.30**
	Thickness (mm)	3.44	3.48	3.49	3.44	3.44	3.48	3.51	3.44	3.44	3.51	-	-	**3.47**	**0.03**
	Diameter (mm)	9.60	9.62	9.59	9.60	9.57	9.60	9.61	9.60	9.61	9.61	-	-	**9.60**	**0.01**
	Disintegration time (sec)	42	49	52	50	48	48	60	60	90	90	90	90	**64.08**	**19.76**
	Friability (%)	0.7062													
7.5	**Hardness (mm)**	151.00	140.00	143.00	156.00	152.00	146.00	149.00	156.00	164.00	146.00	-	-	**150.30**	**7.10**
	Thickness (mm)	3.51	3.62	3.52	3.54	3.52	3.56	3.58	3.52	3.53	3.60	-	-	**3.55**	**0.04**
	Diameter (mm)	9.60	9.61	9.60	9.60	9.60	9.61	9.61	9.59	9.61	9.62	-	-	**9.61**	**0.01**
	Disintegration time (sec)	19	22	20	26	24	30	17	18	20	21	21	21	**21.58**	**3.60**
	Friability (%)	0.6946													
10.0	**Hardness (mm)**	163.00	148.00	156.00	149.00	148.00	152.00	147.00	156.00	151.00	147.00	-	-	**151.70**	**5.21**
	Thickness (mm)	3.60	3.62	3.62	3.58	3.59	3.61	3.61	3.59	3.58	3.58	-	-	**3.60**	**0.02**
	Diameter (mm)	9.59	9.60	9.59	9.59	9.60	9.58	9.59	9.60	9.59	9.59	-	-	**9.59**	**0.01**
	Disintegration time (sec)	15	15	16	16	17	17	17	18	20	20	22	22	**17.92**	**2.50**
	Friability (%)	1.4123													

Table 40 Physical properties of tablets containing Amberlite® IRP69

% w/w	Physical properties	1	2	3	4	5	6	7	8	9	10	11	12	AVG	SD
2.5	**Hardness (mm)**	95.00	132.00	86.00	99.00	125.00	103.00	86.00	119.00	111.00	105.00	-	-	**106.00**	**16.05**
	Thickness (mm)	3.54	3.46	3.46	3.44	3.41	3.40	3.43	3.44	3.47	3.47	-	-	**3.45**	**0.04**
	Diameter (mm)	9.60	9.60	9.61	9.60	9.61	9.61	9.61	9.61	9.61	9.60	-	-	**9.61**	**0.01**
	Disintegration time (sec)	17	21	21	21	25	26	27	27	32	38	42	46	**28.58**	**9.12**
	Friability (%)	0.7418													
5.0	**Hardness (mm)**	77.00	76.00	68.00	80.00	78.00	83.00	75.00	72.00	75.00	75.00	-	-	**76.50**	**6.65**
	Thickness (mm)	3.51	3.50	3.47	3.55	3.53	3.49	3.48	3.43	3.46	3.51	-	-	**3.49**	**0.03**
	Diameter (mm)	9.61	9.63	9.64	9.60	9.64	9.64	9.63	9.63	9.62	9.64	-	-	**9.63**	**0.01**
	Disintegration time (sec)	5	8	11	13	12	15	16	17	22	22	22	22		
	Friability (%)	3.3679													
7.5	**Hardness (mm)**	57.00	55.00	57.00	61.00	50.00	51.00	52.00	74.00	56.00	52.00	-	-	**55.17**	**7.15**
	Thickness (mm)	3.58	3.59	3.55	3.56	3.59	3.59	3.56	3.60	3.62	3.61	-	-	**3.59**	**0.02**
	Diameter (mm)	9.67	9.64	9.65	9.66	9.65	9.66	9.65	9.66	9.67	9.67	-	-	**9.66**	**0.01**
	Disintegration time (sec)	9	8	10	11	12		14	15	16	16	17	18	**13.27**	**3.44**
	Friability (%)	3.2647													
10.0	**Hardness (mm)**	43.00	36.00	46.00	40.00	53.00	40.00	46.00	42.00	50.00	50.00	-	-	**44.75**	**4.86**
	Thickness (mm)	3.69	3.73	3.70	3.72	3.71	3.66	3.69	3.73	3.73	3.68	-	-	**3.70**	**0.02**
	Diameter (mm)	9.66	9.64	9.68	9.64	9.66	9.64	9.66	9.66	9.66	9.66	-	-	**9.66**	**0.01**
	Disintegration time (sec)	9	10	10	12	14	16	16	19	19	21	21	20	**15.58**	**4.50**
	Friability (%)	3.5758													

Table 41 Physical properties of tablets containing Dowex® 1x2-200

% w/w	Physical properties	1	2	3	4	5	6	7	8	9	10	11	12	AVG	SD
2.5	**Hardness (mm)**	133.00	156.00	135.00	135.00	132.00	149.00	135.00	120.00	129.00	131.00	-	-	**133.83**	**10.23**
	Thickness (mm)	3.52	3.50	3.55	3.54	3.50	3.49	3.49	3.48	3.53	3.48	-	-	**3.51**	**0.03**
	Diameter (mm)	9.61	9.60	9.62	9.61	9.61	9.61	9.61	9.61	9.59	9.61	-	-	**9.61**	**0.01**
	Disintegration time (sec)	152	152	152	152	152	152	124	129	136	144	152	166	**146.92**	**11.75**
	Friability (%)	0.9716													
5.0	**Hardness (mm)**	102.00	100.00	107.00	99.00	99.00	104.00	103.00	113.00	100.00	108.00	-	-	**103.50**	**4.60**
	Thickness (mm)	3.74	3.72	3.69	3.73	3.74	3.66	3.69	3.75	3.70	3.65	-	-	**3.71**	**0.03**
	Diameter (mm)	9.59	9.57	9.57	9.59	9.58	9.57	9.59	9.57	9.57	9.59	-	-	**9.58**	**0.01**
	Disintegration time (sec)	11	12	13	14	15	16	13	15	19	19	19	19	**15.42**	**2.97**
	Friability (%)	1.1076													
7.5	**Hardness (mm)**	96.00	94.00	85.00	99.00	90.00	90.00	94.00	94.00	96.00	92.00	-	-	**93.08**	**3.58**
	Thickness (mm)	3.88	3.88	3.87	3.86	3.91	3.86	3.90	3.87	3.93	3.87	-	-	**3.88**	**0.02**
	Diameter (mm)	9.59	9.59	9.59	9.59	9.57	9.57	9.59	9.59	9.59	9.59	-	-	**9.59**	**0.01**
	Disintegration time (sec)	11	11	11	11	11	11	14	14	14	14	14	14	**12.50**	**1.57**
	Friability (%)	1.4965													
10.0	**Hardness (mm)**	75.00	64.00	74.00	78.00	77.00	74.00	81.00	71.00	81.00	76.00	-	-	**75.58**	**4.68**
	Thickness (mm)	3.98	4.01	4.02	3.93	4.04	3.90	3.96	3.95	3.99	3.88	-	-	**3.97**	**0.05**
	Diameter (mm)	9.59	9.60	9.57	9.59	9.60	9.59	9.57	9.59	9.59	9.60	-	-	**9.59**	**0.01**
	Disintegration time (sec)	10	10	10	10	10	10	10	10	10	10	**10**	**10**	**10.00**	**0.00**
	Friability (%)	2.1865													

2. Effect of compression pressure

Table 42 Physical properties of tablets without disintegrant

Compression pressure (Tons)	Physical properties	1	2	3	4	5	6	7	8	9	10	11	12	AVG	SD
0.5	**Hardness (mm)**	15.00	14.00	18.00	20.00	22.00	22.00	24.00	16.00	17.00	15.00	-	-	**18.30**	**3.50**
	Thickness (mm)	3.79	3.79	3.80	3.81	3.81	3.80	3.78	3.79	3.76	3.83	-	-	**3.80**	**0.02**
	Diameter (mm)	9.59	9.58	9.60	9.60	9.58	9.58	9.61	9.60	9.61	9.60	-	-	**9.60**	**0.01**
	Disintegration time (sec)							30 min							
	Friability (%)		9.2888												
1.5	**Hardness (mm)**	46.00	35.00	51.00	51.00	50.00	57.00	53.00	50.00	57.00	50.00	-	-	**50.00**	**6.24**
	Thickness (mm)	3.44	3.44	3.43	3.45	3.43	4.43	3.45	3.42	4.43	4.42	-	-	**3.73**	**0.48**
	Diameter (mm)	9.58	9.60	9.56	9.59	9.57	9.59	9.56	9.58	9.59	9.57	-	-	**9.58**	**0.01**
	Disintegration time (sec)							30 min							
	Friability (%)		2.8947												
3.0	**Hardness (mm)**	101.00	105.00	104.00	113.00	105.00	103.00	107.00	109.00	97.00	104.00	-	-	**104.80**	**4.34**
	Thickness (mm)	3.24	3.26	3.24	3.22	3.23	3.21	3.25	3.24	3.25	3.25	-	-	**3.24**	**0.02**
	Diameter (mm)	9.60	9.60	9.60	9.60	9.57	9.61	9.60	9.60	9.65	9.61	-	-	**9.60**	**0.02**
	Disintegration time (sec)							30 min							
	Friability (%)		1.3513												
4.5	**Hardness (mm)**	260.4	279.8	288.1	256.2	273.5	243.2	280.4	294.4	252.9	289.6	-	-	**271.85**	**17.58**
	Thickness (mm)	3.17	3.20	3.24	3.29	3.19	3.24	3.26	3.26	3.20	3.22	-	-	**3.23**	**0.04**
	Diameter (mm)	9.59	9.56	9.58	9.58	9.59	9.60	9.57	9.60	9.61	9.62	-	-	**9.59**	**0.02**
	Disintegration time (sec)							30 min							
	Friability (%)		0.7698												

Table 43 Physical properties of tablets containing SSG

Compression pressure (Tons)	Physical properties	1	2	3	4	5	6	7	8	9	10	11	12	AVG	SD
0.5	**Hardness (mm)**	20.00	22.00	31.00	25.00	27.00	28.00	20.00	20.00	30.00	29.00	-	-	**25.20**	**4.39**
	Thickness (mm)	3.93	3.93	3.80	3.90	3.95	3.91	3.81	3.98	3.89	3.51	-	-	**3.86**	**0.14**
	Diameter (mm)	9.61	9.58	9.59	9.56	9.58	9.58	9.56	9.57	9.59	9.59	-	-	**9.58**	**0.02**
	Disintegration time (sec)	11	11	11	11	12	12	12	12	13	13	13	13	**12.00**	**0.85**
	Friability (%)	6.0125													
1.5	**Hardness (mm)**	67.00	64.00	58.00	72.00	64.00	69.00	64.00	72.00	64.00	66.00	-	-	**66.00**	**4.24**
	Thickness (mm)	3.61	3.59	3.59	3.57	3.63	3.61	3.62	3.58	3.63	3.58	-	-	**3.60**	**0.02**
	Diameter (mm)	9.56	9.56	9.60	9.60	9.59	9.59	9.62	9.59	9.59	9.59	-	-	**9.59**	**0.02**
	Disintegration time (sec)	19	19	19	19	19	19	20	20	20	20	20	20	**19.50**	**0.52**
	Friability (%)	2.2970													
3.0	**Hardness (mm)**	111.00	119.00	118.00	113.00	123.00	107.00	112.00	113.00	128.00	121.00	-	-	**116.50**	**6.40**
	Thickness (mm)	3.46	3.48	3.45	3.42	3.49	3.43	3.47	3.57	3.44	3.46	-	-	**3.47**	**0.04**
	Diameter (mm)	9.57	9.55	9.56	9.56	9.52	9.56	9.57	9.54	9.55	9.57	-	-	**9.56**	**0.02**
	Disintegration time (sec)	30	30	31	32	32	32	33	33	33	33	34	35	**32.33**	**1.50**
	Friability (%)	3.3486													
4.5	**Hardness (mm)**	155.00	159.00	148.00	163.00	170.00	165.00	149.00	167.00	165.00	154.00	-	-	**159.50**	**7.69**
	Thickness (mm)	3.25	3.26	3.24	3.26	3.23	3.26	3.24	3.23	3.23	3.28	-	-	**3.25**	**0.02**
	Diameter (mm)	9.60	9.60	9.61	9.62	9.60	9.60	9.58	9.58	9.60	9.59	-	-	**9.60**	**0.01**
	Disintegration time (sec)	41	43	48	57	60	68	58	62	65	69	72	77	**60.00**	**11.34**
	Friability (%)	0.7328													

Table 44 Physical properties of tablets containing Amberlite® IRP64

Compression pressure (Tons)	Physical properties	1	2	3	4	5	6	7	8	9	10	11	12	AVG	SD
0.5	**Hardness (mm)**	20.00	21.00	15.00	21.00	25.00	20.00	17.00	20.00	20.00	18.00	-	-	**19.70**	**2.67**
	Thickness (mm)	4.14	4.20	4.24	4.22	4.19	4.20	4.31	4.23	4.28	4.21	-	-	**4.22**	**0.05**
	Diameter (mm)	9.63	9.62	9.59	9.61	9.62	9.61	9.60	9.63	9.60	9.60	-	-	**9.61**	**0.01**
	Disintegration time (sec)	20.00	22.00	22.00	25.00	28.00	20.00	22.00	22.00	25.00	28.00	22.00	22.00	**23.17**	**2.72**
	Friability (%)	7.704													
1.5	**Hardness (mm)**	51.00	65.00	55.00	64.00	59.00	60.00	64.00	57.00	55.00	50.00	-	-	**58.00**	**5.35**
	Thickness (mm)	3.80	3.68	3.84	3.81	3.91	3.85	3.75	3.81	3.76	3.89	-	-	**3.81**	**0.07**
	Diameter (mm)	9.64	9.60	9.64	9.63	9.61	9.64	9.59	9.61	9.64	9.64	-	-	**9.62**	**0.02**
	Disintegration time (sec)	17	18	19	20	22	23	17	18	19	20	22	23	**19.83**	**2.21**
	Friability (%)	2.8034													
3.0	**Hardness (mm)**	121.00	115.00	125.00	123.00	125.00	133.00	131.00	123.00	134.00	120.00	-	-	**125.00**	**6.06**
	Thickness (mm)	3.59	3.54	3.51	3.55	3.53	3.53	3.52	3.51	3.53	3.55	-	-	**3.54**	**0.02**
	Diameter (mm)	9.63	9.64	9.65	9.64	9.63	9.61	9.63	9.64	9.61	9.63	-	-	**9.63**	**0.01**
	Disintegration time (sec)	21	22	24	30	33	33	21	22	24	30	33	33	**27.17**	**5.24**
	Friability (%)	1.4032													
4.5	**Hardness (mm)**	154.00	161.00	161.00	186.00	176.00	154.00	174.00	179.00	169.00	157.00	-	-	**167.10**	**11.30**
	Thickness (mm)	3.44	3.48	3.49	3.44	3.44	3.48	3.51	3.44	3.44	3.51	-	-	**3.47**	**0.03**
	Diameter (mm)	9.60	9.62	9.59	9.60	9.57	9.60	9.61	9.60	9.61	9.61	-	-	**9.60**	**0.01**
	Disintegration time (sec)	42	49	52	50	48	48	48	48	60	60	60	60	**52.08**	**6.27**
	Friability (%)	0.7062													

Table 45 Physical properties of tablets containing Dowex® 1x2-200

Compression pressure (Tons)	Physical properties	1	2	3	4	5	6	7	8	9	10	11	12	AVG	SD
0.5	**Hardness (mm)**	16.00	17.00	18.00	13.00	18.00	17.00	18.00	18.00	16.00	16.00	-	-	**16.70**	**1.57**
	Thickness (mm)	4.13	4.09	4.10	4.08	4.12	4.13	4.11	4.12	4.11	4.10	-	-	**4.11**	**0.02**
	Diameter (mm)	9.59	9.59	9.61	9.57	9.59	9.60	9.59	9.59	9.60	9.60	-	-	**9.59**	**0.01**
	Disintegration time (sec)	25	26	27	27	28	28	25	26	27	27	28	28	**26.83**	**1.11**
	Friability (%)	100.00													
1.5	**Hardness (mm)**	53.00	53.00	50.00	50.00	53.00	35.00	51.00	52.00	50.00	53.00	-	-	**50.00**	**5.44**
	Thickness (mm)	3.80	3.76	3.80	3.77	3.75	3.81	3.77	3.82	3.77	3.80	-	-	**3.79**	**0.02**
	Diameter (mm)	9.56	9.57	9.55	9.58	9.59	9.59	9.59	9.59	9.58	9.58	-	-	**9.58**	**0.01**
	Disintegration time (sec)	8	8	8	9	9	9	8	8	8	9	9	9	**8.50**	**0.52**
	Friability (%)	2.3719													
3.0	**Hardness (mm)**	86.00	93.00	104.00	96.00	104.00	88.00	104.00	108.00	93.00	104.00	-	-	**98.00**	**7.76**
	Thickness (mm)	3.69	3.64	3.63	3.70	3.62	3.69	3.62	3.62	3.63	3.60	-	-	**3.64**	**0.04**
	Diameter (mm)	9.33	9.32	9.31	9.31	9.31	9.33	9.31	9.31	9.32	9.31	-	-	**9.32**	**0.01**
	Disintegration time (sec)	7	7	7	8	8	8	7	7	7	8	8	8	**7.50**	**0.52**
	Friability (%)	1.3627													
4.5	**Hardness (mm)**	102.00	100.00	107.00	99.00	114.00	99.00	104.00	103.00	100.00	108.00	-	-	**103.60**	**4.84**
	Thickness (mm)	3.72	3.69	3.73	3.74	3.66	3.69	3.63	3.66	3.70	3.65	-	-	**3.69**	**0.04**
	Diameter (mm)	9.59	9.57	9.57	9.59	9.58	9.57	9.59	9.57	9.57	9.59	-	-	**9.58**	**0.01**
	Disintegration time (sec)	6	6	6	6	6	6	6	6	6	6	6	6	**6.00**	**0.00**
	Friability (%)	1.1076													

Table 46 Disintegration time of tablets containing 2% SSG

Compression pressure (Tons)	1	2	3	4	5	6	7	8	9	10	11	12	AVG	SD
0.5	8	8	9	9	9	10	8	8	9	9	9	9	8.75	0.62
1.5	11	11	12	13	13	13	10	10	11	11	11	11	11.42	1.08
3.0	20	20	21	21	22	22	23	23	24	25	25	25	22.58	1.88
4.5	39	39	39	40	40	40	38	38	40	43	43	44	40.25	2.01

Table 47 Disintegration time of tablets containing 2 % Amberlite IRP64

Compression pressure (Tons)	1	2	3	4	5	6	7	8	9	10	11	12	AVG	SD
0.5	112	125	128	138	150	159	123	140	140	145	148	148	138.00	13.52
1.5	160	165	170	179	180	180	150	156	167	170	179	180	169.67	10.40
3.0	165	172	190	200	206	215	160	165	168	180	182	182	182.08	17.62
4.5	285	297	310	330	336	350	250	260	269	270	278	230	288.75	36.75

Table 48 Disintegration time of tablets containing 2 % Dowex®1x2-200

Compression pressure (Tons)	1	2	3	4	5	6	7	8	9	10	11	12	AVG	SD
0.5	585	600	612	650	653	660	550	580	580	600	620	620	609.17	33.53
1.5	270	277	300	307	309	315	270	270	285	285	300	300	290.67	16.48
3.0	30	33	34	37	40	40	42	43	50	50	55	57	42.58	8.74
4.5	40	45	48	50	55	57	42	42	45	48	50	50	47.67	5.18

3. Effect of types of diluents

Table 49 Physical properties of tablets without disintegrant

Type of diluents	Physical properties	1	2	3	4	5	6	7	8	9	10	11	12	AVG	SD
DCP	**Hardness (mm)**	270.00	275.00	287.00	248.00	280.00	286.00	298.00	276.00	267.00	281.00	270.00	275.00	**287.00**	**248.00**
	Thickness (mm)	3.24	3.22	3.15	3.16	3.21	3.25	3.19	3.24	3.20	3.23	3.24	3.22	**3.15**	**3.16**
	Diameter (mm)	9.53	9.56	9.54	9.54	9.57	9.56	9.56	9.58	9.57	9.56	9.53	9.56	**9.54**	**9.54**
	Disintegration time (sec)	41	43	48	57	60	68	58	62	65	69	72	77	**41**	**43**
	Friability (%)	0.7698													
SDL	**Hardness (mm)**	326.00	269.00	201.00	240.00	338.00	200.00	213.00	321.00	200.00	342.00	-	-	**265.00**	**61.47**
	Thickness (mm)	4.78	4.81	4.84	4.77	4.83	4.81	4.82	4.76	4.78	4.77	-	-	**4.80**	**0.03**
	Diameter (mm)	9.62	9.62	9.62	9.62	9.62	9.62	9.62	9.62	9.62	9.62	-	-	**9.62**	**0.00**
	Disintegration time (sec)	354	530	692	692	546	556	354	530	692	692	546	556	**561.67**	**119.38**
	Friability (%)	100.00													
MCC	**Hardness (mm)**								N/A						
	Thickness (mm)	4.95	5.01	4.98	4.99	4.98	4.98	4.99	4.97	4.99	5.01	-	-	**4.99**	**0.02**
	Diameter (mm)	9.57	9.57	9.57	9.58	9.57	9.57	9.57	9.58	9.57	9.57	-	-	**9.57**	**0.00**
	Disintegration time (sec)								>30 min						
	Friability (%)	0.0503													
SDRS	**Hardness (mm)**	159.00	137.00	163.00	171.00	154.00	125.00	128.00	113.00	174.00	126.00	-	-	**145.00**	**21.75**
	Thickness (mm)	5.57	5.58	5.63	5.60	5.63	5.70	5.65	5.63	5.65	5.69	-	-	**5.63**	**0.04**
	Diameter (mm)	9.68	9.73	9.70	9.71	9.73	9.77	9.76	9.76	9.70	9.75	-	-	**9.73**	**0.03**
	Disintegration time (sec)	160	170	190	195	195	210	140	160	160	190	220	220	**184.17**	**26.01**
	Friability (%)	100.00													

Table 50 Physical properties of tablets containing SSG

Type of diluents	Physical properties	1	2	3	4	5	6	7	8	9	10	11	12	AVG	SD
DCP	**Hardness (mm)**	155.00	159.00	148.00	163.00	170.00	165.00	149.00	167.00	165.00	154.00	-	-	**159.50**	**8.21**
	Thickness (mm)	3.38	3.33	3.25	3.35	3.29	3.35	3.31	3.30	3.44	3.35	-	-	**3.34**	**0.05**
	Diameter (mm)	9.60	9.60	9.61	9.60	9.60	9.61	9.58	9.58	9.60	9.59	-	-	**9.60**	**0.01**
	Disintegration time (sec)	41	43	48	57	60	68	58	62	65	69	72	77	**54.63**	**9.59**
	Friability (%)	0.7328													
SDL	**Hardness (mm)**	418.00	424.00	374.00	424.00	335.00	385.00	339.00	404.00	393.00	404.00	-	-	**418.00**	**424.00**
	Thickness (mm)	4.77	4.77	4.74	4.77	4.76	4.75	4.76	4.75	4.76	4.76	-	-	**4.77**	**4.77**
	Diameter (mm)	9.61	9.61	9.61	9.59	9.61	9.59	9.61	9.58	9.61	9.59	-	-	**9.61**	**9.61**
	Disintegration time (sec)	354	352	465	473	423	440	533	476	546	636	702	659	**354**	**352**
	Friability (%)	0.2231													
MCC	**Hardness (mm)**							N/A							
	Thickness (mm)	4.97	4.98	4.94	4.98	4.96	4.95	4.94	4.96	4.99	4.94	-	-	**4.96**	**0.02**
	Diameter (mm)	9.57	9.57	9.57	9.59	9.57	9.57	9.57	9.57	9.57	9.57	-	-	**9.57**	**0.01**
	Disintegration time (sec)	192	193	194	195	201	202	186	188	190	196	209	211	**193.88**	**5.59**
	Friability (%)	0.0000													
SDRS	**Hardness (mm)**	294.00	287.00	272.00	305.00	253.00	283.00	264.00	240.00	231.00	286.00	-	-	**274.75**	**21.74**
	Thickness (mm)	5.43	5.39	5.42	5.43	5.43	5.39	5.39	5.43	5.43	5.41	-	-	**5.42**	**0.02**
	Diameter (mm)	9.58	9.54	9.54	9.55	9.59	9.56	9.55	9.60	9.58	9.53	-	-	**9.56**	**0.02**
	Disintegration time (sec)	240	240	270	270	270	270	230	230	240	240	256	256	**252.50**	**19.09**
	Friability (%)	0.0520													

Table 51 Physical properties of tablets containing Amberlite® IRP64

Type of diluents	Physical properties	1	2	3	4	5	6	7	8	9	10	11	12	AVG	SD
DCP	**Hardness (mm)**	154.00	161.00	161.00	186.00	176.00	154.00	174.00	179.00	169.00	157.00	-	-	**167.10**	**11.30**
	Thickness (mm)	3.54	3.49	3.60	3.57	3.53	3.57	3.57	3.55	3.51	3.60	-	-	**3.55**	**0.04**
	Diameter (mm)	9.60	9.60	9.61	9.58	9.59	9.59	9.62	9.56	9.59	9.60	-	-	**9.59**	**0.02**
	Disintegration time (sec)	42	49	52	50	48	48	60	60	90	90	90	90	**64.08**	**19.76**
	Friability (%)	0.7062													
SDL	**Hardness (mm)**	379.00	384.00	360.00	382.00	354.00	371.00	358.00	383.00	378.00	341.00	-	-	**372.11**	**11.81**
	Thickness (mm)	4.85	4.82	4.84	4.84	4.82	4.84	4.83	4.85	4.85	4.86	-	-	**4.84**	**0.01**
	Diameter (mm)	9.61	9.61	9.62	9.61	9.62	9.61	9.61	9.62	9.61	9.62	-	-	**9.61**	**0.01**
	Disintegration time (sec)	851	872	875	938	1033	1033	975	1042	1052	1128	1128	1128	**1004.58**	**101.90**
	Friability (%)	0.2923													
MCC	**Hardness (mm)**							N/A							
	Thickness (mm)	5.08	5.09	5.04	5.03	5.03	5.09	5.05	5.05	5.03	5.07	-	-	**5.06**	**0.02**
	Diameter (mm)	9.56	9.56	9.57	9.56	9.56	9.55	9.55	9.57	9.57	9.56	-	-	**9.56**	**0.01**
	Disintegration time (sec)	1675	1989	1992	2174	2355	2355	1116	1811	1947	2307	2317	2322	**2030.00**	**368.75**
	Friability (%)	0.0000													
SDRS	**Hardness (mm)**	331.00	337.00	272.00	328.00	313.00	335.00	273.00	273.00	328.00	325.00	-	-	**310.00**	**28.80**
	Thickness (mm)	5.49	5.48	5.48	5.47	5.47	5.43	5.49	5.47	5.47	5.48	-	-	**5.47**	**0.02**
	Diameter (mm)	9.56	9.56	9.57	9.56	9.56	9.55	9.55	9.57	9.57	9.56	-	-	**9.56**	**0.01**
	Disintegration time (sec)	210	210	210	210	210	240	195	220	220	220	233	240	**218.17**	**13.66**
	Friability (%)	0.0702													

Table 52 Physical properties of tablets containing Amberlite® IRP69

Type of diluents	Physical properties	1	2	3	4	5	6	7	8	9	10	11	12	AVG	SD
DCP	**Hardness (mm)**	77.00	76.00	68.00	80.00	78.00	83.00	75.00	72.00	75.00	75.00	-	-	**75.90**	**4.12**
	Thickness (mm)	3.51	3.50	3.47	3.23	3.63	3.55	3.53	3.49	3.48	3.43	-	-	**3.48**	**0.10**
	Diameter (mm)	9.61	9.63	9.64	9.60	9.65	9.64	9.64	9.63	9.63	9.62	-	-	**9.63**	**0.02**
	Disintegration time (sec)	5	8	11	13	12	15	16	17	22	22	22	22	**15.42**	**5.85**
	Friability (%)	2.3679													
SDL	**Hardness (mm)**	213.00	193.00	195.00	202.00	214.00	205.00	208.00	190.00	210.00	177.00	-	-	**200.70**	**11.81**
	Thickness (mm)	5.06	4.97	5.06	5.01	4.97	5.03	5.02	5.00	5.06	5.03	-	-	**5.02**	**0.03**
	Diameter (mm)	9.62	9.61	9.62	9.60	9.60	9.59	9.61	9.60	9.61	9.62	-	-	**9.61**	**0.01**
	Disintegration time (sec)	8	8	8	8	9	9	9	9	9	10	10	10	**8.92**	**0.79**
	Friability (%)	0.9552													
MCC	**Hardness (mm)**							N/A							
	Thickness (mm)	5.01	5.01	5.02	5.03	5.02	5.01	5.02	5.01	5.03	5.03	-	-	**5.02**	**0.01**
	Diameter (mm)	9.58	9.59	9.59	9.59	9.58	9.59	9.59	9.59	9.59	9.59	-	-	**9.59**	**0.00**
	Disintegration time (sec)	100	104	113	117	117	117	99	113	138	145	148	173	**123.67**	**22.57**
	Friability (%)	0.000													
SDRS	**Hardness (mm)**	183.00	234.00	194.00	198.00	171.00	147.00	222.00	177.00	121.00	173.00	-	-	**182.00**	**33.13**
	Thickness (mm)	5.57	5.56	5.52	5.46	5.52	5.56	5.60	5.53	5.53	5.54	-	-	**5.54**	**0.04**
	Diameter (mm)	9.66	9.63	9.60	9.60	9.64	9.69	9.71	9.64	9.64	9.64	-	-	**9.65**	**0.03**
	Disintegration time (sec)	120	150	150	180	200	200	130	150	170	170	210	210	**170.00**	**30.75**
	Friability (%)	0.1707													

Table 53 Physical properties of tablets containing Dowex® 1x2-200

Type of diluents	Physical properties	1	2	3	4	5	6	7	8	9	10	11	12	AVG	SD
DCP	**Hardness (mm)**	102.00	100.00	107.00	99.00	99.00	104.00	103.00	113.00	100.00	108.00	-	-	**103.50**	**4.60**
	Thickness (mm)	3.74	3.69	3.73	3.63	3.74	3.67	3.67	3.69	3.73	3.69	-	-	**3.70**	**0.04**
	Diameter (mm)	9.54	9.55	9.56	9.56	9.58	9.58	9.57	9.57	9.57	9.56	-	-	**9.56**	**0.01**
	Disintegration time (sec)	11	12	13	14	15	16	13	15	19	19	19	19	**15.42**	**2.97**
	Friability (%)	1.1076													
SDL	**Hardness (mm)**	251.00	275.00	267.00	280.00	266.00	271.00	248.00	250.00	254.00	260.00	-	-	**262.20**	**11.27**
	Thickness (mm)	5.07	4.99	4.99	5.01	5.01	5.00	4.99	5.01	5.04	5.00	-	-	**5.01**	**0.03**
	Diameter (mm)	9.58	9.58	9.61	9.58	9.61	9.59	9.61	9.61	9.61	9.61	-	-	**9.60**	**0.02**
	Disintegration time (sec)	18	21	22	23	24	25	20	26	26	27	28	35	**24.58**	**4.44**
	Friability (%)	0.6517													
MCC	**Hardness (mm)**							N/A							
	Thickness (mm)	5.04	5.05	5.08	5.07	5.06	5.05	5.05	5.07	5.05	5.08	-	-	**5.06**	**0.01**
	Diameter (mm)	9.56	9.57	9.56	9.56	9.56	9.56	9.57	9.56	9.58	9.58	-	-	**9.57**	**0.01**
	Disintegration time (sec)	170	170	170	170	170	170	125	133	152	165	169	179	**161.92**	**16.63**
	Friability (%)	0.0000													
SDRS	**Hardness (mm)**	196	143	128	216	213	179	110	162	184	208	-	-	**173.90**	**37.07**
	Thickness (mm)	5.77	5.61	5.73	5.74	5.58	5.65	5.71	5.63	5.69	5.60	-	-	**5.67**	**0.07**
	Diameter (mm)	9.74	9.62	9.68	9.69	9.63	9.63	9.65	9.72	9.67	9.66	-	-	**9.67**	**0.04**
	Disintegration time (sec)	120	120	139	160	180	195	120	120	120	120	165	165	**143.67**	**27.82**
	Friability (%)	0.3127													

APPENDIX C

Development of tablet formulations by using IER as tablet disintegrant

1. Dextromethorphan hydrobromide (DMP) tablets

1.1 Physical properties of DMP tablets

Table 54 Physical properties of DMP tablets

Resin type	Physical properties	1	2	3	4	5	6	7	8	9	10	11	12	AVG	SD
SSG	**Hardness (mm)**	140.00	114.00	142.00	156.00	154.00	135.00	156.00	156.00	159.00	135.00	-	-	**144.70**	**14.28**
	Thickness (mm)	3.47	3.47	3.44	3.46	3.46	3.49	3.46	3.48	3.47	3.44	-	-	**3.46**	**0.02**
	Diameter (mm)	9.59	9.70	9.62	9.62	9.61	9.63	9.61	9.61	9.61	9.62	-	-	**9.62**	**0.03**
	Disintegration time (sec)	16	16	16	16	16	16	16	16	16	17	17	17	**16.25**	**0.45**
	Friability (%)	1.5785													
Amberlite® IRP64	**Hardness (mm)**	117.00	115.00	121.00	121.00	128.00	112.00	105.00	115.00	104.00	118.00			**115.60**	**7.31**
	Thickness (mm)	3.52	3.57	3.60	3.57	3.58	3.60	3.56	3.57	3.59	3.55	-	-	**3.57**	**0.02**
	Diameter (mm)	9.61	9.60	9.58	9.58	9.61	9.64	9.72	9.68	9.63	9.61	-	-	**9.63**	**0.04**
	Disintegration time (sec)	23	24	24	25	25	26	26	27	27	28	28	28	**25.92**	**1.73**
	Friability (%)	1.9331													
Dowex® 1x2 - 200	**Hardness (mm)**	81.00	74.00	82.00	81.00	82.00	54.00	84.00	86.00	92.00	81.00	-	-	**79.70**	**10.10**
	Thickness (mm)	3.73	3.73	3.71	3.73	3.75	3.72	3.77	3.72	3.73	3.74	-	-	**3.73**	**0.02**
	Diameter (mm)	9.59	9.59	9.61	9.59	9.59	9.61	9.60	9.63	9.61	9.61	-	-	**9.60**	**0.01**
	Disintegration time (sec)	9	9	9	9	9	9	7	7	7	7	7	7	**8.00**	**1.04**
	Friability (%)	3.1331													

1.2 Dissolution of DMP

1.2.1 Standard curve of DMP

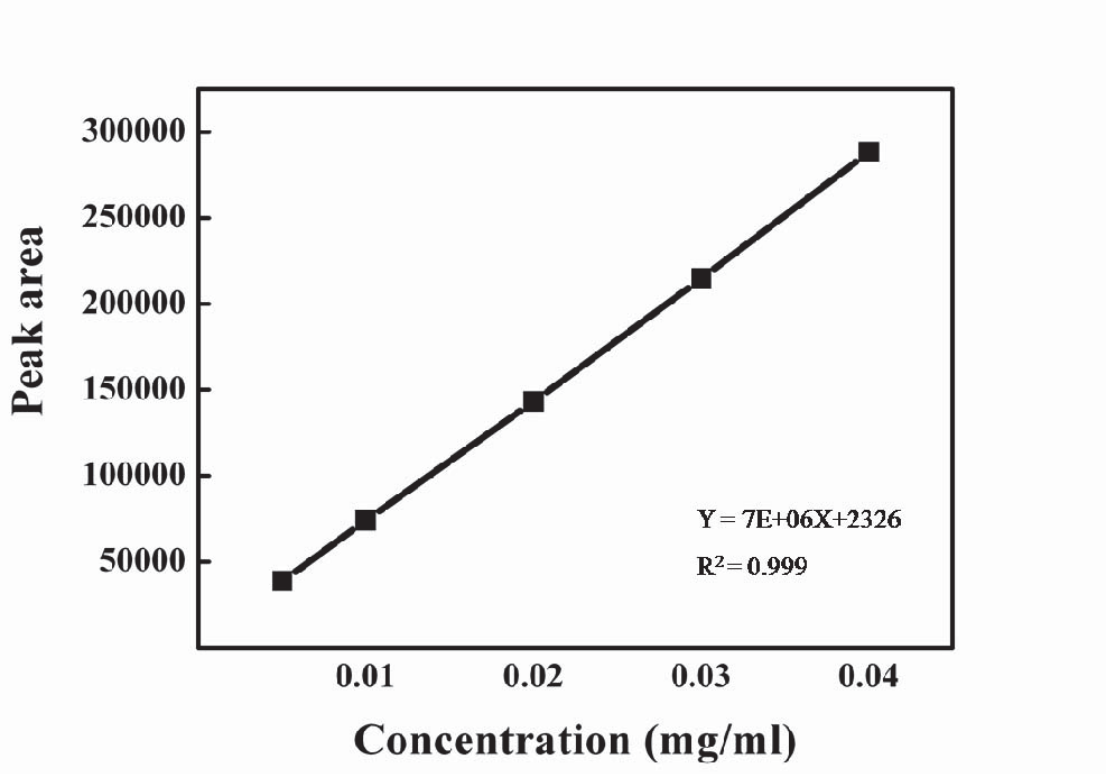
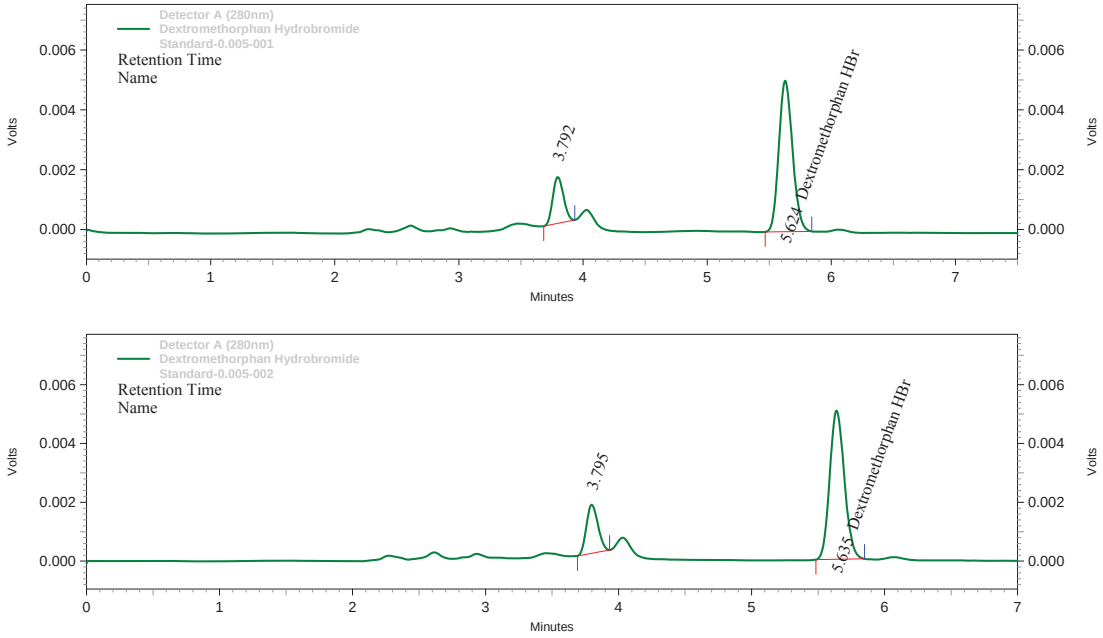


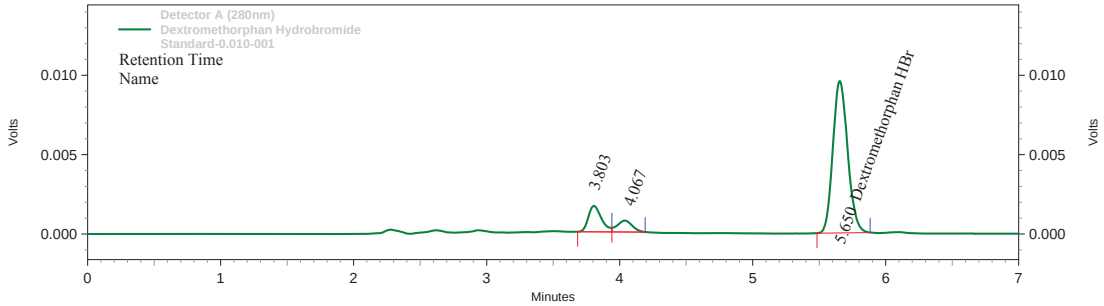
Fig. 33 Standard curve of DMP.

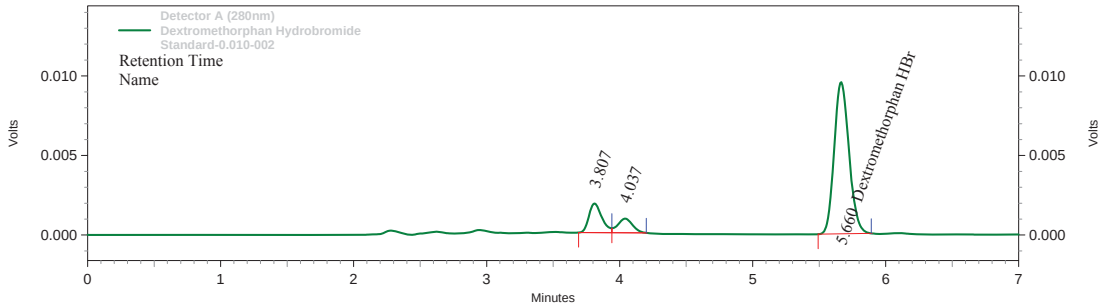
1.2.2 Peak area and chromatogram of DMP standard

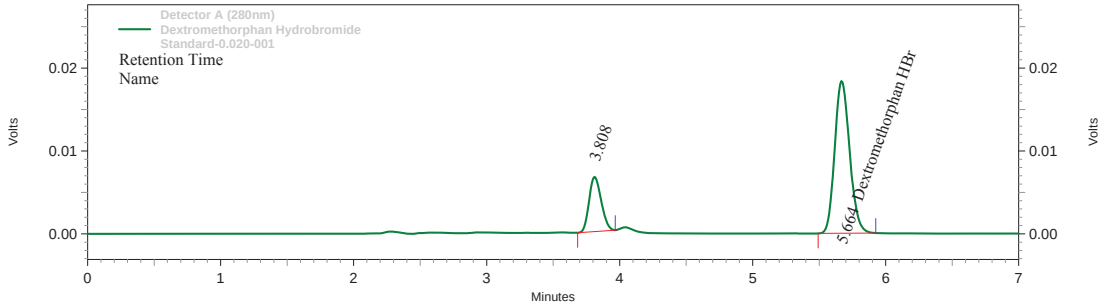
Table 55 Retention time and peak area of DMP standard

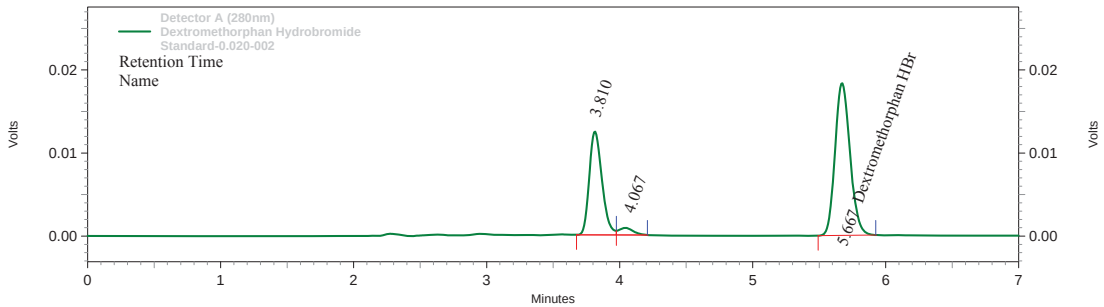
Concentration (mg/mL)	Retention time (min)	Peak area
0.005	5.624	38589
	5.635	38736
0.010	5.650	74035
	5.660	73961
0.020	5.664	143162
	5.667	143140
0.030	5.669	214809
	5.667	214833
0.040	5.663	288268
	5.662	287457

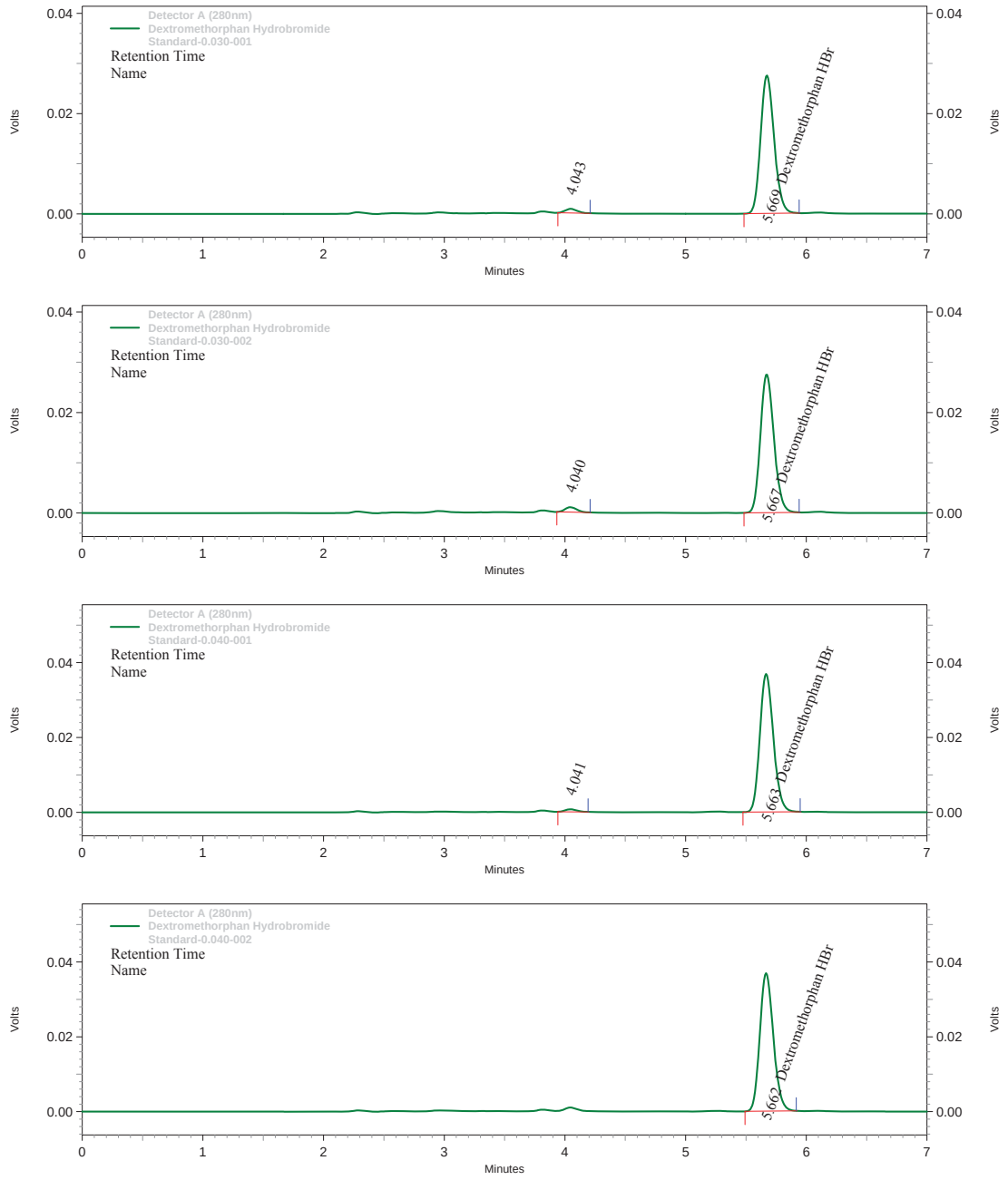



Detector A (280nm)
Dextromethorphan Hydrobromide
Standard-0.010-001
Retention Time
Name
3.803
4.067
5.650
Dextromethorphan HBr
Volts
Minutes


Detector A (280nm)
Dextromethorphan Hydrobromide
Standard-0.010-002
Retention Time
Name
3.807
4.037
5.660
Dextromethorphan HBr
Volts
Minutes


Detector A (280nm)
Dextromethorphan Hydrobromide
Standard-0.020-001
Retention Time
Name
3.808
5.664
Dextromethorphan HBr
Volts
Minutes


Detector A (280nm)
Dextromethorphan Hydrobromide
Standard-0.020-002
Retention Time
Name
3.810
4.067
5.667
Dextromethorphan HBr
Volts
Minutes

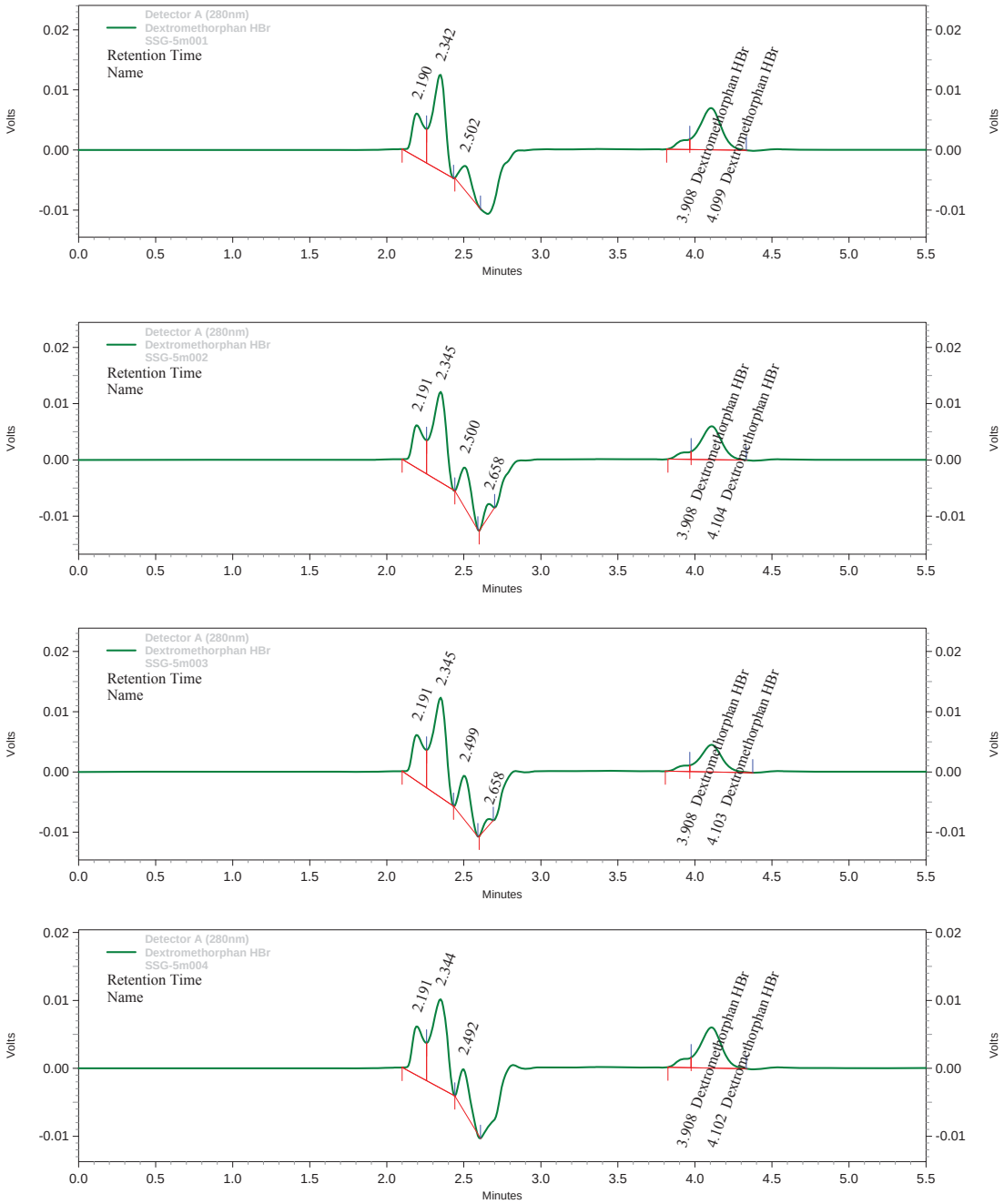

Detector A (280nm)
Dextromethorphan Hydrobromide
Standard-0.030-001
Retention Time
Name
4.043
5.669
Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan Hydrobromide
Standard-0.030-002
Retention Time
Name
4.040
5.667
Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan Hydrobromide
Standard-0.040-001
Retention Time
Name
4.041
5.663
Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan Hydrobromide
Standard-0.040-002
Retention Time
Name
5.662
Dextromethorphan HBr
Volts
Minutes

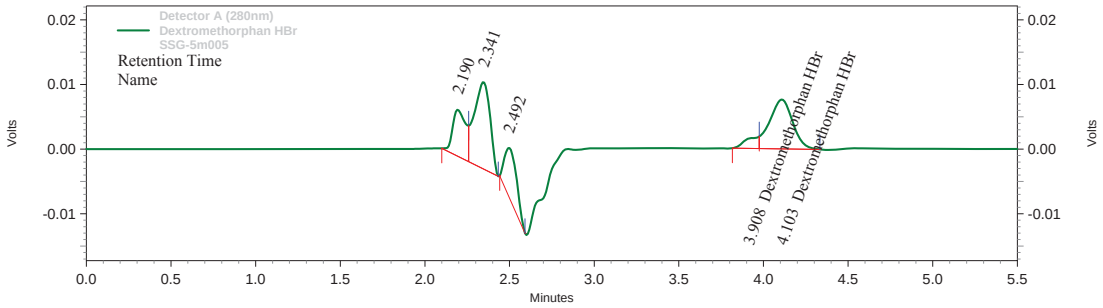
1.2.3 Peak area and chromatogram of DMP released from tablets containing SSG

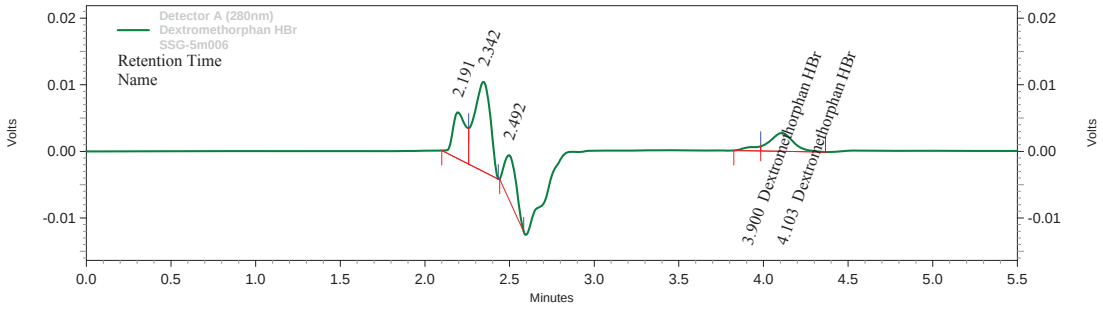
Table 56 Retention time and peak area of DMP released from tablets containing SSG

Sample	Retention time (min)	Peak area	Totals	Sample	Retention time (min)	Peak area	Totals
5m001	3.908	9185	76232	**30m001**	3.917	15140	124755
	4.099	67047			4.104	109615	
5m002	3.908	7784	63672	**30m002**	3.908	14740	117668
	4.104	55888			4.101	102928	
5m003	3.908	5721	49590	**30m003**	3.908	13107	104395
	4.103	43868			4.101	91289	
5m004	3.908	8154	64971	**30m004**	3.908	15157	121704
	4.102	56816			4.101	106547	
5m005	3.908	10571	82087	**30m005**	3.908	15332	123018
	4.103	71516			4.102	107686	
5m006	3.900	3859	29715	**30m006**	3.908	15162	117272
	4.103	25856			4.100	102110	
10m001	3.917	12880	101683	**1h001**	3.908	15943	123946
	4.106	88804			4.100	108002	
10m002	3.908	10040	79978	**1h002**	3.908	16042	124899
	4.106	69938			4.101	108858	
10m003	3.908	8493	66236	**1h003**	3.908	14962	118836
	4.104	57742			4.101	103874	
10m004	3.908	10791	89108	**1h004**	3.908	16640	128186
	4.101	78316			4.100	111546	
10m005	3.908	12588	102591	**1h005**	3.908	15728	125548
	4.103	90003			4.101	109819	
10m006	3.908	8914	65099	**1h006**	3.908	15700	126323
	4.104	56185			4.101	110623	
15m001	3.917	14296	117555	**2h001**	3.900	15322	126073
	4.103	103259			4.097	110752	
15m002	3.908	12675	95796	**2h002**	3.900	16356	126748
	4.103	83121			4.098	110392	
15m003	3.908	9890	78087	**2h003**	3.908	15543	125742
	4.105	68197			4.100	110198	
15m004	3.908	12514	102355	**2h004**	3.908	15066	125719
	4.101	89841			4.098	110653	
15m005	3.917	13753	111558	**2h005**	3.908	16261	129019
	4.103	97805			4.101	112758	
15m006	3.908	10617	86255	**2h006**	3.908	15625	128411
	4.100	75638			4.097	112785	

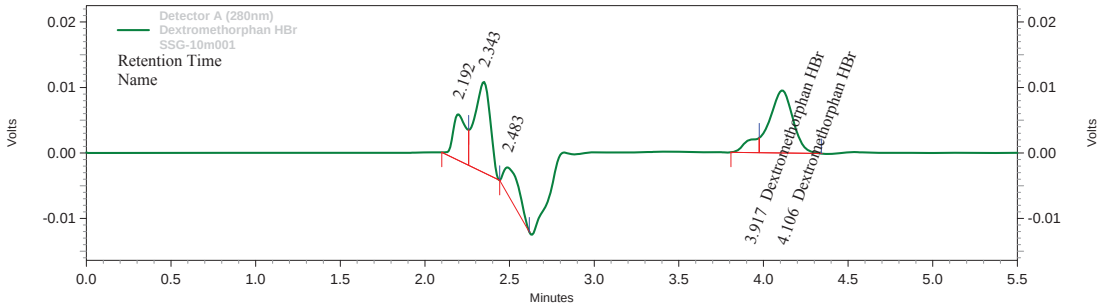
5 min

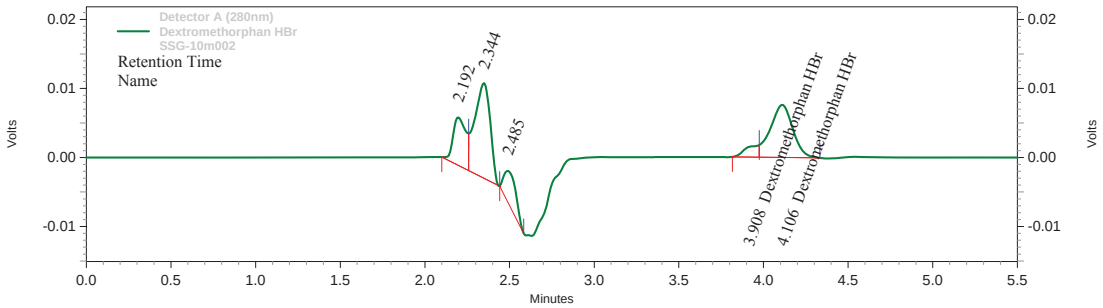

Detector A (280nm)
Dextromethorphan HBr
SSG-5m001
Retention Time
Name
2.190
2.342
2.502
3.908 Dextromethorphan HBr
4.099 Dextromethorphan HBr
Detector A (280nm)
Dextromethorphan HBr
SSG-5m002
Retention Time
Name
2.191
2.345
2.500
2.658
3.908 Dextromethorphan HBr
4.104 Dextromethorphan HBr
Detector A (280nm)
Dextromethorphan HBr
SSG-5m003
Retention Time
Name
2.191
2.345
2.499
2.658
3.908 Dextromethorphan HBr
4.103 Dextromethorphan HBr
Detector A (280nm)
Dextromethorphan HBr
SSG-5m004
Retention Time
Name
2.191
2.344
2.492
3.908 Dextromethorphan HBr
4.102 Dextromethorphan HBr
Volts
Minutes
0.02
0.01
0.00
-0.01
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5

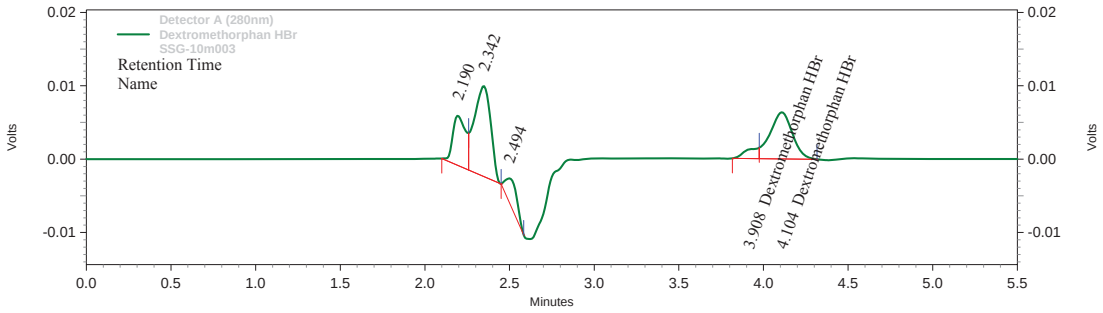

Detector A (280nm)
Dextromethorphan HBr
SSG-5m005
Retention Time
Name
2.190
2.341
2.492
3.908 Dextromethorphan HBr
4.103 Dextromethorphan HBr
Volts
Minutes

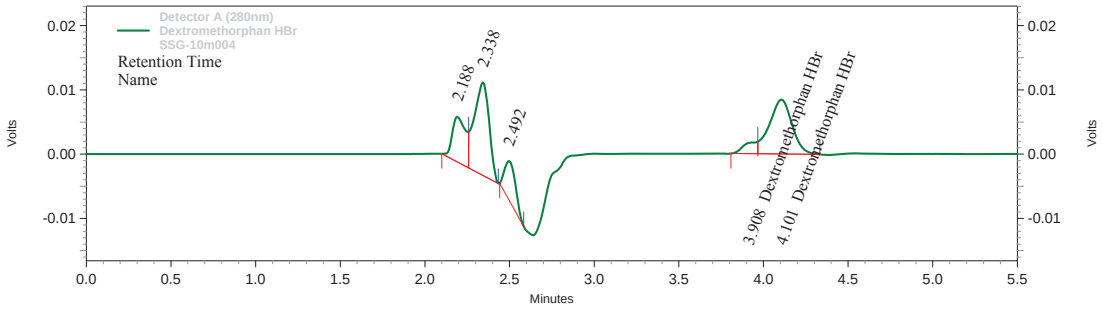

Detector A (280nm)
Dextromethorphan HBr
SSG-5m006
Retention Time
Name
2.191
2.342
2.492
3.900 Dextromethorphan HBr
4.103 Dextromethorphan HBr
Volts
Minutes

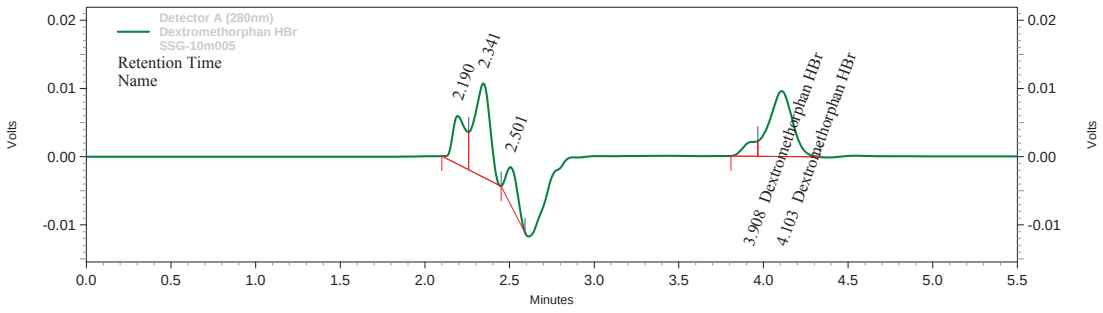
10 min

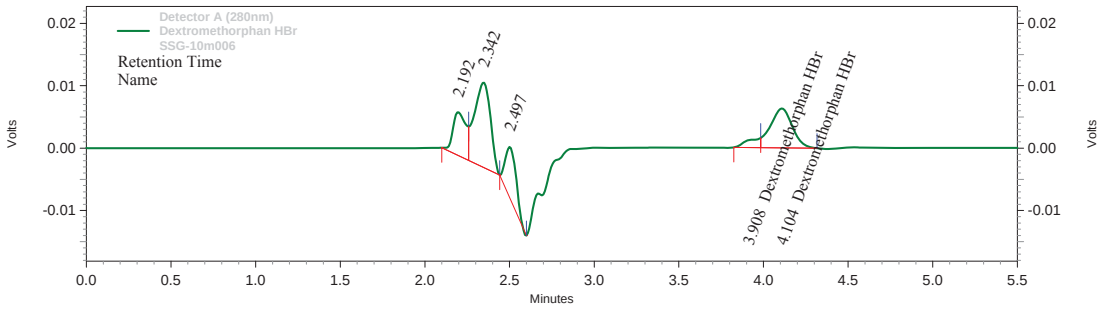

Detector A (280nm)
Dextromethorphan HBr
SSG-10m001
Retention Time
Name
2.192
2.343
2.483
3.917 Dextromethorphan HBr
4.106 Dextromethorphan HBr
Volts
Minutes


Detector A (280nm)
Dextromethorphan HBr
SSG-10m002
Retention Time
Name
2.192
2.344
2.485
3.908 Dextromethorphan HBr
4.106 Dextromethorphan HBr
Volts
Minutes

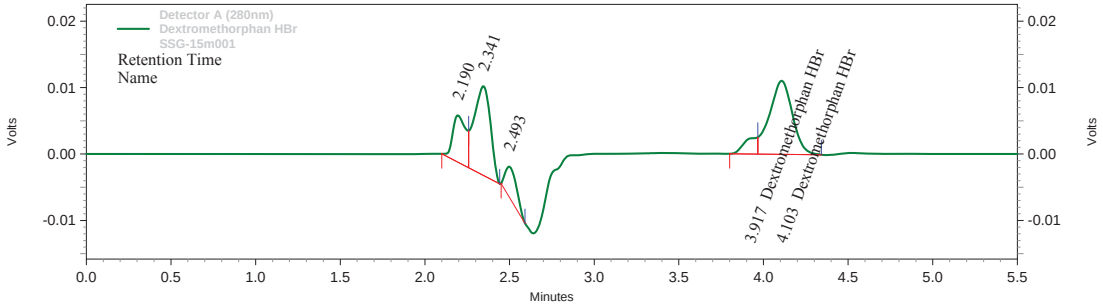

Detector A (280nm)
Dextromethorphan HBr
SSG-10m003
Retention Time
Name
2.190
2.342
2.494
3.908 Dextromethorphan HBr
4.104 Dextromethorphan HBr
Volts
Minutes

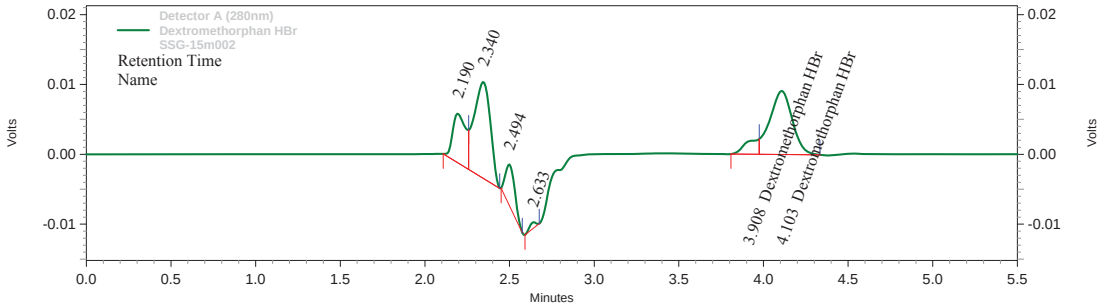

Detector A (280nm)
Dextromethorphan HBr
SSG-10m004
Retention Time
Name
2.188
2.338
2.492
3.908 Dextromethorphan HBr
4.101 Dextromethorphan HBr
Volts
Minutes

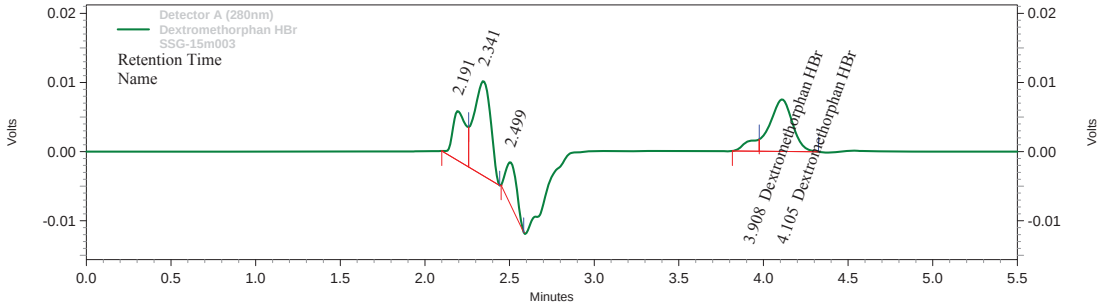

Detector A (280nm)
Dextromethorphan HBr
SSG-10m005
Retention Time
Name
2.190
2.341
2.501
3.908 Dextromethorphan HBr
4.103 Dextromethorphan HBr
Volts
Minutes

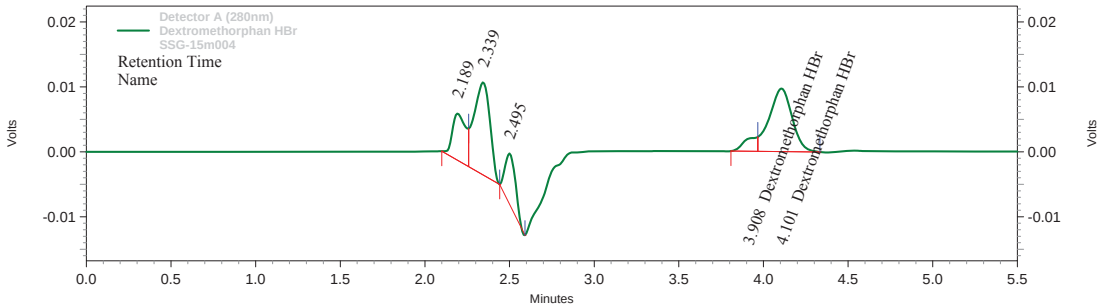

Detector A (280nm)
Dextromethorphan HBr
SSG-10m006
Retention Time
Name
2.192
2.342
2.497
3.908 Dextromethorphan HBr
4.104 Dextromethorphan HBr
Volts
Minutes

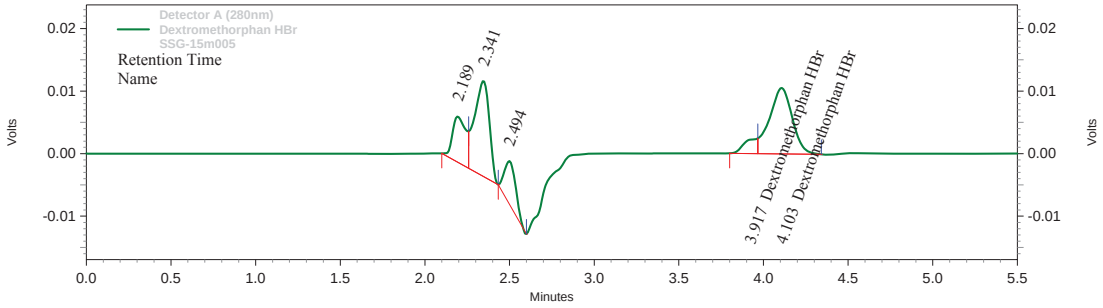
15 min

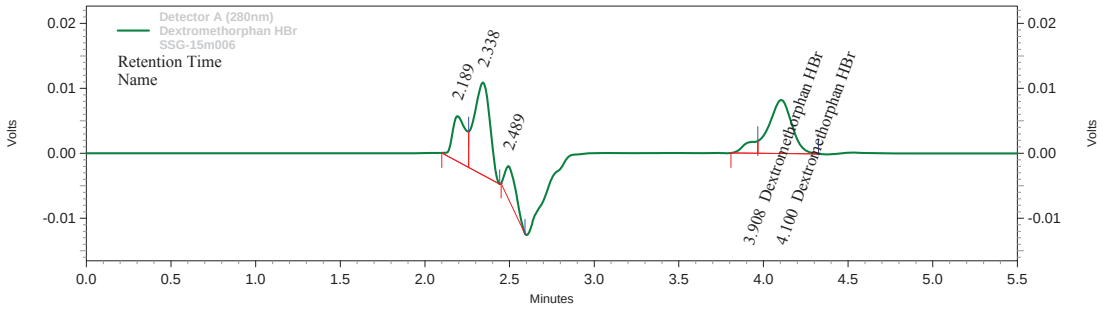

Detector A (280nm)
Dextromethorphan HBr
SSG-15m001
Retention Time
Name
2.190
2.341
2.493
3.917 Dextromethorphan HBr
4.103 Dextromethorphan HBr
Volts
Minutes


Detector A (280nm)
Dextromethorphan HBr
SSG-15m002
Retention Time
Name
2.190
2.340
2.494
2.633
3.908 Dextromethorphan HBr
4.103 Dextromethorphan HBr
Volts
Minutes

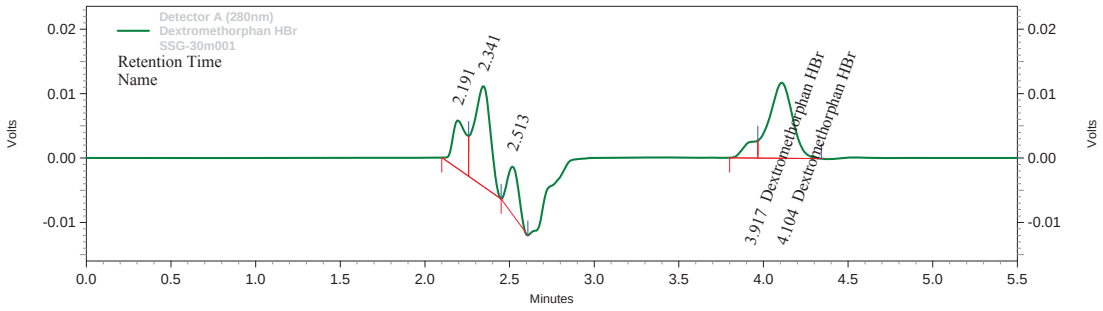

Detector A (280nm)
Dextromethorphan HBr
SSG-15m003
Retention Time
Name
2.191
2.341
2.499
3.908 Dextromethorphan HBr
4.105 Dextromethorphan HBr
Volts
Minutes

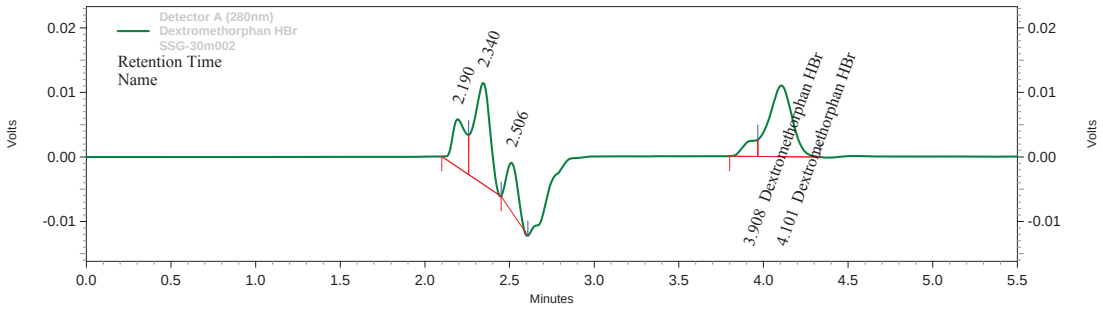

Detector A (280nm)
Dextromethorphan HBr
SSG-15m004
Retention Time
Name
2.189
2.339
2.495
3.908 Dextromethorphan HBr
4.101 Dextromethorphan HBr
Volts
Minutes

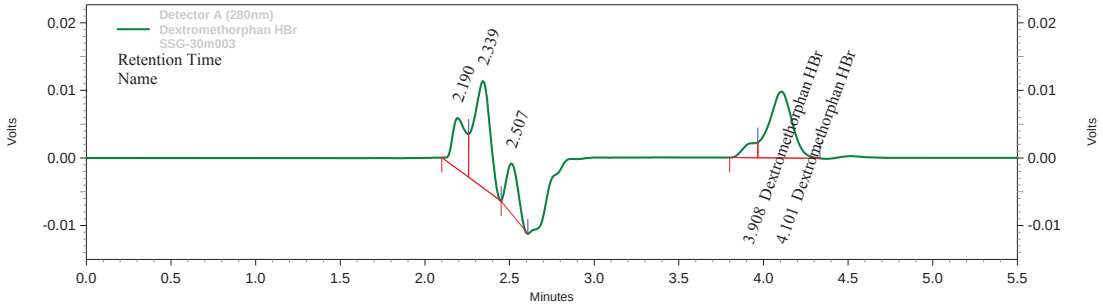

Detector A (280nm)
Dextromethorphan HBr
SSG-15m005
Retention Time
Name
2.189
2.341
2.494
3.917 Dextromethorphan HBr
4.103 Dextromethorphan HBr
Volts
Minutes

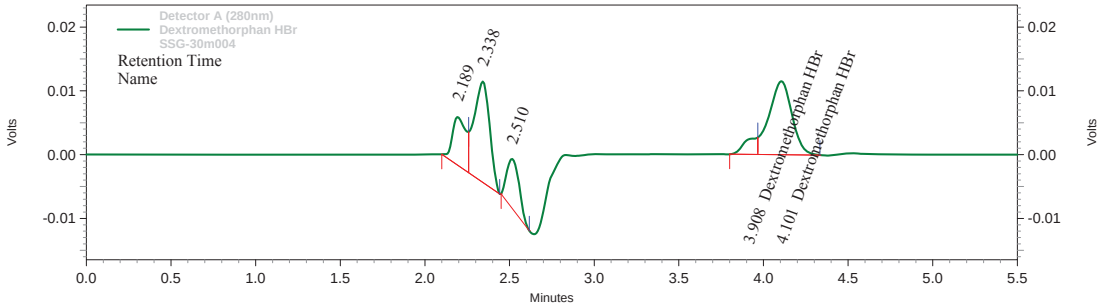

Detector A (280nm)
Dextromethorphan HBr
SSG-15m006
Retention Time
Name
2.189
2.338
2.489
3.908 Dextromethorphan HBr
4.100 Dextromethorphan HBr
Volts
Minutes

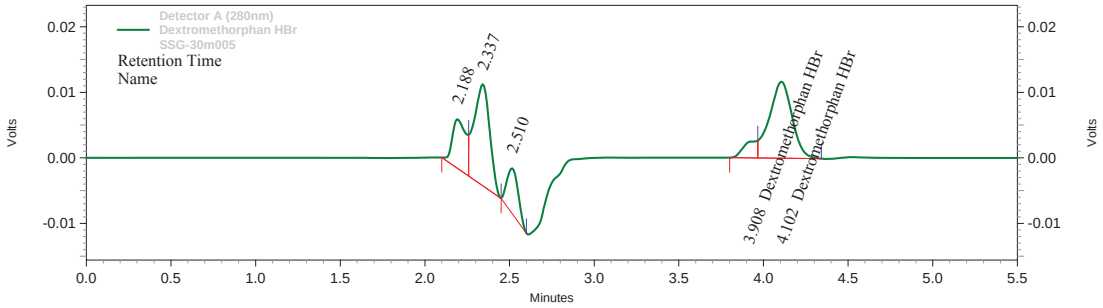
30 min

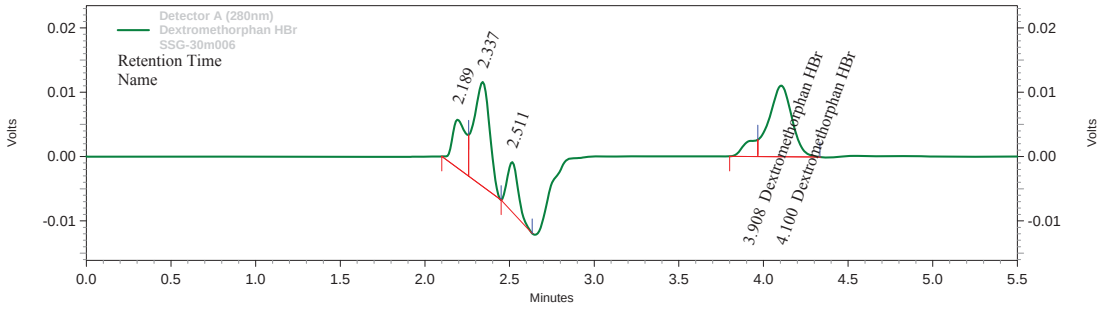

Detector A (280nm)
Dextromethorphan HBr
SSG-30m001
Retention Time
Name
2.191
2.341
2.513
3.917 Dextromethorphan HBr
4.104 Dextromethorphan HBr
Volts
Minutes


Detector A (280nm)
Dextromethorphan HBr
SSG-30m002
Retention Time
Name
2.190
2.340
2.506
3.908 Dextromethorphan HBr
4.101 Dextromethorphan HBr
Volts
Minutes

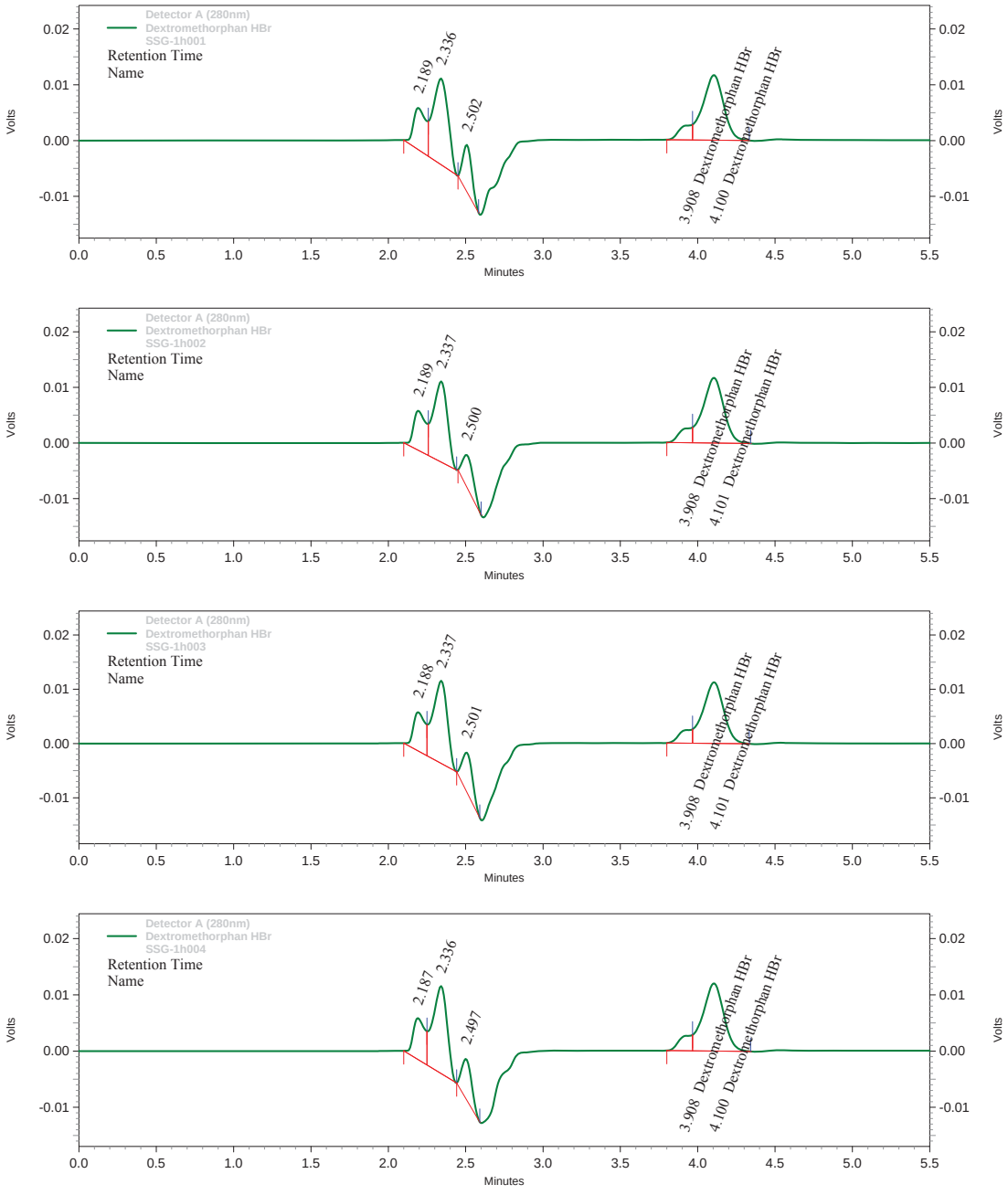

Detector A (280nm)
Dextromethorphan HBr
SSG-30m003
Retention Time
Name
2.190
2.339
2.507
3.908 Dextromethorphan HBr
4.101 Dextromethorphan HBr
Volts
Minutes

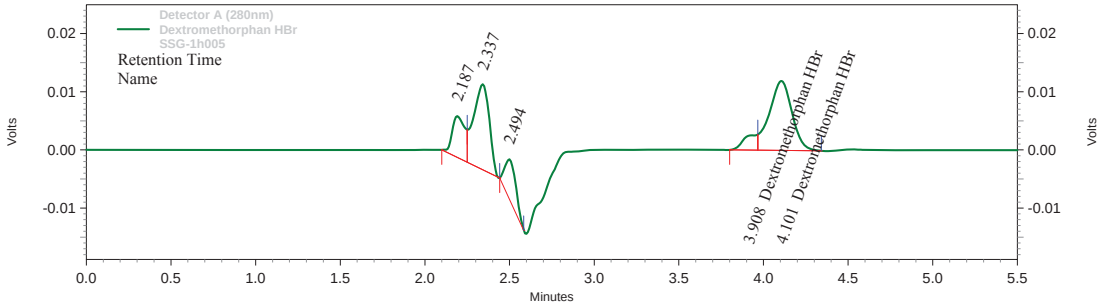

Detector A (280nm)
Dextromethorphan HBr
SSG-30m004
Retention Time
Name
2.189
2.338
2.510
3.908 Dextromethorphan HBr
4.101 Dextromethorphan HBr
Volts
Minutes

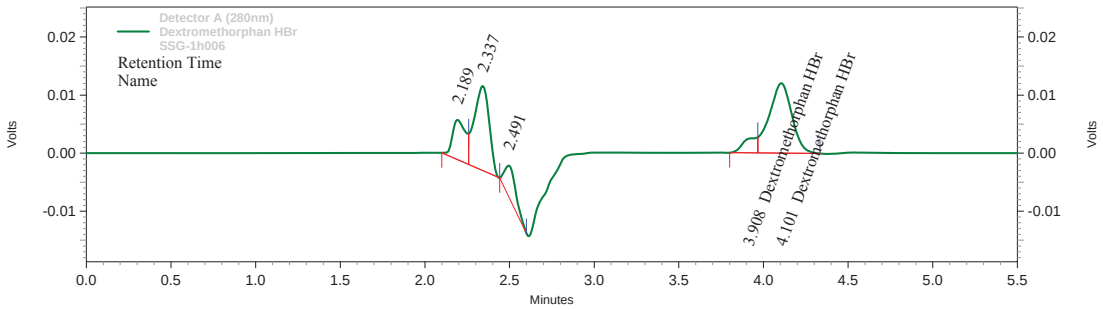

Detector A (280nm)
Dextromethorphan HBr
SSG-30m005
Retention Time
Name
2.188
2.337
2.510
3.908 Dextromethorphan HBr
4.102 Dextromethorphan HBr
Volts
Minutes


Detector A (280nm)
Dextromethorphan HBr
SSG-30m006
Retention Time
Name
2.189
2.337
2.511
3.908 Dextromethorphan HBr
4.100 Dextromethorphan HBr
Volts
Minutes

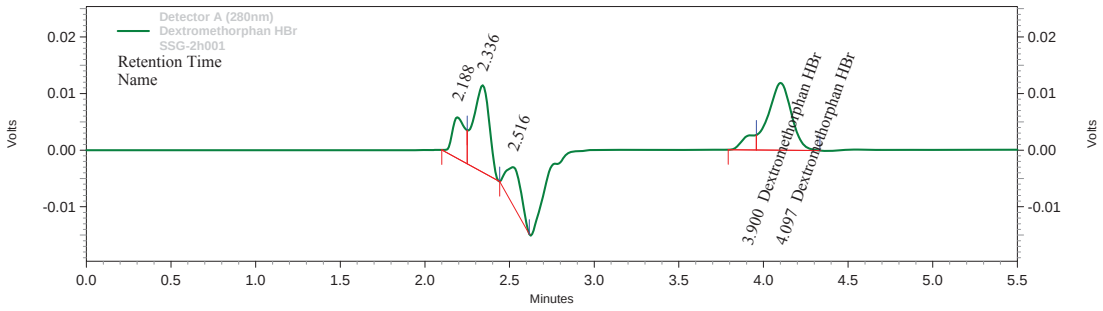
1 h

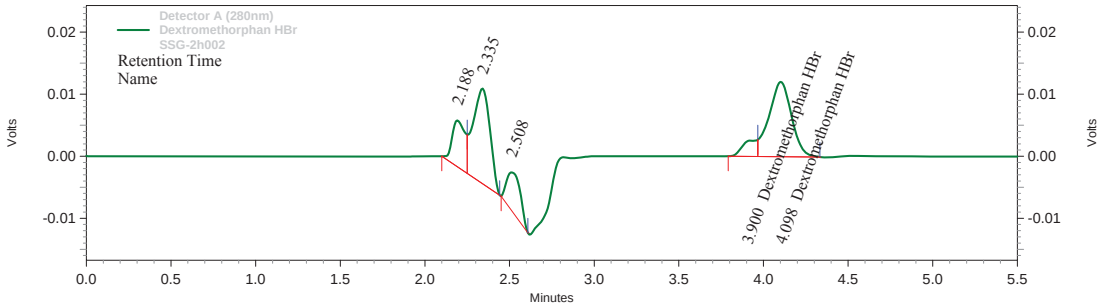

Detector A (280nm)
Dextromethorphan HBr
SSG-1h001
Retention Time
Name
2.189
2.336
2.502
3.908 Dextromethorphan HBr
4.100 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
SSG-1h002
Retention Time
Name
2.189
2.337
2.500
3.908 Dextromethorphan HBr
4.101 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
SSG-1h003
Retention Time
Name
2.188
2.337
2.501
3.908 Dextromethorphan HBr
4.101 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
SSG-1h004
Retention Time
Name
2.187
2.336
2.497
3.908 Dextromethorphan HBr
4.100 Dextromethorphan HBr
Volts
Minutes

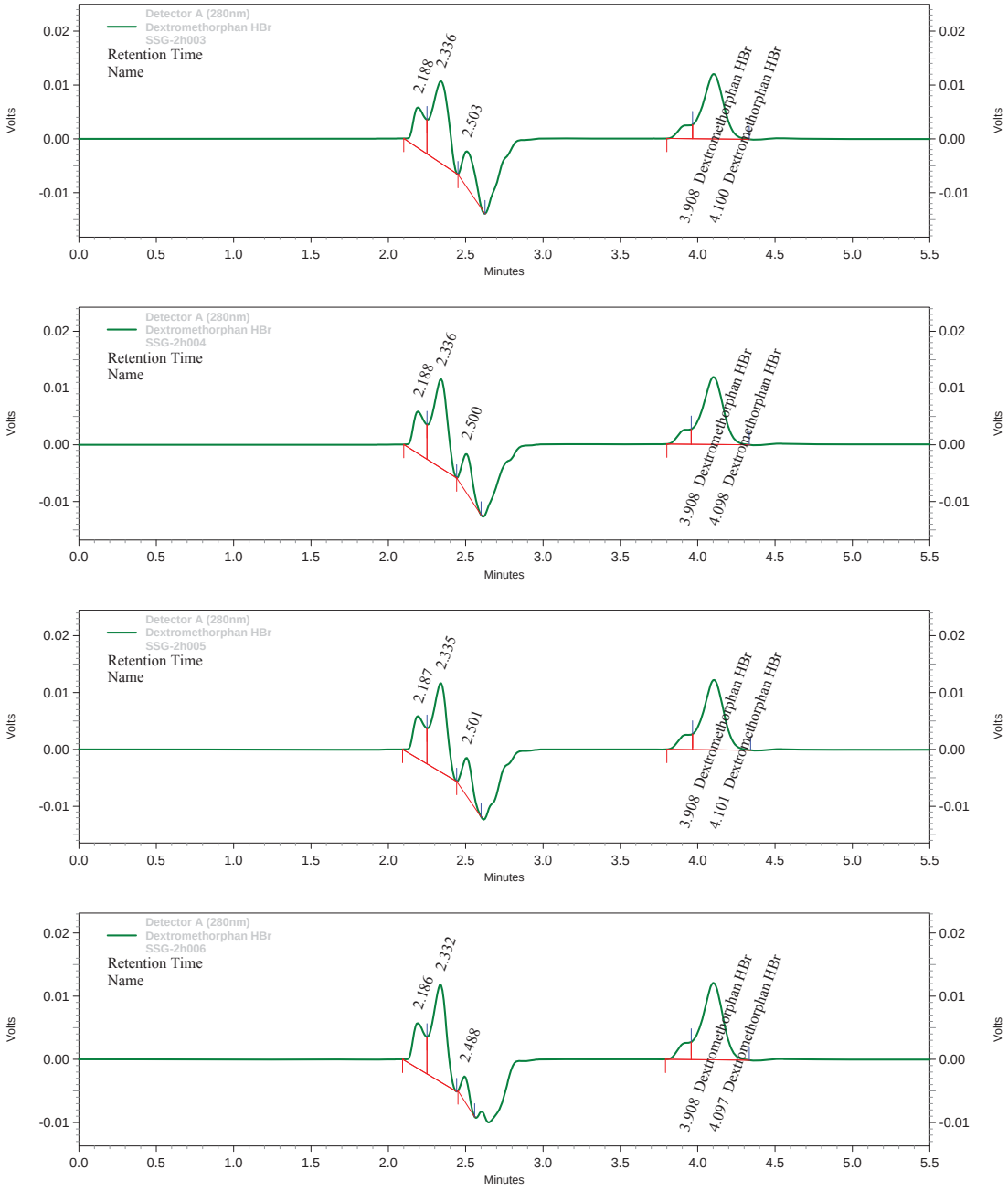

Detector A (280nm)
Dextromethorphan HBr
SSG-1h005
Retention Time
Name
2.187
2.337
2.494
3.908 Dextromethorphan HBr
4.101 Dextromethorphan HBr
Volts
Minutes


Detector A (280nm)
Dextromethorphan HBr
SSG-1h006
Retention Time
Name
2.189
2.337
2.491
3.908 Dextromethorphan HBr
4.101 Dextromethorphan HBr
Volts
Minutes

2 h


Detector A (280nm)
Dextromethorphan HBr
SSG-2h001
Retention Time
Name
2.188
2.336
2.516
3.900 Dextromethorphan HBr
4.097 Dextromethorphan HBr
Volts
Minutes


Detector A (280nm)
Dextromethorphan HBr
SSG-2h002
Retention Time
Name
2.188
2.335
2.508
3.900 Dextromethorphan HBr
4.098 Dextromethorphan HBr
Volts
Minutes

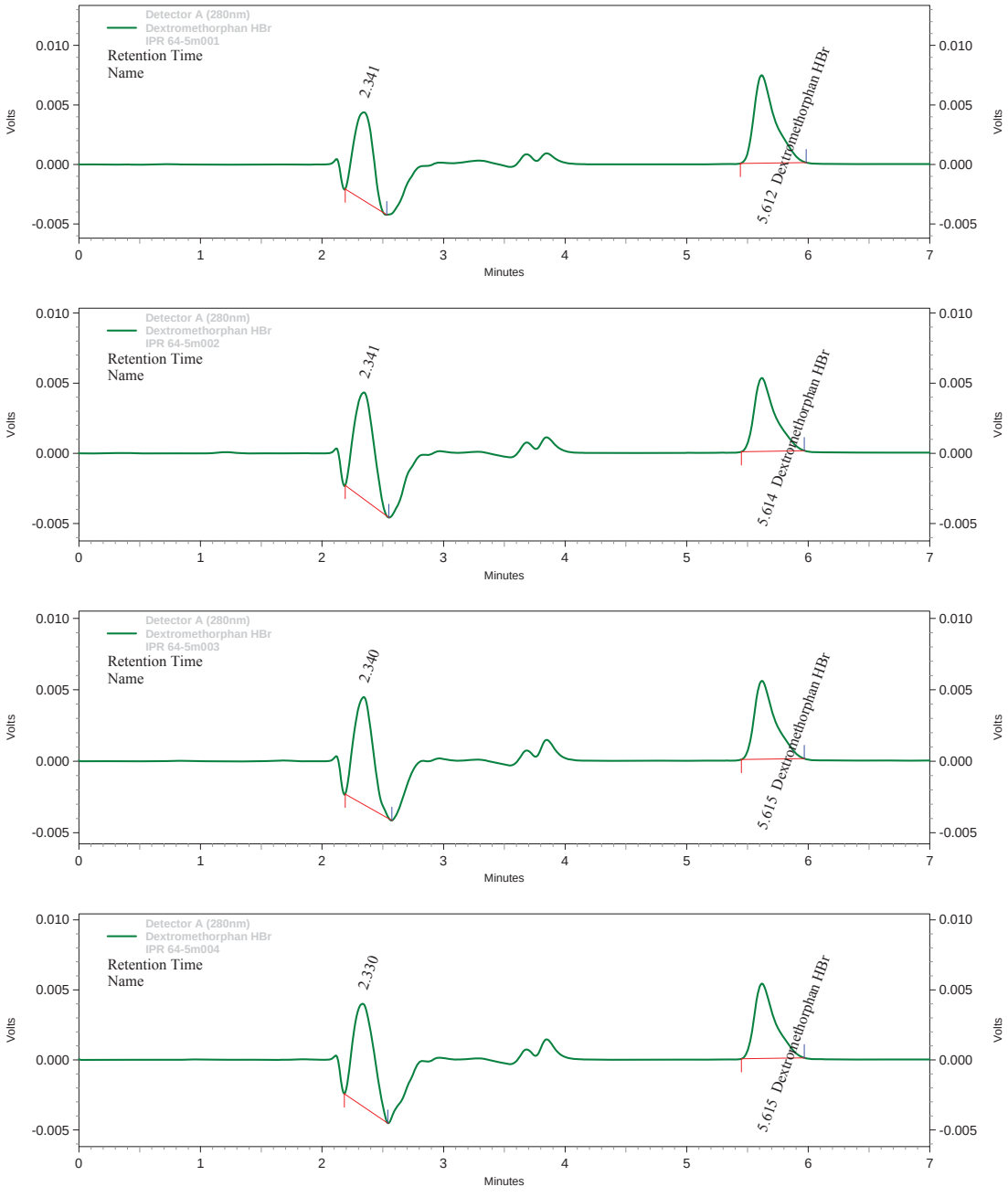

Detector A (280nm)
Dextromethorphan HBr
SSG-2h003
Retention Time
Name
2.188
2.336
2.503
3.908 Dextromethorphan HBr
4.100 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
SSG-2h004
Retention Time
Name
2.188
2.336
2.500
3.908 Dextromethorphan HBr
4.098 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
SSG-2h005
Retention Time
Name
2.187
2.335
2.501
3.908 Dextromethorphan HBr
4.101 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
SSG-2h006
Retention Time
Name
2.186
2.332
2.488
3.908 Dextromethorphan HBr
4.097 Dextromethorphan HBr
Volts
Minutes

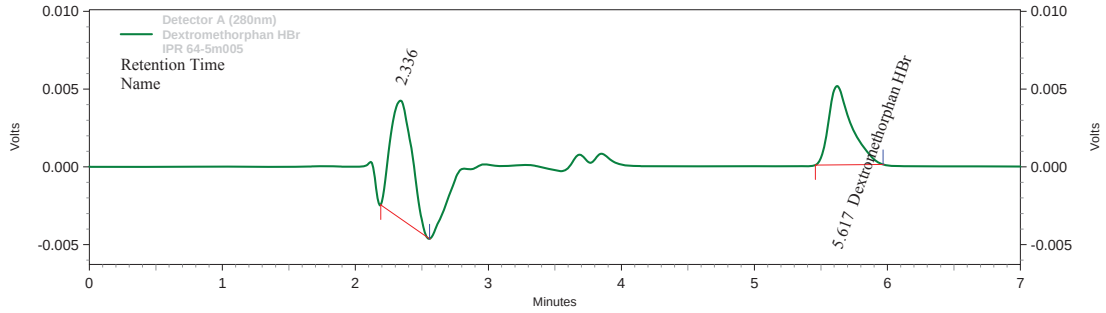
1.2.4 Peak area and chromatogram of DMP released from tablets containing Amberlite® IRP64

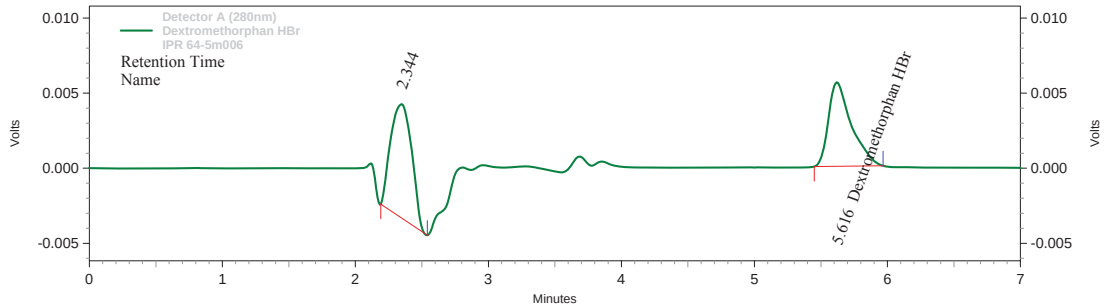
Table 57 Retention time and peak area of DMP released from tablets containing Amberlite® IRP64

Sample	Retention time (min)	Peak area
5m001	5.612	90071
5m002	5.614	63233
5m003	5.615	66156
5m004	5.615	64174
5m005	5.617	60669
5m006	5.616	66813
10m001	5.611	78900
10m002	5.608	71563
10m003	5.613	84375
10m004	5.612	80965
10m005	5.608	90245
10m006	5.610	84755
15m001	5.612	89136
15m002	5.608	81026
15m003	5.614	89089
15m004	5.609	86211
15m005	5.612	103487
15m006	5.609	101779
30m001	5.606	89596
30m002	5.615	85990
30m003	5.605	95942
30m004	5.604	92190
30m005	5.603	107584
30m006	5.600	97017
1h001	5.605	95748
1h002	5.596	91247
1h003	5.605	98683
1h004	5.598	95434
1h005	5.601	110381
1h006	5.598	97745
2h001	5.595	105038
2h002	5.601	96598
2h003	5.597	102137
2h004	5.589	101650
2h005	5.588	118857
2h006	5.589	103827

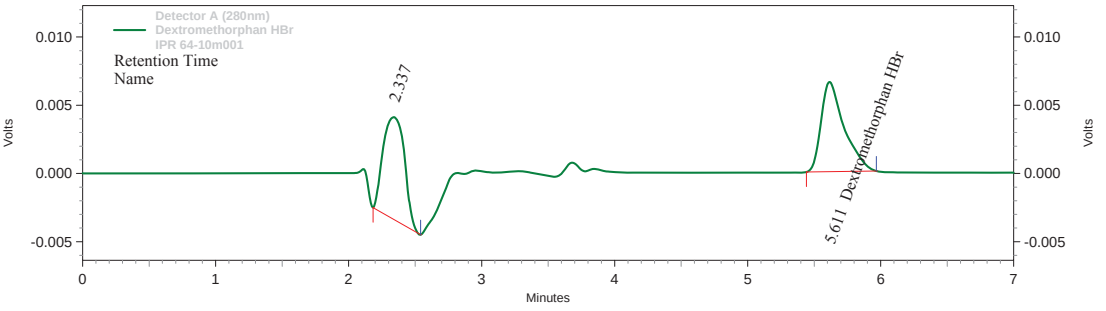
5min

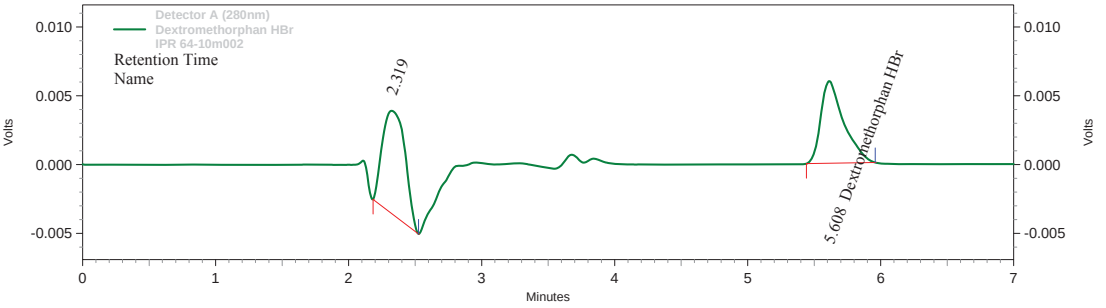

Detector A (280nm)
Dextromethorphan HBr
IPR 64-5m001
Retention Time
Name
2.341
5.612 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
IPR 64-5m002
Retention Time
Name
2.341
5.614 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
IPR 64-5m003
Retention Time
Name
2.340
5.615 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
IPR 64-5m004
Retention Time
Name
2.330
5.615 Dextromethorphan HBr
Volts
Minutes

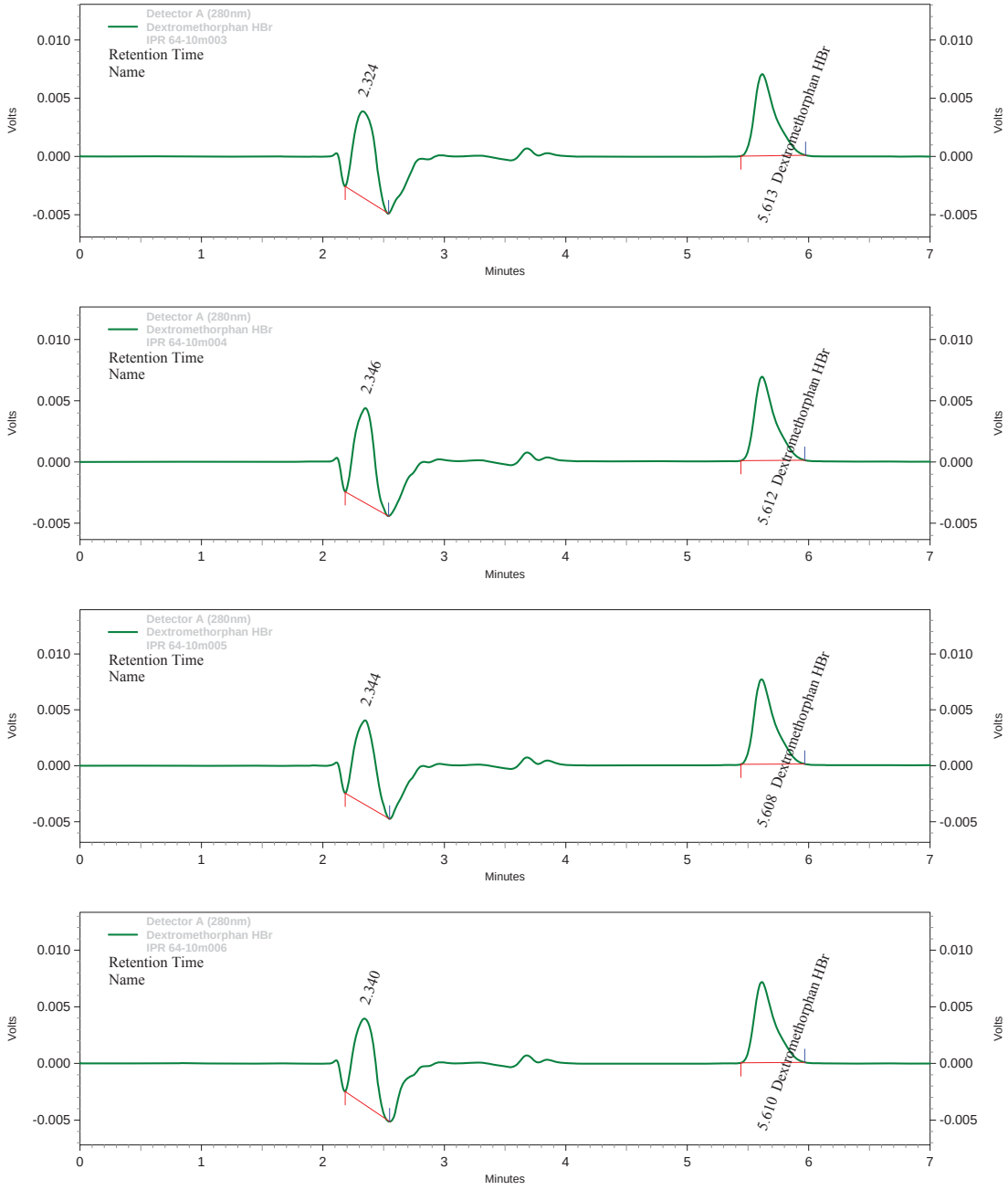

Detector A (280nm)
Dextromethorphan HBr
IPR 64-5m005
Retention Time
Name
2.336
5.617 Dextromethorphan HBr
Volts
Minutes


Detector A (280nm)
Dextromethorphan HBr
IPR 64-5m006
Retention Time
Name
2.344
5.616 Dextromethorphan HBr
Volts
Minutes

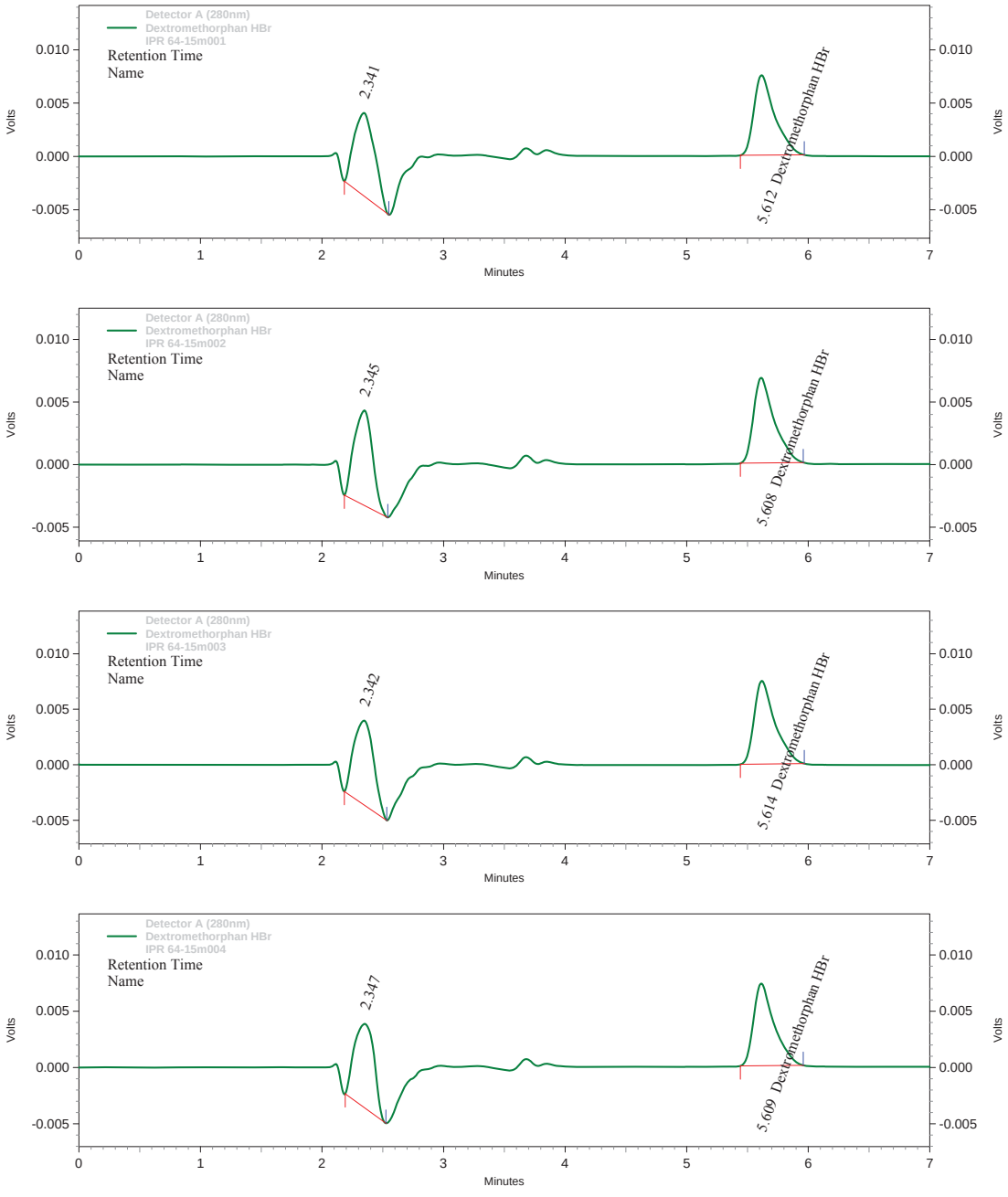
10 min

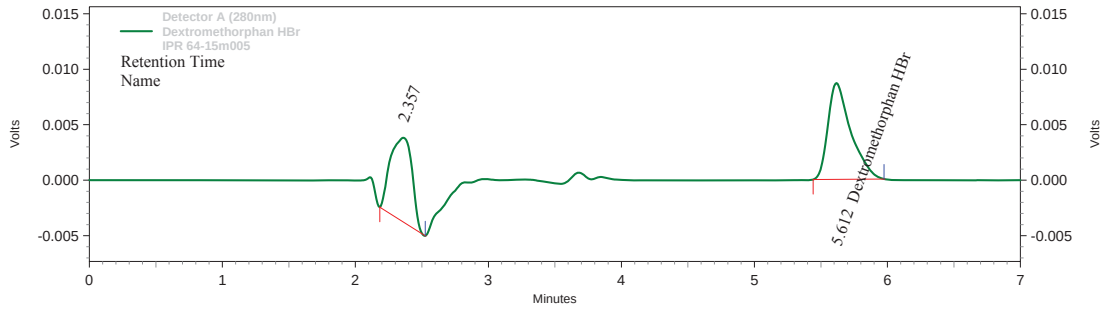

Detector A (280nm)
Dextromethorphan HBr
IPR 64-10m001
Retention Time
Name
2.337
5.611 Dextromethorphan HBr
Volts
Minutes

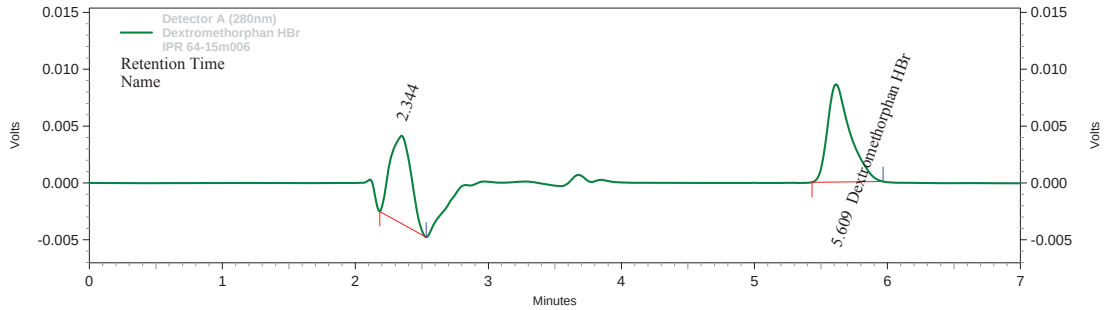

Detector A (280nm)
Dextromethorphan HBr
IPR 64-10m002
Retention Time
Name
2.319
5.608 Dextromethorphan HBr
Volts
Minutes


Detector A (280nm)
Dextromethorphan HBr
IPR 64-10m003
Retention Time
Name
2.324
5.613 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
IPR 64-10m004
Retention Time
Name
2.346
5.612 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
IPR 64-10m005
Retention Time
Name
2.344
5.608 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
IPR 64-10m006
Retention Time
Name
2.340
5.610 Dextromethorphan HBr
Volts
Minutes

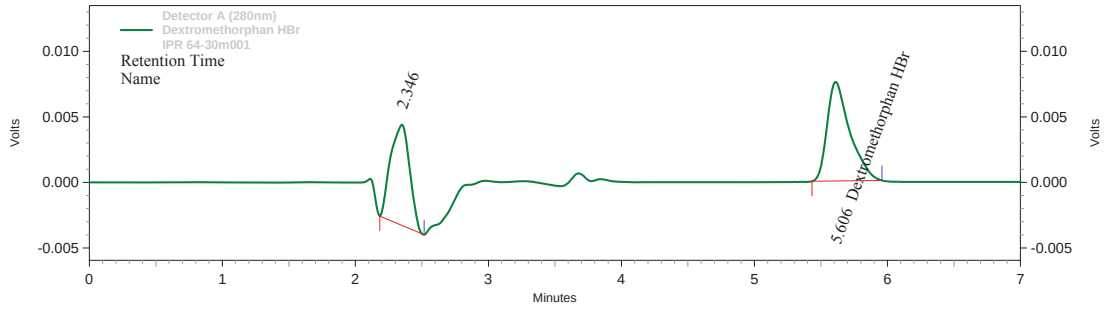
15 min

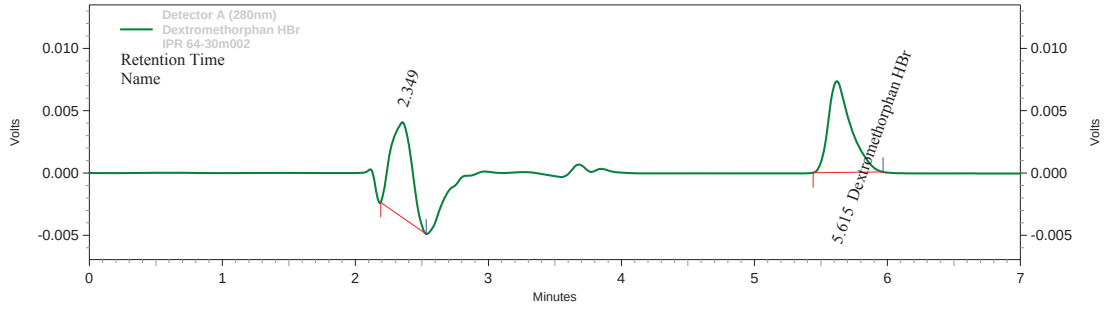

Detector A (280nm)
Dextromethorphan HBr
IPR 64-15m001
Retention Time
Name
2.341
5.612 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
IPR 64-15m002
Retention Time
Name
2.345
5.608 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
IPR 64-15m003
Retention Time
Name
2.342
5.614 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
IPR 64-15m004
Retention Time
Name
2.347
5.609 Dextromethorphan HBr
Volts
Minutes

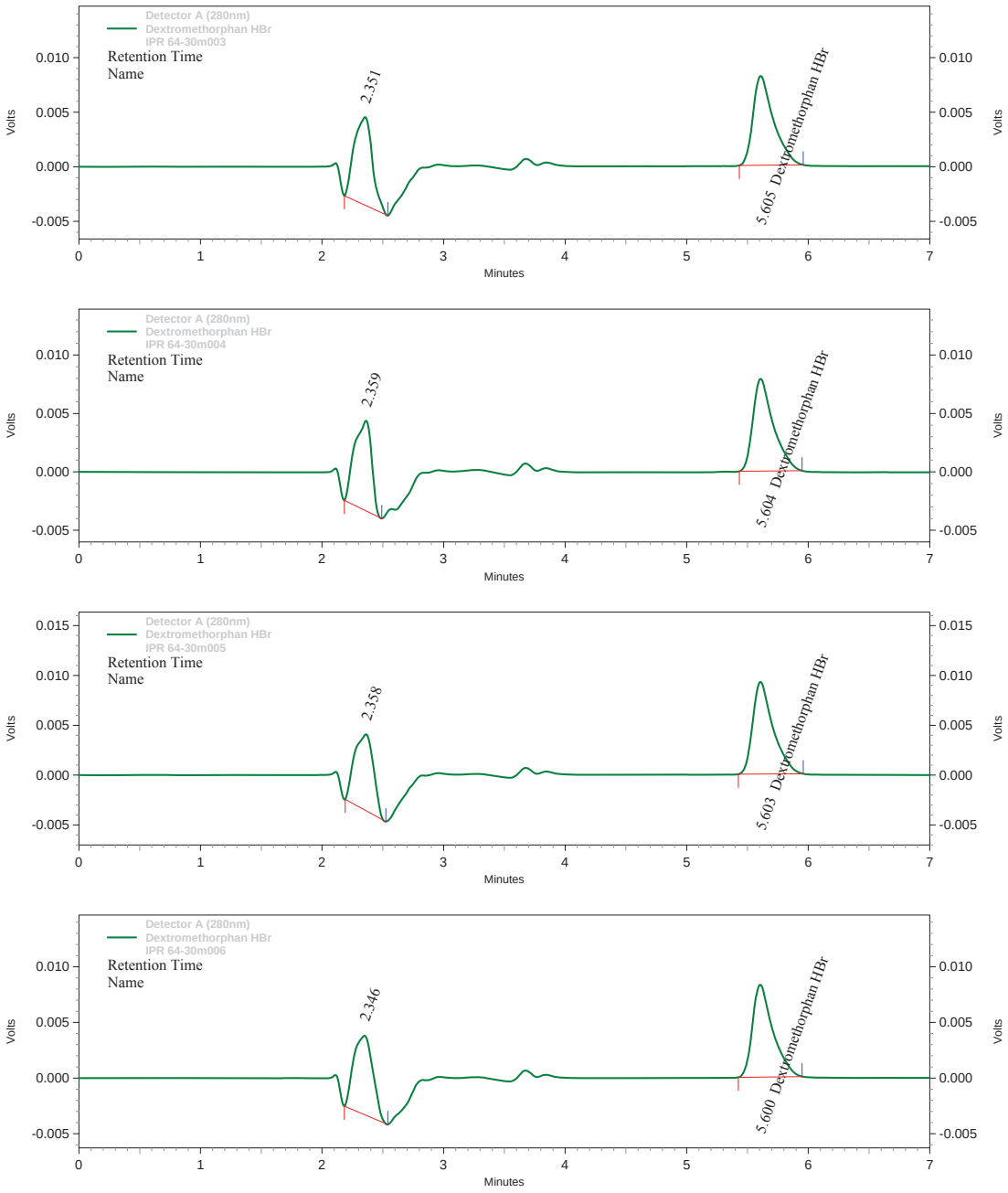

Detector A (280nm)
Dextromethorphan HBr
IPR 64-15m005
Retention Time
Name
2.357
5.612 Dextromethorphan HBr
Volts
Minutes


Detector A (280nm)
Dextromethorphan HBr
IPR 64-15m006
Retention Time
Name
2.344
5.609 Dextromethorphan HBr
Volts
Minutes

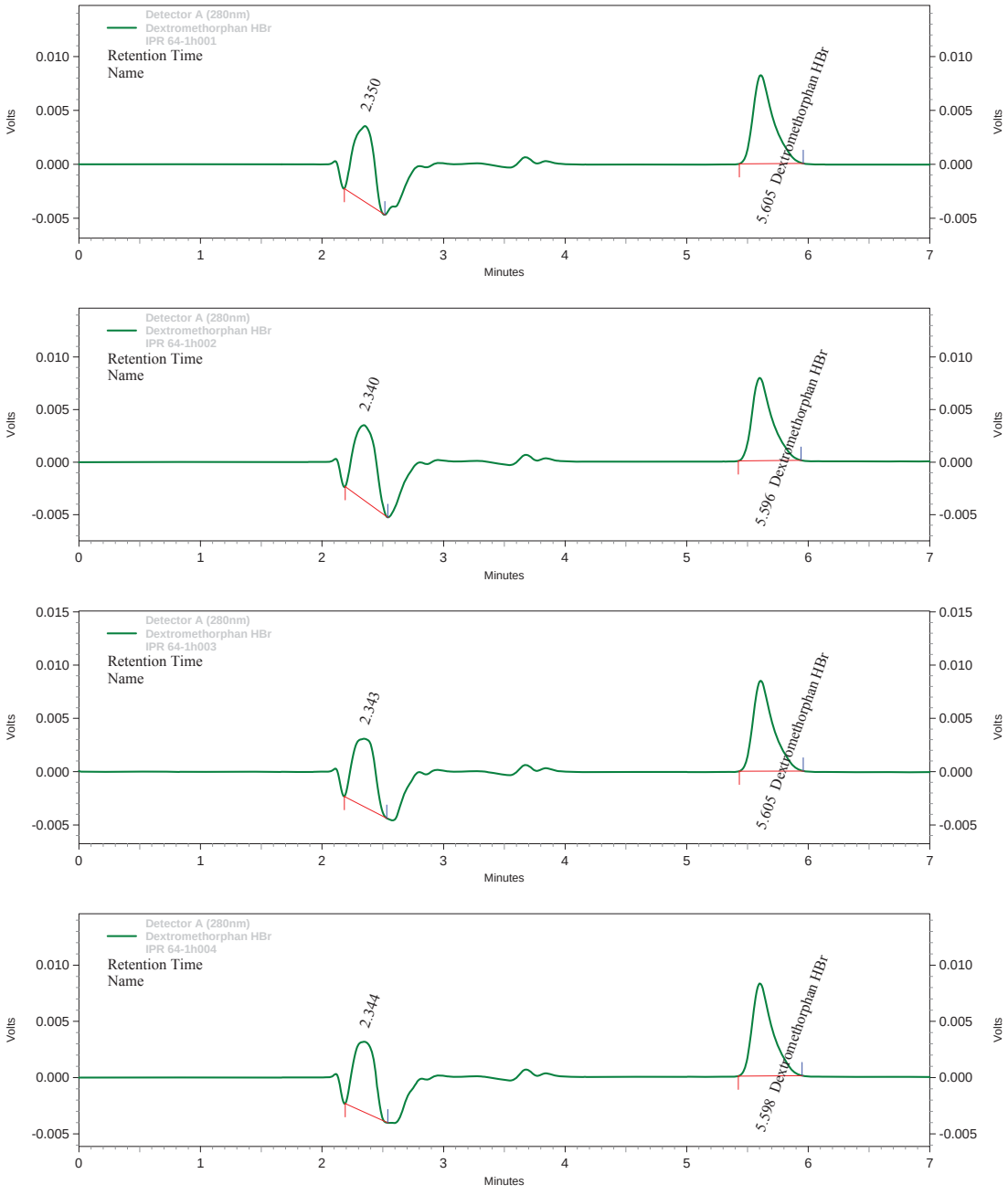
30 min

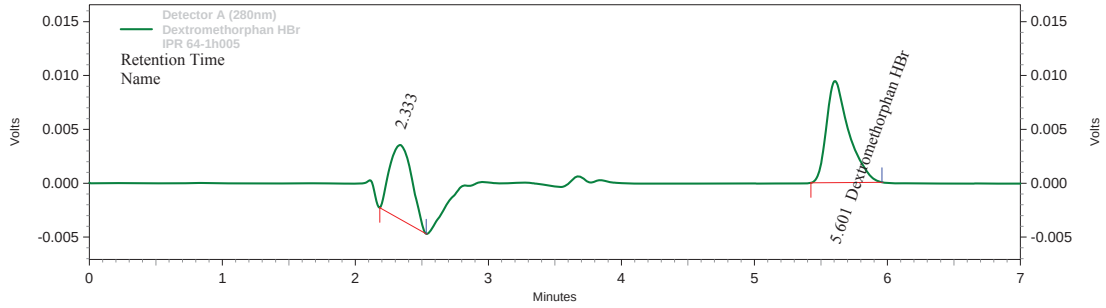

Detector A (280nm)
Dextromethorphan HBr
IPR 64-30m001
Retention Time
Name
2.346
5.606 Dextromethorphan HBr
Volts
Minutes

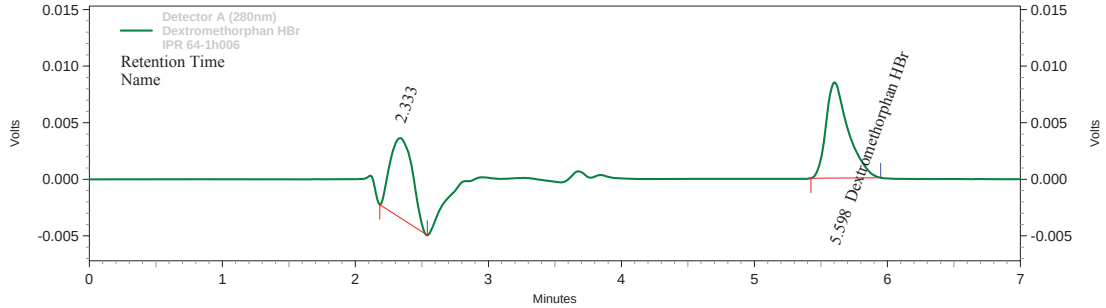

Detector A (280nm)
Dextromethorphan HBr
IPR 64-30m002
Retention Time
Name
2.349
5.615 Dextromethorphan HBr
Volts
Minutes


Detector A (280nm)
Dextromethorphan HBr
IPR 64-30m003
Retention Time
Name
2.351
5.605 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
IPR 64-30m004
Retention Time
Name
2.359
5.604 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
IPR 64-30m005
Retention Time
Name
2.358
5.603 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
IPR 64-30m006
Retention Time
Name
2.346
5.600 Dextromethorphan HBr
Volts
Minutes

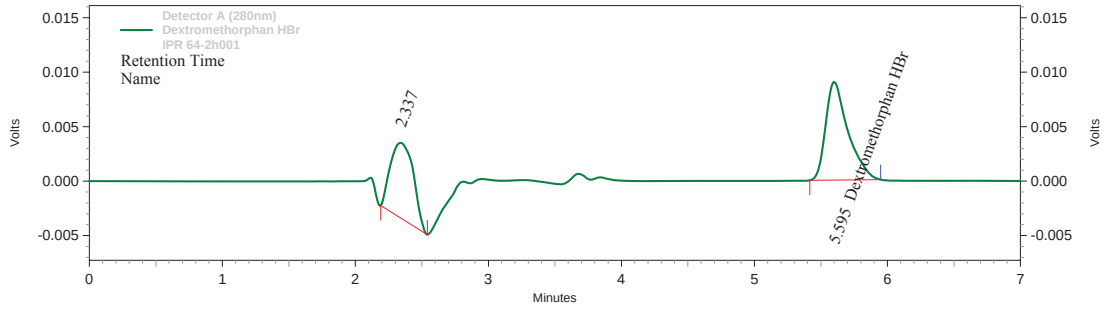
1 h

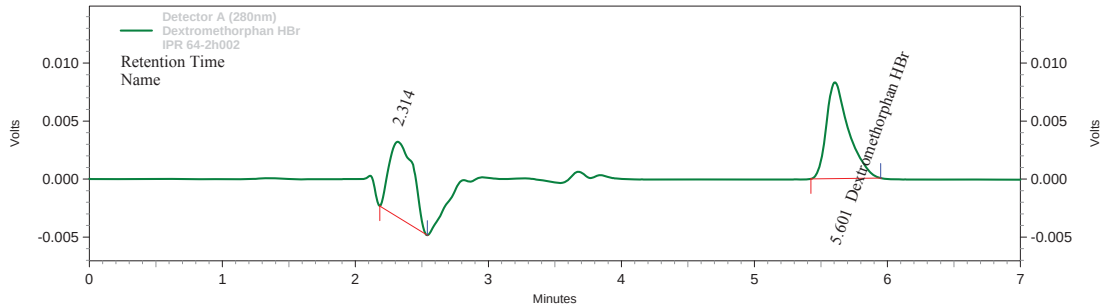

Detector A (280nm)
Dextromethorphan HBr
IPR 64-1h001
Retention Time
Name
2.350
5.605 Dextromethorphan HBr
Detector A (280nm)
Dextromethorphan HBr
IPR 64-1h002
Retention Time
Name
2.340
5.596 Dextromethorphan HBr
Detector A (280nm)
Dextromethorphan HBr
IPR 64-1h003
Retention Time
Name
2.343
5.605 Dextromethorphan HBr
Detector A (280nm)
Dextromethorphan HBr
IPR 64-1h004
Retention Time
Name
2.344
5.598 Dextromethorphan HBr
Volts
Minutes

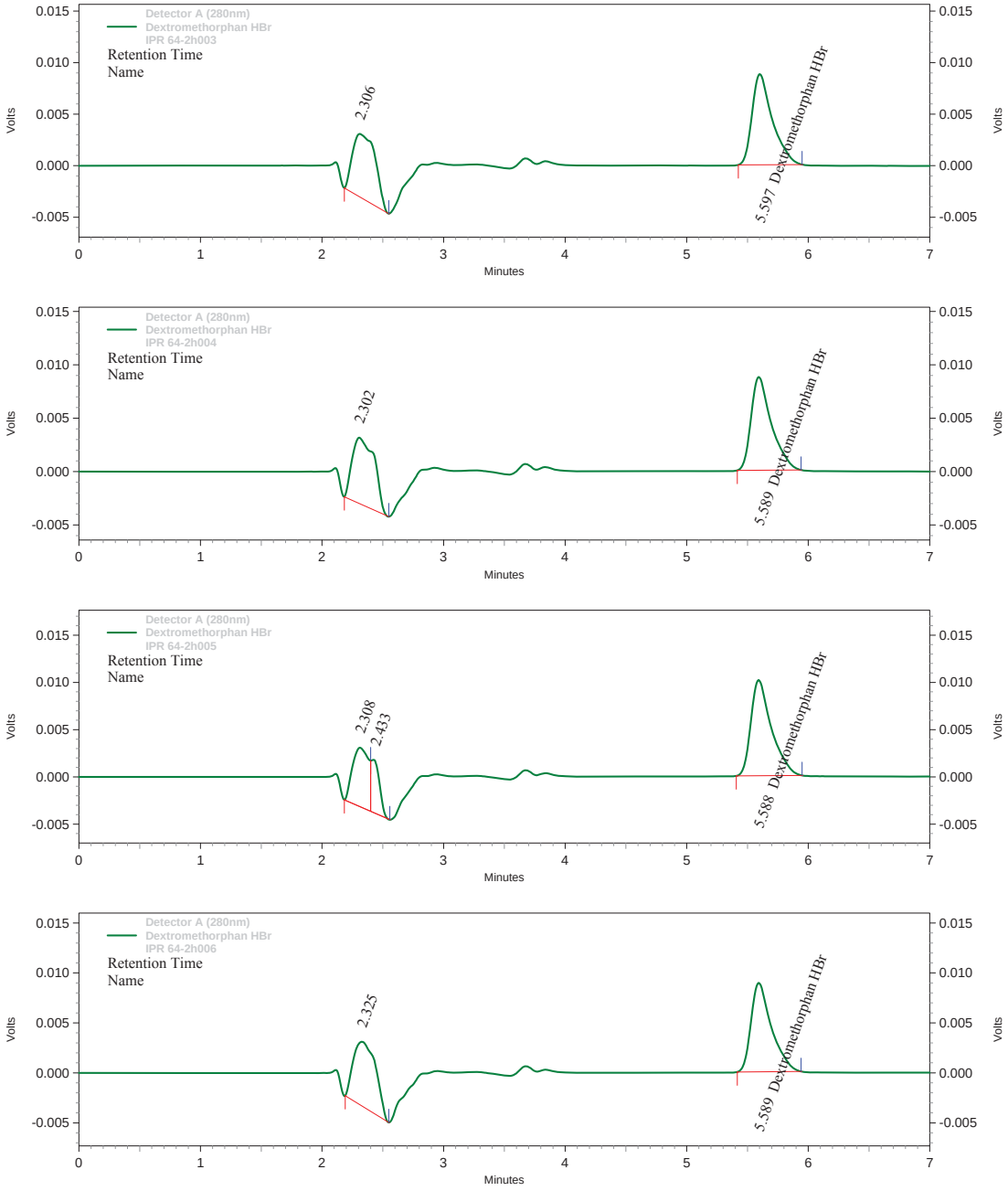

Detector A (280nm)
Dextromethorphan HBr
IPR 64-1h005
Retention Time
Name
2.333
5.601 Dextromethorphan HBr
Volts
Minutes


Detector A (280nm)
Dextromethorphan HBr
IPR 64-1h006
Retention Time
Name
2.333
5.598 Dextromethorphan HBr
Volts
Minutes

2 h


Detector A (280nm)
Dextromethorphan HBr
IPR 64-2h001
Retention Time
Name
2.337
5.595 Dextromethorphan HBr
Volts
Minutes


Detector A (280nm)
Dextromethorphan HBr
IPR 64-2h002
Retention Time
Name
2.314
5.601 Dextromethorphan HBr
Volts
Minutes

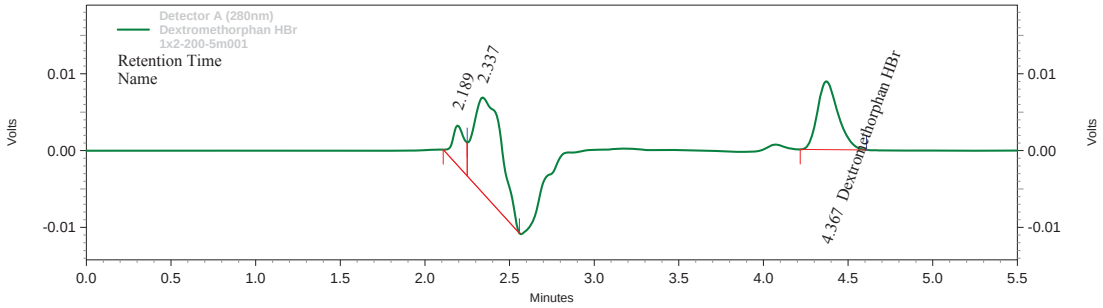

Detector A (280nm)
Dextromethorphan HBr
IPR 64-2h003
Retention Time
Name
2.306
5.597 Dextromethorphan HBr
Detector A (280nm)
Dextromethorphan HBr
IPR 64-2h004
Retention Time
Name
2.302
5.589 Dextromethorphan HBr
Detector A (280nm)
Dextromethorphan HBr
IPR 64-2h005
Retention Time
Name
2.308
2.433
5.588 Dextromethorphan HBr
Detector A (280nm)
Dextromethorphan HBr
IPR 64-2h006
Retention Time
Name
2.325
5.589 Dextromethorphan HBr
Volts
Minutes
0.015
0.010
0.005
0.000
-0.005
0
1
2
3
4
5
6
7

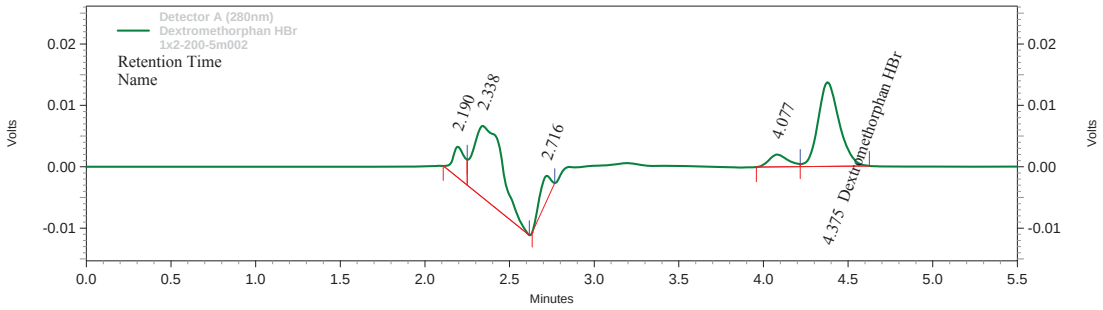
1.2.5 Peak area and chromatogram of DMP released from tablets containing Dowex® 1x2-200

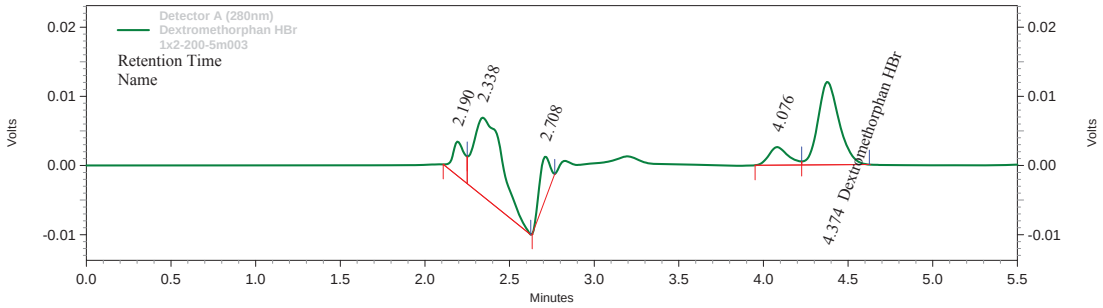
Table 58 Retention time and peak area of DMP released from tablets containing Dowex® 1x2-200

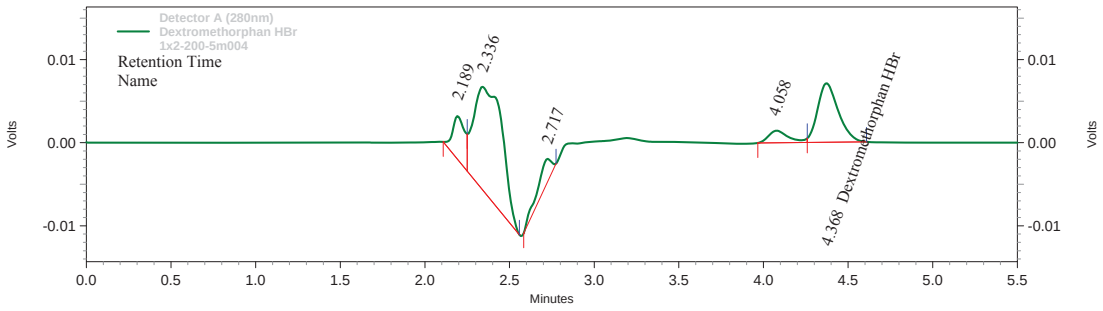
Sample	Retention time (min)	Peak area
5m001	4.367	75073
5m002	4.375	118583
5m003	4.374	103689
5m004	4.368	60276
5m005	4.374	111651
5m006	4.374	116039
10m001	4.373	116233
10m002	4.373	119063
10m003	4.374	123988
10m004	4.366	78555
10m005	4.374	123419
10m006	4.374	121835
15m001	4.373	120035
15m002	4.375	121704
15m003	4.373	127384
15m004	4.373	94989
15m005	4.372	122842
15m006	4.374	124495
30m001	4.371	120643
30m002	4.373	122444
30m003	4.371	122745
30m004	4.372	111976
30m005	4.373	121673
30m006	4.370	122355
1h001	4.372	118492
1h002	4.372	122431
1h003	4.373	123507
1h004	4.372	115405
1h005	4.373	122303
1h006	4.372	123276
2h001	4.372	124221
2h002	4.372	124867
2h003	4.372	121563
2h004	4.372	117966
2h005	4.373	121035
2h006	4.371	122786

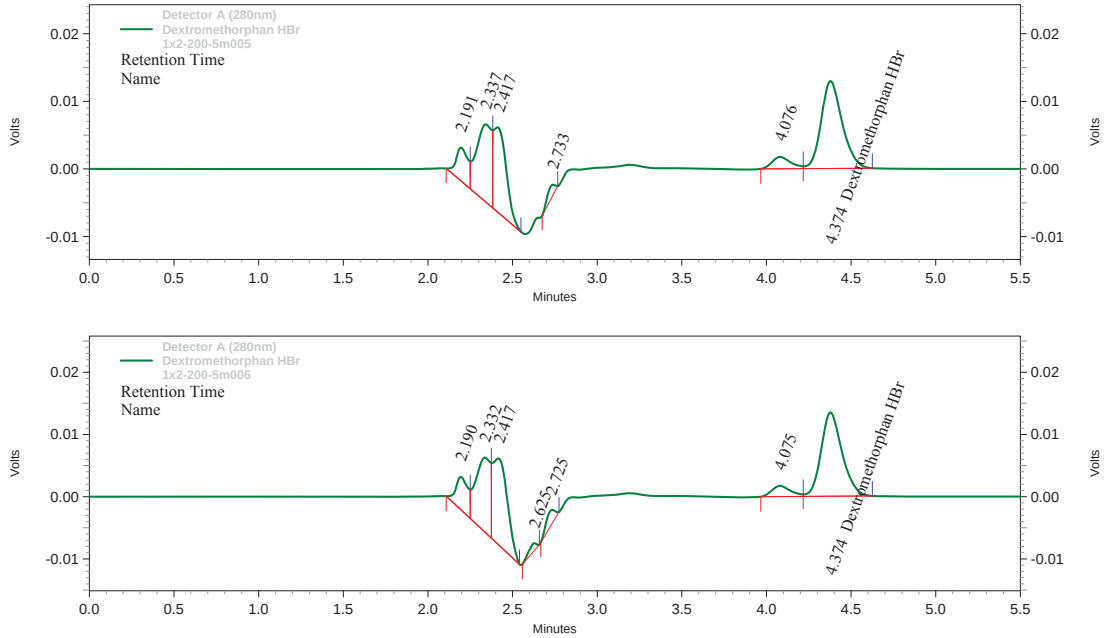
5 min


Detector A (280nm)
Dextromethorphan HBr
1x2-200-5m001
Retention Time
Name
2.189
2.337
4.367 Dextromethorphan HBr
Volts
Minutes

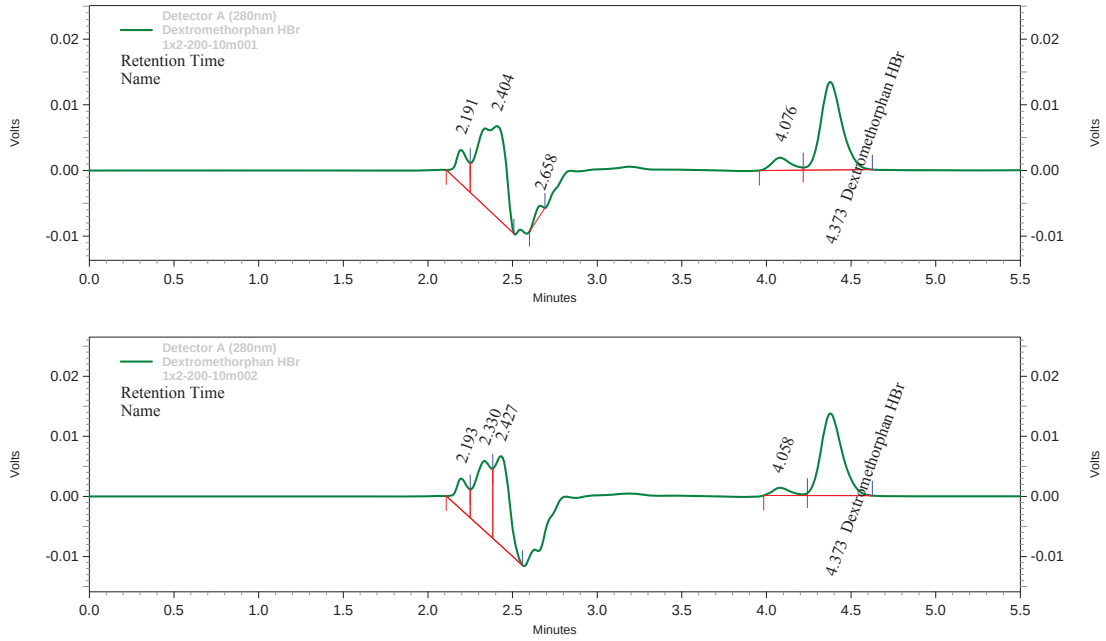

Detector A (280nm)
Dextromethorphan HBr
1x2-200-5m002
Retention Time
Name
2.190
2.338
2.716
4.077
4.375 Dextromethorphan HBr
Volts
Minutes

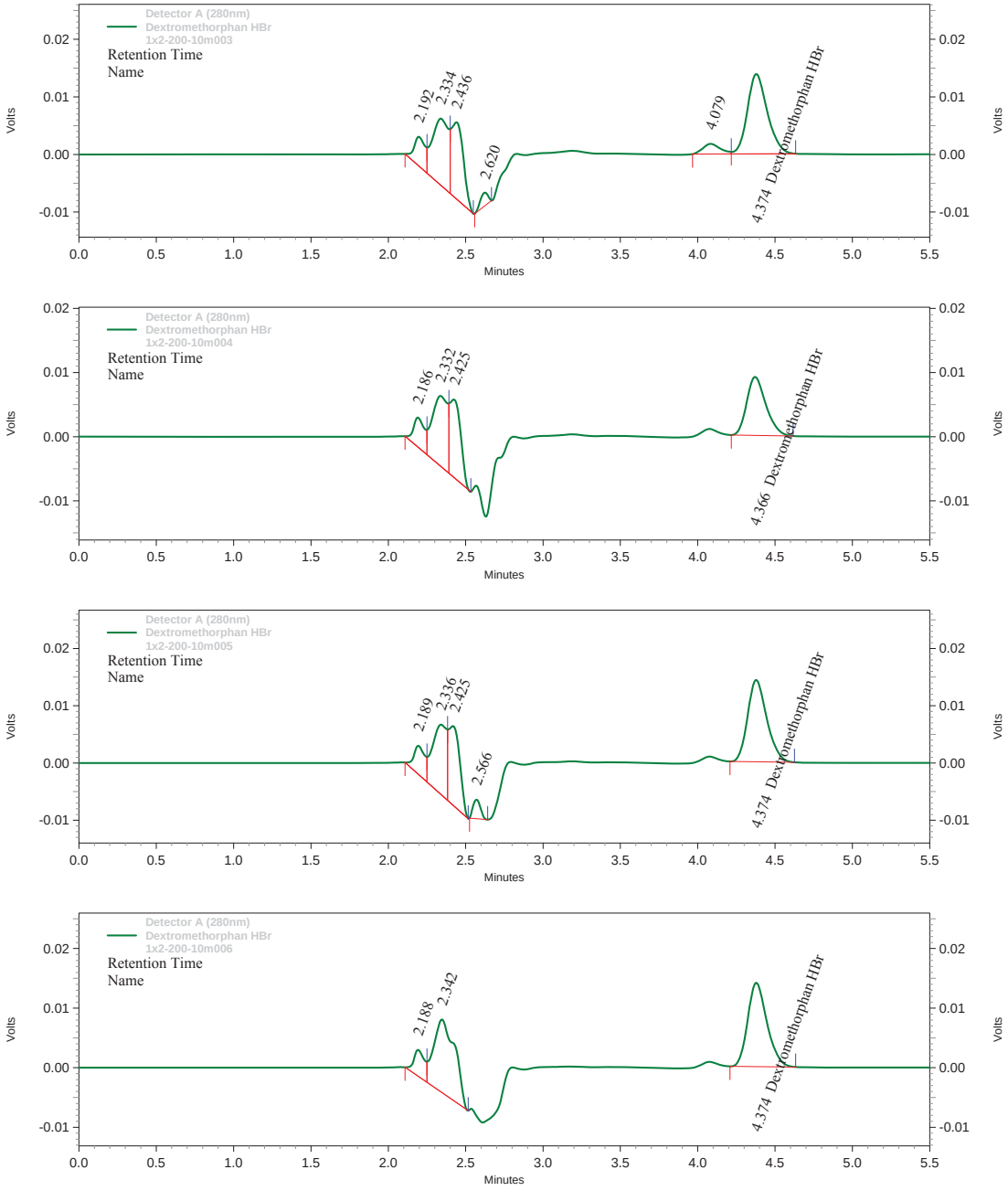

Detector A (280nm)
Dextromethorphan HBr
1x2-200-5m003
Retention Time
Name
2.190
2.338
2.708
4.076
4.374 Dextromethorphan HBr
Volts
Minutes


Detector A (280nm)
Dextromethorphan HBr
1x2-200-5m004
Retention Time
Name
2.189
2.336
2.717
4.058
4.368 Dextromethorphan HBr
Volts
Minutes

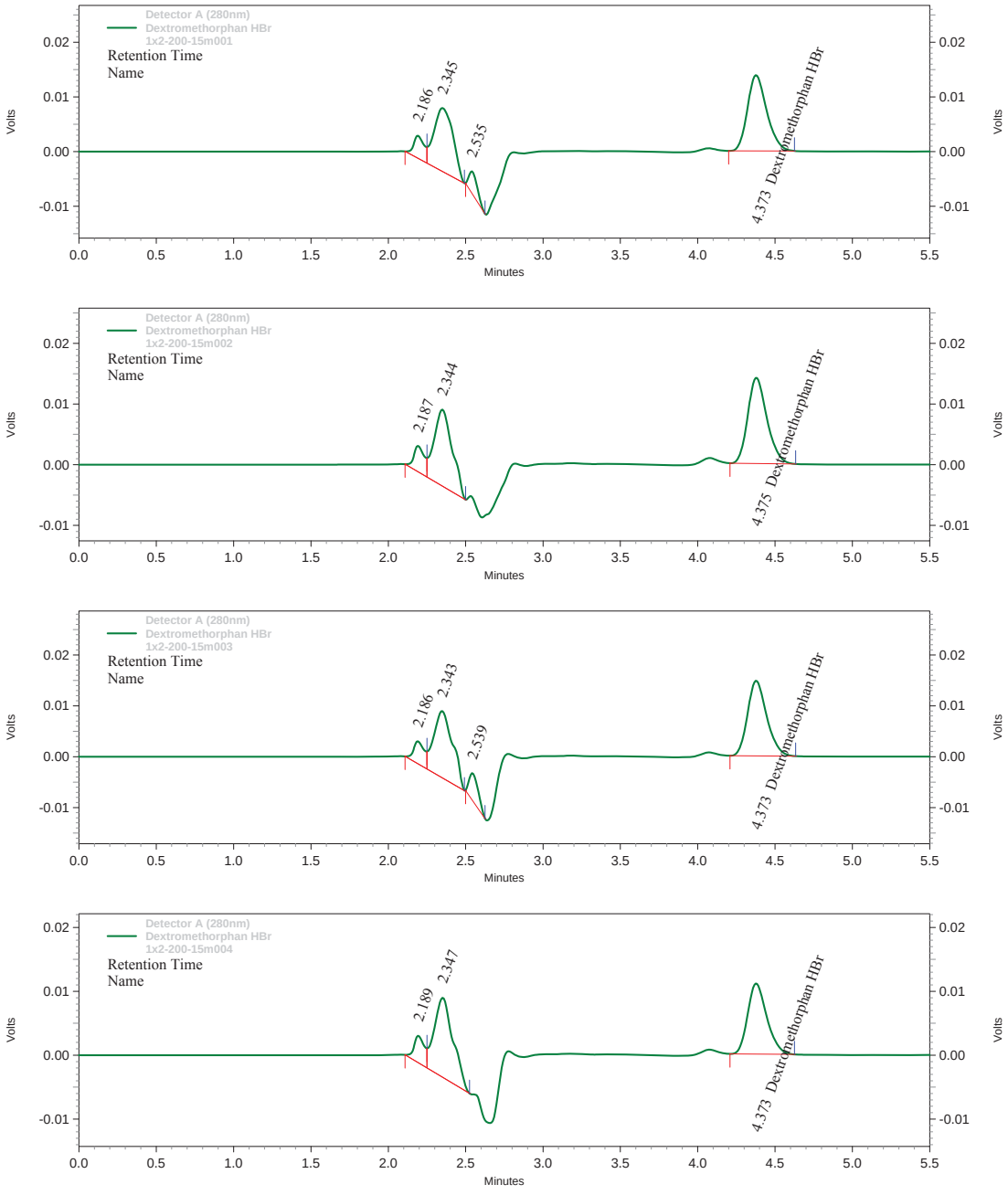

Detector A (280nm)
Dextromethorphan HBr
1x2-200-5m005
Retention Time
Name
2.191
2.337
2.417
2.733
4.076
4.374 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
1x2-200-5m006
Retention Time
Name
2.190
2.332
2.417
2.625
2.725
4.075
4.374 Dextromethorphan HBr
Volts
Minutes

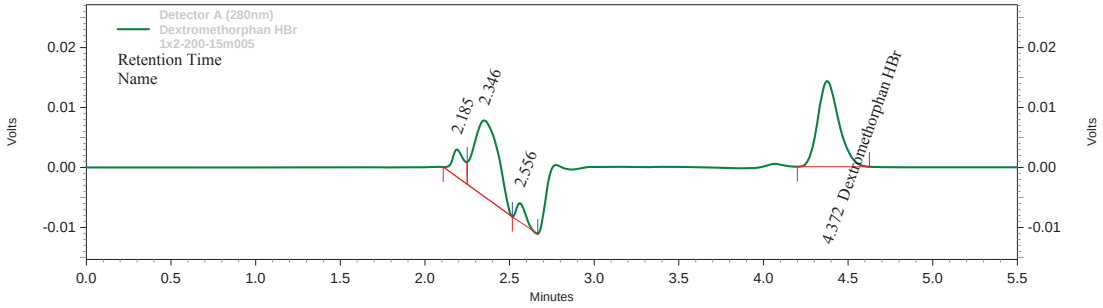
10 min

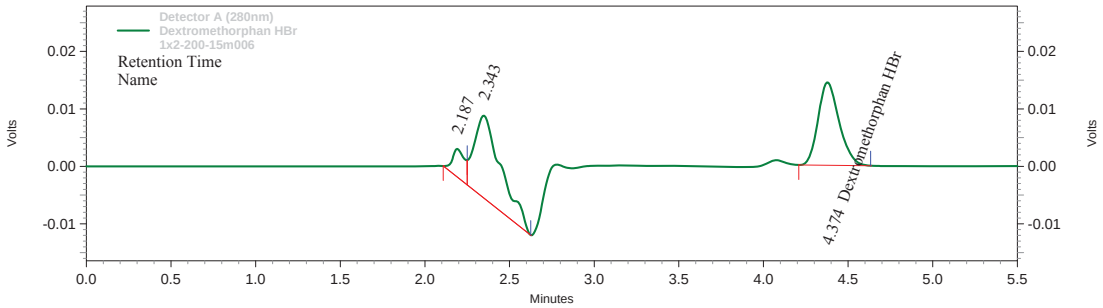

Detector A (280nm)
Dextromethorphan HBr
1x2-200-10m001
Retention Time
Name
2.191
2.404
2.658
4.076
4.373 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
1x2-200-10m002
Retention Time
Name
2.193
2.330
2.427
4.058
4.373 Dextromethorphan HBr
Volts
Minutes


Detector A (280nm)
Dextromethorphan HBr
1x2-200-10m003
Retention Time
Name
2.192
2.334
2.436
2.620
4.079
4.374 Dextromethorphan HBr
Detector A (280nm)
Dextromethorphan HBr
1x2-200-10m004
Retention Time
Name
2.186
2.332
2.425
4.366 Dextromethorphan HBr
Detector A (280nm)
Dextromethorphan HBr
1x2-200-10m005
Retention Time
Name
2.189
2.336
2.425
2.566
4.374 Dextromethorphan HBr
Detector A (280nm)
Dextromethorphan HBr
1x2-200-10m006
Retention Time
Name
2.188
2.342
4.374 Dextromethorphan HBr
Volts
Minutes

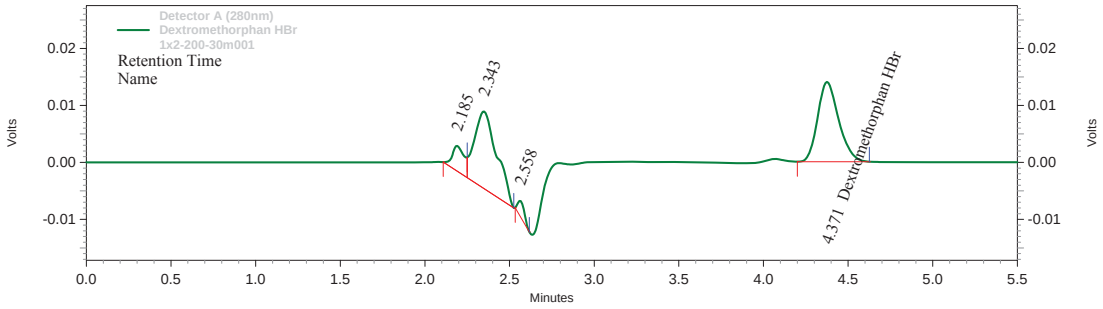
15 min

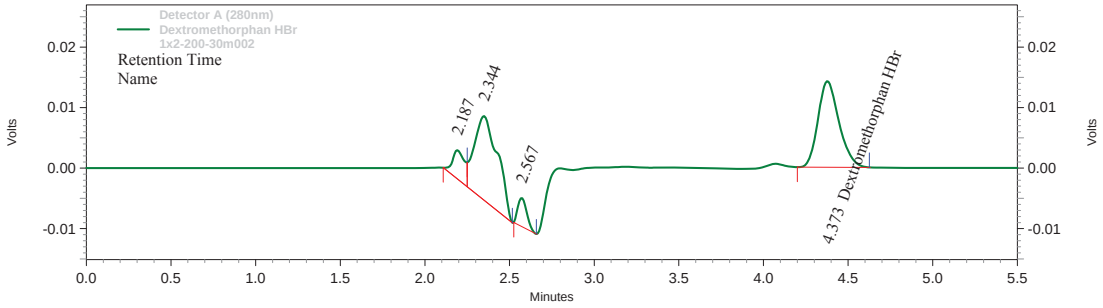

Detector A (280nm)
Dextromethorphan HBr
1x2-200-15m001
Retention Time
Name
2.186
2.345
2.535
4.373 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
1x2-200-15m002
Retention Time
Name
2.187
2.344
4.375 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
1x2-200-15m003
Retention Time
Name
2.186
2.343
2.539
4.373 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
1x2-200-15m004
Retention Time
Name
2.189
2.347
4.373 Dextromethorphan HBr
Volts
Minutes

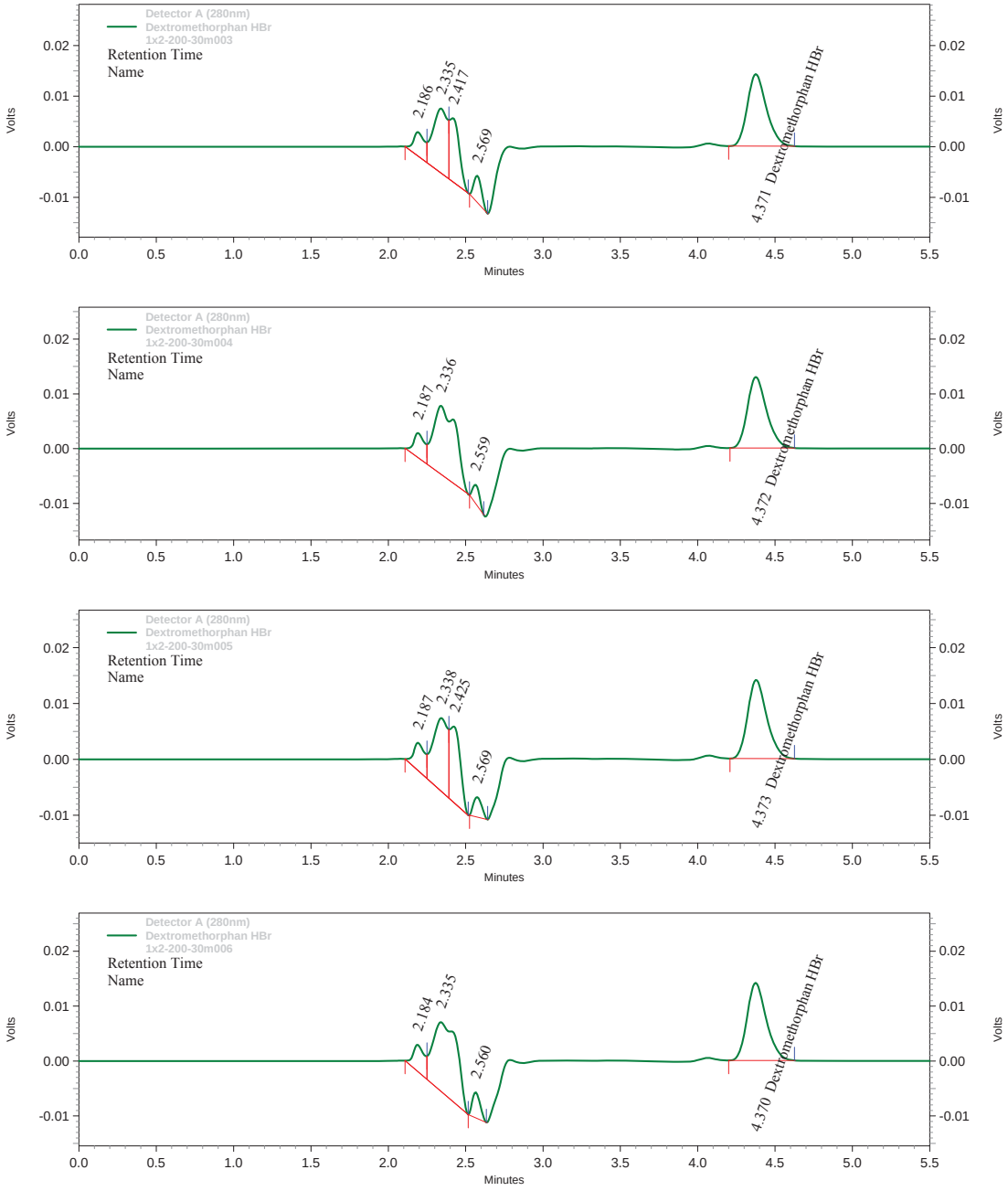

Detector A (280nm)
Dextromethorphan HBr
1x2-200-15m005
Retention Time
Name
2.185
2.346
2.556
4.372 Dextromethorphan HBr
Volts
Minutes


Detector A (280nm)
Dextromethorphan HBr
1x2-200-15m006
Retention Time
Name
2.187
2.343
4.374 Dextromethorphan HBr
Volts
Minutes

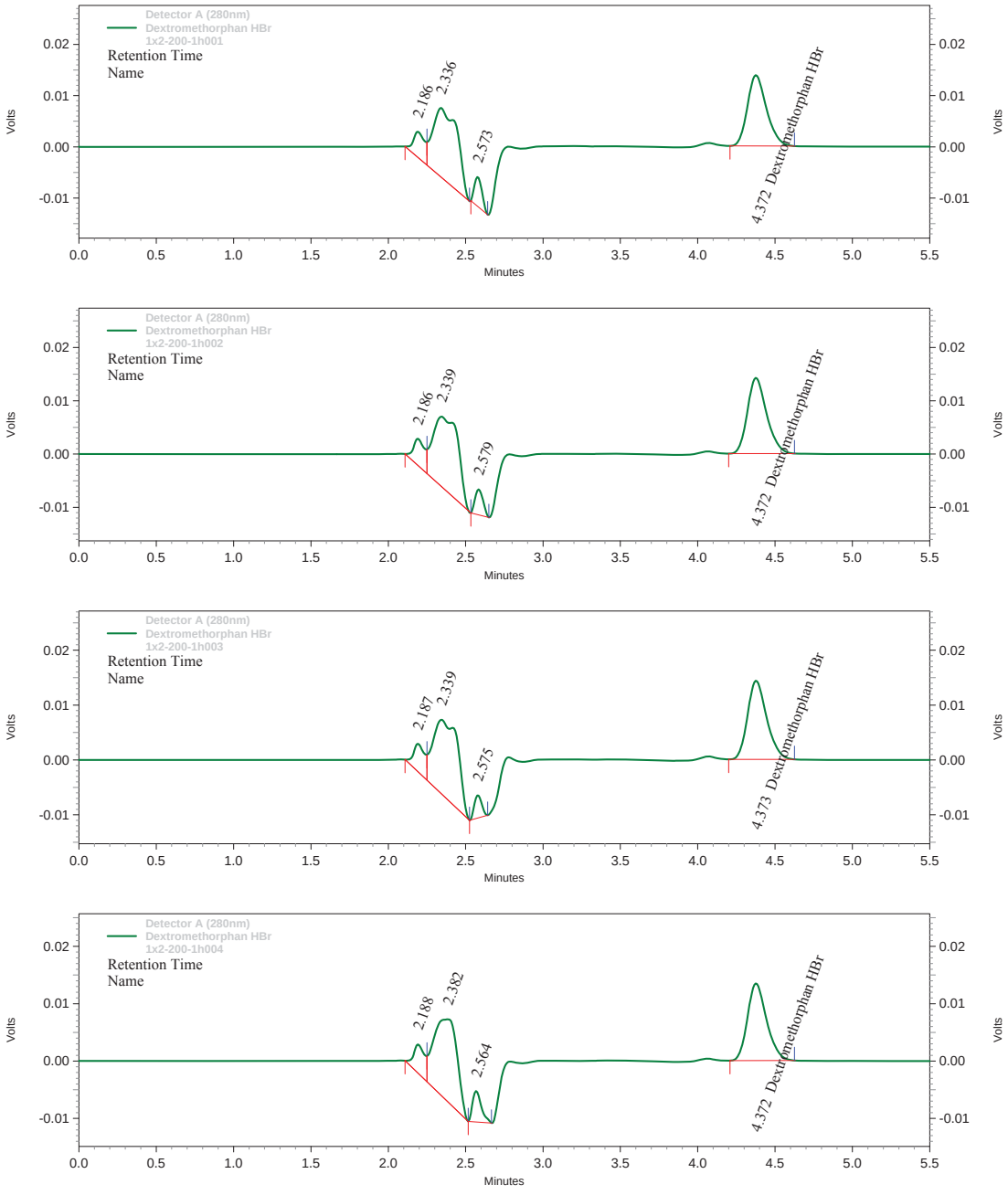
30 min

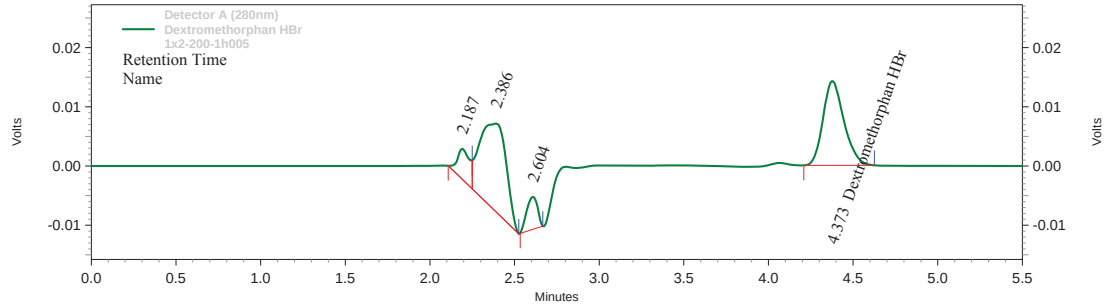

Detector A (280nm)
Dextromethorphan HBr
1x2-200-30m001
Retention Time
Name
2.185
2.343
2.558
4.371 Dextromethorphan HBr
Volts
Minutes

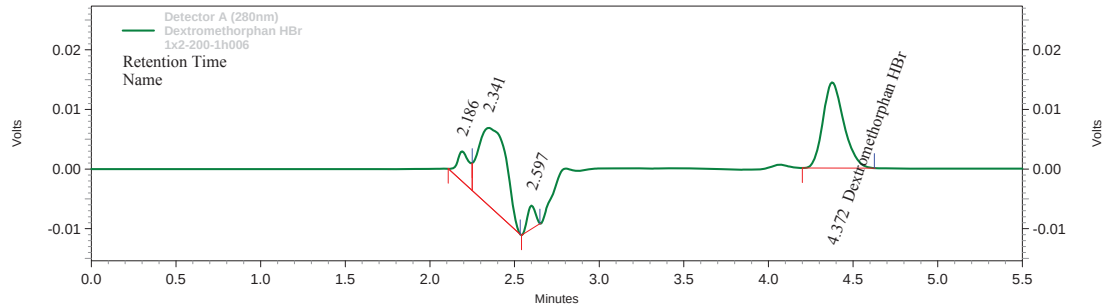

Detector A (280nm)
Dextromethorphan HBr
1x2-200-30m002
Retention Time
Name
2.187
2.344
2.567
4.373 Dextromethorphan HBr
Volts
Minutes


Detector A (280nm)
Dextromethorphan HBr
1x2-200-30m003
Retention Time
Name
2.186
2.335
2.417
2.569
4.371 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
1x2-200-30m004
Retention Time
Name
2.187
2.336
2.559
4.372 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
1x2-200-30m005
Retention Time
Name
2.187
2.338
2.425
2.569
4.373 Dextromethorphan HBr
Volts
Minutes
Detector A (280nm)
Dextromethorphan HBr
1x2-200-30m006
Retention Time
Name
2.184
2.335
2.560
4.370 Dextromethorphan HBr
Volts
Minutes

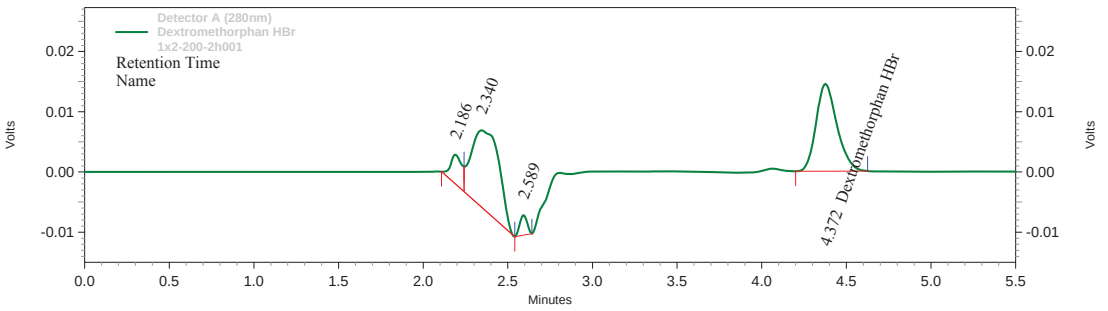
1 h

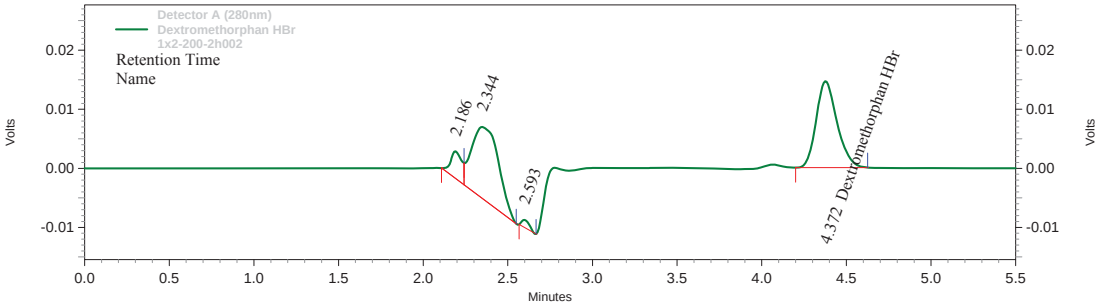

Detector A (280nm)
Dextromethorphan HBr
1x2-200-1h001
Retention Time
Name
2.186
2.336
2.573
4.372 Dextromethorphan HBr
Detector A (280nm)
Dextromethorphan HBr
1x2-200-1h002
Retention Time
Name
2.186
2.339
2.579
4.372 Dextromethorphan HBr
Detector A (280nm)
Dextromethorphan HBr
1x2-200-1h003
Retention Time
Name
2.187
2.339
2.575
4.373 Dextromethorphan HBr
Detector A (280nm)
Dextromethorphan HBr
1x2-200-1h004
Retention Time
Name
2.188
2.382
2.564
4.372 Dextromethorphan HBr
Volts
Minutes
0.02
0.01
0.00
-0.01
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5

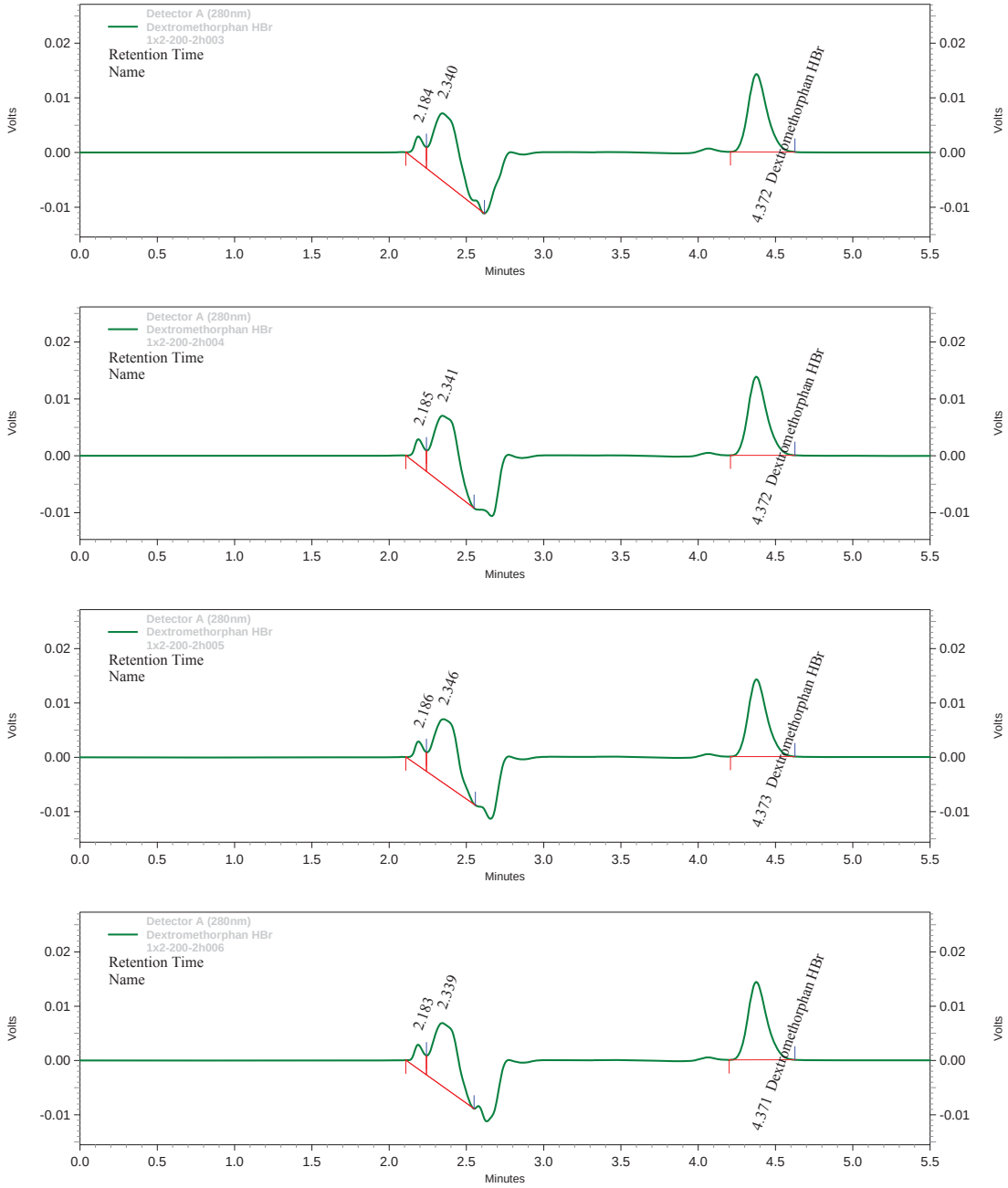

Detector A (280nm)
Dextromethorphan HBr
1x2-200-1h005
Retention Time
Name
2.187
2.386
2.604
4.373 Dextromethorphan HBr
Volts
Minutes


Detector A (280nm)
Dextromethorphan HBr
1x2-200-1h006
Retention Time
Name
2.186
2.341
2.597
4.372 Dextromethorphan HBr
Volts
Minutes

2 h


Detector A (280nm)
Dextromethorphan HBr
1x2-200-2h001
Retention Time
Name
2.186
2.340
2.589
4.372 Dextromethorphan HBr
Volts
Minutes


Detector A (280nm)
Dextromethorphan HBr
1x2-200-2h002
Retention Time
Name
2.186
2.344
2.593
4.372 Dextromethorphan HBr
Volts
Minutes


Detector A (280nm)
Dextromethorphan HBr
1x2-200-2h003
Retention Time
Name
2.184
2.340
4.372 Dextromethorphan HBr
Detector A (280nm)
Dextromethorphan HBr
1x2-200-2h004
Retention Time
Name
2.185
2.341
4.372 Dextromethorphan HBr
Detector A (280nm)
Dextromethorphan HBr
1x2-200-2h005
Retention Time
Name
2.186
2.346
4.373 Dextromethorphan HBr
Detector A (280nm)
Dextromethorphan HBr
1x2-200-2h006
Retention Time
Name
2.183
2.339
4.371 Dextromethorphan HBr
Volts
Minutes
0.02
0.01
0.00
-0.01
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5

1.2.6 % Cumulative released of DMP

Table 59 % Cumulative released of DMP from tablets containing SSG

Time	% Cumulative released of DMP from tablets containing SSG							
	1	2	3	4	5	6	AVG	SD
5 min	62.31	51.72	39.85	52.81	67.24	23.09	49.50	16.03
10 min	84.11	65.75	54.10	73.45	84.90	53.05	69.23	14.05
15 min	97.96	79.45	64.39	85.03	92.93	71.18	81.82	12.78
30 min	104.57	98.33	86.93	101.81	103.10	97.72	98.74	6.37
60 min	104.46	104.97	99.58	107.83	105.80	105.89	104.75	2.79
2 h	106.82	107.10	105.94	106.34	109.31	108.23	107.29	1.26

Table 60 % Cumulative released of DMP from tablets containing Amberlite® IRP64

Time	% Cumulative released of DMP from tablets containing Amberlite® IRP64							
	1	2	3	4	5	6	AVG	SD
5 min	73.97	51.35	53.81	52.14	49.19	54.37	55.80	9.09
10 min	64.97	58.66	69.47	66.59	74.39	69.79	67.31	5.33
15 min	73.95	66.96	73.83	71.38	85.97	84.53	76.10	7.54
30 min	74.75	71.51	80.01	76.81	89.90	80.98	78.99	6.37
1 h	80.34	76.34	82.76	79.97	92.75	82.04	82.37	5.55
2 h	88.61	81.26	86.13	85.64	100.40	87.61	88.28	6.45

Table 61 % Cumulative released of DMP from tablets containing Dowex®1x2-200

Time	% Cumulative released of DMP from tablets containing Dowex®1x2-200							
	1	2	3	4	5	6	AVG	SD
5 min	61.33	98.01	85.45	48.85	92.17	95.87	80.28	20.36
10 min	96.37	98.96	103.04	64.54	102.60	101.28	94.47	14.87
15 min	100.11	101.73	106.47	78.75	102.68	104.09	98.97	10.14
30 min	101.17	102.92	103.15	93.50	102.26	102.86	100.98	3.73
1 h	99.91	103.47	104.36	96.91	103.35	104.19	102.03	2.99
2 h	105.29	106.08	103.28	99.60	102.84	104.35	103.57	2.29

2. Diclofenac sodium (DCN) tablets

2.1 Physical properties of DCN tablets

Table 62 Physical properties of DCN tablets

Resin type	Physical properties	1	2	3	4	5	6	7	8	9	10	11	12	AVG	SD
SSG	**Hardness (mm)**	120.00	123.00	127.00	122.00	123.00	121.00	122.00	122.00	124.00	125.00	-	-	**122.90**	**2.02**
	Thickness (mm)	3.16	3.15	3.13	3.14	3.15	3.13	3.14	3.14	3.16	3.15	-	-	**3.15**	**0.01**
	Diameter (mm)	9.58	9.58	9.60	9.55	9.57	9.60	9.55	9.54	9.57	9.57	-	-	**9.57**	**0.02**
	Disintegration time (sec)	15	15	15	16	16	16	15	15	15	16	16	16	**15.50**	**0.52**
	Friability (%)	1.4668													
Amberlite®	**Hardness (mm)**	94.00	114.00	106.00	85.00	86.00	90.00	92.00	105.00	104.00	106.00	-	-	**98.20**	**9.99**
IRP64	**Thickness (mm)**	3.29	3.23	3.19	3.22	3.28	3.26	3.26	3.20	3.21	3.21	-	-	**3.24**	**0.04**
	Diameter (mm)	9.47	9.47	9.51	9.52	9.52	9.48	9.50	9.51	9.52	9.53	-	-	**9.50**	**0.02**
	Disintegration time (sec)	25	25	25	25	26	27	25	26	26	27	27	28	**26.00**	**1.04**
	Friability (%)	1.8053													
Dowex®	**Hardness (mm)**	80.00	75.00	65.00	76.00	67.00	68.00	67.00	76.00	78.00	72.00	-	-	**72.40**	**5.32**
1x2 - 200	**Thickness (mm)**	3.36	3.40	3.38	3.37	3.42	3.40	3.43	3.37	3.37	3.40	-	-	**3.39**	**0.02**
	Diameter (mm)	9.55	9.55	9.60	9.56	9.59	9.55	9.53	9.60	9.60	9.59	-	-	**9.57**	**0.03**
	Disintegration time (sec)	8	8	9	9	9	9	10	10	12	12	12	12	**10.00**	**1.60**
	Friability (%)	2.9945													

2.2 Dissolution studies of DCN

2.2.1 Standard curve of DCN

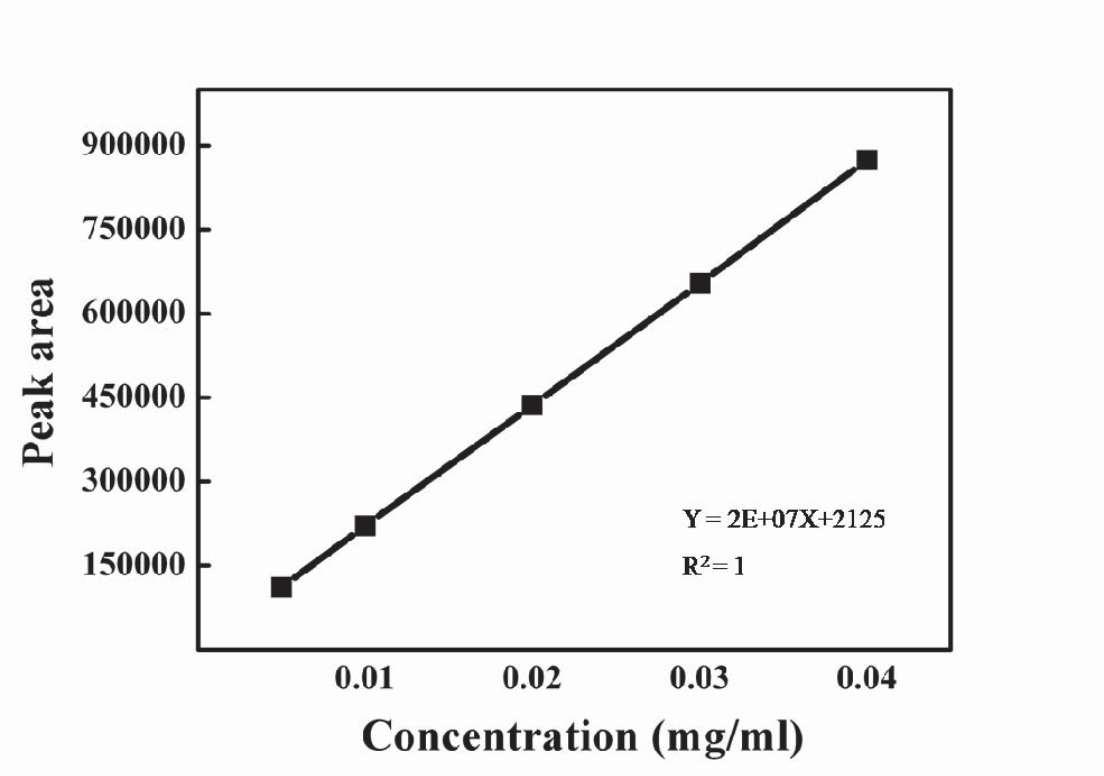
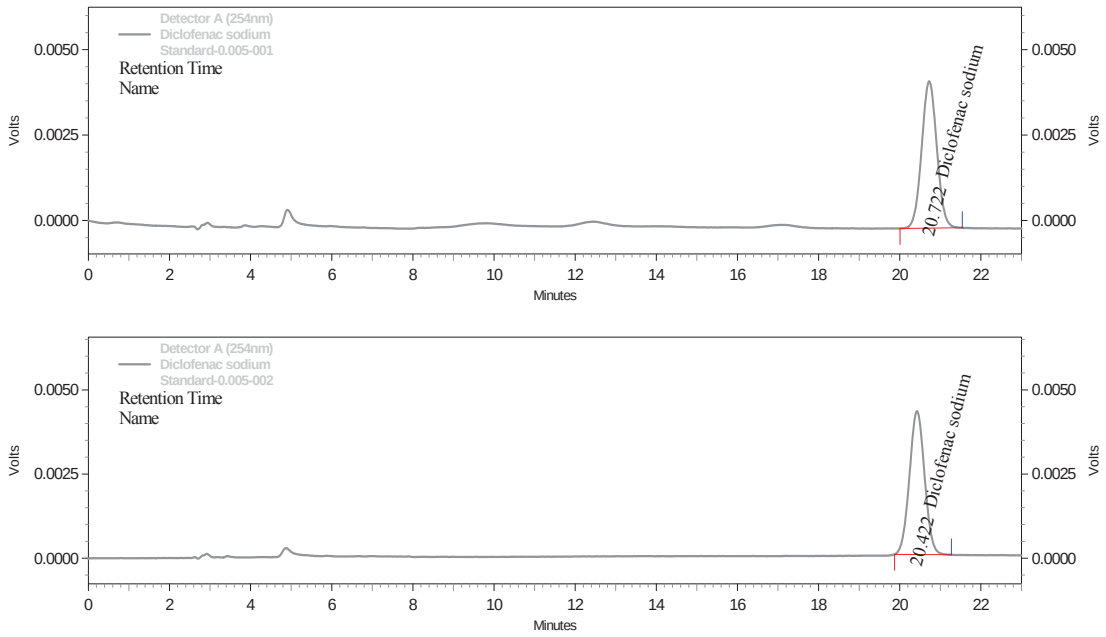


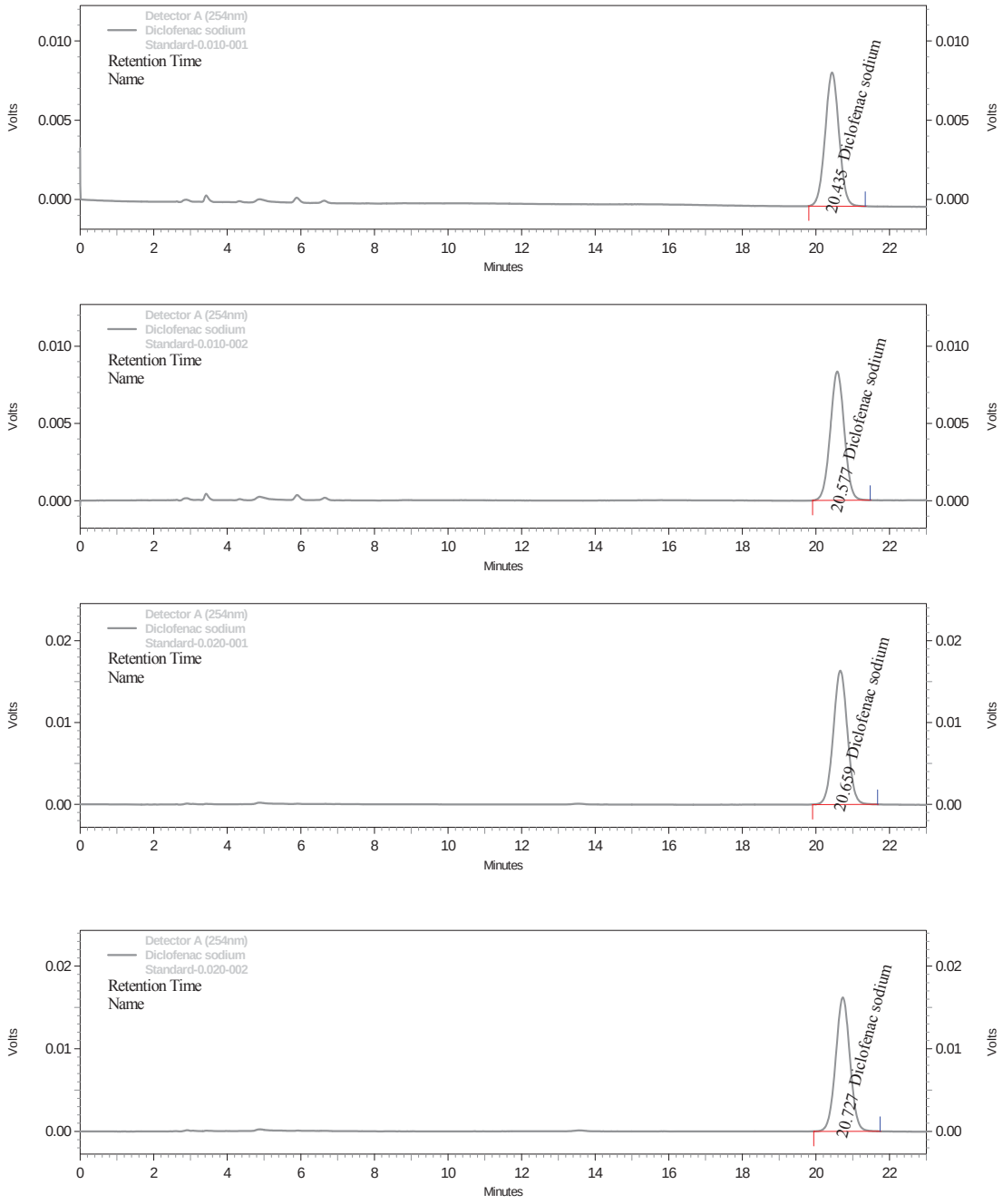
Fig. 34 Standard curve of DCN.

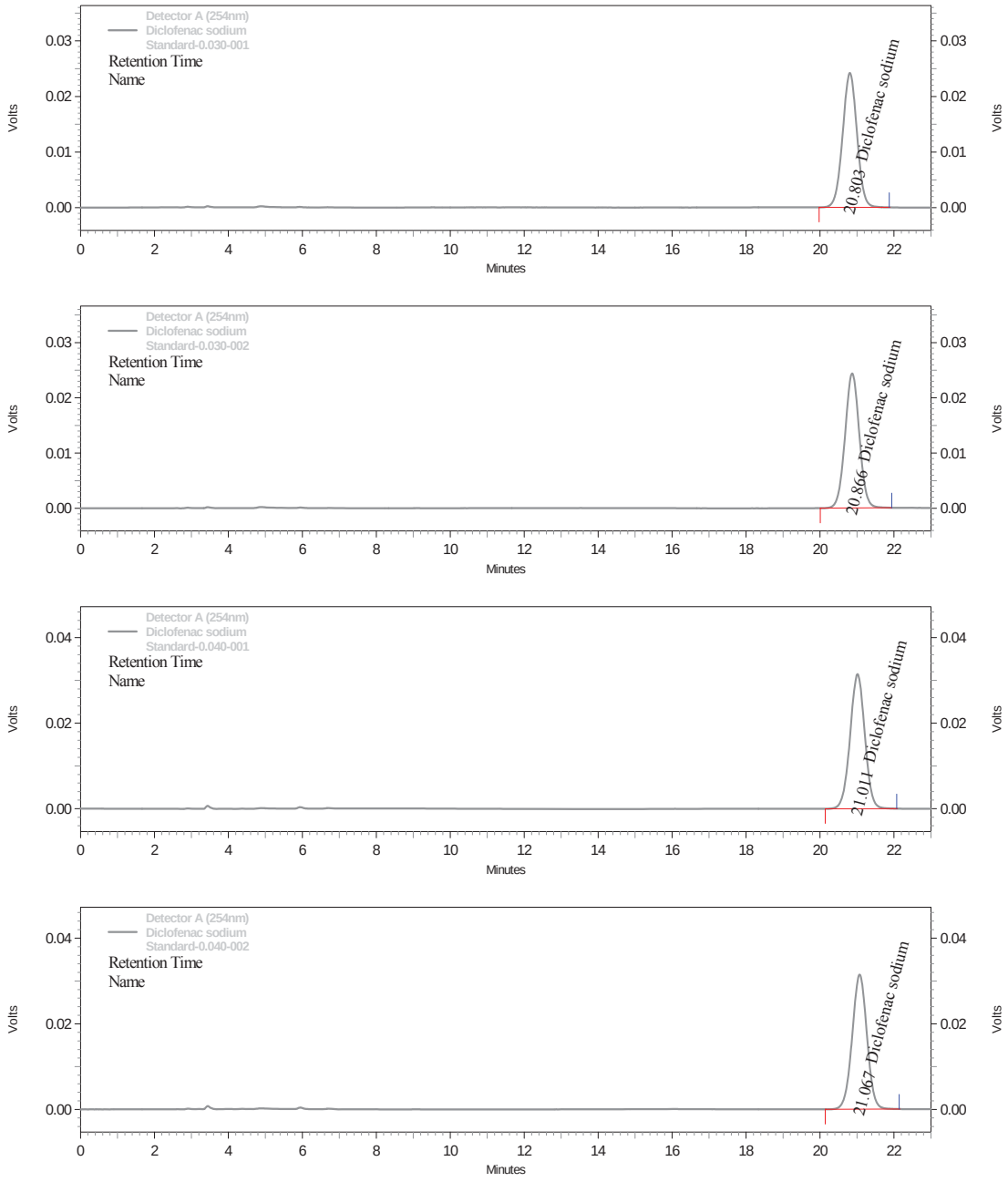
2.2.2 Peak area and chromatogram of DCN standard

Table 63 Retention time and peak area of DCN standard

Concentration (mg/mL)	Retention time (min)	Peak area
0.005	20.722	111503
	20.422	110450
0.010	20.435	220678
	20.577	221154
0.020	20.659	436512
	20.727	436300
0.030	20.803	653810
	20.866	653961
0.040	21.011	873889
	21.067	874157




Detector A (254nm)
Diclofenac sodium
Standard-0.010-001
Retention Time
Name
20.435 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
Diclofenac sodium
Standard-0.010-002
Retention Time
Name
20.577 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
Diclofenac sodium
Standard-0.020-001
Retention Time
Name
20.659 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
Diclofenac sodium
Standard-0.020-002
Retention Time
Name
20.727 Diclofenac sodium
Volts
Minutes

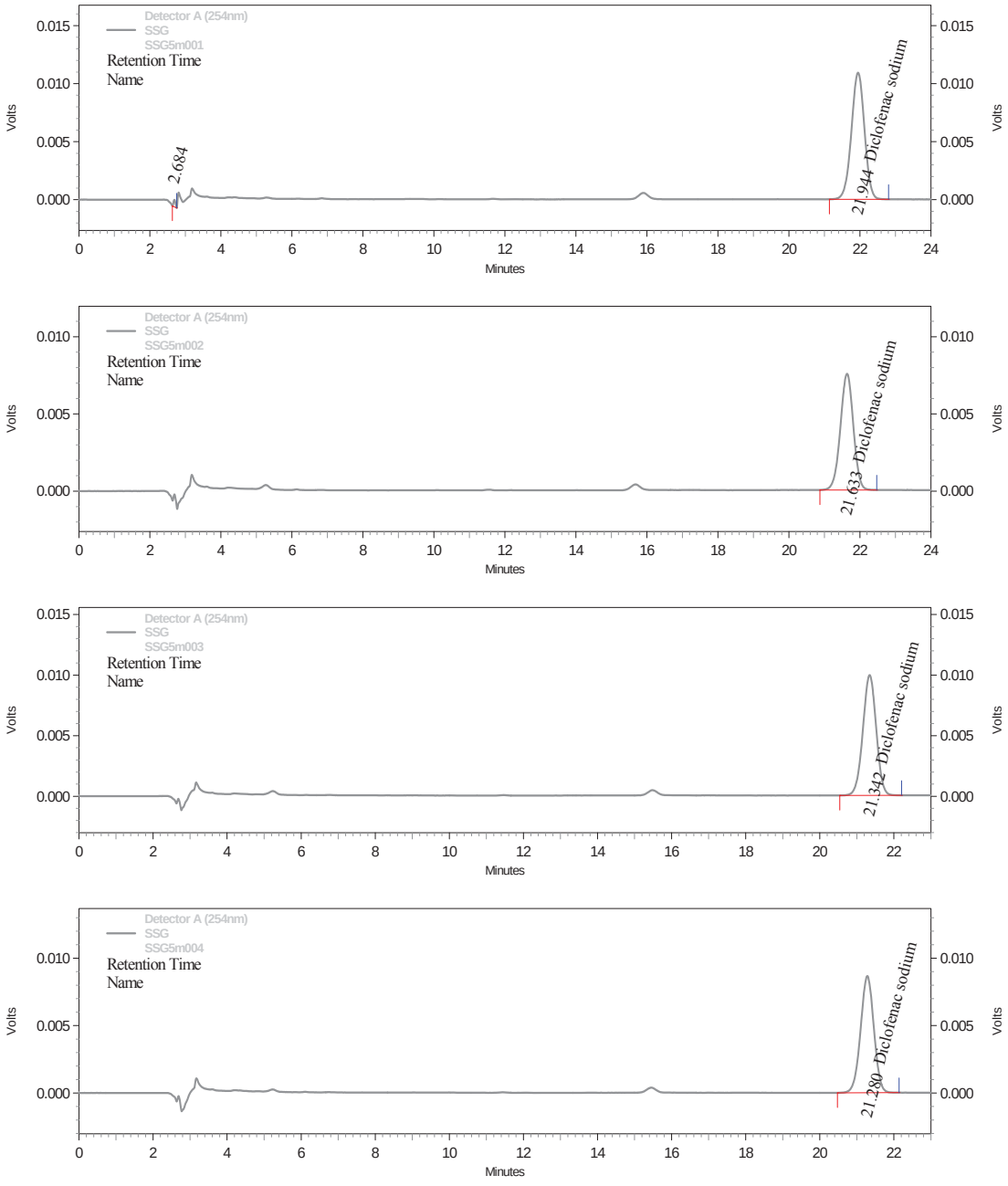

Detector A (254nm)
Diclofenac sodium
Standard-0.030-001
Retention Time
Name
20.803 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
Diclofenac sodium
Standard-0.030-002
Retention Time
Name
20.866 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
Diclofenac sodium
Standard-0.040-001
Retention Time
Name
21.011 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
Diclofenac sodium
Standard-0.040-002
Retention Time
Name
21.067 Diclofenac sodium
Volts
Minutes

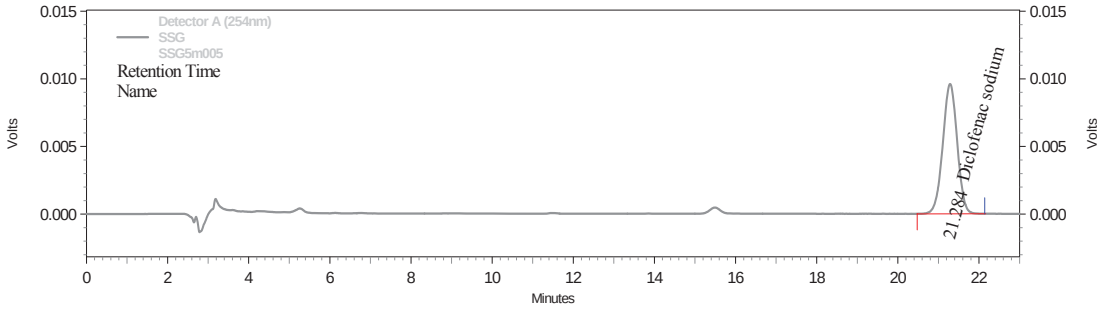
2.2.3 Peak area and chromatogram of DCN released from tablets containing SSG

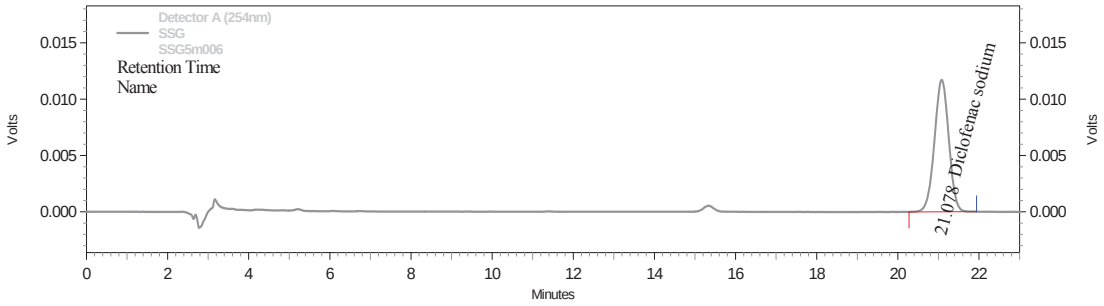
Table 64 Retention time and peak area of DCN released from tablets containing SSG

Sample	Retention time (min)	Peak area
5m001	21.944	279118
5m002	21.633	190941
5m003	21.342	248384
5m004	21.280	215768
5m005	21.284	236707
5m006	21.078	287597
10m001	21.034	345486
10m002	21.097	232648
10m003	21.016	312791
10m004	21.049	318153
10m005	20.961	306549
10m006	20.927	382564
15m001	20.934	423807
15m002	20.912	262962
15m003	20.888	351750
15m004	20.864	357952
15m005	20.895	322390
15m006	20.921	425185
30m001	20.854	543377
30m002	20.928	321664
30m003	20.913	408252
30m004	20.865	425542
30m005	20.869	448568
30m006	20.887	492177
1h001	20.860	568310
1h002	20.868	380202
1h003	20.865	464584
1h004	20.868	495780
1h005	20.980	515419
1h006	20.936	541158
2h001	20.951	589038
2h002	21.118	443425
2h003	20.997	512660
2h004	21.026	534040
2h005	21.093	550317
2h006	21.009	576730

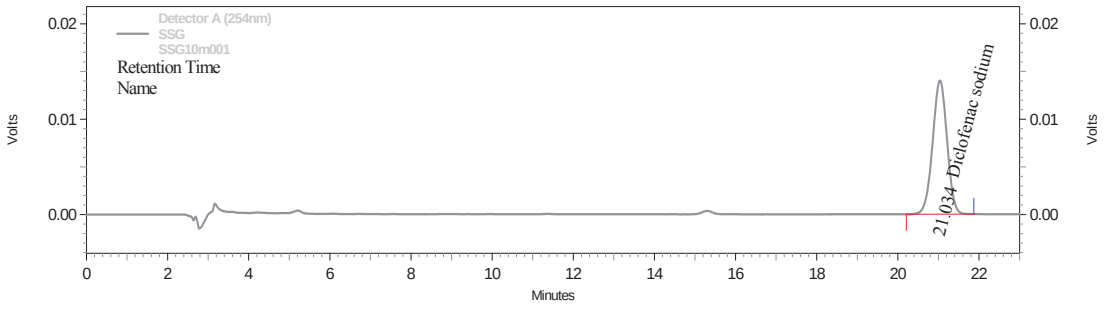
5 min

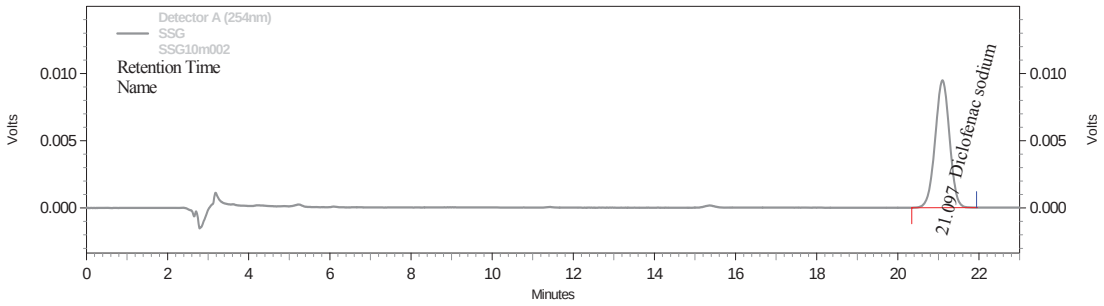

Detector A (254nm)
SSG
SSG5m001
Retention Time
Name
2.684
21.944 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
SSG
SSG5m002
Retention Time
Name
21.633 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
SSG
SSG5m003
Retention Time
Name
21.342 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
SSG
SSG5m004
Retention Time
Name
21.280 Diclofenac sodium
Volts
Minutes

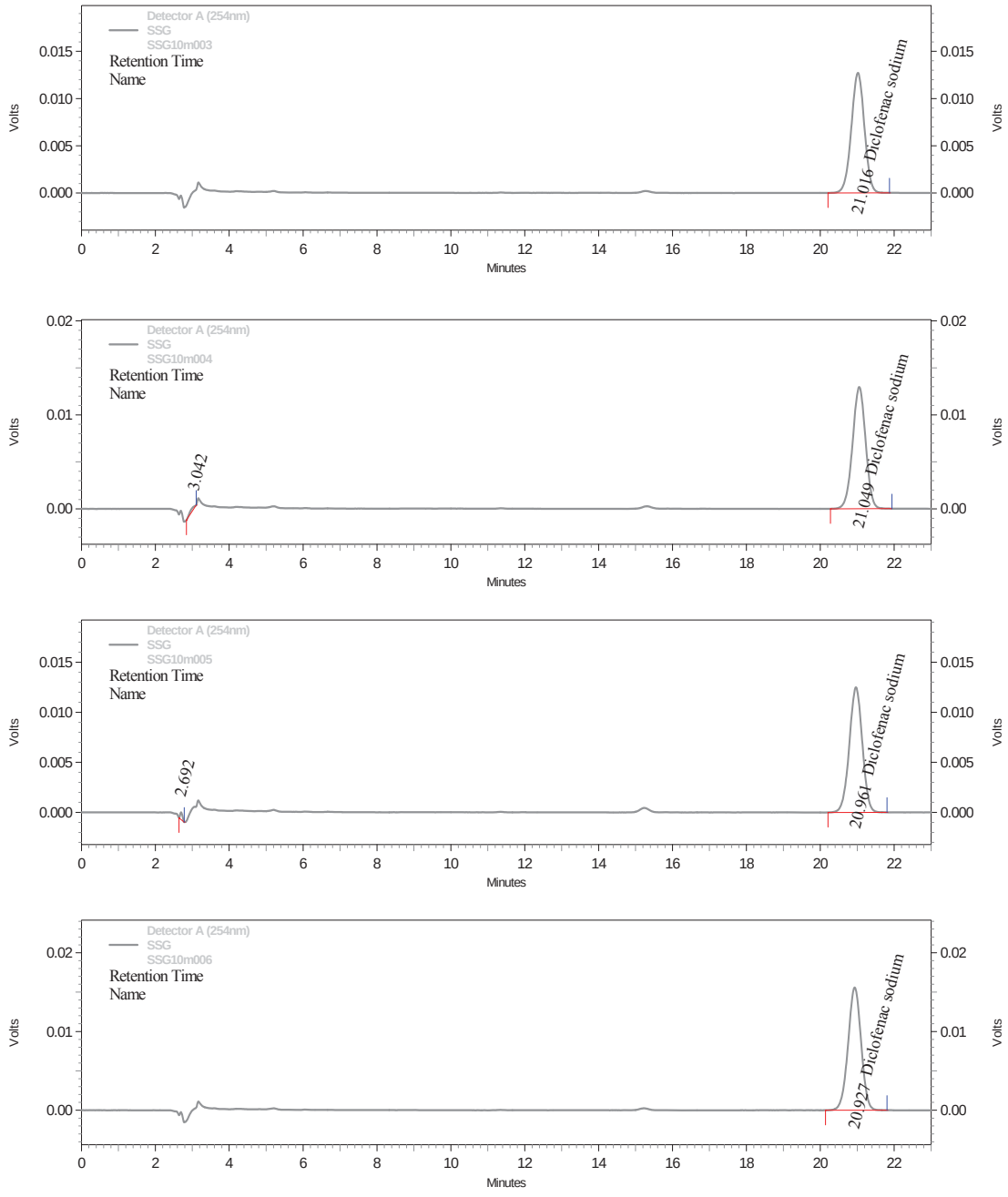

Detector A (254nm)
SSG
SSG5m005
Retention Time
Name
21.284 Diclofenac sodium
Volts
Minutes


Detector A (254nm)
SSG
SSG5m006
Retention Time
Name
21.078 Diclofenac sodium
Volts
Minutes

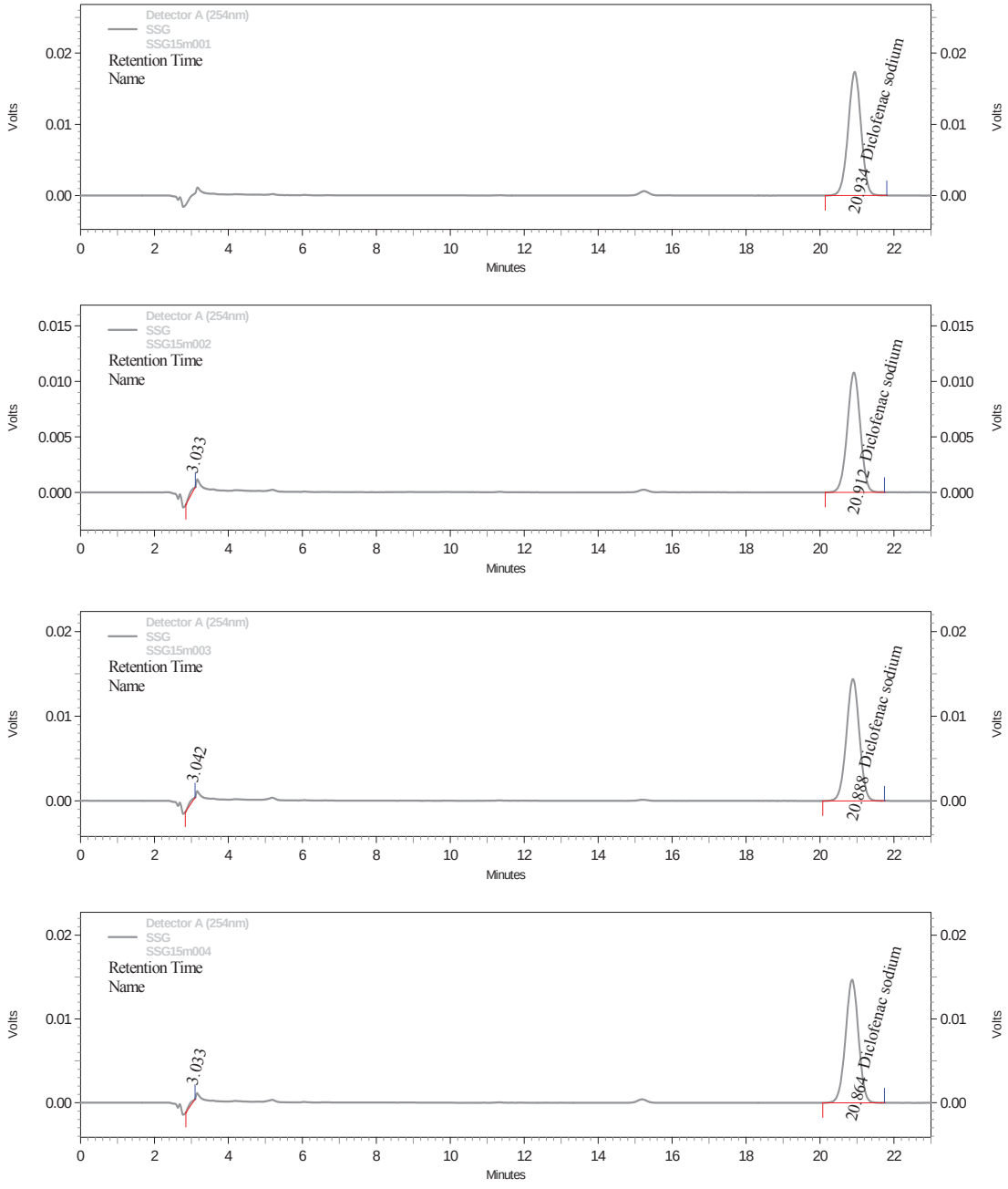
10 min

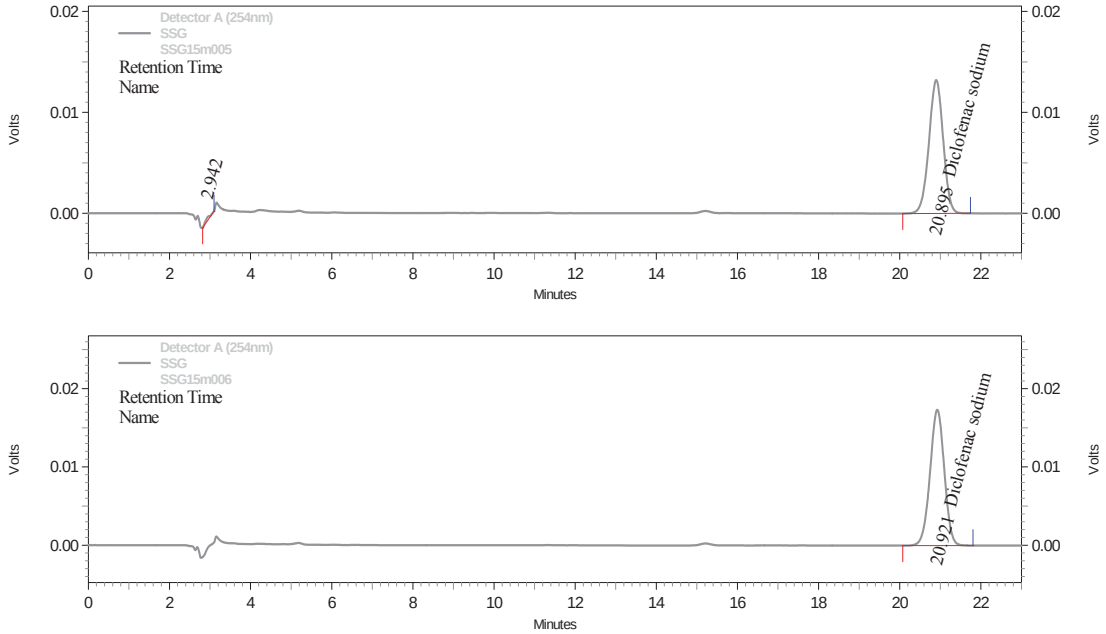

Detector A (254nm)
SSG
SSG10m001
Retention Time
Name
21.034 Diclofenac sodium
Volts
Minutes


Detector A (254nm)
SSG
SSG10m002
Retention Time
Name
21.097 Diclofenac sodium
Volts
Minutes

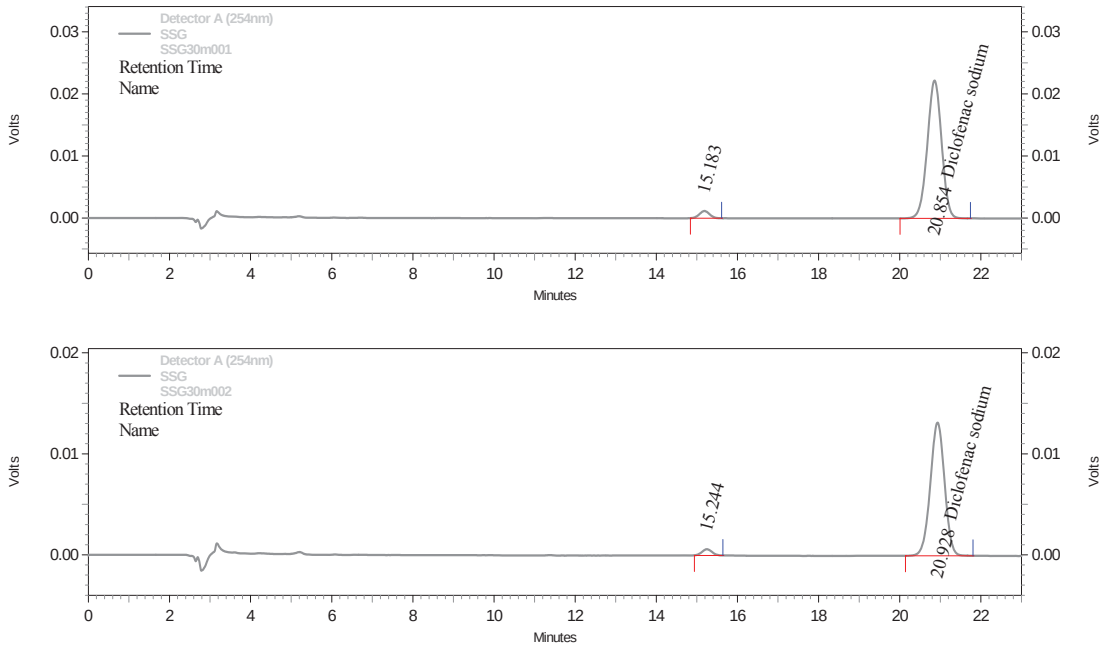

Detector A (254nm)
SSG
SSG10m003
Retention Time
Name
21.016 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
SSG
SSG10m004
Retention Time
Name
3.042
21.049 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
SSG
SSG10m005
Retention Time
Name
2.692
20.961 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
SSG
SSG10m006
Retention Time
Name
20.927 Diclofenac sodium
Volts
Minutes

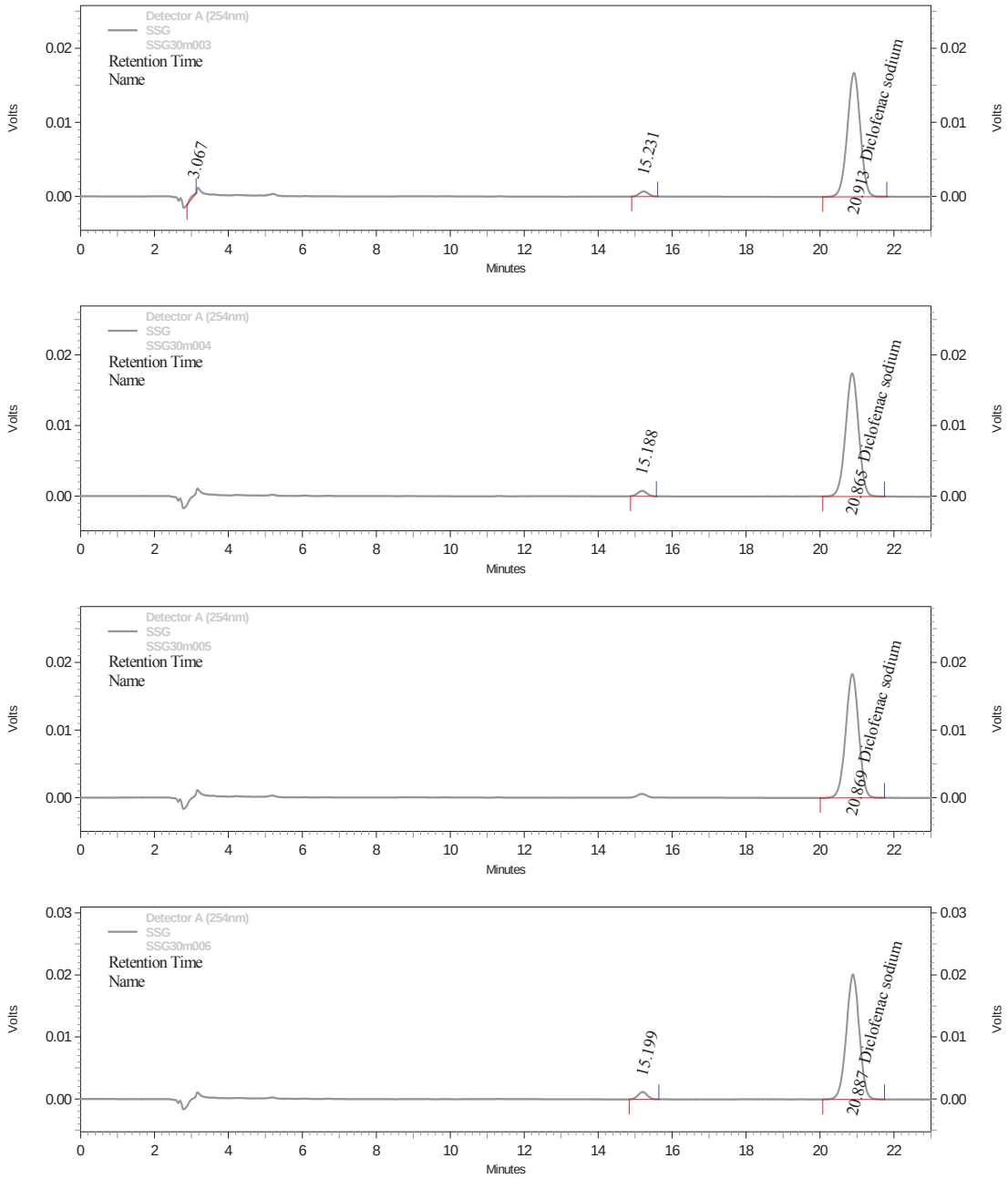
15 min


Detector A (254nm)
SSG
SSG15m001
Retention Time
Name
20.934 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
SSG
SSG15m002
Retention Time
Name
3.033
20.912 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
SSG
SSG15m003
Retention Time
Name
3.042
20.888 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
SSG
SSG15m004
Retention Time
Name
3.033
20.864 Diclofenac sodium
Volts
Minutes

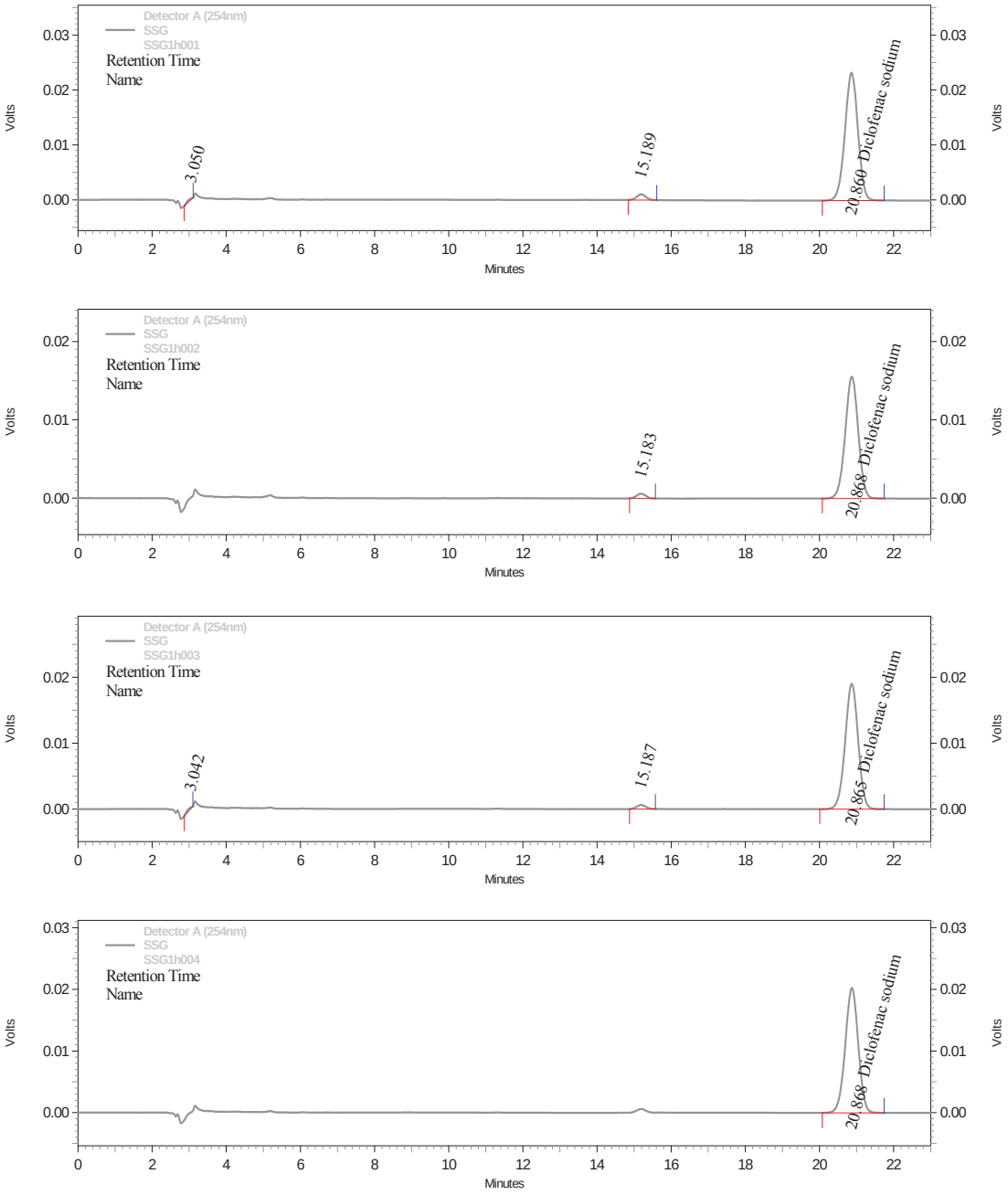

Detector A (254nm)
SSG
SSG15m005
Retention Time
Name
2.942
20.893 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
SSG
SSG15m006
Retention Time
Name
20.921 Diclofenac sodium
Volts
Minutes

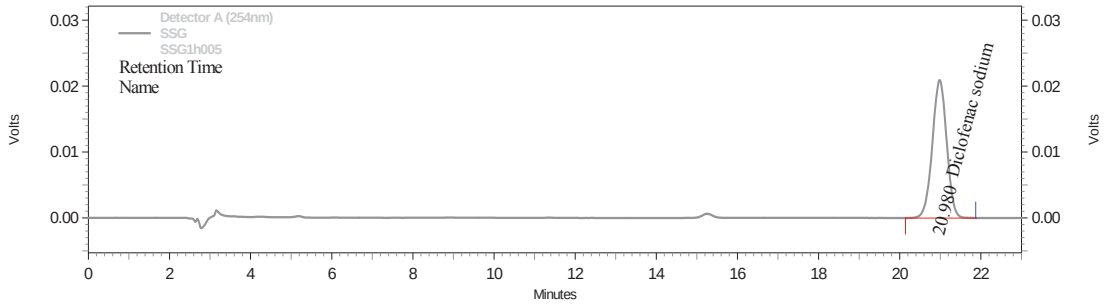
30 min

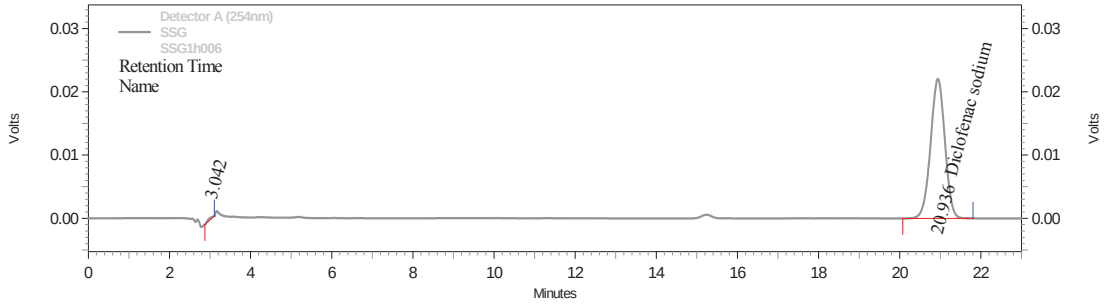

Detector A (254nm)
SSG
SSG30m001
Retention Time
Name
15.183
20.854 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
SSG
SSG30m002
Retention Time
Name
15.244
20.928 Diclofenac sodium
Volts
Minutes


Detector A (254nm)
SSG
SSG30m003
Retention Time
Name
3.067
15.231
20.913 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
SSG
SSG30m004
Retention Time
Name
15.188
20.865 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
SSG
SSG30m005
Retention Time
Name
20.869 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
SSG
SSG30m006
Retention Time
Name
15.199
20.887 Diclofenac sodium
Volts
Minutes

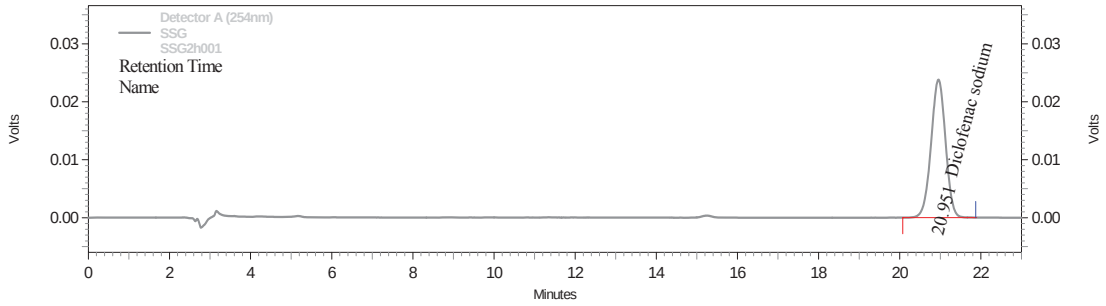
1 h

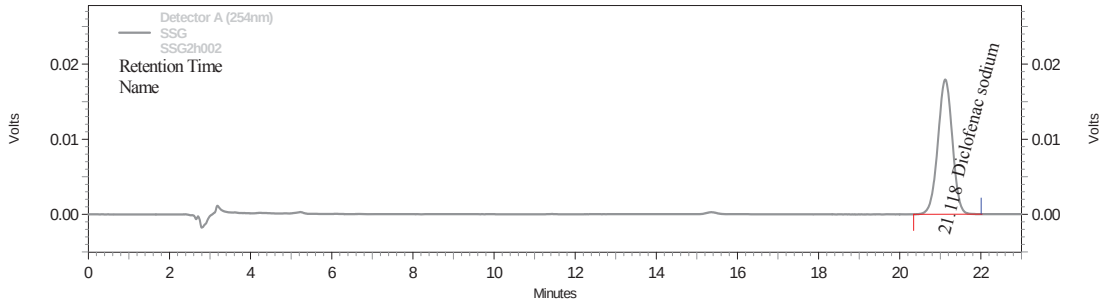

Detector A (254nm)
SSG
SSG1h001
Retention Time
Name
3.050
15.189
20.860 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
SSG
SSG1h002
Retention Time
Name
15.183
20.868 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
SSG
SSG1h003
Retention Time
Name
3.042
15.187
20.865 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
SSG
SSG1h004
Retention Time
Name
20.868 Diclofenac sodium
Volts
Minutes

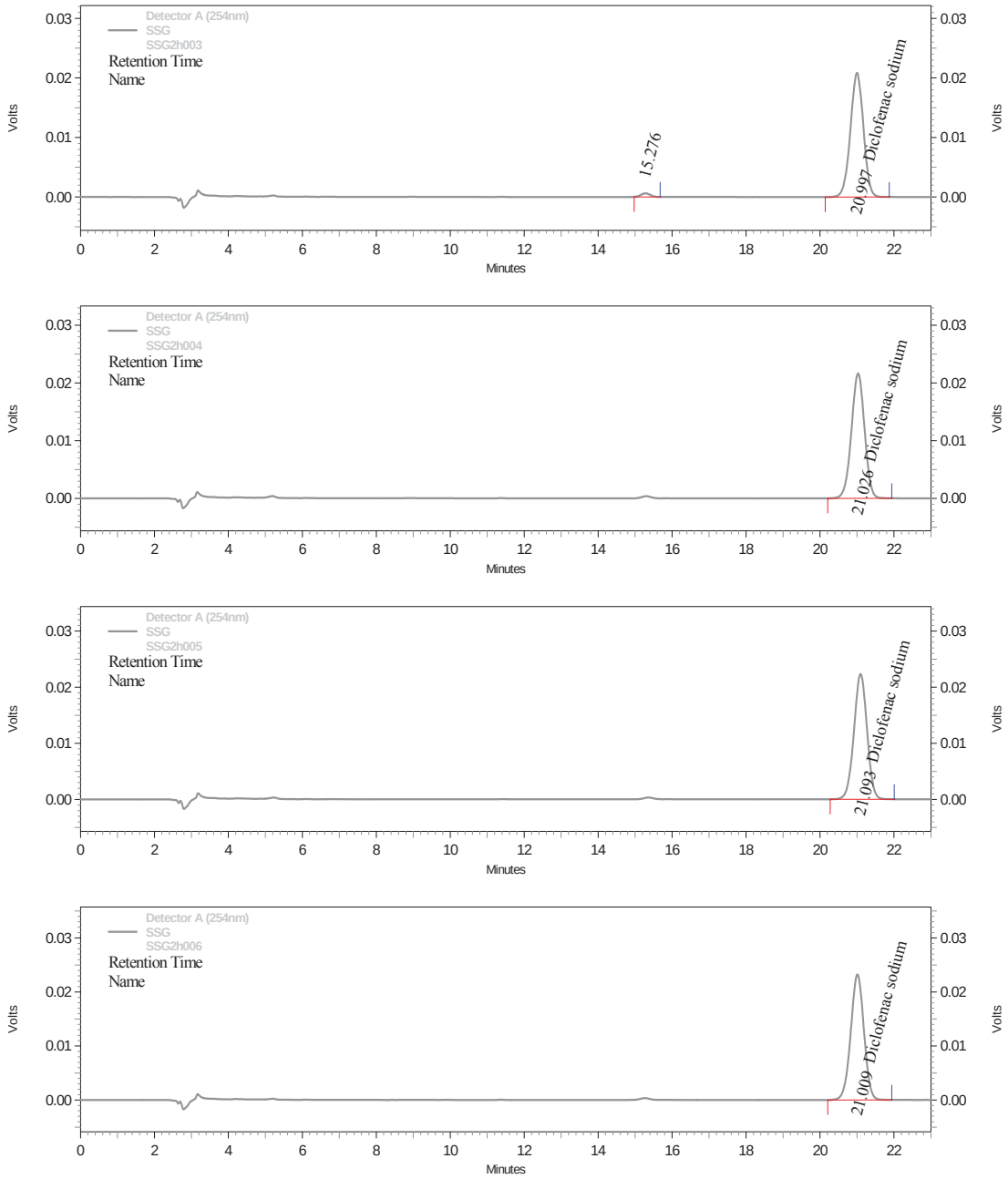

Detector A (254nm)
SSG
SSG1h005
Retention Time
Name
20.980 Diclofenac sodium
Volts
Minutes


Detector A (254nm)
SSG
SSG1h006
Retention Time
Name
3.042
20.936 Diclofenac sodium
Volts
Minutes

2 h


Detector A (254nm)
SSG
SSG2h001
Retention Time
Name
20.951 Diclofenac sodium
Volts
Minutes


Detector A (254nm)
SSG
SSG2h002
Retention Time
Name
21.118 Diclofenac sodium
Volts
Minutes

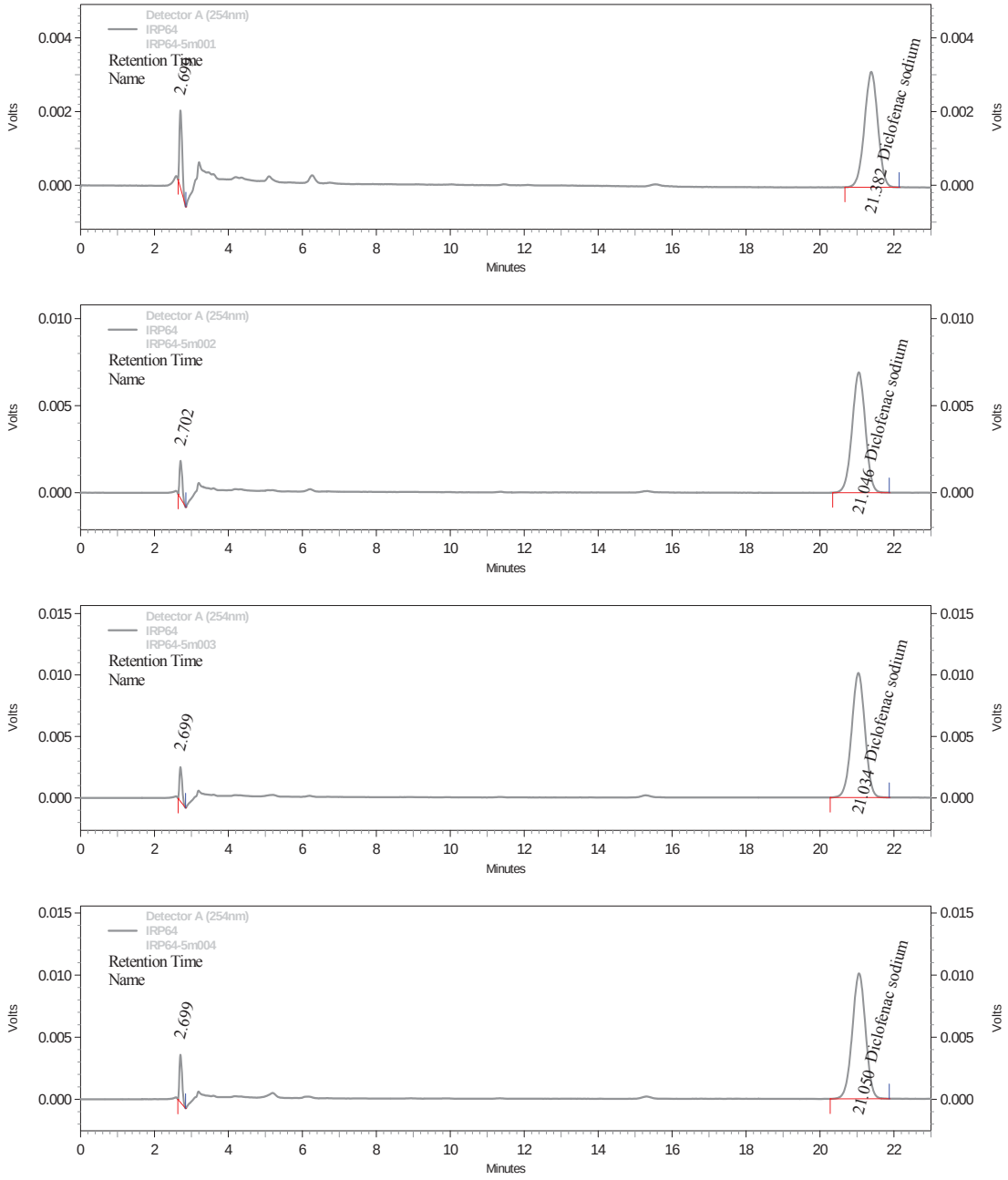

Detector A (254nm)
SSG
SSG2h003
Retention Time
Name
15.276
20.997 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
SSG
SSG2h004
Retention Time
Name
21.026 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
SSG
SSG2h005
Retention Time
Name
21.093 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
SSG
SSG2h006
Retention Time
Name
21.009 Diclofenac sodium
Volts
Minutes

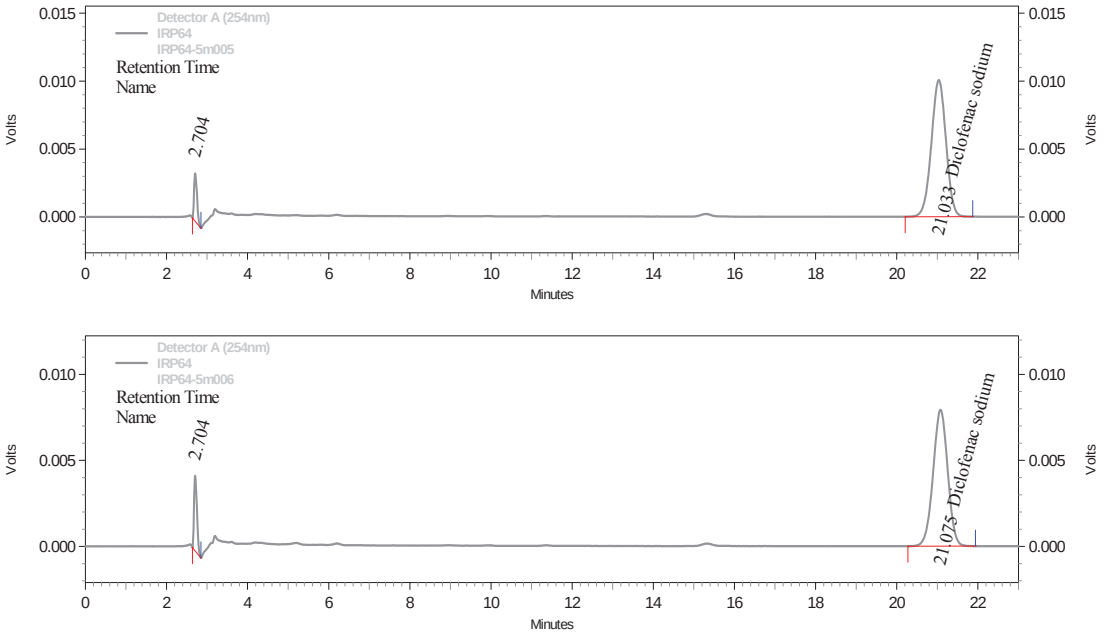
2.2.4 Peak area and chromatogram of DCN released from tablets containing Amberlite® IRP64

Table 65 Retention time and peak area of DCN released from tablets containing Amberlite® IRP64

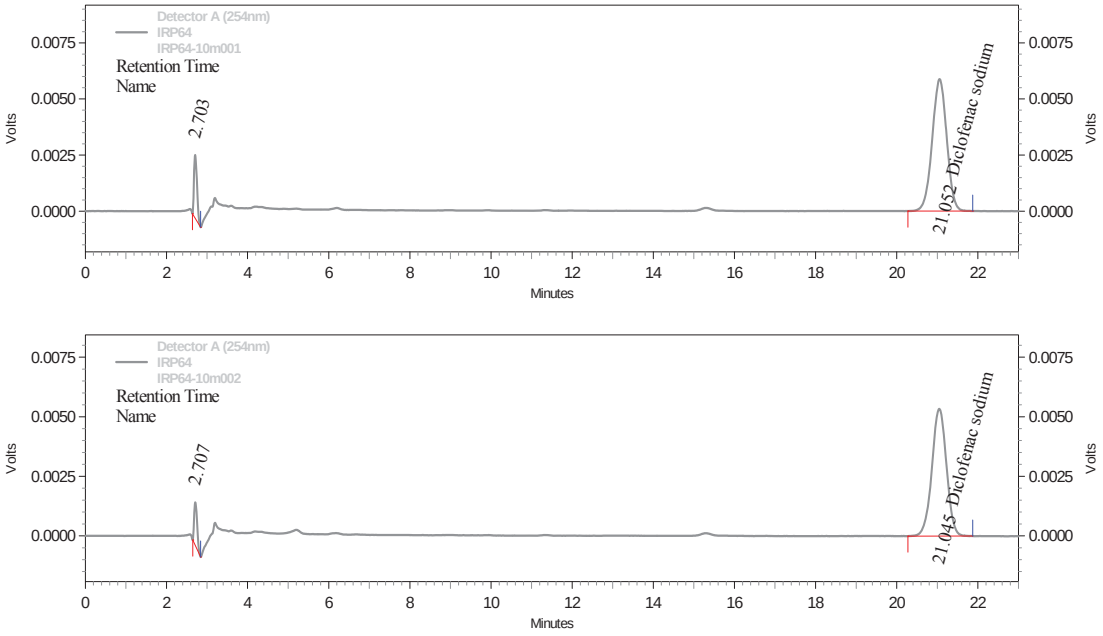
Sample	Retention time (min)	Peak area
5m001	21.382	78823
5m002	21.046	173034
5m003	21.034	253054
5m004	21.050	251751
5m005	21.033	250834
5m006	21.075	197979
10m001	21.052	146748
10m002	21.045	133530
10m003	21.046	277421
10m004	21.050	284559
10m005	21.055	296824
10m006	21.065	252443
15m001	21.065	174090
15m002	21.083	164085
15m003	21.080	290208
15m004	21.070	325765
15m005	21.060	320733
15m006	21.078	293253
30m001	21.110	258973
30m002	21.116	259206
30m003	21.123	339502
30m004	21.116	381141
30m005	20.918	359685
30m006	20.893	382754
1h001	24.502	351525
1h002	22.553	386545
1h003	22.494	419036
1h004	22.255	420885
1h005	22.220	402211
1h006	22.298	417216
2h001	18.386	353482
2h002	18.438	426884
2h003	18.568	388122
2h004	18.712	379236
2h005	18.584	365843
2h006	18.518	376844

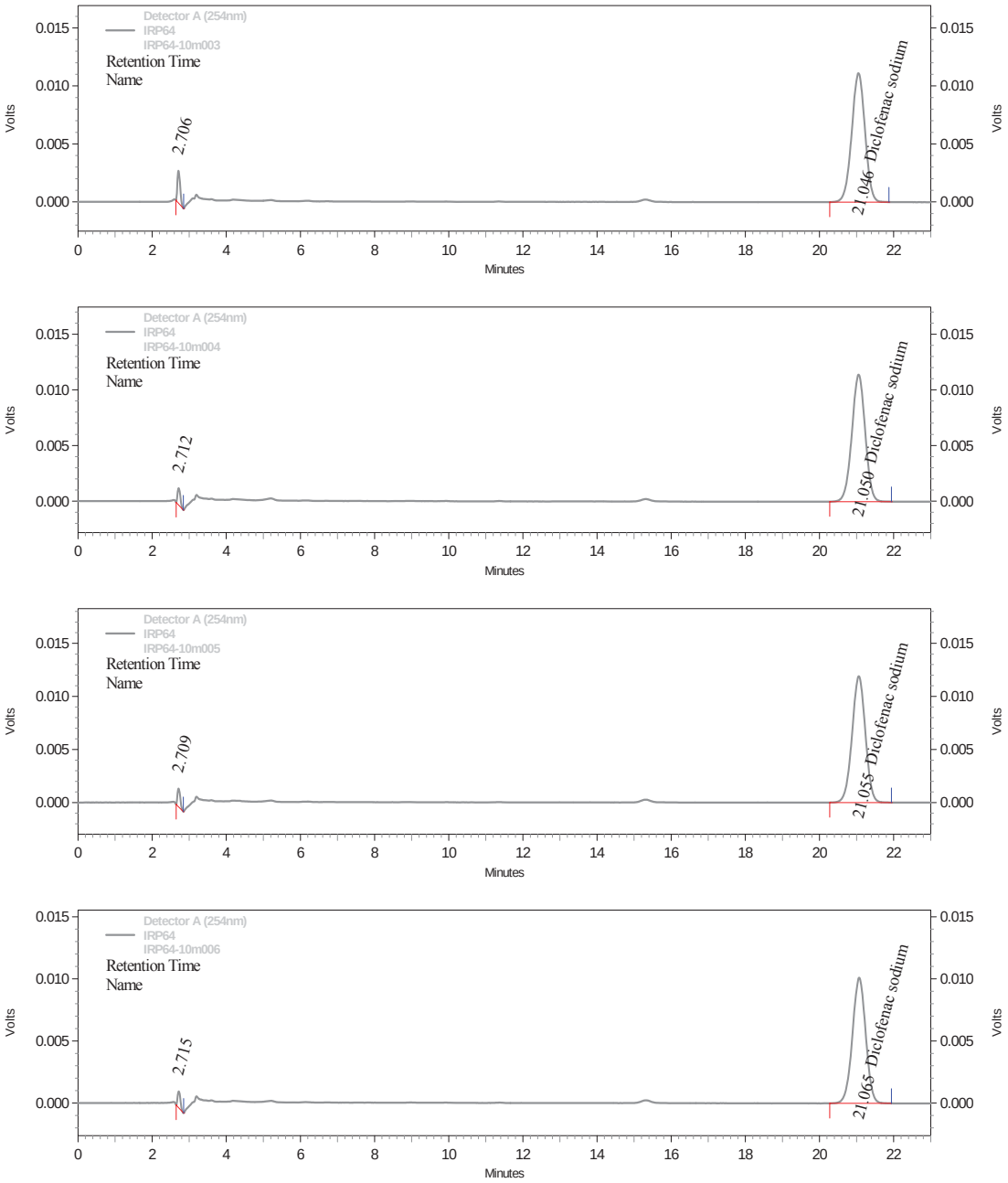
5 min


Detector A (254nm)
IRP64
IRP64-5m001
Retention Time
Name
2.699
21.382 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
IRP64
IRP64-5m002
Retention Time
Name
2.702
21.046 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
IRP64
IRP64-5m003
Retention Time
Name
2.699
21.034 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
IRP64
IRP64-5m004
Retention Time
Name
2.699
21.030 Diclofenac sodium
Volts
Minutes

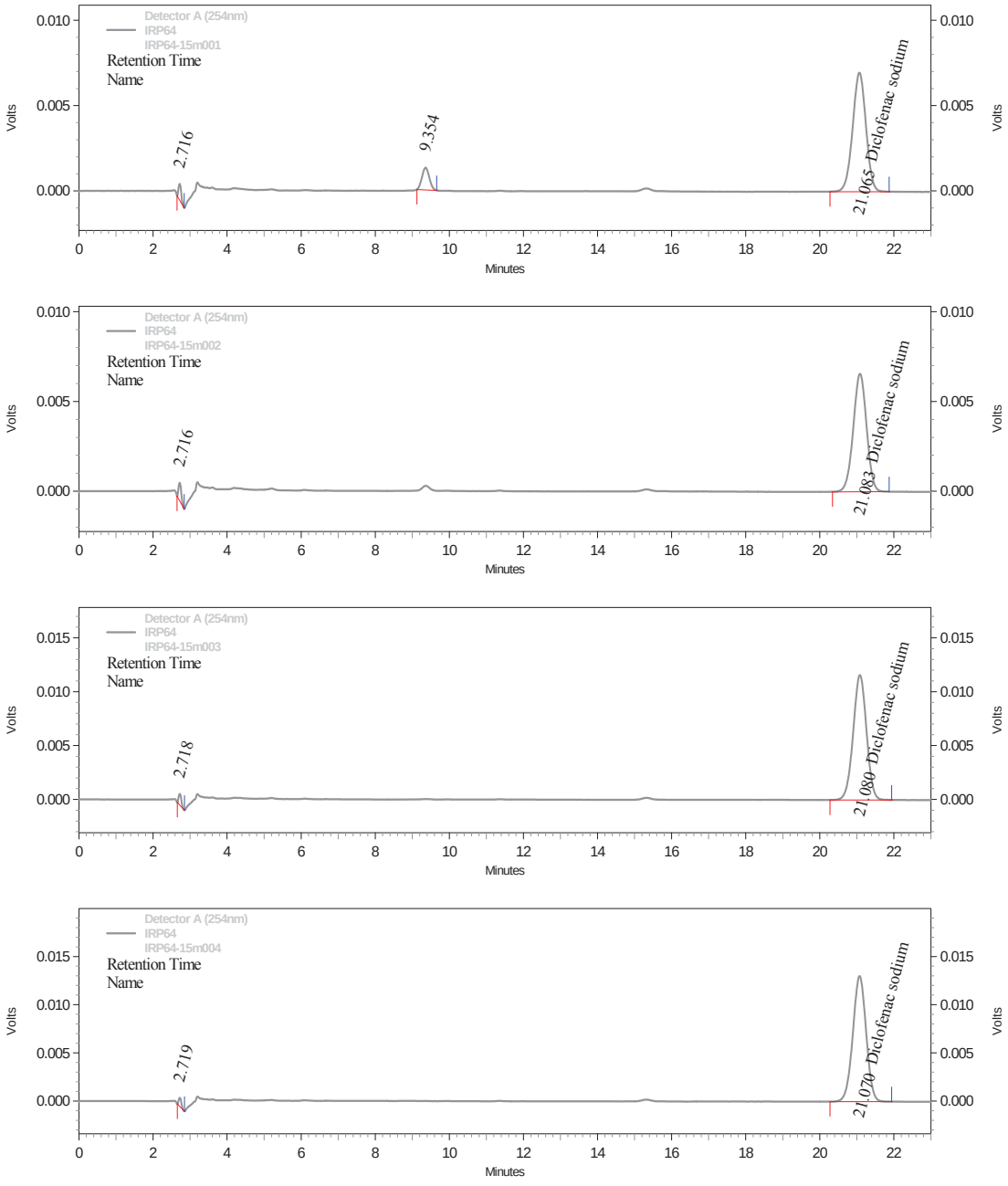

Detector A (254nm)
IRP64
IRP64-5m005
Retention Time
Name
2.704
21.033 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
IRP64
IRP64-5m006
Retention Time
Name
2.704
21.075 Diclofenac sodium
Volts
Minutes

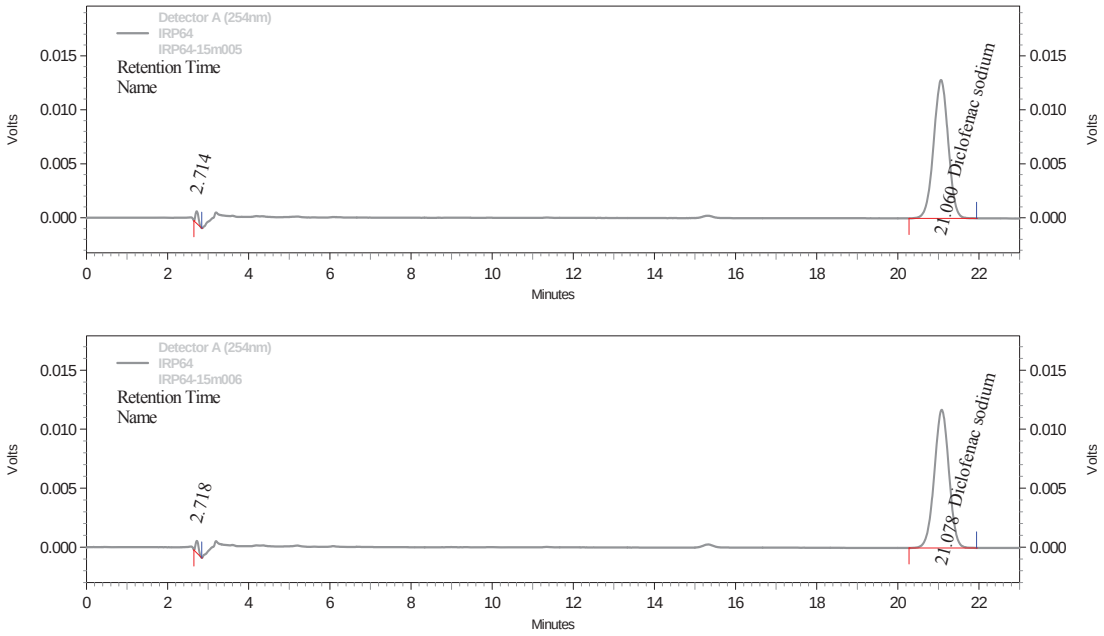
10 min


Detector A (254nm)
IRP64
IRP64-10m001
Retention Time
Name
2.703
21.052 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
IRP64
IRP64-10m002
Retention Time
Name
2.707
21.045 Diclofenac sodium
Volts
Minutes

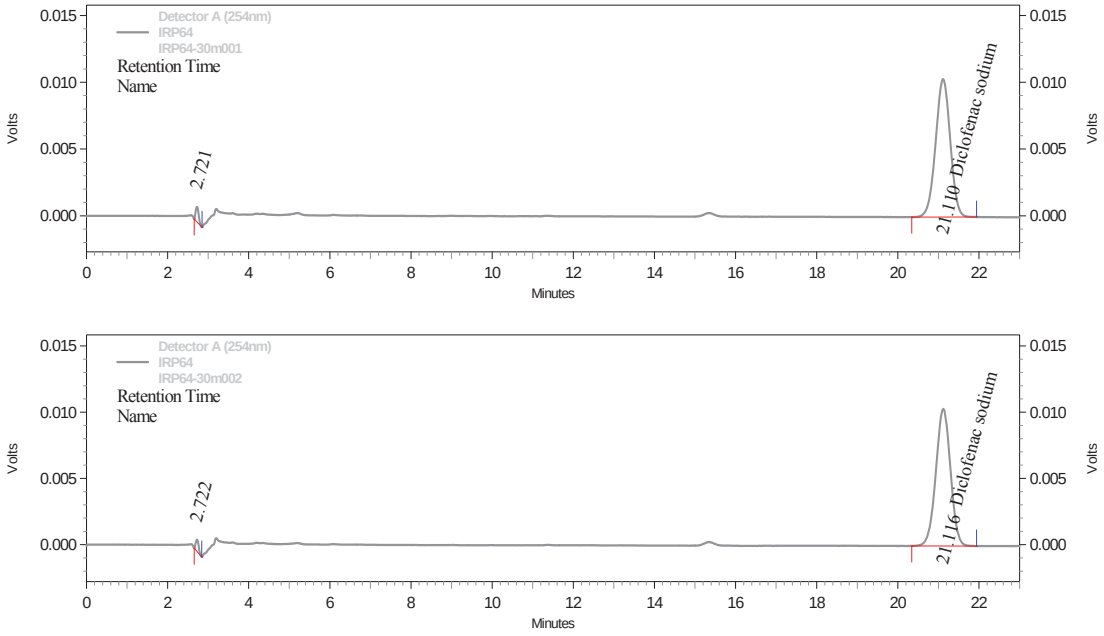

Detector A (254nm)
IRP64
IRP64-10m003
Retention Time
Name
2.706
21.046 Diclofenac sodium
Detector A (254nm)
IRP64
IRP64-10m004
Retention Time
Name
2.712
21.050 Diclofenac sodium
Detector A (254nm)
IRP64
IRP64-10m005
Retention Time
Name
2.709
21.055 Diclofenac sodium
Detector A (254nm)
IRP64
IRP64-10m006
Retention Time
Name
2.715
21.065 Diclofenac sodium
Volts
Minutes
0.015
0.010
0.005
0.000
0
2
4
6
8
10
12
14
16
18
20
22

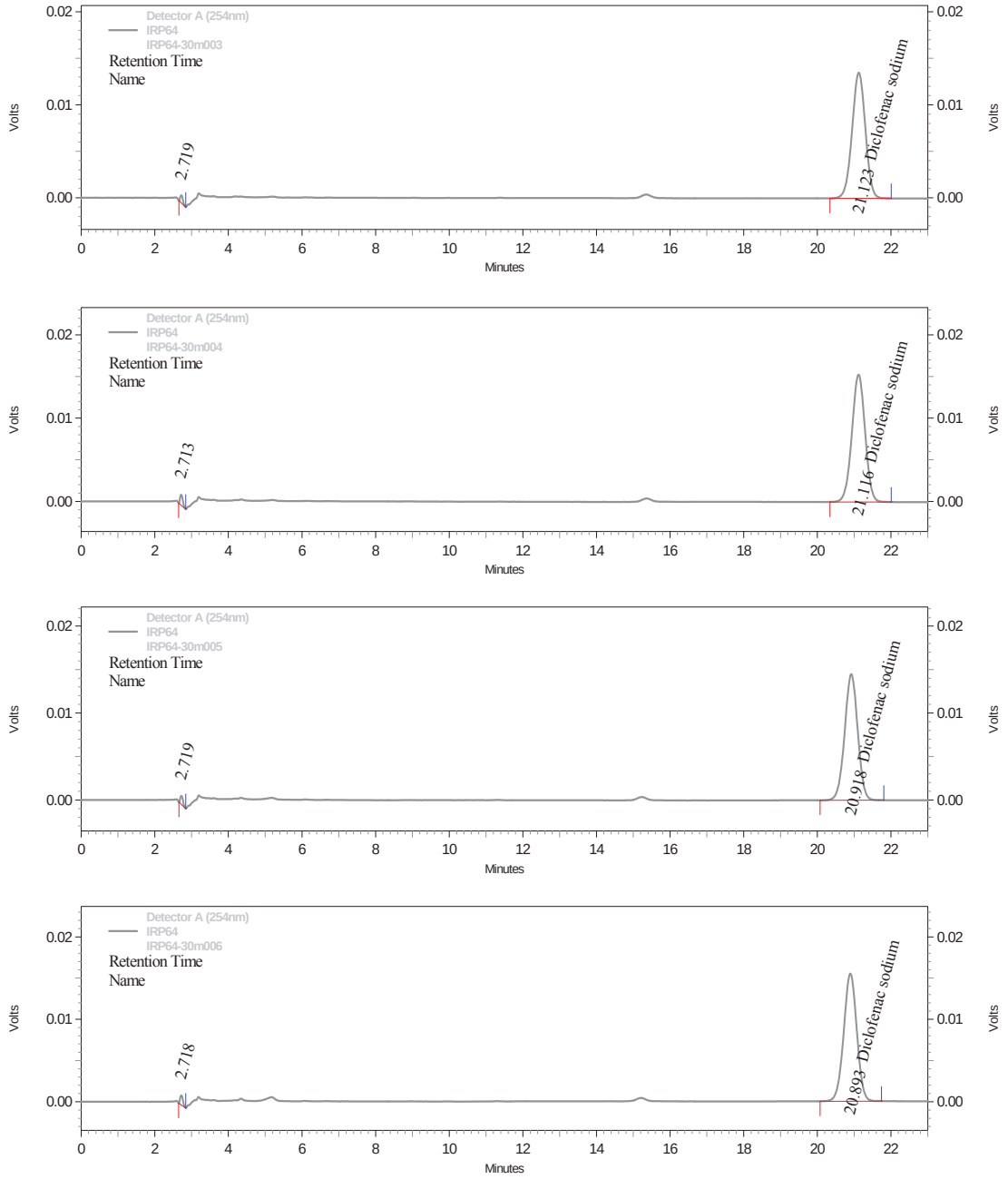
15 min


Detector A (254nm)
IRP64
IRP64-15m001
Retention Time
Name
2.716
9.354
21.065 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
IRP64
IRP64-15m002
Retention Time
Name
2.716
21.083 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
IRP64
IRP64-15m003
Retention Time
Name
2.718
21.080 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
IRP64
IRP64-15m004
Retention Time
Name
2.719
21.070 Diclofenac sodium
Volts
Minutes

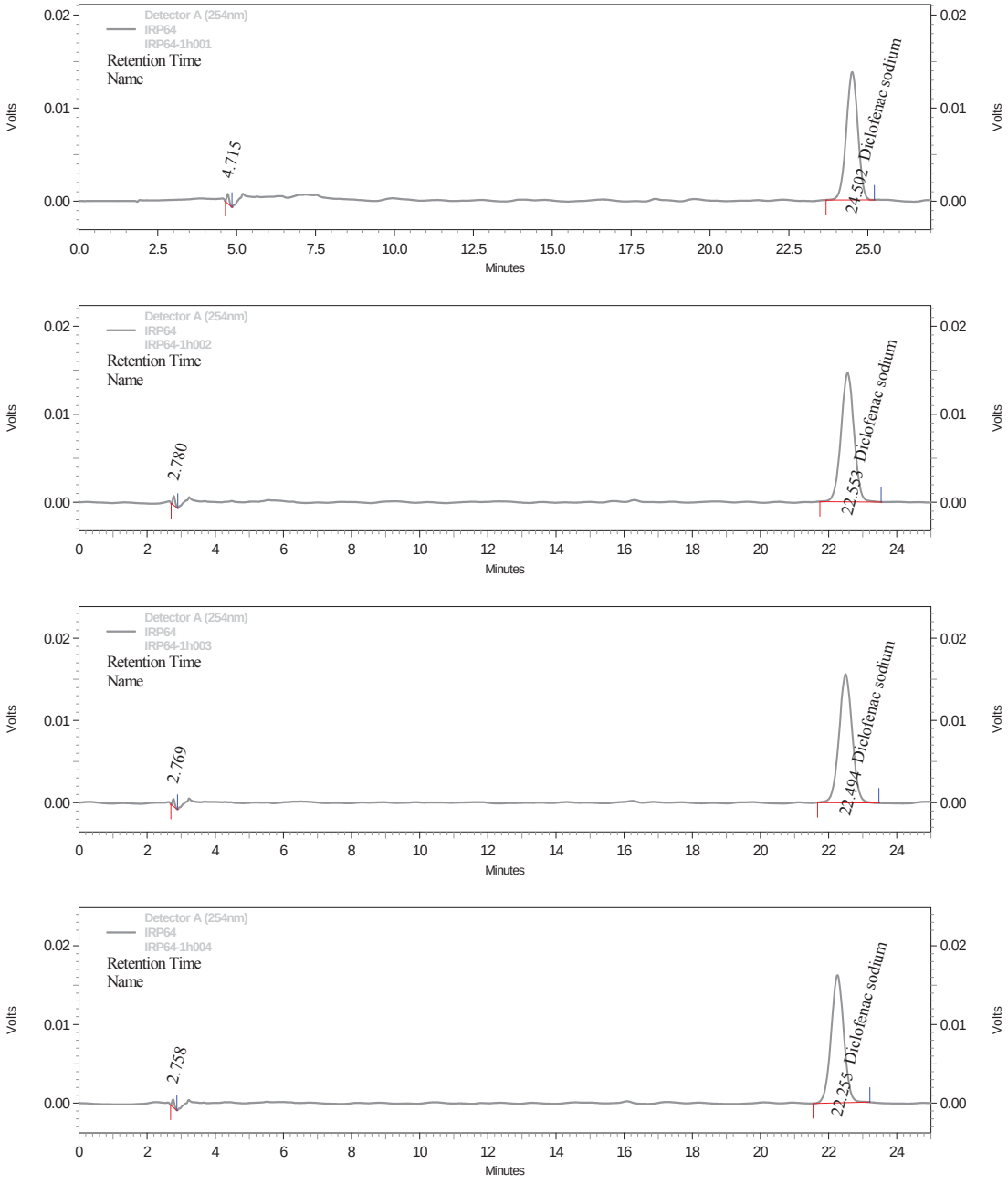

Detector A (254nm)
IRP64
IRP64-15m005
Retention Time
Name
2.714
21.060 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
IRP64
IRP64-15m006
Retention Time
Name
2.718
21.078 Diclofenac sodium
Volts
Minutes

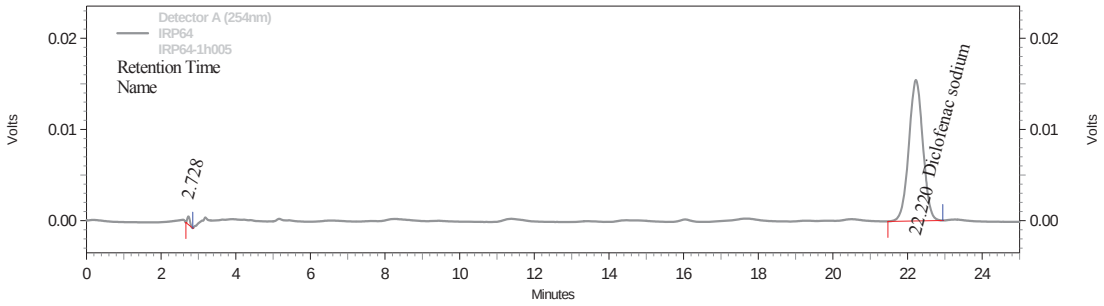
30 min

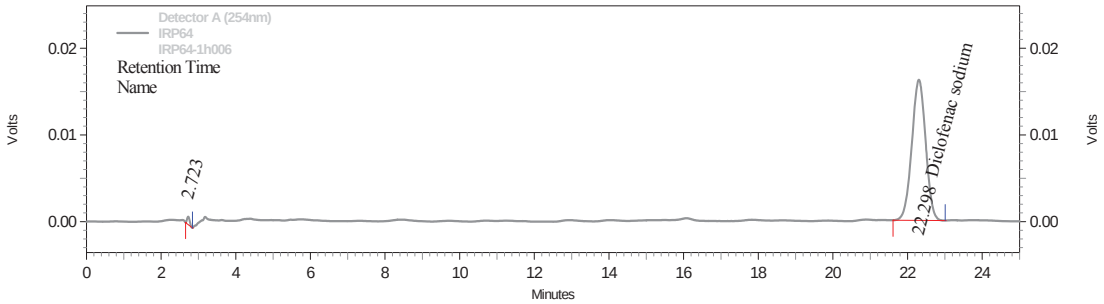

Detector A (254nm)
IRP64
IRP64-30m001
Retention Time
Name
2.721
21.110 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
IRP64
IRP64-30m002
Retention Time
Name
2.722
21.116 Diclofenac sodium
Volts
Minutes


Detector A (254nm)
IRP64
IRP64-30m003
Retention Time
Name
2.719
21.123 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
IRP64
IRP64-30m004
Retention Time
Name
2.713
21.116 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
IRP64
IRP64-30m005
Retention Time
Name
2.719
20.918 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
IRP64
IRP64-30m006
Retention Time
Name
2.718
20.893 Diclofenac sodium
Volts
Minutes

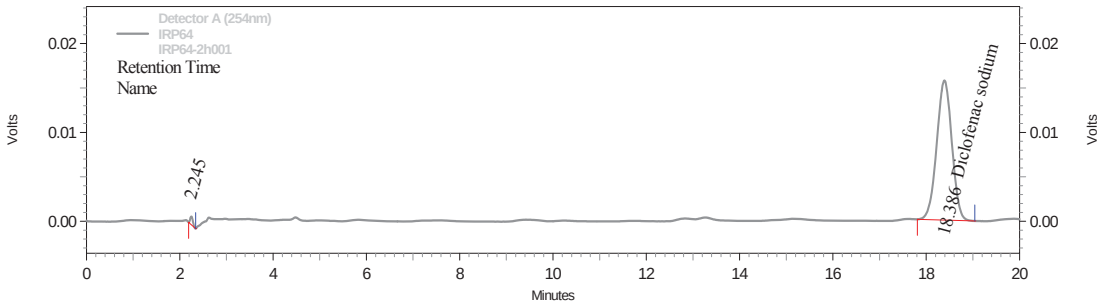
1 h

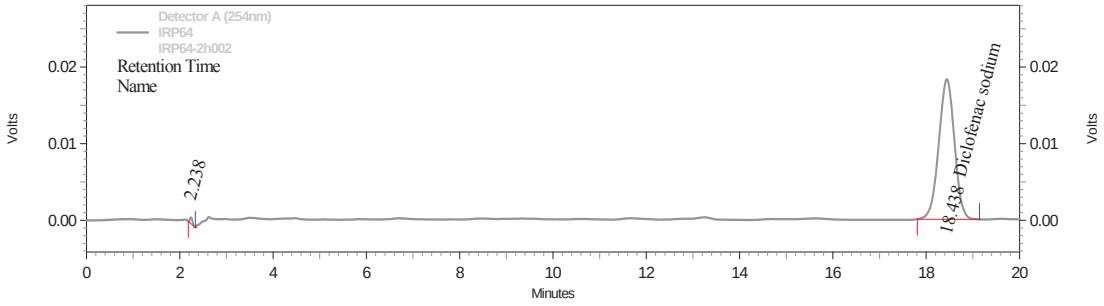

Detector A (254nm)
IRP64
IRP64-1h001
Retention Time
Name
4.715
24.502 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
IRP64
IRP64-1h002
Retention Time
Name
2.780
22.553 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
IRP64
IRP64-1h003
Retention Time
Name
2.769
22.494 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
IRP64
IRP64-1h004
Retention Time
Name
2.758
22.255 Diclofenac sodium
Volts
Minutes

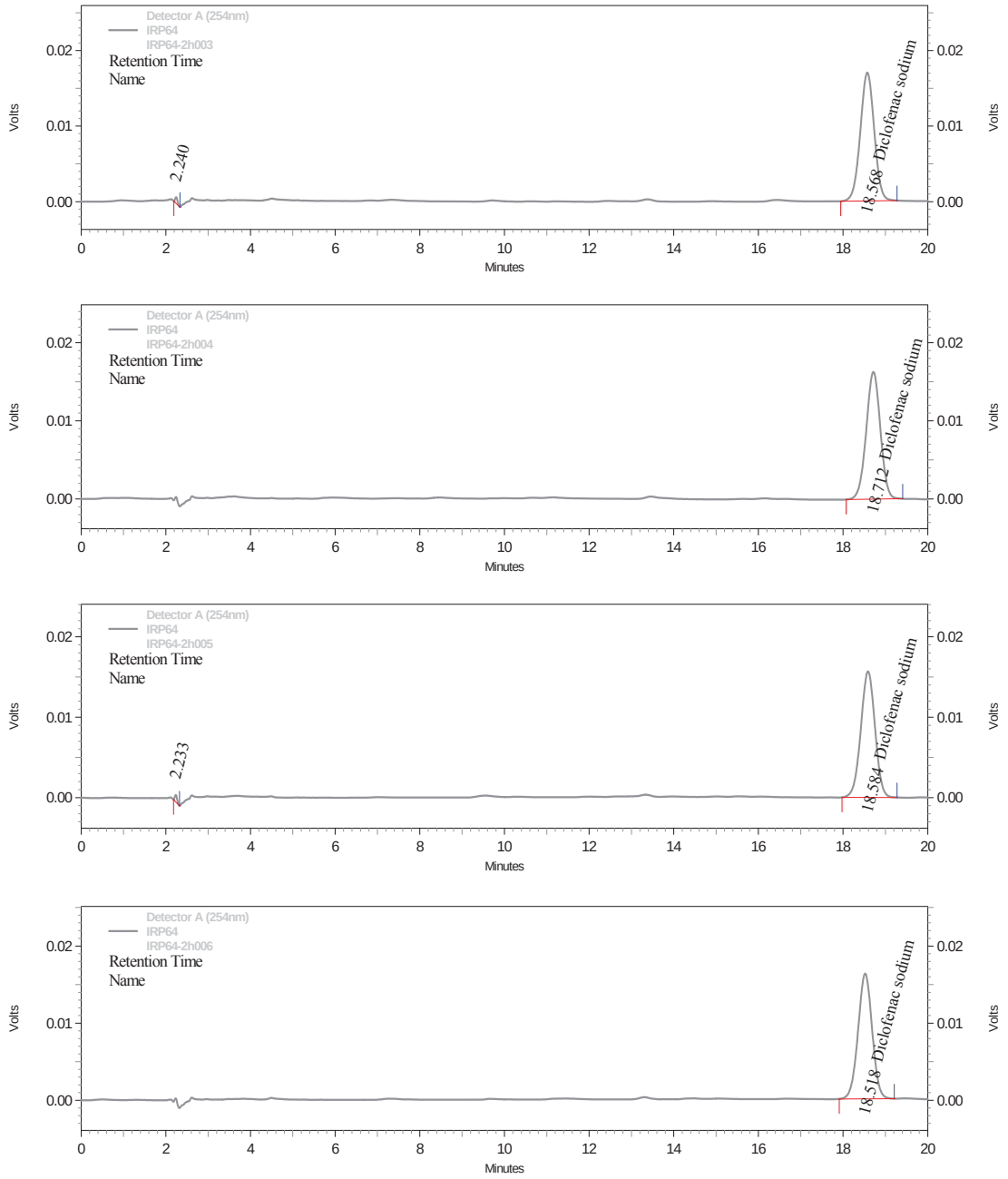

Detector A (254nm)
IRP64
IRP64-1h005
Retention Time
Name
2.728
22.220 Diclofenac sodium
Volts
Minutes


Detector A (254nm)
IRP64
IRP64-1h006
Retention Time
Name
2.723
22.298 Diclofenac sodium
Volts
Minutes

2 h


Detector A (254nm)
IRP64
IRP64-2h001
Retention Time
Name
2.245
18.386 Diclofenac sodium
Volts
Minutes


Detector A (254nm)
IRP64
IRP64-2h002
Retention Time
Name
2.238
18.438 Diclofenac sodium
Volts
Minutes

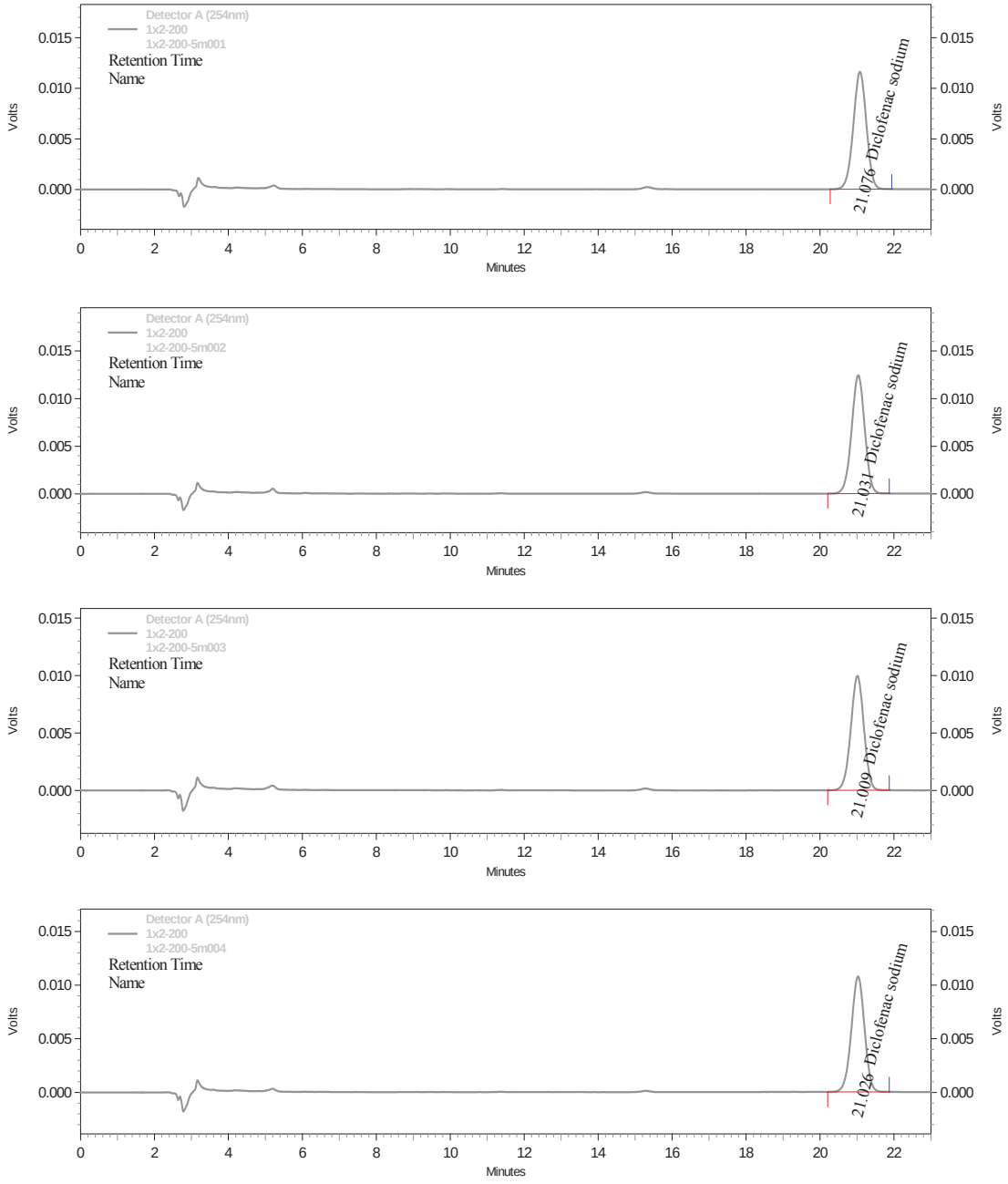

Detector A (254nm)
IRP64
IRP64-2h003
Retention Time
Name
2.240
18.568 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
IRP64
IRP64-2h004
Retention Time
Name
18.712 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
IRP64
IRP64-2h005
Retention Time
Name
2.233
18.584 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
IRP64
IRP64-2h006
Retention Time
Name
18.518 Diclofenac sodium
Volts
Minutes

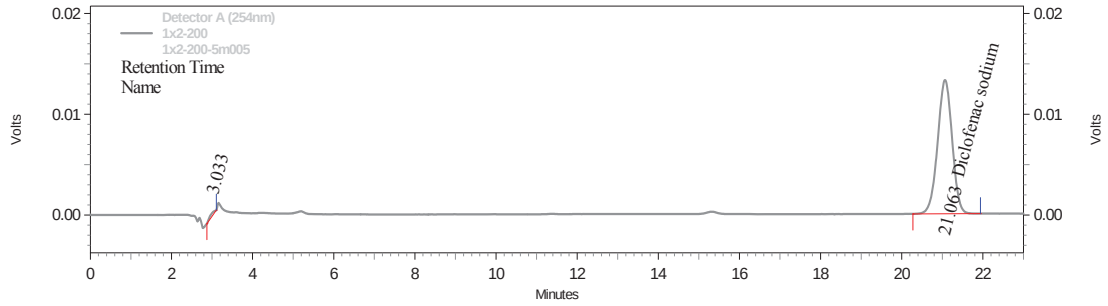
2.2.5 Peak area and chromatogram of DCN released from tablets containing Dowex® 1x2-200

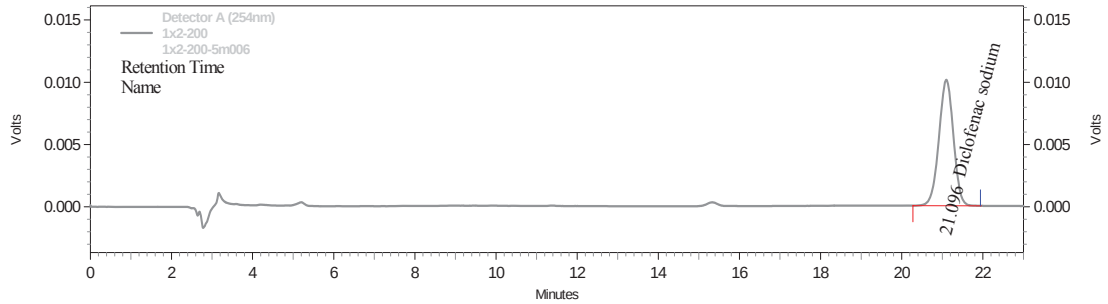
Table 66 Retention time and peak area of DCN released from tablets containing Dowex® 1x2-200

Sample	Retention time (min)	Peak area
5m001	21.076	285840
5m002	21.031	306765
5m003	21.009	245583
5m004	21.026	266042
5m005	21.063	329024
5m006	21.096	251253
10m001	21.197	326930
10m002	20.986	353866
10m003	21.014	291881
10m004	20.994	304784
10m005	21.157	371456
10m006	21.346	315413
15m001	21.512	340804
15m002	21.457	371401
15m003	21.680	313610
15m004	20.139	315473
15m005	19.896	384007
15m006	20.684	343592
30m001	21.056	355344
30m002	21.014	384930
30m003	20.694	336358
30m004	20.500	329963
30m005	20.442	399316
30m006	20.388	375170
1h001	20.360	357532
1h002	20.359	382517
1h003	20.356	345985
1h004	20.311	335997
1h005	20.288	406990
1h006	20.247	374942
2h001	20.253	350828
2h002	20.256	377494
2h003	20.253	347828
2h004	20.183	339538
2h005	20.380	402276
2h006	20.488	367255

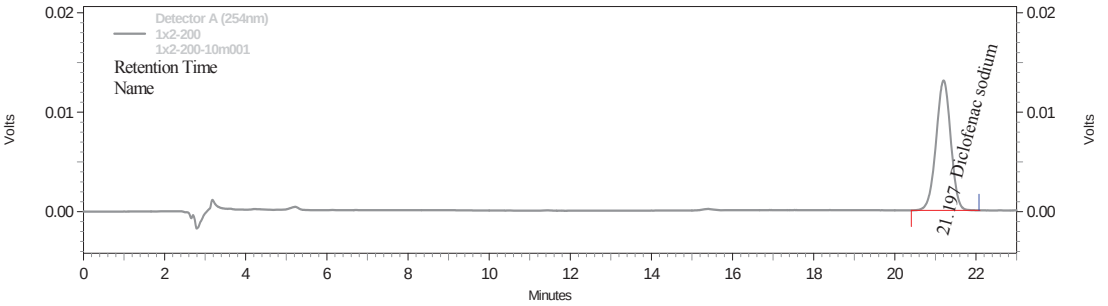
5 min

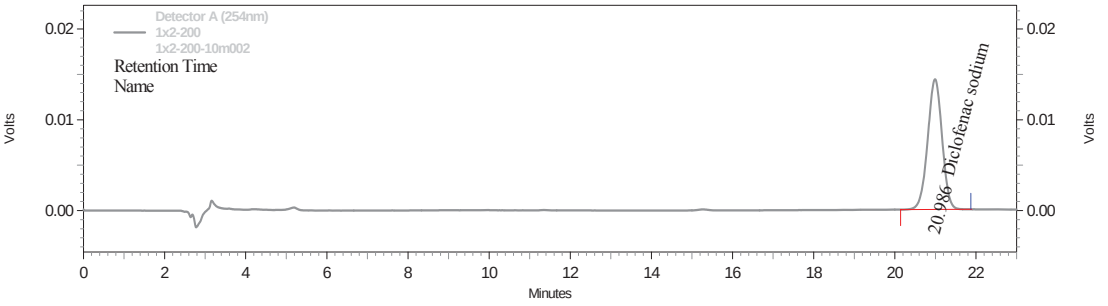

Detector A (254nm)
1x2-200
1x2-200-5m001
Retention Time
Name
21.076 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
1x2-200
1x2-200-5m002
Retention Time
Name
21.031 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
1x2-200
1x2-200-5m003
Retention Time
Name
21.009 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
1x2-200
1x2-200-5m004
Retention Time
Name
21.026 Diclofenac sodium
Volts
Minutes

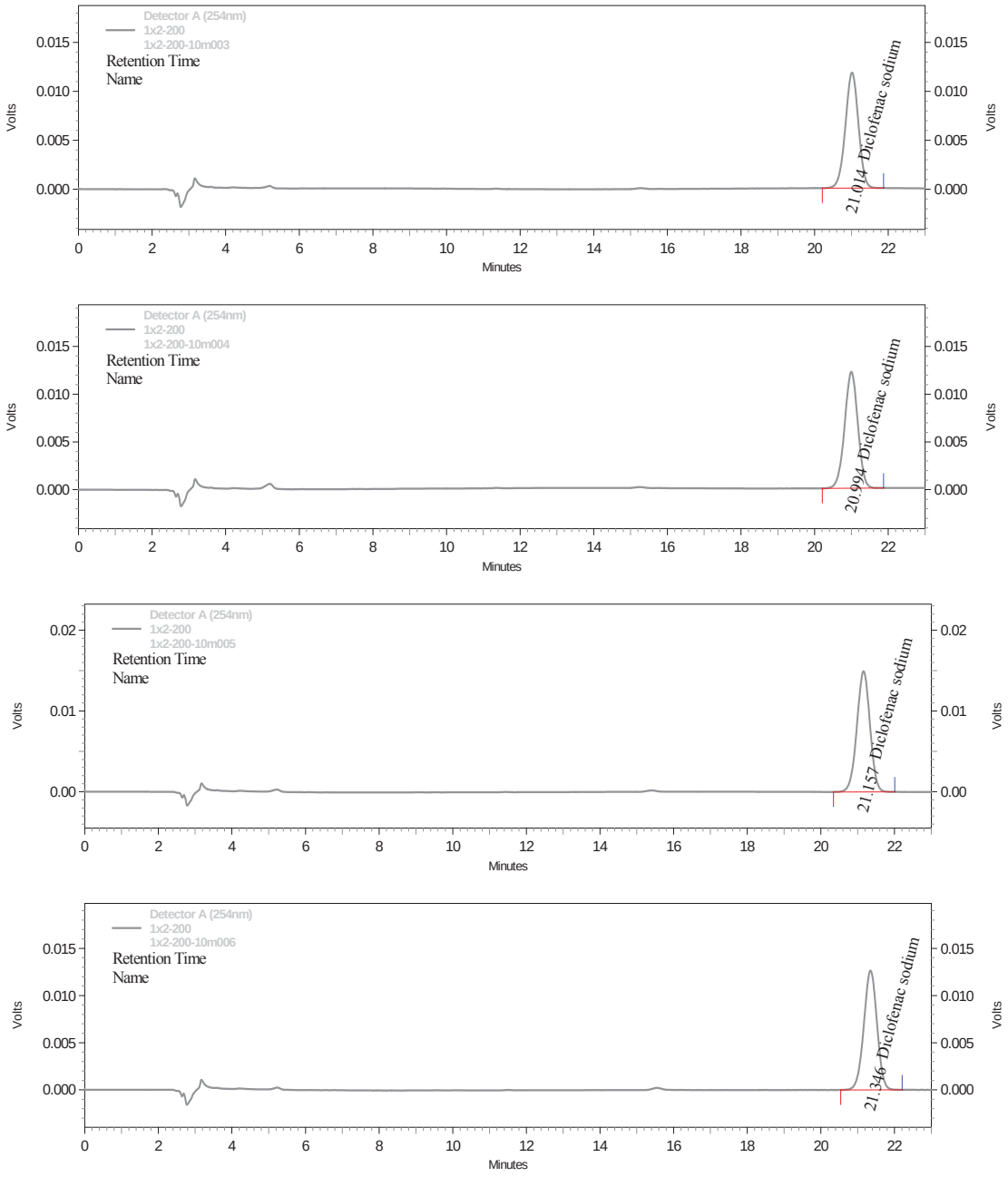

Detector A (254nm)
1x2-200
1x2-200-5m005
Retention Time
Name
3.033
21.063 Diclofenac sodium
Volts
Minutes


Detector A (254nm)
1x2-200
1x2-200-5m006
Retention Time
Name
21.096 Diclofenac sodium
Volts
Minutes

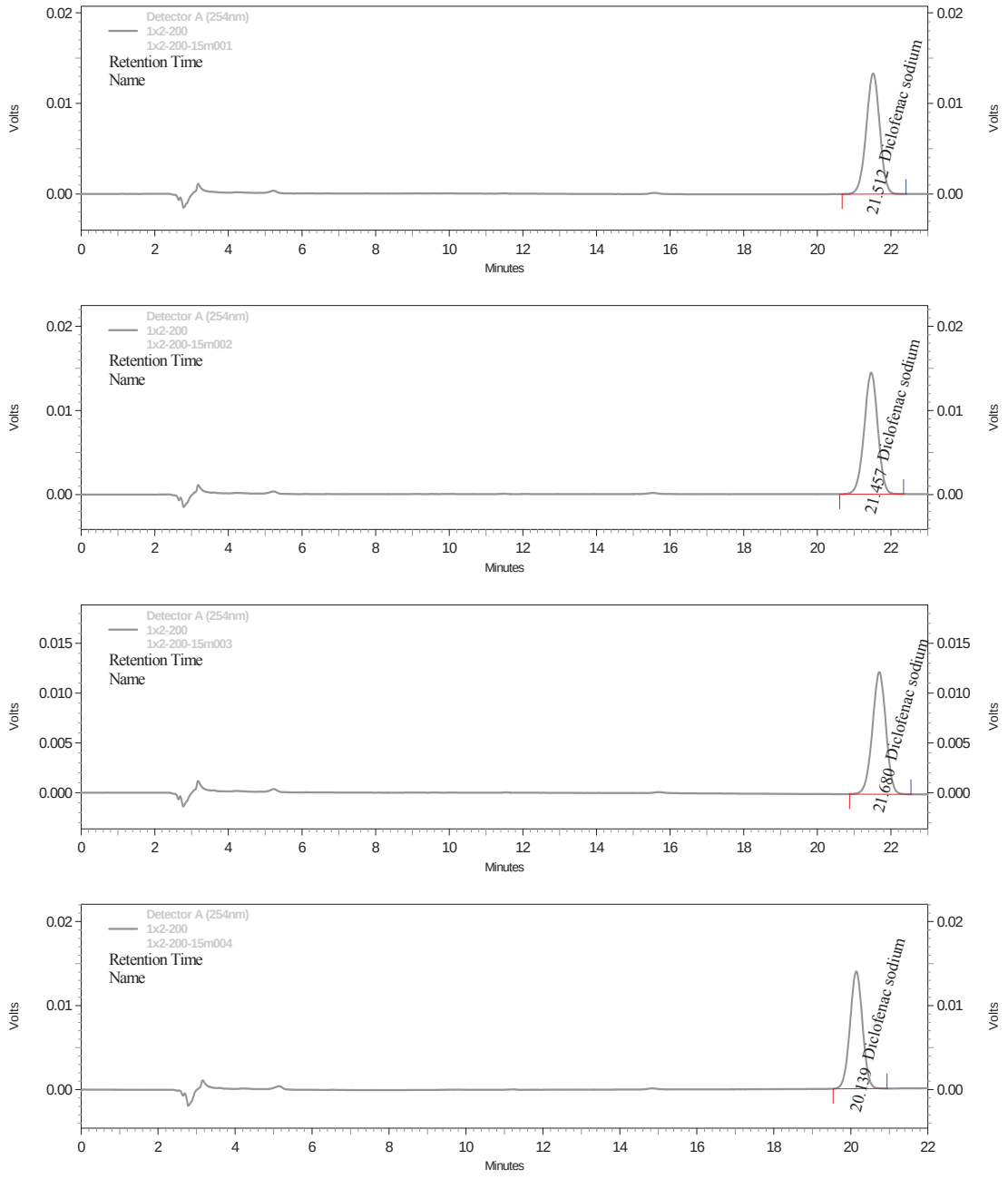
10 min

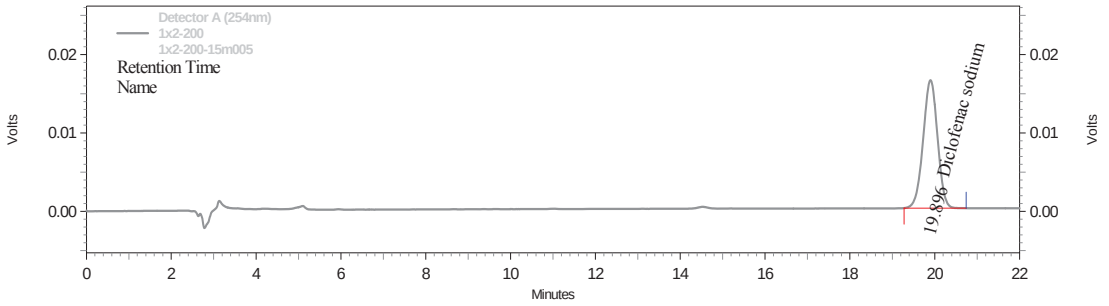

Detector A (254nm)
1x2-200
1x2-200-10m001
Retention Time
Name
21.197 Diclofenac sodium
Volts
Minutes

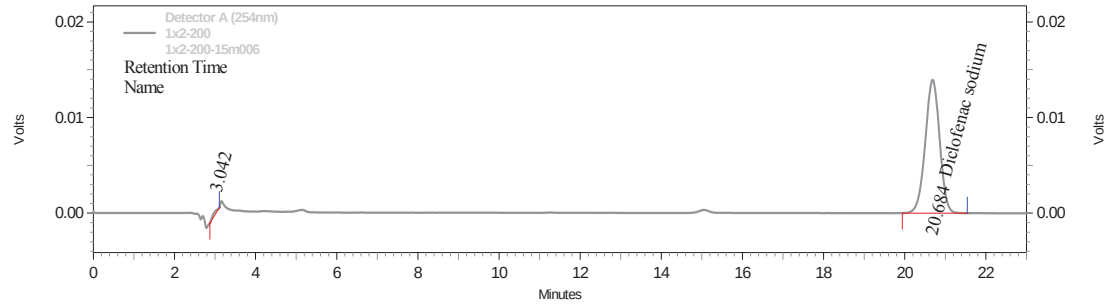

Detector A (254nm)
1x2-200
1x2-200-10m002
Retention Time
Name
20.986 Diclofenac sodium
Volts
Minutes


Detector A (254nm)
1x2-200
1x2-200-10m003
Retention Time
Name
21.014 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
1x2-200
1x2-200-10m004
Retention Time
Name
20.994 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
1x2-200
1x2-200-10m005
Retention Time
Name
21.157 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
1x2-200
1x2-200-10m006
Retention Time
Name
21.346 Diclofenac sodium
Volts
Minutes

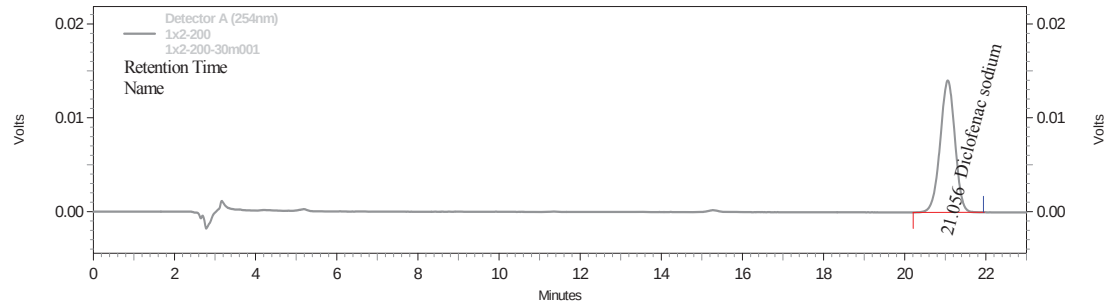
15 min

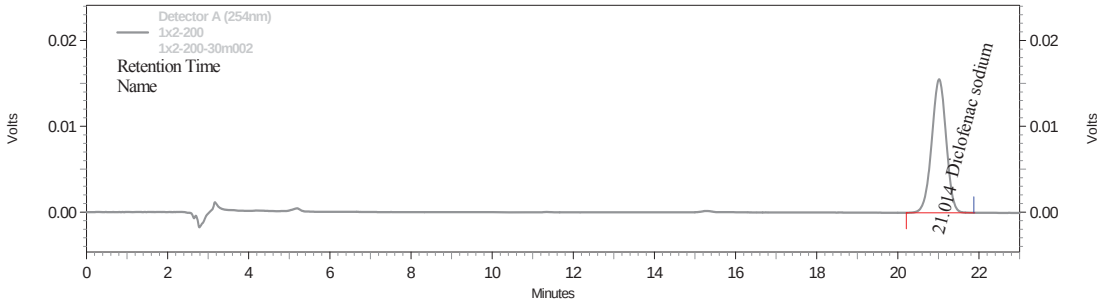

Detector A (254nm)
1x2-200
1x2-200-15m001
Retention Time
Name
21.512 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
1x2-200
1x2-200-15m002
Retention Time
Name
21.457 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
1x2-200
1x2-200-15m003
Retention Time
Name
21.680 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
1x2-200
1x2-200-15m004
Retention Time
Name
20.139 Diclofenac sodium
Volts
Minutes

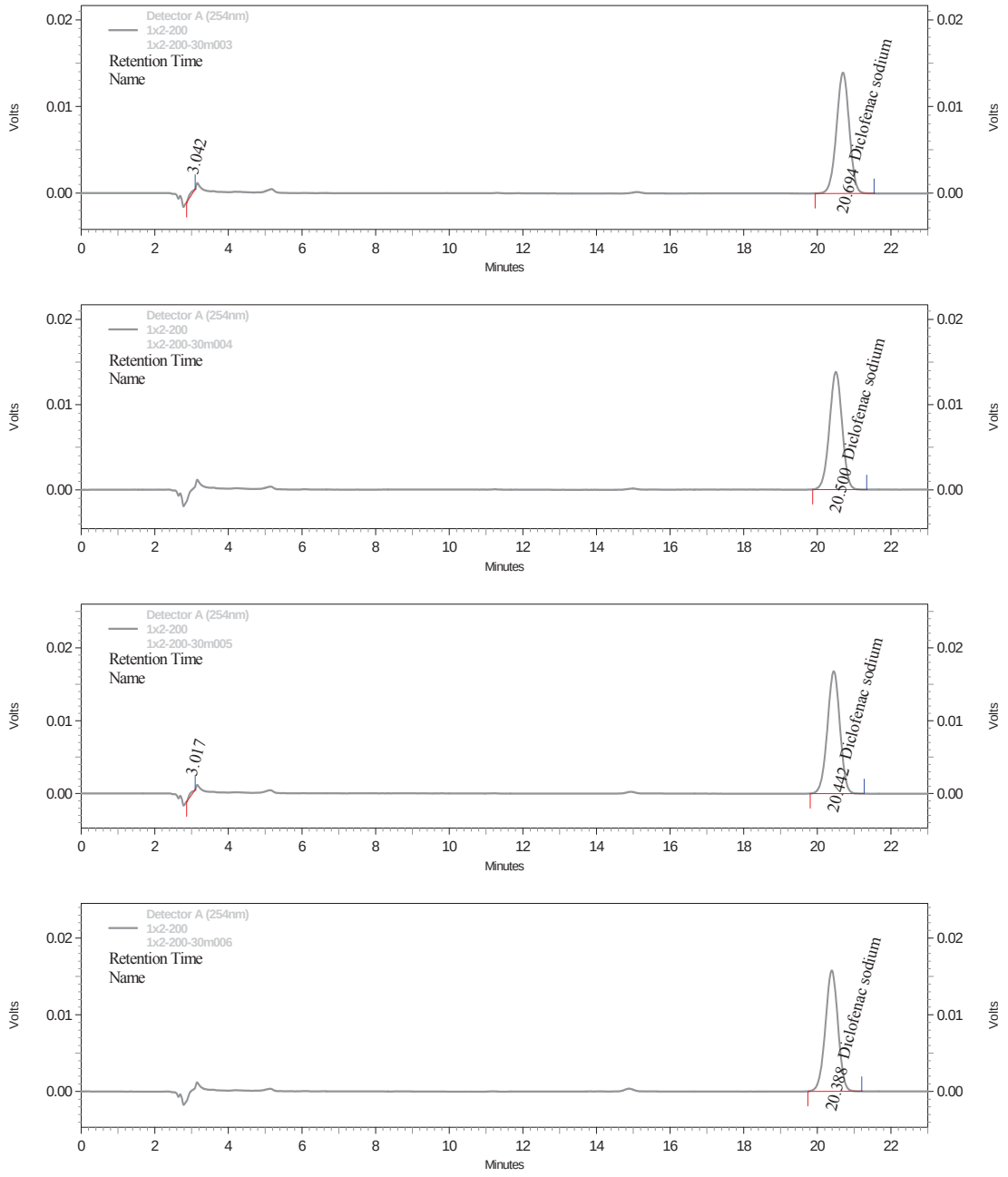

Detector A (254nm)
1x2-200
1x2-200-15m005
Retention Time
Name
19.896 Diclofenac sodium
Volts
Minutes


Detector A (254nm)
1x2-200
1x2-200-15m006
Retention Time
Name
3.042
20.684 Diclofenac sodium
Volts
Minutes

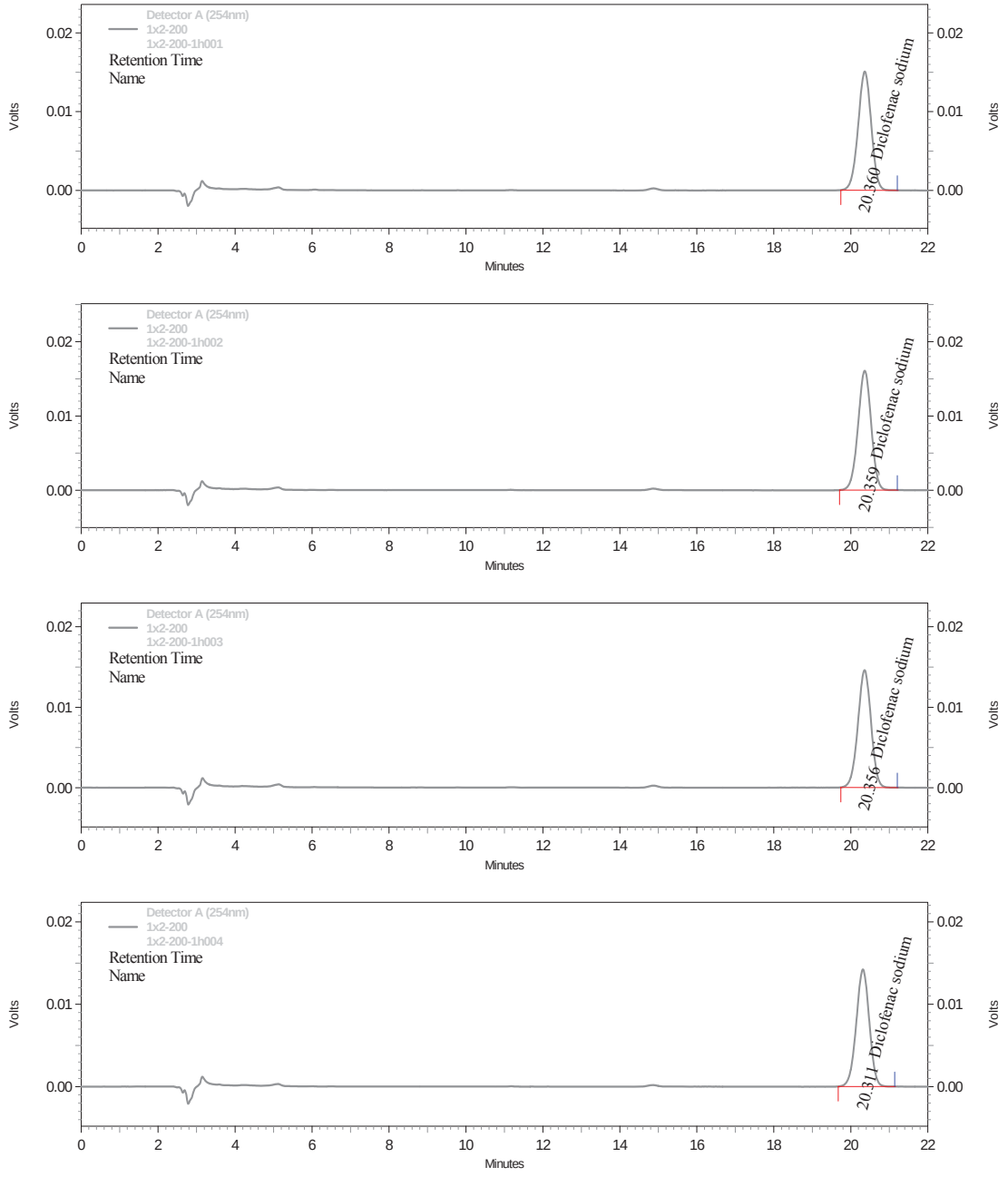
30 min

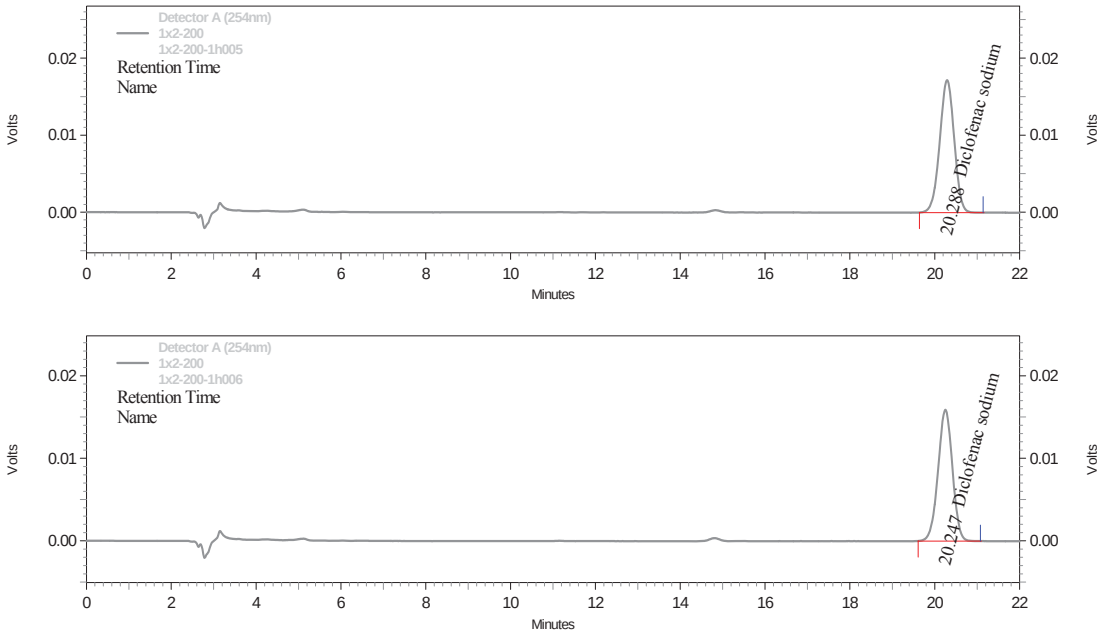

Detector A (254nm)
1x2-200
1x2-200-30m001
Retention Time
Name
21.056 Diclofenac sodium
Volts
Minutes


Detector A (254nm)
1x2-200
1x2-200-30m002
Retention Time
Name
21.014 Diclofenac sodium
Volts
Minutes

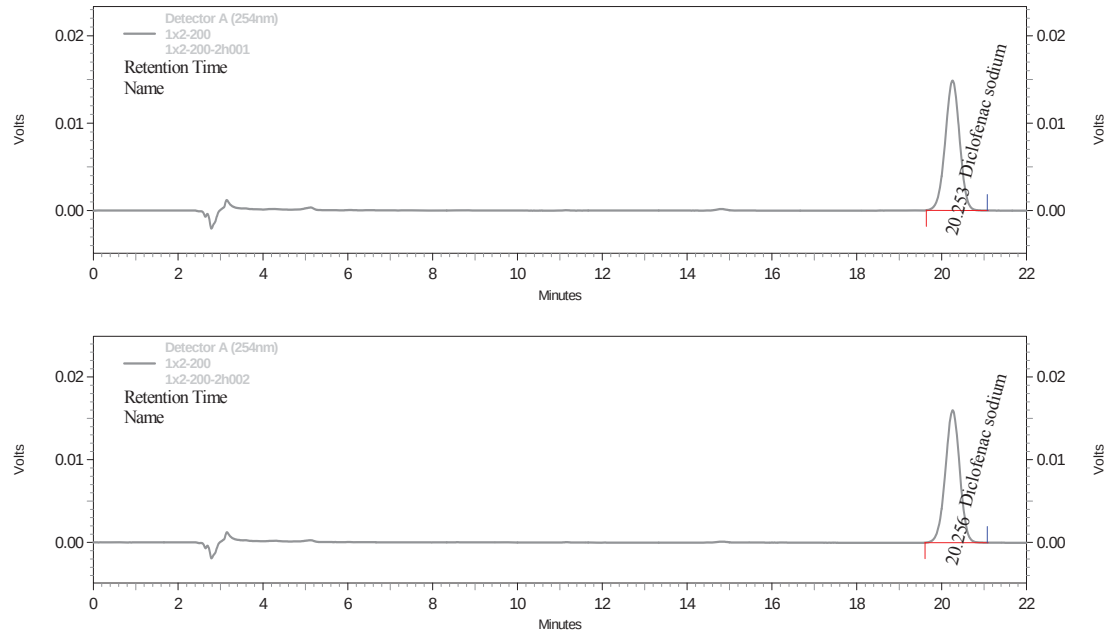

Detector A (254nm)
1x2-200
1x2-200-30m003
Retention Time
Name
3.042
20.694 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
1x2-200
1x2-200-30m004
Retention Time
Name
20.500 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
1x2-200
1x2-200-30m005
Retention Time
Name
3.017
20.442 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
1x2-200
1x2-200-30m006
Retention Time
Name
20.388 Diclofenac sodium
Volts
Minutes

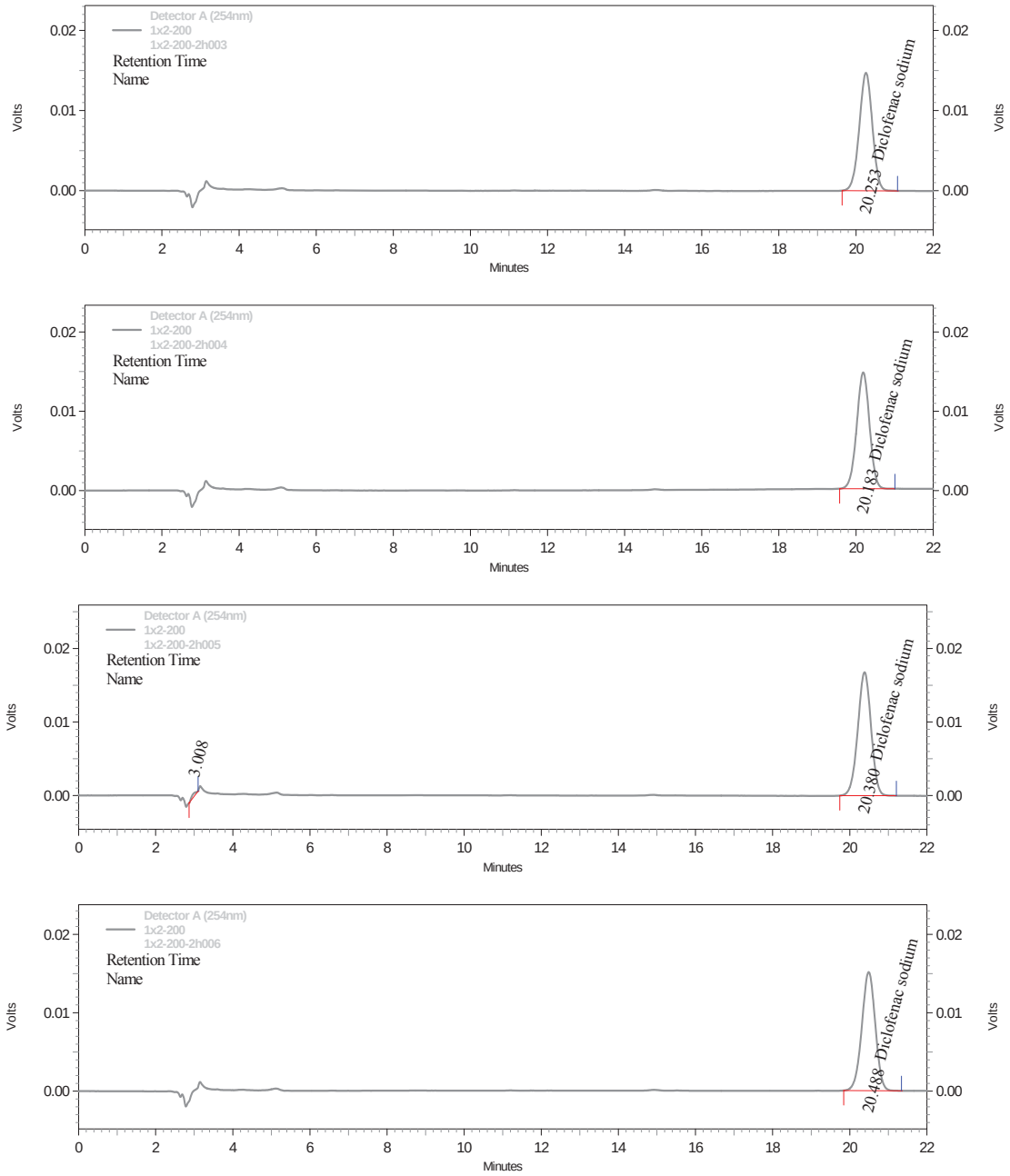
1 h


Detector A (254nm)
1x2-200
1x2-200-1h001
Retention Time
Name
20.360 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
1x2-200
1x2-200-1h002
Retention Time
Name
20.359 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
1x2-200
1x2-200-1h003
Retention Time
Name
20.356 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
1x2-200
1x2-200-1h004
Retention Time
Name
20.311 Diclofenac sodium
Volts
Minutes


Detector A (254nm)
1x2-200
1x2-200-1h005
Retention Time
Name
20.288 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
1x2-200
1x2-200-1h006
Retention Time
Name
20.247 Diclofenac sodium
Volts
Minutes

2 h


Detector A (254nm)
1x2-200
1x2-200-2h001
Retention Time
Name
20.253 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
1x2-200
1x2-200-2h002
Retention Time
Name
20.236 Diclofenac sodium
Volts
Minutes


Detector A (254nm)
1x2-200
1x2-200-2h003
Retention Time
Name
20.253 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
1x2-200
1x2-200-2h004
Retention Time
Name
20.183 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
1x2-200
1x2-200-2h005
Retention Time
Name
3.008
20.380 Diclofenac sodium
Volts
Minutes
Detector A (254nm)
1x2-200
1x2-200-2h006
Retention Time
Name
20.488 Diclofenac sodium
Volts
Minutes

2.2.6 % Cumulative released of DCN

Table 67 % Cumulative released of DCN from tablets containing SSG

Time	% Cumulative released of DCN from tablets containing SSG							
	1	2	3	4	5	6	AVG	SD
5 min	45.77	31.14	40.67	35.27	38.69	47.09	39.77	6.10
10 min	57.03	38.26	51.56	52.33	50.52	63.12	52.14	8.25
15 min	70.23	43.43	58.21	59.25	53.39	70.45	59.16	10.31
30 min	90.41	53.39	67.92	70.75	74.56	81.99	73.17	12.66
1 h	95.03	63.41	77.65	82.80	86.01	90.55	82.58	11.15
2 h	99.05	74.14	86.00	89.56	92.24	96.85	89.64	8.95

Table 68 % Cumulative released of DCN from tablets containing Amberlite® IRP64

Time	% Cumulative released of DCN from tablets containing Amberlite® IRP64							
	1	2	3	4	5	6	AVG	SD
5 min	12.67	28.24	41.51	41.31	40.94	32.34	32.83	11.32
10 min	23.93	21.77	45.68	46.89	48.88	41.57	38.12	12.09
15 min	28.62	26.95	48.08	54.05	53.15	48.58	43.24	12.21
30 min	42.80	42.96	56.58	63.48	59.93	63.56	54.89	9.65
1 h	68.85	75.92	82.63	83.69	78.91	80.76	78.46	5.46
2 h	70.03	83.42	76.35	74.38	71.80	74.27	75.04	4.66

Table 69 % Cumulative released of DCN from tablets containing Dowex® (1x2-200)

Time	% Cumulative released of DCN from tablets containing Dowex® (1x2-200)							
	1	2	3	4	5	6	AVG	SD
5 min	46.87	50.29	40.23	43.63	53.92	41.06	46.00	5.39
10 min	53.95	58.34	48.09	50.22	61.33	52.00	53.99	5.01
15 min	56.47	61.62	51.98	52.36	63.93	56.98	57.22	4.82
30 min	59.16	64.19	56.02	55.13	66.82	62.66	60.66	4.66
1 h	60.18	64.29	58.12	56.38	68.37	62.91	61.71	4.38
2 h	59.37	63.78	58.76	57.40	68.05	62.02	61.57	3.93

BIOGRAPHY

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E-mail address	nunpy038@gmail.com

Education

1997 - 2002	Bachelor of Pharmacy, Pharmaceutical Technology, Mahidol University, Thailand
2003 - 2005	Bachelor of Public Health, Sukhothai thammathirat open University, Thailand
2008 - 2012	Master of Pharmacy, Pharmaceutical Technology Silpakorn University, Thailand

Poster presentations

1. **Nistakan Pattarakan**, Praneet Opanasopit, Tanasait Ngawhirunpat and Prasert Akkaramongkolporn “Application of Ion Exchange Resins as tablet disintegrants” The 35th Congress on Science and Technology of Thailand, 15-17 October 2009, Chonburi, Thailand.

2. **Nistakan Pattarakan**, Praneet Opanasopit, Tanasait Ngawhirunpat and Prasert Akkaramongkolporn "Application of Ion Exchange Resins as tablet disintegrants" The 26th Annual Research Conference in Pharmaceutical Sciences, 4 December 2009, Chulalongkorn University, Bangkok, Thailand.

3. **Nistakan Pattarakan**, Praneet Opanasopit, Tanasait Ngawhirunpat and Prasert Akkaramongkolporn "Application of Ion Exchange Resins as tablet disintegrants" The 1st Current Drug Development International Conference 6-8 May 2010, Woraburi Resort & Spa Hotel, Phuket, Thailand.

Working profile

April 2002 – September 2002	Production supervisor in Skinnex Co. Ltd., Thailand
October 2002 – April 2004	Production supervisor in Bangkok lab and Cosmetics Co. Ltd., Thailand
May 2004 – September 2004	Production manager in Cosmed Innovation Co. Ltd., Thailand
October 2004 - present	Production manager in Pharmatech Co. Ltd., Thailand