EFFECT OF EXERCISE ON FRUCTOSE ABSORPTION FACILITATED BY ALANINE AND PHYSICAL PERFORMANCE

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Ingestion of water and/or beverage both before and during competition or training is important for athletes and their performance. Fructose is a carbohydrate that creates less insulin responses than glucose but is less absorbed in the intestine than glucose. The facilitating effect of alanine on fructose absorption in healthy children is shown in resting condition but there is no report about fructose absorption with facilitating effect of alanine in exercise conditions. Therefore, this study aimed to investigate the effect of exercise on fructose absorption facilitated by alanine and physical performance using a double blind randomized design. Eight physically active college students (VO_2 max = 51.78±2.04 ml/kg/min), were engaged in the experiment in four trials i.e., 6% glucose (G), 6% fructose (F), 6% fructose and half-equimolar alanine (Fa), or 6% fructose and equimolar alanine (FA). Five hundred milliliters of beverage was given at 45 min before exercise and 350 ml immediately prior to exercise. Total fructose/glucose intake was 51 g in each trial. Osmolality of the beverages were 413±6.56, 438±3.85, 594±14.93, and 788±12.47 mmol/L in G, F, Fa, and FA trials, respectively. The intensity of exercise employed was 70% VO_2 max for the first 60 min of exercise on treadmill, followed by an increased of workload 10% every 5 min until exhaustion.

There were no significant differences in heart rate, and ratings of perceived exertion (RPE), blood lactate, plasma free fatty acids, percentage changes in plasma volume, serum osmolality, and body weight loss. Plasma glucose and serum insulin were more significantly increased in G than in F, Fa and FA trials at 15 min after first ingestion ($p<0.05$). Breath hydrogen excretion was more significantly increased in F than in G, Fa and FA trials ($p<0.05$). Gastrointestinal disturbances were reported in F and FA trials in which 4 of subjects could not run until exhaustion due to diarrhea in F trials and severe abdominal distention in the FA trial. However, exhaustion time in the other 4 subjects was not significantly different among trials (74.00±5.05, 73.75±5.30, 72.25±3.68, and 74.75±3.35 min in G, F, Fa, and FA trials, respectively). These results showed that ingestion of either fructose 51 g or high osmolality of 788±12.47 mmol/L before exercise could create gastrointestinal disturbances which apparently limits performance. Alanine has an enhanced effect on fructose absorption in exercise as shown by lowering breath hydrogen excretion. Despite the GI disturbances, physical performance is similar among all trials.

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เครื่องดื่มที่ใช้สำหรับนักกีฬาเป็นสิ่งที่จำเป็นสำหรับนักกีฬาหรือผู้ที่ออกกำลังกาย ฟรุคโตสเป็นสารอาหารคาร์โบไฮเดรตชนิดหนึ่งที่กระตุ้นการสร้างฮอร์โมนอินสุลินน้อยกว่ากลูโคสแต่ดูดซึมช้ากว่า จากการศึกษาที่ผ่านมามีรายงานว่าอะลานีนเมื่อให้ร่วมกับฟรุคโตสมีผลช่วยในการดูดซึมฟรุคโตสได้ดีขึ้นในภาวะที่ไม่มีการออกกำลังกาย จึงน่าจะศึกษาผลดังกล่าวในภาวะการออกกำลังกายและผลต่อประสิทธิภาพการออกกำลังกาย โดยได้ทำการทดลองแบบ double blind randomized design อาสาสมัครเป็นนักศึกษามหาวิทยาลัยมหิดล ที่เข้าร่วมการแข่งขันกีฬาระหว่างมหาวิทยาลัย และฝึกซ้อมสม่ำเสมอตลอดการทดลองจำนวน 8 คน ได้มีการจัดเครื่องดื่ม 4 ชนิดได้แก่ 6%ฟรุคโตส (F), 6% กลูโคส (G), 6% ฟรุคโตสกับอะลานีนที่มีจำนวนโมลครึ่งหนึ่งของฟรุคโตส (Fa) และ 6% ฟรุคโตส กับอะลานีนที่มีจำนวนโมลเท่ากับฟรุคโตส (FA) ในปริมาณ 500 ซีซี 45 นาทีก่อนการออกกำลังกาย และ 350 ซีซี เมื่อเริ่มการออกกำลังกาย ปริมาณกลูโคสหรือฟรุคโตสที่ได้รับในแต่ละการทดลองจะได้เท่ากันในปริมาณ 51 กรัม โดยมีความเข้มข้นของอนุภาคในเครื่องดื่ม (osmolality) 413±6.56, 438±3.85, 594±14.93, และ 788±12.47 mmol/L ในกลุ่ม G, F, Fa, และ FA ตามลำดับ ประสิทธิภาพการออกกำลังกายวัดโดยการให้อาสาสมัครวิ่งบนสายพานเลื่อนที่ 70% ของประสิทธิภาพการออกกำลังกายสูงสุดเป็นเวลา 60 นาที จากนั้นเพิ่มการวิ่ง 10% ทุก 5 นาทีจนกระทั่งไม่สามารถวิ่งต่อไป

ผลการศึกษาพบว่า อัตราการเต้นของหัวใจและระดับความเหนื่อยในขณะออกกำลังกาย น้ำหนักตัวที่ลดลงหลังการทดลอง ปริมาณแลคเตท ปริมาณไขมันอิสระ และความเข้มข้นของอนุภาคในเลือด และการเปลี่ยนแปลงของปริมาณพลาสม่า ไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ ระดับน้ำตาลและอินสุลินในเลือดในกลุ่ม Gเพิ่มขึ้นสูงที่ 15 นาทีหลังจากการได้รับเครื่องดื่มครั้งแรกและพบว่าแตกต่างจากกลุ่มอื่นๆอย่างมีนัยสำคัญทางสถิติ ($p<0.05$) ผลจากการวัดกาซไฮโดรเจนในลมหายใจพบว่าในกลุ่ม F เพิ่มขึ้นสูงกว่าอีก 3 กลุ่มอย่างมีนัยสำคัญทางสถิติ ($p<0.05$) ถึงแม้ว่าอาสาสมัคร 4 คนต้องหยุดวิ่งก่อนที่จะถึงเวลาเหนื่อยที่สุด เนื่องจากท้องเสียในกลุ่ม F และ แน่นท้องมากในกลุ่ม FA ระยะเวลาการวิ่งของอาสาสมัครที่เหลืออีก 4 คน 74.00±5.05, 73.75±5.30, 72.25±3.68 และ 74.75±3.35 นาที ในกลุ่ม G, F, Fa และ FA นั้นซึ่งพบว่าไม่แตกต่างกัน ดังนั้นอะลานีนมีส่วนช่วยในการดูดซึมฟรุคโตสในภาวะการออกกำลังกายจากการที่พบว่าปริมาณไฮโดรเจนในลมหายใจลดลง แต่ไม่มีผลต่อประสิทธิภาพการออกกำลังกายเมื่อเปรียบเทียบกับเครื่องดื่มกลูโคส อย่างไรก็ดี การได้รับฟรุคโตสในปริมาณ 51 กรัม และที่มีความเข้มข้นของอนุภาคในเครื่องดื่มสูง (788±12.47 mmol/L) อาจก่อให้เกิดผลข้างเคียงที่ไม่พึงประสงค์จนมีผลต่อประสิทธิภาพการออกกำลังกายได้

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ACSM	American College of Sports Medicine
BW	body weight
CHO	carbohydrate
CV	coefficient variation
FFA	free fatty acids
F	6% fructose electrolyte solution
Fa	6% fructose and half-equimolar alanine electrolyte solution
FA	6% fructose and equimolar alanine electrolyte solution
G	6% glucose electrolyte solution
GI	gastrointestinal
h	hour
H_2	hydrogen
Min	minutes
PV	plasma volume
RER	respiratorv exchange ratio
RPE	ratings of perceived exertion
V_E	minute ventilation
VO_2 max	maximum oxygen consumption

CHAPTER I

INTRODUCTION

1. Exercise and Health

Regular exercise improves physical fitness and well being across all ages in the life span. Nowadays, people have little physical activity due to the sedentary lifestyle, and accumulating evidence indicates that physical inactivity is a major risk factor for cardiovascular and related disease. However, moderate levels of physical activity confer significant health benefits. Even those who currently meet these daily standards may derive additional health and fitness benefits by becoming more physically active or including some vigorous activity. For those with known cardiovascular disease, cardiac rehabilitation programs that combine physical activity with reduction in other risk factors should be more widely used (1).

Acute and long-term physical activity of a vigorous nature (exceeding 70% of maximum heart rate or age-adjusted maximum heart rate from 20 to 60 min with a frequency of at least 3 sessions per week) consistently reduces anxiety and symptoms of depression for 30 min to several hours after exercise (2).

Diet and exercise studies of premenopausal women have shown reductions in obesity and other cardiovascular disease (CVD) risk factors (3). Exercise thus provides a strong support for successful long-term prevention of cardiovascular risk, particularly, when exercise and fitness training sessions are incorporated into sedentary lifestyles. When organized on a community level, they might have a positive impact on the health behavior of a larger population. Physical activity can help to foster health promotion in a holistic and integrated manner, leading to a healthy lifestyle in the long term (4).

Ideally, the concept of positive attitude in health promotion and prevention should be related to each individual's characteristics and environment together with adequate food and exercise. This principle of positive health should be applied to all people, and not be limited to athletes and the affluent. To promote an optimal life-style and successful aging, the challenge ahead is to create an awareness of and promote good nutrition and regular physical activity from childhood to old age. Abstinence from smoking, alcohol use and other recognized treats to health must be emphasized. The message needs to be clear and then it becomes a matter of personal choice for individuals and communities to adopt a healthy life style integrating nutrition, physical activity and healthy life option (5).

2. Exercise and Fluid

In exercise, the requirements for thermoregulation can be considerable, and the price for failure is death. A drop in deep body temperature of 10 °C and an increase of only 5 °C can be tolerated. This has been vividly illustrated by the fact that between 1960 and 1983, 70 football players have died as a direct result of exercise stress during practice or actual competition. Heat injury is also an unfortunate common occurrence in a variety of long duration athletic events (6).

In thermoregulation, the evaporation of sweat secreted on to the surface of the skin is a very effective way to lose heat. For every 1 litre/1.75 pints of sweat that evaporates, some 600 kcal/2500 kJ of heat energy may be released from the body. As it is possible to lose as much as 2 litres/ 3.5 pints of sweat per hour during prolonged exercise in a hot environment, there is appreciable potential for heat loss by this mechanism. However, not all of the sweat formed during exercise is effective in dissipating heat as some does not evaporate on the skin surface but drop off the skin and hence does not aid heat loss. This can even be a disadvantage to the heavy sweater (7).

Not surprisingly, the greatest decrements in exercise performance occur during prolonged exercise in hot environments at high levels of dehydration, although even low levels of dehydration (1-2%) can have an ergolytic effect on performance (8-9). Physical and cognitive performances are impaired at 1-2% dehydration, and the body

can collapse when water loss approaches 7% (10). Mental performance also deteriorates as a result of heat exposure (11). The effect of heat exposure and dehydration on physiological responses is shown in table 1.

Table 1 Physiological responses to dehydration.

Physiological factor	Response
Ventricular filling (12)	Decreased
Stroke volume (12)	Decreased
Cardiac output (13)	Decreased
Plasma electrolytes (14)	Decreased
Sweating rate (14)	Decreased
Core temperature (15)	Increased
Blood volume (16, 18)	Decreased
Blood pressure (13)	Decreased
Plasma osmolality (17, 18)	Increased
Urine osmolality (19)	Increased
Cortisol and fluid-electrolytes regulatory hormone; aldosterone, renin activity, arginine vaso-pressin (20)	Increased
Skin blood flow (13-14)	Decreased
Gastric emptying (21-22)	Decreased
Incidence of gastrointestinal distress (21)	Increased
Blood flow to exercising muscles (13, 23)	Decreased
Oxygen consumption of exercising muscles (23)	Increased
Skeletal muscle endurance (24)	Decreased
Performance (25)	Decreased

To encourage proper fluid intake behavioral strategies, the American College of Sports Medicine (ACSM) published and released a position stand on fluid intake during exercise (26). Within the position paper are guidelines for developing strategies for athletes and physically active individuals. The guidelines include fluid intake prior and during exercise (Table 2).

Table 2 Fluid intake guidelines before and during exercise.

Timing	Amount	Adaptation
Before exercise (2 h prior)	Drink 500 ml (17oz)	None
During exercise	Drink 600-1200 ml (20-40 oz) per h	Drink 150-300 ml (5-10 every 15-20 min

Source: the American College of Sports Medicine (ACSM): A position stand on exercise and fluid replacement. Med Sci Sports Exerc 1996;28:I-vii.

3. Exercise and Fructose

Not only is fluid needed in exercise, but also are carbohydrate as energy substrate for the body. Carbohydrate is the most important nutrient in an athlete's diet because it is the only fuel that can power intense exercise for prolonged periods, yet its stores within the body are relatively small (27). Exercise leads to a decrease in the body's readily available energy stores. The degree to which such energy stores are depleted or unable to keep up with energy demands depends on the duration and intensity of the exercise. Exercise greater than 2 h duration without appropriate energy replacement may lead to failure of hepatic glucose production to keep up with muscle glucose uptake (28). Provision of water during exercise is beneficial relative to a 'no drink' condition, but that the provision of carbohydrate-containing drinks is more effective in improving performance in a wide range of exercise situations (29). Although it appeared that trained endurance athletes are capable of oxidizing carbohydrate source other than muscle glycogen at high rates during the latter stages of prolonged strenuous exercise.

Many researchers have focused attention on glucose and its polymers in sport drinks. But the anti-lipolytic effects of glucose-induced blood insulin rises have prompted atheletes to consider the use of fructose, a weak insulinotropic sugar which is known to produce lower insulin secretory response than glucose ingestion (30). There is reporting an increased rate of muscle glycogen depletion and decreased endurance if glucose polymer is ingested 30 min prior to endurance cycle exercise. It was postulated that the glucose-induced elevations in plasma insulin concentration just prior to exercise might decrease lipolysis and free fatty acids (FFA) delivery to muscle, thereby increasing the reliance of skeletal muscle on carbohydrate, particularly muscle glycogen, as an oxidative fuel (31) which may lead to premature fatigue (32). Many investigators have shown how to reduce hyperinsulinemia response by use of food matrix on carbohydrate utilization by altering the composition and form of the food supplement in order to slow rate of glucose assimilation (33-34). Furthermore, the results of Thomas et al (35) were shown that the low glycemic index foods consumed before exercise prolonged endurance during strenuous exercise. Additionally, MacLaren et al (36) demonstrated that adding guar gum to the glucose solution has been shown to attenuate postprandial hyperglycemia in normal and diabetic humans. Fructose feeding before and during exercise can enhance performance under certain conditions, however the gastrointestinal discomfort can hinder performance (37).

The mode of absorption of fructose as a free monosaccharide has not been considered an important issue in the past, because of the relatively small amounts of the carbohydrate normally contained in the diet before the introduction of high-fructose syrup (HFS). New methods have made the preparation of HFS and pure fructose less expensive and have resulted in widespread utilization of fructose as a sweetener in prepared foods and beverage (38). This change was motivated primarily by marketing considerations aiming to substitute fructose (the fruit sugar), seen as the healthy carbohydrate, for glucose or sucrose, which had acquired a negative image among the health-conscious population.

Consumption of fructose is steadily increasing. As intake of fructose has risen, recognition of digestive tract symptoms in association with fructose ingestion has led to an interest in the physiology and pathophysiology of fructose absorption. The

excessive consumption of products containing fructose could result in malabsorption symptoms of abdominal discomfort, flatulence, and diarrhea (39-40).

At present, the mechanism of this facilitating effect of glucose on fructose absorption, which is dose dependent (41-43), is not adequately understood. A possible explanation might be fructose profits from the water movement caused by the uptake of glucose through the well-defined glucose-transport system, especially the glucose Na^+ cotransporter (44). Hoekstra and Aker (45) studied the facilitating effect of amino acids on fructose absorption in normal children by using breath H_2 excretion as an indicator of carbohydrate malabsorption found a significant decreased of breath H_2 excretion. Even more positive effect on fructose absorption was obtained with the addition of an equimolar dose of alanine. On further evaluation of their studies, the solution containing half of the previous alanine dose was shown to also promote absorption. However, the mechanism of fructose still needs further study.

Thus the facilitating effect of alanine on fructose absorption in healthy children is shown in resting condition but there is no report about fructose absorption with facilitating effect of alanine in exercise conditions. Hence, it is possible that if fructose is effectively absorbed from the gut by the facilitating effect of alanine, it can improve performance in endurance exercise. The aim of the present study, therefore, is to investigate the effect of fructose and alanine ingested simultaneously prior to exercise on fructose absorption and physical performance.

4. Research Design

In designing the experiment involved carbohydrate-electrolyte beverage and exercises, the following aspects were considered.

4.1 Beverage Concentration

Depending on ACSM recommendation that 30-60 g/h of carbohydrate should be ingested in exercise to maintain oxidation and the solution should contain 4-8% carbohydrates (26-27). As maximal rates of oxidation of exogenous supplied carbohydrate appear to be approximately 60 g/h, therefore supplying larger amounts in drink are not necessary (46). Murray, et al also demonstrated that carbohydrate feeding

at the rates of 26 and 78 g/h was associated with improve exercise performance and there were no dose-response relationship of carbohydrate consumed and exercise performance (47). Moreover, Horswill reported that solution containing up to and including 6% carbohydrate, the absorption rates are similar to or faster than that of water alone while the absorption of fluids that contain 8% carbohydrate or higher tend to be slower (26).

4.2 Amount of Fructose

In rats, at least 2.0 g fructose/kg BW was require to induce malabsorption, whereas a majority of human subjects were unable to absorb amounts of fructose ranging from 0.5-1.0 g/kg/BW (44). Although there are many researchers reported about concentration/amount of fructose solutions ingested in exercise such as 76.3±4.3 g (6% fructose) during cycling exercise (48), 98.9±4.7 g (7% fructose) over the 2-h period of exercise (49), 100 g fructose (diluted in 400 ml of water) 60 min before exercise (50), 140±12 g (7%fructose) during exercise (51), 150 g (25% fructose) during exercise (52), etc. Additionally, concentration of solution is to be considered as 50 g of fructose in a 10% solution created malabsorption less than fructose is provided in a 20% solution (53). The doses of fructose used in this experiment is 51.0 g as the maximum capacity for intestinal absorption of fructose in resting conditions seems to be about 50 g in most subjects (38) and the concentration of the fructose in the solution is only 6%.

4.3 Volume of Ingested

There are recommendations that 600-1200 ml/hr of solutions containing 4%-8% carbohydrate should be ingested during intense exercise lasting longer than 1 h (26, 54). Also Gisolfi 1992 (55) recommended that events lasting between 1 and 3 h, 300-500 ml of water should be ingested as pre-event beverages. Moreover, gastric volume plays a major role in regulation the rate of gastric emptying. In 1985 Grunewald and Tucker reported that larger volumes emptying faster than smaller volumes from stomachs of exercised mice (56). The larger the volume consumed, the greater the gastric emptying rate, up to at least 600 ml (46, 55, 57). The studies of gastric emptying have suggested that carbohydrate content of the ingested solution is

an important factor determining its rate of gastric emptying. However, the findings of recent studies have shown that a repeated drinking will have a significant, possibly major, influence on the rate of both carbohydrate and water delivery from any solution (58). Hence, in this experiment, 500 ml of beverage provided at the first (45 min before exercise) and 350 ml provided 45 min thereafter.

4.4 Osmolality

The osmolality of sport drinks and beverages vary from 240 (Dioralyte^{R}), 250 (Exceed^{R}), 280 (Gatorade^{R}), 296 (Isostar^{R}), 650 (Coca cola^{R}), 690 (orange juice), 890 (cranberry juice) and 10-20 (water) mmol/L (55). The amount of osmolality in the solution that can be tolerated in exercise is not well established. However, the high osmolality glucose solution at 1850 mmol/L (100 g/300 ml) used for diagnosing diabetes, can be tolerated in adult (59).

There are wide ranges of osmolality in the exercise experiments. Sole and Noakes in 1989 (57) investigated 13 different carbohydrate-containing solutions where the osmolality ranges from 2 (water) to 819 (15% Fructose) mmol/L ingested during running at 75% VO_2 max. Jandrain in 1989 (60) studied the beverages ingested at the beginning of prolonged exercise bout which osmolalities were 439, 644, and 1204 mmol/L. However, the high osmolality of beverage is taken on a precaution as it is reported that the high osmolality solution slower gastric emptying than lower osmolality solution (61). It is also reported that the solutions with multiple substrates stimulate several different solute absorption mechanisms yielding greater water absorption than solutions with only one substrate (62).

4.5 Glucose Solution

Carbohydrate solution is proved to be superior to the intake of no drink and water placebo in exercise lasting longer than 1 h. The carbohydrate solution such as glucose or sucrose or starch (e.g., maltodextrin) is recommended from ACSM in effective maintaining carbohydrate oxidation and delaying fatigue (26). The osmolality of maltodextrins is lesser than glucose and it was proposed that because of their lower osmolality, it would be preferable to isocaloric glucose solutions as a source of ingestion of carbohydrate during exercise (46). However, many studies were

shown that glucose polymer (i.e., maltodextrins) solutions do not offer an advantage over free glucose solutions in terms of energy provision of the working muscle (26, 63-67). Maltodextrins has become a popular form of carbohydrate inclusion in sports drinks because they are not very sweet and therefore solution in concentrations of 10 g per 100 ml or more are more palatable for most people. That is the major benefit of maltodextrins to sugars because gastric emptying rates and metabolic responses are not appreciably different (68-50). Simply, maltodextrins is a more palatable than to consume carbohydrate (27).

4.6 Sodium Addition

Inclusion of sodium (0.5-0.7 g/l of water) in the rehydration solution ingested in exercise lasting longer than 1 h is also recommended by ACSM (26). Since it may be advantageous in enhancing palatability, promoting fluid retention, and possibly preventing hyponatremia in certain individual who drink excessive quantities of fluid. In the present experiment, 10 mEq (0.585 mg) of sodium was added in 1000 ml solution.

4.7 Time of Fluid Ingestion

Although there were reports about eating sugar during the hour before exercise that may cause a decline in blood glucose concentration and rise in serum insulin at the onset of exercise. However, several studies have not found the increase muscle glycogen used from those effects (70-72). More importantly, in examining the studies which have measured endurance performance following sugar ingestion during the hour before exercise, only one study has reported a negative effect, four studies have observed no significant effect, and three studies reported improvements in performance. Therefore, there is little support for the idea that sugar ingestion before exercise impairs performance (27). However, precaution must be kept in mind to prevent the hypoglycemia, the 350 ml of solution is provided immediately prior to exercise.

5. Objectives

1. To determine the impact of exercise on the intestinal absorptive capacity of fructose enhanced by alanine.
2. To describe and compare the substrate utilization during exercise between glucose, fructose, fructose and half-equimolar alanine, fructose and equimolar alanine beverages.
3. To evaluate the effect of fructose absorption enhanced by alanine on physical performance using treadmill.

6. Hypothesis

1. Alanine could facilitate fructose absorption by lowering breath H_2 excretion in the exercise test.
2. Ingestion of fructose and alanine beverage can improve performance compare with ingested fructose and glucose beverages.

CHAPTER II

LITERATURE REVIEW

1. Fluid Replacement

Dehydration is a frequent and important problem, commonly seen among athletes. Equally important is the approach research for providing correct rehydration (73). Since adequate hydration before exercise is essential for optimum performance. During prolonged exercise the ingestion of appropriate fluids will improve performance, not just of the elite athlete but of all people involved in sport and physical activity. Carbohydrate beverage ingestion during exercise has the dual aim of supplying water to replace the losses incurred by sweating and providing a source of carbohydrate fuel to supplement the body's limited stores (74).

To minimize risk of thermal injury and impairment of exercise performance during exercise, fluid replacement should attempt to equal fluid loss. During exercise lasting longer than 1 h, carbohydrates and electrolytes (primary NaCl) should be added to the replacement solution. The dilute carbohydrate-electrolyte drinks can be found to provide extra energy and reduce the probability for development of hyponatremia (75).

The characteristics of an appropriate oral rehydration solution for exercise are listed below (76).

- Provide substrate
- Replace electrolytes
- Replace fluids
- Enhance absorption
- Give palatability
- Maintain plasma volume

The process of rehydration depends on both gastric emptying and intestinal absorption. The former has been studied in detail than the latter and is currently considered to be primary factor limiting rehydration (55).

1.1 Gastric Emptying

Gastric emptying is the primary factor limiting the rate delivery to the blood and therefore influences the utilization of exogenous carbohydrate ingested before or during exercise (46). It is highly influenced by several factors: i.e., volume of the stomach and volume ingested, calories, type of nutrients, size, density, temperature, viscosity, osmolality, the amount of acid that the stomach produces, as well as those factors associated with physiologic responses: splanchnic blood flow, body position, posture, and electrolyte balance. For instance, the rate of gastric emptying is decreased by high blood glucose concentrations (77). The main factors influence to gastric emptying of carbohydrate beverages are shown in Table 3 (58). The influence of volume ingested, caloric density, electrolyte content, osmolality of the solution, and exercise variables on gastric emptying will be described.

Table 3 Factors known to influence the rate of gastric emptying.

Constituents of the ingested solution
Volume
Caloric density
Electrolyte content
Osmolality
Temperature
pH
Exercise variables
Intensity of exercise
Mode of exercise
Subject variables
Level of hydration
Individual variability

Source: Noakes TD, Rehrer NJ, Maughan RJ. The importance of volume in regulating gastric emptying. Med Sci Sports Exerc 1990;23:307-13. (Ref 56).

1.1.1 Volume Ingested

Effect of volume ingested on gastric emptying and distention are the issues of concern in athlete.

Ryan et al 1989 studied eight trained male who cyclist completed four 3-h bouts of cycling at 60%VO_2 max in the heat. Either water, 5% glucose, 5% glucose polymer, or 3.2% glucose polymer + 1.8% fructose were provided at a rate of 350 ml every 20 min (3.15 L total volume). The volume retained in the stomach obtained at the end of exercise was similar for all drinks. The 5% glucose trials yielded greater residual volume than water trials. This study demonstrated that during prolonged (3-h) cycling exercise in the heat, large volumes of water and 5% carbohydrate can be emptied from the stomach to help minimize the effects of dehydration (78).

In another study, 6% isotonic carbohydrate-electrolyte solution and cycle exercise at 60.6 ± 3.7 VO_2 max for 85 min, subjects ingested a total of 23 ml/kg BW by drinking 396 ± 34 ml, 5 min prior to exercise followed by 198 ± 17 ml every 10 min during exercise. Mean stomach volume (312 ± 80 ml) and gastric emptying (19.7 ± 2.0 ml/min) did not change significantly after the initial 35 min equilibration period. The result indicated that relatively constant stomach volume can be maintained over a prolonged period of time and can produce relatively constant gastric emptying rates (79).

The effect of volume of ingested beverage was also investigated by Mitchell and Voss in 1991 to determine the effect of ingesting approximately 800, 1200, 1600 ml/h (equivalent to 1.5, 17.1, 23 ml/kg) of a 7.5% carbohydrate solution every 15 min in exercise at 70% VO_2 max. A significant greater volume of fluid was emptied in the high volume trial compared with the other two trials. The rate of gastric emptying in the moderate volume trial was also significantly higher than in the low volume trial. Ratings of stomach fullness were significantly higher in the moderate volume and high volume trials compared with the low volume trial throughout the rides. There were no significant differences in plasma volume changes, sodium, potassium, or blood glucose between three trials. However, there was a significantly

greater decrease in the body weight in the low volume compared with the moderate volume and high volume trials (66).

Thus greater the degree of gastric distention a subject is able to tolerate during exercise, the more carbohydrate and water will be delivered to the intestine from any ingested solution. However, stomach fullness is still a problem. The recommendation by ACSM is therefore, the 150-300 ml drink should be provided in every 15-20 min during exercise (26).

1.1.2 Caloric Density

Caloric density is also the factor that influence on gastric emptying and thus limits the caloric delivered to the body. Many investigators performed study on this factor for the appropriate caloric delivered to the body.

A study by Wheeler and Banwell 1986 used 5.0% glucose polymers and 2.0% fructose, while the other contained 3.6% glucose polymers, 1.8% fructose, and 1.6% sucrose. Both solutions contained similar amount of sodium, chloride, potassium, magnesium and calcium (10, 10, 5, 1.2, and 3.2 mEq/L, respectively). The result showed that the water and mineral fluxes association with these solutions were not different from water alone (80).

Vist and Maughan in 1994 compared the rate of gastric emptying of 600 ml of either 2%, 4%, or 6% glucose solutions with that of water in resting condition by using double sampling gastric aspiration method. All solutions were emptied rapidly in an exponential emptying pattern. The 2% glucose solution was emptied at the same rate as water. After the first 10 min of ingestion (i.e., the rapid emptying phase), 4% and 6% glucose solution were emptied slower than water. The 6% glucose solution had a strong inhibitory effect on the rate of gastric emptying which was not inhibited during the rapid phase of emptying (i.e., the first 10 min of ingestion), where it delivered the same total volume to the small intestine as water. The results indicated that a 2% glucose solution had no effect on gastric emptying, glucose solutions at a concentration of 4% or more delayed gastric emptying (but not in the first 10 min of rapid phase) (81).

Mitchell et al 1988 studied 5%, 6%, and 7.5% carbohydrate solutions on gastric emptying in exercise. Eight trained male cyclists performed 4 trials of intermittent (7 x 12 min bout) cycling at 70% VO_2 max. Each 12-min ride was followed by 3-min rest, during which a drink was consumed (8.5 ml/kg). Of the original 1336 ml ingested during each trial, the volume emptied by the stomach for the four trials were 1306, 1262, 1288, 1278 ml for water, 5%carbohydrate, 6% carbohydrate, and 7.5% carbohydrate respectively. Only the volume in the 5% carbohydrate trial was significantly different from water placebo (82).

Moodley et al 1992 studied 90-min cycling exercise in trained cyclists exercising at 70% VO_2 max when they ingested glucose, sucrose, or glucose polymer solutions at concentration of 7.5%, 10% or 15% at rate 100 ml/min. The gastric emptying decreased with increasing carbohydrate concentration (83).

Mitchell et al 1989 examined the effects of serial feedings of different concentrations of carbohydrate on gastric emptying and to compare the rates of gastric emptying at rest and during prolonged exercise at 70% VO_2 max 120 min of cycling. The solutions of 0, 6, 12, and 18 g of carbohydrate/100 ml were tested. The volumes emptied were 889.2, 1049.8, 1185.6, and 1210.3 ml in 18, 12, 6 and 0 g carbohydrate/100ml respectively. The range of osmolalities of the drinks used in this study was small (310-407 mmol/L) considering the wide range of concentrations. The relative low osmolality in the 12% and 18% carbohydrate solutions was due to the presence of glucose polymer. The comparatively high osmolality of the 6% carbohydrate drink was due to the addition of electrolyte. If osmolality alone were the strongest determinant of gastric emptying, the 6% carbohydrate solution (354 mmol/L) should have emptied at a rate similar to or slower than the 12% carbohydrate drink (310 mmol/L). In addition, based on osmolality, the 6% carbohydrate solution should have emptied substantially slower than the water placebo (35 mmol/L). Regardless of the osmolality, therefore, carbohydrate solutions of a relatively low the concentration and caloric content were emptied by the stomach nearly as fast as water, while more concentrated solutions emptied slower. The data indicated that 12 and 18% carbohydrate solutions impair of gastric emptying and fluid replacement (84).

Vist and Maughan 1995 assessed the effect of osmolality and carbohydrate content on the rate of gastric emptying by using the double sampling gastric aspiration technique. At 40% solution, glucose solution (230 mmol/L) was emptying slower than glucose polymer (42 mmol/L). Additionally, the more concentrated (188g/L) glucose polymer solution (237 mmol/L) emptied faster (t1/2 = 64 ± 8 min) than the corresponding isoenergic glucose solution (1300 mmol/L, t1/2 = 130 ± 18 min). The dilute (40 g/L) glucose solution emptied faster than the concentrated (188 g/L) glucose polymer solution with the same osmolality (230 mmol/L; 237 mmol/L). These results indicated that both osmolality and carbohydrate content influence gastric emptying of liquids in man, but the carbohydrate content appears to have greater influence than osmolality (61).

Similarly, Brouns et al 1995 determined the effect of carbohydrate content on gastric emptying rate in normal healthy subjects by increasing stepwise from 45 to 90 g carbohydrate/L but all with the same osmolality. The result showed a significant negative relation between carbohydrate content and gastric emptying in the six drinks with a uniform osmolality. They concluded that rate of gastric emptying of carbohydrate-containing solutions was triggered by the carbohydrate-energy drink content or by the delivery rate of carbohydrate-energy to the gut (85).

As the rates of gastric emptying vary inversely with carbohydrate concentration. The more carbohydrate concentration induces more elevates in blood glucose. Therefore, MacGregor et al 1976 (86) tested the possibility that hyperglycemia induced by carbohydrate absorption itself contributes to the slowing of gastric emptying. Normal subjects were made acutely hyperglycemia with intravenous loads of glucose during the ingestion of various liquid test meals, and rates of gastric emptying of these meals were compared in the same subjects during periods of induced hyperglycemia with rates of gastric emptying under euglycemia conditions. Induced hyperglycemia significantly slowed the rate of emptying of meals containing fat plus protein, but did not significantly alter emptying of meals containing only NaCl. They included that hyperglycemia does exert some effect on gastric emptying, but that these

effects of hyperglycemia are variable expressed, depending on the presence of other factors which themselves slow gastric emptying.

Another study which demonstrated the delaying gastric emptying mechanism by changing carbohydrate content in the diet, was conducted in rats in 1995 by Raybould and Zittel (87). The response to intestinal glucose was reduced by a high carbohydrate diet, which also increased in the number of Na^+-glucose co-transporters. Therefore, activation of sensors to initiate feedback inhibition of gastric motility may be dependent either on rapid accumulation of glucose within epithelial cells or activation of Na^+-glucose co-transporter.

In conclusion, caloric density influence on gastric emptying 5%, 6, and 7.5% carbohydrate solution has similar gastric emptying (82) the higher caloric density as 12% and 18% carbohydrate impaired gastric emptying (84). The delaying gastric emptying by carbohydrate content might be the results of the hyperglycemia condition (86) as well as feedback inhibition of gastric motility (87).

1.1.3 Osmolality of the Solution

When gastric emptying characteristics of simple carbohydrates are studied, there is a close relationship between the rate of gastric emptying and both carbohydrate concentration and osmolality of ingested solution as mentioned above. Therefore, many investigators studied by controlling the caloric content in the solution and varied the osmolality to determine the effect of osmolality of solution on gastric emptying.

In running and cycling, at 70% VO_2 max 80 min, the isotonic drink continued to empty quickly after the initial 20 min whereas gastric emptying rate of the hypertonic drink decreased after the initial 20 min (57).

In the triathlon survey in 1990, a beverage with osmolality < 325 mmol/L, 11% had severe gastrointestinal symptoms, whereas a hyperosmotic beverage (>325 mmol/L) 42% had severe symptoms, and 80% who consumed a strongly hyperosmotic beverage (>800 mmol/L) had severe gastrointestinal symptoms. Hyperosmotic beverage consumption during triathlon competition is associated with

gastrointestinal symptoms and may be related to increased gastrointestinal secretion (88).

Owen et al 1986 determined the effect of osmotically different beverages on prolonged treadmill exercise (65% VO_2 max) in the heat. There were no significant differences between drink osmolalities 71, 94, 194, and 586 mmol/L and gastric residual volume in running in the heat (68).

Paraskevopoulos et al 1988 controlled intragastric pressure and measured the emptying of solutions of different osmolality and composition from the stomach. They found that hyperosmolar solution of glucose (586 mmol/L) in saline significantly reduced the gastric emptying rate. Therefore, the factors other than the intragastric pressure induced by fundic contraction regulate the rate at which liquids was emptied from the stomach. The slower emptying of hyperosmotic solutions or solutions containing fat could be brought about in part either by an increased resistance of the pylorus and possibly the duodenum or a reduction in the effectiveness of an antroduodenal pump (89).

The duodenum is both sensitive and responsive to its intraluminal content. The motor responses additionally appear to function to clear exclusively stimulating intraluminal material from the duodenal lumen and may also contribute to the 'postpyloric ' resistance which is known to exert control of normal gastric emptying (90).

Lin et al 1993 showed that the inhibition of gastric emptying by hyperosmolar mannitol depend on duodenal resistance, while the inhibitory effect of hyperosmolar glucose depended on nutrient-specific feedback on the stomach (91).

Osmolality of solution is effecting gastric emptying. Although osmolality of solution as high as 586 mmol/L is quite similar in gastric emptying rate to the osmolality of 71 mmol/L in prolonged treadmill exercise at 65% VO_2 max, the osmolality of solution should be in consideration for preparing fluid used in exercise (68).

1.1.4 Electrolyte Content

Adequate rehydration during and after exercise depends upon retaining the osmotic drive for drinking and upon maintaining a low urine output. Rehydration with water alone will dilute the blood rapidly, removing the drive for drinking and stimulating an increase in urine output. Rehydration will occur more rapidly when sodium, the major electrolyte lost in sweat, is taken with fluids (92).

Sodium also promotes retention of ingested fluids and leads to an increased plasma volume response during rehydration (67, 93). The ionic composition appears to be more important than its osmolality for storing plasma volume (94). However, small amounts of sodium added to water does speed gastric emptying and fluid absorption from the intestine (95).

Optimal water and sodium absorption occurred from solutions containing 60-160 mmol/L glucose and 50-120 mmol/L sodium (62). The optimal concentration of electrolytes, particularly sodium, remains unknown. Most currently available sport drinks therefore, provide a low level of sodium (10 to 25 mmol/L) in recognition that sodium intake may promote intestinal absorption of fluid as well as assist in rehydration (96). However, even if research indicates that intestinal glucose transport is optimally stimulated at higher sodium concentrations, concern for the palatability of sports drinks may imposed a lower ceiling for sodium levels. Commercial viability of a sports drink requires that it provides a refreshing and palatable fluid replacement across a wide variety of sports and exercise situations.

1.1.5 Exercise Variables

At 70% VO_2 max, gastric emptying is not limited (97). However, the data from Sole and Noakes in 1989 showed that exercise at 75% VO_2 max decreased the rate of gastric emptying of water but not of 10% glucose-polymer solutions (98). Exercise variables may have different effects on the gastric emptying rates of water and carbohydrate solutions.

After exercise for 10 min, contraction frequencies and the antral areas were significantly reduced compared to the studies without exercise. In addition, after exercise there was closure of the pylorus and tubular narrowing of the gastric

antrum. Closure of the pylorus might be important in explaining the decrease in gastric emptying that occurred with strenuous exercise (99). An exercise lasting more than 1 h significantly depressed postprandial gastric secretion and significantly delayed gastric emptying (100).

Gastric emptying was increased during running (50-70% maximal aerobic uptake, VO_2 max) as compare to rest. Neufer et al 1989 (69) demonstrated that gastric emptying was similarly increased during both moderate intensity (approximate 28% - 65% VO_2 max) walking or running exercise as compared to resting conditions. However, gastric emptying during moderate intensity treadmill exercise might be related to increases in intragastric pressure brought about by contractile activity of the abdominal muscles.

Most gastrointestinal symptoms occurred more frequently and lasted longer during running than during cycling at 75% VO_2 max exercise was reported by Peters et al (101). In contrast to the study of Houmard et al 1991 (102) who studied on ten male biathletes cycled and ran for 1 h at 75% of their mode-specific VO_2 max or rested and consume water of 7% carbohydrate solution at a rate of 10 ml/kg/h (approximately 180 ml every 15 min). No differences were found between cycling with water, cycling with carbohydrate, run with water, run with carbohydrate, and rest with carbohydrate for volume of a drink emptied and gastric emptying rate. A mean of 72.7 ± 5.7% of the total consumed volume was emptied. The gastric emptying rate during rest with water was significantly greater than the other conditions. Substantial volumes of water and a 7% carbohydrate solution are thus emptied from the stomach during prolonged, intense running and cycling, with no differences in gastric emptying between these exercise modes. These data suggest that recommendations concerning gastric emptying are reciprocal between running and cycling bouts.

Cases of acute gastric stasis following running have been reported and gastric physiology during exercise, particularly bicycling, has been more actively investigated. Gastric emptying during exercise is subject to a number of factors including calorie count, meal osmolality, meal temperature and exercise conditions. However, it is generally accepted that light exercise accelerates liquid emptying, vigorous exercise delays solid emptying and has little effect upon liquid emptying until

near exhaustion. Small bowel transit is delayed by exercise measured by breath hydrogen oral caecal transit times and motility may be reduced as well (103).

In summary, the influence of volume ingested, caloric density, electrolyte content, osmolality of the solution, and exercise variables on gastric emptying were described. The volume of fluid ingested is the important regulator of the volume of fluid emptied, at least after ingestion of a single fluid drink. Additionally, the volume of fluid ingested is more important for fluid ingestion than carbohydrate concentration. But the rate of gastric emptying (express as percentage emptied per unit time) is regulated by the carbohydrate content of the solution and the volume of the solution that is emptied is determined by the gastric volume (58). Osmolality of solution is also influencing gastric emptying but the carbohydrate content appears to have greater influence than osmolality (61, 85).

1.2 Fluid Absorption

Absorption rates of water, electrolytes, and carbohydrate are interrelated determinants of how effective oral solutions replenish the loss. Two major factors governing net water transport in the small intestines are osmolality (104) and solute flux (62).

Characteristics that influence intestinal absorption are summarized in Table 4 (54). The proximal small intestine (duodenum & jejunum) is the primary site of fluid absorption. The maximal fluid absorptive capacity of the small intestine is about 1.9 to 2.3 L/h, which is similar to the highest values for gastric emptying. Intestinal fluid absorption is a passive process and can occur against an osmotic gradient which can absorb about 50% to 60% of any given fluid load (105).

Neither gastric emptying nor intestinal absorption appeared to limit exogenous CHO oxidation, and differences in net water absorption were not necessarily reflected in gastric emptying rates. The study of Rehrer et al demonstrated that although net jejunal water absorption was greater from 4.5% glucose than water and than other solutions, there was a greater increase in exogenous carbohydrate oxidation over time (80 min) with 17% glucose and 17% maltodextrin than with 4.5% glucose (106).

Table 4 Factors influencing intestinal absorption of fluids.

Factor	Description	Action
Concentration of carbohydrate	Range of 2.5% to 12% found in commercially available beverages.	Carbohydrates are transported actively across intestinal wall. With saturation of transporters when carbohydrate levels are too high (≥8%), free carbohydrate in gut lumen can counteract fluid absorption.
Type of carbohydrate	Glucose polymers---(maltodextrins), sucrose, glucose, and fructose are typical choices---are optimal, with lesser amounts of fructose (not to exceed 1:1 molar ratio with glucose)	Glucose and fructose (individually or as sucrose) facilitate transportation, possibly by the putative disacchridase-related transport system (DRTS). Solute transport across intestinal membrane creates osmotic pressure that draws water for absorption. Polymers do not offer an advantage over free glucose at the same percent of carbohydrate, based on tracer methodology.
Presence of sodium	Macromineral, which is found in large concentrations in extracellular fluid.	Transported in intestinal membrane via glucose-sodium cotransporterrs. Resultant osmotic pressure draws water for absorption. Unclear whether additional sodium increases fluid absorption rate when carbohydrate mixture activates DRTS. Using intestinal perfusion model, a range of about 180 mEq to slightly over 400 mEq/L stimulates similar rates of fluid uptake in the duodenojejunum.
Osmolality	Particle content of the solution, primarily determined by carbohydrates, and electrolytes.	Osmolality has less of an impact when multiple transportable substrates are present in the fluid compared to when only one substrate is present.

Source: Horswill CA. Effective fluid replacement. Int J Sport Nutr 1998;8:175-95. (Ref 54)

Gisolfi et al in 1992, studied by using segmental perfusion technique on the studying of 2, 4, 6, or 8% solutions of glucose (111-444 mmol/L), sucrose (55-233 mmol/L). A maltodextrin (17-67 mmol/L), or a corn syrup solid (40-160 mmol/L) were perfused at 15 ml/min for 70 min after a 30-min equilibration period. All solutions were made isotonic with NaCl, except 6 and 8% glucose solutions, which were hypertonic. An isotonic NaCl solution was perfused as control. Water absorption (range: 9-15 ml/h/cm) did not differ for the 2, 4, and 6% carbohydrate solutions but was greater than absorption from control (3.0 ml/h/cm). The 8% glucose and maltodextrin solutions reduced net water flux compared with the 2, 4, and 6% solutions, but 8% sucrose and 8% corn syrup solid solutions promoted water absorption equivalent to lower carbohydrate concentrations. Adding different amounts of NaCl to the original solutions to make them isotonic did not influence net water absorption. On the other hand, net water flux correlated significantly with net Na^+ flux, indicating that Na^+ movement was an important determinant of water movement. Na^+ absorption also correlated significantly with K^+ absorption ($r = 0.78$), and, ultimately, net water flux followed net solute flux. However, the absorption that water absorption correlated poorly with [Na^+] in test segment ($r = 0.23$) suggested that carbohydrate absorption played the dominant role in determining water movement in this investigation (107).

Osmolality of solution is not only influence on gastric emptying but also on fluid absorption from the intestinal. The studied of Shi et al 1995 on intestinal absorption of solutions containing either one (glucose, or maltodextrin) or two (fructose, and glucose or sucrose) transportable carbohydrate substrate using segmental perfusion technique. The results were shown that the solutions with multiple substrates produce greater water absorption at a given osmolality (165-444 mmol/L) than those with one (glucose, maltodextrin). They concluded that multiple substrates stimulate several different solute absorption mechanisms yielding greater absorption than solutions with only one substrate (62).

Gisolfi et al 1998 (108) determined the effect of osmolality of an orally ingested fluid-replacement beverage on intestinal fluid absorption from the duodenum and/or jejunum during 85 min of cycling exercise (63.3 ± 9% VO_2 max) in a cool environment. They found that total fluid absorption of 6% carbohydrate-electrolyte

beverages from the duodenojejunum during exercise, within the osmotic range studied (197-414 mmol/L), was not different from water placebo.

In summary, the efficacy of a given drink is limited by the rate of gastric emptying and absorption (109). Ingestion of approximately 30-60 g of carbohydrate during each hour of exercise will generally be sufficient to maintain blood glucose oxidation late in exercise and delay fatigue. Since the average rates of gastric emptying and intestinal absorption exceed 1,250 ml/h for water and solution up to 8% carbohydrate, athlete can be supplemented with both carbohydrate and fluids at relatively high rates. However, runners generally drink only 500 ml/h of fluid and thus allow themselves to dehydrate at rates of 500-1000 ml/h (77).

Many of the recommendations on fluid replenishment have been directed at continuous exercise, and application of these suggestions can be applied on an intermittent exercise. Triathletes should drink at least one cup of fluid 20 min or so before training or competition. Every 15 min during exercise, they should drink fluids containing 6 to 8 % carbohydrate. A small amount of sodium added in the solution may be advantageous in promoting fluid retention (110).

Adequate rehydration during and after exercise depends upon retaining the osmotic drive for drinking and upon maintaining a low urine output. Rehydration with water alone will dilute the blood rapidly, removing the drive for drinking and stimulating an increase in urine output. Rehydration will occur more rapidly when sodium the major electrolyte lost in sweat, is taken with fluids (92).

Adding to sodium and carbohydrate (up to approximately 7%) increased the net intestinal absorption rate. Increasing carbohydrate concentration above this level begins to have a deleterious effect on intestinal absorption of fluid (93).

The volume of ingested fluid is critical for both rapid gastric emptying and complete rehydration, and osmolality (250 to 370 mmol/L), carbohydrate concentration (5 to 7%), and carbohydrate type (multiple transportable carbohydrates) should be considered when choosing an effective beverage for rehydration and carbohydrate supplementation during exercise (111).

2. Fructose Absorption

2.1 Fructose Absorption Mechanism

Water-filled channels (pores) in the luminal border of the intestine epithelial cell are thought to provide the route used by small water-soluble molecules in crossing this otherwise lipoidal barrier. The equivalent pore radius for these channels has been calculated to be 3.2-4.0 A (rat intestine) and therefore monosaccharides and other water-soluble molecules greater than 100 in molecular weight should be limited in their ability to penetrate intestine epithelial cells in the absence of special mechanism has evolved. For the two common dietary monosaccharides, D-glucose and D-galactose are to be rapidly transported against a concentration gradient across this lipoprotein membrane by a common, energy-requiring, saturable mechanism. D-fructose another common dietary monosaccharide, transport system separate from that of glucose (112), is neither absorbed against a concentration gradient nor have most investigators observed a saturable rate of absorption (113). The flux of fructose across the intestinal epithelial cell may be explained by postulating the existence of carriers in the lipoidal membrane (112-113).

There are specific transport systems for the three major dietary hexoses (glucose, galactose, and fructose). Glucose and galactose are transport systems across the microvillus membrane by a Na^+-dependent glucose transporter (SGLT1), which is a membrane of a family of proteins that includes Na^+-dependent nucleoside and myosinositol transporter (114). Glucose taken up by the enterocyte is released across the basolateral membrane into the interstitium via facilitative glucose transporter.

The five facilitative glucose transporters have been designed as GLUT1/erythrocyte type, GLUT2/liver type, GLUT3/brain type, GLUT4/muscle fat type, and GLUT5/small intestine type, and all are pressed in adult human small intestine (115-116).

GLUT5 is a member of the family of facilitative sugar transporters. Each member of this family has distinct biochemical properties and serves a specific role in the regulation of the uptake of glucose and other sugars. Of these facilitative sugar carriers, GLUT2 and GLUT5 are able to mediate the transport of fructose across the

plasma membrane. GLUT2 is also an efficient glucose transporter, whereas GLUT5 is a very poor carrier for this sugar. In the small intestine GLUT2 and GLUT5 may participate in the transepithelial uptake of fructose with GLUT5 being responsible for movement (Figure 1) across the luminal surface of the enterocyte and GLUT2 for transporting fructose across the basolateral membrane. The presence of GLUT5 in the intestine and human GLUT5 in spermatozoa along with the transport data suggests that GLUT5 is the primary fructose transporter in these tissues (117-118).

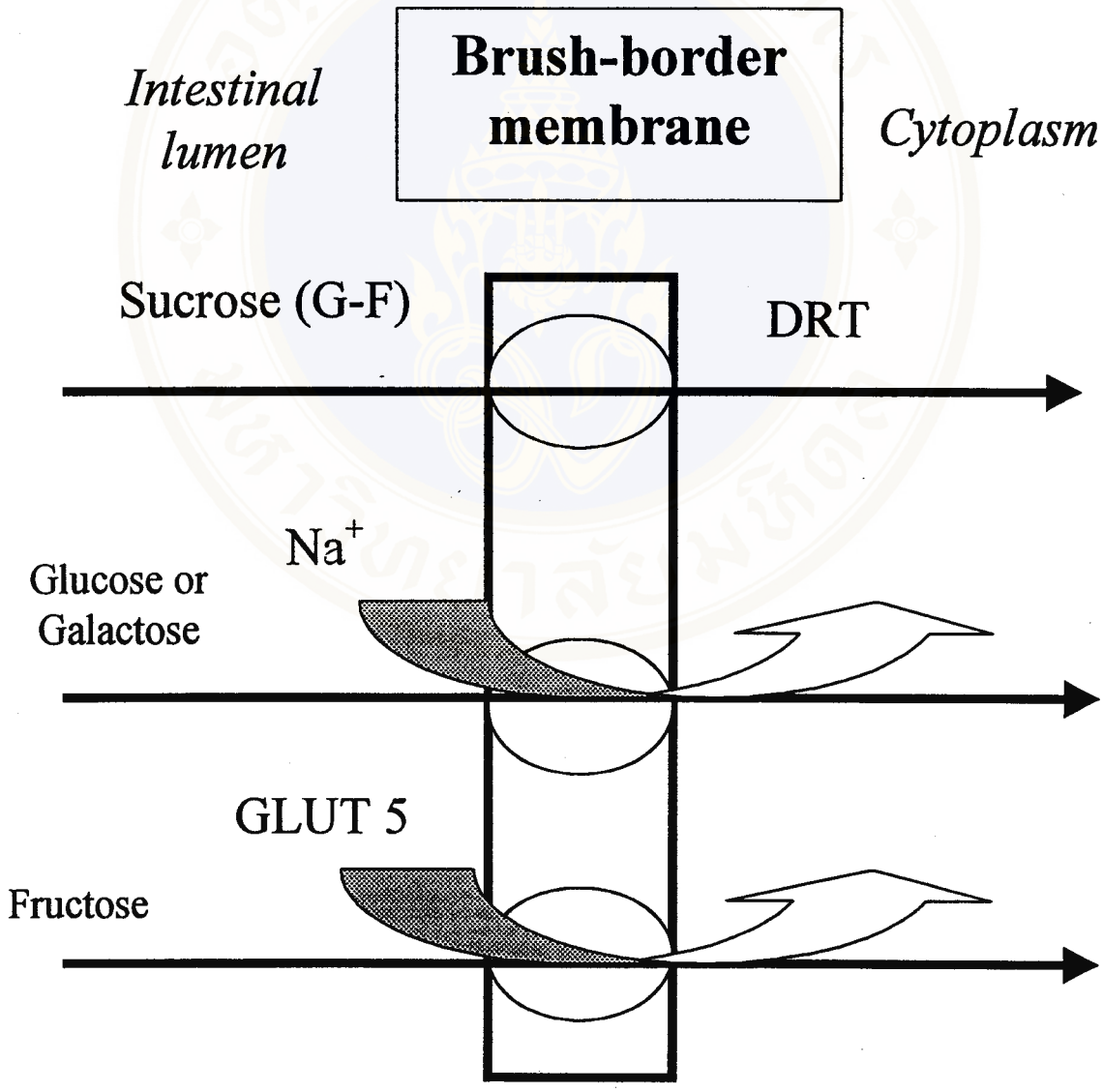


Figure 1 Fructose absorption mechanism. DRT, disaccharidase-related transport system (Adapted from Fujisawa T, Riby J, Kretchmer N. Intestinal absorption of fructose in the rat. Gastroenterol 1991;101:360-7. Ref 44)

2.2 Fructose Absorption Capacity

Fructose absorption has different mechanism from the other monosaccharides and there is limited in its absorption. The malabsorption after fructose ingestion has been reported.

Acute absorption of fructose in rats occurred with doses > 0.6 g (2.1 – 2.4 g / kg BW) (42). A study in children by Kneepkens et al in 1984 (119) demonstrated that 71% of subjects (31 children) failed to absorb fructose completely at the dose of an ingestion of 20% solution at a dose of 2 g/kg BW (maximum 50 g) after a fast of at least six hours.

The effect of exercise on fructose absorption was studied by Fujisawa et al 1993 (120). The data showed that intestinal capacity for absorption of fructose is readily saturated after ingestion of amounts as small as 50 g (50% fructose), and that exercise which reduces intestinal transit time, can cause incomplete absorption of fructose.

Similarly, Truswell et al 1988 confirmed that breath-H_2 production > 20 μl/L, often with diarrhea, abdominal cramps, and/or flatulence, is common after ingestion of 50 g pure fructose (100 ml/L H_2O) in healthy human subjects. Inability to completely absorb fructose is evidently dose dependent. When 21 subjects who produced ≥ 20 μl/L breath-H_2 after 50 g fructose were retested with 25 g fructose, only four showed increased breath-H_2 production. This difference was highly significant at $p< 0.005$. In addition, the highest peak breateh-H_2 in the same 21 subjects was 56 μ l/L after 25 g fructose compared with 155 μl/L after 50 g fructose (121).

The results of several studies demonstrated the determinations of the absorptive capacity of fructose in healthy humans are presented in Table 5 (38). The maximum capacity for intestinal absorption of fructose in resting conditions seems to be ≈ 50 g in most subjects and any reduction in the absorption capacity caused by exercise might therefore be expected to result in incomplete absorption of a 50-g load (120).

Table 5 Frequency of fructose malabsorption.

	Carbohydrate dose/ volume ingested	Proportion of subjects who had malabsorption
Studies in Healthy Adults		
Truswell et al 1988		
Fructose	50 g / 500 ml	58
	25 g / 250 ml	19
Glucose	50g / 500 ml	0
Fructose + glucose	25 g + 25 g / 250 ml	0
Sucrose	50 g / 500 ml	0
Rumessen et al 1986		
Fructose	25 g / 500 ml	52
Sucrose	50 g / 500 ml	0
Rumessen et al 1992		
Fructose	50 g / 500 ml	80
	37.5 g / 370 ml	70
	25 g / 250 ml	50
	20 g / 200 ml	40
	12.5 g / 250 ml	10
Fructose + glucose	50 g + 50 g / 500 ml	0
	50 g + 25 g / 500 ml	30
	50 g + 12.5 g / 500 ml	70
Sucrose	100 g / 500 ml	0
Ravich et al 1983		
Fructose	50 g / 250 ml	71
	50 g / 500 ml	37
	37.5 g / 370 ml	14
	25 g / 250 ml	0
Sucrose	50 g / 500 ml	0
Studies in Healthy Children (1-17 mo)		
Kneepken et al 1984		
Fructose	2 g / kg	71
Fructose + glucose	2 g / kg + 2 g / kg	14

Source: Riby JE, Fujisawa T, Kretchmer N. Fructose absorption. Am J Clin Nutr 1993;58 (suppl):748-53S. (Ref 38).

2.3 Fructose Absorption Facilitated by Glucose

Although fructose absorption is slower than glucose and galactose, studies using perfusion techniques have suggested that sucrose is very efficiently absorbed (122). This may either suggest an effect of the presence of glucose or of the process of hydrolysis or both.

Other perfusion studies have shown that absorption rates of fructose from mixtures of equivalent amounts of fructose and glucose are similar to absorption rates of fructose from a corresponding amount of sucrose (44, 64, 123). This is in accordance with the findings of Rumessen and Gudmand-Hoyer in 1986 (124), which strongly suggested that the presence of glucose is crucial point and also glucose stimulates fructose uptake in a dose dependent fashion.

In children who received an equal amount of either glucose or galactose (50 g fructose + 50 g glucose or 50 g fructose + 50 g galactose) had no symptoms of malabsorption and breath hydrogen test was increased less than 10 ppm (119). When glucose was added (25 g fructose + 25 g glucose) or combined in sucrose, breath hydrogen production was reduced; the greatest reduction was seen with equivalent amounts of fructose and glucose (121).

Fujisawa et al 1991 (44) confirmed that glucose or galactose administered with fructose enhanced the absorption of fructose. The greatest absorption was observed when equal amounts of fructose and glucose were given simultaneously. If glucose was ingested as a polymer (starch or dextrin), the stimulatory effect was dependent on the digestibility of the polymer. Sucrose given with the fructose and glucose diminished the absorption of fructose. Acarbozone, a specific inhibitor of α-glucosidase, including sucrase, also inhibited the facilitating effect of glucose and galactose in absorption of fructose. The facilitating effects of glucose on fructose absorption in many studies are also shown in Table 5.

In exercise, the tested on fructose and glucose absorption was determined by Fujisawa et al 1993 (102). Subjects ingested a total of 50 g carbohydrate: 100% fructose, 95% fructose + 5% glucose, 70% fructose + 30% glucose, and 100% glucose as well as a water placebo. Orange flavor and color and saccharin were added to all solutions as needed to achieve uniformity of taste and

appearance. The substitution of 5% glucose (47.5 fructose + 2.5 g glucose) did not improve absorption significantly, indicating that the facilitating effect exerted by glucose in resting conditions was not present during exercise. The malabsorption of fructose as shown by breath hydrogen tests was found in 100% of subjects both 100% fructose and 95% fructose + 5% glucose solutions. Ingestion of the test solution containing 35 g fructose + 15 g glucose before exercise was followed by malabsorption in 2 out of 7 subjects which demonstrated the facilitating effect of glucose.

Adopo et al 1994 (63) computed the respective amounts of the exogenous glucose and fructose, which are oxidized during exercise when ingested simultaneously, with the use of 13C labeling. Six subjects exercised for 2 h at 60.7 ± 2.9% VO_2 max on a cycle ergometer while ingesting 50 or 100 g of glucose or fructose or a mixture of 50 g of each of glucose and fructose in 500 ml of solution. The solution was ingested in one drink over a 2-min period after 5 min of exercise. The amount of exogenous glucose oxidized increased from 37.8 ± 2.2 to 58.3 ± 8.1 g when the total amount ingested increased from 50 to 100 g. The amount of fructose oxidized was significantly lower (32.2 ± 1.2 and 45.8 ± 2.6 g for the 50 and 100 g ingested, respectively). When the total amount of carbohydrates ingested was increased from 50 to 100 g by adding of fructose to 50 g of glucose, a larger increase in the total amount of exogenous carbohydrates oxidized was observed (37.8 ± 2.2 to 73.6 ± 6.6 g) than when the amount of glucose ingested was increased from 50 to 100 g (37.8 ± 2.2 to 58.3 ± 8.1 g). Compared with the percentage of exogenous glucose oxidized when 100 g of glucose were ingested (58.3 ± 8.1%). The percentage of exogenous hexoses oxidized with the ingestion of 50 g of glucose plus 50 g of fructose was significantly higher (73.6 ± 6.6%) and was not significantly different from that observed when 50 g of glucose were ingested (75.7 ± 4.4%). Accordingly, the contribution of exogenous carbohydrates to the energy increased from 15.7 ±2.9% (100 g of glucose) to 21.9 ± 1.6% (50 g of glucose + 50 g of fructose). From a practical point of view, these data may provide experimental support for using mixtures of carbohydrates in the energy supplements for endurance athletes.

2.4 Fructose Absorption Facilitated by Amino Acids

Fructose may profit from the water movement caused by the uptake of glucose through the well-defined glucose-transported systems, especially the glucose-Na^+ cotransporter (45). Some amino acids are Na^+ cotransporters that may be facilitate fructose absorption as same as glucose.

A study using perfusion technique was performed to quantitate the effect of the amino acids glycine and alanine on sodium and water absorption from human jejunum (125). The results showed that although no net absorption on sodium and water was seen in the absence of non-electrolyte, a significant stimulation occurred in the presence of both free amino acids and dipeptides. In the case of glycine and alanine, sodium and water absorption increased linearly with increasing concentration of the amino acids and saturation was not demonstrated over the range of concentrations studied. Molar ratios for net absorption of free amino acids and sodium were approximately 1:1 for all but the highest concentration was alanine.

Hoekstra and van den Aker (45) studied on the assumption that if the effect of glucose on absorption is mediated by water movement, amino acids should show similar effect. Their results are contrasted to Fujisawa et al (44) that acarbose pretreatment had no effect on fructose absorption from a fructose-glucose solution, which is against the theory of a disaccharidase-related transport system for combinations of fructose and glucose. This result is similar to Shi et al 1997 (126) which supported the evidence that the disaccharidase-related transport system is not used for free fructose and free glucose transport. Moreover, fructose absorption is enhanced by glucose and by the amino acids L-alanine, L-glutamine, L-phenylalanine, and L-proline. (45). The effects of equimolar solution provide an alternative explanation for the facilitating effect of glucose. Sorbitol, structurally related to fructose, was also shown to be enhanced by glucose and L-alanine. They suggested that the facilitating effects of glucose as well as of amino acids on both fructose and sorbitol absorption are a consequence of the water flow through the apical membrane, which is generated by the Na^+-coupled substrate transport. On one hand, there is the so-called solvent drag, The force that requires that water and solute (i.e., fructose) traverse the mucosa through the same pathway.

Another study has explained the solvent drag, which is opening of the tight junctions by glucose absorption and the subsequent movement of luminal fluid through the paracellular pathway (126). The evidence of solution drag in glucose absorption is also reported by Gisolfi et al in 1995 (127). Their studies support the theory that glucose absorption may occur largely via bulk flow through the paracellular pathway rather than through the transcellular pathway. As the concentration of glucose in the human solution was approximately 0.12 mmol/ml. Thus, for every milliliter of water absorbed one would aspect 0.12 mmol of glucose to be absorbed, if glucose was absorbed exclusively via the paracellular pathway. For every 10 ml of water absorbed 1.2 mmol of glucose should be absorbed. But in that study, water absorption averaged 12 ml/h/cm and glucose absorption ranged from 1.3 – 1.4 mmol/h/cm, supporting the notion that glucose absorption occurs predominantly "solution drag" across the paracellular pathway, nor across the cell.

The results of intraluminal intubation experiments on normal human adults can be summarized as follows (128). If the perfusate does not contain either amino acid or sugar, then there is either a small net sodium absorption or secretion or no net movement across the jejunum. The addition of glucose to the perfusate causes an increase in jejunum sodium absorption. Other sugars also increase sodium absorption. Among the simple sugars, glucose and galactose have almost identical absorption effects on sodium. At equivalent concentrations, maltose and glucose have identical effect on water flow, fructose has a small effect. Amino acids increase jejunum sodium and water absorption. The neutral amino acids, leucine, glycine, and alanine, and their peptides have a similar effect. In contrast, the basic amino acids arginine does not stimulate sodium absorption, it may even stimulate secretion.

The effects on water flow of alanine has tested extensively in human although the addition of 30 mmol/L alanine to the standard WHO-ORS produces no further improvement in the outcome of the infants with acute diarrhea compared with those fed the standard WHO-ORS (129). Oral therapy with a glucose-containing solution is generally used. One suitable solution consists of, in mmol/L, Na 90, K 20, HCO_3 30, Cl 80, glucose 110in gram per liter, NaCl 3.5, $NaHCO_3$ 2.5, KCl 0.75,

glucose 20); the measured osmolality is 320 mmol/L. The solution need not be sterile (113).

There are many transport pathways of amino acids in intestine. Based on uptake kinetics and cross-inhibition, it is seen that the brush-border membrane transports amino acids via at least three Na^+-dependent carriers system (130). The transport of both L-alanine and L-phenylalanine is an Na^+-dependent process. Similarly, both L-proline and glycine uptakes are stimulated by an Na^+-gradient (131). In the brush border membrane of the enterocytes, at least six different transport systems have been identified (130) as seen in Table 5 for the neutral amino acids, two Na^+-dependent (NBB and PHE) and one Na^+-independent (L) systems are present. The basic amino acids are taken up by the Na^+-independent y^+ system, the acidic amino acids by the Na^+-dependent imino system. Moreover, considering that no specific inhibitor is presently available and taking into account that "only occasionally does a natural amino acid serve as defining substrate for a given transport system" (131).

The L-alanine transporter is the Na^+-dependent apical NBB system, which is responsible for majority of neutral amino acids (130). Another transporter the PHE system is responsible for the uptake of the neutral amino acids L-phenylalanine (131). The Na^+-dependent IMINO carrier is highly specific for L-proline transport, but it too is less active than the NBB system. Arginine, a basic amino acid does not increase sodium absorption (132). Glycine has been reported in promoting net sodium and water absorption in cholera patients (128). However, Shi et al 1995 (133) have not found that effect in using segmental perfusion techniques in healthy subjects.

The complete mechanism of fructose absorption from the human intestine remains to be fully clarified (134). The facilitation of fructose transport seems to be of physiological significance and most probably explains the well-known observation of a better fructose absorption when consumed in a meal with other nutrients in comparison to similar amounts dissolved in a solution.

3. Substrate Utilization

Substrate utilization is an important issue in exercise as it provides as energy source during exercise. There are involved two major sources for energy used in human. Energy storage in the body is an important source of energy for human activities. However, there are limited in energy utilization from this source. The another source of energy is derived from outside the body, which most of them are from ingestion. Therefore, the study of carbohydrate replacement is widely performed, as carbohydrate is the main source of energy utilization of human.

3.1 Energy Storage

Caloric requirements vary with energy expenditure. A sedentary man weighing 70 kg consumes 2100 to 2500 kcal/d (135). Exercising at 30% VO_2 max, the 70-kg man burn 350 kcal/h. Increasing the intensity of exercise to 80% of VO_2 max increases energy consumption to approximately 950 kcal/h. The highly trained ultra-endurance athlete (male or female) will utilize oxygen at an average of 80% of VO_2 max over the distance of a marathon (42 km), resulting in an energy cost of 0.95 kcal/kg/km or a total of 2793 kcal for a 70-kg man. Consumption of energy during a 24-h ultra-endurance race has been demonstrated to as high as 18,000 kcal. Body energy stores will be used to meet the large caloric requirement of the ultra-endurance athletic performance. The average amount of stored fuels in the nonobese, 70 kg man are given in Table 6 (136).

Body fat stores provide the largest amount of available energy (approximately 80% of total stores). Although energy stored as protein may be as high as 40,000 kcal, its utilization probably is limited. It is estimated that only 3% of body protein is normally available for energy turnover at anytime (136). 10% of total available energy is in the form of carbohydrate stored as glycogen in muscle and liver. A small amount of glucose in circular also is available (135).

Table 6 Sources of substrate stores in humans (70 kg BW).

Source	Weight (kg)	Energy (kJ)
Circulating fuels		
• Glucose (extracellular H_2O_2)	0.020	336
• Free fatty acids (plasma)	0.0004	17
• Triglycerides (plasma)	0.004	168
	Total	521
Tissue stores		
Fat		
• Adipose tissue triglycerides	15.0	588,000
• Intramuscular triglycerides	0.3	11,760
Protein (mainly muscle)	10.0	172,000
Glycogen		
• Liver	0.085	1,470
• Muscle	0.350	6,090
	Total	779,320

Source: Nagle FJ, Bassett DR. Energy metabolism in exercise. In:Hickson JF, Wolinsky I, editors. Nutrition in Exercise and Sport. USA: CRC; 1990. p. 95. (Ref.136).

Glycogen is the main fuel for heavy exercise of a few minutes' duration where performance capacity is limited by the degree of lactate accumulation and intracellular acidosis (137). Oxidation of both glucose and free fatty acids supplies the energy needed for exercise lasting more than two minutes, the relative contribution of lipids increasing with a longer duration or a lower intensity of the muscular work. Intramuscular stores of glycogen and triglycerides may be almost completely depleted in long-lasting exercise, e.g., a 100 km run. Under these conditions, glycogen stores in the liver and triglycerides in adipose tissue contribute approximately 70% of the energy need whereas 5-10% of the supply comes from oxidation of amino acids.

3.2 Substrate Use During Exercise

There are five principal factors dictate the relative utilization of fuel during exercise (138):

- Intensity of exercise of task
- Duration of exercise task
- Type of exercise
- Training status of the individual
- Preceding diet

The use of various substrates is dependent on the intensity of the exercise, which is usually represented as the percentage of the subject's total functional capacity or VO_2 max (37). Training protocols established on an individual's VO_2 max are normally related as low (30-40% VO_2 max), moderate (50-70% VO_2 max) or high (>70 % VO_2 max).

Comparison of substrate utilization during marathon running at two different paces was held by O'brien et al 1993 (139). Subjects were placed into a fast (≤ 2 h, 45 min; 73.3% VO_2 max), or a slow trials (≤3 h, 45 min; 64% VO_2 max) by treadmill running with overnight fast, and only by tap water at a rate of 1 l/h ingested during exercise. The average respiratory gas exchange ratio was higher in fast than slow trial (0.99 ± 0.01 vs. 0.90 ± 10.01, respectively). A direct relationship between carbohydrate oxidation and running speed during marathon running is indicated. There was no significant difference between groups in the amount of total carbohydrate utilized: the higher rate of carbohydrate oxidation in the fast group was compensated by a longer duration in the slow group such that the total carbohydrate combustion were not different. Estimated carbohydrate combustion [fast: 2414.3 ± 43.0 kcal (575 ± 10 g); slow: 2890.0 ± 159.0 kcal (688 ± 38 g)] exceeded estimated glycogen stores in active muscle and liver [(475 g = 375 g (muscle) + 100 g (liver)]. Therefore, total body glycogen stores were made available for combustion. All classes of energy substrates participate, but carbohydrate, not lipid, is the primary fuel for marathon running.

The effects of exercise intensity and duration on substrate utilization were evaluated by Romijn et al 1993 (140) by using isotopic tracer approach. Five

trained subjects were studies during exercise intensities of 25, 65, and 85% VO_2 max for 120, 120, and 60 min respectively. Carbohydrate oxidation rates calculated during 20-30 min of exercise at 25, 65, and 85% VO_2 max increased significantly with exercise intensity. The value of total carbohydrate oxidation at 65 and 85% VO_2 max were significantly higher than the rate of glucose tissue uptake (the maximal amount of plasma glucose available for oxidation). This difference reflects the minimal contribution of muscle glycogen to carbohydrate oxidation, which also increased significantly with increasing exercise intensity. Fat oxidization rates were related differently to exercise intensity than carbohydrate oxidation rates. Fat oxidation after 30 min of exercise was not different at 25 vs. 85% VO_2 max, despite a more than threefold increase in energy expenditure. At 65% of VO_2 max fat oxidation rate was significantly higher than observed during exercise at 25 and 85% VO_2 max. During exercise at 65 and 85% VO_2 max, whole body fat oxidation was significantly higher than tissue FFA uptake, with the difference representing the minimal contribution of muscle triglyceride stored to whole body fat oxidation. The increase in caloric equivalents from glucose tissue uptake with increasing exercise intensities is largely counterbalanced by the relative decrease in plasma FFA uptake. As a consequence, the contribution of plasma substrates to overall energy production remained essential constant at the different levels of exercise, meaning that, at higher exercise intensities, muscle substrate stores (particularly glycogen) become predominant.

The effect of the duration of exercise on the metabolic responses was also evaluated during exercise at 25, 65, and 85% of VO_2 max by Romijn et al 1993 (140). It was not possible at 85% of VO_2 max, because this level of intensity could only be maintained for 30 min, and 20 min of exercise was required before a good isotopic steady state was achieved in all factors. At 25% of VO_2 max, there was no significant alteration in relative contribution of the various substrates to energy production over the 2-h exercise period. On the other hand, during exercise at 65% of VO_2 max, there was a progressively increase on the reliance on plasma FFA and glucose as energy substrates availability over the time. Because the rates of total fat and carbohydrate oxidation did not change over time, it can be assumed that there was a progressive decrease in the reliance on intramuscular triglycerides and glycogen substrates. As a

consequence the contribution of muscle substrate stores to energy production decreases.

Although significant potential energy for exercise exists in the form of stored fat, because of slow fat mobilization during exercise and the rate limiting effects of the diffusion of fat from blood to muscle, fatty acids cannot typically support muscular contraction that elicit > 60% of VO_2 max (141). Thus, athletes most often train and perform at exercise intensities requiring > 70% VO_2 max, and a source of fuel other than fat or protein must be available. That source of fuel is carbohydrate. As exercise intensity increases linearly, there is an exponential increase in the rate of muscle glycogen metabolism during exercise. The rate of muscle glycogen breakdown is 0.7, 1.4, and 3.4 mmol/L/min at 50%, 75%, and 100% VO_2 max, respectively. At exercise intensities ≤60% VO_2 max, fatigue occurs as a result of boredom, dehydration, hyperthermia, or orthopedic injury. At exercise intensities ≥ 90% VO_2 max, fatigue is related to the consequences of increased muscle and blood lactic acid concentrations. However, at 65-85% VO_2 max, fatigue occurs concurrently with the depletion of muscle glycogen. Furthermore, the time to fatigue is directly proportional to the initial muscle glycogen concentration. The pattern of muscle glycogen metabolism during exercise at 75% VO_2 max is curvilinear; the most rapid glycogenolysis occurs during the first 20-30 min, which is followed by a slower decline in muscle glycogen depletion after ≈60 min in untrained subjects.

In exercise at 65-75% VO_2 max in endurance-trained subjects which fasted overnight, about 50% of the energy for exercise at 70% of VO_2 max is derived from fat, with equal contributions from plasma acids and intramuscular triglycerides during the early portions of exercise, the majority of carbohydrate energy is from muscle glycogen (142). As exercise progresses, muscle glycogen is reduced and contributes less to the carbohydrate requirements of exercise and there is increased reliance on blood glucose.

Fat oxidation also appears to provide most of the energy for light work but does not increases parallel to the intensity of exercise (143). Thus, the contribution of fat oxidation first increases and then decreases again, so that in high intensity work the contribution of fat metabolism is very small. The reason suggested for the metabolic

preference for glycogen in supporting hard work is that the efficiency of ATP synthesis from fat oxidation may be lower than from glycogen. Thus, it is possible that in man, where fat is stored at remote locations, glycogen supports short-term high intensity exercise and fat oxidation is reserved for long term energy metabolism.

3.3 Carbohydrate Replacement

In exercise, lipids provide an abundance of stored energy, whereas calories with carbohydrate and accessible protein are far more limited. However, in the high intensity work the contribution of fat metabolism is very small. The primary role of carbohydrate replacement is to maintain blood glucose concentration and enhance carbohydrate oxidation during exercise that lasts longer than 1 h, especially when muscle glycogen is low.

3.3.1 Infusion Studies

The testing for the benefit of fluid replacement and glucose infusion during exercise on cardiovascular system was conducted by Hamillton et al 1991 (65). The subjects were cycling for 2 h at 70% VO_2 max with or without fluid replacement. A sterile 18% (wt/vol.) glucose solution in water was infused into forearm vein beginning at 8 min and ending at 118 min of exercise. The infusion rate was adjusted every few minutes to maintain blood concentration at 10.1 ± 0.4 mmol/L (i.e., 182 ± 7 mg/ 100 ml), whereas blood glucose concentration remained in the euglycemic range (i.e., 3.7 – 4.6 mmol/L) during the trial. The data was shown that the 5-7% increase in heart rate and cardiac output during fluid replacement trial is in response to increased whole body oxidative metabolism in tissues that respond directly or indirectly (i.e., via catecholamines) to blood glucose concentration because the increased in oxidative metabolism was suppressed by the hyperglycemia.

The questions of how much exogenous glucose needed in exercise is still debated. Coyle et al 1991 (144) conducted experimental on the effects of hyperglycemia on muscle glycogenesis and carbohydrate metabolism in well-trained cyclists during 2 h of exercise at 73% VO_2 max. The amount of muscle glycogen utilized in the vastus lateralis during exercise was similar during hyperglycemia and

control trials (no exogenous glucose provided). As exercise duration increased, carbohydrate oxidation declined during control trial but increased during hyperglycemia trial. Consequently, after 2 h of exercise, carbohydrate oxidation was 40% higher during hyperglycemia trial than during control trial. The rate of glucose infusion required maintaining hyperglycemia (10 mmol/L) remained very stable at 1.6 ± 0.1 g/min during the first hour. However, during the 2nd h of exercise, the rate of glucose infusion increased to 2.6 ± 0.1 g/min (37 mg/kg BW/min) during the final 20 min of exercise. Finally, well-trained cyclists have the remarkable ability to "dispose of glucose" during 2 h of intense cycling when hyperglycemic. The finding of Coyle et al as above is in contrast to several studies in rats and humans in which hyperglycemia during exercise has been observed to somewhat attenuate the net decline in muscle glycogen (145-147). Bergstrom and Hultman 1967 (147) intravenously infused glucose into men at ~ 3 g/min during 1 h of one-legged cycling. As a result, blood glucose averaged 21 mmol/L (range 13-30 mmol/L) and the decline in muscle glycogen concentration was reduced by 15 mmol/L compared with control. Winder et al 1988 (145) infused glucose into exercising rats and maintain blood glucose at 10 mM. After 80 min of exercise, muscle glycogen was 8-11 mmol/L higher when hyperglycemic than euglycemic. However, on the basis of Coyle et al (144) it appeared that 10 mmol/L blood glucose did not alter net glycogen use in humans, although it has been suggested that 20 mM blood glucose might attenuate the decline in muscle glycogen (147). The differences between those studies and Coyle et al (144) might be from the different in subjects who were well trained whereas the subjects in the study of Bergstrom and Hultman (148) and the rats used by Winder et al (145) were moderately trained for endurance exercise.

Infusion method can be provided the substrate such as carbohydrate more directly to the blood circulation than ingestion method. Infusion studies of carbohydrate replacement were shown the benefit results both for the cardiovascular system and substrate utilization during exercise. However, the effect of glucose infusion on muscle glycogen is still controversy.

3.3.2 Ingestion Studies

The benefit of carbohydrate replacement was demonstrated as in infusion studies. Therefore, many investigators attempted to study the benefit of carbohydrate replacement in practically based which some are shown in Table 7.

3.3.2.1 The Benefit of Carbohydrate Ingestion

The effects of carbohydrate replacement on muscle glycogen depletion also tested by ingestion. Coyle et al 1986 (28) studied on seven endurance-trained cyclist exercised at 71 $\pm$1% of VO_2 max, to fatigue, while ingesting a flavored water solution (i.e., placebo) during one trial and while ingesting a glucose polymer solution (i.e., 2.0 g/kg BW of 50% solution at 20 min, and 0.4 g/kg BW of 10% solution every 20 min thereafter) during another trial. When plasma glucose was maintained at 4-5 mmol/L through carbohydrate ingestion, the rate of total carbohydrate oxidation was held constant and the subjects were able to exercise strenuously for an hour longer than when they fasted. The pattern of muscle glycogen utilization, however, was not different during the first 3 h of exercise with the placebo or the carbohydrate feedings. The additional hour of exercise performed when fed carbohydrate was accomplished with little reliance on muscle glycogen and without compromising carbohydrate oxidation. They concluded that when ingested carbohydrate, highly trained endurance athletes are capable of oxidizing carbohydrate at relatively high rates from sources other than muscle glycogen during the latter stages of prolonged strenuous exercise and that this postpones fatigue.

Table 7 The benefit of carbohydrate replacement in exercise.

Reference	Exercise test	Carbohydrate feeding	Results
Coyle et al 1983 (151)	74±2% VO_2 max, cycled to fatigue	50% polycose solution 140 ml at 20 min and 6% polycose 300 ml every 30 min thereafter	Time to fatigue 157±5 vs. 134 ±6 min ($p<0.01$), carbohydrate and water trial respectively.
Coyle et al 1986 (28)	70% VO_2 max cycled to fatigue	50% glucose polymer at 20 min and 10% glucose polymer every 20 min	Muscle glycogen depletion was not different as water placebo.
Coggan and Coyle 1989 (152)	70% VO_2 max, cycled 180 min.	3g/kg of 50% glucose polymer at 135 min of exercise	Improve time to fatigue.
Millard-Stafford et al 1990 (153)	Triathletes	7% carbohydrate (5% glucose polymer + 2% fructose) during exercise	Time to fatigue 205±17 vs. 169 ±12 min ($p<0.01$) carbohydrate and water trial respectively.
Millard-Stafford et al 1992 (154)	40 km run in the heat	7% carbohydrate (5% glucose polymer + 2% fructose) 400 ml 30 min prior to exercise and 250 ml every 5 km.	No significant effect on total triathlon performance time Running performance in the last 6 km was significantly faster.
Burgess et al 1991 (148)	70% VO_2 max, cycled 180 min	6, 8, 12, and 18 % carbohydrate solution 2 ml/kg LBM every 15 min.	Attenuate of ratings of perceived exertion.
Murray et al 1991 (47)	65-75 % of VO_2 max for 2 h cycling	20% and 40% carbohydrate solution equal osmolality given	No significant on perceived exertion rates between solutions.
Sherman et al 1991 (155)	70% Of VO_2 max 90 min cycled	1.1 g or 2.2 g/kg 1 h before exercise	VO_2 max was 17% and 11% higher for 40% and 20% carbohydrate solution respectively.
Below et al 1995 (156)	80% of VO_2 max 1- h cycling	1330 ml and 200 ml as equal energy	Faster performance time than small volume.
Roberg et al 1998 (157)	65% of VO_2 max 2- h cycled	0.6 g carbohydrate/kg/h at 0, 30, 60, 90, and 120 min)	Similar exercise performance between solid and liquid formula.

The precise contribution of exogenous substrates to the energy demand of exercise remains a matter debate. For the same intensity of exercise, amounts between 0.15 to 0.84 g/min for ingested glucose have been reported. The wide dispersion could be explained by the diversity of experimental conditions of exercise and carbohydrate ingestion. For example, the oxidation rate of exogenous glucose increased with the amount ingested (149) but not its concentration. It appears also be clear that the oxidation rate of carbohydrates ingested during exercise is determined by the power output sustained by the subject. The influence of the workload is an interesting factors.

The influence of workload on oxidation rate of carbohydrates ingested during exercise was examined by Pirnay et al 1995 (150). The healthy male subjects underwent three exercise bouts, low (45% VO_2 max, 1822 $\pm$ 194 ml O_2 /min for 4 hours), moderate (60% VO_2 max, 2582 $\pm$ 226 ml O_2 /min for 3 hours), and high intensity (75% VO_2 max, 3036 $\pm$ 287 ml O_2 /min for 2 hours). After 10 min of exercise, each subject ingested 100 g of artificially ^{13}C-labelled glucose dissolved in 400 ml of water. Over the four hours of the exercise at 45% VO_2 max, the amount of exogenous glucose oxidized was 89.5 $\pm$ 5 g from the 100 g ingested. In all exercise bouts, the oxidation of exogenous glucose already began during the first 30 min after ingestion and peaked at 120 min. The maximum oxidation average 0.64 $\pm$ 0.07, 0.75 $\pm$ 0.04, and 0.63 $\pm$ 0.08 g/min, and the mean amounts of exogenous glucose oxidized over the first two hours averaged 51.7 $\pm$ 8.0, 61.5 $\pm$ 6.6 and 50.9 $\pm$ 8.45 g at 45, 60, and 75% VO_2 max respectively. The contribution of the oxidation of exogenous glucose to the total energy supply progressively decreased when the power output increased, from 19.6 to 12.2 %. In the meantime, the contribution of total carbohydrates (exogenous + endogenous) progressively increases from 55.1 to 77.8 %. The limitation of the oxidation seems to be localized at the muscular level. The uptake from the blood would be impaired and endogenous glycogen preferably utilized.

In summary, the benefit of carbohydrate ingestion on exercise was well established by many investigators as it can contribute the exogenous substrate to the energy demand during exercise. However, although there are many reports supported the benefit of carbohydrate replacement on physical performance, this issue is still in debated and needed further study.

3.3.2.2 Amount of Carbohydrate Ingestion

The amount of carbohydrate replacement is the important issues involving for the carbohydrate delivery and its oxidation in exercise. Mitchell et al 1989 (158) employed the subjects ingested a water placebo or carbohydrate at the rates of 37 g/h (6% carbohydrate beverage), 74 g/h (12% carbohydrate beverage), or 111 g/h (18% carbohydrate beverage) at regular intervals during 105 min of cycling exercise at 70% VO_2 max. Power output during a final 15 min cycling bout was used as the performance criterion. Mean power outputs with the carbohydrate treatments were 6-10% greater than with the water placebo and reached statistical significance with the 74 g/h treatment. They concluded that there was no evidence of a dose-response relationship between carbohydrate ingestion rates and performance and that carbohydrate feeding at a rate exceeding 37 g/h was required to elicit an improvement in performance.

Murray et al 1991 (47) also studied carbohydrate ingestion by varying rates of carbohydrate consumption. Exercising at 65-75% VO_2 max, subjects ingested either water placebo or carbohydrate solutions formulated to provide glucose at the rates of 26, 52, and 78 g/h (6%, 12%, and 18% glucose solution). To minimize the differences in sweetness and osmolality among the glucose beverages, the 12% and 18% solutions were formulated with combinations of dextrose and maltodextrin (4% dextrose + 8% maltodextrin, and 3% dextrose + 15% maltodextrin respectively). The osmolality of the glucose beverages ranged from 334 to 375 mmol/L. Beverages were ingested at 15 min intervals, beginning at 12 min of exercise. Each serving provide 2.0 ml/kg lean body mass. Fluid ingestion average 440 $\pm$ 21.0 ml/h. Their result indicated that carbohydrate intake of approximately 25 g/h is sufficient to elicit an ergogenic effect by faster mean performance time. The finding is

consistent with Fielding et al 1985 (159) who reported performance benefits association with carbohydrate ingestion rates of 22-25 g/h. There were no significant differences in rating of perceived nauseousness, perceived stomach upset and perceived exertion which may because the study was conducted in a cool environment (10 ^{0}C), where the thermoregulatory strain and need for exogenous fluids are substantially reduced.

When only one hexose is ingested the amount oxidized for a given metabolic rate increases with the total amount ingested. However, the increase in the amount oxidized is slower than the increase in the amount ingested, and accordingly, the percentage of the carbohydrate load that is oxidized decreases. As Pallikarakis et al 1986 (149), the percentage of exogenous glucose oxidized decreased from 69 to 57% (from 137 to 227 g) when the amount ingested was doubled from 200 to 400 g. In the study by Rehrer et al 1992 (106), the percentage of exogenous glucose oxidized decreased from 55 to 19% (from 32 to 42 g) when amount ingested was increased from 58 to 220 g. Adopo et al (63) also found that when the amounts of hexoses ingested were increased from 50 to 100 g, the percentage of exogenous glucose oxidized was reduced from 75.7 to 58.3% (from 38 to 58 g from the 50 and 100 g of glucose, respectively) and that of fructose was reduced from 64 to 46% from 32 to 46 g for the 50 and 100 g fructose ingested, respectively.

3.3.2.3 Volume and Osmolality of Carbohydrate Solution

Volume of beverages to be ingested for exercising is an important factor for exercise performance. As known that the water is lost from the body while exercising by sweating is the main water loss. To determine the influence of fluid replacement for intense exercise, Below et al 1995 (157) studied on four occasions. Eight men cycled at 80 $\pm$ 1% VO_2 max for 50 min. During exercise, the subjects consumed either a large volume (1330 $\pm$ 60 ml; 79% of fluid losses replaced) of a 6% carbohydrate solution (79 $\pm$ 4 g) or water or a small volume (200 $\pm$ 10 ml; 13% of fluid losses replaced) of a 40% maltodextrin (79 $\pm$ 4 g) solution or water. The

fluid that was consumed in the various trials was ingested immediately before exercise (40% of the total volume) at 15 min (20%), at 25 min (20%) and 34 min (20%). Performance times were 6.5% faster during large volume than small volume and 6.3% faster during carbohydrate than no carbohydrate. Large volume fluid replacement attenuated the increase in esophageal temperature and heart rates, which occurred when only a small volume of fluid was ingested.

The influence of the osmolality of glucose solutions on digestive factors such as the rate of gastric emptying and glucose intestinal absorption is still controversial (160). Jandrain et al 1989 (60) tested the same amount of glucose, i.e., 50 g by giving with various amounts of water (200, 400, and 600 ml), leading to osmolality of 1204, 644, and 439 mmol/L for the ingested solutions. The beverages were given orally 15 min after adaptation to exercise in five healthy male volunteers, and exercise was continued for the next 4 h. With the exception of a modest, but sometimes significant, increase in pulmonary ventilation, when large amounts of fluids (400-600 ml) were ingested with no obvious explanation, differences in osmolality of the orally given glucose did not result in any significant change in the many metabolic and hormonal parameters investigated. Total carbohydrate oxidation was similar in the three protocols, as was lipid oxidation. Exogenous glucose oxidation rates were similar under the three experimental conditions and the total amount of exogenous glucose utilized was slightly, but not significantly increased with the more diluted solution. The blood glucose response was similar in the three protocols. Thus, within the ranged investigated in this study, the osmolality of the glucose solution ingested had no significant influence either on its oxidation which was 86-98% of the load ingested) or on the utilization of endogenous carbohydrate, lipid, or protein stores.

In summary, carbohydrate is the most important nutrient for an athlete because it is the only fuel that can power intense exercise for prolonged periods, yet its stores within the body are relatively small. The main factors which could modify the metabolic responses to carbohydrate ingestion and thus affect the exogenous and endogenous carbohydrate utilization during exercise. The impact of these factors are type and intensity of exercise; amount, type and timing of carbohydrate ingestion; pre-exercise nutritional and training status of the participants (161).

Carbohydrate ingested during exercise appears to be readily available as a fuel for the working muscles, at least when the exercise intensity does not exceed 70 to 75% of maximum oxygen uptake. Carbohydrate-containing solutions appear to be more effective in improving performance than plain water. Water and electrolytes are lost from the body major in sweat although the composition of sweat is rather variable, it is invariably hypotonic with respect to plasma (162). Sports drinks containing 6-8 percent carbohydrate maintain circulatory and thermoregulatry function during exercise as well as plain water and provide greater performances benefit than water (163).

Ingestion of approximately 30-60 g of carbohydrate (i.e.; glucose, sucrose, or starch) during each hour of exercise will generally be sufficient to maintain blood glucose oxidation late in exercise and delay fatigue (164). For an exerciser who weighs about 68 kg (150 lb.), the requirements for carbohydrate (i.e.,30-60 g/h) and fluid during prolonged exertion can be met by drinking 625-1250 ml/h of beverages containing 4-8 % carbohydrate. This volume must be adjusted for person of different body weights. For an example, an individual who weighs 50 kg should multiply the above recommendation by 50/68 or 0.74, i.e., 462.5-925 ml/h (165-166). Since the average rates of gastric emptying and intestinal absorption exceed 1250 ml/h for water and solutions containing up to 8% carbohydrate, exercising people can be supplemented with both carbohydrate and fluids at relatively high rates. (167). Higher intake rates could have small advantages with respect to energy provision to the working muscle but may lead to accumulation of carbohydrates and fluid in the stomach (and maybe the intestine) (168).

4. Fructose Replacement

Although glucose is an important metabolic fuel during exercise, there are drawbacks to its use as a supplement: the main factor being its stimulatory influence on insulin release. Therefore, fructose is an alternative for dietary aids to performance as it much less stimulates insulin response than glucose.

4.1 Fructose and Exercise Performance

Athletic competition requires great energy expenditure and the ability to maintain performance depends on an adequate supply of metabolic fuels, which has led to the use of dietary supplements. It shows that fructose before or during exercise can enhance performance under certain conditions (37). Preexercise nutrition seems to be the most important condition to be met. It has been theorized that prefeeding elevates liver glycogen and spares muscle glycogen, which prolongs activity. There is also good evidence to indicate that the addition of fructose to the diet during ultraendurance events can improve performance by 126%. The gastrointestinal discomfort created by large amounts of fructose can hinder performance and has limited research with this supplement. Therefore, even though positive effects have been demonstrated, more research is needed to determine the role that fructose can play role in enhancing athletic performance.

Kovisto et al 1981 (169) examined the effect of various carbohydrates on the metabolic and hormonal response to exercise, 250 ml of 75 g glucose, fructose, or placebo were given to nine well-trained males 45 min before cycle ergometer exercise performed at 75% VO_2 max for 30 min. The glucose ingestion prior to exercise results in hypoglycemia and decreased free fatty acid availability during vigorous exercise. This decline in blood-born fuel availability is mediated, at least in part, by hyperinsulinemia, and fructose ingestion is associated with a modest rise in plasma insulin and does not result in hypoglycemia during exercise.

The effects of preexercise carbohydrate feedings on endurance performance and muscle glycogen utilization during prolonged exercise were studied by Hargreaves et al 1987 (70). Trials consisted of a cycling ride to exhaustion at 75% VO_2 max preceded by the ingestion of either 75 g of glucose in 350 ml of water, 75 g of fructose in 350 ml of water, or 350 ml of an artificially sweetened and flavored placebo. No differences were observed between trials for oxygen uptake, respiratory exchange ratio, heart rate, or exercise time of exhaustion. Muscle glycogen utilization during the first 30 min of exercise and total glycogen uses were similar in the three trials.

Okano et al 1988 (170) studied twelve trained males, in a fed state, were studied to examine the effect of pre-exercise fructose ingestion on endurance capacity

during prolonged cycling exercise. Sixty minutes prior to exercise, subjects ingested either 60 or 85 g fructose or a sweet placebo. Mean exercise intensity initially required 62% VO_2 max and thereafter increased to elicit 72 to 81 % of VO_2 max at 90 and 120 min of exercise, respectively. Exercise time to exhaustion was significantly increased after fructose ingestion, as compared to placebo ingestion (145 ± 4 vs. 132 ± 3 min, respectively). There were also no significant differences in serum free fatty acids and glycerol levels as well as respiratory exchange ratio between fructose and placebo trials during exercise.

The purpose of the study of Murray et al 1989 (48) was to compare the physiological, sensory, and exercise performance responses to ingestion of 6% glucose, 6% fructose, and 6% sucrose solutions during cycling exercise. Twelve subjects completed three sessions consisting of 115 min of intermittent cycle ergometer exercise at 65-80% of VO_2 max followed by a timed performance bout requiring the completion of 600 pedal revolutions. Beverages were consumed at the end of the initial 20-min rest period (6 ml/kg LBM) and during each of the 4-min rest period (3 ml/kg LBM). These fluid consumptions regimen provided a total 1.27 ±0.072 L of fluid during each session, providing a total 76.3 ± 4.3 g of exogenous carbohydrate. Fructose was associated with lower plasma glucose and serum insulin, a larger loss of plasma volume, greater gastrointestinal distress and relative perceived exertion ratings, and higher plasma or serum concentrations of free fatty acids, fructose, and cortisol values than sucrose or glucose. Compared to sucrose and glucose, fructose feeding also resulted in lower lactate and heart rate values during the performance bout. Mean ± SE cycling performance times were faster with sucrose and glucose that with fructose (419.4 ± 21.0S, 423.9 ± 21.2S, and 488.3 ± 21.2S, respectively). Relative to 6% solutions of sucrose and glucose, ingestion of 6% fructose beverage is associated with gastrointestinal distress, compromised physiological response, and reduced exercise capacity.

Bjorkman et al 1985 (165) studied to examine the influence of glucose and fructose ingestion on the capacity to perform prolonged heavy exercise. Eight well-trained healthy volunteers exercised on a bicycle ergometer at 68 ±3% of their VO_2 max until exhaustion, on three occasions, with 8-day intervals. During the exercise they

ingested either glucose (250 ml, 7%), fructose (250 ml, 7%) or water (250 ml) every 20 min in a double-blind randomized study design. Corrected for the sequence effect, total work time until exhaustion was significantly longer with glucose (137 ± 13 min) than with either fructose (114 ± 12 min) or water (116 ± 13 min). When glucose or fructose was ingested, the arterial plasma glucose concentration was maintained at the normoglycemic level; with water ingestion, plasma glucose values fell during exercise in seven subjects and remained at the resting level in the eight subjects. Intermittent glucose ingestion (3 x 17.5 g/h) during prolonged, heavy bicycle exercise postpones exhaustion and exerts a glycogen-conserving effect in the working muscles. In contrast, fructose ingestion during exercise maintains the glucose concentration at the basal level but fails to influence either muscle glycogen degradation or endurance performance.

Ventura et al 1994 (171) studied the effect of prior ingestion of glucose or fructose on the performance of exercise of high intensity and intermediate duration. A group of 11 male recreational sportsmen ran on a treadmill, at intensity corresponding to 82% VO_2 max until exhaustion on three occasions (30 min after ingestion of a beverage containing 75 g of glucose, 75 g of fructose, or water). The mean endurance time was 644 ± 261 sec after the ingestion of glucose, 611 ± 227 sec after the ingestion of fructose and 584 ± 189 sec after ingestion of the water ($P<0.05$ between glucose and water).

In summary, fructose is a monosaccharide as glucose is. In contrast to glucose, fructose ingestion is associated with the modest rise in plasma insulin which is preferable more than glucose ingestion. The study of fructose on exercise is limited as the limited in its absorption and metabolized. However, many researchers had put their effort on investigated fructose ingestion and exercise performance. The physical performance and fructose ingestion is not in absolutely conclusiveness. The gastrointestinal discomfort from the large amounts of fructose ingestion can hinder performance.

4.2 Fructose Oxidation Rate

The consequence of the digestion of sucrose and other fructose containing foods such as honey, fruits, and some vegetables, is absorption and transport of fructose by the intestinal epithelium into the hepatic portal vein (172). Therefore, all fructose absorbed flows through the liver initially. Because of the presence of an active hepatic enzyme system for metabolizing fructose, fructose readily passes into the liver, accounting for a fractional uptake of 55% and 71%, respectively, of fructose presented to the liver after tube feeding fed and starved rats. In human it was shown that the liver metabolized at least half of the fructose injected intravenously. In the perfused rat liver it was found a value of 40% for the fractional extraction of fructose. As a consequence of the high rate of extraction of fructose by the liver, correspondingly low concentrations of fructose are found in the system blood vessels after meals containing fructose or sucrose are consumed. Some 20% of fructose administers intravenously is taken up by the kidney. Thus, somewhat less than this amount would be expected to taken up by this organ after oral feeding where the liver takes up some 50% of the initial flux. A considerably smaller fraction would be available for adipose tissue and skeletal muscle. Experiments with both the perfused liver and catheterized human subjects indicate that in the starved state, $\approx$ 66% of fructose dose is converted to glucose and up to 25% is released as lactate. Up to a further 8% may form glycogen.

Ingestion of exogenous substrates immediately before or during a period of prolonged exercise can postpone fatigue and increase performance in endurance events. The efficacy of this procedure depends in part on the rate at which the exogenous substrate can be oxidized (173). From this concept, there are researches conducted to study the various oxidation substrates including glucose, fructose, sucrose and others. The summary of the studies on oxidation of ingested glucose and fructose during exercise is shown in table 8.

Table 8 Exogenous carbohydrate oxidized during exercise: studies using ^{13}C evaluation.

References	Exercise	Exogenous carbohydrate	Percentages and/or amount of exogenous oxidized
Massicotte et al 1986 (159)	Cycling 180 min at 50±5% VO_2 max	7% solution (140 ± 12 g) during exercise	Glucose 75% (106±11 g) Fructose 56% (79 ± 8 g)
Guezenec et al 1989 (166)	Cycling 120 min at 60% VO_2 max	400 ml (1592 kJ) 60 min prior to exercise	Glucose 67±9 % Sucrose 73±8 % Fructose 54±6 %
Massicotte et al 1989 (167)	Cycling 120 min at 53±2% VO_2 max	1.33 g/kg in 19 ml/kg (98.9±4.7g) during exercise	Glucose 72±15 % Glucose polymer 65±18 % Fructose 54±13 %
Massicotte et al 1990 (168)	Cycling 120 min at 52% VO_2 max	96±9 g of fructose during exercise in the fasted and fed group	Fasted 49±6 g Fed 36±5 g
Jandrain et al 1993 (169)	Running 180 min at 45% VO_2 max	25 g every 30 min = 150 g total	Glucose 81±4 g = 20% Fructose 57±2 g = 14%
Massicotte et al 1994 (170)	Cycling 120 min at 60% VO_2 max	7% solution (97±9 g) during exercise	Glucose56.1±14.2g Fructose 35.7±9.2 g

Although the isotope techniques are widely used, there are still large inconsistencies between the results in those experimental which may be from the fact that in most studies possible 'isotope effects' have not been properly investigated (173). From table 8, when fasted state the using exogenous carbohydrate from fructose is greater than fed state and equaled 31% and 20% of total carbohydrate energy supply

respectively. In exercise, glucose is oxidized more than fructose (table 8) and more than glucose polymer (49). The oxidation rate of exogenous glucose and fructose increased linearly with increasing metabolic rate ($r = 0.7$ and 0.70, respectively, $p < 0.01$) (174).

Massicotte et al 1986 (51) also studied on metabolic response to [^{13}C] glucose and [^{13}C]fructose ingestion during exercise. Seven healthy male volunteers exercised on a cycle ergometer at 50 ±5% VO_2 max for 180 min on three occasions. They ingested either water only, [^{13}C]glucose, or [^{13}C]fructose 2 g/kg BW (140 ±12 g diluted at 7% in water, and evenly distributed every 20 min from 0 to 160 min. The slower availability of fructose was demonstrated by the enrichment of ^{13}C in the expired CO_2. With glucose ingestion the $^{13}C/^{12}C$ ratio increased 20 min following the first ingestion while the delay was 20 min following fructose ingestion. Fructose feeding was less readily available for combustion than glucose feeding; over the 3-h period 75% (106 ±11 g) of ingested glucose was oxidized, compared with 56% (79 ± 8 g) of ingested fructose. As a consequence, carbohydrate store utilizations were similar in the two conditions (174 ±20 g, 173 ± 17 g, 193 ± 22 g for glucose, fructose, and water trials respectively). Fat utilization was greater with fructose than glucose ingestion. However, endogenous carbohydrate utilization was not significantly different with glucose or fructose ingestion. Substrate utilization as well as blood glucose concentration with fructose ingestion 1) resembled that observed with water ingestion in the first 90 min of exercise and 2) resembled that observed with glucose ingestion in the second 90 min of exercise.

The results from many studies using isotopic method demonstrated that fructose ingestion creates less exogenous carbohydrate oxidized than glucose or glucose polymer does. However, the substrate used during exercise is not only from exogenous carbohydrate source. The more exogenous carbohydrate oxidation is not the conclusion of the more benefit for exercise. But the appropriate amount of exogenous and endogenous substrate oxidation is more important issue as it can provide appropriate source of energy to the body as needed during exercise.

4.3 Fructose and Muscle Glycogen

Fructose infusion reduced the muscle glycogen depletion during exercise was demonstrated by Kozlowski et al 1983 (176). They performed on dogs which exercised whilst receiving either the intravenous fructose infusion (2.2 mmol/min) or a slow glucose infusion (0.25 mmol/min) which was given either via the portal or peripheral vein.

Erickson et al 1987 (177) determined by ingesting fluid intake (16 ml/kg) consisting of (1) non-nutrient control; (2) fructose (1g/kg) before exercise; (3) glucose (1g/kg) during exercise. Exercise consisted of 90 min of cycling at 65 to 70% VO_2 max. Fructose is likely to cause gastric upset. Muscle glycogen utilization was greater for control and glucose trials.

The effect of fructose and glucose ingestion and muscle glycogen use during submaximal exercise was also studied by Levine et al 1983 (71). Eight subjects performed treadmill running at 75% VO_2 max for 30 min. Prior to exercise 45 min, subjects ingested 300 ml of 75 g fructose, 75 g glucose or water placebo. The higher rate of perceived exhaustion values during the final minutes of the fructose trial were likely due to the perceptions of two subjects who complained of intestinal distress during that trial. However, muscle glycogen depletion determined by pre-and postexercise biopsies (gastrocnemius muscle) was significantly less during fructose trial than during control or glucose trial.

Koivisto et al 1985 (72) examined the influence of various carbohydrates of fuel homeostasis and glycogen utilization during prolonged exercise. 75 g/ 250 ml of glucose, fructose, or placebo were given orally to eight healthy males at 45 min before ergometer exercise performed for 3 h at 55% VO_2 max. The fructose ingestion, through causing smaller pertubations in plasma glucose and insulin, was no more effective than glucose or placebo in sparing glycogen during long-term exercise. This result is different from Levine et al (71) as differences in methodology and experimental design may be in part.

Hargreaves et al 1985 (178) studied eight healthy males to compare the effects of preexercise fructose and glucose ingestion on muscle glycogen usage during exercise. Subjects performed three randomly assigned trials, each involving 30 min of

cycling exercise at 75% VO_2 max. Forty-five min prior to commencing each trial, subjects ingested either 50 g of glucose, 50 g of fructose, or sweet placebo. Muscle glycogen utilization was greater during glucose than water placebo drinks. No difference was observed between fructose and placebo drinks. There was a trend for muscle glycogen usage to be lower during fructose than glucose solution.

Sonne and Galbo 1986 (179) studied Carbohydrate metabolism in fructose-fed and food-restricted running rats. One week after catheterization the rats were subjected to one of three different dietary regimens. Control rats were fed ad libitum and had their carbohydrate withdrawn 2 h before the experiment. Other rats (fructose fed) were received 2.5 g of fructose dissolved in 1.5 ml of water. The third dietary regimen consisted of food restriction overnight. All rats ran either 75% VO_2 max (moderate-intensity exercise) or 45% VO_2 max (low-intensity exercise). The fructose fed rats, muscular glycogen depletion was lower than in control rats. The muscle glycogen-sparing effect was more marked during running than at rest, indicated that some fructose was mobilized directly in muscle and more during exercise that at rest.

Ahlborg and Bjorkman 1990 (180) studied on muscle fructose metabolism during and after exercise. 12 healthy males performed 90-min bicycling exercise at 30% VO_2 max with a 20-min recovery. The subjects received an intravenous fructose infusion (8.5 mmol/min) from 40 min of exercise to the end of recovery. The fructose infusion rate was chosen to determine whether fructose, if directly utilized by exercising muscle, would also influence glucose uptake. The results showed 1) an increased carbohydrate oxidation from fructose, lactate, and pyruvate in exercise muscle. 2) exerted a glycogenic effect in resting muscle and liver during exercise and in liver and muscle recovering from exercise., and 3) does not interfere with glucose metabolism, and that fructose transport into muscle differs from that of glucose. Although a transient increase in insulin at the onset of fructose infusion cannot be excluded, the metabolism of fructose and the fall in releasing of free fatty acids in this study were regulated without major concomitant changes in arterial insulin as found in glucose.

The effects of preexercise feedings of glucose, fructose, sucrose or unsupplemented water on glycogen contents in the liver and several selected muscles during a 2-h bout of exercise in trained rats was determined by Addington and Grunewald 1987 (178). Male Wistar rats trained to run on a treadmill were fasted overnight and fed by gavage 3 ml unsupplemented water or a solution containing 2 g of glucose, fructose or sucrose 30 min prior exercise. Six rats from each dietary group were killed after 0, 1, or 2 h of exercise. The muscle studied were the soleus, which has predominantly red type I slow twitch oxidative muscle fibers, and the vastus lateralis, which has both red and white portions consisting primarily of red type IIa fast twitch oxidative glycolytic and white type IIb fast twitch glycolytic fibers, respectively. The fructose fed animals exhibited the greatest depletion of liver glycogen and the smallest decline in soleus and red vastus lateralis muscle modified by the type of carbohydrates.

The glycogenic of fructose does not seem to be fructose itself. But in the presence of extra glucose, as would be the case after a sucrose meal, fructose "opens the dorr" for hepatic glucose uptake and synthesis of glycogen. This is achieved, presumbly by activation of glycogen synthase and inhibition of phosphorylase (172).

5. Summary

Fluid replacement is necessary in exercise as can helps maintain hydration and, therefore, promotes the health, safety, and optimal physical performance of individuals (26). The appropriate oral rehydration solution for exercise should provide substrate, replace electrolytes, replace fluids, enhance absorption, give palatability, and maintain plasma volume (75).

Glucose and its polymers are commonly contained in rehydration fluid as the substrate uses during exercise. But the anti-lipolytic effects of glucose-induced blood insulin rises have prompted to consider the use of fructose, a weak insulinotropic (30). Fructose another common dietary monosaccharide, the transport system differed from that of glucose (112). The slower absorption of fructose than glucose is well established and the malabsorption after fructose ingestion is commonly found. Glucose enhances fructose absorption is well demonstrated by the researchers. Amino acids

therefore, are in consideration as stimulate water movement similar to glucose, which may profit for fructose absorption. L-alanine is an amino acid, which was reported the facilitated effect on fructose absorption in resting condition better than the other i.e., L-glutamine, L-phennylalanine, and L-proline (45). Hence, in the present study, fructose in rehydration fluid is studied concurrently with the facilitated effect of alanine in exercise condition.

Amount of fructose in the solution study should around 50 g because at this dose, the malabsorption can be found by breath hydrogen test. Amount of total calorie from carbohydrate source is within the recommendation of ACSM i.e., 30-60 g/h to maintain oxidation of carbohydrate and delay fatigue (26). The concentration of the solution is also followed by ACSM recommendation i.e., 4-8% carbohydrate (g/100 ml) which are supported by many investigators that > 8% carbohydrate (g/100 ml) can delayed its absorption. Additionally, the volume to be ingested in the study is followed by ACSM that should drink 600-1200 ml/h for intense exercise last longer than 1 h.

Therefore, the present study, 6% of fructose/glucose solution is provided 500 ml at 45 min before exercise, and the another 350 ml is provided prior to exercise. Total calorie from carbohydrate source is about 51 g. The amount of alanine added is 1:1 molar ratio to fructose that is similar to glucose: fructose ratio. According to the study of Hoekstra and van den Aker (45), the half-equimolar alanine also enhanced fructose absorption, therefore the half-equimolar alanine also adds in the another fructose solution.

Osmolality of the solution is an important factor in the process of rehydration which depend on both gastric emptying and intestinal absorption (49). The osmolality of the solution as high as 586 mmol/L was similar in gastric emptying to the osmolality of 71, 94, and 194 mmol/L in running at 65% VO_2 max (68). Furthermore, osmolality of the glucose solution as 1850 mmol/L is well tolerated in normal adult (59). For prolonged exercise, osmolality of the solution as 644, and 1204 mmol/L were used in the study of Jandrain in 1989 (60). For absorption, the multiple substrates stimulate and create greater water absorption than the single substrate (62). In the present study, the range of osmolality of the solution is range from 300-800 mmol/L.

CHAPTER III

MATERIALS AND METHODS

1. Subjects

Eight healthy students from College of Sports Science and Technology, Mahidol University, participated in this study. They were informed of the risks and benefits of the experiment. The consent form (Appendix 1) was obtained by committee of the ethical approve, Mahidol University. All subjects were physically active students who habitually engaged in 3-5 hours of endurance type activities each week (soccer, or running). The subjects were instructed to maintain generally constant diet and training schedule throughout the experimental period. Two questionnaires were used for recording and determining their health (Appendix 2) and training status (Appendix 3). Blood pressure, pulse rate, and body temperature are measured before being recruited in the experimental program (Appendix 4) and before the starting in each trial.

1.1 Including Criteria

Qualifying subjects should:

- be male
- in the age between 17-22 years old
- be healthy, no present or chronic illness such as diabetes mellitus, cardio-vascular diseases, respiratory diseases, gastrointestinal diseases, anemia, or other hematological disorder
- have regular exercise
- be willing to participate in the study

1.2 Excluding Criteria

The subject who currently has signs or symptoms of any disease or illness.

2. Preliminary Measurements

Maximal aerobic power (VO_2 max) is the maximal ability of individual to take up, transport, and utilize oxygen by the working muscle (181-182). It is generally considered to be a useful indicator of successful performance an endurance activities (183-184). In order to determine the performance of individuals, measurement of maximal oxygen uptake using treadmill (Quinton Q55, Seattle, USA) and Bruce protocol (185) was provided which grade and/or speed are changed every 3 minutes. The 0% grade is omitted in these healthy subjects (Appendix 5).

The extent to which the classic criteria for plateau in VO_2 is still unclear (186) and is not a reliable physiological marker for maximal effort in all subjects (187). For those reasons a variety of secondary criteria have been used to characterize the oxygen uptake measured for VO_2 max. These secondary criteria include; a) elevated respiratory exchange ratio, and b) achievement of some percentage of age-adjusted estimates of maximal heart rate.

The respiratory exchange ratio has been used as a secondary criterion for having attained VO_2 max. This is based, in part, on the reaction between the rising plasma hydrogen ion concentration and plasma bicarbonate during exercise. As the CO_2 is generated, ventilation increases and the respiratory exchange ratio is increased (186).

Systemic oxygen transport is a function of heart rate, and stroke volume. Physical activity level is the major factor in a healthy subject causing variation in maximal stroke volume during exhaustive exercise. Maximal heart rate may also varied (182). Additionally, some subjects are not being able to achieve the heart rate standard, even when working maximally. For this reason, The American College of Sports Medicine states that predicted maximal heart rates should not be used as an absolute endpoint in the test termination (186).

Therefore, maximum oxygen uptake during the test was designated VO_2 max provided that it met two of the following three criteria (186).

1) RER greater than 1.0
2) An increase in VO_2 of less than 150 ml/min with increases in work load
3) Heart rate within 15 % of age-predicted maximum.

All subjects were familiarized with the experimental procedures. VO_2 max was obtained using the protocol and criteria as mentioned. Thereafter, they were randomly assigned in a double blind randomized selected to four experimental trials that were separated by at least 1 week apart. They were tested for their endurance performance capability by performing a 1 hour at 70% VO_2 max with the following increased in workload.

3. Nutritional status

Body weight (kg) and height (cm) were measured for each subject who enrolled in the study protocol. Skinfolds thickness at four sites: biceps, triceps, subscapular, and suprailiac were measured with caliper (Holtain Ltd, UK). The results were recorded in mm, then be calculated according to the method of Durnin and Womersley (188).

Equations: D = 1.1631 – 0.0632 x [log sum of four skinfold thickness]

Fat mass (kg) = BW (kg) x [4.95/D - 4.5]

Fat free mass (kg) = BW (kg) – Fat mass (kg)

4. Experimental Procedures

4.1 Subjects

The experimental protocol was approved for use in human by the Committee on Human Rights Related to Human Experimentation, Mahidol University, Bangkok, Thailand. The subjects were asked for 2-days dietary record (Appendix 7).

They refrained from alcohol or caffeine beverage on the preceding day. To avoid high breath hydrogen results as the baseline of the experiment, night before the experiment, the subjects were asked to refrain from milk and its product such as ice cream, yogurt, chocolate etc., fruits and juices, pickled, vegetables, fruits, and beans.

For controlling hydration status of the subject, 500 ml of drinking water was provided and the subject had to drink it all at 2 hours before he went to bed at 10.00 p.m. They were fasted after the last drink, about 11 hours before arriving at the laboratory at 07.00 a.m. the next day.

4.2 Beverages

Four types of carbohydrate electrolyte beverage were prepared and provided to the subject in the double blind randomized selected trials, i.e., 6% glucose (G), 6% fructose (F), 6% fructose and half-equimolar alanine (Fa), and 6% fructose and equimolar alanine in (FA). All beverages were added sodium 10 mEq/L and potassium 2 mEq/L. The lemon favor and yellow color were added in the beverage for the similarly taste and appearance.

For each 1 litter of each beverage was prepared by which 850 ml was for the subject and 1 ml was for the osmolality assessment. On a trial, the 500 ml of a beverage was provided to the subject 45 min prior exercise (07.45 a.m.) and another 350 ml immediately before exercise (08.30 a.m.).

4.3 Methodology

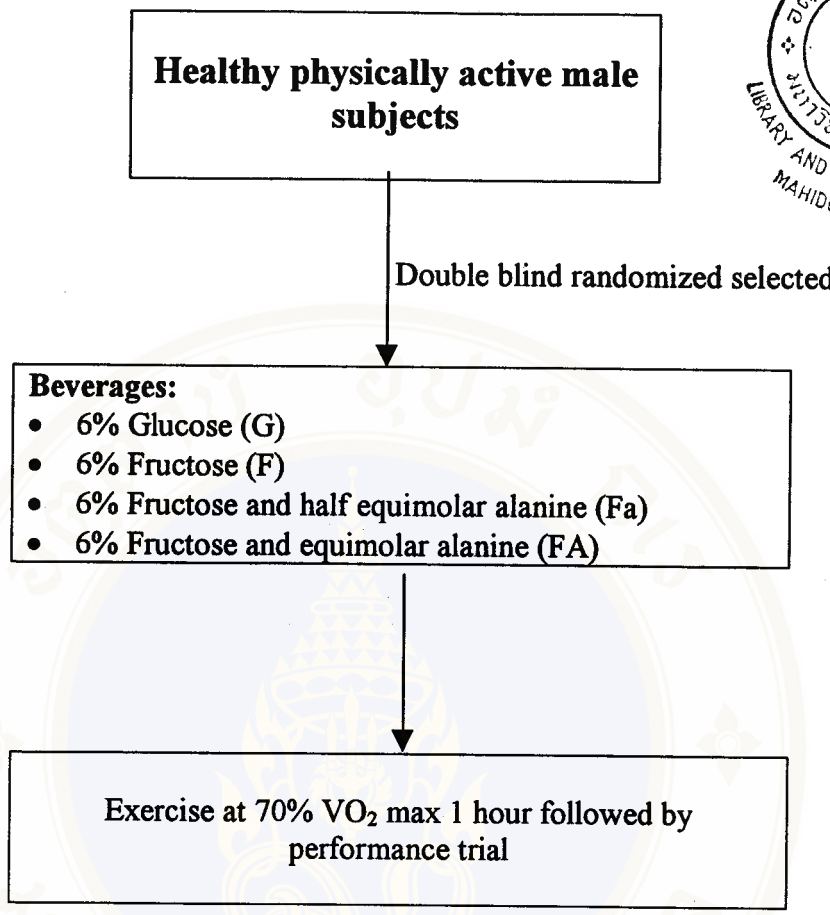
After arriving at the laboratory at 07.00 a.m. the subject was asked to rest by sitting. At 07.20 a.m., body weight was measured with nude, body temperature was measured by sublingual technique, blood pressure, pulse rate and respiratory rate were recorded (Appendix 8). The information of health and illness in two weeks before the experiment was also asked and recorded. The room temperature was controlled at 26^0 C.

At 07.30 a.m. breath H_2 excretion was assessed for baseline data and recorded every 30 minutes for about 3 hours (until 11.30 a.m.) with peak H_2 excretion had been reached. Others gas analysis as V_E was collected by mouthpiece for baseline data and every 30 minutes together with breath H_2 excretion. Then Jelco gauge 18 was

inserted in the forearm vein and 12 ml of blood was drawn for the baseline data for hemoglobin, hematocrit, blood lactate, plasma glucose, serum insulin, plasma free fatty acids, and serum osmolality of each subject and then every 30 minutes until 10.00 a.m. At 07.45 a.m., the subject drank 500 ml of beverage. At 08.00 a.m., the second H_2 gas expired and V_E were collected together with the second blood specimens.

At 08.20 a.m., the subject started warming up by running on the treadmill and later the 70% VO_2 max exercise was started on 08.30 a.m. right after the subject received 350 ml of beverage. Heart rate was monitor and recorded with sport tester (PE3000, Polar Electro Oy, Finland) from the beginning throughout the study. They were on the treadmill at 70% VO_2 max for 1 hour (until 09.30 a.m.), then the speed and/or grade were increased 10% every 5 minutes until subject was not able to continue. Exhaustion time was then recorded. During the exercise period, the movie was shown throughout to reduce boredom of the subject. Post exercise body weight was measured for the nude and dry body of subject.

After finishing the exercise, the subject was asked to sit and watch the movie until gas collection (breath hydrogen excretion and V_E) was completed. During this period, the subject was allowed to drink only water as required.



Physical Performance:
- Exhaustion time
- Ratings of Perceived Exertion (RPE)
- Heart Rate

Fructose absorption:
- Breath hydrogen test
- GI disturbances recorded

Hydration status:
- Plasma volume changed
- Serum osmolality
- Body weight loss

Metabolism:
- Plasma sugar
- Serum insulin
- Blood lactate
- Plasma free fatty acids

Diagram 1 Study design

Sample Collections

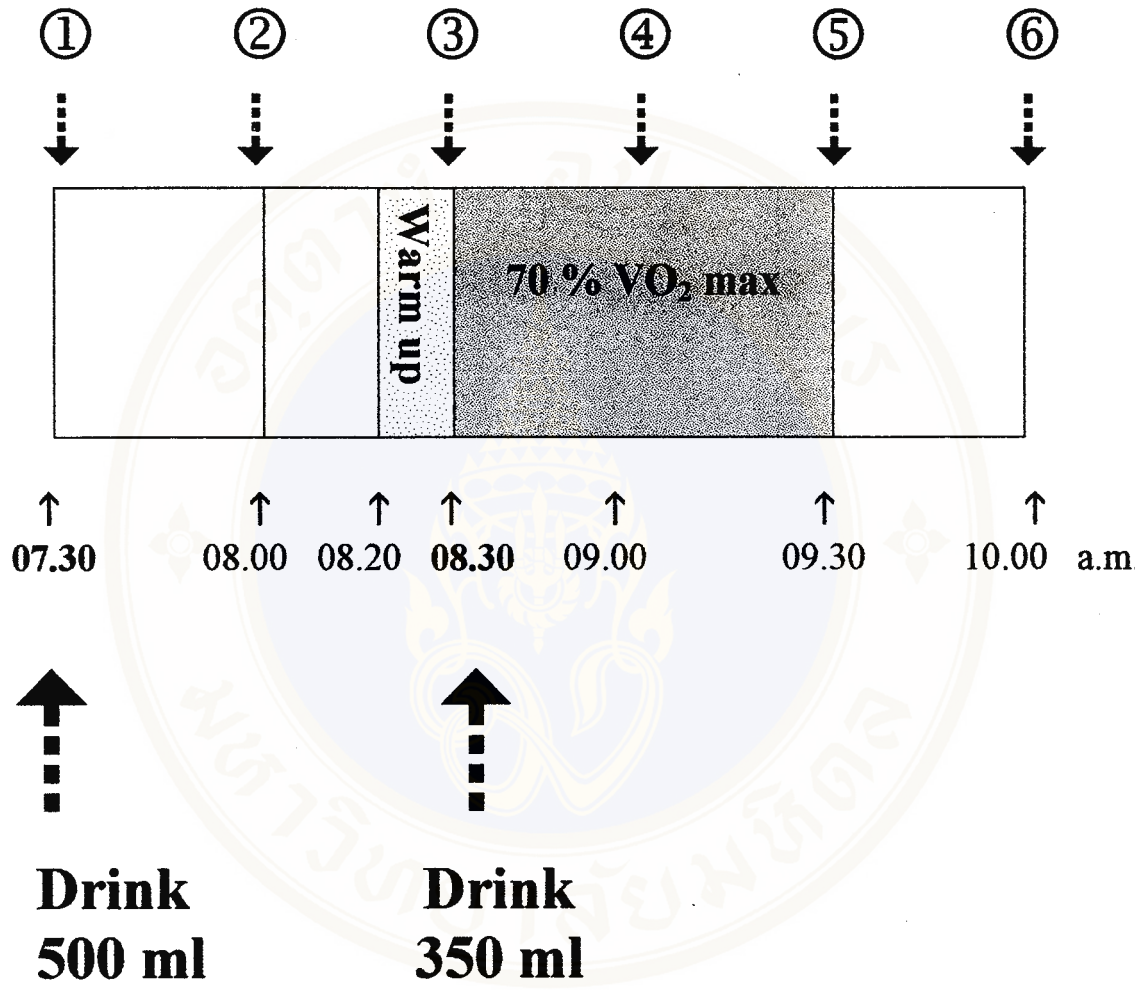


Figure 2 Experimental Design for Sample Collection.

5. Sample analysis

5.1 Performance Test

A continuous protocol at submaximal load (60-90% VO_2 max) until exhaustion is the classical and most common performance trial test. However, the most remarkable finding in Jeukendrup et al (189) was the poor reproducibility of a continuous exercise protocol until exhaustion (CV = 26.6%) while the preloaded time trial protocol had CV of 3.5%. Therefore, in this study, the preloaded time protocol was applied from cycle ergometer to run on the treadmill. The subject performed running on treadmill at 70% VO_2 max for 1 hour, the workload was then increased every 5 minutes until the subject could not maintain his pace. The increment of workload after exercise at 70% VO_2 max was controlled to the same values in each subject through four trials. The finished time was recorded. Total amount of distances after 1 hour steady state (at 70% VO_2 max) was taken as a measure of performance. To avoid test retest influence, the subject receives no information amount of work performed as well as heart rate.

5.2 Breath Hydrogen Test

When carbohydrate is absorbed incompletely by the small intestine and reaches the colon, it is subjected to the enzymatic action of bacteria, and hydrogen is produced by fermentation, providing a volatile marker of intestinal function related to carbohydrate digestion and absorption (190). Therefore, incomplete intestinal absorption of ingested carbohydrate was determined by using the breath hydrogen method. This is a noninvasive and easy procedure and providing a very accurate means of identifying malabsorption of low doses of carbohydrate (191, 192). High fasting excretion of H_2 in breath was a frequent cause of misclassification (193) so the subjects were instructed to avoid fruits, milk, vegetables, bean, pickled, and their products at dinner the day before (194). The samples of expired air were collected directly from the outlet of the metabolic cart into bag fitted one-way valve with three way stopcock and was drawn into 50-ml plastic syringe at 30-min intervals during resting and exercising periods. The collection of gases was done until they reached peak elevation of H_2. For fructose, the peak H_2 is reached about 2.5 hours after

ingestion (195). As breath hydrogen tests are limited by leak of gases from breath samples from standard glass or plastic syringe (196), the sample was determined within that day. The hydrogen concentration was determined by a gas chromatograph (QuinTron Model DP Microlyzer^{TM}, USA) within 8 hours. Because of the increase in minute ventilation (V_E) during exercise inversely effects with H_2 excretion (197), the hydrogen excretion rate (V_EH_2) was used as a more accurate means of comparison of the different treatment (190). $V_EH_2 = V_E [H_2]$/ body wt, where V_E is in L/min measured throughout exercise and rest, $[H_2]$ is the hydrogen concentration of breath samples (μl/L).

5.3 Gas Exchange Analysis

As subjects inhaled through a two-way valve, inspired air volume was measured with CPX/MAX (Medgraphics) that was calibrated early morning before the test, using reference and calibration gases (TIG Company, Thailand). The composition of O_2 and CO_2 were 15.5 ± 0.05% and 4.88 ± 0.02% for calibration gas with certification. The instruments were interfaced with a computer for calculations of the rate of oxygen consumption (VO_2) and respiratory exchange ratio (RER) for preliminary measurement and V_E for treatment protocol.

5.4 Blood Collection and Analysis

The 18-gauge Surflo (Terumo^{TM}) catheter was inserted in the forearm vein and was kept patent by injection 0.5 ml of 10 U.S.P. units/ml of heparin sterile in saline. The first sample of blood was drawn at 07.30 a.m. for baseline data. The following 5 blood samples were collected every 30 minutes until 10.00 a.m. About 12 ml of blood was drawn each time.

About 40 μl of this fresh blood was filled in heparinized micro-hematocrit tube and centrifuge with micro-centrifuge (Micro Hematocrit, IEC MB Centrifuge, Massachusetts) 5 minutes and read the hematocrit value by Micro-hematocrit reader (Micro-capillary reader, International Equipment Company, Massachusetts).

0.5 milliliters of each blood sample were placed in tube (Microgard^{TM}, Becton Dickinson and Company, USA) which contained 1 mg of

ethylenediaminetetraacetic acid (EDTA). Each 25 µl of blood was aspirated and analyzed for blood lactate in duplicate with Glucose and Lactate Analyzer (YSI Model 2300 STAT PLUS, Ohio). The rest of this whole blood was kept in room temperature and analyzed for hemoglobin with Drabkin solution and spectophotometer (AMES^{TM} Minilab V1.1, Miles LTD, England) within 8 hours.

Changes in plasma volume were derived from changes in hemoglobin and hematocrit values using the calculations of Dill and Costill (198).

2 ml of blood was placed in tube that contained sodium fluoride (NaF) 20 mg for anticoagulation and preservative for glucose and antiglycolytic agent. The blood was well mixed and then centrifuged at 3000 rpm with Helttich EBA III centrifuge (Hettlingen, Germany) for 10 minutes. Plasma was separated and kept in 4^0C for glucose analysis within 6 hours by glucose oxidase colorimetric method with reagent kit (Cod 11538,Biosystem, Spain) and AMES spectophotometer.

4 ml of blood was filled in glass tube and centrifuged at 3000 rpm with Hettich centrifuge for 20 minutes, 1 ml of serum was drawn into micro serum tube for further insulin analysis. The rest of blood in glass tube was then centrifuged for the second time for 10 minute and the clear serum was separated for osmolality analyzed.

Serum insulin was analyzed at the Clinical Chemistry Laboratory, Department of Clinical Pathology, Siriraj hospital, Mahidol University. Serum osmolality was analyzed in duplicate by freezing point method using the Osmometer (Advanced Digimatic 3DII, Advanced Instruments, Massachusetts).

Another 4 ml of blood was filled in glass tube contained heparin 80 units. It was then centrifuged at 3000 rpm with Hettich centrifuge for 20 minutes, plasma was immediately separated and kept in –75 ^{0}C for further free fatty acids (FFA) analysis.

Plasma FFA was analyzed using first plasma extraction method as described by Folch et al (199). The dry sample was analyzed using Lowry and Tinsley (200). Palmitic acid was used as the FFA standard. The absorbance was read at 715 nm.

5.5 Gastrointestinal Symptoms

Gastrointestinal disturbances if any, were recorded every 30 min after the first drink until at the end of each trial, and throughout that day. An example of recorded form is given in Appendix 10. The following numbers were used to rate the intensity as follow: 0 for no symptoms, 1 for mild symptoms, 2 for moderate symptoms, and 3 for severe symptoms.

5.6 Ratings of Perceived Exertion (RPE)

Any physiological variable e.g., heart rate, ventilation, oxygen uptake, and lactate threshold linearly related to exercise intensity is correlated quite highly with RPE (201). There is a consensus that RPE is dominated during low intensity exercise by local factors; but as the exercise intensity increases, central factors including sensations associated with increasing blood lactate and hyperventilation play a more significant role. Relative VO_2 and RPE typically correspond at all intensities, independently of exercise mode (202). RPE was found to be a valid means of monitoring and regulating exercise intensity (203) In general, RPE provide a physiologically valid method of regulating exercise intensity (204). The investigation of Glass et al (205) demonstrates that a RPE obtained from exercise can accurately serve as a method of prescribing exercise intensity during level treadmill running and the ease of using RPE appears to be complimented by accuracy in application. Therefore, in this study, RPE were assessed by using Borg's scale (Appendix 9). During the exercise, the subject was asked to rate a numerical scale how he felt in relation to his level of exertion. This scale consisted of numbers from 6-20 in a quanta format with descriptive words printed beside every other number, ranging from "very very light" at 6 to "very very hard" at 20 (202).

6. Statistic Analysis

The data was analyzed with SPSS release 9.00. General linear model with repeated measures was used to determine differences among the treatments. When significant effects were detected, Turkey was used as post hoc analysis to find differences across fluid treatments. Data during each time in each treatment was analyzed by student pair t-test. An alpha level of .05 is used to indicate statistical significance. All values reported are means (± SE).

CHAPTER IV

RESULTS

1. General Characteristics

1.1 Subjects

Eight male volunteers, aged 19-22 years old were recruited. They were the students from College of Sports Science and Technology, Mahidol University. They were all healthy with non-smoking and non-alcoholic and no history of chronic diseases or present illness of any diseases.

1.1.1 General Information

As shown in Table 9, mean height of the subjects was 168.2± 1.62 cm, and their mean weight was 61.7±1.51 kg. Their BMI values were in normal, which range from 20.7 – 22.9 kg/m^2. The highest percent of fat mass was found in the 8th subject, which was 13.7%. However, all subjects have percent of fat free mass ranged from 86.3 – 94.3 %.

Table 9 Subjects' characteristics.

Subject No.	Age (yr.)	Height (cm)	Weight (kg)	BMI (kg/m^2)	Fat mass (%)	Fat free mass (%)
1	22	170.0	62.0	21.5	5.7	94.3
2	20	175.5	67.9	22.0	10.9	89.1
3	20	168.0	58.3	20.7	11.7	88.3
4	21	167.0	59.9	21.5	5.8	94.2
5	20	163.0	55.8	21.0	10.4	89.6
6	20	170.0	64.5	22.3	8.3	91.7
7	21	161.0	58.3	22.5	8.6	91.4
8	19	170.8	66.8	22.9	13.7	86.3
Mean ± SE	20.4 ± 0.32	168.2 ±1.62	61.7 ± 1.54	20.6 ±0.27	9.4 ±0.99	90.6 ± 0.99

1.1.2 Physical Activity

In general, the subjects were physically active. Two were middle distance runners, three were short distance runners and the other three were soccer players. Mean years of experienced in their sports was 7.13±1.13 years, which range from 4 – 13 years (Table 10). They had routinely practiced strenuous exercise everyday at least 3 h a week.

Table 10 Characteristics of exercise practice routinely within the last 3 months in each subject.

Subject No.	Years of experience	Practice 1-3 times/week	Practice 3-5 times/week	Practice > 5 times/week
1	11 runner	Swimming>60 min		Running > 60 min
2	7 soccer		Jogging15-30 min Running 30-60 min	Soccer > 60 min
3	6 running	Swimming 15-30 min		Running > 60 min
4	6 soccer	Running >60 min Swimming>60 min Badminton>60 min		Fast walking15-30 min Soccer >60 min
5	4 runner	Swimming<15 min		Jogging<15 min Running30-60 min
6	13 runner	Cycling<15 mim Swimming30-60 min Badminton 30-60 min		Fast walking 15-30 min Jogging 15-30 min Running 30-60 min
7	5 runner	Cycling<15 min Swimming>60 min Badminton>60 min	Fast walking<15 min	Jogging 15-30 min Running 30-60 min
8	5 soccer	Swimming 15-30 min Badminton 30-60 min		Fast walking 15-30 min Jogging 15-30 min Running 15-30 min soccer>60 min
Mean ± SE	7.13± 1.13			

Average VO_2 max of the subjects was 51.78 ± 2.04 ml/kg/min (Table 11). The minimum VO_2 max were found in soccer players (44.5 and 46.1 ml/kg/min). Mean maximal heart rate at VO_2 max was 179 ± 4.52 beats/min, most of them were within 15% of age-predicted maximum heart rate (192), except for the 4th subject who had mean maximal heart rate at VO_2 max at 153 beats/min which was less than 15% of age-predicted maximum heart rate. RER at VO_2 max was ranged from 1.00 – 1.16.

Table 11 Characteristics at VO_2 max of the subjects

Subject No.	VO_2max (ml/kg/ min)	VO_2 (ml/min)	VCO_2 (ml/min)	HR at VO_2 max (beats per min.)	RER at VO_2max
1	58.0	3602	3962	175	1.10
2	44.5	3021	3231	180	1.07
3	52.5	3059	3500	196	1.14
4	59.5	3564	3781	153	1.06
5	50.1	2794	3241	191	1.16
6	47.0	3028	3330	179	1.10
7	56.5	3293	3291	177	1.00
8	46.1	3078	3289	183	1.07
Mean ± SE	51.78 ±2.04	3179 ±100.07	3453 ±97.41	179.3 ± 4.52	1.09 ±0.02

1.1.3 Food Intake

The 2-day dietary intake was recorded by the subject before engaged in each experimental trial. As seen in Table 12, there was no significantly different in total calories, carbohydrate, protein, and fat intake in the 2-day among the trials.

Table 12 Mean of 2-day dietary intake in G, F, Fa, and FA trials.

Type of Beverage	Dietary Intake			
	Calories (Kcal)	Carbohydrate (g)	Protein (g)	Fat (g)
G	1738.89± 137.70	251.20± 25.56	63.40± 3.88	51.23± 7.38
F	1738.70± 116.63	258.43± 20.65	61.81± 5.60	49.30± 4.38
Fa	1711+.56± 107.37	269.34± 30.32	65.40± 4.87	39.15± 4.46
FA	1701.42± 121.44	243.89± 24.41	65.64± 6.73	49.11± 3.42

1.2 Beverage

The osmolality of Fa beverages was significantly different from G, F, and FA beverages at $p<0.001$ and the osmolality of FA beverages was significantly different from G, F, and Fa beverages at $p<0.001$ (table 13). The osmolality of the beverages were 413±6.56, 438 ± 3.85, 594 ± 14.93, and 788 ± 12.47 mmol/L for glucose (G), fructose (F), fructose and half-equimolar alanine (Fa), and fructose and equimolar alanine (FA) trials respectively.

Table 13 Characteristics of beverages.

Beverage	Glucose (g/L)	Fructose (g/L)	Alanine (g/L)	Osmolality (mmol/L)
G	60	0	0	413±6.56
F	0	60	0	438±3.85
Fa	0	60	14.7	594±14.93*
FA	0	60	29.4	788±12.47**

* = significantly different from G, F, and FA at $p<0.001$

** = significantly different from G, F, and Fa at $p<0.001$

2. Physical Performance

Physical performance was reported as time to exhaustion, distance after exercise at 70% VO_2 max, and RPE.

2.1 Time to Exhaustion, and Distance After Exercise at 70% VO_2 max

As shown in Table 14, in FA trial, two subjects could not run until exhausion because of gastric distress. Additionally, F trial, three of subjects could not maintain their work until exhaustion because of abdominal pain. Therefore, times to exhaustion, and distance after exercise at 70% VO_2 max were reported from only 4 subjects who could run until exhaustion (Table 15). However, all 8 subjects could finish exercising of 1 h at 70% VO_2 max. Hence, the other measurements as heart rate,

blood lactate, plasma glucose, serum insulin, plasma FFA, serum osmolality, plasma volume and breath hydrogen were determined in all subjects.

Table 14 Time to exhaustion (min) in each subject divided by type of beverage.

Subject	Type of beverage				
	G	F	Fa	FA	Mean±SE
1	85	80	77	80	80.50±1.66
2	64	68	67	66	66.25±0.85
3	76	NA*	83	69	76.00±4.04
4	73	73	77	NA*	75.00±2.00
5	67	62	65	73	68.33±2.40
6	80	85	80	80	81.25±1.25
7	63	NA*	70	77	70.00±4.04
8	66	NA*	63	NA*	64.50±1.50

* NA = Stop running before exhaustion.

Time to exhaustion (Table 15) was not significantly different among G (74.00±5.05 min), F (73.75±5.30 min), Fa (72.25±3.68 min) and FA (74.75±3.35 min) trials. Similarly, distances after steady state running at 70% VO_2 max were also not significantly different among G (1.14±0.05 miles), F (1.14±0.05 miles), Fa (1.12±0.04 miles), and FA (1.18±0.02 miles) trials. This distance covered was measured after the 1 h protocol at 70% VO_2 max of each subject.

Table 15 Time to exhaustion, and distance covered after exercise at 70% VO_2 max (n = 4).

Type of beverage	Time to exhaustion (min)	Distance (miles)
G	74.00±5.05	1.14±0.05
F	73.75±5.30	1.14±0.05
Fa	72.25±3.68	1.12±0.04
FA	74.75±3.35	1.18±0.02

2.2 Ratings of Perceived Exertion (RPE)

Exercise was begun, after 10 minutes of warming, at 08.30 a.m. (45 min after the first ingestion), RPE were recorded twice at 30 min interval. It was found that RPE were significantly increased with time in all trials ($p < 0.01$), but there were not significantly different among treatments as shown in Table 16.

Table 16 RPE at 30 and 60 min of exercise of different beverages (mean ± SE).

Beverages	**30 min**	**60 min**
G	11.5 ± 0.42	14.1 ± 0.69*
F	11.7 ± 0.49	14.5 ± 0.91*
Fa	12.0 ± 0.92	14.0 ± 1.13*
FA	11.1 ± 0.72	13.1 ± 0.67*

* = significantly different from 30 min of exercise at $p<0.01$ in its trial.

3. Heart Rate

At finishing warming up which workload reached 70% VO_2 max, there was sharply increased in heart rate at the first 10 min of exercise in all trials (84± 4.07vs.144±4.81, 86±2.71vs.140±5.19, 82±3.96vs.137±4.98, and 82±5.42vs.139±4.22

beats/min at –15vs.0 min in G, F, Fa, and FA trials, respectively). Heart rate was still higher than the beginning throughout exercise. However, as shown in Figure 3 (Table 17), changes in heart rate during exercise period were not significantly different among G, F, Fa, and FA trials. At exhaustion, heart rate reached the highest in all treatments (172±6.33, 172±5.96, 176±5.62, and 171±7.86 beats/min for G, F, Fa, and FA trials, respectively).

Table 17 Heart rate (beat/min) during exercise after G, F, Fa and FA ingestion.

Type of beverage	Time (min)									
	-10	0	15	30	45	60	* 72.25 ±3.68	* 73.75 ±5.30	* 74.00 ±5.05	* 74.75 ±3.35
G	84± 4.07	144± 4.81	149± 5.34	152± 4.50	153± 4.46	155± 4.32			172± 6.33	
F	86± 2.71	140± 5.19	149± 4.93	156± 5.23	157± 4.59	161± 5.35		172± 5.96		
Fa	82± 3.96	137± 4.98	147± 5.22	152± 5.09	156± 5.48	159± 4.82	176± 5.62			
FA	82± 5.42	139± 4.22	147± 4.97	153± 4.72	153± 5.15	158± 4.18				171± 7.86

* n = 4

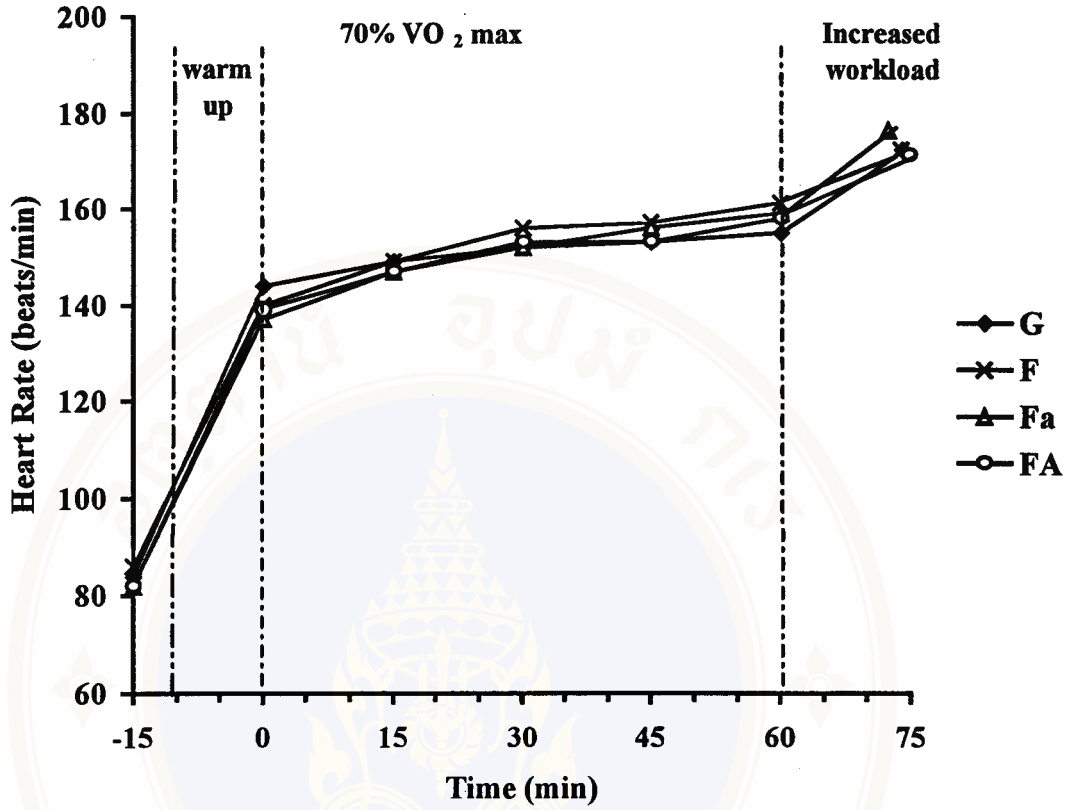


Figure 3 Heart rate (beats/min) during exercise period in G, F, Fa, and FA trials.

4. Blood Lactate

As shown in Figure 4 (Table 18), blood lactate had increased at 15 min after ingestion in all trials (0.56±0.06vs.0.73±0.08, 0.56±0.86vs.0.86±0.09, 0.55± 0.09vs.0.85±0.12, and 0.70±0.08vs. 0.94±0.01 mmol/L at –60vs. –30 min for G, F, Fa, and FA trials, respectively). After warming up, blood lactate was significantly increased in all trials (0.75±0.08vs.1.30±0.13, 0.86±0.09vs.1.36±0.09, 0.85± 0.12vs.1.54±0.11, and 0.94±0.01vs.1.53±0.02 mmol/L at –30 vs. 0 min in G, F, Fa and FA trials, respectively, $p<0.01$).

Table 18 Blood lactate (mmol/L) in G, F, Fa, and FA trials.

Type of beverage	Time(min)					
	-60	-30	0	30	60	90
G	a 0.56 ± 0.06	b 0.73± 0.08	b 1.30± 0.13	1.66± 0.13	1.69± 0.15	a 1.18± 0.29
F	a 0.56± 0.06	b 0.86± 0.09	b 1.36± 0.09	1.71± 0.19	1.60± 0.25	a 1.17± 0.13
Fa	a 0.55± 0.09	b 0.85± 0.12	b 1.54± 0.11	1.83± 0.14	1.70± 0.17	a 1.42± 0.22
FA	a 0.70± 0.08	b 0.94± 0.01	b 1.53± 0.02	1.99± 0.14	1.53± 0.11	1.21± 0.14

a = significantly different between -60 and 90 min at $p < 0.05$.

b = significantly different between -30 and 0 min at $p < 0.01$.

During exercise, there was a continuously increased of blood lactate until it reached the highest values at 30 min of exercise for F, Fa and FA trials (1.71±0.19, 1.83±0.14 and 1.99±0.14 mmol/L for F, Fa, and FA, respectively) and at 60 min of exercise for G trial (1.69±0.15 mmol/L).

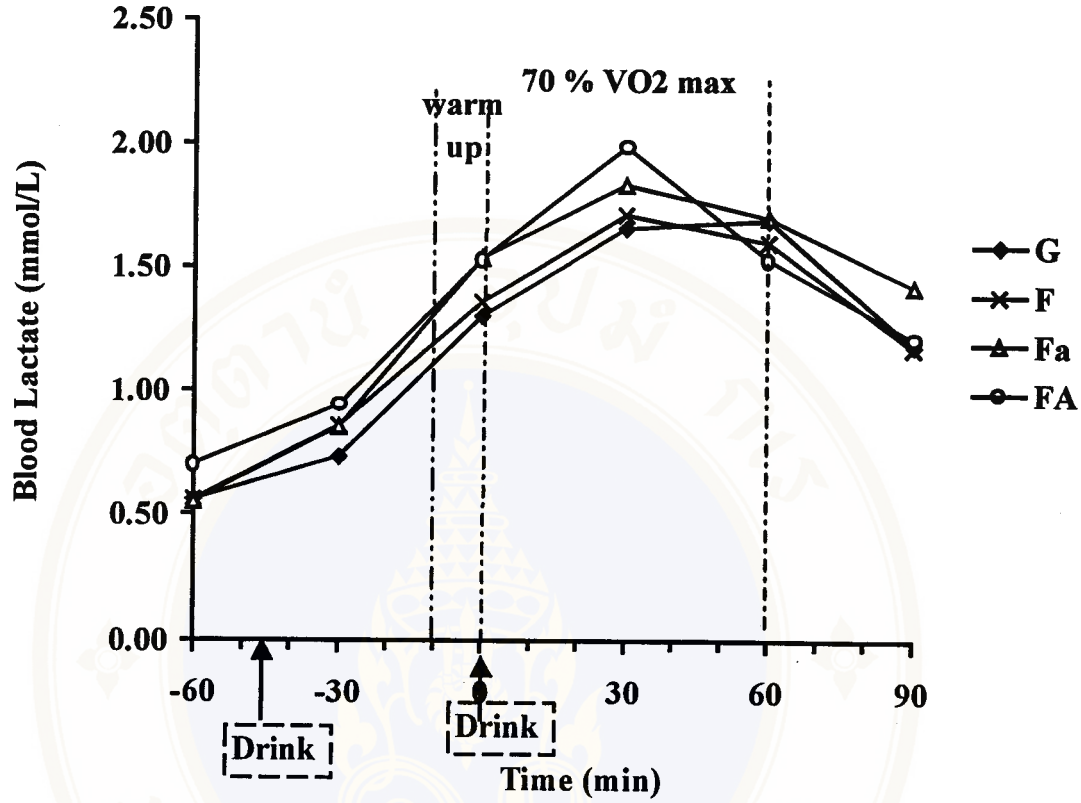


Figure 4 Blood lactate (mmol/L) in G, F, Fa, and FA trials.

After 30 min, of exercise in Fa trial, blood lactate continuously declined from the peak at 30 min to 90 min (1.83±0.14, 1.70±0.17, and 1.42±0.22 mmol/L, at 30, 60, and 90 min, respectively, $p < 0.05$), and in FA trial (1.99±0.14, 1.53±0.11 and 1.21± 0.14 mmol/L for 30, 60 and. 90 min, respectively, $p < 0.05$). Similarly, in G and F trial, after blood lactate reached the peak at 60 and 30 min respectively, it gradually decreased (1.69±0.15,.and 18±0.29 mmol/L for G trial at 60, and 90 min, respectively and 1.71±0.19, 1.60±0.25, and 1.17±0.13 mmol/L for F trial at 30, 60, and 90 min, respectively). At recovery, blood lactate was still significantly over baseline in all trials (0.56±0.06vs.1.18±0.29, 0.56±0.06vs.1.17±0.13, 0.55±0.09vs.1.42±0.22, and 0.70±0.08vs.1.21±0.14 mmol/L at –60 and 90 min in G, F, Fa, and FA trials, respectively, $p<0.05$). However, there were not significant differences in the changes of blood lactate among treatments at any times.

5. Plasma Glucose

There were no differences in baseline (pre-feeding) plasma glucose concentrations among trials (Figure 5, and Table 19). However, 15 min after G beverage ingestion, there were significantly increased in plasma glucose concentrations compare to after F, Fa, and FA ingestion (130.38±5.03, 91.13±2.84, 101.38±4.62 and 95.13±3.86 mg/dl at –30 min in G, F, Fa, and FA trials, respectively, $p < 0.001$). In contrast, in FA trial the plasma glucose concentrations were decreased and significantly lowest at 45 min after first ingestion (93.50±3.08 and 75.50±3.86 mg/dl at –60 and 0 min, respectively, $p<0.01$).

Table 19 Plasma glucose concentrations (mg/dl) in G, F, Fa, FA trials.

Type of beverage	Time(min)					
	-60	-30	0	30	60	90
G	a 90.00± 3.00	a* 130.38± 5.03	* 101.25± 10.55	 86.75± 4.36	* 79.00± 2.82	 85.50± 3.70
F	 91.85± 2.74	* 91.13± 2.84	 93.38± 4.30	 88.38± 3.72	 90.13± 4.26	 90.25± 4.11
Fa	b 88.88± 3.34	b* 101.38± 4.62	 85.63± 6.02	 95.38± 4.23	 90.88± 3.47	 91.38± 3.72
FA	c 93.50± 3.08	d* 95.13± 3.86	cd* 75.50± 3.86	 89.00± 4.58	* 100.13± 5.74	 96.75± 3.95

a = significantly different between -60 and –30 min at $p < 0.001$.

b = significantly different between-30 and –30 min at $p < 0.01$.

c = significantly different between -60 and 0 min at $p < 0.01$.

d = significantly different between -30 and 0 min at $p < 0.01$.

* = significantly different from G ingestion at $p < 0.001$.

After plasma glucose concentrations in G trial were significantly peaked at 15 min after first ingestion and then decreased throughout 90 min. Additionally, plasma glucose concentrations were lowest at 60 min and which were less than baseline (90.00±3.00, and 79.00±2.82 mg/dl at baseline and 60 min, respectively). For F trial, there were no significance changes between baseline, after ingestion, throughout exercise and recovery period which were ranged from 88.38±3.72 to 93.38±4.30 mg/dl.

The significantly increased from baseline in plasma glucose at 15 min after ingestion was also found in Fa trial (88.88±3.34, 101.38±4.62 mg/dl for baseline and at -30 min, respectively, $p < 0.01$). However, this value was still significantly lower than the increased in G beverage ingestion (130.38±5.03 and 101.38±4.62 mg/dl for G and Fa trials, respectively, $P < 0.001$) and had no significance differences neither from F nor FA trials (101.38±4.62, 91.13±2.84, and 95.13±3.86 for Fa, F, and FA, respectively).

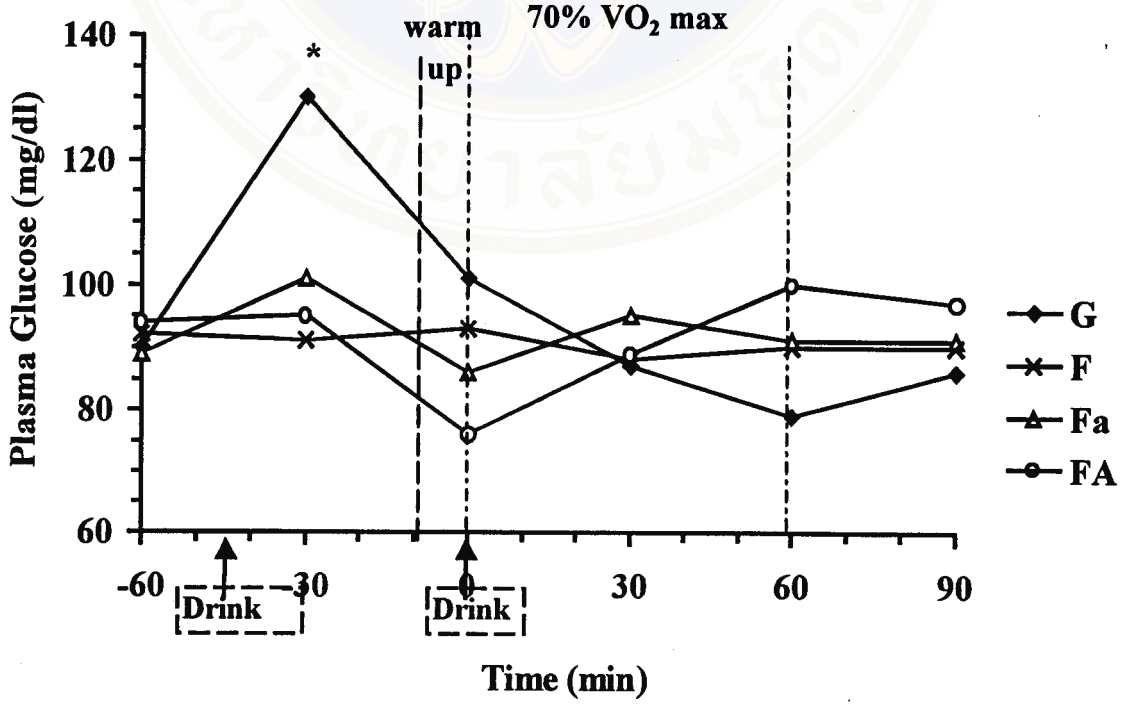


Figure 5 Plasma glucose concentrations (mg/dl) in G, F, Fa, and FA trials.
* = significantly different from F, Fa, and FA trials ($p<0.001$).

The plasma glucose was increased at -30 min in Fa trial, and decreased afterward. The changes in plasma glucose concentration in Fa trial during exercise and recovery period were slightly increased (85.63±6.02, 95.38±4.23, 90.88±3.47, and 91.38±3.72 mg/dl at 0, 30, 60, 90 min, respectively). In contrast to the other trials, there were not increased in plasma glucose after FA beverage ingestion at -30 min but there was significantly declined in plasma glucose from -30 min to 0 min after ingestion (95.13±3.86 and 75.50±3.86 mg/dl at -30 and 0 min, respectively, $p < 0.01$) and at 0 min there were also significantly lower than before ingestion (93.50±3.08 and 75.50±3.86 mg/dl for -60 and at 0 min, respectively, $p < 0.01$). After the beginning of exercise, in FA trial, plasma glucose concentrations were gradually increased from the beginning of exercise (75.50±3.86, 89.00±4.58, 100.17±5.74 and 96.75±3.95 at 0, 30, 60, and 90 min, respectively). While plasma glucose concentrations in FA trial were the highest, plasma glucose concentration in G trial were lowest which made plasma glucose differ significantly between G and FA trial at 60 min (79.00±2.82vs.100.13± 5.74 mg/dl, $p<0.05$). At recovery period, plasma glucose concentrations were similar to the baseline in all trials (90±3.00 vs. 86±3.70, 92±2.73 vs. 90±4.11, 89±3.34 vs. 91±3.72, and 94±3.08 vs. 97±3.95 mg/dl for baseline vs. recovery period in G, F, Fa, FA trials respectively).

6. Serum Insulin

Similar to plasma glucose, there were no significant differences in baseline (pre-feeding) serum insulin among treatments (Figure 6, and Table 20). Together with increasing in plasma glucose, serum insulin were increased at 15 min after G ingestion and significantly higher than F, Fa, and FA ingestion (37.59±3.09, 13.24±3.32, 18.56± 2.91, and 13.73±3.15 μU/ml at -30 min for G, F, Fa and FA, respectively, $P < 0.01$). After increased in serum insulin in G trial at 15 min after ingestion, there were declined in serum insulin throughout the period until near the baseline data at 60 min (8.64±3.05, and 8.12±2.71 μU/ml at –60, and 60 min, respectively). In contrast to G trial, the changes of serum insulin in F, Fa, and FA trials were in the normal fasting value (3.00-25.00 μU/ml) (201).

Table 20 Serum insulin (μU/ml) in G, F, Fa, and FA trials.

Type of beverage	Time(min)					
	-60	-30	0	30	60	90
G	a 8.64 ±3.05	a* 37.59 ±3.09	17.55 ±4.63	12.46 ±3.62	8.12 ±2.71	6.72 ±3.26
F	b 8.66 ±2.48	b* 13.24 ±3.32	11.95 ±3.41	12.20 ±2.15	7.37 ±2.92	9.28 ±2.49
Fa	c 7.70 ±2.12	c* 18.56 ±2.91	12.03 ±1.82	8.18 ±1.83	5.52 ±1.19	11.53 ±1.80
FA	d 8.39 ±1.76	* 13.73 ±3.15	d 18.36 ±2.40	12.35 ±2.57	8.51 ±1.74	10.92 ±1.89

a = significantly different between –60 and –30 min at $p < 0.001$.

b = significantly different between -60 and –30 min at $p < 0.005$.

c = significantly different between -60 and –30 min at $p < 0.001$.

d = significantly different between -60 and 0 min at $p < 0.001$

* = significantly different from G ingestion at $p < 0.01$.

In F and Fa trial, there were significantly increased after 15 min of ingestion (8.66±2.48vs.13.24±3.32, and 7.70±2.12vs.18.56±2.91 μU/ml at –60 vs. –30 min at $p < 0.005$, and at $p<0.001$ in F and Fa trials, respectively). In FA trial, there were also increased in serum insulin but significantly different from baseline at 45 min of ingestion (8.39±1.76 and 18.36±2.40 μU/ml at –60 and 60 min, respectively, $p < 0.005$). During exercise at 70% VO_2 max, there were decreased in serum insulin after ingestion before exercise in all trials (17.55±4.63vs.12.45±3.62vs.8.12±2.71, 12.03± 1.82vs.8.18±1.83vs.5.52±1.19, and 18.36±2.40vs.12.35±2.57vs.8.51±1.74 μU/ml at 0,

30, and 60 min in G, Fa, and FA trials, respectively and 11.95±3.41vs.7.37±2.92 μ U/ml at 0 vs. 60 min in F trial).

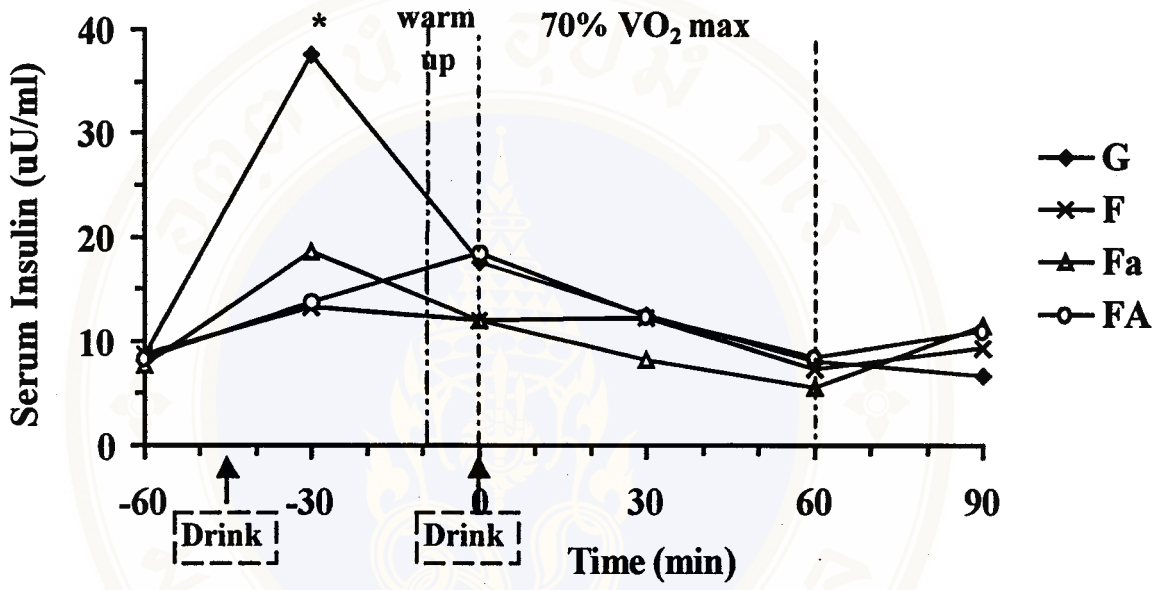


Figure 6 Serum insulin (uU/ml) in G, F, Fa, and FA trials.
* = significantly different from F, Fa, and FA trials ($p<0.01$).

7. Plasma Free Fatty Acids

As shown in Figure 7 (Table 21), there were no significant differences in plasma FFA concentration among the trials in any time. After 15 min of ingestion in all trials, there were slightly declined in plasma FFA concentrations (0.29± 0.02vs.0.25±0.03, 0.43±0.07vs.0.24±0.02, 0.38±0.06vs.0.32±0.04, and 0.34± 0.03vs.0.28±0.03 μmol/ml at –60 vs. –30 min in G, F, Fa and FA trials, respectively).

Table 21 Plasma free fatty acids (μmol/ml) in G, F, Fa, and FA trials.

Type of beverage	Time(min)					
	-60	-30	0	30	60	90
G	0.29 ±0.02	0.25 ±0.03	0.30 ±0.03	0.24 ±0.02	0.24 ±0.04	0.49 ±0.06
F	0.43 ±0.07	0.24 ±0.02	0.21 ±0.03	0.25 ±0.03	0.26 ±0.02	0.38 ±0.06
Fa	0.38 ±0.06	0.32 ±0.04	0.22 ±0.06	0.19 ±0.03	0.19 ±0.04	0.30 ±0.02
FA	0.34 ±.003	0.28 ±0.03	0.28 ±0.05	0.22 ±0.04	0.24 ±0.04	0..37 ±0.07

After the second drink, in all trials except F trial, there were slightly decreased (0.30±0.03vs.0.24±0.02, 0.22±0.06vs.0.19±0.03, and 0.28±0.05vs.0.22±0.04 μmol/ml at 0 vs. 30 min in G, Fa and FA trials, respectively) and still steady during exercise period. In F trial, although the second drink, there were slightly increased in plasma FFA concentration through the exercise and recovery period (0.21±0.03, 0.25±0.03, 0.26±0.03, and 0.38±0.06 μmol/ml at 0, 30, 60 and 90 min, respectively). At recovery period, there were increased in plasma FFA in all trials but not significantly different from baseline in any trials (0.29±0.02vs.0.49±0.06, 0.43±0.07vs.0.38±0.06, 0.38± 0.06vs.0.30±0.02 and 0.34±0.03vs.0.37±0.07 μmol/ml at –60 vs. 90 min in G, F, Fa and FA trials, respectively).

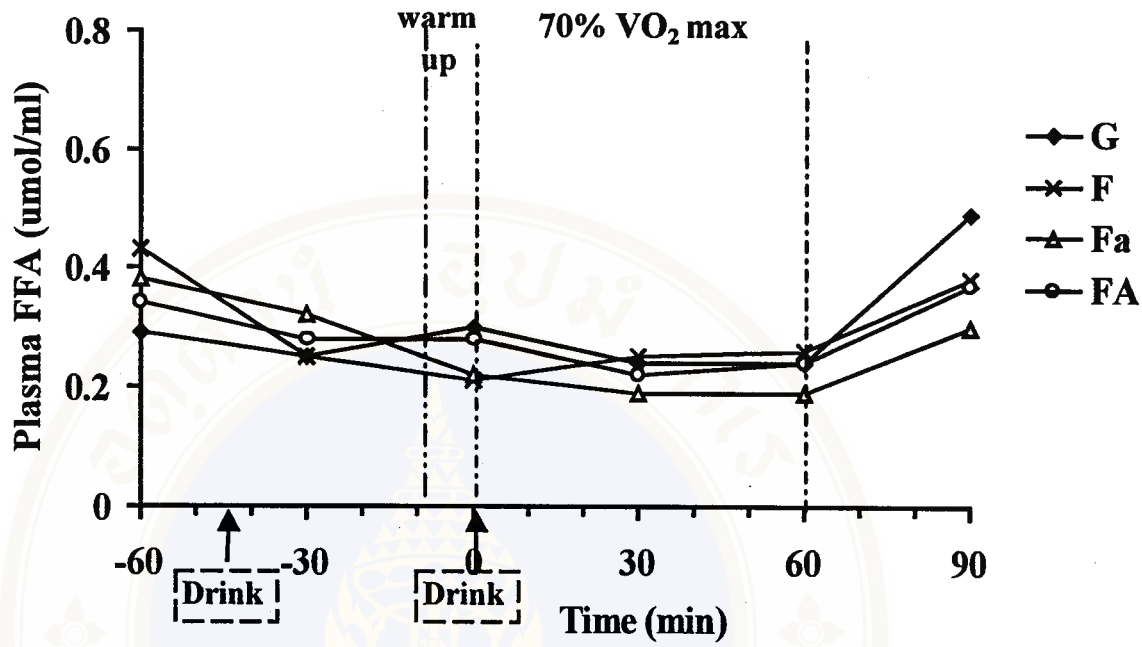


Figure 7 Plasma FFA (umol/ml) in G, F, Fa, and FA trials.

8. Serum Osmolality

There were no significant differences in baseline (prefeeding) serum osmolality among the four trials as shown in Figure 8 (Table 22) and there were no significant differences among the four beverages at any time. After 15 min of ingestion in G, F and FA trials, there were slightly increased in serum osmolality (281±1.32vs.285±1.50, 281±1.45vs.282±1.70, and 281±1.11vs.284±1.04 mmol/L in G, F, and FA trials, respectively).

During exercise, in G trial, there were slightly increased in serum osmolality (285±1.33, 286±1.44, and 287±1.60 mmol/L at 0, 30, and 60 min, respectively). In contrast, in F, Fa, and FA trials, there were significantly increased in serum osmolality (284±1.36vs.287±1.96, 283±0.65vs.289±1.67, and 287±0.53vs.292±1.34 mmol/L at 0 vs. 30 min in F, Fa, and FA trials, respectively, $p<0.05$).

Table 22 Serum osmolality (mmol/L) in G, F, Fa, and FA trials.

Type of beverage	Time(min)					
	-60	-30	0	30	60	90
G	281± 1.32	285± 1.50	285± 1.33	286± 1.44	287± 1.60	283± 1.57
F	281± 1.45	282± 1.70	a 284± 1.36	a 287± 1.96	288± 1.90	284± 1.67
Fa	281± 1.19	280± 1.45	a 283± 0.65	a 289± 1.67	287± 1.86	284± 2.51
FA	b 281± 1.11	284± 1.04	287± 0.53	292± 1.34	289± 2.10	b 286± 1.19

a = significantly different between 0 and 30 min at $p < 0.05$.

b = significantly different between -60 and 90 min at $p < 0.05$.

At recovery period, all trials except FA trial, there were declined in serum osmolality until closed to baseline data (281±1.32vs.283±1.57, 281±1.45vs.284±1.67 and 281±1.19vs.284±2.51 mmol/L at –60 vs.90 min for G, F, and Fa trials, respectively). Serum osmolality in FA trial at recovery was still significantly more than baseline period (281±1.11, and 286±1.19 mmol/L for –60 and 90 min, respectively, $p < 0.05$). However, serum osmolality in all trials were in normal range, which ranged from 275 to 295 mmol/L (201).

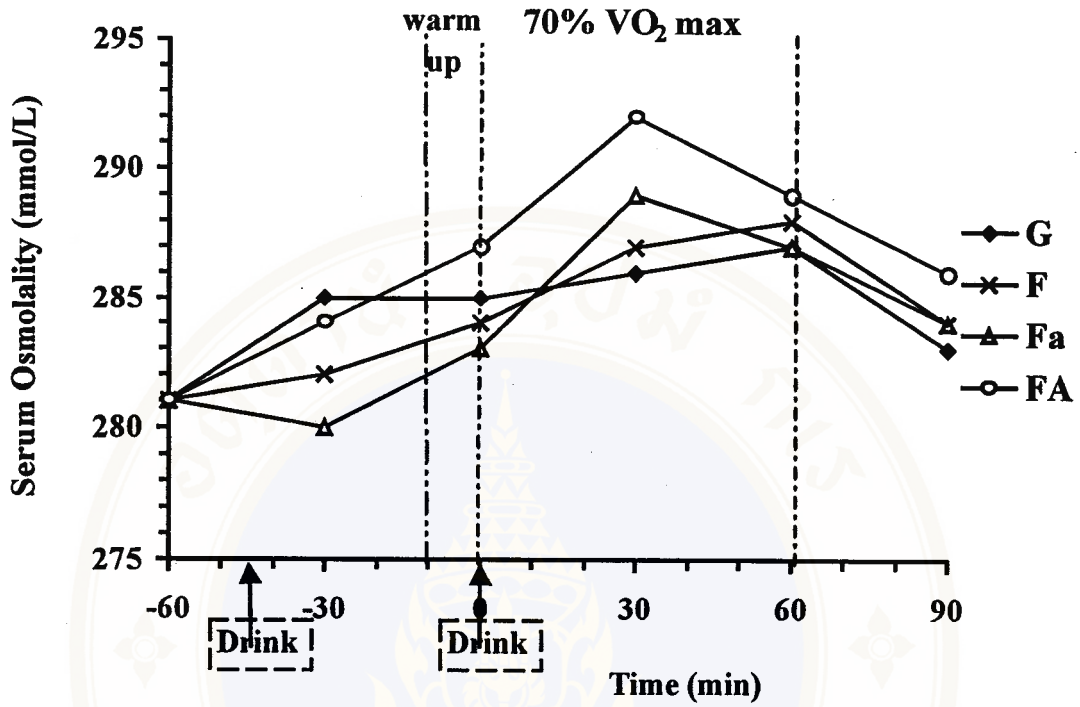


Figure 8 Serum osmolality (mmol/L) in G, F, Fa, and FA trials.

9. Plasma Volume

Percentage changes in plasma volume (PV) have shown in Figure 9 (Table 23), there were not significant differences among the four trials. There were significantly decreased in plasma volume after 15 min of first ingestion in F and FA treatments (-5.23±1.23, -and –5.30±1.41% for F, and FA, respectively, $p<0.05$). In G and Fa trials there were slightly decreased (-1.93±0.93 and –2.16±1.65 % at –30 min for G and Fa trials, respectively). In G and Fa trial, the significantly decreased in PV from baseline were seen at 45 min after first drinking (-5.58±1.22, and –7.98±1.33 % at 0 min for G and Fa trials, $p<0.05$). In F,and FA trials, after significantly decreased from baseline at 15 min after first ingestion, there were still decreased from –30 to 0 min (-5.23± 1.23vs.-10.53±1.82, and –5.30±1.41vs.10.59±1.86 % at –30 vs. 0 min for F, and FA trials, respectively).

Table 23 Percentage changes in plasma volume (%) in G, F, Fa, and FA trials.

Type of beverage	Time (min)					
	-60	-30	0	30	60	90
G	a 0	-1.93± 0.93	a -5.58± 1.22	-6.09± 1.89	c -6.70± 1.57	c -1.95± 1.94
F	b 0	b -5.23± 1.23	-10.53± 1.82	-9.81± 1.33	c -8.75± 2.08	c -4.55± 1.52
Fa	a 0	-2.16± 1.65	a -7.98± 1.33	-9.98± 1.93	c -8.03± 1.93	c -4.45± 1.72
FA	b 0	b -5.30± 1.41	-10.59± 1.86	-10.28± 1.01	c -7.80± 1.38	c -3.19± 1.11

a = significantly different between -60 and 0 min at $p < 0.05$.

b = significantly different between –60 and -30 min at $p < 0.05$.

c = significantly different between 60 and 90 min at $p < 0.05$.

During exercise, the decreased in PV in G trial were slightly during exercise (-5.58±1.22, -6.09±1.89 and –6.70±1.57 % at 0, 30, and 60 min, respectively). In Fa trial, there were slightly decreased in PV after 30 min of exercise then there were slightly increased in PV (-7.97±1.33, -9.98±1.93, and –8.03±1.93 % at 0, 30, and 60 min, respectively). The lowest values of PV in G and Fa trial were found during exercise in G, and Fa trials (at 60 min in G trial and 30 min in Fa trial). These changes in PV were not similar to F and FA trials which the lowest PV were found at the beginning of exercise (-10.53±1.82 and –10.59±1.86 % at 0 min for F and FA trials, respectively).

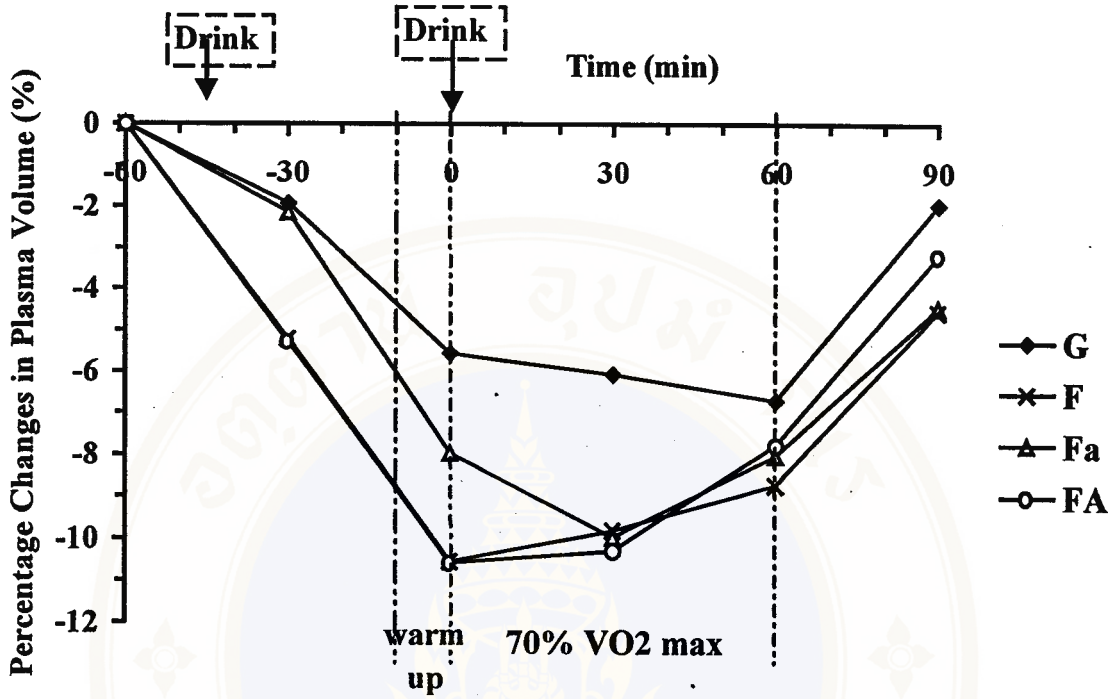


Figure 9 Percentage changes in plasma volume in G, F, Fa, and FA trials.

At recovery period, there were significantly increased in PV from exercise period in all trials which were closed to before exercise (-1.93±0.93vs—1.95±1.94, --5.23±1.23vs.-4.55±1.52, --2.16±1.65vs.-4.45±1.72 and —5.30±1.41vs.—3.19±1.11 at -30 vs.90 min for G, F, Fa and FA, respectively, $p<0.05$).However, theses increased at the recovery period, the changes in PV were still less than baseline.

10. Body Weight

After finished exercise, body weight was measured again and compared to the baseline. There were no significant differences in body weight loss over exercise period among the four trials (0.80±0.10, 0.75±0.14, 0.79±0.09, and 0.80±0.08 kg for G, F, Fa, and FA respectively).

11. Breath Hydrogen Excretion

As shown in Figure 10 (Table 24), from the baseline data, there were no significant differences among the four trials. However, there were significantly different between F and Fa trial at 30 min (2.74±0.63, and 1.02±0.16 µl/min/kg in F, and Fa trials, respectively, $p < 0.05$), F and G trial at 60 min (3.44±0.68, and 1.22± 0.25 µl/min/kg in F, and G, respectively, $p < 0.01$), and F and FA at 90 min (2.44±0.53 and 0.62±0.12 µl/ min/kg in F and FA trials, respectively, $p < 0.01$).

Table 24 Changes in breath hydrogen expired (µl/min/kg) before, during and after ingestion each beverage.

Type of beverage	Time(min)								
	-60	-30	0	30	60	90	120	150	180
G	1.44± 0.53	0.85± 0.30	1.30± 0.38	1.77± 0.38	* 1.22± 0.25	0.89± 0.39	0.58± 0.28	0.51± 0.28	0.44± 0.18
F	a 0.76± 0.17	0.94± 0.47	1.42± 0.37	* 2.74± 0.63	a* 3.44± 0.68	* 2.44± 0.53	1.56± 0.46	1.86± 0.53	1.06± 0.25
Fa	0.65± 0.24	0.53± 0.15	1.02± 0.16	* 0.96± 0.16	2.26± 0.51	1.24± 0.42	1.41± 0.55	1.26± 0.51	0.86± 0.25
FA	0.84± 0 23	0.85± 0.29	1.73± 0.50	1.76± 0.35	2.23± 0.54	* 0.62± 0.12	0.82± 0.20	0.73± 0.20	0.48± 0.09

a = significantly different between -60 and 60 min at $p < 0.005$.

* = significantly different from F ingestion at $p < 0.05$.

In F trial, there were significantly increased and peaked from baseline data at 60 min of exercise (0.76±0.15 and 3.44±0.68 μl/min/kg for baseline and 60 min, respectively, $p < 0.005$). Then there were progressively declined in breath hydrogen excretion (3.44±0.68, 2.44±0.53, 1.56±0.46, and 1.06±0.25 μl/min/kg at 60, 90, 120 and 180 min, respectively). Although, in Fa and FA trials, there were found the significance peak at the 60 min of exercise same as F trial (2.26±0.51 and 2.23±0.54 μ l/min/kg in Fa and FA trials, respectively) but it was not significant difference from baseline and also from G, or F trials.

At recovery period, similar to F trial, there were progressively declined in breath hydrogen excretion in G, Fa, and Fa trials and significantly from the peak which were found during exercise (1.77±0.38vs.0.44±0.18 μl/min/kg at 30 vs. 180 min in G trial, 2.26±0.51vs.0.86±0.25 and 2.23±0.54vs.0.48±0.09 μl/min/kg at 60 vs. 180 min in Fa and FA trials, respectively).

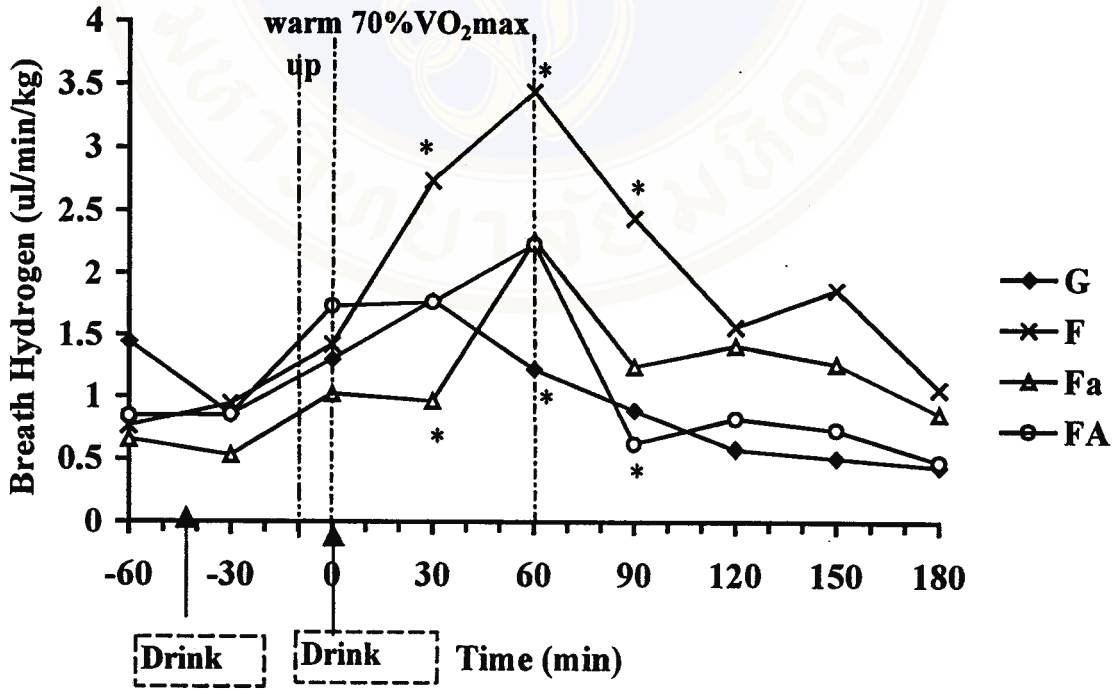


Figure 10 Hydrogen excretion rate (ul/min/kg) preceded by ingestion of different solutions (G, F, Fa, and FA solutions).

* Treatments sharing the same subscript are significantly different at $p<0.05$.

12. Gastrointestinal Disturbances

There were no signs or symptoms of GI disturbances after G ingestion (Table 25, and also Table 14). In contrast to G trial, 5 of 8 subjects in F trial reported abdominal distress at 30 min after the beginning of exercise, three of them could not maintain their work and stop running before exhaustion and then had diarrhea immediately after stopped exercise. One of 5 who had abdominal distress in F trial, the 2nd subject, could run to exhaustion but had diarrhea 2 hours after finished exercise, only one of them felt better after finished exercise. Similarly, in FA trial, 4 of subjects reported abdominal distention at 10-30 min after second ingestion, two of them could not maintain their work and stop running before exhaustion. Only one in the 4 subject who suffered from abdominal distention in FA trial, the 5th subject, felt better after finishing exercise but none of them reported about diarrhea. In Fa trial, there were also reported of mild abdominal distention at 10-20 min after beginning exercise in 4 subjects but they felt better after 30 min and were able to run until exhaustion without any GI disturbances after exercise or had not had any diarrhea reported.

Table 25 Incidence of GI disturbances in G, F, Fa and FA trials.

Beverage	GI disturbances		Note
	No (%)	Yes (%)	
G	8(100.0)	0(0.0)	
F	3(37.5)	5(62.5)	3 out of 5 stopped exercise because of diarrhea
Fa	4(50.0)	4(50.0)	
FA	4(50.0)	4(50.0)	2 out of 4 stopped exercise because of severe GI disturbance

CHAPTER V

DISCUSSION

The facilitating effect of amino acids on fructose absorption in healthy children is shown in resting condition but there is no report about fructose absorption with facilitating effect of amino acids in exercise condition. Hence, it is possible that if fructose is effectively absorbed from the gut by the facilitating effect of amino acids, fructose can improve performance in endurance exercise. The present study studied the effect of fructose and amino acids ingested simultaneously prior exercise on fructose absorption and physical performance.

1. Effect of Exercise on Fructose Absorption Facilitated by Alanine

1.1 Breath Hydrogen Excretion

Incomplete fructose absorption can be determined by using breath hydrogen test because the appearance of hydrogen gas in the breath is the indication of fructose fermentation by bacteria. As shown in Figure 10, there was significantly increased in breath hydrogen excretion after F ingestion higher than Fa ingestion at 30 min (2.74±0.63, and 0.96±0.16 μL/min/kg in F, and Fa trials, respective, $p<0.01$), higher than G ingestion at 60 min (3.44±0.68 and 1.22±0.25 μL/min/kg in F, and G trials, respectively, $p<0.01$) , and higher than FA ingestion at 90 min (1.56±0.46 and 0.82±0.20 μL/min/kg in F, and FA trials, respectively, $p< 0.01$). These data demonstrated the malabsorption after F ingestion compared to ingestion of other solutions. Peak hydrogen values of F trial and also Fa and FA trials were found at 60 min of exercise (105 min after first ingestion) which is supported by Truswellet al's study (121) that peak hydrogen values occurred at 75 or 105 min after 50 g fructose ingestion in resting condition.

When added alanine in either equimolar or half-equimolar doses (FA or Fa trials, respectively), the changes of breath hydrogen excretion in FA and Fa trials were not significantly different from G trial but significantly less than F trial. Therefore, adding alanine in equimolar and half-equimolar doses to fructose solution can enhance fructose absorption as demonstrated by lowering breath hydrogen excretion.

The changes in breath H_2 excretion in FA trial were similar to G trial except the peak of breath H_2 excretion in FA trial is higher than G trial (although not significantly different from G trial) and closed to Fa trial. These results were different from the study in resting condition performed by Hoekstra and van den Aker (45) who showed that adding equimolar alanine in 50 g fructose solution resulted in significantly decreased of breath H_2 excretion with no peak was found. However, the unexpected peak of breath H_2 excretion in FA trial was shown in the exercise condition in this study. These result were concurred with Fujisawa et al (120) who demonstrated that the substition of 5% glucose (47.5 g fructose + 2.5 g glucose) in 50 g carbohydrate beverage ingested 30 min before exercise at 70% VO_2 max for 30 min did not improve absorption as shown by breath hydrogen excretion which similar to 50 g fructose ingestion. Their study was contrast to Truswell et al (121) who reported that the addition of 4 g glucose to the 50 g fructose in the test solution in the resting condition decreased incidence of malabsorption nearly by half. In the present study, the facilitating effect exerted by equimolar alanine in resting condition is not fully present during exercise.

The influence of exercise on fructose absorption facilitated by alanine might be from the physiologic response of GI tract from exercise. In exercise, the contraction frequencies and the antral areas were significantly reduced compared to that of without exercise (99). Additionally, an exercise lasting more than 1 h significantly depressed postprandial gastric secretion and significantly delayed gastric emptying (100). There were also reported the cases of acute gastric stasis following running. Furthermore, small bowel transit is delayed by exercise measured by breath hydrogen oral caecal transit times and motility may be also reduced (103), as well as the splanchnic blood flow is inversely related to heart rate or oxygen uptake, celiac and mesenteric arterial blood flow (206).

The adverse effect of exercise on fructose absorption is well demonstrated in Fig 10 which showed the rapid increased in breath H_2 excretion immediately after the beginning of exercise. The peak breath H_2 excretion was found after 60 min of second ingestion. After the stop of exercise, breath H_2 excretion in all trials was gradually decreased.

1.2 GI Disturbances

The malabsorption of fructose is always reported in various studies. The crucial factor with respect to symptom production may be from the colonic response to malabsorbed carbohydrate. Colonic factors that may be significance include metabolic events related to bacterial fermentation of the malabsorbed carbohydrate and the reabsorptive capacity of the colon. The capacity of the colon to remove carbohydrates and to compensate an osmotic load varied among individual (40). Carbohydrate malabsorption results in the deposition of osmotically active material in the large intestine (207). Since the osmolality of fecal water is only slightly greater than that of plasma, failure to absorb or metabolize this carbohydrate in the colon results in an osmotic diarrhea. The development of cramping may be dependent on the individual's intrinsic response to bowel distention. However, there is a poor correlation between the development of symptoms and the absolute height of breath hydrogen excretion (39).

In the present study, 30 g of fructose was used in the first drink followed by another 21 g at 45 min thereafter. Totally 51 g of fructose were ingested in each F, Fa, and FA trials. Five of eight subjects (62.5%) reported abdominal cramps in F trial with four of them had had diarrhea. This was similar to the study in resting condition that diarrhea, abdominal cramps, and/or flatulence, was common after ingestion of 50 g pure fructose (100 ml/L H_2O) in healthy human subjects (121). The study of 50 g of fructose in water was taken by 103 healthy volunteers showed that 60 subjects (58%) were unable to absorb the fructose completely (incomplete absorbers), showing an increase above basal breath hydrogen of 20-155 µl/L. Levine et al (71) also reported two out of eight subjects had complained intestinal distress after ingestion 75 g fructose 45 min before exercise.

In the study of Levine et al (71) was found the less incidence of intestinal distress despite the more fructose ingestion than in this study. However, the duration of exercise employed in their study was only 30 min while it was more than 60 min in the present study. This should be the result of the human intestinal capacity for fructose absorption in the absence of glucose is quite different in the general population (38).

It seems that there is a greater fructose absorption in rats than in humans. At least 2.0 g fructose/kg BW was required to induce malabsorption in the rats, whereas a majority of human subjects were unable to absorb amounts the fructose ranging from 0.5-1.0 g/kg BW (44). The present study also demonstrated the fructose malabsorption at the dose of 51 g (~ 0.83 g/kg BW) as shown by GI disturbances. However, fructose malabsorption is also related to the concentration of the solution as reviewed by Riby et al (38) that 10% fructose (50g /500 ml) induced 37% malabsorption (by breath hydrogen excretion $\geq$ 20 µl/L) but when increased the concentration to 20% fructose (50 g/ 250 ml), malabsorption increased to 71%. In the present study, the concentration in the solution was only 6%, the malabsorption indicated by GI disturbances was reported about 62.5%.

GI symptoms are common during endurance exercise, such as long-distance running and triathlon. In most study, incidence rates vary from 10 to 81%, depending on factors such as type, duration, and intensity of exercise performed (110). The frequency of GI symptoms is much higher during running than others endurance sports like cycling, rowing, or swimming, where the up and down movements are more limited. Recently there was a report that GI symptoms were significantly related to the subjects' experience (number of prior participation to the event), body weight loss and several components of diet before and during the event (208). In the present study, the subjects were fasted at least 10 h before exercise, and BW losses, together with the intensity of exercise were similar individually, hence the solution provided in the experiment should be responsible for the occurrence of GI disturbances.

Alanine added in the test solutions (in Fa, and FA trials) in the present study should be considered on the occurrence of GI disturbance. The study of amino acids: glycine, β-alanine, L-lysine, L-leucine, and DL-methionine with the concentration were 0.1 M, 0.2 M, 0.5 M, and 1.0 M (osmolality ranged from 100-1010

mmol/L) was found that all amino acids in concentrations of 0.2 M delayed emptying significantly when compared with test meals containing water and phenol red only. The mixture of essential amino acids totaling 160 mmol/L was within the range found in a 60-g protein meal. The delay in emptying was related to the molar concentration of the amino acid in the test meal and unrelated to the molecular weight of amino acid or to the amount of acid secreted. The results of these studies indicated that gastric emptying of amino acids was related to their osmolar concentration. In the present study, alanine was added in FA and Fa trials as 0.33, and 0.17 mmol/L, respectively. Therefore, it is probably that the alanine contained in FA solution reduced gastric emptying but should not be effected on Fa solution.

The osmolality of the beverage in the present study was varied from 413±6.56, 438±3.85, 594±14.93, and 788±12.47 mmol/L, for G, F, Fa, and FA, respectively. Therefore, the osmolality of the solution should be considered as a factor influence the occurrence of GI disturbances. Zarling et al (210) studied in subjects aged 18-35 yrs old during resting condition, the enteral formular which the osmolalities ranged between 325 and 690 mmol/L, there were well tolerated for which shown by no carbohydrate malabsorption was detected as measured by breath hydrogen and occurrence of GI disturbances.

Gastric secretion and emptying rate were not affected by varying the type of dietary carbohydrate and the dietary osmolality from 280 to 680 mmol/L as shown in the study of Steven et al in resting condition (211). Moreover, it has been demonstrated that the rate of gastric emptying is not affected by diet osmolality but directly related to caloric density of the diet (67, 212-213). Similar to the study of Case et al (214) that intragastric dilution and gastric emptying were not effected by diet osmolality (340-700 mmol/L) in Miniature pigs, which had a gastrointestinal tract similar to human.

Although high osmolality of solution was well tolerated in resting condition, in the exercise condition, there was not similar. In the present study, there were much different in osmolality of each beverages. G and F trials have similar osmolality at 413±6.56, and 438±3.85 mmol/L. In F trial, however, 5 subjects reported GI disturbances while no occurrences were found in G treatment, it was because of different in absorption. The same amount of fructose was presented in Fa, and FA

trials but no diarrhea reported. This might be the malabsorption of fructose was not appeared in either Fa or FA trials as the result of the facilitation of alanine to fructose absorption. Incidences of gastric fullness were found in Fa and FA trials. In Fa trial, 4 of subjects (50%) reported slightly gastric fullness at 10-20 min after they received the second drink immediately prior to exercise but they felt better thereafter. However, in FA trial the incidences of GI disturbance were similar to Fa trial but the severity was much greater and last longer than Fa trial that 2 out of 5 had to stop exercise before exhaustion. The highly different in osmolality between Fa, and FA trial (594±14.93 and 788±12.47 mmol/L for Fa and FA, respectively, $p<0.001$) should be corresponded in the occurrence of gastric fullness in Fa, and FA trials as described above.

2. Substrate Utilization

2.1 Plasma Glucose, and Serum Insulin

In the present study, plasma glucose and serum insulin were significantly increased after 15 min of G ingestion (90±3.0 vs. 130±0.03 mg/dl, and 9.09±3.49 vs. 33.65±4.89 μU/ml for baseline vs. at -30 min in plasma glucose and serum insulin, respectively, $p<0.05$). Plasma glucose and serum insulin in G trial were significantly higher than in F, Fa and FA trials ($p<0.05$).

Following G ingestion, plasma glucose concentration increased significantly but then declined rapidly in a linear fashion. These declines have been demonstrated to be primarily due to an over-production of insulin in response to a concentrated blood glucose challenge. Over compensation in production of insulin is defined as a hyperinsulinemic response and may result in a hypoglycemic response (215). The magnitude of the response appeared to be related to either the amount of carbohydrate ingested or the insulin response (216). It was also shown that in the present study the reduction of plasma glucose lower than baseline but did not found hypoglycemic state as the glucose used was 33 g which was ingested 45 min before exercise and another 21 g ingested immediately prior to exercise.

For the F trial, blood glucose was not significantly elevated over time, its' ranged between 82 to 92 mg/dl. Presumably, by the elevation of blood glucose from fructose ingestion is not sufficient to initiate a large production and thus no

significant changes in blood glucose concentration were observed. Additionally, as we all realize, fructose creates much less blood glucose response than does glucose (39, 52, 120).

The pattern of plasma glucose in F, and G trial is similar to the result shown by Guezennec et al (50) who provided 100 g fructose or glucose (diluted in 400 ml) 60 min before the beginning of exercise. However, the peak of serum insulin in their study was higher as carbohydrate provided was more than in the present study. The plasma insulin response was significantly correlated with the load of glucose ($r=0.86$, $P<0.001$) whereas such correlation was not observed with the blood glucose response.

In the Fa trial, blood glucose was significantly elevated at 15 min after first ingestion and slightly declined 30 min thereafter and remained steady throughout the study without significant differences from the baseline values. For FA trial, plasma glucose was not changed after 15 min of first ingestion but unexpectedly significantly declined at 45 min after first ingestion ($p<0.05$). Thereafter, there were significantly increased (89±4.58, 100±5.74 and 97±3.95 mg/dl at 30, 60 and 90 min, respectively, $p<0.05$). In the post-exercise ingestion of 100 g alanine, it caused mild sustained increases in plasma glucose concentrations of usually not more than 2.0 mmol/L (217). Moreover, the elevation in plasma glucose did not reach significant level until 1.5 h post-ingestion (218). The significant increase in plasma glucose in Fa trial might be from high absorption after the 500 ml solution in the first drink as the osmolality of Fa trial was in the ranged (<680 mmol/L) that did not effect in gastric secretion and emptying rates as demonstrated in the studies in resting condition (211, 214).

In FA trial, since the high osmolality of the solution as shown by the increase of serum osmolality and the highest decreased in PV. Therefore, plasma glucose significantly decreased at 60 min after first ingestion because of slow absorption from high osmolality. After the secondary ingestion, plasma glucose increased and peaked at 1.5 h after second ingestion. However, the increased in plasma glucose was not as much as 50 g glucose since 50 g alanine ingestion caused increased in plasma glucose only 2.0 mmol/L (36 mg/dl). In the present study, alanine was added only 24.99 g (29.49 g/L), and 12.50 g (14.79 g/L) in FA, and Fa trials, respectively.

2.2 Plasma FFA

Hyperglycemia per se has no effect on free fatty acid turnover. Changes in lipolysis that occur coincident with hyperglycemia are probably due to changes in other circulating substrates or hormones known to affect lipolysis (219). Preexercise hyperinsulinemia also has the long-lasting effect of reducing the release of free fatty acids from adipocytes and the rate of fat oxidation during exercise. Thus, there is a shift in blood-borne fuels from fatty acids to glucose (142).

The present study, there were no significant differences in plasma FFA concentrations among the trials at anytime, although hyperinsulinemia was found in G trial. Similar to the study of Koivisto et al (169) on 75 g fructose, fructose, or placebo solution ingested 45 min before cycle ergometer exercise at 75% VO_2 max for 30 min. The results were shown that despite the differences between plasma insulin response to exercise with fructose ingestion, or with glucose ingestion, there was no significance observed in fat utilization. The study of Massicotte et al (49) demonstrated that ingestion of about 98.9 g (1.33g/kg in 19 ml/kg) of fructose, glucose, glucose polymer compared to water during 2 h of exercise at 53±2% VO_2 max, the plasma fat utilization was not significantly different.

The study of Jandrain et al (52) demonstrated that fructose or glucose ingested every 30 min during long duration moderate-intensity exercise (45% VO_2 max) in men. The ingestion of the first 25 g load of glucose was followed by a modest decreased in FFA levels, which thereafter slightly increased again until the end of the test but never became significantly higher than basal values. No significant difference in plasma FFA values was found between the protocols of glucose and fructose, but with fructose ingestion, FFA levels continuously increased throughout the exercise period. The present study, in adding alanine in Fa, and FA trials, there were slightly less FFA concentrations than G and F trials. The possibly reason may be the gluconeogenic precursor of alanine which enhances gluconeogenesis in Fa and FA trials.

2.3 Blood Lactate

Lactate formed in active muscle cells during exercise with high rates of glycogenolysis and glycolysis becomes an energy source and gluconeogenic precursor for the body. In the present study, the results demonstrated that blood lactate increased significantly at the 15 min after the first ingestion of the solutions in all trials (0.56± 0.06 vs. 0.73±0.08, 0.56±0.06 vs. 0.86±0.09, 0.55±0.09 vs. 0.85±0.13, and 0.7±0.08 vs. 0.94±0.01 for baseline vs. -30 min for G, F, Fa, and Fa, respectively, $p< 0.05$). There is active turnover rate during resting post-absorptive condition. As after a meal, net hepatic lactate output will be present (215). Therefore, there were increase in blood lactate after the first ingestion in all trials. However, the increased of lactate in this study for all trials were within the normal range as in the resting condition which was about 1 mmol/L (220).

Blood lactate continued to increase until it reached the peak and there was slightly decreased thereafter. The increased in blood lactate found in initial stages of exercise which was directly related to the intensity of exercise (221), and then declined when oxygen was available (222). Additionally, as exercise continued, gluconeogenesis was accelerated and the liver gradually shifts from a lactate producing to a lactate consuming state (215). Therefore, during continuous submaximal power output, blood lactate rose and then declined toward resting levels (223). However, there were no significant differences in blood lactate between the solutions over time in this study.

As the exercise, it was employed for high intensity exercise at 70% VO_2 max, the rate of lactate production was greatly exceed the capacity for lactate removal and therefore accumulated. During submaximal exercise, steady state might be achieved, and lactate would stabilize at moderately increased levels. Lactate was removed faster when exercise was continued at submaximal intensity. The largest clearance had been observed at an intensity of 60% of VO_2 max. The increased clearance was probably the results of uptake by active muscle, in which lactate served as substrate for both oxidation and glycogen resynthesis (224).

It was reported that more lactate is formed from fructose than from glucose in infusion study. This increase in lactate production occurs because of the increase in fructokinase activity, the rate-limiting step for glycolysis

(phosphofrutokinase) is bypassed, and pyruvate kinase activity is stimulated by accumulation of fructo-1-phosphate (225). Koivisto et al (72) provided either 75 g fructose or 75 g glucose 45 min before 2-h exercise at 55% VO_2 max. The blood lactate in glucose trial was highest as 1.6±0.3 mmol/L while the highest in fructose trial was 2.1±0.5 mmol/L. The higher in blood lactate in fructose found in Koivisto et al study was higher than that of in this study (1.71±0.19 mmol/L) which might be due to the lower fructose consumption in the present study. However, they also did not found the significant difference between the trials. There was a report that the rise in blood lactate after fructose administration was dose dependent (226).

An amino acid given simultaneously during fructose infusion was decreased lactate production from liver. The most pronounced decrease was observed when the amino acid infusion was started before the simultaneous administration of fructose and amino acids. The explanation of the phenomenon is thought to be a stimulation of gluconeogenesis by amino acids (227). The infusion is directly applied to blood circulation whereas alanine was ingested in the study (24.99 g and 12.50 g in FA, and Fa trials, respectively). As the slower absorption of FA solution (as previously described), the effect of alanine on blood lactate was not present. In contrast, blood lactate in FA trial was slightly higher than the other trials that might be the consequence of the higher rates of glycolytic flux from slower rates of FA absorption.

The fall in insulin stimulates hepatic glycogenolysis, and as a consequence of glycolytic flux, and as a result, hepatic lactate output was accelerated (215). The present study, although there was a significantly fall in serum insulin in G trial but it was not the result in higher lactate concentration than other trials. This is similar to the study of Koivisto et al (72) that plasma glucose was not much decreased to the hypoglycemic state. Therefore the glycolytic flux was not fully stimulated.

3. Effect of Alanine and Fructose Absorption on Hydration Status

The hydration status in the present study was determined by plasma volume, serum osmolality and body weight loss from exercise.

In G trial, there was slightly increased in serum osmolality and decrease in PV at 15 min after first ingestion, which reflected the replacement from both solute and fluid from solution that entered the blood circulation.

In FA trial, at 15 min after first ingestion, PV was significantly decreased from the baseline together with a significantly increased of serum osmolality. These reductions in PV together with increased serum osmolality in this trial presumably due to water shift from blood to GI tract. The comparable studies by Case et al (214) and Steven et al (211) who showed that the osmolality of 280-680 mmol/L were not affected both gastric secretion and emptying rate. However, in the present study the osmolality was somewhat higher at 788±12.62 mmol/L and demonstrate the GI disturbance in 4 out of 8 subjects after FA ingestion.

In Fa trial, PV was declined similarly to G trial that was less than F and FA trials. These probably from the similar water absorption to G trial although the osmolality in Fa trial was higher than G trial but it was not shown the incidence of gastric secretion as found in FA trial.

In F trial, serum osmolality were slightly increased while PV was significantly decreased as 15 min after first ingestion similar to Fa trial. In contrast, the osmolality of F solution is closed to G solution, therefore, this might not be the result of the osmolality in F solution. The decreased in PV at 15 min after first ingestion should be from the malabsorption of fructose itself, which created water movement from the blood into GI tract and caused 4 out of 8 subjects had diarrhea.

At the onset of exercise, there were significantly decreased in PV in all trials. Because at the beginning of exercise, there was a reduction in PV due to a redistribution of fluids from the vascular to the interstitial space. However, in most cases this shift was the result of movement to an upright exercise body position or to an increase in mean arterial pressure related to exercise intensity. Fluid uptake by the muscle is quite rapid. With exercise, the vasodilatation in muscle might increase the capillary hydrostatic pressure by almost 20 mmHg, and the effect filtration surface

would increase. Although the high intramuscular hydrostatic pressure during contraction would counteract extravasation of fluid, there was a net driving force for filtration out of the vascular bed between contraction (223).

During exercise, the PV in G trial was slightly decrease (-5.58±1.22, -6.09± 1.89 and –6.70±1.57 % at 0, 30, and 60 min, respectively). In Fa trial, there was slightly decreased in PV after 30 min of exercise then there were slightly increased in PV (-7.97±1.33, -9.98±1.93, and –8.03±1.93 % at 0, 30, and 60 min, respectively). The lowest values of PV in G and Fa trial were found during exercise in G, and Fa trials (at 60 min in G trial and 30 min in Fa trial). These changes in PV were not similar to F and FA trials which the lowest PV were found at the beginning of exercise (-10.53±1.82 and –10.59±1.86 % at 0 min for F and FA trials, respectively). After the initial fluid shift from the onset of exercise, an equilibrium is reached between vascular fluid influx and efflux resulting a constant plasma volume. A 'true' decrease in PV usually only occurs as a result of total body dehydration due to prolonged exercise, high sweat rates, and heat stress. Either the onset of exercise or the decrease in PV stimulates the release of neuroendocrine hormones associated with fluid and electrolyte balance. The release of these hormones, i.e., arginine vasopressin, arterial natriuretic peptide, and aldosterone, is related to the intensity of the exercise and during prolonged exercise is related to a decrease in cardiac filling pressure. The increase in the plasma concentration of these hormones and the constancy of the plasma volume during continuous exercise suggests an active regulation of the vascular fluid volume for the purpose of maintaining cardiac output and mean arterial pressure (228).

In FA, and F trials the lowest PV were found at the beginning of exercise, and during exercise, there were slightly increased in PV. These might be from the rapid decreased in PV from the water excreting to GI tract and from the physiologic change at the onset of exercise as previously described. The decrease in PV in F, and FA trial, therefore, stimulates the release of neuroendocrine hormones associated with fluid and electrolyte balance earlier than G, and Fa trial which had less decreased in PV at the beginning of exercise.

While PV was decreased, serum osmolality was concurrently increased during exercise in all trials. Serum osmolality passively increase as PV decreases (229).

Serum osmolality tended to progressively increase throughout exercise when subjects ingested carbohydrate-electrolyte beverage as seen in G, trial. In Fa, and FA trial, there were slightly increased in serum osmolality after 30 min of exercise, which probably from the solute in Fa, and FA absorption. After 30 min of exercise, there were slightly decreased in serum osmolality. It might be from the high osmotic pressure in the vascular that pulled the water to the blood (230).

At recovery period, there was no significant difference between before exercise and recovery period in all trials. These results were from the "starling forces", the pulling effect from the osmotic pressure simply return the PV to preexercise conditions (230). However, serum osmolality in FA trial were still significantly different from baseline while the other trials were returned to near the baseline. This high serum osmolality in FA trial may be from the solutes in the solution as found that there were no diarrhea reported in this trial. Therefore the FA solution could be absorbed but in the slower rate than other trials.

The changes in heart rate were not significantly differences same as body weight losses between solutions. The hydration status might not different between the solution as measured by changes in heart rate, and body weight losses. Accordingly, there were no significant differences among trials in PV changes and serum osmolality.

4. Physical Performance

Factors related to physical performance are type and intense of exercise, amount and timing of carbohydrate ingestion, the composition of the beverage, pre-exercise meal, and training status. In the present study, the subjects were the same persons in all trials. Their physical activities were similar throughout the experiment and the same in 2 days food intake before engaged in each experiment. On experiment, they were fast about 10 h then running on treadmill in the same workload of the same subject in the four trials. Additionally, time and amount of carbohydrate solution intake was ingested at the same time, and same amount at each trial. Therefore, the compositions of these solutions were only the factor involved in the physical performance of the subjects in the four trials.

The present study demonstrated that physical performance was not significantly different among the G, F, Fa, and FA trials. Additionally, RPE which was significantly increased with the time of exercise, but there was not significantly different between the trials.

Fructose and exercise was studied by many investigators but most of their studies focused on oxidation rate and muscle glycogen depletion. The oxidation rates of fructose was reported similarly that lowered than glucose oxidation in many investigations (49-52, 174) which was from the slower absorption and had to be metabolized in the liver. In contrast, muscle glycogen depletion was lowered than in glucose trial (71, 176-180). Only few investigators investigated about fructose and exercise performance as might be due to the GI disturbance occurrence. Okano et al (170) provided fructose ingestion 60 min before exercise and found that time to exhaustion was significantly increased after fructose ingestion as compared to placebo ingestion (145±4 vs. 132±3 min, respectively, $p<0.05$). Murray et al (48) compared fructose ingestion with glucose and sucrose. They found that cycling performance times were faster with sucrose and glucose than fructose (419.21.0 s, 423.9±21.2 s, respectively, $p<0.05$). Gastrointestinal distress might reduce exercise capacity in their study. Bjorkman et al (165) also agreed with those, that total work time until exhaustion was significantly longer with glucose than with either fructose or water (133±13, 114±12 and 116±13 min, respectively).

In contrast to carbohydrate and fat, amino acids and protein were believed to have little or no role as a source of fuel for muscle contraction, but it now appears that they may contribute as much as 5-10% of the energy needed to run a marathon. Their source may be the free amino acids found in muscle, blood, and liver produced by the deamination of proteins in liver and skeletal muscle. Gluconeogenesis via the glucose-alanine pathway is a possible energy source during prolonged exercise (231).

Role of amino acids in hepatic gluconeogenesis is reported. The amino acids alanine, glutamine, glutamate, glycine, serine, and threonine can be taken up by the liver and converted to glucose. After an overnight fast, alanine and glutamine appear to be the most quantitatively important during exercise. The release of alanine and glutamine from the working limb increases with exercise intensity, thereby providing more gluconeogenic substrate to the liver (232).

Hypoglycemia may be affected physical performance but as reported of Coggan and Coyle (233) and Felig et al (234) that neither mild CNS (central nervous system) symptoms of hypoglycemia nor blood glucose levels < 2.5 mmol/L, the men can continue exercise. However, although there were much decreased in plasma glucose in G trial but not low as hypoglycemia. Therefore, hypoglycemia was not affected physical performance in this study. GI disturbance from malabsorption of fructose in F solution and high osmolality in FA solution, the physical performance was affected as shown by 4 subjects had to stop exercise before exhaustion.

As known that dehydration and substrate used are affected physical performance. In the present study, there were not significant differences in body weight losses, heart rate, blood lactate, and plasma FFA among the trials. Therefore, these results indicated the similar in dehydration status and substrates used (except blood glucose) which subsequently similar time to fatigue and RPE in those trials.

CHAPTER VII

CONCLUSION

Not only fluid that is needed in exercise but also carbohydrate as energy substances for the body in prolonged exercise. Carbohydrate is the most important nutrient in an athlete's diet because it is the only fuel that can power intense exercise for prolonged periods, yet its stores within the body are relatively small. Many researchers are centered on glucose and its polymers in sport drink. But the anti-lipolytic effects of glucose-induced blood insulin rises have prompted atheletes to consider the use of fructose, a weak insulinotropic sugar, which is known to produce lower insulin secretory response than glucose ingestion.

The facilitating effect of amino acids on fructose absorption in healthy children is shown in resting condition but there is no report about fructose absorption with facilitating effect of amino acids in exercise condition. Hence, it is possible that if fructose is effectively absorbed from the gut by the facilitating effect of amino acids, fructose can improve performance in endurance exercise. The present study demonstrated the effect of fructose and amino acids ingested simultaneously prior exercise on fructose absorption and physical performance.

The solutions contained the same amount of sodium and potassium in accompany with either 6% glucose (G), 6% fructose (F), 6% fructose and half-equimolar dose of alanine (Fa) or 6% fructose and equimolar alanine (FA). Each 500-ml solution given to the subject at 45 min before exercise, and another 350 ml of the drink was given immediately prior to exercise for 1 h at 70% VO_2 max followed with performance test. Totally 850 ml was given at each occasion which about 100% replacement of sweating rate (as compared with body weight losses). The 6% carbohydrate given is the optimal dosage for improving physical performance as suggested by many investigators.

The results demonstrated the hyperinsulinemia and hyperglycemia only occurred in G trial. However, blood lactate, heart rate, RPE, serum osmolality, changes in PV, body weight loss, and time to exhaustion were not significant differences among trials. Adding alanine enhanced fructose absorption as shown by lowered breath hydrogen excretion in Fa and FA trials than in F trial. However, there were increased in breath hydrogen excretion during exercise in Fa trial, which is not similar to the resting condition. These data demonstrated that exercise might have affected on facilitating effect of alanine in fructose absorption.

GI disturbance was found in F, and FA trials. In F trial, the osmolality is similar to G trial. There were no GI disturbances in G trial. Therefore, GI disturbance in F trial was from the different absorption from glucose absorption. The high osmolality in the test solutions especially in FA trials caused GI disturbance during exercise.

In summary the use of fructose alone (51 g) or in high osmolality in the solution can cause gastrointestinal distress in exercise. Both 51 g fructose and high osmolality (about 788 mmol/L) are the exercise-limiting condition. Therefore, in exercise, people should avoid ingesting pure fructose solution (about 51 g) and high osmolality beverage as in FA trial (788±12.47 mmol/L), although 3 subjects were well tolerated with both kinds of the solution. Adding alanine in fructose solution either equimolar (FA) or half-equimolar (Fa), although did not improve the performance time compare to glucose solution in this study, it is interesting to further study as the benefit of fructose metabolism and alanine as the gluconeogenesis precursor during exercise.

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APPENDIX 1

หนังสือยินยอม

(INFORMED CONSENT FORM)

ชื่อโครงการ ผลของอะลานีนต่อการดูดซึมฟรุคโตสในภาวะการออกกำลังกาย และต่อประสิทธิภาพของการออกกำลังกาย

ชื่อและนามสกุลผู้เข้าร่วมโครงการ .....

อายุ ..... ปี ชั้นปีที่ศึกษา ..... รหัสประจำตัว.....

คำยินยอมของผู้เข้าร่วมโครงการ

ข้าพเจ้านาย .....ได้รับทราบรายละเอียดของโครงการการทดลอง ตลอดจนประโยชน์และข้อเสี่ยงที่จะเกิดขึ้นต่อผู้ถูกทดลองแล้วได้แก่

1. รายละเอียดของโครงการการทดลอง และประโยชน์ที่ได้รับ

ผู้เข้าร่วมโครงการได้รับรายละเอียดของโครงการที่เป็นลายลักษณ์อักษร ได้แก่ ชื่อโครงการวิจัย ชื่อและที่ทำงานของผู้วิจัยหลัก สรุปย่อโครงการวิจัย ความเป็นมาและความสำคัญของโครงการ เหตุผลที่ต้องทดลองในคน ประโยชน์ที่จะได้รับจากการทดลอง วัตถุประสงค์ของโครงการ สถานที่ทำการทดลอง การวางแผนการวิจัย เกณฑ์การคัดเลือกอาสาสมัครเข้าร่วมโครงการ เกณฑ์การคัดเลือกอาสาสมัครออกจากโครงการ เกณฑ์การให้เลิกจากการศึกษา ขั้นตอนการดำเนินการวิจัย ระยะการศึกษาวิจัย และชื่อและที่อยู่ของผู้ทดลอง

2. ความเสี่ยงที่อาจเกิดขึ้นได้จากการทดลอง

2.1 การออกกำลังกายขนาดปานกลางโดย cycle ergometer เป็นระยะเวลาโดยประมาณ 60 นาที เป็นการออกกำลังกายที่ปฏิบัติกันเป็นปกติในนักกีฬาโดยทั่วไป โดยปริมาณและขนาดการออกกำลังกายในการทดลองนี้จึงไม่มีผลเสียต่อสุขภาพร่างกายของผู้ถูกทดลองซึ่งเป็นนักศึกษาวิทยาศาสตร์การกีฬาที่เล่นกีฬาและออกกำลังประจำ แต่ทั้งนี้จะมีการทดสอบสมรรถภาพของผู้ถูกทดลองก่อนการเข้าร่วมโครงการ

2.2 เครื่องดื่มที่ให้กับผู้เข้าร่วมการทดลองที่มีความเข้มข้น 6 เปอร์เซนต์ฟรุคโตส (51 กรัมต่อการทดลอง) นั้นเป็นความเข้มข้นที่ต่ำ การศึกษาของ Fujisawa และคณะ (1991) พบว่าคนปกติจะเกิดอาการผิดปกติเมื่อได้รับฟรุคโตสได้ในปริมาณมากกว่า 2.1-2.4 กรัมต่อน้ำหนักตัว 1 กิโลกรัม

2.3 อะลานีน เป็นกรดอะมิโน ซึ่งเป็นสิ่งที่มีประโยชน์แก่ร่างกาย ทั้งนี้สารอะลานีนที่นำมาใช้ในการทดลองเป็นสารอะลานีนที่ตรวจสอบความบริสุทธิ์และสิ่งเจือปนโดยบริษัทอายิโนะโมะโตะแล้วพบว่าอยู่ในระดับมาตรฐาน ไม่มีสารอันก่อให้เกิดอันตรายต่อผู้บริโภคได้ ทั้งนี้ปริมาณของอะลานีนที่ใช้เป็นปริมาณที่มีการใช้ศึกษาในเด็กปกติโดย Hoekstra และ van den Aker (1996) มาก่อนแล้ว

2.4 ผู้ทดลองจะปกปิดข้อมูลและสถานภาพของผู้ถูกทดลองแต่ละคนไว้เป็นความลับ

ข้าพเจ้านาย .....ยินยอมเข้าร่วมโครงการทดลองที่มีชื่อข้างต้น และข้าพเจ้ารู้ว่าถ้ามีปัญหาหรือข้อสงสัยเกิดขึ้น ข้าพเจ้าสามารถถามผู้ทดลองได้ และข้าพเจ้าสามารถที่จะไม่เข้าร่วมโครงการทดลองนี้เมื่อใดก็ได้

ลงชื่อ ..... ผู้เข้าร่วมโครงการ

(.....)

..... พยาน

(.....)

วันที่ .....

ข้าพเจ้าได้อธิบายรายละเอียดของโครงการ ตลอดจนประโยชน์ของการทดลองรวมทั้งข้อเสี่ยงที่อาจเกิดขึ้นแก่ผู้ถูกทดลองแล้วตามรายละเอียดข้างต้น

ลงชื่อ.....(ผู้ทดลอง)

วันที่.....

คำอธิบายของผู้ทดลอง

1. ผู้เข้าร่วมการทดลองจะได้รับรายละเอียดของโครงการที่เป็นลายลักษณ์อักษร ได้แก่ ชื่อโครงการวิจัย ชื่อและที่ทำงานของผู้วิจัยหลัก สรุปย่อโครงการวิจัย ความเป็นมาและความสำคัญของโครงการ เหตุผลที่ต้องทดลองในคน ประโยชน์ที่จะได้รับจากการทดลอง วัตถุประสงค์ของโครงการ สถานที่ทำการทดลอง การวางแผนการวิจัย เกณฑ์การคัดเลือกอาสาสมัครเข้าร่วมโครงการ เกณฑ์การคัดเลือกอาสาสมัครออกจากโครงการ เกณฑ์การให้เลิกจากการศึกษา ขั้นตอนการดำเนินการวิจัย ระยะการศึกษาวิจัย และชื่อและที่อยู่ของผู้ทดลอง

2. ข้อพิจารณาด้านจริยธรรม

2.1 การออกกำลังกายขนาดปานกลางโดย cycle ergometer เป็นระยะเวลาโดยประมาณ 60 นาที เป็นการออกกำลังกายที่ปฏิบัติกันเป็นปกติในนักกีฬาโดยทั่วไป โดยปริมาณและขนาดการออกกำลังกายในการทดลองนี้จึงไม่มีผลเสียต่อสุขภาพร่างกายของผู้ถูกทดลองซึ่งเป็นนักศึกษาวิทยาศาสตร์การกีฬาที่เล่นกีฬาและออกกำลังประจำ แต่ทั้งนี้จะมีการทดสอบสมรรถภาพของผู้ถูกทดลองก่อนการเข้าร่วมโครงการ

2.4 เครื่องดื่มที่ให้กับผู้เข้าร่วมการทดลองที่มีความเข้มข้น 6 เปอร์เซนต์ฟรุคโตสนั้นเป็นความเข้มข้นที่ต่ำ การศึกษาของ Fujisawa และคณะ (1991) พบว่าคนปกติจะเกิดอาการผิดปกติเมื่อได้รับฟรุคโตสได้ในปริมาณมากกว่า 2.1-2.4 กรัมต่อน้ำหนักตัว 1 กิโลกรัม

2.5 อะลานีน เป็นกรดอะมิโน ซึ่งเป็นสิ่งที่มีประโยชน์แก่ร่างกาย ทั้งนี้สารอะลานีนที่นำมาใช้ในการทดลองเป็นสารอะลานีนที่ตรวจสอบความบริสุทธิ์และสิ่งเจือปนโดยบริษัทอายิโนะโมะโตะแล้วพบว่าอยู่ในระดับมาตรฐาน ไม่มีสารอันก่อให้เกิดอันตรายต่อผู้บริโภคได้ ทั้งนี้ปริมาณของอะลานีนที่ใช้เป็นปริมาณที่ไม่เกินความต้องการของดปรตีนต่อวัน ในคนปกติ

2.4 ผู้ทดลองจะปกปิดข้อมูลและสถานภาพของผู้ถูกทดลองแต่ละคนไว้เป็นความลับ

APPENDIX 2

แบบสอบถามเกี่ยวกับสุขภาพ

แบบสอบถามเกี่ยวกับสุขภาพและความเจ็บป่วย

ชื่อ.....นามสกุล.....

วันที่.....

1 . ประวัติความเจ็บป่วยในครอบครัว

ก. บิดา ชื่อ ..... อายุ .....ปี

มีชีวิต เสียชีวิต (ระบุสาเหตุ).....

มีโรคประจำตัวหรือไม่ (ระบุ).....

ข. มารดา ชื่อ ..... อายุ .....ปี

มีชีวิต เสียชีวิต (ระบุสาเหตุ).....

มีโรคประจำตัวหรือไม่ (ระบุ).....

ค. ท่านมีหรือพี่น้องรวม.....คน (รวมตัวท่าน)

ง. พี่/น้องของท่าน (ไม่รวมตัวท่าน)

คนที่ 1 มีชีวิต เสียชีวิต (ระบุสาเหตุ).....

มีโรคประจำตัวหรือไม่ (ระบุ).....

คนที่ 2 มีชีวิต เสียชีวิต (ระบุสาเหตุ).....

มีโรคประจำตัวหรือไม่ (ระบุ).....

คนที่ 3 มีชีวิต เสียชีวิต (ระบุสาเหตุ).....

มีโรคประจำตัวหรือไม่ (ระบุ).....

2. ท่านมีโรคประจำตัวต่อไปนี้หรือไม่ (ถ้ามี ระบุจำนวนปีที่เป็น)

ก. เบาหวาน ไม่มี มี ..... ปี

ข. โรคหัวใจ ไม่มี มี.....ปี

ค. โรคความดันโลหิตสูง ไม่มี มี.....ปี

ง. ความผิดปกติของเม็ดเลือด ไม่มี

มี (ระบุชนิดและระยะเวลาที่เป็น).....ปี

จ. โรคโลหิตจาง ไม่มี มี.....ปี

ฉ. โรคหอบ/หืด ไม่มี มี.....ปี

ช. โรคกระเพาะอาหาร ไม่มี มี.....ปี

ซ. ท้องเสียหรือท้องเดินเรื้อรัง ไม่มี มี.....ปี

ฌ. อื่นๆ (ระบุชนิด และระยะเวลาที่เป็น).....

3. ปัจจุบันท่านรับประทานยาเป็นประจำหรือไม่ (ถ้ามี ระบุ)

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4. ท่านเคยได้รับการผ่าตัดหรือไม่ (ถ้ามี ระบุชนิด และปีที่ทำ)

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5. ท่านเคยได้รับอุบัติเหตุร้ายแรงใดๆหรือไม่ (ถ้ามี ระบุชนิด และ ปีที่เป็น)

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6. ในรอบปีที่ผ่านมา (1 มิ.ย. 2541 – 1 มิ.ย. 2542) ท่านเคยเจ็บป่วยด้วยโรคร้ายแรงใดๆหรือไม่ (ถ้ามี ระบุชนิด และเดือนที่เป็น)

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7. ในรอบ 1 เดือนที่ผ่านมา ท่านมีการเจ็บป่วยด้วยโรคใดๆหรือไม่ (ถ้ามี ระบุ)

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8. ในรอบ 1 เดือนที่ผ่านมา ท่านรับประทานยาใดเป็นประจำหรือไม่ (ถ้ามี ระบุ)

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9. ปัจจุบันท่านรับประทานยาหรือวิตามินใดเป็นประจำหรือไม่ (ถ้ามี ระบุ)

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APPENDIX 3

แบบสอบถามการออกกำลังกาย

ชื่อและนามสกุล.....

อายุ.....ปี

วันที่.....

1. ขณะนี้ท่านเป็นนักกีฬาใช่หรือไม่
   - ▫ ไม่
   - ▫ ใช่ (ระบุชนิดกีฬา).....
2. ถ้าใช่ ท่านเป็นนักกีฬาดังกล่าวมา.....ปี
3. ก่อนหน้านี้ท่านเคยเป็นนักกีฬาชนิดใดมาก่อนหรือไม่
   - ▫ ไม่
   - ▫ ใช่ (ระบุชนิดกีฬา).....
     ตั้งแต่ปี พ.ศ.....ถึง พ.ศ.....

ในรอบ 3 เดือน กิจกรรมใดต่อไปนี้ที่ปฏิบัติเป็นประจำ

ชนิดกิจกรรม	อาทิตย์ละ <3 ครั้ง ครั้งละ (นาที)				อาทิตย์ละ 3-5 ครั้ง ครั้งละ (นาที)				อาทิตย์ละ >5 ครั้ง ครั้งละ (นาที)			
	<15	15-30	30-60	>60	<15	15-30	30-60	>60	<15	15-30	30-60	>60
วิ่งเหยาะ												
วิ่ง												
Treadmill												
จักรยาน												
ว่ายน้ำ												
ฟุตบอล												
วอลเล่ย์บอล												
แบดมินตัน												
เทนนิส												
ยกน้ำหนัก												
อื่นๆระบุ												

APPENDIX 4

แบบบันทึกการตรวจร่างกายแรกเข้า

วันที่.....

ชื่อและนามสกุล.....อายุ.....ปี

1. น้ำหนัก ส่วนสูง

- ✓ น้ำหนัก.....กิโลกรัม
- ✓ ส่วนสูง.....เซนติเมตร

2. การตรวจร่างกายทั่วไป

- ✓ อุณหภูมิ.....องศาเซนเซียส
- ✓ ชีพจร.....ครั้งต่อนาที
- ✓ ความดันโลหิต...../.....มิลลิเมตรปรอท
- ✓ หายใจ.....ครั้งต่อนาที

3. Body density and fat mass

การวัด (skinfold measurement)

- ✓ Biceps.....mm
- ✓ Triceps.....mm
- ✓ Subscapular.....mm
- ✓ Suprailiac.....mm

การคำนวณ

Equation for man

Age range 17-19 yr D = 1.1620 - 0.630 x [logΣ]

20-29 yr D = 1.1631 - 0.632 x [logΣ]

D = ...g/mL

Σ = sum of skinfold measurement at four sites as mentioned above

Fat mass = BW [kg] x [4.95/D – 4.5]

= .....kg

Fat free mass = BW [kg] - fat mass [kg]

= .....kg

APPENDIX 5

แบบบันทึก HR และ WORK RATE FOR VO_2 MAX

วันที่.....สิงหาคม 2542 เวลา.....น. ครั้งที่ .....

ชื่อนาย.....นามสกุล.....

เวลา(นาที)	Heart Rate(beats/min)	เวลา(นาที)	Heart Rate(beats/min)
0.00	1.7 / 5*	12.00	4.2 / 16*
0.30		12.30	
1.00		13.00	
1.30		13.30	
2.00		14.00	
2.30		14.30	
3.00	1.7 / 10*	15.00	5.0 / 18*
3.30		15.30	
4.00		16.00	
4.30		16.30	
5.00		17.00	
5.30		17.30	
6.00	2.5 / 12*	18.00	5.5 / 20*
6.30		18.30	
7.00		19.00	
7.30		19.30	
8.00		20.00	
8.30		20.30	
9.00	3.4 / 14 *	21.00	6.0 / 22*
9.30		21.30	
10.00		22.00	
10.30		22.30	
11.00		23.00	
11.30		23.30	

* speed (mph) / grade (%)

APPENDIX 6

การเตรียมตัวเพื่อเข้าร่วมการทดลอง

ชื่อและนามสกุล.....

วันที่.....

เข้าร่วมครั้งที่ **1 2 3 4**

2 วันก่อนมา	รับประทานอาหารและทำกิจวัตรตามปกติ
	จดบันทึกอาหารที่รับประทานทั้ง 2 วันนี้ในแบบฟอร์มที่แจก
1 วันก่อนมา	งดการออกกำลังกาย หรือการใช้แรงงานที่หักโหม
	งดเครื่องดื่ม แอลกอฮอล์ และเครื่องดื่มที่มีคาเฟอีน (ได้แก่ กาแฟ เครื่องดื่มชูกำลัง โค้ก/เป๊บซี่ เป็นต้น)
อาหารมื้อเย็นก่อนมา	ห้ามกินนมและผลิตภัณฑ์จากนมหรือใส่นม เช่น นม เนย
	โยเกิร์ต ครีม ไอศกรีม โอวัลติน ชอคโกแลต
	ห้ามกินผลไม้ และน้ำผลไม้ทุกชนิด
	ไม่กินอาหารดองทุกชนิด
	ไม่กินถั่วทุกชนิด
	ไม่กินอาหารย่อยยาก เช่น ตะน้า เป็นต้น

รับประทานผักได้เล็กน้อย หรือพยายามหลีกเลี่ยงผักทุกชนิด

ก่อนนอน 2 ชั่วโมง	ดื่มน้ำจำนวน 500 ซีซี ที่ให้ไป
เวลานอน	ควรนอนตามปกติ และห้ามนอนดึกเกินกว่า 4 ทุ่ม
	งดอาหารทุกชนิดจนกระทั่งมารายงานตัวที่ห้องออกกำลังกายในตอนเช้า และรับประทานอาหารได้เมื่อได้รับคำอนุญาตจากผู้วิจัย
วันเข้าร่วมการวิจัย	มาที่ห้องออกกำลังไม่เกิน 07.30 น

หมายเหตุ ***ข้อแนะนำทั่วไป***

1. *ควรหัดดื่มน้ำครั้งละ 500 ซีซี หรือ 2 แก้วปกติ*
2. *ควรฝึกซ้อมและออกกำลังสม่ำเสมอ ยกเว้นวันที่ระบุห้ามไว้*
3. *ควรปฏิบัติตัวตามข้างต้นอย่างเคร่งครัด มิฉะนั้นจะเป็นผลเสียทั้งต่อตัวท่านและการวิจัย*
4. *ท่านสามารถแลกวันและเวลาการเข้าร่วมวิจัยได้ตามความจำเป็นกับผู้เข้าร่วมการวิจัยอื่น แต่ทั้งนี้ท่านต้องแจ้งล่วงหน้าอย่างน้อย 2 วันเพื่อให้ผู้อื่นเตรียมตัวอย่างถูกต้องครบถ้วน*
5. *หากมีปัญหาหรือข้อขัดข้องติดต่อผู้วิจัยทันทีได้ทุกเวลา*

APPENDIX 7

แบบบันทึกรายการอาหารที่รับประทาน ใน 48 ชั่วโมง

ชื่อ ..... นามสกุล .....

บันทึกวันที่ .....

คำแนะนำการบันทึกอาหารในรอบ 2 วัน

1. บันทึกรายการอาหารมื้อหลักและอาหารว่างที่รับประทาน ทุกรายการใน 1 วัน
2. กรณีรับประทานอาหารสำเร็จรูปเป็นจาน ให้บันทึกปริมาณของส่วนประกอบส่วนใหญ่ที่สังเกตเห็น เช่น ข้าวผัด ส่วนประกอบคือ
   - ข้าวสวย 1 ถ้วยตวง
   - หมู 4 ชิ้น
   - ไข่ 1 ฟอง
   - ผักคะน้า 2 ช้อนโต๊ะ
3. ขนมขบเคี้ยว ให้ระบุยี่ห้อ และปริมาณที่รับประทาน (ถ้าเป็นไปได้โปรดเก็บซองที่บรรจุให้คณะวิจัย)
4. อาหารที่เป็นผลไม้ให้ระบุจำนวนชิ้น, จำนวนลูก และขนาด
5. บันทึกเครื่องดื่ม เช่น ชา กาแฟ น้ำหวาน น้ำอัดลม น้ำผลไม้ (ในปริมาณที่ไม่รวมน้ำแข็ง)

				เจ้าหน้าที่กรอก	
มื้ออาหาร/เวลา	รายการ	ส่วนประกอบ	นน./กรัม หรือ ปริมาณ	Food Code	นน.ดิบ (กรัม)

APPENDIX 8

แบบบันทึกการตรวจร่างกาย
ในวันเข้าร่วมการทดลอง

วันที่.....

ชื่อและนามสกุล.....อายุ.....ปี

เข้าร่วมครั้งที่ **1 2 3 4**

เครื่องดื่มที่ได้รับ **A B C D**

1. การตรวจร่างกายทั่วไปก่อนการทดลอง (หลังการปัสสาวะแล้ว)
   - น้ำหนัก.....กิโลกรัม
   - ชีพจร.....ครั้งต่อนาที
   - หายใจ.....ครั้งต่อนาที
   - ความดันโลหิต...../..... mmHg
   - อุณหภูมิ.....องศาเซลเซียส

2. การซักประวัติ
   - ในรอบ 1-2 อาทิตย์ที่ผ่านมาท่านมีความเจ็บป่วยหรือไม่ (ระบุชนิด / เวลาที่เป็น)

_____

_____

_____

_____

- ในรอบ 1-2 อาทิตย์ที่ผ่านมาท่านได้รับประทานยาใดหรือไม่ (ระบุชนิด / ปริมาณที่รับประทานใน 1 วัน)

_____

_____

_____

_____

_____

3. การตรวจร่างกายหลังการทดลอง

ก. เวลาที่บันทึก.....น.

- น้ำหนัก.....กิโลกรัม (ก่อนการปัสสาวะ)
- ชีพจร.....ครั้งต่อนาที
- หายใจ.....ครั้งต่อนาที
- ความดันโลหิต...../..... mmHg
- อุณหภูมิ.....องศาเซนเซียส

ข. เวลาที่บันทึก.....น.

- น้ำหนัก.....กิโลกรัม (หลังการปัสสาวะ)

APPENDIX 9

The RPE Scale

ชื่อ.....นามสกุล.....

อายุ.....ปี

วันที่.....ชนิดของเครื่องดื่ม A B C D

A 15-grade scale for ratings of perceived exertion, The RPE scale from Borg 1982 (Astrand 1991).

Score	เวลา 09.30	เวลา 10.00	เวลา 10.30	Subjective Rating
6				
7				Very very light
8				
9				Very light
10				
11				Fair light
12				
13				Somewhat hard
14				
15				Hard
16				
17				Very hard
18				
19				Very very hard
20				

APPENDIX 10

แบบบันทึกอาการผิดปกติในทางเดินอาหาร

ชื่อ.....นามสกุล.....

วันที่..... เข้าร่วมการทดลองครั้งที่ 1 2 3 4

ชนิดของเครื่องดื่ม A B C D

ครั้งที่ (เวลา)	อาการ												
	ปวดท้อง/ เสียดท้อง			เรอ/ ผายลม			คลื่นไส้/ อาเจียน			อาการอื่นๆ			หมายเหตุ
	1	2	3	1	2	3	1	2	3	1	2	3	
08.00 น													
08.30 น													
09.00 น													
09.30 น													
10.00 น													
10.30 น													
11.00 น.													
11.30 น													

0 ไม่มีอาการ

1 อาการเล็กน้อย

2 อาการปานกลาง

3 อาการหนัก

BIOGRAPHY

NAME	Capt. Jeeranun Suwanwaree
DATE OF BIRTH	May 15, 1962
PLACE OF BIRTH	Nakorn Nayok, Thailand
INSTITUTIONS ATTENDED	Chiangmai University, 1980-1984 Bachelor of Science (Nursing & Midwifery) Mahidol University, 1987-1989 Master of Science (Public Health Nutrition) Mahidol University, 1996-2000 Doctoral of Science (Nutrition)
POSITION & OFFICE	1984-1991, Nurse, Thai Army Hospital, Bangkok, Thailand 1991-1996, Nursing Instructor, Assumption University, Bangkok, Thailand