CHAPTER 5

CONCLUSION

In this work, Ontology-based Expert system for a generic drug Production of Immediate Release Tablet (OXPIRT) has been proposed. The system has been particularly implemented to assist those pharmacists who attempt to produce a generic drug tablet that is pharmaceutically equivalent to its original product. OXPIRT is also designed to recommend a production of herbal tablet which is only made from herbal powder, as well. Aside from existing expert systems in pharmaceutical field, OXPIRT can be claimed that it is the first expert system which is developed for generic drug production and focused on pharmaceutical equivalence. Moreover, it has been implemented as web based application for easy access and worldwide usage. To help a novice pharmacist, the output of the system is a list of all ingredients with their particular amount, a manufacturing process and a sequence of instruction. In case of the non-pharmaceutically equivalent recommended output, tablet producer can fill in a dissolution profile of the fail tablet alongside its quality control information to OXPIRT for another improved output.

To cover both generic drug tablet production and herbal production, OXPIRT consists of three parts: 1). pharmaceutical tablet production ontology (PTPO); 2). decision rules and 3). intelligent system.

The PTPO is a knowledge stored relevant details of tablet production in ontology representation. In PTPO, a general knowledge related to tablet ingredients

and their properties is kept following a Handbook of Pharmaceutical Excipients. Beside, information of the original product from patent and literature reviewing is also written in PTPO. With this two types of knowledge, PTPO is designed to share ingredient class, role class (function of ingredient based on weight) and relation class as a schema. Into PTPO, the data of each class are instantiated with an ingredient name, its functions, its range amount between minimum and maximum, its properties and the compatibility of ingredients. In total, forty one classes, five relations and ten role concepts are designed for PTPO.

The decision rule is a set of production rules that assists the system to resolve a recommendation based on the knowledge in PTPO and criteria from input. It is written in an if-then format which is only executed once the condition is exactly met. However, the set of rule is split into two; rule for generic tablet generation and rule for improving the recommendation. The rule for generic tablet generation is a set of rule only related to decide an amount of each ingredient, a manufacturing process, and manufacturing instructions. Differently, the rule for improving the recommendation is only applied once the recommendation of OXPIRT is brought to action and result non-pharmaceutical equivalence. The improving rule attempts to adjust an amount of some excipients that relate to a problem or add another excipient to commit a better recommendation based on the equivalence and quality control laboratorial testing result.

With the previous two mentioned parts, OXPIRT takes the knowledge to infer a recommendation precisely. Jess inference engine is exploited in the system to act as a brain to assign a yet unknown value of each excipient, process and instruction. Aside of inference engine to generate a generic tablet formulation, OXPIRT includes

a module to compute a pharmaceutical equivalence between the recommended produced tablet and its original tablet according to a difference factor (F_1) and similarity factor (F_2) of both tablets' characteristics.

To test an ability of OXPIRT on generic drug tablet production, four original drug tablet samples were selected. They were selected based on two factors: 1). a percentage weight of API (active pharmaceutical ingredient) compared with tablet weight and 2). a solubility of API. From these two factors, four original tablets were chosen as follows: 1). metformin hydrochloride (Glucophage®); 2). paracetamol (Tylenol®); 3). hydroxyzine hydrochloride (Atarax®) and 4). atorvastatin calcium (Lipitor®). With OXPIRT's recommendation, the generic productions of the first three samples were correctly given in the first attempt in terms of pharmaceutical equivalence and quality control.

However, the first attempt on generic production of atorvastatin calcium tablet was not acceptable since it is not pharmaceutically equivalent to the original one for its different dissolution profile and disintegration time. For second attempt, OXPIRT ignored to adjust an amount of solubilizer since it was already set to optimum. It; however, chose to add another wetting agent excipient for a half amount of current solubilizer and reduced amount of another solubilizer to half for improving dissolution profile. In the point of disintegration time, OXPIRT went differently since it found out that the disintegrant was already set to maximum, but one of another given excipient can perform as a role of disintegrant if the amount can be set higher. Therefore, it increased that excipient amount to improve a disintegration time. The third attempt finally made the produced tablet to become pharmaceutical equivalence.

In conclusion of testing a production of generic drug tablet, OXPIRT can significantly recommend a correct formulation and instruction for successful generic drug production. This confirms that OXPIRT works well in terms of reducing time consuming and expertise requirement for suggesting a production of generic tablet. It is also easy to use since only information and characteristic of original product are required to fill in, and formulation and instruction are returned automatically. In addition, it can intelligently improve a fail result to another better result for reducing a burden of pharmacists on finding an error original by their own.

From evaluating herbal tablet productions, two samples which are ginger and Fa-tha-lai-chon are selected. Both of them were recommended with a formulation and instruction. Since herbal tablets do not need a pharmaceutical equivalence due to no original tablet to compare with, standards of quality control are mainly focused including weight variation, disintegration time and friability. Recommendations of those two samples were produced into tablets and tested against standards. They were both passed the quality control in the first attempt. Without other criteria, all excipients assigned in formulation are all selected based on rule. Note that the suggested formulations are not the only acceptable formulations, but other possible formulations for those herbal tablets are widely open.

The Ontology-based Expert system for a generic drug Production of Immediate Release Tablet (OXPIRT); however, still have a limitation. It can be expanded to serve another pharmaceutical dosage form by adding more information and data into knowledge represented in ontology. For improving system performance, the system might perform better if experts design more on the excipient information for its major and minor function since OXPIRT limits a function of excipients in drug

formulation to one function for each. Moreover, current system requires a lot of expertise knowledge to review a patent of original product and a load for expertise to inform ontology which role of each excipient can be. It is better to find an automatic tagging system for assigning a role on each drug's excipient to reduce such burden of experts.