Preliminary Evaluation of *Halal* Status in Respiratory, Immunological Products and Vaccines in Malaysia

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ABSTRACT

Introduction: Muslim consumers and patients are showing a growing interest on the *halal* (permissible) status of pharmaceuticals. This descriptive study was done to explore the *halal* status of selected respiratory and immunological products, and vaccines available in 2 government hospitals in Malaysia.

Methodologies: The *halal* status of products was determined based on the sources of their active pharmaceutical ingredients (API) and excipients. Information regarding sources of active ingredients and excipients was obtained from product leaflets, feedback from manufacturers and standard references such as US Pharmacopeia, British Pharmacopeia and Merck Index. These products were categorized as *halal, mushbooh* (dubious) or *haram* (prohibited) based on their contents.

Results: There were 123 medications included in this study (91 were respiratory products while 32 were immunological products and vaccines). Out of 91 respiratory products, 56% were *halal*, whereas 44% were *mushbooh*. Out of the 32 immunological products and vaccines, 96.9% were *mushbooh* and one product was *haram*. No *halal* product was found under immunological products and vaccines in this study. There was 49 API in respiratory products and 79.6% were considered *halal* and 20.4% were *mushbooh*. From 124 excipients used, 83.1% were *halal* and 16.9% were *mushbooh*. Under the immunological products and vaccines, from 32 products analysed, 96.9% were *mushbooh* and 3.1% were *haram*. As of the 42 APIs under this product category, 100% were *mushbooh*. From the 52 excipients, 57.7% were *halal*, 40.4% *mushbooh* and 1.9% *haram*. Lactose, magnesium stearate, ethanol, polysorbate 80 and amino acids are the most common *mushbooh* ingredients. *Haram* ingredients were of porcine origin.

Conclusion: This study concluded that although most excipients are *halal*, but the status of medicines becomes *mushbooh* due to the presence of certain excipients which may actually be replaced with *halal* alternatives.

Keywords: *Halal* pharmaceuticals, active pharmaceutical ingredients, excipients

INTRODUCTION

Products which comply with the *halal* concept are widely accepted by communities as they are considered safe, of high quality and prepared with hygienic procedures (Azmi & Hadeer Akram, 2013). *Halal* pharmaceutical products should not only be free from *haram* (non-*halal*) constituents, but they should also be thoyyib, a term given to goods and products which meet certain quality standard and are considered as clean according to Shariah Law (Waarden & Dalen 2010). A previous study has shown that 26% of the 50 Muslim patients in a UK primary care setting would take a medicine even if they were unsure as to whether it was *halal* or not, 42% of patients stated that they would not take the medications if they were not sure it were *halal*, and 58% of them stated that they would stop taking the medication if they found out it was *haram* (Bashir et. al., 2001). Hence this indicate that *halal* status of medicines is as important as *halal* status of food.

The term *halal* refers to 'lawful or permitted' under the Shariah Law (Islamic rules). *Haram* is the opposite of *halal* which means unlawful or forbidden. However, there is one category that falls between *halal* and *haram*

which is referred to as *mushbooh*. *Mushbooh* means doubtful or suspicious. Products categorized as *mushbooh* are questionable because the origin of some or their constituents may be unknown, possibly containing products from unacceptable animal sources such as porcine (Jusmaliani & Nasution, 2009). The consumption of pharmaceutical products which result in hazardous effects to the patient is also not allowed in Islam. The balance between benefit and harm to treatment modalities should be considered (Kasule, 2002).

Respiratory medications are defined as the prescription drugs for conditions and diseases relating to the lungs or breathing. Usually powder or solution is used together with special device designed to carry the drugs to the target site effectively (Abdul Aziz et. al., 2014). The immune system and immunological products play a critical role in defending the human body against pathogenic organisms (Marcos et. al., 2003). Vaccines are preparations of antigenic materials that are given with the object of inducing in the recipient active immunity to specific infecting agents or toxins. They may contain living or killed micro-organisms, bacterial toxoids, or antigenic materials from particular parts of the infecting organism, which may be derived from the organism or produced by recombinant DNA technology (Martindale, 5th edition).

Religious and moral objections to vaccination are the key in understanding vaccine refusal today. Opposition to immunization programs of selected Muslim communities was detected during the poliovirus immunization programs in Nigeria, Pakistan and Afghanistan in 2003 (Warraich, 2009). Ultimately it falls upon Muslims in the pharmaceutical profession to carry out research into this issue and come up with *halal* alternatives for active ingredients or excipients, so that the question of the dubious nature of medicinal ingredients does not arise. Responsibility also falls on the rest of the society to lobby for the use of *halal* ingredients in medicinal preparations (Gambles, 2010).

This study was carried out to assess the *halal* status of respiratory products, immunological products and vaccines available with regard to their APIs and excipients where sources of APIs and excipients were identified and classified into *halal*, *mushbooh* or *haram*. Also, to identify common types of ingredients that are categorized as *haram* and *mushbooh*.

METHODOLOGIES

This descriptive exploratory study was done in two government hospitals located in Klang Valley. After getting approval from the hospitals, the hospital formulary was obtained, and products screened and sorted out according to the selected therapeutic areas of the study. Data were collected from product information leaflets and packages which are available at the pharmacy store, and the in-patient and out-patient pharmacy. The collected data such as generic name, brand name, dosage form, strength, APIs, excipients and manufacturer were filled into developed Data Collection Form.

There were two approaches used to obtain details about the products. The first was through enquiry letters and response forms sent to respective manufacturers to be completed with the details regarding the products. They were also required to provide *halal* certificates to prove the ingredients used were *halal*. The feedback received from the manufacturers about the source of ingredients was included in the data collection form as the first priority. If the manufacturers did not respond within the research period, the analysis was performed using the second approach.

Through the second method, the source of each active ingredient and excipient was determined by using the standard pharmaceutical references such as British Pharmacopeia, *Halal* Index, Merck, Martindale, Excipient Handbook, Remington and US Pharmacopeia. Sources of ingredients were classified into eight main categories, namely plant, animal, synthetic, semi-synthetic, natural chemical, mineral, microorganism and Genetically Modified Organism (GMO). They were then classified into *halal*, *mushbooh* or *haram* following guidelines and definition in MS2424:2012, *Halal* Pharmaceuticals-General Guideline.

The *halal* status of pharmaceutical products would depend on *halal* nature of active ingredients and excipients. If both APIs and excipients were *halal,* the product would be categorized as *halal*. If APIs or excipients consist of *mushbooh* then the product would be categorized as *mushbooh*. If any of these is of *haram* origin, the product would be classified as *haram*. The same product found in both hospitals was regarded as one product. The data collected were analysed using Microsoft Office Excel and Google document where descriptive analysis involving frequencies and percentages were generated to present the results of the analysis.

RESULTS AND DISCUSSIONS

There were 123 medications considered in this study; 91 respiratory products, and 32 immunological products and vaccines. For the respiratory products, 56% (N=51) were considered *halal* and 44% (N=40) *mushbooh*. There was no *haram* product reported. With regard to 49 APIs contained in the 91 products, 79.6% (N=39) were reported as *halal*

while 20.4% (N=10) *mushbooh*. On the other hand, of the 124 excipients analysed, 83.1% (N=103) were found to be *halal* and 16.9% (N=21) *mushbooh*.

Of the 32 immunological products and vaccines, 96.9% (N=31) were reported as *mushbooh* and 3.1% (N=1) *haram*. There was not a single *halal* product in this product category. On the 42 APIs of the 32 products, 100% were *mushbooh*, i.e., there were no *halal* or *haram* APIs reported. However, from 52 excipients studied, 57.7% (N=30) were reported as *halal*, 40.4% (N=21) *mushbooh* and 1.9% (N=1) *haram*. Table 1 summarizes the *halal* status of the respiratory products, immunological products and vaccines.

Table 1: Summary of *halal* status of the respiratory products, immunological products and vaccines

Status	*Halal*	*Mushbooh*	*Haram*
Respiratory products (N = 91)	56%	44%	0%
API respiratory (N = 49)	79.6%	20.4%	-
Excipients (N = 124)	83.1%	16.9%	-
Immunological products and vaccines (N = 32)	-	96.9%	3.1%
API respiratory (N = 42)	-	100%	-
Excipients (N = 52)	57.7%	40.4%	1.9%

This study showed that generally most of the respiratory products were *halal* followed by *mushbooh*. No *haram* products were indicated under the respiratory product group. However, there was no *halal* option among immunological products and vaccines. The majority of immunological products and vaccines were *mushbooh*, while one product was *haram*.

Halal and *haram* are clearly stated and defined in the Quran (Azmi & Hadeer, 2013). Even though respiratory pharmaceutical products or medications are among the most commonly used products in the community and hospital settings, Muslims are required to avoid any food or medication that originates from doubtful sources. Products which contain questionable or unknown sources of ingredients are classified as *mushbooh* depending on the nature of the product and how it is made. For instance, lactose was found to be the major substance that contributed to the assertion of *mushbooh* category in this study. According to a previous study, lactose is a *halal* substance but because some of the preparation processes involve the use of bones or bone related substances, it is categorized as mushboo (Waarden & Dalen, 2010). In this study, only three companies clarified that lactose used in their products were derived from *halal* sources which were Noripharma Sdn. Bhd., Malaysian Pharmaceutical Industries Sdn. Bhd. and UPHA Pharmaceutical (CCM) Sdn. Bhd.

Another example of *mushbooh* substance found in this study was magnesium stearate. Magnesium is one of the most widely used lubricants in the tablet production of pharmaceutical products (Bashir et al., 2001). It can be obtained either from plant or animal, or both sources. Due to the uncertainty of its origin, the *halal* status of magnesium stearate has become controversial. Other than that, products containing alcohol as excipients are also categorized as *mushbooh*. It is known that ethanol can be derived from two processes, either synthetically produced from the laboratory or naturally from winemaking processes. Alcohols obtained from the winemaking industry are forbidden in Islam while alcohols which are purely synthesized from laboratory are considered permissible (Jusmaliani & Nasution, 2009).

Also, gelatine is widely used as a binding agent for tablets, pastilles, micro-encapsulation and sugar-coated pills in the pharmaceutical industry (Kasulse, 2002). The most widely used gelatines originate from porcine and bovine sources. Since gelatine is derived from animal bones, skin and tendons, it is likely to be *haram* unless it is from animals or birds that are allowed to be eaten by Muslims, and which have been slaughtered in a *halal* way (Abdul Aziz et al., 2014). However, there are some alternatives available that can be used to replace the animal-based gelatine such as plant-based gelling substances which include Carrageenans (carrageenins), agar-agar (seaweed), pectin or modified forms of starch and cellulose. Another alternative is to use Hypromellose (HPMC; E-Number: E464) isolated from natural sources such as plant materials or bacterial cell cultures (Gambles, 2010).

CONCLUSION

This study indicated that most excipients were *halal*, but medicines became *mushbooh* due to the presence of certain excipients which could have been replaced with *halal* alternatives. This insight should encourage pharmaceutical manufacturers to go for *halal* certification to meet the demand for *halal* medications. This study also provides additional information from existing research regarding *halal* pharmaceutical products available in Malaysia. It may also serve as a platform for future researchers to explore other aspects that were not covered in this study such as *halal* compliance during manufacturing and preparation processes, and the potential harmfulness of the pharmaceutical products.

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