

PORCINE AND BOVINE-DERIVED INGREDIENTS: ISLAMIC RULES IN HALAL PHARMACEUTICAL PRODUCTS

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ABSTRACT

For Muslims, ingesting or utilising any products derived from porcine is forbidden as it is considered unclean. Besides, although bovine is halal to be consumed, this ruling is only applicable if it is slaughtered strictly according to Islamic law (Shari'ah). Given Islam's imposing certain restrictions on the consumption of porcine- and bovine-based products, for Muslims who are seeking medication, this could limit their therapeutic options as many pharmaceutical products are sourced from both animals. This will eventually make it difficult for them to get treatment and will endanger their lives. Hence, every Muslim must have knowledge and understanding of the views of Islamic jurists (Fuqaha') regarding the Islamic rules on pharmaceutical products containing porcine- and bovine-derived ingredients. In this article, a clear narration regarding porcine and bovine-derived pharmaceutical products, accompanied by a review of Islamic rules based on Islamic jurists, is presented.

Keywords: Halal, halal pharmaceuticals, porcine, bovine, non-halal ingredients

1. INTRODUCTION

Islam imposed certain laws and restrictions upon its followers not to burden their everyday lives but for their benefit. The restriction applies to the consumption and use of haram animals and their derivatives for any purpose, including foods and pharmaceutical products. In principle, the prohibition of ingesting pork is to take care of cleanliness and purity (*taharah*) for the sake of our health as well as for the environment since cleanliness is an essential component in Islam (Mohd Kashim et al., 2015). Consuming only halal and *toyyib* foods and pharmaceutical products can keep us away from getting

diseases, and more importantly, it is an act of obedience and worship to Allah SWT (Wan Chik and Ali, 2015). In the command of prohibition, Allah SWT tests us with the act of leaving those things and not practising them (Nurdeng 2009). In addition, it is important to reflect on and take lessons from the living creation of those animals. For example, we can observe how pigs live their lives and take lessons from them, which can remind us to always practice good hygiene in our daily lives.

Muslims should always be aware of and careful with anything that enters their bodies. Having awareness and knowledge about halal and haram are important not only when consuming food, but also when taking medicines. They should not treat their illnesses with haram materials and their derivatives. This has been mentioned by the Prophet Muhammad (peace and blessings be upon him), according to the hadith reported by Abu Darda', *"God has sent down both the disease and the cure, and He has appointed a cure for every disease, so treat yourselves medically, but use nothing unlawful."* In a situation when something is doubtful, Muslims should be careful and better not consume it. This is similar to pharmaceutical products that contain ingredients whose halal status is unclear. Al-Hasan ibn Ali reported that the Messenger of Allah (peace and blessings be upon him) said: *"Leave what makes you doubt for what does not make you doubt."* *The grade of this hadith is Sahih (The Book of Drinks, n.d.).*

In modern medicine, Muslims seem to be unable to escape from animal-based materials mainly derived from pigs and cattle since they play crucial functions either as main ingredients or aiding substances in many pharmaceutical products (Hassanein & Anderson, 2020). The common porcine- and bovine-derived ingredients that can be found in many pharmaceuticals include gelatin, collagen, insulin, pancreatic enzymes, and heparin. This has been a major concern when they must deal with medicines that contain non-halal animals.

In Malaysia, two reference documents shall be the guidelines for halal pharmaceuticals, namely Malaysian Standard (MS) 2424:2019 Halal Pharmaceuticals - General Requirements (First revision), and the User Guide of Medicines Containing Non-Halal Sources for Muslim Patients at Ministry of Health Malaysia (*Panduan Penggunaan Ubat-Ubatan Yang Mengandungi Unsur Tidak Halal Kepada Pesakit Muslim Di Kementerian Kesihatan Malaysia*). Halal pharmaceuticals are defined as products that contain ingredients permitted under *shari'ah* law and fatwa and do not contain any parts or products of animals that are non-halal or any parts or products of animals that are not slaughtered according to *shari'ah* law and fatwa (MS 2424:2019). Generally, MS 2424:2019 describes the general requirements for the manufacturing and handling of halal pharmaceuticals, whereas the user guide is the reference for

clinical practitioners about the use of medicine containing non-halal ingredients. In this article, we aim to review the common porcine and bovine-based ingredients namely gelatin, collagen, insulin, pancreatic enzymes, and heparin used in the manufacturing of pharmaceutical products and how Islam rules on this matter.

2. LITERATURE REVIEW

Gelatin, collagen, insulin, pancreatic enzymes, and heparin are substances used as ingredients in pharmaceutical products. The sources of these ingredients are from animals, mainly porcine and bovine. Nevertheless, Muslim consumers are still lacking in awareness and knowledge about the ingredients and manufacturing process of halal pharmaceuticals, making it difficult to choose products for their usage (Saha et al., 2019).

2.1 *Collagen and gelatin*

Collagen is a protein found in humans and animals but cannot be found in plants (Silvipriya et al., 2015). The majority of collagen is derived from porcine and a small percentage from other animals, including cows, chickens, kangaroos, rats, alligators, and sheep. Porcine collagen is a major concern among Muslim consumers. The concern about bovine collagen is due to the outbreak of bovine diseases such as bovine spongiform encephalopathy (BSE), and foot-and-mouth disease (FMD) which can also cause an allergic reaction (EFSA et al., 2020). Recently, marine animals have been researched to substitute porcine and bovine collagen since they also exhibit more advantages than land animal sources (Coppola et al., 2020). Collagen exhibits unique features such as weak immunogenicity, antigenicity, biodegradability, and biocompatibility, making it suitable for many industrial applications (Sangeetha et al., 2020). Collagen is widely used in the manufacturing of pharmaceutical drugs and devices, mainly in the drug delivery system (Chak, 2013). Collagen is also used as a wound dresser as it can strengthen the wound (Sangeetha et al., 2020).

The main product of collagen is gelatin, a natural polymer of highly purified protein (Alipal et al., 2021). Gelatin is made up of 18 varieties of complex amino acids, predominantly about 57% of glycine, proline, and hydroxyproline, while the remaining 43% are other distinguished amino acid families such as glutamic acid, alanine, arginine, and aspartic acid (Alipal et al., 2021). To obtain gelatin, collagen is subjected to an extraction process either acidic or alkaline treatment at high temperature and pressure conditions (Karim & Bhat, 2008). During the treatment, the fibrous structure of collagen is degraded, cross-linkages between different polypeptide chains develop, and the formation of gelatin occurs

(Karim & Bhat, 2008).

Gelatin exhibits appealing properties like gelling, stabilising, healing, ointment, capsule, and coating, widely used in food, pharmaceutical, and cosmetic products. (Alipal et al., 2021). Gelatin is used in the application of drug delivery systems (Foux & Zilberman, 2015), and the making of hard and soft capsule shells, tablets, granulation, and syrups. In addition, gelatin acts as a stabiliser in the vaccine manufacturing process (Gomez & Robinson, 2018). About 46% of the gelatin sources are pig skin, 29.4% are cow skin, 23.1% are bone, and only 1.5% are from other sources (Karim & Bhat, 2008). The use of porcine and bovine gelatin has become a heated debate, particularly among Muslim consumers. Bovine gelatin is mostly avoided because of doubts about its slaughtering method. Therefore, fish gelatin has now been given attention and pharmaceutical products containing gelatin made from fish are more receivable because the source is permissible (Ali et al., 2017).

2.2 *Insulin*

Insulin is a polypeptide hormone produced in the pancreas of animals and humans (Kamour et al., 2020). Insulin consists of 51 amino acids comprising two polypeptide chains, A (with 21 amino acid residues) and B (with 30 amino acid residues) (Dagasan & Erbas, 2020). Insulin is essential in the regulation of carbohydrate metabolism which functions to transport blood sugar glucose into the body cells, where it will be utilised for energy afterwards (Kamour et al., 2020). When the body is unable to produce sufficient insulin or cells in the body stop responding to insulin, a disease called diabetes mellitus arises, and these are the conditions where insulin therapy is required (Ahmad, 2014). At an earlier time, the source of insulin was obtained from the dog's pancreas (Quianson & Cheikh, 2012). Due to the effectiveness of dog insulin, animals were widely used in the process of making insulin, and porcine and bovine were mostly used (Kumar & Bhat, 2003). However, this has led to shortages in animals because the clinical demand for insulin is constantly increasing (Landgraf & Sandow, 2015). In consequence, the use of animal insulin is declining and has been replaced with human insulin (Hirsch et al., 2020).

As the source of insulin is porcine, its consumption is prohibited in Islam. Meanwhile, in the case of bovine insulin, although Islam does not prohibit its consumption, the cattle slaughtering process is doubtful, whether it is by the provisions of *shari'ah* law or not. Semisynthetic insulin was introduced with a modification of animal insulin (Zieliński et al., 2019). The insulin used in clinical settings is a recombinant human insulin made by recombinant DNA (rDNA)

technology, replacing both animal and semisynthetic insulins (Sandow et al., 2015). Nowadays, the actual human insulin gene has been replaced with the cloned human insulin gene through the proinsulin gene cloning method (Riggs, 2021). The insulin is free from animal materials, which is acceptable in Islam.

2.3 *Pancreatic Enzymes*

Pancreatic enzymes are enzymes made by the animal pancreas mainly protease, amylase, and lipase which function to digest protein, starch, and fat from food (Ketwaroo & Graham, 2019). The enzymes are widely used in pharmaceuticals, foods and beverages, detergents, and chemicals (Chapman et al., 2018). Proteases (trypsin, pepsin, and chymotrypsin) are the most used in the pharmaceutical industry for example in the vaccine production process as cell dissociating agents to remove adherent cells from a culture surface before harvesting (Vaidya et al., 2016).

Some Muslims are sceptical about getting vaccinated due to the use of porcine or bovine trypsin in vaccine production (Mardian et al., 2021). For example, COVID-19 vaccine, Ulama (clerics) issued fatwas (decrees) to provide clear guidance and avoid confusion among Muslims. In Indonesia, Sinovac is the only vaccine that was granted a halal certificate by the Indonesian Ulama Council (MUI), as they claimed that porcine trypsin or other animal enzymes were not included during its manufacturing process (Majelis Ulama Indonesia, 2021). Meanwhile, Pfizer, AstraZeneca, and Sinopharm have been issued as haram-permittable as porcine trypsin has been used, but their use is permissible during emergencies (Majelis Ulama Indonesia, 2021). On the other hand, the fatwa committees of the National Council for Islamic Religious Affairs Malaysia issued a fatwa stating that the use of the COVID-19 vaccine is permissible and its use is obligatory for certain groups of people (Ismail & Baharuddin, 2022). There has been research recommending the replacement of trypsin with accutase, an enzyme from invertebrate animals that can serve a similar function as a cell-dissociating agent (Mohamad Ros et al., 2020; Arifin, 2010).

2.4 *Heparin*

Heparin is used as an anticoagulant drug, a medicine used to prevent blood clot formation for the treatment and prevention of diseases related to anticoagulation problems, for example, deep vein thrombosis and pulmonary embolism (Onishi et al., 2016). Heparin can be extracted from animals' lungs, liver, ileum, skin, lymph, and thymus, mostly from pig intestines and some from cows and sheep (Kouta et al., 2019).

There are 3 classes of heparin used clinically: unfractionated heparin (UFH), low molecular weight heparin (LMWH), and ultra-low molecular weight heparin (ULMWH) (Lindhart & Liu, 2012). UFH is produced from both porcine and bovine, where the porcine intestine is the most common source (Oduah et al., 2016), while LMWH is merely sourced from porcine (Awang et al., 2019;). ULMWH is manufactured by chemical synthesis and is free from animal components (Oduah et al., 2016). LMWH used in clinical settings are clexane (enoxaparin), dalteparin, tinzaparin nadroparin, certoparin, parnaparin, reviparin, and bemiparin (Qiu et al., 2021). Compared to UFH and LMWH, ULMWH is considered the best anticoagulant because it has high consistency and controllability (Qiu et al., 2021). The most common ULMWHs are fondaparinux (arixtra), AVE5026, and RO-14 (Liu et al., 2014). Arixtra was decided permissible to be used as an alternative to enoxaparin (clexane) by the Fatwa Committee Muzakarah of the National Council for Islamic Religious Affairs Malaysia due to the source of clexane, which comes from pigs, and concern on some ethical issues.

3. FIQH DISCUSSION

There are five main objectives of Islamic law (also known as *maqasid al-shari'ah*), which are the protection of religion, life, intellect, lineage, and wealth (Al-Khadimiy, 2001). Based on the order of priority, the protection of religion is the first and primary objective (Al-Khadimiy, 2001). Taking care of health is the one under the protection of life and comprises the preservation of health, and intellect from harm and death (Wan Muhammad et al., 2016). Thus, seeking medication is obligatory for Muslims who suffer from illnesses. As the protection of religion comes first, the religious aspect needs to be taken into consideration before consuming any medication to protect life (Ahmad Sarkawi et al., 2017). Based on the application of fiqh, there are two conditions to determine the status of pharmaceutical products that contain unclean materials, either halal or haram, which are the Darurah situation (state of emergency), and *istihalah* or *istihlak* (Figure 1).

3.1 *Darurah Situation*

Darurah is a situation when one encounters destruction, harm, or risk that can lead to death (Zuhayli, 1997). Darurah can happen when consuming medicines that contain non-halal sources in conditions where i) the patient's health will be at real risk if he or she does not take the medicines containing non-halal ingredients, ii) there are no halal medicines available, and iii) the absence of halal medicines is proven by qualified and reliable Islamic medical

experts (Yusuf Al-Qaradawi., 1980). The fatwa committees of the National Council for Islamic Religious Affairs Malaysia (MKI) (Rosman et al., 2020), Indonesian Ulama Council (MUI) (Mardian et al., 2021), United Arab Emirates Fatwa Council (UAE Fatwa Council, 2020) and most Saudi Arabian Muslim scholars (Zainul Abidin, 2019) are among those who incline toward the darurah principle. They issued fatwas stating that medicines that are produced with unclean ingredients are prohibited from being consumed unless no halal medicines are available and a darurah situation takes place during that time.

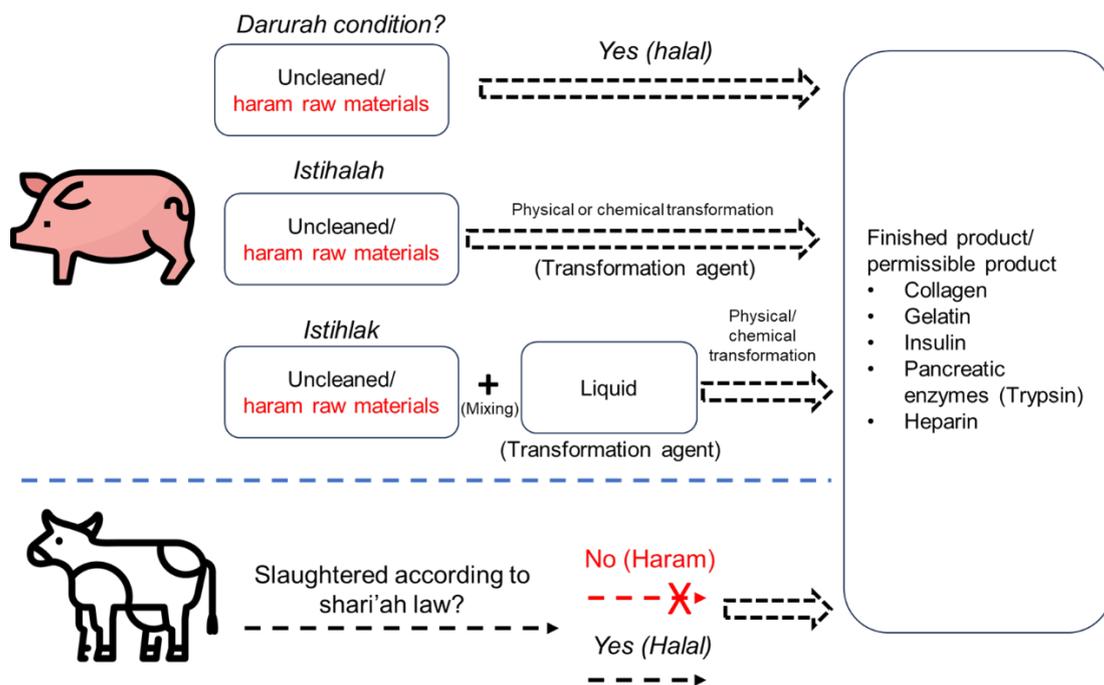


Figure 1. Conditions that allow the use of pig and bovine products and their derivatives in pharmaceutical products. For porcine, two conditions are darurah and istihalah, whereas, for bovine, the animal must be slaughtered according to shari'ah law.

3.2 Istihalah and Istihlak

The application of *istihalah* and *istihlak* methods is supported by the European Council of Fatwa and Research in determining the status of medicines that contain non-halal substances (European Council of Fatwa and Research, 2003). For example, the council claimed that a polio vaccine composed of pig trypsin is permissible. The decision justified the fact that halal components in the vaccine are more dominant than the haram component (porcine trypsin), eventually resulting in a halal vaccine (Rosman et al., 2020; Mamat, 2021).

Istihalah means a transformation, either by physical or chemical process, from filthy or unclean material to pure material, involving the change of the material's properties and characteristics (Zuhayli, 1997). Whereas *istihlak* gives a more specific definition, the loss of properties and characteristics of the original material as a result of being dissolved in a larger quantity of water or liquid, ultimately resulting in a change of ruling (Hukm) (Mamat, 2019). In fact, *istihlak* is a part of *istihalah* (Al-Qaradaghi, 2017). *Istihalah* consists of three elements: raw material, conversion or transformation agent, and finished product (Figure 1) (Jamaludin et al., 2011; Rosman et al., 2020). For example, in the transformation process of alcohol into vinegar, the raw material is ethanol, the conversion agent is the natural condition (oxygen), and the finished product is acetic acid or vinegar. The prohibited raw material (ethanol) has undergone physical and chemical changes in terms of odour, taste, and colour and changed to vinegar completely (Jamaludin et al., 2012; Rosman et al., 2020).

There are different opinions on the application of *istihalah* among the four Islamic schools of thought. The Syafi'ie and Hanbali schools of thought viewed that *istihalah* could only be applied if the process is a natural transformation, for example, the natural transformation of alcohol to vinegar, but not transformations that involve synthetic processes (Al-Syarbini, 1994). Both persisted that inherent filth (najis al-ayn) such as pigs do not apply the *istihalah* method although it has undergone conversion that transforms it into a clean product (Ibn al-Naqib, 1982). In contrast, the Hanafi and Maliki schools of thought accepted that *istihalah* can occur in both natural and synthetic processes of transformation (Ibn Taymiyyah, 2005). Both agreed that all unclean or haram materials can turn into clean materials when undergoing the *istihalah* process taking into consideration the common plight (Al-Zayla'iy, 1984).

Istihalah has been used in determining the halal status of pharmaceutical products in most countries with a Muslim minority population. For example, the European Council of Fatwa and Research issued fatwas stating that products that are produced from unclean or haram animals, if they have undergone chemical transformation, then they have turned into clean and halal products (Mamat, 2021). On the contrary, Malaysia has different views on the application of the *istihalah* method when discussing halal issues related to pharmaceutical products that are prone to implement darurah conditions (Table 1). The issuance of fatwas does not apply the principles of *istihalah* and *istihlak*. Muftis are required to prioritise qawl muktamad (final opinion) from asy-Syafiiyyah school of thought when issuing a fatwa, based on the guidelines for fatwa issuance in Malaysia (Garis Panduan Pengeluaran Fatwa di Malaysia. (2017). The prioritisation of qawl refers to the view of the asy-Syafiiyyah school of thought that the limitation of both *istihalah* and *istihlak* to merely certain

issues is preferred when issuing fatwas regarding products that are sourced from haram substances (Mamat, 2019).

Table 1. Example of Malaysian fatwas on pharmaceutical products containing non-halal ingredients from porcine and bovine.

Issue	Muzakarah, year	Fatwa
Injection of highly purified porcine insulin	The 6 th Muzakarah, 1983	Permissible to inject and to be injected in a <i>darurah</i> situation for the treatment of diabetes mellitus
Gelatin in medicines	The 8 th Muzakarah, 1984	Permissible due to <i>darurah</i> situation. Haram if there are halal materials that can execute the similar function of gelatin
Rubella vaccine	The 21 st Muzakarah, 1988	The vaccine is not najis (ritually impure); the injection is permitted.
Hepatitis-B vaccine	The 22 nd Muzakarah, 1988	The source of vaccine from yeast and not Najis; the injection is permitted.
Meningococcal Meningitis Mencevax vaccines	The 53 rd Muzakarah, 2002	The source of the vaccine from cattle; the injection is permitted.
BioThrax and Rotateq vaccines	The 81 st Muzakarah, 2008	The source of vaccines from pigs; the use of vaccines is not permissible as there are alternatives and their use is non-emergency.
Clexane and fraxiparine in preventing and treating blood clots	The 87 th Muzakarah, 2009	The source of drugs from pigs; the use of drugs is not permissible. arixtra (i.e., synthetic heparin and not from animal sources) is used as alternative medicine.
COVID-19 vaccine	The 10th Special Meeting of the MKI Muzakarah Committee, 2020	The ruling of vaccine is permissible due to <i>the darurah</i> situation of COVID-19 pandemic emerged around the world

Nevertheless, some fatwas issued by the Fatwa Committee contradict the Malaysian National Medicines Policy (MNMP). In the policy, all people, regardless of their backgrounds, shall have access to all medicine. For example, the decision on the substitution of clexane with arixtra in treating blood clot sufferers has imposed difficulties and burdensome upon the poor as arixtra is

more expensive than clexane (Awang et al., 2019). This fatwa, which could lead to harm among the poor, absolutely does not adhere to the MNMP. Even though the usage of clexane is impermissible according to the Malaysian fatwa, its effectiveness, feasibility and accessibility are the reasons why it is still used for blood clot therapy in Malaysia today, especially in government hospitals (Mohd Yusof et al., 2021).

4. CONCLUSION

Concerning the conditions of *darurah*, *istihalah* and *istihlak* that are applied in determining the halal and haram status of porcine and bovine-derived ingredients, there is no right or wrong in both applications. The authorised Islamic jurists nowadays have used their wisdom to apply any conditions that can prioritise the benefit of Muslims, as well as the customs and environment of their region. *Istihalah* and *istihlak* methods are applicable to determine the status of pharmaceutical products that are produced from the combination of halal and haram substances. This will not only facilitate Muslims in seeking treatments but also facilitate Muslim scholars to determine the status of new medicines consisting of haram ingredients in the future.

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