Halal Certification of Food, Nutraceuticals, and Pharmaceuticals in the Arab World

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Abstract

Food is an organic need and essential to our survival, whereas nutraceuticals and pharmaceuticals play an important role in disease prevention and cure. The food processing and healthcare industries are often linked together for economic growth and health promotion. However, the complexity of the ingredients and processes led communities to question their motivation, accuracy, and imposed standards. Different standards are often applied to ensure high quality, reproducibility, and traceability. Many processed products contain ingredients derived

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I. Laher (ed.), *Handbook of Healthcare in the Arab World*,
https://doi.org/10.1007/978-3-319-74365-3_36-1

from animals, where the consumption of such products is prohibited by several religions and lifestyles. Patients who want to avoid certain medications derived from animal need to know the source of origin and detailed ingredients contained in their medicines. Recently many Muslim and non-Muslim countries have realized the value of Halal products and led to an increase in Halal awareness. This chapter aims to provide more insight into the issue of Halal status of food and medications in the context of healthcare and describe the process of certification and the list of ingredients and drugs with potential non-Halal sources. Traceability procedure and identification of a long list of ingredients is a challenge but also key for verifying the Halal status of the end product. Implementation of Halal-Tayyib concept is essential to determine the Halalness of food and pharmaceuticals. To increase confidence, eliminate suspicion, and improve trust with producers, Halal certification is required. However, exerting 100% effort is possible, whereas achieving products that are 100% clean and pure and comply with Shari'ah is debatable.

Keywords
Halal pharmaceuticals · Food · Halal standard · Tayyib · Halal certification

Introduction

Human is rational by nature and seeks a rational path that would fill the heart with tranquility. A human being's vision of life varies from nation to nation, and Islamic vision is based on the idea that humanity is created by Allah, life is mortal, hell and paradise are real, and ticket of entry is solely dependent on human deeds and action during life: "Whosoever does an evil deed shall be recompensed only with the like of it, but whosoever does a righteous deed, whether male or female, while he is a believer, those shall enter Paradise, being given provision therein without account" (Ghāfir 40:40). The main mission of humans is to civilize the earth and create a continuous relationship between man and man: ". . .He has raised you from the earth and settled you in it, enabling your dignity and prosperity. . .." (Hud 11: 61). The pillars of civilization have been clearly described by Prophet Muhammad (PBUH): "Whosoever begins the day feeling secure, having good health; and possessing enough food for his day is as though he possessed the whole world" (Al-Tirmidhi). Health, food, and security play essential roles in evaluating and shaping the living standard of different societies. Health is a state of well-being, and maintaining strength and good health is a basic human right: "Your body has a right over you" (*Sahih al-Bukhari*). Eating food is an organic need and essential to our survival; thus promoting health and food will have a positive impact on the progress and growth of societies. Meanwhile, security is responsible for creating peace, jollity, and tranquility. Prophet Ibrahim made a devout and humble supplication to Allah to bless the city of Mecca. He prayed: "I beseech You, Allah, my Creator, to make this city a safe retreat affording security and peace of mind. And provision its people with the earth's kind fruits" (Al-Baqara 2: 126).

The Halal term is frequently used in the Muslim and non-Muslim worlds; however, Halal is regarded as a concept for Muslims, an idea for non-Muslim, and an issue for certifying bodies. Halal concept means permissible and covers all human actions and deeds, which include eating, wearing, seeing, and talking. For Muslims, Qur'an is a book of signs; interestingly, whenever the concept of Halal is presented in the context of food, the concept of Tayyib is explicitly coupled; therefore it is necessary when Halal food is presented, the combined expression, Halal-Tayyib, is used. The concept Tayyib refers to being clean, pure, and compliant with Shari'ah (Arif and Ahmad 2011), whereas Halal concept organizes behavior; hence what we eat will have an impact on our character (Jiang et al. 2014), *duaa* (supplication) acceptance, and personality. The phrase "you are what you eat" has been frequently used by many and supported by Qur'an: "O you Messengers! Eat of the clean and pure (Tayyib) and act righteously" (Al-Muminun 23: 51). The contrary of Tayyib is "Khabith" which connotes to everything impure, harmful, and disgusting: ". . .makes lawful to them the pure things and makes unlawful to them impure things. . .." (Al-Aʿrāf 7: 157). The concept of Halal-Tayyib has been described frequently in many publications (Arif and Ahmad 2011, Arif and Sidek 2015), and most opinions suggest that Tayyib is related to food safety (Demirci et al. 2016). In this chapter, we would like to present a detailed description of Halal in the context of food, nutraceuticals, and pharmaceuticals, discuss the process of Halal certification, and give a general view about ingredients and drugs either potentially derived from animal or suspended in ethanol.

Halal-Tayyib Relationship

The core definition of Halal is based on general Islamic principles where it says everything is permissible (*mubah*) by nature: "And He has also made subservient to you all that is in the heavens and the earth, most surely there are signs in this for a people who reflect" (Al-Jāthiyah 45: 13), non-Halal has been specified as the exception, and the main exceptions of Halal are *khamr* (ethanol) (Alzeer and Abou Hadeed 2016), blood, pork, carnivores and omnivore animals, food contaminated with non-Halal ingredients, and food with potentially toxic ingredients that may expose human health to danger. Islam emphasized strongly on the issue of food safety and contamination, therefore frequently associate Halal concept with Tayyib when Halal is related to food: "O ye who believe! Eat of the clean and pure that We have provided for you, and be grateful to Allah, it is Him ye worship" (Al-Baqarah 2: 172). Tayyib in Arabic means clean and pure; therefore the concept of Tayyib, concerning food, represents a process through which the food passes through, to achieve both objectives: maximum hygiene (clean) and minimum contamination (pure) with any potential toxic, Najis (ritually unclean), and Khabith (impure) ingredients; thus how Halal, which is a subject, is being processed will determine if Halal is Tayyib or not. Chicken as a subject is Halal, but how the chicken is handled, treated, fed, and slaughtered will determine if the chicken is Halal-Tayyib or not. As both objectives are targets for Muslim and non-Muslim industries, what

makes Tayyib unique for Muslims is its goal, which is to create calmness and comfortable feelings when food is taken. "We only wish to eat therefrom to reassure and comfort our hearts" (Al-Māidah 5: 113). The comfortable feeling cannot simply be achieved through a healthy and safe diet, which is essential; however pleasant and comfortable feeling is achievable if what we eat is compatible with what we believe. Comfort food that is selected and influenced by what we believe is known to improve our mood, make us feel better, and give us a sense of well-being (Wansink et al. 2003; Bublitz et al. 2013). Therefore, the Tayyib processing of Halal will have a positive impact on mood, health, and faith practicing: "Verily Allah the Exalted is pure (Tayyib). He does not accept but that which is pure (Tayyib)" (Sahih Muslim-a). The contrary of Tayyib is Khabith. According to the Arabic dictionary, Khabith refers to everything which is disgusting and cannot be used as a source of food such as snakes, lizards, scorpions, pests, beetles, and mice. Thus, the concept of Khabith concerning food reflects unpleasant and uncomfortable feelings with disgusting consequences resulting from the incompatibility of food and lifestyle (faith). This is a natural reflection, mostly occurring to people following specific lifestyle such as vegetarian, vegan, kosher, and Halal. Anything disgusting and repulsive by human nature or has the potential to harm human health, no matter if it is described or not in Qur'an and Hadeeth, is considered Khabith and non-Halal. Interestingly, cancer in Arabic is also called Khabith; thus any potentially carcinogenic ingredients are Khabith as well. Therefore, eating Halal-Tayyib is the path toward achieving complete satisfaction; however disgusting and repulsive feeling is unhealthy and may lead to stomach discomfort (Alzeer et al. 2018a). Qur'an strongly recommends eating Tayyib and avoiding Khabith: "Not equal are the khabith and the Tayyib, although the abundance of Khabith might impress you" (Al-Māidah 5: 100).

An ancient Greek philosopher, Hippocrates, proposed a notion: "let food be thy medicine and medicine be thy food"; the Qur'an supported the notion by describing honey as a source of food and cure: ". . .There comes out of their (Bees) bellies a drink of different colors, wherein is a cure for mankind. Indeed in that is a sign for a people who give thought" (Al-Nahl 16: 69). Food may also act as a potential vehicle for disease transmission; thus the implementation of Tayyib concept (clean and pure), as a public health priority, is essential for the protection of human health and improvement of life quality. Tayyib takes into consideration, safety, contamination, pesticides, and hygiene; meanwhile it complies with Shari'ah and enriches societies with spiritual, moral, and human values.

Halal Production

Nutrients play an important role in human life. It acts as a source of energy, enables us to perform work, and provides the body with diverse building blocks for DNA, proteins, fats, minerals, vitamins, and antioxidants. Inundation of body with random and uncontrolled diet will have an impact on body weight and oxidative stress; long-term effects may lead to DNA damage, protein cross-linking, and lipid oxidation, ultimately leading to onset and progression of diseases. Many nutrients are based on

regional, religious, and cultural influences (Alonso 2014), and the relation of the nutrient contents and benefits of various diets on health and attitude has been studied by many groups (Alzeer et al. 2018b).

The production and consumption of Halal are obligatory for all Muslims. Lack of knowledge (Sadeeqa and Sarriff 2014), awareness, and understanding of the Halal-Tayyib concept may cause loss of interest and appreciation to Halal products, particularly by the non-Muslim manufacturers. In general, Halal food is healthy and contains all necessary building blocks such as minerals, fats, carbohydrates, amino acids, and vitamins which are required for biochemical reactions and involved in the production of DNA and functional proteins. Previously, many understood that food and drugs are Halal as long as they do not contain pork or ethanol; this notion is not enough to declare they are Halal unless the entire process fulfills the following criteria:

1. Ingredients are safe and free from ethanol, blood, pork, carnivores, omnivore animals, and human parts.
2. Maximum hygiene and minimum contamination with any potential toxic, Najis (ritually unclean), and Khabith (impure) ingredients are applied.
3. The process of cultivation, manufacturing, preparation, packaging, storage, and distribution must be ensured to be clean, pure, and compliant with Shari'ah.
4. The whole Halal production must be physically separated from non-Halal production.
5. Any potential cross-contamination between Halal and non-Halal ingredients and products must be completely avoided.

In general, Muslims do not eat animals that are classified as a carnivore (consume only meat) and omnivore (consume both meat and plant). Dead animals and birds with claws or birds that feed by snatching and tearing are also prohibited. All forms of water, fruits, and vegetables are Halal and can be taken except fermented ethanol, blood, and any poisonous, intoxicating, and harmful drinks. Additionally, there are animals and insects forbidden to be killed in Islam and thus prohibited to be eaten such as ants, bees, frogs, and woodpeckers (Rahim 2018). Any source of food reflects to be repulsive, disgusting, and decayed may classify as Khabith and forbidden to be eaten. Clearly, reading labels and envisaging the content are not enough to realize the Halal status, and many consumers demand to know the process and the source of their food; therefore Halal certification is necessary to ensure quality with regard to processes, ingredients, and compliance with Shari'ah (Mursyidi 2013).

Halal Certification

The main goal of food and pharmaceutical manufacturers is to keep their products profitable and irresistible; therefore industries are innovative and adaptive to help products stay in compliance. Manufacturers are facing a growing demand for

natural, clean, and safe products that may comply with various lifestyles. Qur'an addresses all human beings including Muslim and non-Muslim to search for Halal: "O mankind, eat of the good and lawful things on earth and do not follow the footsteps of Satan. Indeed, he is to you a clear enemy" (Al-Baqarah 2: 168). The basic issues in Halal production are cleanliness, purity, and compliance with Shari'ah (Riaz and Chaudry 2004), as defined in Qur'an: "Eat from the pure and lawful things that God has given to you. Have fear of God in Whom you believe" (Al-Māidah 5: 88).

The production of Halal products is a new challenge for food and pharmaceutical companies (Norazmi and Lim 2015). Muslim countries recently start demanding Halal certificates for products coming from non-Muslim countries. Halal certifying bodies are growing in numbers and endeavor to improve Halal guidelines to comply perfectly with Shari'ah (Jais 2016). In principle, Halal certificates could be issued for meats, ingredients derived from fruits and vegetables, naturally and chemically synthesized ingredients, cosmetics, nutraceuticals, and pharmaceutical drugs (Mohamad 2015). The process of certification is developed to ensure zero suspicion of a manufactured product that is clean, safe, and compliant with Shari'ah. The main stage in Halal certification is conducting the site audit which can be classified into three steps:

1. *Documentation review*: All documents will be reviewed; in this context, all ingredients are being classified into three categories:
   (a) Highly critical: Contain either ethanol or derived from animal, where only Halal certificate is required
   (b) Critical: Processed ingredients either extracted from the natural products or synthesized in the lab where Halal certificate or questionnaire is required
   (c) Noncritical: Natural and non-processed ingredients where Halal certificate or questionnaire or declaration is required

   During documentation control, all ingredients with regard to safety, toxicity, and Halal status will be evaluated, the validity of Halal certificates is checked, and questionnaires are studied. Finally, the compatibility of storage, lubricant, cleaning agents, and packaging material to Halal-Tayyib is verified.
2. *Physical/on-site audit*: During the on-site visits, the production line is followed stepwise, and manufacturing premises, equipment, and other facilities are ensured to be clean and free from filth, dirt, and harmful and non-Halal elements. All standard operating procedures (SOP) for maintaining hygiene and safety are ensured to adhere to Halal guidelines (Halim et al. 2015).
3. *Review/closing meeting*: At the end of the audit, critical remarks are mentioned, missing documents are presented, and requests for special procedures are pointed out. The final report will be submitted to the Halal expert committee and a decision will be made.

Certifying bodies insist on both physical and spiritual cleanliness: ". . .He loves those who keep clean" (Al-Baqarah 2: 222) and "And purify your clothes" (Al-Mudathir 74: 4); thus, utilizing both concepts, Halal-Tayyib (Yunus et al. 2010), is

essential for the Halal certification process and for the determination of the Halal status of food and pharmaceutical products (Sadeeqa 2015**)**. Halal certification cannot be solely done by religious scholars, as they are unable to deal with the complex ingredients and traceability issues (Majid et al. 2015); certification require highly qualified scientists (Muslims and non-Muslims) in the field of chemistry, food technology (Khattak et al. 2011), or other related science with biotechnological or pharmaceutical background and experts in religious jurisprudence to cover all Halal issues (Norazmi and Lim 2015).

Islamic Views on Healthiness and Halalness

By nature, humans are healthy, and disease is a temporary condition in which the body becomes unable to function collectively; such a situation potentially deteriorates if the immune system could not resist or inappropriate medication was used. The strength of physical competence is crucial to play a productive role in society. The strength and capability of Prophet Musa (PBUH) have been described in the Qur'an and promoted him (besides being trustful) to get married and find a job: "One of the women said, O my father, hire him. Indeed, the best one you can hire is the strong and the trustworthy" (Al-Qasas 28: 26). Allah regarded the human body as a trust to profit from it but must be kept in the best state; therefore mankind is responsible to keep their body away from any harm, danger, and diseases. Maintaining good health and avoiding killing ourselves is Allah's order as stated in Qur'an: ". . .And do not kill yourselves [or one another]. . ." (Al-Nisa 4: 29).

Medicines play a vital role in human development and influence morbidity and mortality as well as improve the quality of life. From an Islamic perspective, preserving human life and reducing suffering and pain is a noble act: ". . .We decreed upon the Children of Israel that whoever kills a soul unless for a soul or for corruption in the land, it is as if he had slain mankind entirely. And whoever saves one, it is as if he had saved mankind entirely. . ." (Al-Māidah 5: 32). Prophet Muhammad (PBUH) requested us to seek medicine if our body got sick and clearly manifested that Allah created for every disease a remedy: "take medicine, for Allah Almighty has not created a disease without having created a remedy for it except one disease, Old age" (Al-Tirmidhi). The disease ends when the proper cure is applied, indicating that when the two opponents meet, proper remedy and disease, recovery from illness occurs: "Every illness has a cure, and when the proper cure is applied to the disease, it heals by Allah's Will" (Sahih Muslim-b). Those statements have inspired Muslim scientists through the centuries to pursue medical knowledge.

Seeking treatment is highly recommended, but when treatment is certain to be beneficial, and illness could lead to disability, death, or contagious disease, then it is obligatory: "Indeed Allah has sent down both illness and its cure, and He has appointed a cure for every illness, so treat yourselves medically, but use nothing unlawful" (Sunan Abu Dawud 3874). Islam has made it a priority to use medicines derived from Halal ingredients for effective treatment, whereas non-Halal ingredients may lead to discontinuation of medications (Sattar et al. 2004) and relapse of

symptoms, thus leading to noneffective treatment: “Indeed Allah has not placed cure in that which He has made unlawful for you” (Sahih Ibn Hibban). Medicine is a combination of active ingredients and excipients, obtained from a variety of sources: animals, plants, or synthetic origin. Medicine is like food, which could be potentially non-Halal; thus pharmaceutical companies are requested to take suitable steps in the production of Halal medicine that comply with Halal standards (Sadeeqa and Sarriff 2014).

Potential Non-Halal Ingredients in Food and Pharmaceutical

Many ingredients are involved in the food processing and used as flavoring, stabilizing, or coloring agents, whereas additives in pharmaceutical drugs are used as part of the formulation process to stabilize active ingredients and facilitate absorption, distribution, and elimination of the drug. Many of those ingredients are either naturally extracted or chemically synthesized, whereas other ingredients are derived from the animal. Thus, ingredients could be classified (Table 1) into highly critical, critical, and noncritical. Criticality is determined by the source, nature, and the process being used during the production. In general, highly critical is potentially non-Halal until proven otherwise. A critical ingredient that needs further evaluation is *mushbooh*, whereas noncritical is Halal. Ingredients, process, and location are strongly correlated with the Halal-Tayyib systems, which are the basic principles for understanding and producing Halal products.

Main sources of non-Halal ingredients are:

1. Ingredients derived from pork
2. Ingredients derived from an animal not slaughtered properly
3. Ingredients which are genetically modified
4. Ingredients which are extracted with ethanol or derived from blood

In general, ingredients are listed in descending order of predominance; the complete ingredient list is difficult to obtain from the label. Ingredients present in trace amount are not included in the list. FDA (Food and Drug Administration) does not define “trace amounts”; however, there are some exemptions for declaring ingredients present in “incidental” amounts in a finished product. If an ingredient is present at an incidental level and has no functional or technical effect in the finished product, then it does not need to be declared on the label. Note that major food allergens, regardless of whether they are present in the food in trace amounts, must be declared. Sulfites added to any food or to any ingredient in any food and that have no technical effect in that food are considered to be incidental only if present at less than 10 ppm. It is not necessary to specify spices and flavor; they are declared in ingredient lists by using the declarations “spices,” “flavor” or “natural flavor,” or “artificial flavor.”

Table 1 An alphabetical list of potential non-Halal ingredients

Ingredients	Halal status	Remarks
Adrenaline	Highly critical	*It is used* for circulatory support, correction of hypervolemia, metabolic acidosis, and hypoxia or hypercapnia. It is normally produced by animal or synthesized from epinephrine
Aprotinin	Highly critical	It is a small protein bovine pancreatic trypsin inhibitor (BPTI), obtained from bovine lung
Bacon	Highly critical	It is used as a flavor component and prepared from pork belly
Beractant	Highly critical	It is a modified bovine pulmonary surfactant containing bovine lung extract
Cholecalciferol	Critical	It is vitamin D3 used as a supplement and produced by the irradiation of 7-dehydrocholesterol
Cholesterol	Highly critical	*It is used* to build up cells and certain hormones in the body, derived from animal origin
Co-trimoxazole	Highly critical	It is used for the treatment of *Pneumocystis jiroveci* (*carinii*) pneumonitis and contains 13.2% vol. ethanol (alcohol)
Curosurf (poractant alfa)	Highly critical	It is used as a natural surfactant, prepared from porcine lungs
Diglyceride	Critical	It *is used* with defatted flour as emulsifier. It could be derived from animal and plant origin
Fluenz Tetra nasal spray (vaccine)	Highly critical	It is influenza vaccine, contains a very small amount of gelatin that comes from pork
Fragmin (dalteparin sodium)	Highly critical	It *is used* to prevent blood clots, derived from sodium heparin which potentially could be obtained from porcine
Gelatin (Jell-O Gelatin)	Highly critical	It is used in capsule production and usually derived from animal origin, mostly from pig
Glycerol	Critical	Glycerol is generally obtained from plant and animal sources where it occurs as triglycerides
Glycerine	Highly critical	It *is used* as a laxative, naturally prepared from tallow, a form of beef
Heparin sodium	Highly critical	It *is used* to treat and prevent blood clots, derived from porcine intestinal tissue
Indigo carmine	Critical	It is used as coloring agent, derived from indigo by sulfonation; indigo is a blue coloring agent derived from natural products
Lard	Highly critical	It is commonly used as a cooking fat or shortening, derived from pork
Magnesium stearate	Critical	It has binding and lubricating properties that help lubricate and aid the ejection of tablets and could be derived from animal
Monoglycerides	Critical	It *is used* as an emulsifier, a dispersing agent, and a stabilizer, and it could be derived from animal and plant origin

(continued)

Table 1 (continued)

Ingredients	Halal status	Remarks
NovoSeven (eptacog alfa)	Highly critical	It *is used* for the treatment and prevention of bleeding, *derived* from hamster kidneys
Nutrizym 22, Pancrease HL, Pancrex (pancreatin)	Highly critical	It *is used* to treat chronic pancreatitis, enzymes (lipases, proteases, and amylases), derived from porcine pancreas
Oleic acid	Critical	*It is used* in manufacturing of surfactants, soaps, and plasticizers and produced from saturated fatty acid that occurs naturally in various animal and vegetable fats and oils
Oxytocin	Critical	It *is used* for induction and augmentation. Derived synthetically
Pancreatin (Creon)	Highly critical	It *is used* as a digestive aid, *is derived* from beef or pork pancreas
Pepsin	Highly critical	It is used to break down proteins into smaller peptides, is derived from animal tissues particularly from pork stomach
Polyethylene glycol	Critical	It is used as a humectant, laxative, stabilizer, and bulking agent and produced by the interaction of ethylene oxide with water, ethylene glycol, or ethylene glycol oligomers
Polyoxyl hydrogenated castor oil	Critical	It is used as solubilizer and produced from castor seeds
Polysorbate	Critical	*It is used* as emulsifier and produced from fatty acids
Priadel liquid (lithium citrate)	Highly critical	It *is used* for manic-depressive disorder, contains 5% ethanol
Propylparaben	Critical	It is *used* in many cosmetics and may be found in lipsticks, foundations, and eye shadows, produced from plants and some insects
Rennin (rennet)	Highly critical	*It is used* to curdle milk, produced mostly from stomach lining of a calf, ewe, or plant sources
Sorbitol	Critical	*It is used* as a sweetener and produced synthetically from glucose or naturally derived from placenta
Sorbitan trioleate	Critical	It is used as nonionic surface agent, dispersing agent, co-emulsifier, and stabilizer, for mineral oil used in food and cosmetics, and used as excipients in veterinary medical products prepared from sorbitol and fatty acid
Stearic acid	Critical	It *is used* as an emulsifying agent, solubilizing agent, and tablet and capsule lubricant. *Derived* from either tallow or vegetable sources
Shortening	Critical	It is used in backing and it is fat mostly derived from vegetable oils
Sodium biphosphate	Highly critical	It has multiple uses, originates from several sources including animal bones or bone ash, bovine origin
Sodium glutamate	Critical	It is used as a flavor enhancer and produced either synthetically or by bacterial fermentation

(continued)

Table 1 (continued)

Ingredients	Halal status	Remarks
Sodium starch glycolate	Critical	It is used in tablets to disintegrate and dissolve them to be absorbed by the body. It is made from a number of different starchy foods, including corn, wheat, rice, and potatoes
Triacetin	Critical	It is *used* mainly as a plasticizer and a gelatinizing agent in polymers, *produced* from a multistage reaction sequence involving glycerine, acetic acid, and acetic anhydride as raw materials
Vanilla	Critical	It is used as flavoring and mostly derived from plants and extracted with ethanol
Vitamins	Critical	*Vitamins are used* for stress, allergies, fatigue, and building the immune system, derived mostly from plants
Vaccines	Highly critical	In the preparation of vaccines, animal sera are frequently added to culture media to provide nutrients for microbial growth

Drugs with Animal-Derived Ingredients

Pharmaceutical drugs are derived from a variety of sources, including natural and man-made ingredients. Some of the drugs derived from animal ingredients are listed in Table 2. The animal ingredients could exist as active drug constituents or part of inactive excipients. Many of those ingredients would have implications for patients with a different lifestyle. Pharmaceutical companies are becoming increasingly aware of these limitations; therefore animal ingredients have been replaced by synthetic alternatives. Inactive ingredients, including those containing ethanol, gelatin, or stearic acid, are still a challenge for pharmaceuticals.

Most ingredients are chemically manufactured to keep control of the process and maintain the purity of the active ingredients. There are exceptions such as insulin used to treat diabetes, which is derived from the animal sources, usually from pigs. Gelatin, a common active substance in pharmaceutical products, is manufactured from bones, skin, and connective tissue of animals, mainly pigs, cattle, and fish, and used in the manufacture of capsules and tablets. Collagen is another ingredient, produced from animal bones, and used in arthritis and for improved skin elasticity, skin moisture, and skin texture (Porfirio and Famaro 2016). Hormones like estrogen and estradiol are produced from female hormones of pregnant mares and used in a variety of medical uses (Cox 1996). Heparin is used as a blood anticoagulant drug and derived from mucosal tissues of the porcine intestine or bovine (cow) lung (Tovar et al. 2013). Stearic acid, made from the fat of cows and pigs (tallow), is often used in a salt form such as magnesium stearate which has binding and lubricating properties that help lubricate and aid in the ejection of tablets from the tablet press (Li and Wu 2014). Lactose, the most common animal-derived ingredient, is widely used as a filler or diluent in tablets and capsules. Cysteine, an amino acid, is derived

Table 2 An alphabetical list of selected drugs with potential animal ingredients

Product name (generic name)	Comment
Advate (octocog alfa)	It is a human coagulation factor VIII, produced by recombinant DNA technology in *Chinese hamster* ovary
Aldurazyme (laronidase)	It is a recombinant form of human α-L-iduronidase and is produced by recombinant DNA technology using mammalian *Chinese hamster* ovary
Aranesp (darbepoetin)	It is an erythropoiesis-stimulating protein produced in *Chinese hamster* ovary cells
Avastin (bevacizumab)	It is an angiogenesis inhibitor produced in a *Chinese hamster* ovary
Avonex (interferon beta-1a)	It is an immunomodifier protein produced by recombinant DNA technology using genetically engineered *Chinese hamster* ovary cells
BeneFIX (nonacog alfa)	It is a hemostatic agent, contains recombinant coagulation factor IX derived from a *Chinese hamster* ovary
Cerezyme (imiglucerase)	It is an enzyme replacement therapy, generated from transduced *Chinese hamster* ovary cells
Clexane (enoxaparin)	It is an anticoagulant, antithrombotic medication, made from heparin
Creon (pancrelipase)	It is a digestive pancreatic enzyme prepared from porcine-derived lipases, proteases, and amylases
Curosurf (poractant alfa)	It is a respiratory agent, used as a surfactant and extracted from porcine minced lungs
Elonva (corifollitropin alfa)	*It* is a pituitary hormone, produced in *Chinese hamster* ovary (CHO)
Enbrel (etanercept)	It is a recombinant human soluble tumor necrosis factor receptor fusion protein derived by introducing human DNA into Chinese hamster ovary cells
Ethical Nutrients Digestion Plus	It is a digestive enzyme used to assist protein digestion in the stomach and contains betaine, gentian, lutea, and pepsin
Fragmin (dalteparin)	It is an anticoagulant made from heparin
Gelofusine (gelatin succinylated)	It is a volume expander, contains 4% solution of *succinylated bovine gelatin*
Heparin sodium injection	It is an anticoagulant made from heparin
Heparinized saline	It is an anticoagulant made from heparin
Heparinized saline injection	It is an anticoagulant made from heparin
Haemaccel (polygeline)	It is a plasma volume expander, a derivate of gelatin, from *bovine*-derived bone
Insulin	It *is used* to treat people who have type 1 diabetes, derived from genetically modified yeast, cow, or pork
Orgaran (danaparoid)	It is hemostatic agent, isolated from animal mucosa (porcine)
Panzytrat 25000	It is a digestive supplement (amylase, lipase, pancrelipase, protease), contains a *porcine* pancreatic enzyme
Prothrombinex-VF	It is hemostatic agent, with active ingredients factor IX; factor II; factor X; antithrombin III, human; heparin; factor V; factor VII
Rotarix	It is a *live* oral *rotavirus vaccine* developed from a single protective *human* strain, contains porcine circovirus type 1 (PCV-1)

(continued)

Table 2 (continued)

Product name (generic name)	Comment
RotaTeq	It is a live, oral pentavalent vaccine, contains a porcine-derived material
Travelan	*Travelan* is an antidiarrheal natural product, derived from *bovine colostrum*
Varivax (varicella zoster vaccine)	It is a vaccine, contains inactive components including hydrolyzed gelatin and traces of bovine serum
Vivaxim	It is a hepatitis A vaccine, contains bovine serum albumin
Zostavax (zoster virus vaccine live)	It is a live attenuated virus vaccine, contains hydrolyzed porcine gelatin
Zyderm collagen implants (collagen)	It is a sterile device composed of highly purified bovine dermal collagen

from hair that could come from animal source and used in hair-care products, creams, in some bakery products, and in wound-healing formulations.

Drugs with Ethanol Content

Ethanol is an important organic solvent and substrate that is widely used in food, pharmaceutical, cosmetic, and many other industrial applications. Many active ingredients are suspended in ethanol solutions such as cough remedies, mouth-washes, or children's medicines. Halal status of ethanol is highly controversial, and many Muslim scholars consider ethanol as non-Halal, no matter how it has been prepared. More rational studies revealed the Halalness of ethanol is dependent on the source and concentration (Alzeer and Abou Hadeed 2016). According to Alzeer studies, any ethanol produced by anaerobic fermentation and ranging between 1% and 15% is considered to be non-Halal, whereas ethanol produced by natural fermentation and less than 1% is considered a preserving agent and its Halal status is allowed. Any ethanolic solution higher than 15% is treated as a toxic solution; therefore it is strictly forbidden to drink, and attempts to drink toxic solution is considered suicide attempts and strongly forbidden in Islam. On the other hand, toxic ethanol solution is allowed to be prepared, held, transferred, and used for disinfection and other industrial use. An ethanolic solution prepared by dilution from absolute or denatured ethanol is allowed for industrial use but toxic for human consumption. However, any concentration varying from 0.1% to 100% prepared with the intention to be used as a beverage drink is considered non-Halal. Drugs with a significant amount of ethanol have been summarized in Table 3.

A study was conducted to evaluate the Halal status of selected cardiovascular, endocrine, and respiratory drugs stored at the pharmacy of a Malaysian state hospital (Sarriff and Razzaq 2013). The study showed the proportions of Halal (noncritical), *mushbooh* (critical), and *haram* (highly critical) products were at 19.1%, 57.1%, and 23.8%, respectively. The concept *mushbooh* is used when the Halal status is doubtful

Table 3 An alphabetical list of selected drugs with ethanol content (Sober Link)

Drug	Ethanol%
Actol Expectorant Syrup	12.5
Alamine	5.0
Alertronic	0.5
Alomine C	5.0
Alomine Expectorant	7.5
Alurate Elixir	20.0
Ambenyl-D	9.5
Ambenyl Expectorant	5.0
Anahist	0.5
Aromatic Elixir	22.0
Anaspaz-Pb Liquid	15.0
Asbron Elixir	15.0
Atarax Syrup	0.5
Bactrim Suspension	0.3
Benedryl	14.0
Belladonna	67.0
Benadryl Elixir	14.0
Benedryl Decongestant	5.0
Bentyl-Pb Syrup	19.0
Benylin Expectorant	5.0
Black Draught	5.0
Breacol	10.0
Brondecon Elixir	20.0
Bronkelixir	19.0
Butibel Elixir	7.0
Calcidrine Syrup	6.0
Cas Evac	18.0
Aromatic Cascara Sagrada	18.0
Carbrital Elixir	18.0
Dr. Caldwell's Senna Laxative	4.5
Cerose & Cerose DM Expectorant	2.5
Citra Forte Syrup	2.0
Cetro-Cerose	1.5
Cheracol & Cheracol D	3.0
Choledyl Elixir	20.0
Chlor-Trimeton Syrup	7.0
Codimal DM	4.0
Coldene Cough Syrup	15.0
Cologel Liquid	5.0
Coltrex	4.5
Coltrex Expectorant	4.7
Conar Expectorant	5.0
Contact Severe Cold	25.0

(continued)

Table 3 (continued)

Drug	Ethanol%
Contrex	20.0
Copavin Cmpd Elixir	7.0
Coryban D	7.5
Cosanyl DM & Cosanyl Syrup	6.0
Cotussia	20.0
Darvon-N Suspension	1.0
Daycare	10.0
Decadron Elixir	5.0
Demazin Syrup	7.5
Dexedrine Elixir	10.0
DIA Guel	10.0
Dilaudid Cough Syrup	5.0
Dimetane Expectorant	3.5
Donnagel-PG	5.0
Doxinate Liquid	5.0
Dimetapp Elixir	2.3
Dimacol Liquid	4.8
Donnatal Elixir	23.0
Dramamine Liquid	5.0
Endotussin NN	4.0
Ephedrine Sulfate Syrup USP	3.0
Feosol Elixir	5.0
Fer-ln-Sol Drops	0.3
Fer-ln-Sol Syrup	5.0
Fletcher's Castoria	3.5
Formula 44 Cough	10.0
Formula 44 D	20.0
Geriplex-FS	18.0
Gevabon Liquid	18.0
GG Tussin	3.5
G Tussin DM	1.4
Halls	22.0
Head & Chest	5.0
Hycotuss Expectorant & Syrup	10.0
Hydryllin Comp.	5.0
Iberet Liquid	1.0
Ipecac Syrup	2.0
Isuprel Comp. Elixir	19.0
Kaon Elixir	5.0
Kaochlor	3.8
Kay-Ciel Elixir	4.0
Lanoxin Elixir Pediatric	10.0
Liquid Lomotil	15.0

(continued)

Table 3 (continued)

Drug	Ethanol%
Luffyllin-GG Elixir	17.0
Marax Syrup	5.0
Mediatric Liquid	15.0
Mellaril Concentrate	3.0
Mercodol w/Decaprin	5.0
Mesopin Elixir	12.5
Minocin Syrup	5.0
Modane Liquid	5.0
Naldecon Dx	5.0
Nembutal Elixir	18.0
Night Relief	25.0
Nortussin	3.5
Nicol Elixir	10.0
Nico-Metrazol Elixir	15.0
Novahistine DH	5.0
Novahistine Expectorant	5.0
Novahistine Elixir	5.0
Novahistine DMX	10.0
Novafed	7.5
Novafed A	5.0
Nyquil Cough Syrup	25.0
Mol Iron Liquid	4.8
Organidin Elixir	23.8
Ornacol Liquid	8.0
Tincture Paregoric	45.0
Pabizol with Paregoric	9.6
Parapectolin	0.7
Parelexir	18.0
Parepectolin	0.6
P.B.Z. Expectorant with Ephedrine	6.0
Pediquil	5.0
Percy Medicine	5.0
Periactin Syrup	5.0
Pertussin 8 Hour Syrup	9.5
Pinex	3.0
Phenergan Expectorant Plain	7.0
Phenobarbital Elixir	14.0
Phenergan Expect. w/Codeine	7.0
Phenergan Expectorant VC Plain	7.0
Phenergan Expectorant VC w/Codeine	7.0
Phenergan Expectorant Pediatric	7.0
Phenergan Syrup Fortis (25 mg)	1.5
Polaramine Expectorant	7.2

(continued)

Table 3 (continued)

Drug	Ethanol%
Propadrine Elixir HCI	16.0
Quibron Elixir	15.0
Quelidrine	2.0
Quiet Nite	5.0
Quintess	0.9
Robitussin Syrup	3.5
Robitussin AC Syrup	3.5
Robitussin DM and Robitussin CF	1.4
Robitussin PE	1.4
Romilar CF	0.0
Rondec DM Syrup and Drops	0.6
Roniacol Elixir	8.6
Senecot Syrup	7.0
Serpasil Elixir	2.0
SK APAP Elixir	8.0
Sudafed Cough Syrup	2.4
Tedral Elixir	15.0
Temaril Syrup	5.7
Tempra Syrup & Drops	10.0
Terpin Hydrate Elixir	42.0
Theo Organidin Elixir	5.0
Tolu-Sed	10.0
Tolu-Sed DM	10.0
Tonecol	7.0
Triaminic Expectorant	5.0
Triaminic Expectorant DH	5.0
Trind DM	5.0
Tussend Liquid	5.0
Tussar-2 Syrup	5.0
Tussar SF Syrup	2.0
Tussi-Organidin Expectorant	5.0
Tussar SF Syrup	2.0
Tylenol Liquid & Drops	7.0
Tuss-Ornade Syrup	7.5
Tylenol Elixir	7.0
Tylenol with Codeine Elixir	7.0
Tylenol Drops	7.0
Ulo-Syrup	6.7
Valadol Liquid	9.0
Valpin-PB Elixir & Valprin	5.3
Vicks Cough	5.0
Viromed Liquid	6.6
Vita Metrazol Elixir	5.0

(continued)

Table 3 (continued)

Drug	Ethanol%
Vitamin – Ce-Vi Drops	5.0
Vitamin – Fumeral	5.0
Vitamin – Ganatrix	15.0
Vitamin – Geralix Liquid	15.0
Vitamin – Geriplex FS Liquid	18.0
Vitamin – Geritol	12.0
Vitamin – Geritonic	20.0
Vitamin – Gevrabon	18.0
Vitamin – Gerizyme	18.0
Vitamin – Mol from liquid	4.8
Vitamin – Niferix Elixir	10.0
Vitamin – SSS Tonic	12.0
Vitamin – Zymalixer	1.5
Vitamin – Zymasyrup	2.0
Vicks Formula 44	10.0
Wal-Act	5.0

or unclear whether it is Halal or *haram* (consumption is prohibited). The highly critical ingredients are present substantially in many drugs, and their compatibility with Halal status is questionable. Therefore, it would be pertinent to look into various items of human consumption, and the production of Halal drugs needs to be re-evaluated and optimized to produce drugs that comply with Shari'ah.

Halalopathy

Halalopathy is a holistic form of medicine that aims to make the prevention and/or healing of diseases more effective by integrating the principles of naturopathy and allopathy and by incorporating the principles and practices of the halal guidelines (Alzeer 2019). *Naturopathy* employs natural means and natural therapies to correct the structural, physiological, and psychological balance. As naturopathy is a holistic treatment, the patients are given recommendations for their diet, exercise, and lifestyle. The *allopathic* approach focuses on the physical signs and symptoms, the pathological changes, and infection caused by microorganisms. The core of allopathy is a chemical drug designed rationally to adjust the speed of biological functions in the body. Drugs can either speed up or slow down biochemical reactions in the body, mostly by binding to receptor sites to either activate (agonists) or inhibit (antagonists) receptor function and regain a dynamic equilibrium state (Alzeer 2018).

Halalopathy or permissible therapy offers a new option to prevent diseases by controlling the entropic state ("a state of disorder") and/or to treat diseases by applying the concept of permissible drugs. A high entropic state leads to internal disorders, while the permissible drug provides a compatible relation between therapeutic medicine and the human lifestyle. The compatibility between drugs and an individual's beliefs enhances trust and lowers entropy, which are essentials for activating the placebo effect and increasing potential energy, respectively. The placebo effect initiates the healing process, whereby the potential energy provides an important energy source to activate the immune system. These are the favorable circumstances that work cooperatively with the prescribed therapeutic drugs to promote the healing process toward recovery. The healing power of halalopathy is not limited to a strong placebo effect but is based on a synergistic effect in which each component contributes to the overall healing process and enhances the total drug effect (Fig. 1).

Production of permissible drugs is achieved by evaluating ingredients and monitoring the production process to ensure specific and well-defined standards, depending on the requirement of the lifestyle or belief of the patient. Halalopathic principles are mostly adapted from Islamic references, but many of these are shared with other religions (Alzeer 2019). The guidelines for the production of permissible therapy "halal pharma" have been implemented in many Muslim countries. The production of drugs complying with halalopathic concepts is a straightforward process, as many of the existing drugs have the potential to be Halal. It is recommended that the processing and formulation of newly approved drugs occurs according to the standards of Halal-Tayyib. Drugs labeled with "Halalan-Tayyiban" are preferred by Muslim patients. The "Halalan-Tayyiban" label is intended to convey to the patient that the medication has been manufactured under maximum

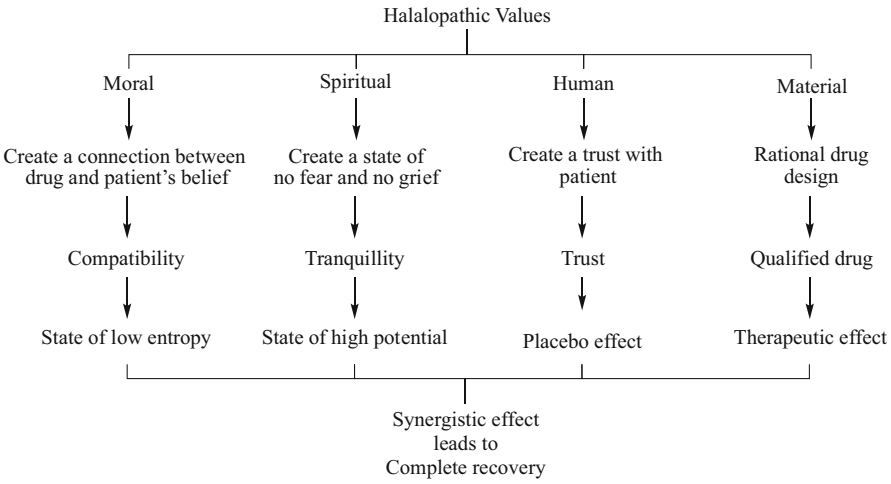

Fig. 1 Halalopathic path toward complete recovery

hygiene and minimum contamination, and that the entire process is clean, pure, and follows Islamic principles. This knowledge will create trust, establish a compatible system between drugs and belief, and eventually, tranquility.

The core principle of halalopathy is to build a compatible system between drug, patient, and mind. Often, higher efficacy can be achieved either by increasing the dose or by extending the duration of action; however, increasing the dose tends to result in a higher incidence of side effects. The tolerant system resulting from the compatibility between therapy and mind often creates a state of existing together, and may lead to treating the drug as a compatible entity; consequently, the rejection mechanisms are reduced and the duration of action is prolonged.

Necessities Overrule Prohibitions

Allah has honored and preferred mankind over other creation: "And We have certainly honored the children of Adam and carried them on the land and sea and provided for them of the good things and preferred them over much of what We have created, with [definite] preference" (Al-Isra 17: 70). The preservation of human life is indispensable and has the highest priority in Islam. Under severe circumstances, Islam is flexible and tolerable. Though eating Halal is mandatory for Muslims, if there is nothing to eat and the Muslim's life is in danger, then Islam allows Muslims to eat non-Halal food: "if one is forced by necessity, without willful disobedience, nor transgressing due limits, then he is guiltless. For Allah is Most Forgiving and Most Merciful" (Al-Baqarah 2: 173). Based on the Islamic principle "Necessities overrule prohibitions," many Muslim scholars allowed patients to use medicines from non-Halal sources provided that the medicine is prescribed by a reliable physician, that human life is at risk, and that no alternative medicine is available (Halim et al. 2014, 2015; Halib et al. 2016).

Conclusion

The Halal production of food, nutraceuticals, and pharmaceuticals in Muslim countries is a growing concept with high demand. Many ingredients involved in the production of food and medications are either non-Halal or produced by the non-Halal process. Drug formulations and food processing are complex and difficult to ascertain with accuracy the origin of some of the ingredients used in medication and food preparations. A potential solution is to establish reassurance on traceability and production processes that may help to promote confidence in the integrity and origin of the ingredients. The implementation of the Halal-Tayyib concept is essential for the determination of Halal status. The process will have to comply with maximum hygiene and minimum contamination, whereas Halal ingredients are used throughout the process. The production process needs to be monitored by qualified scientists with Halal quality assurance experience. Further research is needed to identify alternative ingredients in compliance with Halal standards. The rational design

could be used to replace non-Halal ingredients with reasonable alternatives, to eliminate any potential suspicion and remove *mushbooh* substances. Halal certification remains a necessary step to ensure quality in terms of processes, ingredients, and Shari'ah compliance. However, if there are necessities and the non-Halal product is lifesaving, then all treatment options are approved regardless of the origin.

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