

# Critical Points of Vitamin C Production and Long-Acting Pharmaceutical Preparations

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## ABSTRACT

Vitamin C offers numerous benefits, including its role in the immune system. This factor necessitates the intake of exogenous vitamin C because the human body cannot synthesize it endogenously. Long-acting drugs are known to provide long-term therapeutic effects. The halal and haram aspects of Islam are of great importance because of the potential doubt or syubhat between the two. There are different methods for producing vitamin C, such as Reichstein's method or classical two-step fermentation. Generally, vitamin C synthesis involves biotransformation by microorganisms. One approach to creating long-acting preparations is to coat them with gelatin. A product's halal or haram status is determined by its raw materials, additives, and manufacturing processes. Vitamin C production typically involves fermentation using microorganisms; therefore, a halal growth medium must be considered. Long-acting vitamin C preparations that use gelatin should also be evaluated for halal status. If gelatin originates from halal animals, the law depends on the production process. However, if gelatin comes from haram animals, the law is haram.

**Keywords:** vitamin C, pharmaceutical preparation, long-acting preparation.

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## 1 Introduction

Vitamin C, commonly known as ascorbic acid, has various vital roles in the health of the human body. Vitamin C plays a role in the cellular function of the immune system and has antioxidant properties that can protect the body from endogenous and exogenous oxidative exposure [1]. Vitamin C is one of the cofactors that support the activity of hydroxylating enzymes, such as DNA and histones, which indirectly affect epigenetic modifications that impact cell health and function [1]. Vitamin C also plays a role in several processes related to collagen synthesis, hormone synthesis, carnitine synthesis, and iron reduction in the digestive tract [2]. Vitamin C plays a significant role in the functioning of the human body. Vitamin C deficiency can cause mouth ulcers, weakness, lethargy, muscle pain, and other symptoms [3]. Based on the many benefits vitamin C has for the body, the need for vitamin C must be met. The inability of humans to synthesize vitamin C endogenously leads to the need for vitamin C intake through daily consumption.

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Vitamin C or ascorbic acid has the visual characteristics of a powder and is white or slightly yellow. Vitamin C has a molecular weight of 176.12, a pleasant, sharp, sour taste, and no odor [4]. Vitamin C has good water solubility and belongs to the soluble category. However, vitamin C tends to be unstable in aqueous solutions and can undergo degradation. Vitamin C can also undergo significant degradation due to heat. Ascorbic acid degradation involves a complex series of oxidation reactions and intermolecular restructuring. This phenomenon is one of the main factors leading to quality and color changes during processing and storage [5].

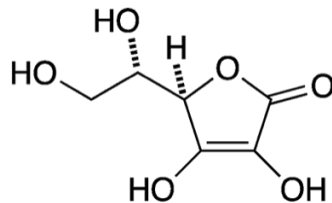


Fig. 1 Ascorbic Acid Chemical Structure

Long-acting drugs have long-acting effects that are absorbed gradually after administration and maintain their therapeutic effects over a prolonged period. The term "long-acting" in the context of drug delivery refers to the application via various oral, topical, and parenteral routes, such as intravenous, intramuscular, subcutaneous injection, and implantable devices. In general, to be considered a long-acting therapy, oral drugs must be administered at least once a week. Long-acting drugs have specific pharmacokinetic and pharmacodynamic properties that support their release. Apart from requiring a good safety profile, long-acting drug formulations also require low water solubility because drugs with good water solubility facilitate the release process. Long-acting drugs should also potentially minimize the need for high plasma concentrations and a long pharmacokinetic half-life to minimize rapid elimination [6].

Islam etymologically means "salvation" and is a religion recognized by Allah SWT. The realization of the meaning of Islam requires guidance or guidelines that cover all aspects of human life. One of the crucial aspects in the life of mankind, especially Muslims, is the matter of being halal and forbidden, both in attitude and in food or drink. These two aspects are fundamental to understand because there is something between them called syubhat (doubt or uncertainty between halal and haram) [7]. The Prophet Muhammad SAW encouraged his people to pay attention to halal things and avoid everything that is haram so that they can understand the difference between the two, including things that are syubhat. Therefore, this article will discuss halal, haram, or syubhat products from vitamin C and pharmaceutical preparations that have a long working period or long-acting.

## 2 Materials and methods

The method used to collect data was a literature review, which involved searching for literature in the last ten years. Literature uses books, articles, information from the Internet, or other data sources related to the topics discussed.

### 3 Results and discussion

#### 3.1 Vitamin C Production

Vitamin C, also known as ascorbic acid, was first commercially produced through the Reichstein process using d-glucose as the initial substrate. In this process, the hydrogenation of D-glucose and hydrogen occurs to synthesize D-sorbitol. D-sorbitol is then converted to L-sorbose by D-sorbitol dehydrogenase (SLDH) from *Gluconobacter oxydans* or other *Acetobacter* sp. L-sorbose is then oxidized to 2-KLG through protective oxidation reactions and converted to L-ascorbic acid through esterification and lactonization. In addition to the Reichstein process, ascorbic acid can be produced through classical two-step fermentation. In principle, the two methods are almost identical. In the classical two-step fermentation process, two steps are required. In this process, d-sorbitol is converted into L-sorbose by *G. oxydans*. L-sorbose is then converted into 2-KLG through a mixed culture fermentation process with *Ketogulonigenium vulgare* (gram-negative bacteria) and *Bacillus megaterium* (gram-positive bacteria) rather than through a pure chemical reaction [8].

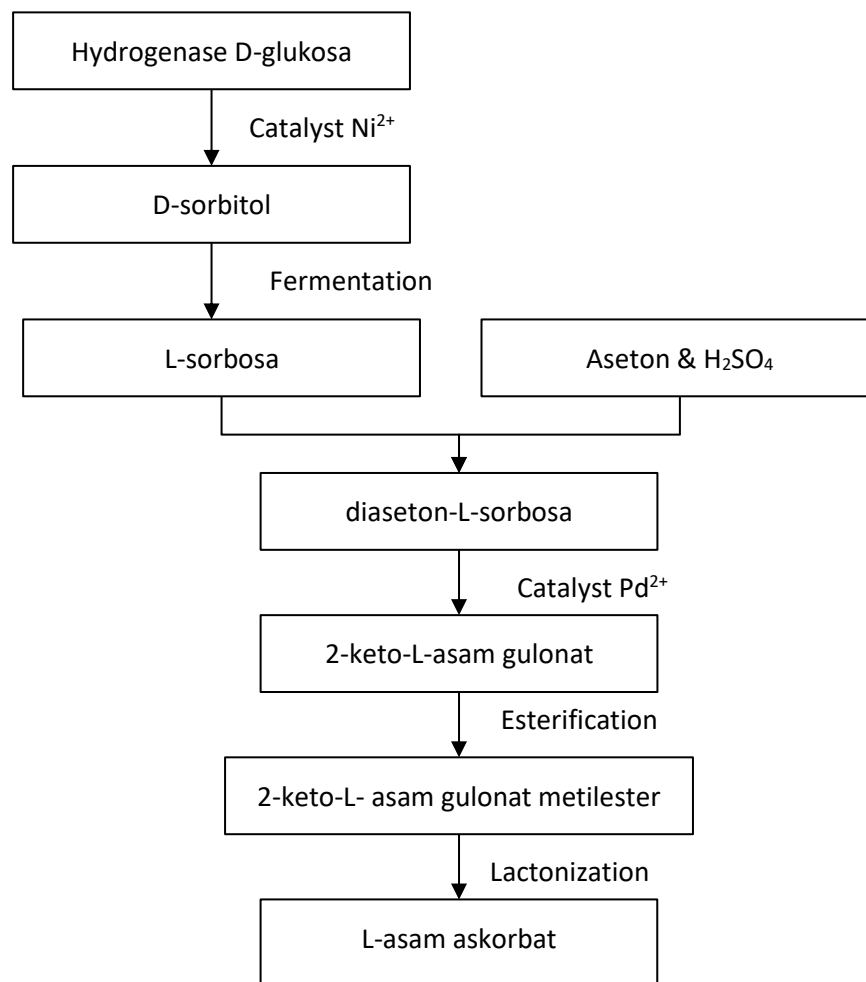


Fig. 2 Ascorbic Acid Synthesis Process Reichstein Process

For ascorbic acid production, it is necessary to consider processes involving chemical synthesis and biotransformation. In ascorbic acid synthesis, there is a trend towards using biotransformation involving microorganisms developed in special growth media. These growth media require carbon and nitrogen sources and other components that must be

verified in terms of their halal status [9]. Based on MUI fatwa number 1 of 2010, microbial products are haram if produced with growth media that utilize pig elements.

### 3.2 Vitamin C Preparations

In Indonesia, single preparations of vitamin C (ascorbic acid) are available in tablets, lozenges, and injections. Meanwhile, in combination with other vitamins, vitamin C is available in various dosage forms, such as tablets, lozenges, effervescent tablets, caplets, capsules, syrups, and topical preparations in the form of serum. Along with the development of drug delivery technology, vitamin C preparations are available in conventional form and in modified release, such as long-acting.

Long-acting pharmaceutical preparations are drug preparations whose effects can last long and include various dosage forms. Long-lasting drug effects can be obtained by using a controlled drug delivery system, one of which is by making extended-release products. Extended-release products are designed to release drugs in a controlled manner at a predetermined rate, duration, and location to achieve and maintain optimal therapeutic drug levels in the blood. Over the years, many terms such as sustained release (SR), sustained action (SA), prolonged action (PA), controlled release (CR), extended-release (ER), timed release (TR), and long-acting (LA) have been used by pharmaceutical manufacturers [10].

Pharmaceutical preparations with a long duration of action (long-acting) can be found in the form of slow-release preparations. This type of preparation is usually in tablets or capsules with a controlled release mechanism. This preparation was formulated to provide an initial therapeutic dose followed by a longer and more stable drug release to reduce the frequency of drug administration [11]. Various methods can be used to create slow-release preparations, including the masking process. Shrouding uses materials that can function as drug-release control membranes.

One of the dressing materials used in vitamin C preparations is gelatin. Gelatine is a substance obtained by extracting collagen from the cartilage or skin of animals, such as cows, goats, fish, and pigs. The law of using gelatin in food or other products depends on the source of the gelatin. If it comes from halal animals that need to be slaughtered, such as cows or goats, the law depends on the process of slaughtering the animals [12]. However, if gelatin comes from pigs, the legal status will become haram because pigs are forbidden from using any part of them. Pig products and their derivatives are forbidden in Islam, as stated in Surah Al-Baqarah verse 173:

إِنَّمَا حَرَّمَ عَلَيْكُمُ الْمَيْتَةَ وَالدَّمَ وَلَحْمَ الْخِنْزِيرِ وَمَا أُهْلَ بِهِ لِغَيْرِ اللَّهِ فَمَنْ اضْطُرَّ غَيْرَ بَاغٍ وَلَا عَادٍ فَلَا إِثْمَ عَلَيْهِ إِنَّ اللَّهَ غَفُورٌ رَّحِيمٌ

Meaning: Verily, Allah has only forbidden carrion, blood, pork, and animals, which (when slaughtered) are called by a name other than Allah. However, whoever is compelled to eat them and does not desire to do so, nor does he transgress the limits, there is no sin on him. Indeed, Allah is Forgiving and Merciful

#### 4 Conclusion

The halal-haram law of a product is determined not only by its primary raw materials but also by the additives and materials used in the manufacturing process. In the production process of vitamin C, a fermentation process is needed that uses microorganisms so that the growth media needs to be considered. Vitamin C can be harmed if the microorganism growth medium originates from haram materials. Long-acting vitamin C preparations that use pork gelatin as an additional ingredient are also harams. In choosing vitamin C products, attention is needed regarding halal labeling and the product's composition.

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