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Original Article

Development and Evaluation of Herbal-Enriched Nutraceutical Gummies for Pediatric Health

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ABSTRACT

Background: Nutraceuticals, which combine the nutritional benefits of food with the therapeutic effects of pharmaceuticals, offer a promising approach to enhancing children's health and well-being. Among these, herbal-enriched nutraceuticals stand out due to their potential to deliver a range of health benefits derived from natural plant sources. **Aim:** This study aimed to develop gummies with *Elettaria cardamomum, Amomum subulatum* Roxb*, Zingiber officinale, Beta vulgaris* L. using different concentrations of gelling agents, plasticizers and pH modifiers. **Materials and Methods:** Gelatin was tested at concentrations of 8% and 10%. The objective was to assess concentration of gelling agents that affect the physical properties of the gummies, such as visual appearance, dispersion time, and texture profile (hardness, chewiness, and gumminess). The gummies were heated and allowed to set before being evaluated using a randomized method. The type and concentration of the gelling agents, as well as their interaction, had significant effects on dispersion time, appearance, hardness, gumminess, and chewiness. **Conclusion:** Gummies made with 8% gelatine were found to be the best formulations, meeting all physical property requirements, showing no syneresis, and having the most pleasant texture.

Keywords: *Elettaria cardamomum*, *Amomum subulatum* Roxb, *Zingiber officinale*, *Beta vulgaris* L., Herbal gummies, Swelling ratio, Ph, Syneresis study, Disintegration study.

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INTRODUCTION

The body is protected from infection by the structures, biochemical processes, and mediators that make up the immune system. Pre-existing immune responses to infection that have developed to identify pathogens and safeguard children are referred to as innate immunity. On the other hand, acquired immunity is unique to each foreign agent and occurs later, following exposure. The main components of innate immunity are various plasma proteins, phagocytic cells, dendritic cells, Natural Killer (NK) cells, and epithelial barriers. Nutraceuticals, which are bioactive compounds derived from edible sources, possess therapeutic properties that can modulate the immune system. These nutraceuticals have shown immunity-boosting effects, including active modulation and antiviral, antibacterial, and antifungal properties. Additionally, nutraceuticals can support the mental and physical development and well-being of toddlers. The preparation of the gummy formulation involves using several key tools and equipment to ensure precision and quality. Essential instruments include spatulas, 100 mL and 50 mL beakers, and measuring cylinders, which are crucial for accurate measurement and handling of ingredients. A weighing balance is used to precisely weigh the raw materials, ensuring the correct proportions are used. A muffle-equipped dissolution apparatus is also employed to thoroughly dissolve and blend the ingredients, achieving a uniform mixture essential for the consistency and effectiveness of the final gummy product. These tools and equipment facilitate a controlled and efficient production process, ensuring the formulation meets the desired specifications and quality standards. This methodical approach underscores the importance of precision and accuracy in creating a consistent and high-quality gummy formulation.

Elettaria cardamomum, both small and large varieties, boasts an array of therapeutic properties that have been recognized for centuries. Small cardamom is renowned for its efficacy in treating gum and throat infections, as well as reducing inflammation in the lungs, alleviating symptoms of pulmonary tuberculosis, and aiding in digestive disorders. Studies have demonstrated that ethanolic aqueous extracts of cardamom possess anti-inflammatory effects, particularly against conditions like paw edema induced by carrageenan in rats.[1,2] Remarkably,

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research indicates that *Elettaria cardamomum* may serve as an antidote against venomous snake and scorpion bites, showcasing its potential in emergency medical scenarios. Furthermore, large cardamom is valued for its ability to address gastrointestinal issues due to its cooling properties. Methanolic extracts of cardamom seeds have exhibited analgesic effects, offering relief from pain.[3-5] In addition to its analgesic properties, cardamom (*Elettaria cardamomum*) has been investigated for its potential as an antidepressant, with ongoing studies evaluating its efficacy in the marble burying test for rats, which assesses antidepressant activity. Moreover, cardamom oil is recognized for its digestive benefits and laxative properties, aiding in the relief of colic and soothing gastrointestinal discomfort.[6-11] *Elettaria cardamomum* 's sweet flavour isn't just for culinary use-it also harbours carminative properties that support gastrointestinal health, helping to alleviate issues such as diarrhoea induced by castor oil and magnesium sulphate. In hot water extracts, cardamom fruit demonstrates its effectiveness in addressing gastrointestinal problems, highlighting its versatile and holistic therapeutic potential.[12]

The pharmacological properties of greater *Amomum subulatum Roxb* included pulmonary antiseptic, neuromuscular antispasmodic, aphrodisiac, expectorant, anthelminthic, antibacterial (varying), cephalic, cardiotonic, diuretic, emmenagogue, sialagogue, and stomachic effects. The little cardamom pod is used to relieve gum and throat infections, as well as lung inflammation, pulmonary TB, and digestive disorders.[13] Rats with paw edema caused by carrageenan showed an anti-inflammatory response to a cardamom extract in an ethanolic aqueous media. As an Antidote, certain studies have indicated that it is also efficacious against the venom of snakes and scorpions. anti-ulcerogenic Additionally, the huge cardamom is used to treat gastrointestinal disorders. The analgesic effect of cardamom seed methanolic extract is due to its cooling impact.[14]

Zingiber officinale, a spice and medicinal herb that is widely used worldwide, is the root of the *Zingiber officinale* roscoe plant, which is a member of the Zingiberaceae family. Primary pharmacological properties of *Zingiber officinale* and the chemicals derived from it include anti-inflammatory, anti-tumorigenic, anti-apoptotic, anti-hyperglycaemic, anti-lipidemic, and anti-emetic properties.[15] While *Zingiber officinale* lacks protein and other minerals, it is a great source of antioxidants. For this reason, studies have indicated that *Zingiber officinale* can lessen oxidative stress in a variety of ways. When the body produces an excessive amount of free radicals, oxidative stress results. Free radicals are harmful compounds that are created by several processes in metabolism. *Zingiber officinale* has been shown by researchers to be highly beneficial in preventing the formation of prostate cancer cells.[16]

Beta vulgaris L., belonging to the Chenopodiaceae family, boasts a vibrant crimson hue. Also referred to as beet, chard, spinach beet, sea beet, garden beet, white beet, and Chukander (in Hindi), beetroot possesses potent therapeutic properties that positively impact human health.[17] The integration of traditional remedies with conventional medicines has been cited in numerous medical treatises for treating various ailments, illnesses, and diseases. *Beta vulgaris* L., a well-known culinary plant, offers significant health benefits due to its rich natural components. It contains antioxidants, vitamins, and minerals that provide essential antidepressant, antibacterial, and anti-carcinogenic properties. Furthermore, beetroot pigment is widely used as a culinary dye.[18]

Apis mellifera Linnaeus is a natural product renowned for its medicinal properties. It is reported to contain over 200 chemical compounds. Primarily composed of fructose and glucose, honey also includes fructo-oligosaccharides, amino acids, nutrients, minerals, and enzymes. Honey exhibits biological activities, including antioxidant properties.[19] Scientists recognize that free radicals can cause molecular changes and gene alterations in a variety of organisms. Oxidative stress is known to contribute to numerous diseases, leading researchers to seek natural sources with active components that can mitigate its effects on cells. Natural honey is rich in flavonoids (such as apigenin, pinocembrin, quercetin, galanin, chrysin, and hesperidin) and phenolic acids.

Gelatine type A, is a powder made from the acidic breakdown of collagen. It also contains a heterogeneous collection of water-soluble proteins with large average molecular weights, such as glycine, proline, and hydroxyproline.[20] Gelatin has been employed in *in vitro* coated cell culture to increase cell line adhesion. This compound can be employed as a blocking reagent in numerous biological methods, including immunity chemistry, ELISA, and western blotting. The material can be used in microencapsulation experiments as a delivery vehicle for the release of active biomolecules because it is a biocompatible polymer.[21]

The gummy formulation relies on ingredients sourced in their raw form from the local market in Kalyanpur, Kanpur Uttar Pradesh. This approach ensures that all necessary components are procured directly and are likely fresh and unprocessed. Once these raw ingredients are acquired, they undergo a grinding process to achieve the desired consistency and texture suitable for the gummy formulation. The grinding process is crucial as it prepares the raw materials for further processing and incorporation into the final product. By sourcing locally, the process supports local markets and potentially ensures better control over the quality and origin of the ingredients used. This method emphasizes a straightforward and potentially more sustainable approach to ingredient procurement and preparation, likely contributing to the overall quality and consistency of the gummy formulation. Thus, the formulation process is closely tied to the local supply chain, reflecting an integration of traditional market resources with modern production techniques.

MATERIALS AND METHODS

Materials

The main material used in this study were *Elettaria cardamomum, Amomum subulatum* Roxb, *Zingiber officinale, Beta vulgaris* L., *Apis mellifera* Linnaeus (Figure 1), procured from local market of Kalyanpur, Kanpur and passed through a 500-mesh screen after grinding. The other excipients used were pharmaceutical grade or food-grade, namely gelatin (Nitta Gelatin India Ltd., Kerala), propylene glycol (Fengda Chemicals Corp., China), sodium benzoate (Sigmaaldrich, India).

Method of preparation of nutraceutical herbal gummies

The manufacturing process begins with dispersing required amount of *Elettaria cardamomum, Amomum subulatum* Roxb, *Zingiber officinale, Beta vulgaris* L. in 100 mL of solvent while heating at 70°C. Gelatin and *Apis mellifera Linnaeus* was added to solution while maintaining temperature (Table 1). A homogenous mass mixture is generated by gradually adding propylene glycol while stirring continuously. And last, the mixture was mixed with sodium benzoate and citric acid. Poured gradually into the silicone mould shaped like a teddy bear was the chewable gummy mass mixture. The gummies set at room temperature after 15 min. The refrigerator chiller was used for 15 min to keep the mould preparations (Figure 2). The preparation was then taken out of the mould and its physical properties were examined. Gummies were then placed in a room temperature storage for a whole day.[21-23]

Evaluation of herbal gummies

Determination of physical appearance

Visual inspection was conducted on all produced gummies to assess their appearance, including colour, transparency, homogeneity, and uniformity. By gently rubbing the prepared jelly between the thumb and index fingers, grittiness and stickiness were assessed.[24]

Determination of gel pH

A digital pH metre was used to measure the gummy's pH. Gummy was dissolved in distilled water and electrode of pH was dipped into dissolved gummy.

Swelling ratio

By calculating gummy's starting weight, the development index was calculated. The amount of liquid in the gummy structure that can be absorbed is determined by the swelling index. Next, at a regulated room temperature of 25°C to 30°C, gummy mixture was immersed in 100 millilitres of filtered water for 10 sec. Following soaking, a chewable gummy is taken out and cleaned with filter paper to remove any remaining water that may have stuck to the gummy's surface.

$$Swelling\ ratio = \frac{Ws - Wd}{Wd}$$

Ws=weight of chewable gummy after soaking.

Wo=weight of chewable gummy before soaking.

Figure 1: Major ingredients used for development of herbal nutraceutical gummies.

Texture analysis

With the use of a texture analyzer (V-TECH Texture Analyser, India), the textural characteristics of gummy were identified, including its stiff mouthfeel. With the use of probe P100 and parameters including a trigger of 5 g, deformation of 1.2 mm, and speed of 1.0 mm/s, a texture profile analysis was obtained by compression analysis.[24] The maximum force value on the graph can be used to measure firmness.

Syneresis study

When the gel structure undergoes syneresis, water molecules are liberated. The gel structure contracts or shrinks, which causes syneresis. The preparation's poor instability and rapid texture softening were indicated by the large proportion of chewable gummy syneresis. By affixing filter paper to the chewable gummy's surface, the preparation's syneresis % was measured over the course of 48 hr at a regulated room temperature.[25] The following formula determines the amount of syneresis based on the weight differential between chewable gummy before and after contact with a filter paper:

$$\%\ Syneresis = \frac{Initial\ weight - Final\ weight}{Initial\ weight} * 100$$

After being stored at room temperature for 48 hr, syneresis was carried out to detect any changes in the gummy consistency or size shrinking. So, gummies that experience syneresis would not be allowed to participate in any more assessment experiments.

Table 1: Formulation design of gummies.

Ingredients	Uses	F1	F2
Beta vulgaris L. (g)	Antioxidant and anti-inflammatory activity.	15	10
Zingiber officinale (g)	Antioxidant, anti-inflammatory activity and immunomodulatory activity.	3	5
Elettaria cardamomum (g)	Antibacterial and anti-inflammatory activities.	1.70	2
Amomum subulatum Roxb (g)	Antioxidant, cytotoxic activity.	2	4
Apis mellifera Linnaeus (g)	Immunostimulant	10	3
Gelatin (g)	Thixotropic agent	8	10
Propylene glycol (%)	Plasticizer	2	4
Citric acid (%)	Acidity modifier	1	1
Sodium benzoate (%)	Preservative	0.5	0.5
Purified water (mL)	--	100	100

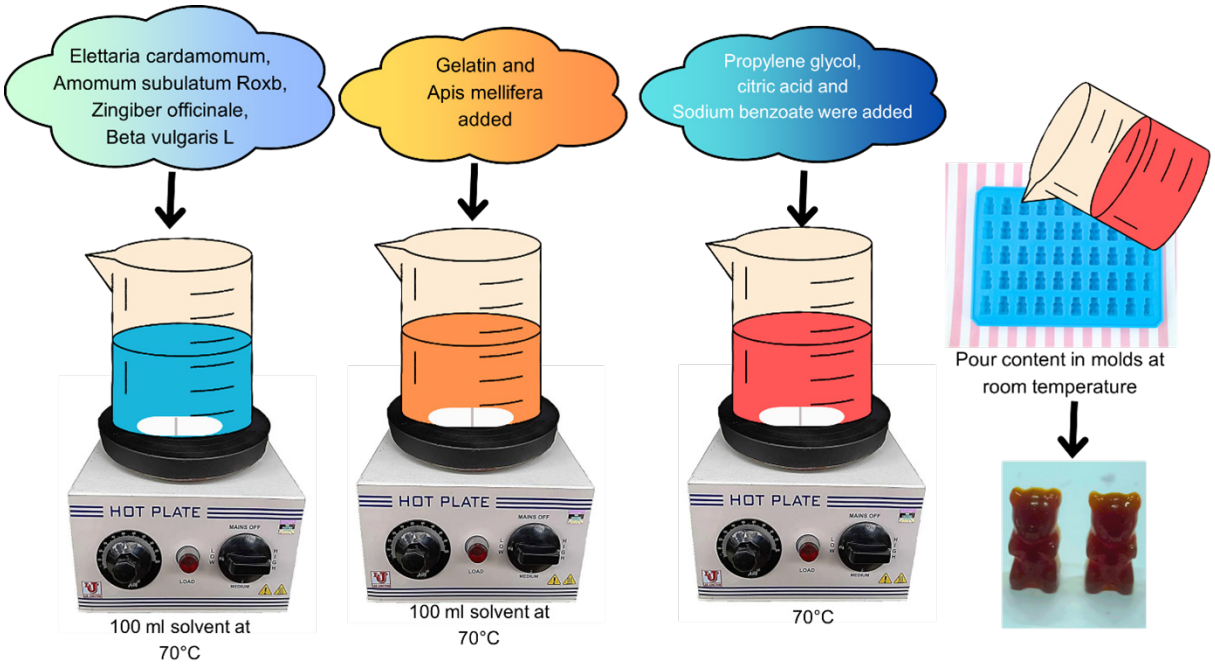

Figure 2: Steps to develop nutraceutical herbal gummies.

Disintegration time

Evaluation of disintegration time was used to predict the speed of disintegration of gummies in aqueous media while ensuring the release of the active ingredients from the gel matrix. The disintegration test was performed using a magnetic stirrer in a flask with 50 mL of purified water at 37°C.[26] The chronometer was used to monitor the dissolving process and determine the dissolution time. The experiment was carried out with gummy bears that had been maintained at room temperature.

Ash value

Three grams of the drug were placed in a silica crucible and heated over a burner flame. The charred material was then transferred to a muffle furnace and heated at 600-650°C for about 6 hr. The resulting whitish ash, free of carbon, was allowed to cool and then weighed using ashless filter paper.

Table 2: **Physico-chemical parameters of herbal gummies.**

Parameters	Observations	
	F1	F2
Colour	Reddish brown	Reddish brown
Flavour	Sweet	Sweet
Shape	Teddy shape	Teddy shape
Texture	Non-sticky	Slightly sticky
Evaluation parameters	F1	
	Test value	Standard value
Moisture content	16.20%	9% to 18%
pH	5.92±0.356	3 to 6
Swelling index	1.0234±0.2301	
Dissolution time (min.)	7±1.21	5-10
Viscosity (cps)	3942±1.051	--
Ash value	0.02335%	0.03% to 0.07%

$$\% \, Ash = \frac{(Initial\ weight - Final\ weight)}{Initial\ weight} * 100$$

RESULTS

As seen in Figure 3, manufactured gummies were 2 cm long, reddish brown in colour, and scented well. The criteria of appearance are included in Table 2. Among both gummy preparations, only F1 displayed acceptable homogeneity without noticeably sticking when holding. For this reason, formula F2 was not included in any more testing. Gummies' pH value, as indicated in Table 2, was discovered to be 5.92.[27]

To make the gummy mass more elastic, plasticizers like propylene glycol are frequently added to chewable gummy formulations.[28] The disintegration time reported by the gummy was less than 15 min, which is the optimal disintegration period for nutraceutical gummy. Percentage ash was found to be 1.02345±0.9657.

DISCUSSION

Because citric acid was used as a pH modifier to improve the gelling power of the gelatin, this is regarded as somewhat acidic. The capacity of the nutraceutical gummy to expand in water was assessed using the swelling index. Gummy disintegration time and syneresis parameter are linked to the swelling index. By forming a barrier to prevent water loss from the chewable gummy structure, the plasticizer can affect the bonding microstructure of the gelling agent. By doing this, the texture of the chewable gummy remains unchanged from when it was initially kept. Because sucrose at the prepared pH immobilises free water, an increase in propylene glycol reduces the syneresis potency. However, formula (F2) demonstrated syneresis; hence, it was not included in the analysis. In about 7 to 8 min, gummies broke down in cleaned water. The more rapidly the gummy dissolves in the medium, the faster the medication releases. Numerous factors, including as content, size, and ambient temperature, can affect how quickly gummies dissolve. Generally, gummies disintegrate

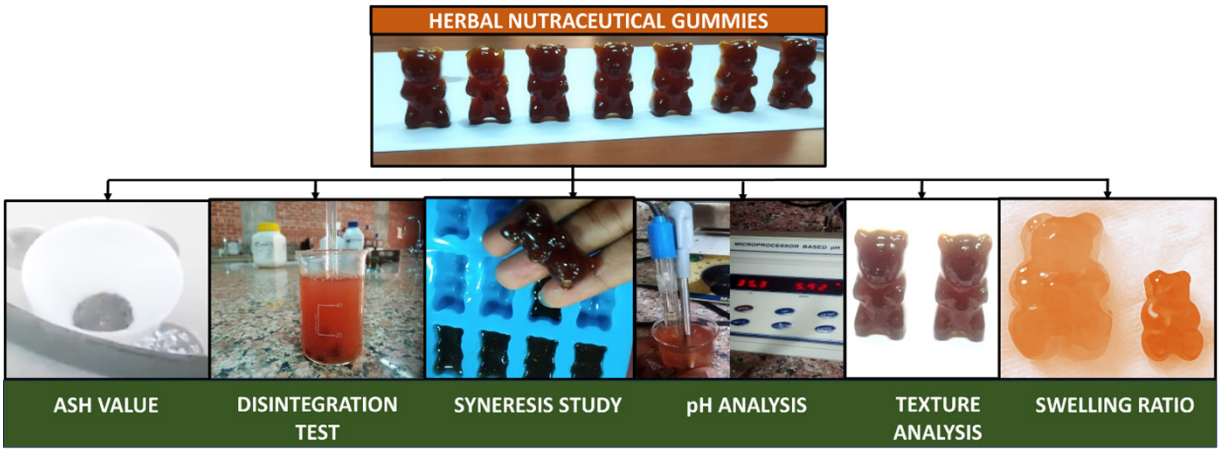

Figure 3: Evaluation parameters of herbal nutraceutical gummies.

relatively slowly compared to other types of candies due to their gel-like consistency.[29] In a typical scenario where a gummy is placed in the mouth, it starts to dissolve as saliva breaks down the gelatin and other ingredients. The rate of dissolution can be influenced by factors such as temperature, pH of saliva, and the presence of enzymes in saliva that can break down the gummy material.[30] Humans require a variety of elements and minerals, many of which are derived from plant sources. For this reason, it is essential to determine whether kinds of plant materials meant for human consumption contain adulterants, residuals, and crude materials. The human body needs both organic and inorganic materials to function properly. Our diet primarily consists of proteins, carbohydrates, and fats, along with essential vitamins and minerals.[31] The quality of our food depends on the types and amounts of organic and inorganic substances and minerals it contains. These nutrients are vital for preventing diseases, coping with environmental pollutants, and enhancing our ability to work, contributing to a healthy diet (e.g., phosphorus, calcium, sodium, potassium). However, some elements can be toxic or harmful (e.g., mercury, lead, aluminum, cadmium). Minerals are widely used to address various health problems. Depending on the age and treatment of the plant, there may be differences in the kind and amount of ash that remains after plant extracts are burned.[32] The inorganic part of the plant is represented by its ash content, which varies over time and among different plant organs. Calculating the ash value for inorganic solutes is important for materials used in medical applications. Plant ash is used in several herbal remedies because inorganic salts, unlike organic plant components, are often essential in medicine. Results indicates that adulteration of raw ingredients by substances. An interesting characteristic of ash is its varying solubility in different solvents. Therefore, this study evaluated the solubility of ash in both water and hydrochloric acid.

CONCLUSION

The development of gummies represents a significant advancement in the nutraceutical and pharmaceutical industries. Their increasing popularity demonstrates their appeal and effectiveness as a delivery vehicle for vitamins, minerals, and other supplements. Gummies are a pleasurable and handy alternative to traditional supplement forms such as tablets and capsules, which some people find difficult to swallow. Creating high-quality gummy formulations is a rigorous procedure that requires carefully acquiring fresh ingredients from reputable local markets. Precise measurement and thorough blending are required, with specialist equipment such as dissolving machines and pH meters. These tools ensure that the combination is homogenous and the pH levels are minimax suitable, which improves the overall quality and stability of gummies. Quality control procedures must be strictly enforced throughout the manufacturing process. Monitoring the physical qualities, such as hardness, gumminess, and chewiness, maintains consistency between batches. Furthermore, preventing syneresis during storage is critical for preserving product quality over time.

Ultimately, a high-quality product that meets consumer expectations is produced through the laborious process of creating gummy formulations, which includes precise measurement, ingredient procurement, and quality control. Gummies boost their standing in the supplement industry by offering a convenient and tasty way to ingest nutrients and supplements, in addition to being an efficient means of delivering these products to consumers.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

RH: Research Highlights; **F1:** Formulation 1; **F2:** Formulation 2; **Ws:** Weight of chewable gummy after soaking; **Wd:** Weight of chewable gummy before soaking; **NK:** Natural Killer; **ELISA:** Enzyme-Linked Immunosorbent Assay; **ORCID:** Open Researcher and Contributor ID; **cps:** Centipoise; **pH:** Potential of Hydrogen; **UV:** Ultraviolet; **HPLC:** High-Performance Liquid Chromatography; **GC-MS:** Gas Chromatography-Mass Spectrometry; **NMR:** Nuclear Magnetic Resonance; **IR:** Infrared Spectroscopy; **XRD:** X-Ray Diffraction; **SEM:** Scanning Electron Microscopy; **TEM:** Transmission Electron Microscopy; **DSC:** Differential Scanning Calorimetry; **TGA:** Thermogravimetric Analysis; **FTIR:** Fourier-Transform Infrared Spectroscopy; **HPTLC:** High-Performance Thin-Layer Chromatography; **UPLC:** Ultra-Performance Liquid Chromatography; **MALDI-TOF:** Matrix-Assisted Laser Desorption/Ionization Time-of-Flight; **LC-MS:** Liquid Chromatography-Mass Spectrometry; **GLP:** Good Laboratory Practice; **GMP:** Good Manufacturing Practice; **ICH:** International Council for Harmonisation; **FDA:** Food and Drug Administration; **WHO:** World Health Organization; **USP:** United States Pharmacopeia; **EP:** European Pharmacopoeia; **BP:** British Pharmacopoeia; **IP:** Indian Pharmacopoeia.

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