

The regulatory framework for phytopharmaceuticals



**Saba Wahid A.M. Khan*¹, Roja Rani Budha¹,
GSN Koteswara Rao²**

¹Department of Pharmaceutics, M.E.S H.K College of Pharmacy,
Jogeshwari (W), Mumbai, Maharashtra-400102

²Professor & Head, Dept. of Pharmaceutics, Shobhaben Pratapbhai Patel
School of Pharmacy and Technology Management, SVKM's NMIMS, Vile Parle (W),
Mumbai-400056, Maharashtra
Email: khansabawahid@gmail.com

Abstract

Phytopharmaceuticals, classified as purified and standardized plant-based drugs containing multiple bioactive compounds, are emerging as a vital category in modern medicine. In India, the regulatory framework for these drugs, overseen by the Central Drugs Standard Control Organization (CDSCO), ensures that phytopharmaceuticals meet stringent standards for quality, safety, and efficacy, similar to synthetic drugs. This approach contrasts with traditional AYUSH medicines, as phytopharmaceuticals emphasize scientific validation and standardization of plant materials. The introduction of regulatory provisions through the Drugs and Cosmetics Act (D and C Act) supports the development of botanical-based drugs, fostering innovation in the field. Phytopharmaceuticals promoting their acceptance in the global market and encouraging research into plant-derived therapeutics. This regulatory framework presents a promising avenue for the integration of traditional knowledge with modern science, advancing the development of effective, plant-based therapies.

Keywords: Regulatory, Ophthalmic drugs, Safety, Standardization, Bioactive

1. Introduction

Phytopharmaceuticals are characterized by the purification and production of fractions containing at least four bioactive or phytochemical compounds that have been well and quantitatively evaluated. These drugs are obtained from the extraction of medicinal plants or their parts and are intended for internal or external use by humans or animals. Their purpose includes the diagnosis, treatment, cure or prevention of diseases or conditions unless administered parenterally (1-3).

2. Regulatory framework and standards for phytopharmaceuticals in India

Phytopharmaceutical drugs in India come under the supervision of the Central Drugs Standard Control Organisation (CDSCO), which grants special approval to these products. The gazette notification outlines the need for scientific data on efficacy, safety and effectiveness to ensure that herbal medicines, similar to synthetic drugs, are rigorously evaluated. This equation contrasts traditional medicine, which is often viewed with suspicion, with traditional AYUSH medicine, which has long relied on herbal medicines. Herbal medicine refers to the reusability and standardization of plant materials used in the development of medicine while embracing traditional knowledge. The extracts are standardized, measured and qualitatively assessed. These drugs are obtained from medicinal plants and are intended for use in diagnosing, treating, alleviating or preventing diseases or disorders in humans or animals, but do not include parenteral administration (3-5).

In Schedule Y, the newly added Annex I B specifies the information required for medicinal practices or the import and manufacture of herbal medicines in India. Regulatory requirements for new drug applications (NDAs) for botanicals include standard procedures such as safety data, drug data, and human studies including clinical trials. Additional emphasis is given to: Information on botanical origin, formulation, route of administration, dosage, therapeutic class, and drug claims procedure. Once approved by the CDSCO, these drugs will have the same commercial status as compounded drugs under international regulations in countries such as the United States and China. This change encourages scientific research, innovation, and the creation of new herbal medicines, thus promoting greater acceptance of herbal products in modern medicine (6-12).

Acts D and C of October 24 establish the regulatory framework for the identification and approval of herbal medicines. This policy includes the scientific evaluation of herbal medicines (similar to synthetic drugs). Although this policy is not yet in force, some botanical products such as Guggulu tablets (for hypercholesterolemia), Ginkgo biloba leaves (for memory loss) and silymarin capsules (for liver disease) have been found to do well by the CDSCO. However, the approval process for these products is taking a long time due to the need to make regulators aware of the unique challenges faced by botanicals compared to synthetic products (13-15).

Especially medicines derived from traditional knowledge such as Ayurveda, which has a long history of safe use. In August 2008, the Government of India appointed Nitya Anand and DBA Narayana as interlocutors to consider these policies. The expert panel emphasized the importance of creating herbal medicines inspired by Ayurvedic wisdom but measured against modern science. It does not affect the application of Ayurvedic, Siddha and Unani (ASU) medicines subject to Section IVA. These regulations provide another avenue for the development of botanical medicines, support scientific research and drug development, and allow ASU products to continue to be managed under the same criteria that are already there (16,17).

3. Standardization and characterization of phytopharmaceuticals

Standardization of botanical medicine includes detailed information about herbal products including inspection of harvesting areas, growing and processes such as washing, drying and storage. Other important factors include certification of herbal products, presence of phytotoxins and tests such as sensory evaluation, ash value and microbial count.

According to Indian Pharmacopoeia (2014), the extraction process should be adjusted within a certain tolerance according to the biomarker or drug marker content. Similarly, the United States Pharmacopoeia (USP) and the European Pharmacopoeia provide guidelines for the standardization of botanical products to ensure efficacy and therapeutic effectiveness (18,19).

4. Integrated approach and global alignment

The development of plant medicine requires an integrated approach that draws on traditional knowledge, modern scientific data, bioassays, and decisions such as biodiversity and international management. Plant-based phytopharmaceuticals comply with national regulations, such as those in the United States and China, to ensure that these products are scientifically evaluated and not based on traditional knowledge.

This policy encourages innovation in medicine, especially for industry and scientists working on plant-based lead. With well-controlled clinical trials to maintain safety and efficacy measures, botanical drugs can be expected to gain wider acceptance in today's medical community. The Drugs Inspector General of India considers these drugs to be similar to synthetic drugs and wants to expand their use and encourage more research in this area.

The botanical medicine research initiative responds to the global interest in phytotherapeutics and has the potential to address unmet medical needs and lead to future change (20,21).

5. Limitations of phytopharmaceuticals

The development of phytopharmaceuticals faces major challenges, especially for small and medium-sized enterprises (SMEs) facing financial constraints. The significant costs of clinical trials, international certification and international product registration all require significant financial support.

Additionally, lack of regulatory oversight hinders progress in scientific research needed to develop effective, evidence-based herbal medicines. Complex and restrictive patent laws are a barrier to innovation and business growth. The Biodiversity Act of 2002 adds an additional layer of complexity that impacts current and future development in the phytopharmaceutical sector (17,19).

6. Requirements for submission of application for clinical trials, import, or manufacture of a phytopharmaceutical drug

6.1. PART I: Data to be submitted by the applicant

- 6.1.1. Medical information:** A brief summary of the botanical drug, including botanical name (by use or spelling), composition, application, dosage, medical classification, and administration schedule.
- 6.1.2. Published literature:** Documented information on the use of plants or drugs in traditional or ethnomedicine, including licenses and information on ingredients, dosage, and administration.
- 6.1.3. Contraindications and side effects:** Information from traditional or current use indicating known contraindications, side effects, or adverse reactions.
- 6.1.4. Research reports:** Published studies on the safety and medicinal properties of drugs. This should include: Information on normal use or procedures.
- 6.1.5. Usage history:** Information on current use including details of the product, manufacturer, sales, human exposure and duration on the market.
- 6.1.6. Pharmacological information:** Information on pharmacodynamics, clinical studies and human trials (if applicable).
- 6.1.7. Monographs:** A monograph of a plant, product or extract with English translation is required (17,19,23).

6.2. PART II: Data generated by applicant

- 6.2.1. Identification and origin of plant material:** Taxonomic description with botanical name (genus, species, family) followed by evidence and confirmation by a taxonomist.
- 6.2.2. Operation and handling:** Details of plant growth, harvesting stages, harvesting techniques, drying, storage and transportation. This will also include details of collision, inspection and finishing of small parts.
- 6.2.3. Quality characteristics:** Foreign products, ash, pesticide residues, heavy metals, microbial content and chromatographic fingerprints. testing procedures and quality control procedures.
- 6.2.4. Extraction process:** Detailed extraction and fractionation process, good properties of the starting material, physical examination and physical and chemical allergies.
- 6.2.5. Production and final product:** Detailed information on the composition and proportion of the purified product.
- 6.2.6. Manufacturing process:** Description of the manufacturing process for the pharmaceutical form, including environmental controls, in-process quality control, and volume details.
- 6.2.7. Stability data:** Stability testing at various conditions (e.g., 40°C and 75% RH) for both the phytopharmaceutical drug and its dosage form, monitored over specific time periods.
- 6.2.8. Safety and toxicity data:** Animal toxicity data (28- to 90-day repeated dose oral toxicity studies). Investigation for teratogenicity (if the drug is intended for use during pregnancy).
- 6.2.9. Clinical studies:** Clinical studies were conducted in accordance with the rules and guidelines used for new drugs. This includes: Phase I studies to determine the maximum antibiotic dose and toxicity. The safety of the test is short.

- 6.2.10. Regulatory and commercial information:** Status of botanical medicines in other countries, regardless of whether they are classified as food, dietary supplement or approved drug. Detailed information on packaging, labelling and post-marketing surveillance plans, including regular safety updates.
- 6.2.11. Other important information:** Other details about herbal medicines under regulatory authority. These include substances such as carotenoids, flavonoids, terpenoids, omega-3, fatty acids, etc. (17,19,22,23).

7. Conclusion

The regulation of phytopharmaceuticals encourages the development of plant-based drugs using modern techniques such as solvent extraction and advanced formulation. With approval from regulatory bodies like CDSCO, these products can be marketed as new chemical entity-based drugs. This regulatory framework aligns with global standards, promoting innovation and investment in phytopharmaceutical drug development.

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