www.ijarp.com ISSN 2456-9992 Page: 01-19

International Journal Advanced Research Publications

Review Article

Volume: 02
Issue: 04

STABILITY TESTING OF HERBAL MEDICINE

***Miss. Komal Yadav, Mr. Awan Kumar Pandey**

India.

Article Received: 03 March 2026, Article Revised: 21 March 2026, Published on: 11 April 2026

***Corresponding Author: Miss. Komal Yadav**

India.

DOI: https://doi-doi.org/101555/ijarp.4017

ABSTRACT

The uniformity in the quality of pharmaceutical products is crucial to ensure their intended therapeutic effectiveness. However, due to the physicochemical complexity and natural variability of herbal products, maintaining consistent quality is a significant challenge. Regulatory authorities worldwide have established guidelines and standards for stability testing parameters and procedures for herbal products stored under recommended conditions.

The testing parameters and methodologies for these herbal products are described in the guidelines issued by five major international organizations and fifteen countries/regions, namely the Association of Southeast Asian Nations (ASEAN), Eurasian Economic Commission (EEC), European Medicines Agency (EMA), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), and World Health Organization (WHO), along with Australia, Brazil, Canada, China, Egypt, Hong Kong, India, Japan, Kenya, South Korea, the Philippines, Qatar, Switzerland, the United States, and Zambia.

Comparative evaluation of physical, chemical, and biological stability parameters across various dosage forms has been conducted, and the testing conditions—including temperature and relative humidity for long-term, intermediate, and accelerated studies—are specified within these guidelines. Tools such as PMC Labs can be explored for further comparison and insights.

This review provides a comprehensive understanding of the global perspective on quality assessment of herbal products, particularly in relation to storage stability.

KEYWORDS: region of organistion and countries, stability testing parameters, factors.

INTRODUCTION

Maintaining the quality of herbal products during storage is essential to ensure their therapeutic effectiveness. Stability testing is conducted to evaluate how herbal formulations preserve their properties under defined storage conditions influenced by factors such as temperature, humidity, light, oxygen, and other environmental conditions, as well as physical stress (e.g., vibration or freezing) and packaging characteristics.

Herbal products are formulated in a wide range of dosage forms, including tablets, powders, liquids for oral use, and topical preparations such as creams. Therefore, stability evaluation specific to each dosage form is necessary, as different formulations exhibit distinct degradation mechanisms and require appropriate analytical approaches.

The stability of herbal products is assessed by examining properties that are sensitive to storage conditions, including:

- Physical parameters (appearance, sensory characteristics, physical state, particle size)
- Chemical properties (active constituent content, pH, identification, and purity)
- Microbiological quality
- Toxicological attributes

These factors directly influence the quality, safety, and efficacy of herbal products, making stability testing essential for determining their shelf life.

In recent years, there has been increased emphasis on the global harmonization of stability testing standards in herbal medicine development. However, achieving international uniformity requires collaborative efforts and exchange of regulatory knowledge and scientific data among countries.

Therefore, this study presents a detailed overview of stability testing parameters and methodologies for herbal products across different dosage forms, as specified in guidelines issued by international and national regulatory bodies. These include the Association of Southeast Asian Nations (ASEAN), Eurasian Economic Commission (EEC), European Medicines Agency (EMA), International Council for Harmonisation (ICH), World Health Organization (WHO), as well as regulatory authorities in Australia, Brazil, Canada, China (including Hong Kong), Egypt, India, Japan, Kenya, South Korea, the Philippines, Qatar, Switzerland, the United States, and Zambia.

Purpose and Objectives

Ensuring consistent quality of medicinal products is vital for achieving the desired therapeutic outcomes and maintaining uniformity in drug performance. Herbal products pose unique challenges due to their complex composition and inherent variability.

To address these challenges, regulatory agencies worldwide have established guidelines and standards for stability testing parameters and procedures for herbal products under recommended storage conditions. These guidelines, issued by five international organizations and fifteen national authorities, outline the required testing methods and quality criteria.

This review aims to:

- Compare physical, chemical, and biological stability parameters across various herbal dosage forms
- Examine testing conditions, including temperature and relative humidity, for long-term, intermediate, and accelerated stability studies
- Analyze the global regulatory framework governing herbal product stability testing
- Additionally, tools such as PMC Labs may be utilized for further evaluation and comparison of stability data.

Overall, this review contributes to a better understanding of the global scenario of quality control practices for herbal products, particularly in relation to their stability during storage.

Overview of Stability Testing of Herbal Dosage Forms (Rewritten)

Guidelines and regulatory frameworks were reviewed from international authorities and various countries where stability testing is mandated to ensure the quality and safety of herbal products (or finished herbal formulations). The test parameters, also referred to as quality control indicators, play a critical role in maintaining the standard of herbal products and vary depending on the type of dosage form.

Key storage conditions such as temperature, relative humidity, and duration of storage are compared across different global authorities and national regulations. Guidelines that focus exclusively on synthetic or chemical pharmaceuticals were excluded from this evaluation.

Stability Testing Parameters

1. ASEAN

The Association of Southeast Asian Nations (ASEAN) provides stability testing guidelines to

ensure the preservation of quality in finished herbal products (traditional medicines) within their specified packaging systems under recommended storage conditions and durations.

The evaluation parameters vary according to dosage forms and include:

- Oral powders: sensory attributes, laboratory characteristics, potency, and microbial limits
- Capsules (hard and soft): appearance, physicochemical properties, solubility, disintegration, content uniformity, and microbial quality
- Tablets (coated and uncoated): organoleptic properties, hardness, friability, dissolution/solubility, disintegration, content, and microbial limits
- Suspensions: sensory characteristics, viscosity, pH, microbial quality, and particle size variation
- Solutions and emulsions: appearance, viscosity, pH, and microbial content
- Semisolid preparations (ointments, creams, gels, lotions, pastes): organoleptic properties, viscosity, pH, and microbial limits
- Plasters: appearance, microbial quality, and adhesion properties
- Granules/particles: content, particle size distribution, and microbial contamination
- Herbal sachets/infusions: sensory properties, content, and microbial limits
- Lozenges: organoleptic characteristics and microbial quality

2. EEC

The Eurasian Economic Commission (EEC) requires comprehensive documentation of stability studies for herbal preparations in accordance with pharmaceutical regulations. Stability evaluation includes assessment of physical, chemical, biological, and microbiological characteristics, along with the content of preservatives (e.g., antioxidants and antimicrobial agents) and the functionality of drug delivery systems.

General parameters include evaluation of:

- Appearance
- Active pharmaceutical ingredients (APIs)
- Degradation products
- Preservative and antioxidant levels Specific dosage form requirements include:
- Pills: dissolution, disintegration, content, and resistance to abrasion
- Hard gelatin capsules: brittleness, dissolution, disintegration, content, and microbial purity

- Soft gelatin capsules: dissolution, disintegration, pH, leakage integrity, adhesion, and microbial quality
- Oral liquids (solutions, suspensions, emulsions): sedimentation, pH, viscosity, extractables, microbial purity, and transparency
- Suspensions: dispersion characteristics, rheology, particle size distribution, and polymorphic changes
- Emulsions: phase separation and droplet size distribution
- Powders and granules: content and reconstitution efficiency
- Metered-dose inhalers: dose uniformity, valve performance, particle size distribution, microbial contamination, and container integrity
- Aerosols: particle morphology, agglomeration, contamination, and container corrosion
- Nasal sprays: clarity, pH, microbial purity, particle size distribution, and dose uniformity
- Topical, ophthalmic, and otic preparations: transparency, viscosity, pH, sterility, and microbial quality
- Suppositories: softening point and disintegration time
- Parenteral formulations: color, clarity, sterility, endotoxins, pyrogenicity, and volume
- Transdermal patches: drug release rate, adhesion, integrity, and microbial sterility

3. EMA

The European Medicines Agency requires specific stability studies under defined storage conditions to ensure the quality of herbal products. These requirements are described in official guidelines such as *Guidelines for New Active Substances and Medicinal Products Stability Testing* and *Guidelines for Stability Testing of Existing Active Substances and Finished Products*.

According to EMA standards, herbal products must be evaluated to confirm compliance with specifications including description, identification, assay, impurities, and microbiological limits.

The key stability parameters for various dosage forms include:

- Tablets (coated and uncoated) and hard capsules: dissolution, disintegration, hardness, friability, uniformity, content, and microbial limits
- Oral suspensions: uniformity, pH, microbial quality, preservative content (antimicrobial and antioxidant), extractables, alcohol content, dissolution (for suspensions),

redispersibility (for dry powders), particle size distribution, dispersibility, rheological behavior, viscosity, density, reconstitution time, and content

- Herbal infusions: loss on drying, identification, purity, uniformity, assay, particle size, and microbiological quality.

4. ICH

The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use provides general principles for stability testing of pharmaceutical products, including parameters such as description, identification, assay, and impurity profiling.

Although primarily designed for synthetic drugs, these guidelines are widely applied to herbal products because many international regulatory frameworks (such as EMA, Australia, Japan, and Switzerland) are based on ICH standards.

The major stability parameters include:

- Tablets and hard capsules: dissolution, disintegration, hardness, friability, uniformity of dosage units, moisture content, and microbial limits
- Oral liquids (solutions and suspensions): dosage uniformity, pH, microbial limits, preservative content, antioxidant levels, extractables, alcohol content, dissolution, particle size distribution, redispersibility, rheological properties, viscosity, reconstitution time, and assay
- Parenteral preparations: dosage uniformity, pH, sterility, endotoxins, pyrogens, particulate matter, assay, preservative content, extractables, functionality of delivery systems (e.g., prefilled syringes or auto-injectors), osmotic pressure, particle size distribution, and reconstitution characteristics

5. WHO

The World Health Organization publishes technical reports and guidelines on good herbal processing practices and stability testing of pharmaceutical preparations.

General stability requirements for finished products include evaluation of appearance, assay, degradation products, and preservative content (antioxidants and antimicrobials). Additionally, specific parameters are defined based on the type of dosage form.

Liquid Herbal Dosage Forms:

Include extracts, decoctions, infusions, tinctures, syrups, and oral solutions, evaluated for:

- Precipitation
- Clarity
- pH
- Viscosity
- Extractables
- Microbial contamination
- Oral suspensions: precipitation, clarity, pH, viscosity, extractables, microbial limits, dispersibility, rheology, particle size distribution, and polymorphic changes
- Oral emulsions: phase separation, transparency, pH, viscosity, microbial quality, and droplet size distribution
- Powders and granules for reconstitution: content and reconstitution time

Solid Herbal Dosage Forms:

Include herbal powders, granules, capsules, tablets, lozenges, and herbal sachets:

- Hard gelatin capsules: friability, dissolution, disintegration, content, and microbial limits
- Soft gelatin capsules: dissolution, disintegration, microbial quality, pH, leakage, and film integrity
- Tablets: dissolution, disintegration, hardness, friability, and content

Semisolid and Other Dosage Forms:

Include ointments, creams, and gels, evaluated for:

- Transparency
- Uniformity
- pH
- Consistency
- Viscosity
- Particle size distribution
- Microbial contamination
- Sterility
- Weight variation
- Ophthalmic and otic products: sterility, particulate matter, and extractables

- Inhalation products: dose uniformity, delivery performance, particle size distribution, leakage, and microbial quality
- Transdermal patches and dressings: drug release rate, adhesion, leakage, sterility, and peel strength

Country-Level Regulatory Organizations

1. Australia

The Australian government provides mandatory guidelines for stability testing of herbal products across various dosage forms. These guidelines cover formulations such as solutions, suspensions, creams, ointments, tablets (prepared by direct compression or granulation methods), capsules (produced by dry blending or granulation), and soft gelatin capsules (containing solutions, suspensions, or powder mixtures).

The stability evaluation requirements are largely aligned with the recommendations of the European Medicines Agency, particularly the guideline on stability testing of existing active substances and related finished products. These standards ensure that herbal formulations maintain their quality, safety, and efficacy throughout their shelf life under specified storage conditions.

2. Brazil

In Brazil, the regulatory authority National Health Surveillance Agency recognizes that the stability of herbal products is influenced by both environmental factors (such as temperature, humidity, and light) and product-related factors (including the physicochemical properties of active ingredients and excipients, formulation type, manufacturing process, and packaging materials).

ANVISA requires that stability studies be conducted under both accelerated and long-term conditions to determine appropriate shelf life and storage requirements.

The specified stability parameters for different herbal dosage forms include:

- Tablets and pills: description, disintegration, dissolution, hardness, friability, assay (content), uniformity of dosage units, and average weight
- Capsules: description, disintegration, dissolution, assay, dosage uniformity, and average weight
- Granules: description, particle size distribution, content, friability, flow properties, bulk

density, dosage uniformity, and average weight

- Tinctures and syrups: description, pH, viscosity, relative density, sucrose content, dosage uniformity, and active ingredient content
- Semisolid preparations (creams, ointments): description, pH, dosage uniformity, average weight, phase separation, and content uniformity
- Transdermal patches: description, dosage uniformity, adhesion, tensile strength, and active ingredient content
- Intravaginal suppositories: description, disintegration, dissolution, pH, softening point, dosage uniformity, and average weight
- Medicinal soaps: description, pH, dosage uniformity, average weight, and active ingredient content

3. Canada

The Canadian regulatory authority, Health Canada, mandates shelf-life and stability testing for natural health products and non-prescription medicines to establish their expiry period under defined packaging and storage conditions.

These evaluations include assessment of:

- Purity and physical characteristics
- Concentration of active ingredients
- Dosage uniformity
- Potency and effectiveness

Specific stability parameters for different dosage forms include:

- Immediate-release tablets, lozenges, and capsules: description, disintegration, and weight variation or average weight
- Fast-dissolving tablets: description, dissolution, and weight variation
- Modified-release (extended, delayed, or controlled-release) tablets and capsules: description, dissolution, weight variation, and dosage uniformity
- Sustained-release and enteric-coated formulations: description, disintegration, and weight variation
- Oral solutions and suspensions: description and preservative effectiveness
- Topical formulations: description and preservative efficacy
- Transdermal patches: description, dosage uniformity, and adhesion/peel strength

- Metered-dose systems: number of actuations per container and dose uniformity

4. China

The Chinese regulatory system requires both accelerated and long-term stability studies to determine the shelf life and appropriate storage conditions of herbal medicines. These requirements are based on standards outlined in the Chinese Pharmacopoeia and enforced by authorities such as the National Medical Products Administration.

The stability testing parameters for various dosage forms of traditional herbal products include:

- Pills: description, identification, disintegration, assay (content), and microbial limits
- Powders: description, identification, uniformity of appearance, content, particle size, and microbial limits (including sterility for topical use)
- Granules: description (including moisture sensitivity), identification, content, solubility, particle size, and microbial limits
- Tablets: description, identification, hardness, disintegration, assay, and microbial limits
- Concentrated decoctions: crystallization tendency, phase separation, identification, density, insoluble matter, and microbial limits
- Colloids: description, identification, content, and microbial limits
- Syrups: description, identification, density, pH, assay, and microbial limits
- Transdermal systems: identification, heat resistance, excipient properties, adhesion, and microbial limits
- Liquid formulations: transparency, identification, density, pH, content, and microbial limits
- Soft capsules and drop pills: description, identification, disintegration, content, and microbial limits
- Herbal alcoholic preparations (tinctures, medicinal liquors): ethanol/methanol content, total solids, identification, and microbial limits
- Extracts: identification, assay, and microbial limits
- Semisolid forms (gels, ointments): pH, viscosity, phase stability, particle size, sterility (for wound applications), and microbial limits
- Topical preparations (liniments, lotions): density, pH, ethanol content, refractive index, and microbial limits

- Suppositories: disintegration, assay, and microbial limits
- Nasal and ophthalmic products: pH, sterility, particulate matter, foreign contaminants, and microbial limits
- Aerosols and sprays: spray performance, particle size distribution, dose uniformity, sterility, and microbial limits

5. India

The Government of India establishes quality control and stability testing requirements for herbal products used in traditional systems such as Ayurveda, Siddha, and Unani, based on their respective dosage forms.

The specified evaluation parameters include:

- Tablets: description, labeling compliance, weight uniformity, uniformity of size/diameter, disintegration testing, and assay (content determination)
- Capsules*: description, identification, weight uniformity, size/diameter consistency, disintegration testing, and assay
- Parenteral preparations: clarity, pH, identification, fill volume, sterility testing, pyrogen testing, toxicity evaluation, and assay.

6. United States

The United States Food and Drug Administration requires the application of validated analytical techniques and bioassays in stability studies to monitor the stability of botanical raw materials and finished pharmaceutical products. These requirements also support the quality evaluation of botanical drug products to ensure appropriate design and compliance of clinical studies during Phase I, II, and III trials.

General quality attributes assessed include:

- Physical appearance
- Chemical identification
- Quantification of active constituents or characteristic markers
- Bioassay evaluation (where applicable)
- Content expressed on a dry-weight basis (API concentration)
- Microbiological limits

- In addition, dosage form-specific parameters are considered, such as:

- Solid oral dosage forms: dissolution testing
- Parenteral (injectable) preparations: sterility, non-pyrogenicity, and safety evaluation (including animal testing where required).

General Importance of Stability Testing

In general, stability testing is essential to determine the duration for which a drug product remains safe and effective for use. Medicines cannot be used indefinitely, as their quality and potency decline over time, and some products may remain stable only for a limited period.

In 1984, Rhodes identified several key reasons for restricting the shelf life of pharmaceutical products, including:

- Loss of drug substance (e.g., degradation due to hydrolysis or oxidation)
- Loss of excipients or carriers (e.g., evaporation of volatile components)
- Physical instability (e.g., aggregation in suspensions or phase separation in emulsions)
- Changes in bioavailability (particularly in tablets, where aging may reduce therapeutic effectiveness)
- Alterations in appearance (such as discoloration or changes in texture)
- Formation of toxic or irritating degradation products resulting from chemical reactions
- Microbial contamination or growth

It is therefore crucial to recognize the potential instability of pharmaceutical products, especially after their expiration period. Proper storage conditions and clearly defined shelf life must be established to ensure effective inventory management and maintain product integrity during distribution, including appropriate packaging selection.

The primary purposes of stability testing include:

- Ensuring patient safety and therapeutic efficacy
- Safeguarding the reputation and reliability of manufacturers
- Generating a scientific database of formulation stability, which can be useful for the development of future products

Factors Affecting Product Stability – Physical Degradation

Drug components, including active pharmaceutical ingredients (APIs) and excipients, may exist in different microscopic physical states with varying levels of stability. The rate of transformation between these states depends on the chemical potential, which is influenced

by differences in free energy and the energy barrier required for conversion (similar to activation energy in chemical reactions).

Experimental evidence indicates that elevated temperatures can adversely affect the physical stability of pharmaceutical formulations, leading to changes such as phase transitions, crystallization, or aggregation.

1. Chemical Stability

Chemical degradation of active ingredients typically results in a reduction in therapeutic efficacy. For example, β-lactam drugs undergo hydrolysis, leading to loss of activity. Various chemical reactions can contribute to degradation of APIs and excipients, with oxidation and hydrolysis being the most common. In many cases, multiple degradation pathways may occur simultaneously.

Environmental factors that significantly influence chemical stability include:

- Temperature
- Light exposure
- Humidity
- Oxygen
- Carbon dioxide

Formulation-related factors affecting stability include:

- Particle size (especially in suspensions and emulsions)
- pH of the system
- Solvent composition and polarity
- Compatibility of ionic species (anions and cations)
- Concentration of components
- Packaging materials
- Presence of stabilizers or additives
- Molecular interactions and diffusion of drug and excipients

2. Hydrolysis

Hydrolysis is a major degradation pathway, particularly for compounds containing ester and β-lactam bonds. For instance, Aspirin undergoes hydrolysis in the presence of moisture to

form salicylic acid and acetic acid.

In dry conditions, hydrolysis is minimal; however, the rate of hydrolysis increases with environmental moisture (humidity).

3. Epimerization

Epimerization occurs when a drug in solution is exposed to a moderate pH range (generally above pH 3), leading to a change in the spatial configuration of molecules. This reaction is commonly observed in compounds such as tetracyclines, where structural rearrangement can reduce biological activity.

4. Decarboxylation

Decarboxylation involves the removal of carbon dioxide (CO_2) from carboxylic acid groups, particularly under elevated temperatures. For example, p-aminosalicylic acid may undergo this reaction, resulting in reduced pharmacological activity.

5. Dehydration

Dehydration reactions, often acid-catalyzed, lead to the formation of products that may lack therapeutic activity and potentially exhibit toxicity. This process can significantly compromise drug safety and effectiveness.

6. Oxidation

Oxidation is a common degradation process affecting compounds with structures such as:

- Phenolic (hydroxyl) groups attached to aromatic rings
- Conjugated dienes
- Heterocyclic aromatic systems
- Nitroso and nitrite derivatives
- Aldehydes

CONCLUSION

Stability testing of herbal products with well-defined chemical composition is generally comparable to that of conventional pharmaceutical active ingredients (APIs). However, herbal medicines are inherently more complex and variable in nature, which presents additional challenges in quality evaluation. Despite these complexities, the fundamental principles of stability assessment for herbal and chemically defined products remain similar.

The distinctive characteristics of stability testing for herbal medicines include:

- Evaluation based on two batches of raw materials and three batches of finished products
- Absence of intermediate testing points (e.g., no requirement for 3-month testing at 30°C/65% RH)
- Stability studies for herbal raw materials are typically conducted under standard conditions (25°C/60% RH) without the need for accelerated or intermediate testing
- Use of advanced analytical techniques, including a combination of methods such as chromatographic fingerprinting, for identification and quality assessment
- Emphasis on semi-quantitative or qualitative evaluation rather than fixed numerical specifications (e.g., percentage of standardized extracts instead of precise API values)
- Requirement for continuous or ongoing stability monitoring to ensure product quality over time.

REFERENCES

1. World Health Organization. Quality assurance of pharmaceuticals: a compendium of guidelines and related materials; World Health Organization, 1997, 1.
2. Silva J, Fernandes AR, Baptista PV. Application of nanotechnology in drug delivery. Application of nanotechnology in drug delivery,2014:25:128-54.
3. World Health Organization, WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations.
4. Fan TP, Deal G, Koo HL, Rees D, Sun H, Chen S, Dou JH, Makarov VG, Pozharitskaya ON, Shikov AN, Kim YS. Future development of global regulations of Chinese herbal products. Journal of ethnopharmacology,2012:140(3):568-86.
5. Chauhan SK, Tyagi A, Singh B, Agarwal S. Accelerated stability studies of a polyherbal preparation (eazmovr) capsule. Ancient science of life,1999:18(3- 4):210. 49Kim JH, Lee K, Jerng UM, Choi G. Global comparison of stability testing parameters and testing methods for finished herbal products. Evidence-Based Complementary and Alternative Medicine, 2019, 20.
6. Kim JH, Lee K, Jerng UM, Choi G. Global comparison of stability testing parameters and testing methods for finished herbal products. Evidence-Based Complementary and Alternative Medicine,2019:20:2019.
7. Kim JH, Lee K, Jerng UM, Choi G. Global comparison of stability testing parameters and testing methods for finished herbal products. Evidence-Based Complementary and

Alternative Medicine, 2019, 20.

8. Zakharochkina ER, Garankina RY, Bekhorashvili NU, Lisovskaya SB, Lavrenteva LI, Chukreeva NV. The common pharmaceutical market of the Eurasian economic union: regulatory analysis. Journal of Advanced Pharmacy Education & Research|,2020:10(2):189.
9. Vinokurov E. Common Markets within the Eurasian Economic Union: Movement of Goods, Services, Labour, and Capital. InIntroduction to the Eurasian Economic Union Palgrave Macmillan, Cham, 2018, 67- 107.
10. Knoess W, Wiesner J. The globalization of traditional medicines: Perspectives related to the European Union regulatory environment. Engineering,2019:5(1):22-31.
11. Kumadoh DO, Ofori-Kwakye KW. Dosage forms of herbal medicinal products and their stability considerations-an overview. J Crit Rev,2017:4(4):1-8.
12. Rahman N, Azmi SN, Wu HF. The importance of impurity analysis in pharmaceutical products: an integrated approach. Accreditation and Quality Assurance,2006:11(1):69-74.
13. World Health Organization. Regulatory situation of herbal medicines: a worldwide review.
14. Kim JH, Lee K, Jerng UM, Choi G. Global comparison of stability testing parameters and testing methods for finished herbal products. Evidence-Based Complementary and Alternative Medicine,2019:20.
15. The Federative Republic of Brazil Agência Nacional de Vigilância Sanitária. Consolidado de normas da COFID (Versão IV) Brasilia, Brazil: The Federative Republic of Brazil Agência Nacional de Vigilância Sanitária, 2013.
16. Maciel A. Medicamentos líquidos orais pediátricos contendo etanol: bases para o registro no Brasil.
17. Bardala S. Natural Health Products: The Gap between Perceptions and Reality. UBCM. 2015:11.
18. Disch L, Drewe J, Fricker G. Dissolution testing of herbal medicines: challenges and regulatory standards in Europe, the United States, Canada, and Asia. Dissolut. Technol,2017:1(24):6-12.
19. Liao S, Zhang Z, Li G, Zhou L, Jiang J, Zhang N et al. Chinese Herbal Formula Xuefu Zhuyu for Stable Angina (CheruSA): Study Protocol for a Multicenter Randomized Controlled Trial. Evidence-Based Complementary and Alternative Medicine,2020:31:2020.

20. Jin LU, Fei YA, Fu-dong KE. Stability of salicylic acid collodiun. Anhui Medical and Pharmaceutical Journal, 2012, 10. 21. Alostad AH, Steinke DT, Schafheutle EI. Herbal medicine classification: policy recommendations. Frontiers in medicine,2020:11:7:31.
21. Fung VS. Integrating traditional Chinese (herbal) medicines into risk based regulation-With focus on nonclinical requirements to demonstrate safety. Journal of Traditional Chinese Medical Sciences,2020:7(2):88- 94.
22. World Health Organization. Experts' Consultation Meeting on Regional Strategy for Traditional Medicine in the Western Pacific Region, Hong Kong Special Administrative Region (China) 18-19 November 2010: report. Manila: WHO Regional Office for the Western Pacific, 2010.
23. Kim JH, Lee K, Jerng UM, Choi G. Global comparison of stability testing parameters and testing methods for finished herbal products. Evidence-Based Complementary and Alternative Medicine, 2019, 20.
24. Ministry of Health, Labour and Welfare. About partial revision of about the statement of application for prescription for over-the-counter products with approval criteria and the handling of attached materials. Drug Pharmacopoeia 0331, 2017, 19.
25. Ministry of Health, Labour and Welfare. About revision of stability test guidelines. Medical Review. 20030603001
26. Mokaya EG. A Retrospective Review of Pharmaceutical Product Dossiers Submitted at the Pharmacy and Poisons Board Between 2010 and, 2014. (Doctoral dissertation, University of Nairobi).
27. Code MF. Ministry of Food and Drug safety. Republic of Korea, 2010.
28. Republic of Korea Ministry of Food and Drug Safety. Stability Test Standards for Medicines, Republic of Korea Ministry of Food and Drug Safety, 2014, 59.
29. Zarsuelo MA, Zordilla ZD, Anacio DB. Review of regulatory policies on and benefits of herbal medicine in the Philippines. Acta Medica Philippina,2018:28:52(5).
30. Sharma S. Current status of herbal product: regulatory overview. Journal of pharmacy & bioallied sciences,2015:7(4):293.
31. Sarhan N. Cultural Sensitivity and Global Pharmacy Engagement in the Arab World. American Journal of Pharmaceutical Education,2019:20:83(4):619-36.
32. Bansal G, Kaur I, Kaur J. Herbal health products quality through stability studies: a global regulatory concern. Applied Clinical Research, Clinical Trials and Regulatory Affairs,2017:4(1):26-35.
33. Wu C, Lee SL, Taylor C, Li J, Chan YM, Agarwal R et al. Scientific and regulatory

approach to botanical drug development: a US FDA Perspective. Journal of natural products,2020:24;83(2):552-62.

34. Food US. Drug Administration Centre for Drug Evaluation and Research (FDA) Guidance for Industry: Bioavailability and Bioequivalence Studies for Orally Administered Drug Products–General Considerations, Office of Training and Communications, Division of Communications Management. Drug Information Branch, HFD-210, Rockville MD. 2003 Mar;20857.
35. Authority PR. Guidelines on application for registration of herbal medicines, 2008.
36. Guideline E. Stability testing: of existing active substances and related finished products. issued as CPMP. QWP/122/02, 2003.
37. Diaz DA, Lynch M, McMahon M, Oblessuc R, Colgan ST. Science and Risked-Based Stability Testing Strategies—a Test Case on the Global Implementation and Regulatory Reception. The AAPS Journal,2020:22(6):1-1.
38. Kim JH, Lee K, Jerng UM, Choi G. Global comparison of stability testing parameters and testing methods for finished herbal products. Evidence-Based Complementary and Alternative Medicine, 2019, 20.
39. Enayatifard R, Asgarirad H, Kazemi Sani B. Microbial quality of some herbal solid dosage forms. African Journal of Biotechnology,2010:9(11):1701-1705. doi: 10.5897/ajb10.1673.
40. Guimarães R, Barreira JCM, Barros L, Carvalho AM, Ferreira ICFR. Effects of oral dosage form and storage period on the antioxidant properties of four species used in traditional herbal medicine. Phytotherapy Research,2011:25(4):484-492. doi: 10.1002/ptr.3284.
41. Kim HJ, Jang HN, Bae JY, Park SN. A study on the stability of the cream containing Glycyrrhiza uralensis extract. Journal of the Society of Cosmetic Scientists of Korea,2013:39(2):117-125. doi: 10.15230/scsk.2013.39.2.117.
42. Pushpalatha H, Shyam R, Sundaram R, Pramod K. Pasteurization as a tool to control the bio-burden in solid herbal dosage forms: a pilot study of formulating Ashoka tablets with an industrial perspective. Journal of Advanced Pharmaceutical Technology & Research,2014:5(4):191-195. doi: 10.4103/2231- 4040.143039.
43. Winfield AJ, Richards RME. Pharmaceutical practice. 3rd ed., Elsevier health sciences, 2003, 113.
44. Yoshioka S and Stella VJ. Stability of drug and dosage forms. Kluwer Academic publishers. New York, 2002, 139-140

45. Pandey A, Rath B, Dwivedi AK. Pharmaceutical Preformulation Studies with special emphasis on Excipients compatibility. International Journal of Pharmacy and technology,2011:3(2):1029-1048. www.ijptonline.com
46. Christopher R. Physicochemical characterization and mechanism release of theophyllin from melt extruded dosage forms based on methacrylic acid polymer. International journal of pharmaceutics. Elsevier, 2005, 301(1). www.deepdyve.com
47. Beezer AE, Gaisford S. Pharmaceutical Micro calorimetry, Applicationsto Long Term Studies. IJPSR,1999:179(2):159-165.Discovery.ucl.ac.uk
48. Walter L. The Pharmaceutical Codex-Principles and Practice of Pharmaceutics. 12thed. Great Britain: The pharmaceutical Press, 1994, 277-288.
49. Chauhan SK, Tyagi A, Singh B, Agarwal S. Accelerated stability studies of a polyherbal preparation (eazmovr) capsule. Ancient science of life,1999:18(3- 4):210.
50. Kim JH, Lee K, Jerng UM, Choi G. Global comparison of stability testing parameters and testing methods for finished herbal products. Evidence-Based Complementary and Alternative Medicine,2019:20:2019.