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Stability Testing of Ayurvedic Drugs: An Indian Regulatory Perspective

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Abstract The safety and effectiveness of a product are greatly influenced by its stability. Ayurvedic, Siddha, and Unani (ASU) medicine includes single-herb or polyherbal formulations with or without mineral medications and/or drug ingredients derived from animals. Pharmaceutical products have currently undergoing stability testing in accordance with the guidelines of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The First Schedule of the Drugs and Cosmetics Act, 1940 includes a concept of shelf life and stability study. According to Rule No. 161-B of the Drugs & Cosmetics Act 1940 and Rules 1945, a person applying for a license or renewing an existing license for the manufacturing of patent & proprietary ASU medicines must provide the scientific data based shelf life or date of expiry of the medicine based on the Real-time stability tests to the State licensing authority. The Ayurvedic Pharmacopoeia of India (API), Part I, Vol. VIII, specifies the guideline for stability testing and shelf life determination for both new and old Ayurvedic Siddha and Unani medicines. Stability tests should be performed on the dosage form contained in the container and closure system that are intended for marketing. At least three primary batches should be the subject of formal stability studies. For accelerated long-term study, the recommended storage conditions are 40^0 C ± 2^0 C / 75 % RH ±5 % RH for at least 6 months, and for long-term study, the recommended storage conditions are 30^0 ± 2^0 / 60 % RH ± 5% RH for at least 12 months. A product is considered to be stable if "no significant change" occurs at any time of testing.

Keywords Stability, Shelf life, Ayurveda, Unani, Siddha, Drugs & Cosmetic Act, 1940 and Rules, 1945

Drug Stability and Stability Testing [1, 2, 3]**:**
A capacity of formulation to maintain its physical, chemical, microbiological, toxicological, and therapeutic requirements in a certain container or closure system under defined storage conditions is known as stability.
Objective of Stability Testing [4]**:** To Provide evidence on how the quality of drug substance of drug product varies with time under the influence of a variety of environmental factors such as Temperature, Humidity and Light, and enables recommended storage conditions, re-testing periods & shelf lives to be established
Selected Definitions: [4,5,6,7,8,9,10]

1) *Shelf Life (Expiry Date period):* The time period during which a drug product is expected to remain within the approved shelf life specification, provided that it is stored under the conditions provided on the container label.
2) *Re-test Date:* Date after which samples of the drug substance should be examined to ensure that the material is still in the compliance with the specifications and thus substance can be used to formulate the drug product.
3) *Re-Test period:* The time period for Re-test of drug sample.
4) *Shelf Life (Expiry Date period):* The time period during which a drug product is expected to remain within the approved shelf life specification, provided that it is stored under the conditions provided on the container label.

5) *Re-test Date:* Date after which samples of the drug substance should be examined to ensure that the material is still in the compliance with the specifications and thus substance can be used to formulate the drug product.
6) *Re-Test period:* The time period for Re-test of drug sample.
7) *Accelerated testing:* Study designed to increase the rate of physical or chemical degradation of the drug substance or its formulations by using exaggerated storage conditions as part of formal stability studies.
8) *Intermediate testing:* Studies conducted at 30° C/ 65% RH and designed to moderately increase the rate of physical or chemical degradation of the drug substance or its formulations intended to be stored far a longer time at 25° C.
9) *Long term testing:* Stability testing under the recommended storage conditions for the retesting period or shelf life proposed (or approved for labeling.
10) *Stress testing (Drug testing):* studies undertaken to elucidate the intrinsic stability of the drug substances. Normally carried out under severe stress conditions than that used for accelerated testing.
11) *Stress testing (Drug Product):* Studies undertaken to assess the effect of severe conditions on the drug substances. Such studied include Photo stability testing and specific testing on certain products. (metered dose inhalers, creams, emulsions and refrigerated aqueous liquid products).
12) *Container closure systems:* The sum of packaging components that together contain and protect the dosage form.
13) *Formal stability studies:* Long term and Accelerated (and intermediate) studies undertaken on the primary and/or commitment batches according to the prescribed stability protocol to establish or confirm the re-test period of the drug substance of the shelf life of the drug product.
14) *Commitment Batch:* Production batches of drug substance or drug product for which the stability studies are initiated or completed post approval through a commitment made in the registration application.
15) *Primary Batch:* A Batch of Drug substance or Drug product used in a formal stability study from which stability data are submitted in the registration application for the purpose of establishing the Re-test period or shelf life.
16) *Pilot scale Batch:* A Batch of Drug substance or Drug product manufactured by the procedure fully representative of the production scale batch.
17) *Production Batch:* A Batch of Drug substance or Drug product at the production scale by using production equipments in the production facility as specified in the application.
18) *Specification-Release:* The combination of Physical, chemical, biological and Microbiological tests and acceptance criteria that determines the suitability of a drug product at the time of release.
19) *Specification-Shelf Life:* The combination of Physical, chemical, biological and Microbiological tests and acceptance criteria that determines the suitability of a drug substance throughout the re-test period or the product should meet throughout the shelf life.
20) *Impermeable containers:* Containers the provide permanent barrier to passage of gases and solvents. E.g.: Sealed aluminum tubes for semisolids, sealed glass ampules for solutions
21) *Semi-Permeable containers:* Containers the provide passage of solvents usually water while preventing loss of solutes. Eg: LDPE (Low Density Poly ethylene) pouches for Large Volume Parenteral (LVP's), LDPE ampules and bottles.

The World Wide Zones and Temperature & Humidity Conditions are given in table 1 and Countries belonging to various zones is specified in table 2 [4,5,6].

Table 1: Temperature and Humidity conditions of World Wide Zone

Zone	Temperature	Average Yearly Humidity (% RH)
Zone I (Moderate)	21° C	45
Zone II (Mediterranean)	25° C	60
Zone III (Hot and Dry)	30° C	35
Zone IV (Very Hot and Moist)	30° C	70

Table 2: Regions and countries related to World Wide Zones

Regions	Zone I and Zone II	Zone III and Zone IV
Europe	All Countries	---
America	Argentina, Bolivia, Canada, Mexico, USA	Brazil, Columbia, Cuba, Jamaica
Asia	Afghanistan, China, Iran, Nepal, Turkey	India, Bahrin, Hongkong, Oman, Pakistan, Srilanka, UAE
Africa	Egypt, Algeria, South africa, Libia	Angola, Benin, Congo, Uganda, Sudan, Somalia, Senegal

Stability and Shelf Life in Classical Text and Current Scenario:

The concept of shelf life can be traced from classical texts (Table 3) [11].

Table 3: Ayurvedic Dosage form Shelf Life (Saviryta Avadhi) as per Classical Texts [12,13,14,15,16,17].

CLASSICAL TEXTS	DOSAGE FORM	Shelf Life Period
Vangasen	Avaleha (semisolid oral dosage)	12 months
	Ghrita (medicated ghee) and Taila (medicated oil)	6 months
Sharangdhara Samhita	Churna (powder)	2 months
	Vati (tablets/pills)	12 months
	Avaleha (semisolid oral dosage)	12 months
	Ghrita (medicated ghee) and Taila (medicated oil)	16 months
	Asav-Arista (tincture/ fermented oral liquid)	Long term stability
Yogaratnakar	Kvaath (decoction)	03 hours
	Kalka (paste)	03 hours
	Swarasa (expressed juice)	03 hours
	Anjana (collyrium)	3 months
	Churna (powder)	3 months
	Avaleha (semisolid oral dosage)	6 months
	Ghrita (medicated ghee) and Taila (medicated oil)	12 months

The concept of an expiration date or shelf life was first implemented to ASU medications in 2005. The Rule no. 161- B regarding the shelf life of ASU medications was incorporated into the notification GSR 764(E) dated October 15, 2009. It was amended in 2016 by the Gazette notification GSR 789 dated August 12, 2016. [18,19,20] According to the Rule, Ayurvedic, Siddha, or Unani medicines must prominently display the date of expiration on its container or box, and after that date, no medicine may be marketed, sold, distributed, or consumed. The shelf life or expiration date of an Ayurvedic, Siddha, or Unani medication as defined in clause (a) of section 3 of the Act shall be as specified under the Rule, unless otherwise decided on the basis of scientific facts [20].

According to clause (h) of section 3 of the Drug and Cosmetic Act, 1940, Ayurvedic, Siddha, or Unani medicines are all the medicines that are manufactured exclusively in accordance with the formulae described in the authoritative texts of the Ayurvedic, Siddha, and Unani Tibb systems of medicine, which are listed in the First Schedule, and that are intended for internal or external use for or in the diagnosis, treatment, mitigation, or prevention of disease or disorder in humans or animals [21].

The increasing period of their shelf life or date of expiry of Ayurvedic, Siddha or Unani medicine respectively as givenin the Rule 161-B, is shown in Table 4 [20].

Table 4: Different formulations ASU Medicine and their Shelf Life [20]

Shelf life/ Date of expiry	Formulation Category	Formulation
1 year	**Ayurvedic**	Anjana made from Kasthaushadhi, Arka, Netrabindu
	Siddha	Kallikkam /Mai /Kalimbu /Neer /Venney, Kattu (Medicated bandage cloth)/ Seelai/ Varthy/ Thiri, Nasi- yathuli/Kanthuli/ Sevithuli, Oothal/ Nasigaparanam/ Thoopasarakku, Pakkuvam, Thennoral, Tinir
	Unani	Arq (except Arq-e-Ajeeb), Murabba, Burood, Qutoor, Sufoof (Containing salt)
2 years	**Ayurvedic**	Anjana made from kasthaushadi along with Rasa/ Uprasa/ Bhasma, Churna, Kwatha Churna, Lepta Churna, Danta Manjan (Churna), Dhoopan, Ghrita, Karna/ Nasabindu, Sattva (derived from medicinal plant), Shveta parpati, Varti
	Siddha	Araippu Karpam (e.g. Irunelli Karpam), Karam (Karanool), Karuppu containing only Mooligai ingredients (e.g. Vasambu Sutta Kari), Kutinir Curanam /Adai Curanam/ Kanchi Curanma/ Utkali Curanam/ Pittu Curanam/ Podithimirthal Curanam/ Podi/ Pattru Curanam/ Pottanam or Kizhi Curanam /Ottratam Curanam / Vethu Curanam/ Pugai Curanam /Kali Curanam/ Thuvalai Curanam, Mattirai/ Vatakam containing only Mooligai ingredients (including Kudineer Curanam Mattirai) (e.g. Nilavembu kutinir Mattirai), Mooligai Karpam (e.g. Karisalai Karpam, Thiripala Karpam), Ney/ Ghiruthan/ Kadugu, Parpam/ Centuram containing only Mooligai ingredients (e.g. Kungiliya Parpam), Peechu, Rasa-Paadana Marunthugal (All Mercurial Preparation) containing Moo- ligai ingredients along with Thathu, Porutkal/ Parpam/ Centuram/ Cunnam/ Kattu/ Kalanku, Satthu derived from Mooligai (e.g. Seenthi Satthu), Sutigai, Tiravakam (derived from ThathuPorutkal)
	Unani	Ayarij/ Sunoon/ Zuroor/ Ghazah, Marham/ Zimad/ Qairooti, Shiyaf, Sufoof (Without Salt)
3 years	**Ayurvedic**	Anjana made only from Rasa/ Uprasa/ Bhasma, Avaleha, Khanda, Paka, Guda, Gutika or Vati containingonly Kasthaushadhi (including Lepa Gutika and Ghan Vati), Malahar, Pravahi Kwatha, Sharkar/ Panak/ Sharbat, Taila
	Siddha	Idippu Meluku (e.g. Rasa Gandhi Meluku/Idi Vallthi Meluku), Ilakam/Lagiyam/Iracayanaam, Kutinir/Kiyazham (with preservatives), Manappaku/Panagam, Mooligai Meluku (e.g. Malaikudara Meluku), Tailam/Ennai/Poochu
	Unani	Habb, Halwa, Itrifal, Khamira, Laboob, Laooq, Majoon/ Dawa, Mufarreh, Qurs, Raughaniyat/ Tila, Sharbat/ Sikajabeen, Surma/ Kohal, Tiryaq
4 years	**Ayurvedic**	-
	Siddha	-
	Unani	Jawarish
5 years	**Ayurvedic**	Dravaka, Lavana, Kshara, Guggulu, Gutika or Vati containing Kasthaushadi along with Rasa/Uprasa/Bhasma/Guggulu (including Lepa Gutika and Ghan Vati), Naga Bhasma, Vanga Bhasma and Tamra Bhasma, Rasayoga Containing Rasa/Uprasa/Bhasma along with Kasthaushadhi/Guggulu
	Siddha	Araippu Kulampu (e.g. Agathiya Kulampu), Araippu Meluku (e.g. Linga Meluku), Erippu Kulampu (e.g. Ku- matti Kulampu), Karuppu containing Mooligai ingredients with Jeeva Porutkal (e.g. Kasthuri Karuppu, Pattu,

		Karuppu), Karuppu con-taining Mooligai ingredients with Thathu Porutkal (e.g. Sivanar Amirtham, Thalaga Karuppu), Mattirai/Vatakam containing Mooligai ingredients along with Thathu Porukal/ Jeeva Porukal/ Parpam/ Centuram/ Cunnam. (including Kutinir Curanam Mattirai), Mooligai based Patankam (e.g. Sambirani Patankam), Mooligai Thathu Karpam (e.g. Aya Bringaraja Karpam), Satthu derived from Jeeva Porutkal (e.g. Sembu Satthu derived from Poonagam, Mayiliragu)
	Unani	Arq-e-Ajeeb, Jauhar/ Jawahir
10 years	**Ayurvedic**	Asava/Arista, Gutika/ Vati containing only Ras/ Uprasa/ Bhasma except Naga, Vanga and Tamra Bhasma, Kupipakva Rasayana, Madura-Lauha, Parpati, Pishti and Bhasma except Naga, Vanga and Tamra Bhasma, Rasayoga Containing only Rasa/Uprasa/ Bhasma except Naga, Vanga and Tamra Bhasma
	Siddha	Kattu/Kalanku/Cunnam, Mattirai/ Vatakam containing only Thathu Porutkal/ Parpam/ Centuram/ Cun- nam/ Kattu/ Kalanku., Panda Vaippu, Parpam/ Centuram containing Mooligai ingredients with Jeeva Porutkal (e.g. Sangu Parpam), Parpam/ Centuram containing Mooligai ingredients with Thathu Porukal/ Parpam/ Centuram/ Cunnam/ Kattu/ Kalanku (e.g. Aya Centuram), Rasa based Patankam (e.g. Rasa Centuram), Rasa-Paadana Marunthugal (All Mercurial Preparation) containing only Thathu Porutkal/ Parpam/ Centuram/ Cunnam Kattu/ Kalanku, Satthu derived from Thathu Porutkal (e.g. Aya Satthu, Eya Satthu, Thurusu Satthu)
	Unani	Kushta, Nabeez

The Drugs and cosmetics Rules, 1945 gives shelf life or expiry date of formulations of textual reference (classical medicine). The shelf life or expiry date of patent and proprietary medicines are not specified in the rule. According to Clause (h) of Section 3 of the Act, A patent or proprietary medicine which relates to the Ayurvedic, Siddha, or Unani Tibb systems of medicine is any formulation that uses only the ingredients listed in the formulae described in the authoritative books of the Ayurvedic, Siddha, or Unani Tibb systems of medicine listed in the First Schedule. It excludes medications that are administered parenterally and formulations that are listed in authoritative publications as described in clause (a) [21].

Stability studies are now mandatory under Rule 161-B of the D & C Act 1940 and Rules 1945, as a prerequisite for obtaining a manufacturing licence for patent and proprietary ASU medicines. According to Rule No. 161-B, a person applying for a license or renewing an existing license for the manufacturing of patent & proprietary ASU medicines as defined in clause (h) of section 3 of the Act, must provide the scientific data based shelf life or date of expiry of the medicine based on the Real-time Stability Studies of Medicines after three years from the date of notification of the rules, to the State Licensing Authority [20].

Protocol for Stability Study

Stability of Medicines are determined a number of factors like the nature of the product, the ingredients, the packaging material, and the environmental conditions. Stability testing is a complex set of procedures as variety of factors influence the stability of a product. The formulations themselves are complex, and potential interactions between various components of formulation could make the degradation reactions more complicated. Studying the rate of degradation of each element separately would be challenging, time-consuming, and expensive. The primary objective of stability testing is to establish a retest period for drug substances or a shelf life for drug products as well as to provide evidence regarding how the quality of a drug substance or drug product varies over time under the influence of various environmental factors, such as temperature, humidity, and light.

It is not necessary to determining the mechanism of degradation. In most cases, it is sufficient to use the kinetic expression provided to follow a particular feature of deterioration as a function of time at various elevated

temperatures before extrapolating the data to ambient conditions to determine an estimate of the product's shelf life. [1, 2, 3. 22, 23].

Stability testing is performed in accordance with well designed regulatory guidelines that serve as the basis for experimental design, data analysis, and the type of documentation required satisfying regulatory requirements.

Pharmaceutical products have currently undergoing stability testing in accordance with the guidelines of the ICH (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use), WHO (World Health Organization), ASEAN (Association of South East Asian Nations), and EMEA (European Agency for Evaluation of Medicinal and Health Products). The industry now commonly uses ICH guidelines to assess the stability of a drug substance or drug product. [1, 3, 4, 5. 6, 7, 8, 9].

All licensed ASU medicines must undergo stability testing and have their shelf life determined according to the guidelines prescribed in the Ayurvedic Pharmacopoeia of India, Part-I, Volume- VIII under appendix 3.9. [10].

Guideline for Stability Testing and Shelf Life Determination of Asu MediCine

Studies on stability are conducted to show that, when stored according to the instruction(s) listed on the box, the medication will stay safe for consumption for the duration of its shelf life. It is assumed that a product can be stored at room temperature if the product label makes no mention of any particular storage requirements (below 30^0) [10].

Selection of Samples and batches

There are two Approaches that can be used to check the product's stability. The first approach is to periodically analyze samples of the same batch of material stored under standard storage and accelerated storage conditions. The shelf life or expiration date may be determined once the results have been evaluated. The second approach, termed as "cross sectional method," is appropriate for already-existing items without a specified shelf life. The approach is to choose samples from batches manufactured throughout the course of the previous five years, spanning six months, and evaluate them all simultaneously. The shelf life or expiration date can be calculated based on the results.

For formal stability tests, a minimum of three primary batches of the same formulation as the one proposed for marketing are required. There should be at least two batches selected yearly for the cross-sectional approach. For new products, the batches should be manufactured at a minimum in pilot scale (at least 1/10 the size of the commercial batch), following the same manufacturing process and steps as would be utilised for production batches. The overall quality of the medicine batches used in formal stability tests should be indicative of the quality of the substance produced on a large scale. Whenever possible, batches of drug product should be manufactured by using different batch size of drug substance. Unless bracketing and matrixing are applied, stability tests should be conducted on each specific strength and container size of the product. There should be at least two batches chosen annually for the cross-sectional approach. For instance, eight batches should be chosen if stability is to be tested over a four-year period [10].

Container and closure system

The drug product must be packaged for stability studies in the same container and closure system as are recommended for the marketing of the dosage form, including with any necessary secondary packaging and container labels. Unless bracketing and matrixing designs are used, each individual strength and container size of the proposed packaging configuration should be placed on stability. If the container for a pharmacological substance is too big, stability studies should be conducted in a container and closure system that is similar to or replicates the packaging that is suggested for storage and distribution [10].

Specification

Specifications are the set standards of quality that a product must meet in order to be released or used. It contains a collection of tests, a description of the testing process, and suggested acceptance standards. Tests on medication

properties that are susceptible to change during storage and could affect quality, safety, or efficacy should be included in a stability study. Physical, chemical, biological, and microbiological properties should all be tested as necessary. Validated stability indicating analytical techniques should be employed.

The findings from validation trials will determine whether and to what extent replication should be done. The physical characteristics included in the specification need not be restricted to just taste, colour, and appearance. Chemical parameters should comprise colour reaction, pH level, weight variation, disintegration, bulk density, extractive values, estimation of active or marker or category component by acceptable procedures, and chromatographic profiling. Where possible, a relevant bioassay may be employed. Products should be accepted within the pharmacopoeia-specified parameters. Limits should be taken from the release specification if they are not available. Acceptance criteria for shelf life should be determined after taking into account all stability data.

Based on the stability analysis and the changes noticed during storage, it can be permissible to have justifiable variations between the shelf life and release acceptability requirements.

The choice of an anti-microbial preservative should be made based on a number of factors, including the formulation's pH, interactions with the other ingredients, and container. A validated correlation between chemical content and preservative effectiveness demonstrated during the development of the product in its final formulation (except for preservative concentration) intended for marketing should be used to support differences between the release and shelf life acceptance criteria for anti-microbial preservative content [10].

Storage Condition

Real-time (long-term) testing is normally performed for a longer duration in order to allow for significant degradation of the product under specified storage conditions. Accelerated testing is performed at high temperatures, humidity, light intensity etc. The accelerated testing should be then carried out at least 10^0 C more than the long term storage condition along with appropriate relative humidity condition for that temperature. The reference samples for the above study should be stored in a temperature less than 10^0 C.

Recommended storage conditions are for Real time and accelerated stability testing as per API is shown in Table: 5.

Table 5: Recommended storage conditions for ASU medicines

S. No.	Study	Storage condition	Minimum time
1	Accelerated	40º C ± 2º C 75 % RH ± 5% RH	6 months
2	Long Term	30º C ± 2º C 60 % RH ± 5% RH	12 months

Other storage conditions may be used if properly justified. A medicine intended to be stored for a long time at 25°C must undergo intermediate testing in order to moderately increase up the rate of degradation. These tests are typically carried out when the accelerated studies for general cases fail to meet of the acceptance standards.

In stress testing, the effect of temperature (higher than that employed in accelerated study), humidity (e.g., ≥75% RH), oxidation, photolysis, and hydrolysis is considered. Forced degradation testing is carried out with the objectives of assessing the intrinsic stability of the drug, illuminating potential degradation routes by identifying plausible degradation products, and gaining insight into the stability of the analytical process used to analyse the drug. Temperature-sensitive products should be stored at lower temperatures, which will subsequently serve as the designated long-term storage temperature. [10]

Testing frequency

Frequency of testing should be sufficient for long-term studies to determine the stability profile of the drug. The frequency of testing at long-term storage conditions for drugs with a proposed shelf life of at least 12 months should normally be every six months over the first year, the second year, and annually thereafter through the proposed re-test period or shelf life.

A minimum of three time points, including the initial and final time points (e.g., 0, 3, and 6 months) from a 6 month study, are advised at the accelerated storage condition. If justified, reduced designs, such as matrixing or bracketing, can be used. In these cases, the testing frequency is reduced or certain factor combinations are not applied at all [10].

Reduced Designs: Bracketing and Matrixing

The Ayurvedic Pharmacopoeia of India, Part-I, Volume- VIII allows applying reduced stability study designs like bracketing and matrixing. Bracketing and matrixing can be utilised to simplify testing while still producing enough stability data to evaluate shelf life during the design of stability studies. Bracketing is the design of a stability schedule such that only samples onthe extremes of certain design factors (e.g., strength, container size and/or fill) are tested at all-time points as in a full design. The design assumes that the stability of any intermediate levels is represented by the stability of the extremes tested.

Matrixing is the design of a stability schedule such that a selected subset of the total number of possible samples for all factor combinations would be tested at a specified time point. At a subsequent time point, another subset of samples for all factor combinations would be tested.

The design assumes that the stability of each subset of samples tested represents the stabilityof all samples at a given time point. The differences in the samples for the same drug product should be identified as, for example, covering different batches, different strengths, different sizes of the same container closure system, and possibly, in some cases, different container closure systems [7].

Evaluation

The purpose of stability is to determine a retest period that will be applicable to all subsequent batches of the drug substance, or a shelf life and label storage instructions that will be applicable to all subsequent batches of the drug product made and packaged under identical conditions. An Ayurvedic, Siddha or Unani drug can beconsidered to be stable if "no significant change" occurs during at any time of testing at accelerated storage condition or at real time storage condition [10].

"Significant change" for a drug is defined as

1. A ± 20 % change from the initial assay value when thedrug is analysed for its marker.
2. A ± 15 % change from the initial assay value when thedrug is analysed for its active compound).
3. Completely disappearance of existing spot or appearance of new spots in identification by TLC (when compared with the sample stored in less than 10^0).
4. The physicochemical parameters (moisture, ash, particle size) shall not vary beyond 25 % of the initial value.
5. Failure to meet the acceptance criteria as per individual monographs or specification.
6. Failure to meet acceptance criteria for appearance (Physical attributes, and functionality tests *e.g*., Colour, phase separation, caking, hardness).

Discussion

Ayurveda, Siddha, and Unani (ASU) systems of medicine are becoming more popular today for the prevention, identification, and treatment of a wide spectrum of illnesses. The formulation must be stable in order to have the effective efficacy and safety. Stability is the capacity to remain unchanging, although it is a well-known fact that all things, even formulas, change or deteriorate with time and spoil after a certain amount of time. When a formulation satisfies its established specifications, it is regarded as stable. Shelf life is a term used to describe stability. The Indian Ayurvedic Pharmacopoeia, part I, volume VIII, specify the standards for stability testing of ASU drugs. Stability has been established when there are "no significant changes" in the marker compound, active compound, TLC spot, physicochemical parameters, or acceptability requirements according to monographs or specifications. The challenges in conducting stability studies include the complex chemical composition of formulation, the absence of research on the interactions between the constituents, the unavailability of markers, and the unavailability of validated analytical procedures.

Conclusion

ASU medicines may lose some of their efficacy with time. It is essential for a product to be stable physically, chemically, microbiologically, therapeutically, and free from toxicity in order to have effective efficacy and safety. Rule 161-B of the Ayurvedic Pharmacopoeia of India, part-I volume-VIII, prescribes the shelf life in the textual references of ASU medicine and specify the determination the shelf life of patent and proprietary medicines. Stability is confirmed when there is "no significant changes" in marker compound, active compound, TLC spot, physicochemical parameters, acceptance criteria as per mono- graphs or specification.

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