Shelf life of Ayurvedic dosage forms - Traditional view, current status and prospective need

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The concept of Saviryta Avadhi (shelf life) for different Ayurvedic dosage forms are not specified in major classics like Charaka, Sushruta, etc. but after 13th century, it was considered in various authentic Ayurvedic texts like Vanga Sen, Shrangdhar Samhita and Yogaratnakar. Along with the indication of best before use duration, the importance of quality of package and storage condition is also emphasized in classics. Nowadays, due to development and adaptation of packaging and storage technology by Ayurvedic industries, a need arise to re-study and re-establish the newer ones criteria. Recently, Government of India has also issued a Gazette notification and proposed the shelf life of the Ayurvedic formulations, which seems to be unscientific and the authority has not properly considered the current development in this field. There is also a need to develop a specific guideline for the assessment of shelf life of Ayurvedic drugs. Some of the studies show that the shelf life of these types of dosage forms can be increased by utilizing current advanced pharmaceutical technologies. Through the paper, a trial is made to explore the knowledge of shelf life of Ayurvedic drugs in classics, the current efforts and the potential need.

Keywords: Ayurvedic dosage, Saviryta Avadhi, Ayurvedic drugs shelf life, Packaging, Storage

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Ayurvedic therapeutic system includes various types of dosage forms, depending upon the consistency and its shelf life, viz. Vati (tablet), Churna (powder) as solid dosage forms; Swarasa (juice), Kwatha (decoction), Hima and Phanta (cold and hot infusion, respectively), Asava and Arishta (preparation containing alcohol) as liquid dosage forms where as semi-solid preparation includes Kalka (paste) and Avaleha (electuary), etc. Amongst of them, basic dosage forms like Swarasa, Kalka, Kwatha, Hima and Phanta are prescribed in fresh condition because of having short shelf life; while the derived formulations like Asava, Arishta and Avaleha, etc. can be used throughout year or more because of prolonged stability. In Ayurvedic literatures, ‘Saviryata avadhi’ term is mentioned in context of the time period during which the Virya (potency) of any drug remains unaffected1 due to environmental/microbial deterioration; whereas in the contemporary system, the term ‘Shelf life’ is used to indicate the time period during which an API (Active Pharmaceutical Ingredient) or FPP (Finished Pharmaceutical Product) is expected to remain within the approved stability specification, provided that it is stored under the conditions defined on the container label2. Also as per the citation given in the renowned Ayurvedic text Sushruta samhita, a drug whether it is fresh or old, can be utilized for therapeutic purpose up to which its qualities (appearance, taste, smell, etc.) remains in intact condition3. These characteristics are just the subjective parameters of the physicochemical properties of drug which are generally utilized as the quality parameters of today’s era. This reference directs that shelf life of any drug can be considered up to that period until which it attains the sub potent level and not up to its deterioration.

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Shelf life of Ayurvedic formulations

There is no any clear idea about shelf life of different Ayurvedic formulations in the classical texts before of 11th century AD. After about 12th AD, the scholars have provided a specified shelf life/stability period of different dosage forms (Table 1) [1,3,5]. As per these texts, the Kwatha, Kalka and Swarasa are remain stable for up to one Prahara (3 hrs) while Churna (powder) formulation are having only 2-3 months of stability in its potency whereas nowadays, the airtight packed spices (turmeric, pepper, coriander, etc. powder) are used comparatively for longer period. Also the stability period of the Vati (pills) is mentioned to be up to one year which seems to be lesser in comparison to the tablets of allopathic system of medicine. Ayurvedic Formulary of India (AFI) also has specified some time period during which the formulation retains its efficacy [6]. The longer stability in recent dosage forms is naturally the gift of the present packaging technology which was not much more developed in the ancient time. Also, the modern science has made some advances to control and regulate various aspects of pharmaceutical processing so as to minimize or even eliminate the drawbacks of ancient packaging.

Packaging

As per the reference in Charaka smahita, a drug should be packed in such type of Bhajana (vessel/packaging media) which has Anurupa Guna that is the packing material should not interfere with the physical, chemical or biological property of the drug being packed inside [7]. Beside this, some of the indications are found for the airtight packaging of Churna, Taila, etc. types of preparations, in a new Kalash (earthen vessel with broader body & narrow mouth) and storage in airtight and dark place [8]. So, it has a great role in obtaining a product of suitable purity and potency because unsatisfactory packaging permits or fasten the degradation in the product. Any package must possess sufficient quality so that it can conquer the mechanical hazards like shock, compression, vibration, etc. and environmental hazards like temperature, moisture, light, infestation, contamination and exposure to oxygen [9]. Unlike to the ancient era, great advances in design and development of packaging technology has developed packaging materials, which have requisite barrier properties to build stability of the formulations. Various packaging media are available that can be selected according to nature of product being packed inside. These includes metal foils especially aluminum, plastics, glass bottle with closures, tin packs, collapsible tube, rubber, paper and board. Certain photosensitive drugs must be protected from light. There are numerous types of transparent, opaque and coloured containers, available for packaging. Amber glass will usually screen out ultra violet radiation very effectively and is usually the colour recommended for protection from light [10].

Storage conditions

The most important point in the evaluation of the stability study of a product is its storage conditions. It should simulate the conditions under which the drug substance or drug product is subjected from manufacturing up to its final application. Storage conditions are derived from real climatic situation. Because most of the chemical reactions follow logarithmic and not linear functions, this

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<td>Vati (pills)</td>
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characteristic must be taken into consideration while defining the appropriate conditions. Hence, the present packaging and storing technology development are playing a great role in the comparatively longer stability of the raw or finished drug materials. Nowadays, the Ayurvedic industries are also utilizing these technologies for the packaging and storage of their formulations which ultimately enhances the shelf life of the products. After the development and incorporation of these techniques, there is a need arises for the study and revision of the shelf life of Ayurvedic formulations as during those periods, the drugs were stored in the earthen pots or by tying in cloths, etc. which are not as much viable to stabilize the qualities of the drug for longer period. The scenario in the pharmaceutical industry has also been changed tremendously during past few years. Excellent advancement has been made in the pharmaceutical technology as well as therapeutic, which are facilitating progress in the manufacture and use of drug. Pharmaceutical products over the period have become more complex, potent, specific and targeted. Apart from product safety, efficacy and ethical issues that have been taken root intricacies in the stability testing have also increased making it necessary before launching it into market for the treatment of ill beings.

Guidelines for stability study

The purpose of stability testing is to provide evidence on how the quality of a drug or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity, light and to reset period for the drug substance or a shelf life for the drug product and recommended storage conditions. Currently, there are two guidelines namely ICH and WHO guidelines that provide sufficient details regarding parameters on which stability study can be done. These studies are done over the final dosage form with the final packing in which the drug is prescribed for marketing.

Prediction of shelf life

It is based on the application of the Arrhenius equation \( \log k = \log Z - \frac{E}{2.303R} \times \frac{1}{T} \) that explains the effect of temperature on the rate constant, \( k \), of a chemical reaction. Here, \( Z \) is a constant that is termed the frequency factor, \( E \) is the energy of activation, \( R \) is the gas constant, and \( T \) is the thermodynamic temperature. A graph between reciprocal of thermodynamic temperature, \( 1/T \), versus \( \log k \), is a straight line. When the slope of this line is determined from the results of accelerated tests at high temperatures it is possible to determine the value of the rate constant at other temperatures by extrapolation. Substitution of this value of \( k \) into the appropriate order of reaction allows the amount of decomposition after a given time to be calculated. However, this approach involves knowledge of order of reaction which is taking place in that particular dosage form.

Current status

Till date, no specific guidelines are available regarding the stability/shelf life estimation of the pure Ayurvedic formulations from any Government organization except a Gazette notification issued by Government of India on 20\(^{th}\) October, 2009 with slight modification in the earlier draft notification, issued on 26\(^{th}\) November, 2005. In this notification, the department of AYUSH, Ministry of Health and Family Welfare has implemented the rule namely 161B to display the date of expiry of the ASU drugs and propose shelf life of the Ayurvedic formulations like Churna/Kwatha Churna (fine/course powder drugs) as 2 yrs, Gutika (pills) containing Kastha Aushadhi (herbal drugs) only as 3 yrs and along with Guggulu (exudates of Commiphora mukul Engl.) or Rasaushadhis as 5 yrs, 3 yrs for Avalaha, etc. however, Asava-Arista (Ayurvedic preparations containing alcohol), Rasaushadhis, Kupipakva rasayana, Parpati and Pisti-Bhasma (Ayurvedic mineral/metallic preparations) with no expiry date, and further mentioned that these became more efficacious with the passage of time. Here, it is also specified that Bhasma start solidifying after 5 yrs and they need 1 or 2 Pata again before using in the dosage form. This too did not include the specific guidelines regarding methodology for the estimation of the shelf life of ASU formulations. There is also a need for the reestablishment of the stability period based on some study data. Some of the reported studies have been discussed here in which attempts were made to establish the stability study of some of the formulations using different packing and storage conditions. In the first study, it has selected Kutaki (Picorrhiza kurroa Royle ex. Benth) Churna for the accelerated study in two different packing materials. The first one was food grade polythene bag while another was plastic container having aluminum foil covering. The study was carried out up to 3 months with storage...
specification of temperature and relative humidity of 40°C and 75%, respectively. The testing frequency was 0, 1, 2, and 3 month. The water soluble extractsive obtained were considered as the concentration of drug, as the active principle of the Kutaki is soluble in the water. The rate of degradation of the drug was more in the polythene pack than in the foil pack while no change in colour was observed in both of the samples14. In another study, it has been carried out accelerated studies of the tablet dosage form developed from Gandhaka Rasayana15 (herbo-inorganic preparation). The tablets were packed in food grade polythene bags and kept in stability shelf. The storage conditions applied were temperature 40 ± 2°C and relative humidity 75 ± 5%. The drug was tested at three intervals 0, 3 and 6 months. The study concludes no change in appearance, colour and disintegration of the tablets during this period16.

**Ancient verses modern views and prospective need**

The concept of Virya explained in ancient Ayurvedic literatures is very clear and it denotes the main property which is solely responsible for all the therapeutic actions of the drug17. Savirya avadhī is indicative of that specific period during which the Virya of the drug remains above certain threshold provided that it is stored in the mentioned condition. Beyond that time limit the drug may lose its potency up to some extent but it is not completely devoid of it. There are also some scientific reasoning behind the specific stability/shelf life indication of different formulations like Churna, Vati, Avaleha, Ghrita-Taila and Asava, etc. by ancient knowledge maestros. The main basics behind the development of different Ayurvedic dosage forms, is supposed as to increase its therapeutic efficacy, shelf life and palatability. Churna preparations were mentioned to have only 2-3 months of stability rather than there raw herbal materials. It may be due to greater exposed surface area while the raw materials have its external coating of cuticle or cork, etc. which protect them from environmental or microbial deterioration. The Churna preparation was developed due to its lesser particle size and larger open surface area needed for its efficient absorption. These are further developed in Vati form using different kind of resinous materials like Guggulu (exudates of Commiphora mukul Engl.), Shilajatu, etc. as the bioactive binding agents. These are pharmaceutically required to fix its dose and increase its stability again up to 1 year. Likewise also in case of Avaleha the concentrated sugar solutions or honey, are protecting the formulation from early deterioration. The oleaginous preparations like Ghrita-Taila were mentioned to have comparatively improved shelf life from 1 to 1½ yrs because of the relatively low environmental oxidation and rancidity rate. These are also remaining unaffected by microbial infestation until it develops some moisture which can facilitate the microbial growth. In recent era due to some misconception using the quotation of Acharya Sharangdhara about the shelf life of Asava-Dhatu-Rasa, that its have unlimited shelf life, is totally baseless and unscientific. The alcoholic biomedicines like Asava-arishtha are a kind of fermented products prepared by the development of wild genre of specific microbe in the media. These wild therapeutically beneficial microbes may hinder the non-beneficial others to infest. The shelf generated alcohol content of the product can also work as a preservative agent. Thus theses may retain the quality of the active ingredients for comparatively longer period but not for unlimited period. As one of the deteriorating factor, i.e. microbes may not be easily developed in these types of preparations due to competition with the already present of more wild microbial organisms responsible for its preparation. But the environmental factors like temperature variation; humidity, etc. may gradually facilitate other microbes to deteriorate the product. Likewise it should also be assumed in case of metallic and mineral preparations (Bhasmas and Kupipakva rasayanas) as these types products might have lesser effect of microbial deterioration but previously mentioned environmental factors may effects stability of its quality. The ancient seers have given the shelf life of the products as per the packaging and storage facilities of that era. Thus the shelf life of these products should again be revised using more equipped latest tools of packaging and storage.

While commenting on a verse, Adhamalla has clearly mentioned that all of the Churnas may not have same shelf life and it depends upon the ingredients which it contains; like the drugs which contain Lavan (salts) may have lesser shelf life because of its hygroscopic nature. This can also be supported by a study done in which accelerated stability testing of packaged solid dosage forms was carried out. In the study, the relative humidity inside high density polyethylene (HDPE) bottles stored
under accelerated condition (40°C/75%RH) was determined over a period of 6 months. The bottles, which were either capped tightly by hand or induction sealed at a pre-specified torque with polypropylene caps, were used to package either placebo tablets or anhydrous calcium chloride while one group of bottles did not contain anything. Each bottle contained a humidity-indicating strip that was read to determine the relative humidity of the headspace inside the bottle at 1, 3 and 6 month intervals. The study indicated that the relative humidity of the headspace inside the bottles increases with time and the rate depends on method of sealing and on contents of the package. Therefore, package and seal integrity test should be an important aspect to ensure the stability of a packaged product, especially for a moisture labile material. In another study in which ginger juice was studied for stability on different altered pH using proper amount of 1.0N HCl or KOH solution. The study indicated that the ginger solutions had better physical and chemical stability between pH 4.0-5.0. This kind of ideas for stability could also be utilized in Ayurvedic pharmaceutics, where the primary formulation like Swarasa and Kwatha are used as the base liquid media for the preparation of some derivative formulation like Asava and Arista (fermented alcoholic liquid biomedicines). These alcoholic formulations possess comparatively greater shelf life due to its altered pH and alcohol content which acts as preservative. These kinds of pharmaceutical modifications could be utilized for improving the shelf life of such types of primary formulations, provided that by doing so any undesirable change in the therapeutic efficacy of these dosage forms should not be observed.

Several difficulties and limitations are involved in accelerated studies as there is always possibility that the application of high stress may cause reaction that would not take place under the normal storage conditions. Therefore, while ensuring the stability of a drug in a formulation and the effectiveness of the drug product through out its usual shelf life the principle of physical pharmacy, chemistry, microbiology, pharmaceutical technology along with packaging science must be keep in account. The formulation must be in such form so that all the components could be physically, chemically as well as biologically compatible including the active therapeutic agents, the pharmaceutics ingredients and the packaging materials. The data generated by these studies should be sufficient so that it must be assured that the packaged product will be stable for its anticipated shelf life.

The other problem in case of the Ayurvedic formulation is that as most of the formulations contain more than one ingredient so it is quite difficult to determine the single active ingredient which creates problem in predicting the shelf life because we cannot fix the rate of reaction that is taking place in the formulation and cannot apply the Arrhenius equation for the determination of the expiry period. Now a days, markers are proved as a fruitful tool to assess the quality and stability of an herbal drug or its formulation. In case of a polyherbal formulation, one may consider markers from the main/principle drug used in the formulation as each poly ingredient formulation there are some could not be substituted and some can be substituted if not available. This may be supported by the views of ancient seer Acharaya Charaka that the main drug act like a king and the remaining drugs are acting as the associates of the king. The Ayurvedic polyherbal formulations mainly act on the basis of the pharmacological properties of the main drug and the rest of the drugs are used either for the enhancement of its therapeutic properties or reduction of its untoward effects which may not be needed in the prescribed condition. Thus, this marker based quantification and fingerprinting of the formulation using latest techniques like HPTLC, HPLC, etc. are also supposed as a good tool along with the physicochemical parameters in the establishment of the shelf life. Also in one such type of study an attempt was made for the determination of shelf life of a multi ingredient traditional Chinese medicine. The study proposes a statistical method for determining the shelf-life of a drug product with multiple active ingredients following similar idea as suggested by the FDA and assuming that these active ingredients are linear combinations of some factors. Stability data observed from a traditional Chinese medicine were analysed to illustrate the proposed method. These methods can be adopted as an initiative for the determination of shelf life of Ayurvedic drugs. This can also be help in the globalization of Ayurveda because for every drug product on the market, the United States Food and Drug Administration (FDA) requires that
an expiration dating period (shelf life) must be indicated on the immediate container label.

**Discussion and conclusion**

Thus, in the present scenario, one may consider the *Saviryata avadhi* as an indicative of ‘Best before use date’. This is the time limit after which one or more properties of the formulations would have shown considerable changes/degradation which can be seen or perceived by the consumers/patients and lead to doubts about the quality of the product and ultimately on its efficacy. However, if a drug is *Avipanna* (not influenced by environmental factors) and haves its original *Gandha* (smell), *Rasa* (taste), *Rupa* (physical state) can be used even it is older one because it may indicate that there is no change in the physical or chemical characters. Though Ayurveda has judiciously explained the subjective criteria for the assessment of *Virya* of a drug, but those are not sufficient to assess the potency. Those parameters described by them in that period were really admirable, scientific, and show their keen observation but in today’s era such parameters are not sufficient and hence new objective parameters for measuring these properties are to be search out. Packaging and storage conditions should be specific and *Anurupa Guna* (similar quality) according to dosage form and the API which the drug contains so that the unwanted effects of these factors be overcome. In the ancient period when there was no industrialization and Vaidyas themselves used to prepare the drug in small scale for the treatment of their patient and there main objective of formulation of, a drug, was to achieve the desire action rather than secondary mean of palatability or shelf life but in today in the era of globalization and large scale production, there is need to re-determine the revised stability period of these kinds of Ayurvedic formulations by following a suitable guidelines.

A deep scanning of the past and present scenario of shelf life determination of Ayurvedic dosage forms, a need is required to reestablish some more fruitful and scientific newer one utilizing new developed and specified package and storage conditions by following suitable guidelines. It is also required to thoroughly conducting such type of study on each and every particular formulation separately as all the formulations are varying in their composition and each ingredient have some specific stability period which may ultimately affect the formulation.

**References**