



A global comparison of stability testing parameters and testing methods for herbal products viz, anti acne cream and anti acne gel

Arshdeep Kaur Sidhu, Deepak Khichar, Rahul Rangila, Jitender Singh, Jagtar Singh Chohan*

Department of Pharmaceutics, Lord Shiva College of Pharmacy, Sirsa, Haryana, India

Abstract

Present study was started with a focus on Global comparison of Stability Testing Parameters and testing Methods for Herbal Products along with a focus on various evaluation and stability testing Methods or tests reported in the literature. Qualities of drug products are essential for therapeutic activities and achieving consistent qualities for herbal cosmetics is challenging because of their physicochemical variability. Now, it was interesting to know about the stability testing guidelines as regulatory requirements implemented in various countries of the world. These testing parameters and methods are detailed in the guidelines and regulations issued by 5 Global authorities and 15 countries. This review aims at understanding of the Global situation regarding the testing of herbal cosmetics.

Keywords: Anti acne cream and anti acne gel

Introduction

- 1. Semi -solid Dosage Form:** Semi solids are the topical dosage form used for the therapeutic protective or cosmetic function. Semi solid dosage form is advantageous in terms of its easy application^[1]. Creams are semi solid dosage forms that contain one or more drug substances dissolved or dispersed in a suitable base (O/W) emulsion and are cosmetically and aesthetically acceptable. Gels are semi solid dosage forms consisting of suspensions of small inorganic particles interpenetrated by a liquid.
- 2. Cream:** Creams are classified as oil in water emulsion or water in oil emulsion. A cream is defined as semi solid dosage form intended for external application^[2]. Creams are used to protect the skin against different environmental conditions, acne, soothing effect, moisturizing effect etc^[3].
- 3. Gels:** A gel is a semi solid preparation that can have properties ranging from soft and weak to hard and tough^[4].
- 4. Anti acne cream:** Anti acne cream may be formulated using various extracts for instance papaya, neem, turmeric, Tulsi etc. These ingredients have anti-inflammatory, anti-bacterial, and moisturizing properties^[5].

Formulation and evaluation of Anti acne cream

- 1. Herbal Anti acne cream:** Anti acne cream is formulated incorporating various extracts such as papaya, neem, turmeric, Tulsi etc. These ingredients may have many actions such as anti-inflammatory, anti-bacterial, moisturizing properties etc^[5].
- 2. Formulation:** Formulation process of anti acne cream comprises of a well thought planning along with, selection of suitable herbs, extraction of phytoconstituents, preparation method, and evaluation of final product.

2.1. Selection of Herbs: The market for herbal cosmetics or medication products is growing day by day as a result of availability of various novel herbal ingredients available and also has the financial benefits for creating and launching profitable products. One of the most important and significant medical system that uses Herbal plants is Indian Ayurvedic System^[6].

From the Prehistoric times, *Aloe vera* used to treat burns and infections. It is a miraculous plant for giving ingredients to cosmetic preparations as it contains almost 20 amino acids. Clove oil, Tea tree oil, these ingredients also have anti acne properties. Aloe Vera has moisturizing, anti-acne smoother, skin properties^[7].

2.2. Herbal Ingredients: The ingredients of a variety of herbal species can be used in formulation of herbal anti acne cream. We found various such instances during our study. Some important herbals are reported here;

- a. Aloe Vera:** Aloe vera contains vitamins, minerals, enzymes, carbohydrates, amino acids, saponin, Lignin etc. There are various uses of Aloe vera, anti-bacterial, anti-acne for the treatment of acne, also have anti-inflammatory properties. All these facts support it to be a suitable candidate for including in anti-acne preparation^[8].
 - b. Clove:** Extract of clove collected from buds and flowering parts of *Eugenia caryophyllus* is very important in the anti acne preparations. It contains volatile oil, tannin and eugenol. It possess properties of antiviral, antioxidant and antimicrobial which makes it appropriate for use in the formulation^[9].
 - c. Rose Oil:** Rose oil contains variety of chemical constituents such as terpenes, Glycosides, Vitamin C, Flavonoids etc. It is used for its anti-aging, fragrance and it is also used for its skin restoration property^[10].
- 3. Evaluation Tests for Anti acne Cream:** Every herbal product is required to be evaluated or tested for

establishing its stability, safety and efficacy. We came across various evaluations tests reported as under;

- 3.1. Physical evaluation:** There are various physical parameters like odor, colour, consistency ^[11].
- 3.2. Viscosity:** Viscosity is measured by Brookfield viscometer at room temperature. Measurements were taken in 3 sets at 100 rpm in ratio of (n:3). The viscosity values were recorded in centipoises ^[11].
- 3.3. pH of Cream:** pH of herbal Anti acne cream should be in the range of 5.6 – 5.8, to avoid irritancy of skin. pH of formulated herbal cream is measured by using digital pH meter. pH meter is calibrated by using standard buffer solution ^[11].
- 3.4. Greasiness:** This parameter is used to check, whether the cream is greasy or oily ^[12].
- 3.5. Homogeneity:** Herbal creams are tested for the homogeneity by visual appearance and by touch ^[12].

Formulation and evaluation of Herbal Anti acne Gel-

- 1. Herbal anti acne gel:** Anti acne gel is formulated incorporating various extracts such as garlic, neem, aloe, Tulsi etc. These ingredients may have many actions such as anti-inflammatory, anti-bacterial, moisturizing properties etc.
- 2. Formulation:** Formulation process of anti acne gel comprises of a well thought planning along with, selection of suitable herbs, extraction of phytoconstituents, preparation method, and evaluation of final product.

Methods of Formulation of herbal anti acne gel ^[13]

- Procurement of plant material
 - Extraction procedure
 - Formulation of Gel.
- 2.1. Selection of herbs:** Depending upon the requirements of herbal formula, different species are selected for collecting raw materials in order to prepare extracts such as Garlic, Neem, Carbapol, PEG400, Methyl paraben, Glycerine etc.
 - 2.2. Herbal ingredients ^[13]:** The ingredients of a variety of herbal species can be used in formulation of herbal anti acne cream. We found various such instances during our study. Some important herbals are reported here:
 - a. Chief constituents:** These are the main pharmacologically active compounds which will give the gel its anti acne action on our face. These are the herbal drugs which are acquired from natural sources.
 - **Neem:** It is obtained from the leaves of *Azadirachta indica* is very important in the anti acne preparations. It is used as Anti-viral, also have good Antiseptic properties.
 - **Garlic:** It is obtained from the bulbs of *Alium sativam*. It is very useful in the anti acne preparation. It contains

various chemical constituents such as Allicin, Allin, volatile oil. It is used as a disinfectant and anti-bacterial agent.

- b. Excipients:** Excipients are used for the formulation of herbal gel as binding agent, protective, thickening agents, and gelling agents. To illustrate, Carbapol 940 finds a role as Gelling agent, PEG 400 may be incorporated not only as Humectant but also as a solvent, likewise Methyl paraben is a useful Preservative in herbal products and off course distilled water is used as a vehicle.
- 3. Evaluation of Herbal Anti acne Gel-** Every herbal product is required to be evaluated or tested for establishing its stability, safety and efficacy. We found some evaluations tests to report as under:
 - 3.1. Spreadability:** Spreadability signifies the extent of area to which the gel was expanded or spread on affected part ^[14].
 - 3.2. Skin Irritancy Test:** Skin irritation test highlighted symptoms of rashes, odema, and inflammation ^[14].
 - 3.3. pH:** pH of Herbal gel ranges between 6.1 to 6.6 hence after evaluation results must comply.
 - 3.4. Anti acne activity:** Anti acne activities or anti-bacterial activities determined by using modified agar well diffusion method. Nutrient agar plates are seeded with 0.2ml for 24hour with broth culture of *S. aureus*. Agar plates settle to solidify. 0.5ml of Formulations, herbal gel added into the Wells at randomly. Plates are incubated at 37°C for 24 hours. Activities evaluated by measuring the zones of inhibition ^[15].

Regulatory Compliance of Herbal Products –

Regulatory compliance is the process of complying with regulations, applicable laws, policies, and procedures and other rules issued by Government and regulatory bodies like FDA.

A Review of the regulatory status of Herbal Products *viz.* herbal anti acne cream and herbal anti acne gel was done for few countries Asia, Europe, Australia, Africa, and America. The Regulatory system of cosmetic items ensuring the product safety and efficacy are the mandatory elements for the development of cosmetic herbal products.

1. A Review of the Regulatory status of herbal products in India ^[16]

Herbal products are regulated under the Drug and Cosmetic Act (D and C) 1940 and Rules in 1945. Department of AYUSH is the Regulatory authority that works with authorization for manufacturing and marketing of Herbal Products done after obtaining manufacturing license. GMP (Good Manufacturing Practices) also followed for the manufacturing of herbal products.

2. Global Comparison of Stability Testing Parameters and Testing Methods.

Comparisons of global regulations and guidelines addressing stability testing are rudimentary for the international harmonization of herbal products and global

situation regarding the testing of herbal product quality with regard to storage.

There are the various Guidelines and regulations issued by 5 Global authorities and 15 countries.

Global authorities are –

2.1. ASEAN – Association of Southeast Asian nations.

2.2. EEC- Eurasian Economic Commission

2.3. EMA- European Medicines Agency

2.4. ICH- International Council for harmonization

2.5. WHO- World Health Organization

The Stabilities of herbal products can be determined by testing for properties susceptible to storage conditions and include Physical Parameters (organoleptic), chemical (pH), microbial and toxicological properties. These properties which affected the quality, safety, and. Efficacy of herbal products and thus shelf life of herbal products should be proceeding by stability testing^[17].

Global Harmonization of Stability Testing recently point out in the context of herbal product development^[17].

3. An Overview of Stability Testing^[18]

We checked Guidelines and regulations from global authorities and countries where the stability testing of herbal products is mandatory for quality maintenance of herbal products. Conditions for long-term accelerated and intermediate testing (storage, temperature etc), reported as follows:

1. It is observed from evaluating the different various articles and reviews of research published by different formulators that the global regulations for the stability testing of herbal products under the long term, accelerated, and intermediate conditions sufficient to produce or establish an herbal anti acne cream stability profile throughout its proposed shelf life.
2. Herbal anti acne cream should be evaluated in terms of thermal stability based on consideration of duration of storage and use.
3. The effects of storage temperature and relative humidity should be well enough and these are the most persuasive for quality of herbal products.
4. Herbal creams packed in semi permeable (allow moisture migration) or impermeable containers which impacts on storage and relative humidity.

We searched guidelines and regulations from various global authorities and countries where the stability testing is required for maintenance of herbal preparations.

4. Stability Testing Parameters

1. **ASEAN:** The provision of ASEAN gives the stability testing guidelines to ensure quality of herbal products to recommended storage conditions and times. As per ASEAN the herbal products must be evaluated for organoleptic characteristics. Assay is performed as given protocols apart from that evaluation for pH, viscosity, and microbial content etc. Evaluation must be addressed^[19].

2. **EEC:** According to the EEC, that all the herbal products should be evaluated in terms of appearance, preservatives, degradation products, active ingredients and anti-oxidant contents. Also the physical, chemical, biological, and microbiological contents also determined according to the EEC Guidelines. Dosage forms such as creams, gels, homogeneity, pH value, transparency, ability to resuspend must be evaluated.²⁰

3. **EMA:** Guideline on stability testing of existing active substances and related herbal products (CPMP /QWP/122/02 and EMEA /CVMP/846/99). Descriptions, assay, identification and microbial contents should be addressed according to the EMA guidelines^[21].

4. **ICH:** ICH guidelines are also applicable to herbal products as global documents regulated by EMA, Switzerland, Japan, Australia are conducted in accordance with ICH guidelines. ICH guidelines gives general requirements for the storage stability testing of new herbal products that cover with respect to identification, description, assay and impurity content must be evaluated^[22].

5. **WHO:** General Requirements of the stabilities if herbal products include preservatives, anti-oxidant, appearance, assay and microbial or degradation content. Certain Parameters are also provided according to dosage form of product, that is liquid, solid or semi solid. WHO published technical reports annually for herbal preparations and guidelines on good herbal processing practices for herbal products and stability testing or evaluating methods. According to WHO, Creams are tested for clarity, pH, homogeneity, sterility, extractable volume and particulate matter must be addressed^[23].

6. **Australia:** Stability testing for determined shelf life and storage conditions is performed as determined in the EMA guidelines. The Australian government also provided the obligatory guidelines for the stability testing of herbal anti acne cream such as pH, and microbial content^[24].

7. **Brazil:** The Brazilian Health Regulatory Agency (ANVISA) adopts the position that the stability of herbal preparations depends upon Product related parameters, environmental factors. ANVISA gives stability testing parameters for semi solid preparations (creams and gels) uniformity of dose, pH, description, phase separation^[25].

8. **Canada:** Canadian government provides guidelines for topical preparations creams and gels. Testing parameters includes description and preservative efficacy must be tested^[26].

9. **China:** Chinese Government required accelerated and long term stability testing to provide shelf life of herbal preparations and essential storage conditions. Anhui Provincial Food and Drug Administration provides stability testing parameters for herbal cream as given as odor, colour, particle size, phase separation,

identification, and microbial limits. For gels viscosity, assay, pH, description, must be tested^[27].

10. **Egypt:** Egyptian Drug authority required that herbal preparations (anti acne cream and gels) satisfied minimum specifications includes -Specific quality parameters for semi solid preparations that is Consistency and common quality parameters such as physical appearance, water content, qualitative determination, microbial contamination^[28].
11. **India:** Indian government specified the requirements for the quality test for herbal products that are used in Ayurvedic, Siddha and Unani system of medicines according to the various dosage forms. Testing of herbal products includes various parameters physical evaluating (description, viscosity, pH, odor)^[29].
12. **Hong Kong:** The legislative council of Hong Kong proposed storage conditions as described by Product Quality documents technical guidelines. Skin irritation test for herbal anti acne cream and gels is provided by the Hong Kong Government.³⁰
13. **Kenya:** General specifications which includes tests for microbiological contamination, physical appearance, identifications and tests for residual solvents. Consistency is one such testing parameter for herbal preparations. The Guidelines prescribed that the physical and chemical stabilities after long term storage period should comply with ICH guidelines^[31].
14. **Qatar:** The Qatar Government provided the requirements for quality specifications of herbal products which includes the identification, physical examination, microbial limits and other quality standards according to dosage form which includes pH, spreadability, viscosity should be addressed^[32].
15. **The Philippines:** The food and drug Bureau of the Philippines required stability studies conducted under recommended conditions and should also determine the most suitable conditions for storage. Government required tests, physical description, and quality standards which includes organoleptic and macroscopic descriptions, pH, and moisture content. In addition, the Philippines government also provided the specific parameters for specifications of creams – palpability, pH, melting point, homogeneity, allergenicity must pass all requirements specified in Pharmacopoeias of other countries^[33].
16. **Republic of Korea:** MFDS (Ministry of Food and Drug Safety) provides general specifications for all herbal dosage forms includes identification, description, assay, purity testing. For Creams and gels particle size distribution, uniformity, microbial content must be addressed^[34].

5. Stability Testing Methods

Herbal products should be evaluated in terms of thermal stability or moisture susceptibility based on consideration of durations of storage, transportation, and use. The effects of storage temperature and relative humidity should be

adequately considered as they are the most influential factors for quality of herbal products. Long term testing is carried out for less than 12 months by most of the authorities, though some included are ASEAN, China, Hong Kong, Korea conducted long term testing for more than 12 months. Most global authorities and countries conducted accelerated testing for <6 months, except Korea.

Conclusions

From our current study, we have focused stability testing parameters and methods provided by 5 global authorities and 15 countries including India, China, Australia, Japan, etc. In this present study, we have provided regulatory guidelines of various authorities which are mandatory for the standard herbal preparations to improve the qualities of herbal products. We have understood the requirements of stability parameters and stability testing methods. Stability tests are carried out to ensure that the herbal cosmetics or herbal preparations in recommended storage and shelf life conditions are safe and effective throughout their shelf life. Therefore, the stability test should be conducted based on various regulatory guidelines and comprehension of current regulatory requirements. We hope that the information provided for further understanding and collaborative studies on the stability testing of herbal products in their various dosage forms. Our study can be of some help to the new herbal manufacturers who wish to launch their products globally.

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