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A Review on Stability Testing of Herbal Medicine: Curcuma Longa:

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ABSTRACT :
The assurance of maintaining product quality, safety, and efficacy throughout its shelf life is crucial for the acceptance and approval of any pharmaceutical product. Thus, stability studies are considered a prerequisite and should be carried out following guidelines from reputable agencies such as ICH, WHO, or other regulatory bodies. These studies should be well- planned to ensure the accuracy and validity of the results. The significance of various methods used in stability testing of pharmaceutical products, as well as guidelines issued for stability testing, have been summarized in this review. Additionally, other aspects related to the stability of pharmaceutical products have been presented in a concise manner.
Keyword: Curcuma Longa, Stability Testing, TLC, HPLC

I. INTRODUCTION :

Herbal drugs contain various constituents and often have low concentrations of active components in the finished product. Assessing the stability of herbal drugs is challenging because the entire herb or product is considered the active ingredient, even if specific therapeutic constituents are not known. The key factor in evaluating stability is the product's storage conditions, which can be determined based on the climate. Stability testing aims to demonstrate how a herbal product's quality changes over time due to environmental factors such as temperature, light, oxygen, moisture, contaminants, and container leaching. It also establishes recommended storage conditions and shelf-life. Long-term stability is assessed by testing at least three production batches of the product under natural atmospheric conditions. Modern analytical techniques like spectrophotometer, HPLC, and HPTLC can be used to generate reliable stability data and predict shelf-life, improving the acceptance of herbal products worldwide[1,2]

CURCUMA LONGA:

Turmeric is a most commonly used spice derived from the dried rhizomes of Curcuma longa, a perennial herb belonging to the Zingiberaceae family. In the literature, turmeric has been widely acknowledged for various pharmacological activities such as anti-inflammatory, anti- oxidant, antimicrobial, anticancer, hepatoprotective, and antidiabetic. The bioactivities of turmeric extract have been attributed to the presence of three phenolic compounds namely curcumin (CUR), demethoxycurcumin (DMC), and bisdemethoxycurcumin (BDMC). These phenolic compounds are collectively known as curcuminoids or a curcuminoid mixture. In general, it is believed that CUR, one of the most extensively studied curcuminoids, is responsible for the therapeutic success of turmeric in a wide range of disorders [2]

It is a perennial herb that measures up to 1 m high with a short stem, distributed throughout tropical and subtropical regions of the world, being widely cultivated in Asiatic countries, mainly in India and China. In India is popularly known as “Haldi”, in Malaysia, Indonesia and India has been well studied due to its economic importance. Its rhizomes are oblong, ovate, pyriform, and often short-branched and they are a household remedy in Nepal 1 . It is a sterile plant and does not produce any seeds. The plant has oblong, pointed leaves with funnel- shaped yellow flowers [3] .
Turmeric was described as C. longa by Linnaeus and its taxonomic position is as follows:

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Kingdom	Plantae
Class	Liliopsida
Subclass	Commelinids
Order	Zingiberals
Subfamily	Zingiberoideae
Tribe	Zingibereae
Genus	Curcuma
Tribe	Curcuma longa

Fig 1. Curcuma Longa

Curcumin, a polyphenol, has been shown to target multiple signaling molecules while also demonstrating activity at the cellular level, which has helped to support its multiple health benefits.It has been shown to benefit inflammatory conditions , metabolic syndrome , pain , and to help in the management of inflammatory and degenerative eye conditions [4]

Properties of Curcumin :

Curcumin is a bioactive compound found in the spice turmeric, which is commonly used in Indian and Southeast Asian cuisine. It has been extensively studied for its health benefits, and its antioxidant, anti-inflammatory, antiviral, and antifungal properties have been well-documented.

Studies have shown that curcumin is safe for human consumption and does not cause toxicity even at high doses. Its anti-inflammatory properties are thought to be due to its ability to inhibit the activity of several molecules that play a role in the inflammatory process, such as cytokines and enzymes [5].

The Main Product of Curcuma longa [5]:

Product name	**Appearance**	**Chemical constituents**	**Uses**
Whole rhizome (dried form	Orange-brown, red-yellow	3.5%–14% curcuminoids, and 1.5%–5% essential oils	High Therapeutic value
Ground C. longa	Yellow or red-yellow	Reduction of Curcuminoids and essential oils during its manufacturing, as well as by light exposure. The powder must be protected from in a UVlight.	Used as a nutrient.
C. longa oil	Yellow to brown oil	Monoterpenes and sesquiterpenes are essential oils in leaves and rhizomes, respectively	Used as a spice in making food, medicine, and dietary supplement

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C. longa oleoresins	Dark yellow, reddish-brown	24.5% of essential oiland 37.3%–55.5% of curcuminoids	Used as a food dye, medicine, and dietary supplement
Curcumin	Yellow to orange-red colored crystallinepowder	Curcumin and its bisdemethoxy and demethoxy derivatives.The three primary curcuminoids may account for up to 90%of the total curcuminoids. Oils andresins may make up a small percentage of the total composition.	Used as medicine anddietary supplement

Stability Testing :

The process of stability testing for pharmaceutical products is a complex and expensive undertaking that requires a significant amount of scientific expertise. It is essential for ensuring the quality, efficacy, and safety of drug formulations. In order to successfully develop a pharmaceutical product, it is necessary to have a thorough understanding of the drug development process and the various tasks and milestones that are involved. Key steps in this process include pharmaceutical analysis and stability studies, which are necessary for determining and ensuring the identity, potency, and purity of ingredients, as well as the formulated products themselves. The stability of a pharmaceutical product refers to its ability to maintain its physical, chemical, microbiological, toxicological, protective, and informational characteristics within specific container and closure systems[7].

It is important to conduct stability testing to ensure that the product remains safe, effective, and maintains its desired attributes such as appearance, potency, purity, and stability under various environmental conditions. These studies provide crucial information for formulating appropriate storage recommendations and determining expiry dates for herbal products, which can help ensure consumer safety and regulatory compliance.[3]

Stability Testing Methods:

Stability testing is a standard process that is conducted on both drug substances and products, and it is used at different stages of product development. During the early stages of development, accelerated stability testing is carried out, which involves subjecting the drug substance or product to high temperatures and/or humidity conditions. The purpose of this testing is to identify the potential degradation products that may arise during long-term storage[6].

Real-Time stability testing:

Real-time stability testing is conducted over a prolonged period to observe significant product degradation under recommended storage conditions. The test period should be long enough to identify any measurable degradation and allow the distinction between degradation and inter-assay variation. The data is collected at an appropriate frequency to allow trend analysis to detect instability and distinguish it from day-to-day variability. The inclusion of a single batch of reference material with established stability characteristics can increase the reliability of data interpretation [7].

Accelerated stability testing:

Accelerated stability testing is a method used to predict the shelf life of a product by subjecting it to elevated temperatures that accelerate the degradation process. The amount of heat required to cause product failure is determined, and this information is used to estimate the product's shelf life or to compare the relative stability of different formulations.

By exposing the product to conditions that simulate the effects of aging and degradation over time, accelerated stability testing can provide an

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early indication of a product's shelf life. This information can help developers make informed decisions about the formulation, packaging, and storage conditions of their products, which can help to optimize their stability and extend their shelf life.

One of the key benefits of accelerated stability testing is that it can shorten the product development schedule by providing early indications of shelf life. This can help to speed up the development process and reduce the time and resources required to bring new products to market.

Overall, accelerated stability testing is a valuable tool for product development and quality control, as it provides important information about a product's stability and can help to optimize its formulation, packaging, and storage conditions to ensure a longer shelf life[7].

ICH Climatic zones and long term stability conditions:

Climatic Zone	Climate/ Definition	Major Countries /Region	MAT*/Mean annual partial water vapors pressure	Long-term testing conditions
I	Temperature	United Kingdom Northern Europe Russia Unitedstates	<11hPa	21°C/45%RH
II	Subtropical and Mediterranean	Japan Southern Europe	>15-22°C >11-18 hPa	25°C/60%RH
III	Hot and Dry	Iraq India	>22°C/	30°C/35%RH
IVa	Hot and Dry	Iran Egypt	>22°C/>15-27	30°C/65%RH
Vb	Hot and very humid	Brazil Singapore	>22°C/>27 hPa	30°C/75%RH

Table.1: ICH Climatic zones and long term stability conditions [7]

Stability Testing of Curcuma:

1. Chromatographic-based methods :

Thin layer chromatography (TLC) an (HPTLC) :

Curcuma rhizomes are widely used in traditional medicine and in the food industry for their medicinal and culinary properties. Curcumin, the main bioactive compound in Curcuma rhizomes, is known for its anti-inflammatory, antioxidant, and anticancer properties. The quality control of Curcuma rhizomes is essential to ensure the safety and efficacy of their use. Thin-layer chromatography (TLC) coupled with high-performance liquid chromatography (HPLC) is a powerful tool for the analysis of curcumin in Curcuma rhizomes.

Several recent research studies have investigated the use of TLC coupled with HPLC for the analysis of curcumin in Curcuma rhizomes. For example, a study published in the Journal of Chromatography B in 2019 developed a TLC-HPTLC method for the analysis of curcumin in Curcuma rhizomes. The method was found to be accurate, precise, and reliable for the analysis of curcumin in different samples of Curcuma rhizomes[7].

High performance liquid chromatography :

An Agilent HPLC 1200 instrument (Agilent Technologies, Palo Alto, CA) was used for HPLC determinations, equipped with a diode array detector (DAD) detector, an auto sampler, a column heater, and a Welch Ultimate XB-C18 (250 mm × 4.6 mm, 5 μm) column. The mobile phase consisted of two solvents: solvent A (acetonitrile) and solvent B (4% glacial acetic acid aqueous) (V/V). The optimal separation was achieved using a mobile phase composition of 48% solvent A. The flow rate was 1.0 mL·min−1 and the injection volume was 10 μL. The column temperature was set at 30◦ C. The wavelengths were monitored at 425 nm using the diode array detector[6].

The preferred method for determining curcumin levels is through the use of HPLC (High Pressure Liquid Chromatography) techniques, with the most commonly utilized detectors being UV or

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PDA due to curcumin's absorbance in the visible range[16]. It has been reported that the quantity of curcumin in C. longa extract is 30.76 mg/g, which is equivalent to 3.06%.[8] .

Liquid chromatography coupled with mass spectrometry (LC/MS):

TLC methods have been developed and can be employed as a quality control technique for Curcuma rhizomes. LC/MS is a useful tool for detecting trace amounts of curcumin in biological fluids, food, and other complex matrices. As an online technique, it provides rapid and accurate analysis, and is capable of differentiating between various curcuminoids. In addition to identifying and quantifying known curcuminoids, LC/MS can also be used to identify unknown curcuminoids in extracts from turmeric or related plant material.

2. Curcumin Degradation:

Oxidation of curcumin:

The autoxidation of curcumin can lead to the formation of several compounds, including the bicyclopentadione, dihydroxy cyclopentadione, hemiacetal cyclopentadione, ketohydroxy cyclopentadione, spiroepoxide cyclopentadione, and vinylether cyclopentadione. The major product of this process is the bicyclopentadione, which is formed by the double cyclization of the heptadienedione chain connecting the two methoxyphenol rings of curcumin[9].

Degradation of curcumin in buffered solutions :

The rate of decomposition of curcumin was dependent on the pH of the environment, with faster decomposition occurring under neutral-basic conditions. The stability of curcumin was found to be greater at acidic pH levels, but decreased as the pH increased. In particular, the pH of 1.2 was found to be the most stable, with less than 1% of the curcumin decomposing within 6 hours in the absence of light.

Photo degradation of curcumin :

Exposure to visible light leads to more degradation of curcumin than exposure to UV light. A study exposed solid-state curcumin to sunlight for 120 hours and identified vanillin (34%), ferulic aldehyde (0.5%), ferulic acid (0.5%), vanillic acid (0.5%), p-hydroxybenzaldehyde, and p-hydroxybenzoic acid as degradation products. Curcumin was found to be more stable in its dried form compared to when in a solution under sunlight exposure.

In addition to photo-sensitivity, curcumin is also susceptible to self-degradation in the absence of light. Self-degradation is more pronounced under basic conditions and is significantly influenced by the concentration of salt, particularly NaCl.

2.4.Thermal degradation of curcumin :

Based on current research, it is known that curcumin is heat sensitive and can undergo thermal degradation when exposed to high temperatures, especially during roasting and pressure cooking. The degradation products of curcumin under these conditions are vanillin, ferulic acid, and 4-vinyl guaiacol.

If curcumin is used as a food coloring agent, the processing temperature of the food should not exceed 190°C to prevent significant degradation. Heat processing of turmeric has been shown to result in a loss of around 27-53% of curcumin, with the highest loss observed in pressure cooking for 10 minutes[13].

3. Physical evaluation:

Every monograph offers comprehensive botanical, macroscopic, and microscopic details about the physical traits of each plant. These details serve the purpose of confirming both the authenticity and purity of the plant. Moreover, the descriptions are supported by intricate illustrations and photographic images that offer visual evidence of precisely identified specimens[14].

4. Microscopic evaluation:

A comprehensive physical examination is necessary for a complete and precise characterization of plant material. Microscopic analysis plays a vital role in confirming the plant's identity and serves as a primary method for detecting impurities during the initial screening test[13].

5. Capillary electrophoresis (CE) :

Various chromatographic techniques are currently in use for separating and analyzing curcuminoids, as discussed earlier. However, they are not without limitations. Some methods require extensive sample preparation and are heavily reliant on the sample matrix. Others necessitate the use of sophisticated detectors, particularly in LC-MS/MS analysis. Consequently, there is a need for more sophisticated methods that can effectively separate and quantify curcuminoids in a wide range of sample matrices[11].

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II. RESULT :

The study investigated the stability of curcumin under acidic conditions similar to the pH of the stomach and basic conditions similar to the pH of the intestine and colon. Curcumin solutions were prepared in 0.1 N HCl and pH 6.8 or 7.4 phosphate buffer, and their stability was assessed under accelerated conditions at temperatures of 37, 60, 70, and 80 °C. To determine the degradation kinetics of curcumin, graphs were plotted for the percentage of remaining curcumin (zero-order), the natural logarithm of the percentage of remaining curcumin (first-order), and the reciprocal of the percentage of remaining curcumin (second-order) versus time, and the coefficient of determination (r2) was calculated [5].

REFERENCE :

[1]. Kumar Ashutosh and Sachan kumar Anupam, "Stability testing of herbal products" Published in "Journal of Chemical and Pharmaceutical Research",2015,511-514.

[2]. Palkar B Mahesh and Jalalpure S.Sunil, "Stability studies of pure and mixture form ofcurcuminoids by reverse phase – HPLC method under various experimental stress conditions" Published in "Food Sci Biotechnol",2017,591-602.

[3]. J.suresh and Redy Sri Vasavi, "A Review on Curcuyma longa" Published in "Research J.Pharm and Tech",2012,158-165

[4]. Hewling J. Sushan and Kalman S. Douglas, "Curcumin: AReview of Its Effect on Human Health"Published in "Journal of food"2017,377-4522

[5]. Akram.M and Udin shahab, "Curcuma longa and Curcumin : A review article"Published in "Journal of Bucharest",2010,vol.55,65-70.

[6]. Bajaj Sanjay and single Dinesh, "Stability testing of Pharmaceutical Products",Published in"journal of applied Pharmaceutical science",2012,129-138.

[7]. chen Zhimin and Zhao Youngfeng, "Study on quality standard of Processed Curcum Longa Radix",published in " Hindawi",2017,1-6.

[8]. Zaghary A Waffa and Henna T Emily, " Curcumin: Analysis and stability",Published in "Journal of advanced Pharmacy Research",2019,47-58.

[9]. Haq Nazrul and Shakeel Faiyaz, "Greener Sablity –Indicating HPLC Approach for thedetermination of curcumin in –housing Developed Nanoemulsion and Curuma longa

[10]. l.extract" published in "Journal of separation"2023,2-15.

[11]. Du Zheyuan and kharat Mahesh, " Physical and chemical stability of curcumin in aqueoussolution and emulsion : Impact of Ph, temperatue, and molecular environment" published in "Depatment of Food science"2020,105

[12]. Treesinchai Sakonja and Pitaksuteepog Tasana, "Determination of curcumin stability in various gastrointenstinal ph by arrehnius equation using HPLC method", Published in " Journal of Pharmaceutical sciences Asia",2020,86-96.

[13]. Kotra Rao subba Venkata and Satyabanta Laishram, "A critical review of analytical methods for determination of curcuminoids in turmeric", Published in "journal of food science and technology"2019,5153-5166.

[14]. Fuloria shivkanya and Mehta jyoti, "A comprehensive Review on the Therapeutic Potential of curcuma longa linn. In relation to its Major Active constituent Curcumin" Published in "Frontiers in Pharmacology",vol.13,2022,1-27.

[15]. Bajaj Sanjay and single Dinesh, "Stability testing of Pharmaceutical Products",Published in "journal of applied Pharmaceutical science",2012,129-138.

[16]. Folashade Oluyemisi and Egharvba, " standardization of herbal medicine" Published in " International journal of Herbal Medicines"2012,page.no101-111.