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FORMULATION AND EVALUATION OF ANTI-PEPTIC ULCER CAPSULES OF *CURCUMA LONGA* HERBAL PRODUCT

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ABSTRACT

Curcuma longa has been used in traditional remedy for a wide range of ailments, including wound healing, urinary and gastrointestinal tract infections, and liver ailments and variety of symptoms such as inflammation, gastritis and gastric ulcer. When *Curcuma longa* extract was administered per oral to pylori-ligated rat stomachs, it reduced gastric acid secretion and protected against the formation of gastric mucosal lesions. *Curcuma longa* extract inhibits gastric ulcers by blocking the H2 histamine receptor. *Curcuma longa* is commonly used in traditional medicine for a wide range of ailments including gastritis and gastric ulcer. Anti-peptic ulcer of ethanolic extract of *Curcuma longa* was prepared and evaluated at the dose of 100mg/kg and showed a significant activity. *Curcuma longa* was *f*ormulate as capsules and evaluate for organoleptic properties of ethanolic extract of *Curcuma longa*. The results show that the formulation of extract capsules of *Curcuma longa* was sparingly soluble, particle size was very fine, tapped density was m /V1250 g /ml, flowability of extract powder moisture content was 4%. Dissolution and stability under various storage condition were also performed.

KEYWORDS: *Curcuma longa*, Extract, Capsules, Anti-peptic ulcer, Herbal Medicines**.**

INTRODUCTION

There has been a great interest in the last few decades in using plants to cure diseases in general, and to consider it as a main source in the Alternative Medicine to cure the chronic diseases in particular.[1] prescriptions that contain compounds refer to chemical groups produced by plants are called Botanical Products.

According to the World Health Organization (WHO), "Herbal Preparations" contain plant parts or plant material in the crude or processed state as active ingredients and may contain excipients (foreign substances.[2] Combinations with chemically defined active substances or isolated constituents are not considered herbal preparations.[3]

Plant medicines are generally considered to be safer and less damaging to the human body than synthetic drugs. Furthermore, there is a current upsurge of interest in plants that is further supported by the fact that many important drugs in use today were derived from plants or starting molecules of plant origin: digoxin / Digitoxin, the vinca alkaloids, reserpine and tubocurarine are some important examples.[4]

Curcuma Longa and Peptic Ulcer

C. longa has been used in traditional remedy for a wide range of ailments, including wound healing, urinary and gastrointestinal tract infections, and liver ailments and variety of symptoms such as inflammation, gastritis and gastric ulcer. When C. longa extract was administered per os to pylori-ligated rat stomachs, it reduced gastric acid secretion and protected against the formation of gastric mucosal lesions. C. longa extract inhibits gastric ulcers by blocking the H2 histamine receptor.[5,6]

The antiulcer activity of ethanol extract of Curcuma longa was evaluated at the doses of 125, 250 and 500mg/kg in several ulcerated rat models. The high dose of ethanol extract of Curcuma longa at dose of 500mg/kg was more effective compared to the low and medium dose (125mg/kg and 250mg/kg). The efficacy in high dose of the extract(500mg/kg) appeared to be as good as Omeprazole (8mg/kg) and Misoprostol (50mg/kg) and more than that of sucralfate (500mg/kg). The ethanolic extract of C. longa (125,250,500mg/kg) showed significant anti-ulcer activity in the all rate models, especially in Ethanol induced gastric ulcer model (125,250,500mg/kg) and indomethacin induced gastric ulcer model (125,250,500mg/kg) than cysteamine induced duodenal ulceration (500mg/kg dose only). the

effect appears to be dose dependent. It was confirmed that ethanol extract of Curcuma longa possess potent anti-ulcer activity.[7]

Rafatullah et al., reported that an oral dose of 500 mg/kg of the ethanol extract of turmeric produced significant antiulcerogenic activity in rats subjected to hypothermic restraint stress, pyloric ligation indomethacin, and reserpine administration. He suggested that turmeric extract not only increased gastric wall mucus but also restored the non-protein sulfhydryl content in the glandular stomachs of rats, and finally concluded that the extract has significant antiulcer, antisecretory, and gastroprotective effects in rats.[8]

Curcumin Gastroprotective Potentials

Curcumin has been defined as the most active component in C. longa and has considerable gastroprotective and antiulcerogenic effect. Its anti-ulcer potential activity was recently confirmed and reviewed in our laboratory. [9] The anti-ulcer activity of curcumin was displayed by attenuating the different ulcerative effectors including gastric acid hypersecretion, total peroxides, myeloperoxidase activity, IL-6, and apoptotic incidence, along with its inhibitory activity for pepsin. [10] The presence of both phenolic OH and CH2 groups in β-diketone moiety of this natural compound contributes significantly to its potent antioxidant properties. [11] The gastroprotective potentials of curcumin might protect patients from the adverse gastric side effects of many anti-inflammatory drugs, thereby improving the quality of life for patients and decreasing the treatment costs significantly. [1]

One study carried out with curcumin and dimethoxycurcumin to investigate the major functional group in curcumin reported that phenolic OH plays a major role in the activity of curcumin. It is evident that the antiulcer activity of curcumin arises from its antioxidant activity. Since, the antioxidant or scavenging reactive free radicals' ability of curcumin arise whether from the phenolic OH group or from the CH2 group of the b-diketone moiety.[2,3]

Free radical-mediated peroxidation of membrane lipids and oxidative damage of cellular molecules are believed to be associated with various chronic pathological complications such as cancer, ulcer, and other inflammatory diseases. Curcumin is assumed to play a vital role against these pathological conditions, and could be an antiulcer potent agent.[15]

A study also indicated that indomethacin inactivates gastric peroxidase to induce reactive-oxygen-mediated gastric mucosa injury, and concluded that indomethacin-induced oxidative

damage by ROS as shown by increased lipid peroxidation and thiol depletion was almost completely blocked by curcumin. That is, curcumin protects gastric peroxidase from inactivation by indomethacin for efficient enzymatic removal of H2O2 to block gastric damage by ROS.[5,6]

Surprisingly, curcumin showed immense therapeutic potential against H. pylori infection, as it was highly effective in the eradication of H. pylori from infected mice as well as in restoration of H. pylori-induced gastric damage. Curcumin does this by Preventing the growth of H. pylori cagA + Strain to control H. pylori-mediated ulcer, suggesting its antiulcer potential.[7]

It has been suggested that NSAIDs could induce gastric injury through increases in inflammatory cytokines and leukocyte adhesions. Curcumin, an antioxidant herbal substance, can Prevent these adverse effects and hence might be used as a Preventive method for NSAIDs-induced gastropathy. It was also reported that curcumin is more active against COX-2 and TXA2 compared to COX-1. This is supported by the findings of Morimoto et al. that curcumin possesses COX-2 and TXA2 inhibitory activity without affecting COX-1 activity. That is, curcumin can only block the inflammatory prostaglandin (PGI2) synthesis without affecting the synthesis of protective prostaglandin (PGE2), which is a protective mediator against gastric-induced damage. Equally, it was reported that the anti-inflammatory effect of curcumin is most likely mediated through its ability to inhibit COX-2, lipoxygenase (LOX), and inducible nitric oxide synthase (iNOS). COX-2, LOX, and iNOS are important enzymes that mediate inflammatory processes. Recently, it has been suggested that curcumin affected. [8]

Arachidonic acid metabolism by blocking the phosphorylation of cytosolic phospholipase and decreasing the expression of COX-2. Furthermore, it also inhibited the catalytic activities of 5-LOX. These activities may contribute to the anti-inflammatory and antiulcer actions of curcumin and its analogs. This could also serve as an evidence that curcumin is a potent antiulcer agent.[9,10]

Safety

Many researchers have proposed the use of turmeric and curcumin for improving the quality of health throughout the world. Clinical trials have shown that turmeric and curcumin are safe for humans even at high doses (12g/day). [11]

Curcuma Longa

Botanical Origin

Turmeric (Curcuma longa) is a rhizomatous herbaceous perennial plant of the ginger family, Zingiberaceae.[12] It is native to the Indian subcontinent and Southeast Asia, And requires temperatures between 20 and 30 °C (68–86 °F)and a considerable amount oannual rainfall to thrive. Plants are gathered annually for their rhizomes and propagated from some of those rhizomes in the following season. [13] Turmeric is a perennial herb indigenous to Southeast Asia. It thrives in tropical climates, growing in moist, well-drained soil; however, it can be cultivated in greenhouses in temperate climates. India produces 94% of the world's supply of turmeric. It is also cultivated in China, Taiwan, Burma, Indonesia, Jamaica, Haiti, Japan, and Hawaii.[14]

History of Turmeric

Turmeric has been used in India for at least 2,500 years. It was recorded in China by 700 AD, East Africa by 800 AD and West Africa by 1200. It was introduced to Jamaica in the 18th century. Today, turmeric is widely cultivated throughout the tropics. Turmeric was probably cultivated at first as a dye and then became valued as a condiment as well as for cosmetic purposes. In the 13th century Marco Polo wrote of this spice, marveling at a vegetable that exhibited qualities so similar to saffron. Familiar to the contemporary world as a prime component of curry powder, the orange-yellow rhizome's striking colour lent it a special aura in ancient India. It has always been considered an auspicious material in the subcontinent, both amongst the Aryan cultures (mostly northern) and the Dravidian cultures (mostly southern), and its value may extend far in history to the beliefs of ancient indigenous peoples. Turmeric's common name in the north, haldi , derives from the Sanskrit haridra, and in the south it is called manjal , a word that is frequently used in ancient Tamil literature. Turmeric has a long history of medicinal use in South Asia, cited in Sanskrit medical treatises and widely used in Ayurveda and Unani systems. Suzutan's Ayurvedic compendium, dating to 250 BC, recommends an ointment containing turmeric to relieve the effects of poisoned food.[15]

Phytochemistry

Turmeric powder is approximately60–70% carbohydrates,6–13%water,6–8% protein,5–10% fat,3–7% dietaryminerals, 3–7% essential oils, 2–7% dietary fiber, and 1–6% curcuminoids.[16,17]

Phytochemical components of turmeric include diarylheptanoids, a class including numerous curcuminoids,such as curcumin,demethoxycurcumin, and bisdemethoxycurcumin., Curcumin constitutes up to 3.14% of assayed commercial samples of turmeric powder (the average was 1.51%); curry powder contains much less (an average of 0.29%). Some essential oils are present in turmeric, among which turmerone, germacrone, atlantone, and zingiberene are major constituents.[18,19]

Medicinal Properties

Anti-inflammatory, analgesic, antiarthritic, antioxidant, aromatic, antispasmodic, bitter tonic, carminative, choleretic, cholagogue, cholesterol lowering, hepatoprotectant, antihepatotoxic, analgesic, antibacterial, antiviral, antiseptic, immunomodulant, antimutagenic, anticarcinogenic, antimetastatic, and vulnerary. [20]

Folk Medicine and Traditional Uses

In India, turmeric has been used traditionally for thousands of years as a remedy for stomach and liver ailments, as well as topically to heal sores, basically for its supposed antimicrobial property. In the Siddha system (since around 1900 BCE) turmeric was a medicine for a range of diseases and conditions, including those of the skin, pulmonary, and gastrointestinal systems, aches, pains, wounds, sprains, and liver disorders. A fresh juice is commonly used in many skin conditions, including eczema, chicken pox, shingles, allergy, and scabies. The active compound curcumin is believed to have a wide range of biological effects including anti-inflammatory, antioxidant, antitumour, antibacterial, and antiviral activities, which indicate potential in clinical medicine.[21]

Turmeric has been used for many conditions in traditional medicine in India, Pakistan and Bangladesh. The rhizome is the part that is most widely used. It can be prepared in various ways and is reputed to alleviate asthma and coughs. Many of its traditional uses are supported by scientific evidence. Hot water extracts of the dried rhizome have been taken orally in Ayurveda medicine to reduce inflammation. Turmeric is also regarded as a 'rasayana' herb, which is a branch of Ayurvedic medicine and is used to counteract ageing processes. In Unani medicine, turmeric has been used for conditions such as liver obstruction and jaundice and has been applied externally for ulcers and inflammation. Roasted turmeric has been used as an ingredient of a preparation used to treat dysentery. Turmeric has also been used in tooth powder or paste.[22]

A hot water extract of the dried rhizome taken orally was reputed to slow lactation, regulate fat metabolism, help symptoms of diabetes, diarrhea and liver diseases, and as a tonic calm the stomach. The fresh juice taken regularly on an empty stomach has been used to prevent stomach disorders. A hot water extract of the dried rhizome was reputed to have an abortion-promoting effect when taken orally or in the form of a pessary (when inserted into the vagina). Externally, the dried rhizome has been applied to fresh wounds and insect stings and to help the healing process in chickenpox and smallpox. Turmeric was reputed to improve complexion of the skin and has been applied externally to remove hair, act as a tonic and alleviate itching. Inhalation of turmeric smoke is reputed to relieve hiccups. Turmeric rhizomes have also been mixed with other plants to produce traditional remedies for a range of conditions including tonsillitis, headaches, wounds, snake bites, stings, sprains and fractured bones.[23]

Western Medicine

Turmeric is not widely used in Western medicine, but has been investigated as a treatment for some conditions. Studies show that the rhizomes contain compounds that may have therapeutic effects, which appear to support some of its uses in traditional medicine.

Turmeric has been shown to have anti-bacterial, anti-fungal, antioxidant and anti-inflammatory effects, to which can be added possible anti-ulcer, wound-healing, liver-protective and anti-cancer properties. It contains yellow pigments called curcuminoids. One example of a curcuminoid is curcumin. Turmeric and curcumin are being investigated for any beneficial effects they might have on conditions such as cancer, dementia and irritable bowel syndrome and for potential cholesterol-lowering effects.[24,25]

Some studies suggest that components of the essential oil, such as ar -tumerone, have anti-snake venom activity. The essential oil is also reported to have some insect repellent and insecticidal activity.[25]

Cultural/ Spiritual Uses

Yellow and yellow-orange are colours that have sacred and auspicious connotations on the Indian subcontinent. Turmeric is important in Hindu and Buddhist ceremonies.

Turmeric is associated with fertility and prosperity and considered to bring good luck if applied to a bride's face and body, as part of the ritual purification before a wedding.

Turmeric roots may be given as a present on special occasions, such as a visit to a pregnant woman. Turmeric powder is also sprinkled on sacred images. The use of turmeric is prohibited in a house of mourning.[25,26]

Cosmetics Uses

Extracts have been added to creams as a colouring agent, and traditionally women would rub turmeric into their cheeks to produce a golden glow. One of the main yellow pigments in turmeric is curcumin. It is reported that washing in turmeric improves skin tone and reduces hair growth.[27]

Prior to the development of dosage forms, it is essential that certain fundamental physical and chemical properties of the drug molecule and other derived properties of the drug powder are determined. This first learning phase is known as pre-formulation. [28] Pre-formulation is an important step in the development of a new drug. It influences the safety, effectiveness, controllability stability and compliance of the drug.[29-39]

This study *Curcuma longa* freeze-dried extract powder solid dosage forms were prepared formulation anti-peptic ulcer capsules and analyzed in the pre-formulation study activity against *peptic ulcer*.

MATERIALS AND METHODS

The rhizome's ethanol extract of *Curcuma longa* with the following concentration were prepared: 100 mg/kg. Freeze-dried dried extract of *Curcuma longa*, hard gelatin capsules (Size 0; Color: Red body. Black Cap); Starch, Colloidal Silicon Dioxide (Aerosil), Magnesium Stearate, Sodium Lauryl Sulphate**,** Hydrochloric Acid (0.1NHCl), pH6.8 buffer Solution, and Ethanol. were obtained from Sigma Aldrich. All chemicals used were all of analytical grade and other materials were gift from (Global Pharmaceutical Industry Company-Yemen).

Equipment's: Includes, Oven (Giffin & Geong L-TD) (Metler-Made in Germany); Disintegrator (Erweka- Germany); Dissolution apparatus (SCIENTIFIC Model-DA.60) (Metler- Germany); Balance (Sortorius BP310S NO:91206635- Germany); Balance2 (DENVER Instrument APX-100 - Germany); Hot Plate (Vision Scientific Co. LTD); Freezer (KELON-Model- KDR-20W); Freeze -Dryer (LABONCO Freeze Drier System/LYPH Lock 4.5); Light Microscope; Sieves; Water Bath (CFL 1083 - Germany), UV Spectrophotometer

(SHIMADZU Model-UV-1601PC); Capsule filling machine, PH meter (Sartorius PB-11); Chamber 40C" (LAB TECH-LHI-0250E); Chamber 30C" (LAB TECH-LBI-300M).

Determination of The Organoleptic Properties of The Extract Powder

The following organoleptic properties of *Curcuma longa* materials such as physical appearance, odor and taste were inspected and assessed using the natural senses (e.g. eyes, nose, mouth).

Fig. 1: *Curcuma Longa* (Turmeric).

Determination of The Solubility of The Extract Powder[30-39]

Solubility is an important factor for drug absorption. It is described by the Noyes- Whitney equation.

The equilibrium solubility of the freeze -dried extract of *Curcuma longa* determined as follows: A saturated solution obtained by stirring excess extract powder solute with distilled water for 3 hours at the required temperature (25C°, 37C°) by using water bath until equilibrium has been attained. Samples are withdrawn every 30 minutes and filters. Absorbance of the sample was measured at (425nm for *Curcuma longa)* using UV-VIS Spectrophotometer. The absorbance reading should increase until one gets to a maximum when equilibrium is reached. This indicates the time required for equilibration.

The solubility was obtained by the following equation: Solubility = (weight of initial powder - weight of dried residue) / volume of solvent x100%.

Particle Size Determination of The Extract Powder

One of the most fundamental and easy methods for determining particle size is a sieving method. This method involves passing the material being sized through openings of a particular standard size in sieves. So the degree of fineness of powders is determined by sieving. The sieve receiver and the sieves of number 2.4, 2, 1.6, 0.125, 0.1 were arranged in a descending order on the sieve shaker, then 10g of *Curcuma longa was* poured in the top

sieve. The process of shaking took 30 minutes. Thereafter the powder collected on each of the sieves was weighed and the percentage(w/w) of each fraction determined.

Determination of The Density of The Extract Powder

A simple test has been developed to evaluate the flowability of a powder by comparing the poured density (bulk density) and taped density of a powder and the rate at which it packed down. A useful empirical guide is given by Carr's compressibility index equation: ('compressibility' is a misnomer, as compression is not involved).

Carr's index (%) = (Tapped density - Poured density) / Tapped density

In study the density of *Curcuma longa* extract powder was determined as follows: *Curcuma longa* extract powder was poured into the tared cylinder on apparatus up to a volume between 8-10ml before compacting. The cylinder was then weighed and the weight of extract recorded. Thereafter the cylinder was secured in its holder and the reading of unsettled apparent volume, V0, was taken to the nearest milliliter. The machine was switched on, the powder in the cylinder tapped for approximately 1250 times and the final volume V1250, again taken to the nearest milliliter. The bulk and tapped densities were then calculated using the following equations.

Bulk density (poured density): m /V0, in g per ml

Bulk density = weight of the powder / bulk volume

Tapped density: m /V1250, in g per ml.
Tapped density = weight of the powder / tapped volume.

Determination of Flowability of The Plant Extract Powder

The angle of repose (^{o}) is another important parameter that can be used to describe the flowability of a powder. In the present study a special apparatus was used for the test. The apparatus consisted of a glass cylinder kept in the center of the plate, a plate with scale and a ruler for measuring the height of powder mound. To determine the angle of repose, the glass cylinder was filled with 4 g of plant extract, the cylinder smoothly lifted allowing the powder to flow out at the bottom unto the plate leaving a conical mound. The height and radius of the mound was measured and angle of repose then calculated using the following equation: $\tan \theta = h / r$ θ: Angle of repose, h: height of the conical mound, r: radius of the conical mound.

Determination of The Moisture Content of Extract Powder

About 0.5g of the *Curcuma longa* powdered extract was finely powdered and rapidly weighed in a fiat-bottomed dish. The extract was then dried in an oven at 100- 105 ℃ for 3 hours, allowed to cool (approximately 10 minutes) in a desiccator over anhydrous silica gel, weighed and the weight recorded. The moisture content as determined by this gravimetric method was then calculated using the following equations

Moisture weight = Initial weight (before drying) - Final weight (after drying), Moisture content = (Moisture weight / Initial weight) 100%.

Determination of The Dose of Freeze -Dried Extract Per Capsule

Formulated capsules of *Curcuma longa* that contain an amount of active ingredient equal to that approved in the effectiveness in treatment of peptic ulcer, the amount of freeze -dried extract to be used in the of *Curcuma longa* capsules was decided as 100mg/kg which reported in Anti-peptic ulcer activity study. Then we converted rat dose to human dose as shown in Table 1.

Table 1: Dose Conversion.

Species	Cat 2kg	Monkey 4kg	Dog 12kg	Man 70kg
Mouse 20g	29.231	61.53846	123.0769	384.6154
Rat 200g	4.2222	8.888889	17.77778	55.55556
Guinea pig 400g	1.4902	3.137255	6.27451	19.60784
Rabbet 1.5kg	1.0857	2.285714	4.571429	14.28571
Cat 2Kg	1	2.105263	4.210526	13.15789
Monkey4kg	0.475	1	2	6.25
Dog 12kg	0.2375	0.5	1	3.125
Man 70kg	0.076	0.16	0.32	1

Formulation and Manufacture of The *Curcuma Longa* Capsules[30-39]

The selection of the capsule size, the filling machine, the filling method and the excipients where carried out in which 100mg of this drug mixed with excipients as shown in Table 2**,** place manually in a separate size "0" capsules, then taken four capsules daily to provide the desired dose. The study provide that the lethal dose is above 2.78g which consider as safe extract.

Table 2: Formulation of *Curcuma Longa* Capsules.

Ingredient mg / Capsule	Amount/ Unit
Extract	100mg
Starch	152mg
Aerosil	43mg
Magnesium Stearate	3mg
Sodium Lauryl Sulphate	2mg
Total Weight of Capsules	300mg

Evaluation of the Manufactured *Curcuma Longa* Capsules

Determination of Uniformity of Weight and The Amount of Material in The Capsules

For the determination of the uniformity of weight, the British Pharmacopoeia method was used. In which Twenty of the *Curcuma longa* capsules prepared as described above were taken at random, their contents individually weighed and the average weight (mass) of the content determined. Not more than two of the individual weights (masses) had to deviate from the average weight (mass) by more than 7.5% and none of the deviates by more than twice that percentage. The amount of powder actually filled into the capsules was also compared with the desired quantity and the difference (in percentage) between the desired and actual quantity calculated. According to the formulation, 100mg *Curcuma longa* extract was to be filled in one capsule each. Twenty capsules were thus randomly chosen, their contents weighed, the percentage difference between this and the desired weight calculated and averaged for the 20 capsules to assess the accuracy of the filling process.

Determination of Moisture Content of *Curcuma Longa* Capsules

For this study, the shell of the capsules was removed and the moisture level of the contents of the capsules determined by using the moisture content analyzer.

Determination of The Dissolution Profile of *Curcuma Longa* capsules

In this study the basket method was used. Further, the quantitation of the amount of plant material dissolved was measured based on uv absorbance measured at 425nm, the wavelengths for maximum uv absorption of solutions of the *Curcuma longa* extract determined by using a uv- vis spectrophotometer.

Determination of Stability of *Curcuma Longa* Capsules.

In which the capsules were stored in a glass bottle container under two conditions by using a climate chamber as shown in Table 3.

Table 3: The Storage Conditions for The Stability Study.

Batch	Temperature ^{o}C	Relative humidity (RH)	Container
1	30±2 ^{o}C	70%±5% (RH)	Glass Container
2	45±2 ^{o}C	70%±5% (RH)	Glass Container

The manufactured *Curcuma longa* capsules were stored under the afore-mentioned conditions and every 2 weeks ,6 weeks ,10 weeks and 12 weeks' samples of capsules were taken from each site and assessed for organoleptic properties (i.e. gross physical nature, color and odor of the powder content and overall size, shape and appearance of the capsule).

At 6 weeks and at the end of 12 weeks the moisture content of the capsules were determined. The organoleptic properties and the moisture level of the content of the test capsules were compared with that of the content of *Curcuma longa* capsules before storage.

RESULTS AND DISCUSSION

Yield of Freeze -Dried Extract of *Curcuma Longa*

The yields of freeze -dried extract obtained from *Curcuma longa* using the method are summarized in Table 4, on percentage yield 120 % of extract was obtained from *Curcuma longa* crude.

Table 4: Yield of Freeze -Dried Extract of *Curcuma Longa*.

Weight of The Dry Powder (g)	Yield of Freeze- Dried Extract	
G	G	%
100	25	120

The Organoleptic Properties of The Freeze -Dried Extract *of Curcuma Longa*

As shown in Table 5, the freeze -dried extract and a summary of the organoleptic properties.

Table 5: The Organoleptic Properties of Extract of *Curcuma Longa*.

Properties	*Curcuma Longa*
Physical Appearance	Free-fFlowing, Small Particulate Powder
Color	Dark Yellow, Darker than Ground Leave Powder
Odor	Spicy Odor and Characteristic
Taste	Bitter Spicy Taste

The bitter taste and unpleasant odors normally result in poor patient acceptance of dosage forms. Hopefully these negative characteristics still present in the extract can be masked when incorporated in capsule form.

The Solubility of The Freeze -Dried Extract of *Curcuma Longa*

For oral solid dosage forms, aqueous solubility is a crucial factor influencing the bioavailability of drugs. The results obtained in the solubility testing of the freeze -dried extract of *Curcuma longa* show that the extract is being soluble in pH 6.8 buffer.

The Size of Particles The Freeze -Dried Extract of *Curcuma Longa*

Particle size and shape are crucial parameter. They are important for the manufacture of the dosage forms, influence dissolution and bioavailability. Particles can be classified under four different classes as shown in Table 6.

Table 6: British Pharmacopoeia 2013 Appendix XVII A. Particle Size of Powders.

Coarse Powder	Not less than 95% by weight passes through a number 1400 sieve and not more than 40% by weight passes through a number 355sieve.
Moderately Fine Powder	Not less than 95% by weight passes a number 355 sieve and not more than 40% by weight passes through a number 180 sieve.
Fine Powder	Not less than 95% by weight passes a number 180 sieve and not more than 40% by weight passes through a number 125 sieve.
Very Fine Powder	Not less than 95% of the powder by weight passes a number 125 sieve and not more than 40% by weight passes through a number 90 sieve.

The above terms are used in the description of powders and the results of the particle size study as shown in Table 7.

Table 7: Particle Size of *Curcuma Longa* Freeze -Dried Extract Powders.

European Sieve No.	ISO Sieve No. (mm)	Wt. Retained
2800	2.5	0
2000	2	0
1400	1.6	0
125	0.125	0.2g
90	0.1	4.5g

According to the above results, the *Curcuma longa* freeze -dried extract powders were very fine powders based on the British Pharmacopoeia standard.

The Densities of The Freeze - Dried Extract Powders

According to Carr's index %= (Tapp dins. -pour density) / Tapp dins. = 15.79%

The Carr's index of Compressibility for *Curcuma longa* extract is 15.79 %.

The density study researches show that the extract of *Curcuma longa* freeze -dried extract powders can all be categorized as having excellent flow properties.

The Flowability of The Freeze -Dried Extract Powder

The *Curcuma longa* freeze -dried extract powders had angles of repose of 26.7^{o}. Therefore, had good flow properties. This implicated that the *Curcuma longa* freeze -dried extract powders possessed appropriate excellent flowability for the manufacture of capsule dosage form as shown in Table 8.

The Moisture Content of The Extract

The results of moisture content were 4 %.

Table 8: The Summary of Pre-Formulation Testing Results of *Curcuma Longa*.

Testing	***Curcuma longa***
The Solubility of Extracts	Soluble
Particle Size	Very Fine Powder
Carr's Index (%)	15.79%
Angle of Repose (°)	26.7^{o}
The Moisture Content (%)	4%

We have divided the total dose into small doses. Which will be suitable to be filled in capsule, the chosen capsule size was (0) and we will need for 4 capsule each one will be contain 100mg of *Curcuma longa* freeze dried.

Uniformity of Weight and Content of The Capsules

The results of the uniformity of weight and content of the *Curcuma longa* capsules the average deviation in weight from average for *Curcuma longa* capsules were 0.87% and amount of content of capsule was *100.11%,* respectively. According to the British Pharmacopoeia, the limit on the acceptable deviation in weight from average for capsules is ± 8.7% and the limits on the amount of content in the capsules 99% to 102%. The afore-mentioned results thus indicated that the *Curcuma longa* capsules met the British Pharmacopoeia specifications.

Moisture Level of The Content of *Curcuma Longa* Capsules

After the capsules were filled the moisture level of its contents were again tested just to ascertain if there had been changes in moisture level during the manufacturing procedure. The results of these tests are given and indicated that the moisture level of the contents of the *Curcuma longa* capsules were 4 % and When analyzed in the pre-formulation study, the moisture content for the *Curcuma longa* extract were however4%. Thus, appeared to have a slight increase in the moisture level of the *Curcuma longa* material after encapsulation. This

suggested that this extract absorbed some moisture during the filling procedure, presumably because it was hygroscopic.

Dissolution Profile of *Curcuma Longa* Capsules

The results of the dissolution studies on the *Curcuma longa* capsules are summarized in Table 9 and Figure 2 showed that >50% of the *Curcuma longa* capsule contents dissolved in the dissolution medium within 45 minutes**.**

Table 9: Dissolution Profiles of *Curcuma Longa* Capsules.

Time (min)	%Amount Dissolve
15	45.16%
30	50.10%
45	59.15%
60	60.08%

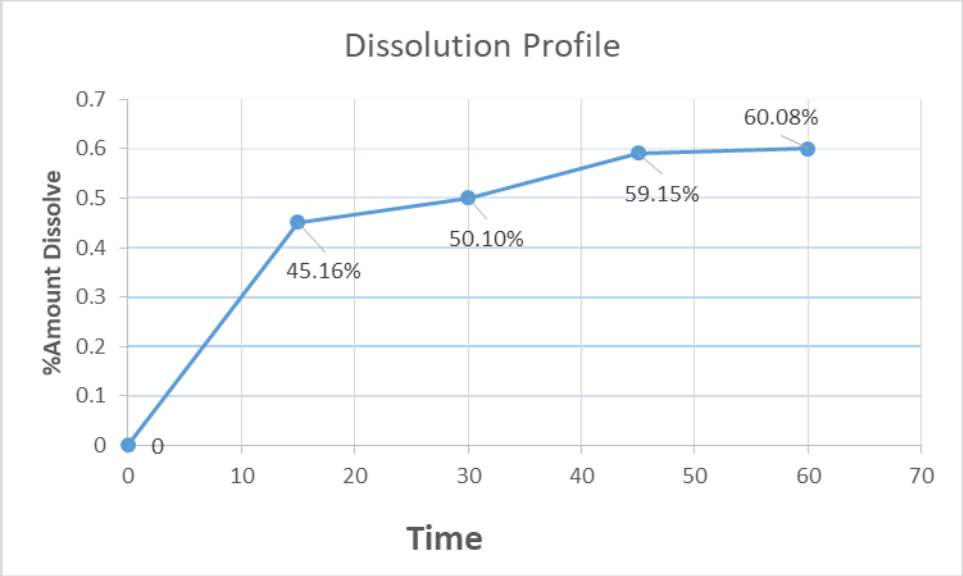

Fig. 2: Dissolution Profile of *Curcuma Longa* Capsules.

Stability of *Curcuma longa* Capsules

For the study of Stability, two batches of capsules were stored under the different conditions. And the results of the organoleptic properties, moisture content tested during stability study are given below.

The Organoleptic Properties of The *Curcuma Longa* Capsules

When *Curcuma longa* capsules were stored in the glass container, whether at 30±2℃ / 70%±5% RH and 45±2℃ / 75%±5% RH, the organoleptic properties of the plant material

remained relatively unchanged during the 12 weeks' storage the results were shown in Table 10.

Table 10: Organoleptic Properties *Curcuma Longa* Capsules During Storage.

No Week	Size, Shape of Capsule	Gross Nature of Powder in Capsule	Color of Powder	Odor of Powder
0	Regular '0' size & shape	Powder	Dark Yellow	No change
2	No change	Powder	Dark Yellow	No change
6	No change	Powder	Dark Yellow	No change
10	No change	Powder	Dark Yellow	No change
12	No change	Powder	Dark Yellow	No change

The Moisture Content of *Curcuma Longa* Capsules

The moisture levels of the *Curcuma longa* capsules contents at 6 weeks and at the end of 12 weeks were determined in Table 11**.** The results were compared with that of the content of *Curcuma longa* capsules before storage.

Table 11: The Moisture Levels of The *Curcuma Longa* Capsules.

Time	Percentage of Moisture%
Before Storage	4%
After 6 weeks at 30±℃ / 70%±5%(RH)	4.1%
After 6 weeks at 45±℃ / 75%±5%(RH)	4.1%
After 12 weeks at 30±℃/ 70%±5%(RH)	4.1%
After 12 weeks at 45±℃/ 75%±5%(RH)	4.2%

From the results above there was no large change in the moisture levels of the *Curcuma longa* capsules stored in the glass bottle containers under high temperature 45±2℃ / 75%±5% (RH) and 30±2℃ / 70%±5% (RH) during storage, and it is strongly suggested that storage in glass bottle containers protect *Curcuma longa* capsules against moisture.

CONCLUSION

Freeze -dried extract powders of *Curcuma longa* have good flowability, regular particle size and shape, is soluble with high wetability, on average contained 4 % moisture for *Curcuma longa*. Elegant capsules that were uniform in content and weight, respectively, Moreover, the manufactured capsules and release solid oral dosage forms and had good bioavailability. The results showed that the extract *Curcuma longa* was suitable as raw materials of the plants as far as manufacture of capsules were concerned, but that the stability of these extract containing capsules was acceptable. The flowers extract *Curcuma longa* provide that the extract has high anti-peptic ulcer activity. the freeze dried of extract and make it as a powder

to enhance density, solubility, flowability to became suitable to formulated as capsules dosage form.

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