

Formulation and Pharmacological Evaluation of Herbal Ointment containing Curcuma Caesia & Piper Nigrum

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Abstract: The annual herb *Curcuma caesia* Roxb has large leaves. Traditional medicine uses rhizomes. Fresh rhizomes smell camphoraceous. According to accounts, Camphor, (Z)-ocimene, ar-curcumin, 1,8-cineole, elemene, borneol, and bornyl acetate are all major components of this plant. The herb has been claimed for its antifungal, anti-asthmatic, smooth muscle relaxant, antibacterial, antioxidant, analgesic, locomotor depressant, anticonvulsant, and anti-inflammatory qualities. It is now a major source of natural chemicals for drug development. Topical ointments are more suitable since patients comply better owing to antioxidants and anti-inflammation. *Curcuma Caesia* may revitalise skin by restoring its natural radiance. Similarly, *Piper nigrum* treats acne and skin infections with antibacterial and anti-inflammatory effects. Trituration was used to make ointment from an oily base. The formulation also contained 0.7gm *Curcuma Caesia* and 0.2gm *piper nigrum* extract. The physicochemical parameters revealed good spreadability, extrudability, washability, solubility, drying loss, and others. The formulation was further tested for stability at 2°C, 25°C, and 37°C for four weeks. Spreading ability, diffusion research, and irritating effect did not change. Thus, an ointment using *Curcuma Caesia* and *piper nigrum* extract could effectively exploit these herbs' therapeutic capabilities.

Keywords: Herbal ointment, Ethnopharmacology, Turmeric, antifungal activities, etc.

1. Introduction

Chemistry and pharmacology meet at the intersection of medicinal or pharmaceutical chemistry, and it is concerned with the development, production, and creation of pharmaceutical drugs. Medicinal chemists search for new therapeutic chemical entities and work to create them from scratch [1]. It also includes studies of the biological properties and quantitative structure-activity correlations (QSAR) of commercially marketed drugs. Pharmaceutical chemistry is concerned with the quality of pharmaceuticals and tries to ensure that they are fit for their intended usage. Most pharmaceuticals rely on organic compounds, such as biopolymers and small organic molecules. Inorganic and metal-containing compounds, however, have been found to have medicinal value [2]. For instance, cis-platin class platinum compounds have been used as cancer treatments. Organic chemistry, biochemistry, computational chemistry, pharmacology, pharmacognosy, molecular biology, statistics, and physical chemistry all come together in medicinal chemistry, making it a highly interdisciplinary field. There are thousands of plants that indigenous people used to produce medicines from, but it's crucial to

determine whether or not these medicines were effective treatments or harmful poisons. Numerous studies have been conducted on the chemistry, pharmacology, pharmacology, and clinical applications of ayurvedic medicinal herbs.[3,4] It is critical to leverage systems biology technology to expedite the development of medications derived from natural constituents, which has become a focus for many of the world's major pharmaceutical corporations. Traditional knowledge-driven drug development can benefit from the application of reverse pharmacology to speed up the process and save costs.[5] The drug discovery and development process as a whole is expected to benefit most from developments in lead structure identification and drug target elucidation. The most significant purpose of traditional knowledge is to serve as a powerful search engine, making it much easier to conduct deliberate, targeted, and safe natural product research to rediscover the drug discovery process[6]. Ayurveda is one of the oldest medical traditions still in use today and is based on sound philosophical principles; it is widely practised in countries like Sri Lanka and India.

Herbal medicine today [7]

Herbal medicine is nothing more than the modernised version of age-old trade secrets. Herbal treatments have gained popularity as an alternative to conventional medicine and surgical procedures for many people. Rather than employing a whole plant, pharmacologists locate, isolate, extract, and synthesise particular components, thus capturing the active principles. Minerals, vitamins, volatile oils, glycosides, alkaloids, bioflavonoids, and other compounds found in plants are just as crucial to the medical effects of a herb as the active elements themselves[8]. In addition, these factors serve as a crucial natural defence. It takes a far larger amount of a whole herb, with all of its components, to become hazardous than it does an isolated or synthesised active molecule. However, herbs are medicines and can have profound benefits when used properly[9].

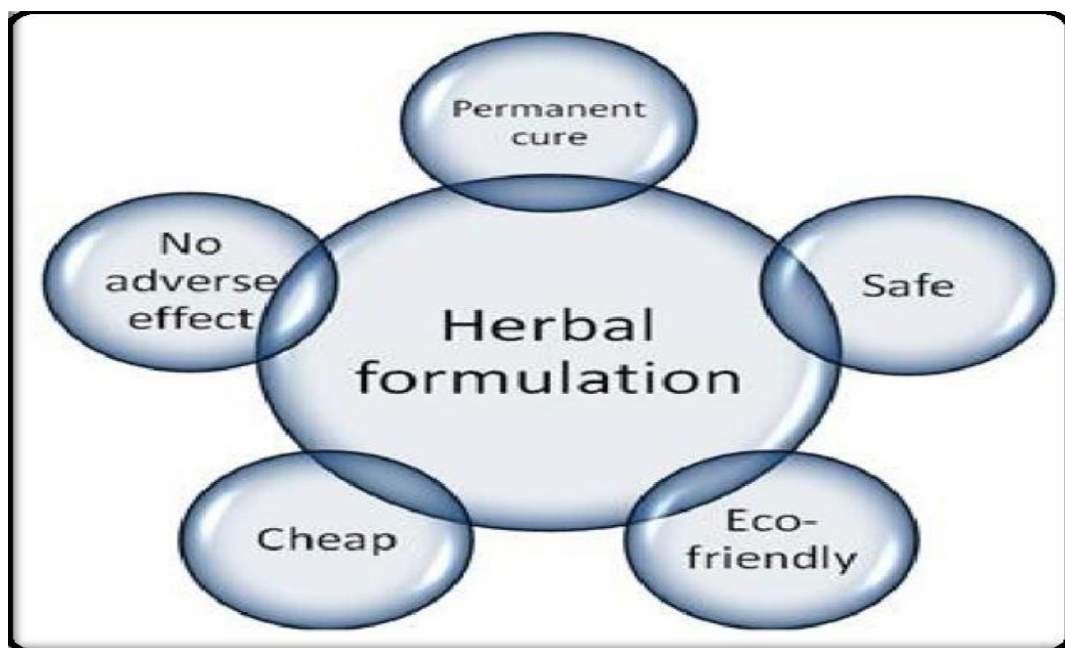


Fig.1 Herbal formulations are important as depicted in the diagram

Many therapeutic plants have had their efficacy confirmed by scientists from Europe and the Orient. Thanks to current technology, research can now discover some of the unique features and interactions of plant elements[10]. Now that we have this scientific evidence, we can understand why particular herbs are useful in treating particular diseases. Research confirming herbal medicine, however, is currently limited to studies conducted in Germany, Japan, China, Taiwan, and Russia[11]. When it comes to licencing novel pharmaceuticals (or substances for which therapeutic characteristics are claimed) for use in the United States, the Food and Drug Administration (FDA) typically does not accept or recognize discoveries from outside.

American medical professionals and government bodies want more research into a plant's medicinal potential before they will acknowledge it[12]. Despite the fact that a great deal of study is being done in other nations, American pharmaceutical firms and research facilities have not invested heavily in botanical studies. As a result, herbal medicine in the United States does not enjoy the same respect or popularity as it has in other parts of the world.

Medicinal importance of Curcuma Caesia and Piper nigrum[13]

Rhizomes from the Curcuma Caesia plant, both dried and fresh, are what we know as turmeric. Family: Zingiberaceae. The Curcuma Caesia plant is a perennial herbaceous rhizomatous herb of the ginger family. Essential oils and fibre make up 7% of the total, while curcuminoids make up 1-6%. Its multipurpose properties include those of an antibacterial, anti-inflammatory, expectorant, condiment, or spice. Curcuma longa has been used to treat arthritis, liver diseases, Alzheimer's disease, and depression thanks to its high antioxidant content[14]. Curcuma Caesia, owing to its possession of antioxidant, anti-inflammatory, antimutagenic, antibacterial, and anticancer properties, has been extensively employed as a medicinal herb in Asian regions throughout history. The curry spice Curcuma Caesia contains the active ingredient curcumin, which is prized more for its aesthetic than for curative qualities in many regions of Asia[15]. Curcuma Caesia has antioxidants and anti-inflammatory components. Because of these qualities, it can make the skin look healthier and more radiant. Curcuma Longa can also be used to restore the skin's natural radiance. The fruit of Piper nigrum, a flowering vine in the family Piperaceae, is harvested and used as a spice or flavouring after being dried. The primary component of piper nigrum, piperine, is a powerful antioxidant and anti-inflammatory. Piper nigrum has shown promise in the lab for promoting better health in a variety of organ systems, including the brain and digestive tract[16]. Acne and other skin infections can be treated because of its antibacterial and anti-inflammatory characteristics. The poor bioavailability of curcumin is a serious issue, but piperine, the main active component of Piper nigrum, has been linked to a 2,000% increase in curcumin bioavailability[17]. Therefore, it appears that the issue of limited bioavailability can be resolved by combining curcumin with active substances that boost bioavailability, such as piperine. To more efficiently and conveniently utilise the therapeutic benefits of Curcuma Caesia and piper nigrum extract, an ointment containing these herbs has been formulated and evaluated in this study[18].

Formulation of Herbal Ointment[19]

Herbal medications come in a variety of application types, including ointment. Ointments are semisolid preparations that can be applied topically to different parts of the body. The skin and the ocular, vaginal, auricular, and nasal mucosae all fall under this category. The active ingredient in medicated ointments is encapsulated in a thick, fatty foundation. Ointments have a wide range of topical applications, including but not limited to protectants, antiseptics, emollients, antipruritics, keratolytics, and astringents [20]. Medications in ointment bases typically come in the form of suspension, solution, or dispersion, and the bases themselves are virtually invariably anhydrous. The bases of ointments might be either hydrocarbon (oleaginous) or a water-removable or soluble type of material. They are broken down into three groups according to their depth of action: epidermal, endodermal, and diadermal. The purpose of an antiseptic ointment is to kill or slow the spread of microorganisms [21].

Analyzing phytochemicals with modern technology[22]

The separation, identification, and structural determination of physiologically active compounds have been facilitated by the continuous development of chromatographic and spectroscopic methods of analysis. To harvest and prepare herbs and medicinal plants, as well as to extract, fractionate, and chromatographically analyze compounds taken from these sources, the phytochemistry unit functions as a laboratory[23]. Furthermore, this unit effectively managed the process of gathering, categorising, and conducting phytochemical analysis on plants, working closely with other units within HMRC and IMR. Phytochemicals, often called phytonutrients, are plant-based chemical components that have been shown to provide health benefits. Examples of phytochemicals include beta-carotene, which is abundant in fruits and vegetables. Beta-

carotene, lycopene, and resveratrol are all examples of phytochemicals (also known as phytonutrients).[24]. Since the beginning of human history, plants have been used as a source of medicine.

2. Materials and Methods[25]

Collection of materials

Curcuma caesia (turmeric) rhizomes and *piper nigrum* (black pepper) berries were purchased from local Nashik market vendors, inspected for quality, and then used without further processing. All of the extraction solvents and chemicals were of analytical grade and purchased from the Merck Company in India.



Fig.1 Dried Rhizomes of *Curcuma caesia* (turmeric) and dried fruits of *piper nigrum*

Preparation of extract[26]

Preparation of *Curcuma longa* extract

1. Requirements for the *Curcuma caesia* extraction are ethyl acetate, petroleum ether, and Soxhlet apparatus. The extraction process is conducted, which is subsequently followed by the grinding of the desiccated rhizomes to obtain a powdered form. Oil and unsaponifiable substance were extracted from the powder using petroleum ether. After the marc had been soaked in ethyl acetate for around 2 hours, the crude curcuminoids were extracted once more. Two times, a very small amount of pet.ether was used to wipe away the residue. Curcuminoids are acquired through the process of recrystallization of turmeric powder using ethanol as the solvent. Put it in an airtight container after it has been evaporated.
2. Preparation of *Piper nigrum* extract
Extracting piperine from *Piper nigrum* required the use of solvents like petroleum ether and alcohol. The *Piper nigrum* fruit was ground and the powder was extracted with 250ml of petroleum ether in the Soxhlet equipment for 2hr. After distillation assembly reduced the extract to a fifth of its initial volume, oily residue formed. Piperine will precipitate out if you decant the supernatant, concentrate to around 20-30 ml, and then let it cool. To get rid of oil, filter the leftovers and then treat them with 20-40ml of petroleum ether. Piperine can be re-crystallized using alcohol.

Formulation of Herbal Ointment[27,28]

Procedure for preparation of herbal ointment

To begin, white petroleum was measured out and placed in an evaporating dish in a water bath to serve as the ointment base. After the white petroleum had melted, the remaining white wax was added and gently swirled to aid in the melting and mixing homogeneously, and then the ointment base was allowed to cool. Table No. 1 lists the quantities of each item used to make the ointment base.

Table no.1 Formulation of herbal ointment as per standard.

Sr.No.	Name of Ingredients	Quantity taken	Use
1	<i>Extract of Cucuma Caesia</i>	0.7gm	API
2	<i>Extract of Piper Nigrum</i>	0.2gm	API
3	Propyl paraben	0.1gm	Preservative
4	Ointment base	Q.S upto 10gm	Base

Evaluation parameter of herbal Ointment[29]

Colour, smell, consistency, pH, spreadability, extrudability, diffusion study, LOD, solubility, washability, non-irritancy test, and stability study were just few of the criteria used to assess the final ointment (table no. 4).

Organoleptic characteristics of herbal ointment[30]

The resulting ointment formulation was assessed for several characteristics like colour, odor, ambience, texture, and any probable phase separation by visual inspection. Pressing a tiny bit of the ointment on the finger and thumb gives an idea about its texture and homogenous nature.

Analysis of Colour[31]

Visual examination, using a black and white background, has been used to test the accuracy of colour evaluation.

Analysis of Smell

The ointment's aroma was evaluated on three willing participants for more precise analysis.

Assessment of consistency

No signs of greed or roughness in the finished ointment were detected.

Analysis of pH[32]

In a beaker, we mixed around 2 grams of the ointment with 100 millilitres of distilled water. The ensuing solutions were warmed to 70 degrees Celsius. Ointments' pH levels are measured with digital pH metres. The measurements were taken three times for accuracy.

Analyzing spreadability

Excess sample was squeezed to uniform thickness between two slides for a predetermined amount of time and weight to measure spreadability. Spreadability was defined as the time it took to split the slides in half.

Spreadability was calculated by the following formula $S = M \times L / T$

Where, S= Spreadability

M= Weight tide to the upper slide L= Length of glass slide

T= Time taken to separate the slides

Testing for Extrudability

The ointment composition was placed into squeezable tube containers. The ability to extrude a 0.5 cm tape of ointment in 10 seconds was used to quantify the extrudability of the ointment.

A Look at Diffusion

In order to conduct a diffusion test, an agar nutritional medium was made. The ointment was kept in a dish with a hole cut out of its centre. After one hour, we timed how long it took for the ointment to spread.

Checking for LOD

The formula was dried at 105 degrees Celsius in a petri plate in a water bath to calculate the LOD.

Analysis of Solubility

The solubility was calculated using a quick and easy procedure.

Two volunteers had the formulation applied to their skin, and then the ease with which it washed off with water was evaluated.

Non-Irritation Assessment

Two test subjects had herbal ointment applied to their skin while researchers monitored the results.

Evaluating Stability[33]

For four weeks, the herbal ointment was subjected to a physical stability test in temperatures as low as 2 degrees Celsius and as high as 37 degrees Celsius. After four weeks, the herbal ointment was proven to be physically stable at three different temperatures: 2 degrees Celsius, 25 degrees Celsius, and 37 degrees Celsius. Table No.3 shows the findings of stability analysis.

Physicochemical evaluation of ointment

Table no.2 Stability study of an herbal ointment

Time(Hr.)	Temperature	Physicochemical parameters			
		Colour	Odour	Ph	Stability
		Creamish	Characteristic	5.5	
7 days	3°C	No change	No change	5.1	Stable
	28°C	No change	No change	5.1	Stable
	36°C	No change	No change	5.1	Stable
14 days	3°C	No change	No change	5.6	Stable
	28°C	No change	No change	5.6	Stable
	36°C	No change	No change	5.6	Stable
21 days	3°C	No change	No change	5.6	Stable
	28°C	No change	No change	5.3	Stable
	36°C	No change	No change	5.3	Stable
28 days	3°C	No change	No change	5.3	Stable
	28°C	No change	No change	5.6	Stable
	36°C	No change	No change	5.3	Stable

TableNo.3 A physicochemical assessment of a herbal ointment was conducted

Sr.No.	Physiochemical Parameters	Observation
01	Colour	Creamish white
02	Odour	Characteristic
03	Consistency	Smooth
04	Ph	5.5
05	Spreadability	12(seconds)
06	Extrudability	0.4gm
07	DiffusionStudy	0.7cm
08	LossonDrying	28%
09	Solubility	Insoluble in ether and boiling water, soluble in aqueous solution, alcohol.
10	Washability	Good
11	Non-irritancy	Non-irritant
12	Stabilitystudy	Stable

Drug release kinetic modeling at 241nm[34]

On comparison of kinetic modelling and release profile data it was evident that herbal ointment formulation was found to release the drug in accordance to Higuchi kinetics model, the regression coefficient 'r' suggests that the drug release from the in situ gels followed a diffusion-controlled process. This is evident from the larger values of 'r' for the Higuchi order compared to the zero order., Hixson, kors-peppas and first model. The regression coefficient was not determined to be exactly near to 1, which could be owing to influence of certain other factors.

Table No.4 Drug release kinetic modeling for Formulation at 241 nm

Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumulative % drug remaining	log time	log Cumulative % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
15	23.51	76.49	3.873	1.885	1.176	1.366	23.22	4.250	0.392
30	29.27	70.73	5.477	1.855	1.477	1.453	5.15	4.153	0.489
45	37.10	62.9	6.708	1.808	1.653	1.552	7.29	4.007	0.635

60	42.10	57.9	7.746	1.768	1.77 8	1.617	5.71	3.885	0.75 7
90	50.11	49.89	9.487	1.701	1.95 4	1.697	8.44	3.689	0.95 3
120	58.39	41.61	10.95 4	1.629	2.07 9	1.759	7.66	3.491	1.15 1
180	64.50	35.50	13.41 6	1.577	2.25 5	1.794	4.74	3.356	1.28 6

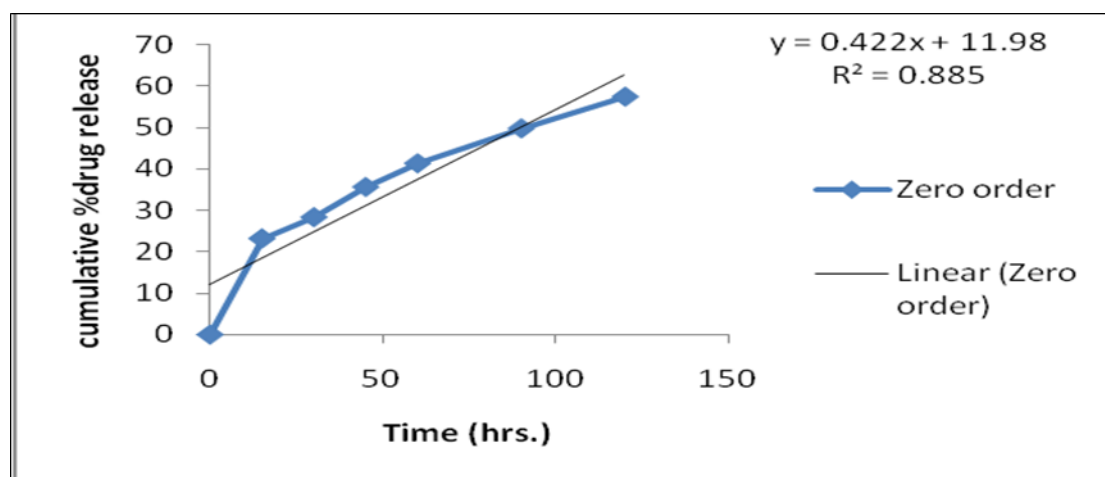


Fig.2 Zero order kinetics of formulation

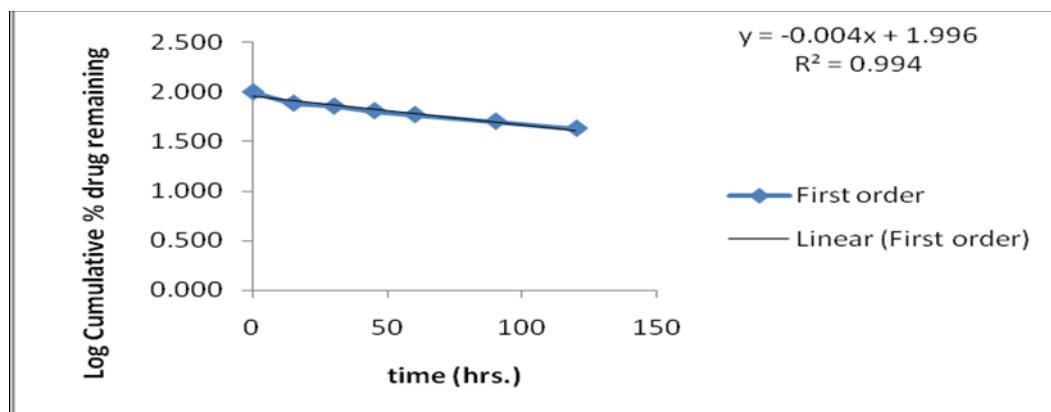


Fig 3. First order kinetics of herbal formulation

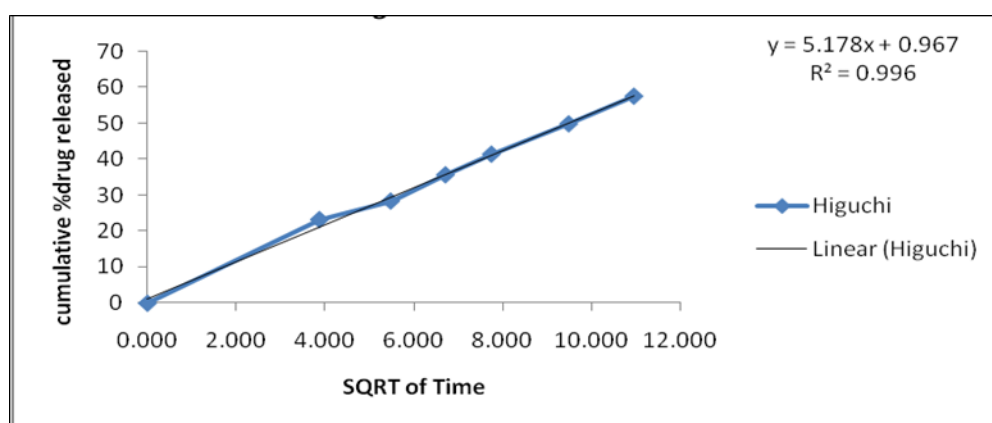


Fig.4 Higuchi model of herbal formulation

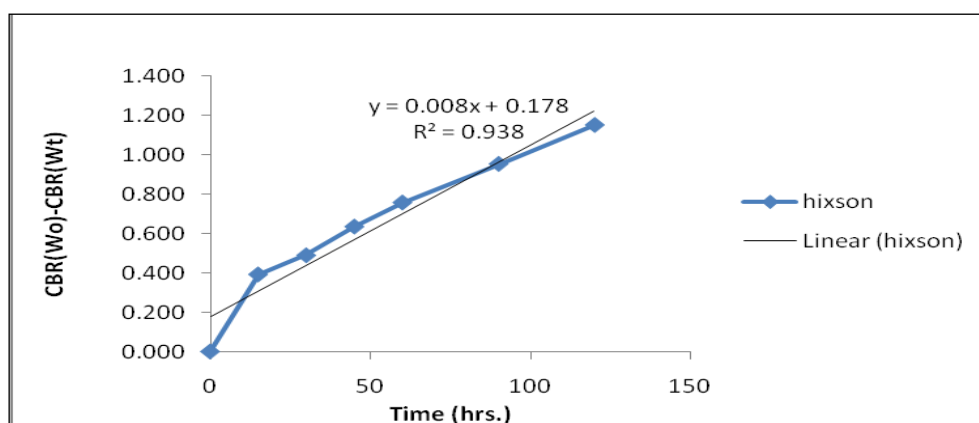


Fig.5 Hixson model of herbal formulation

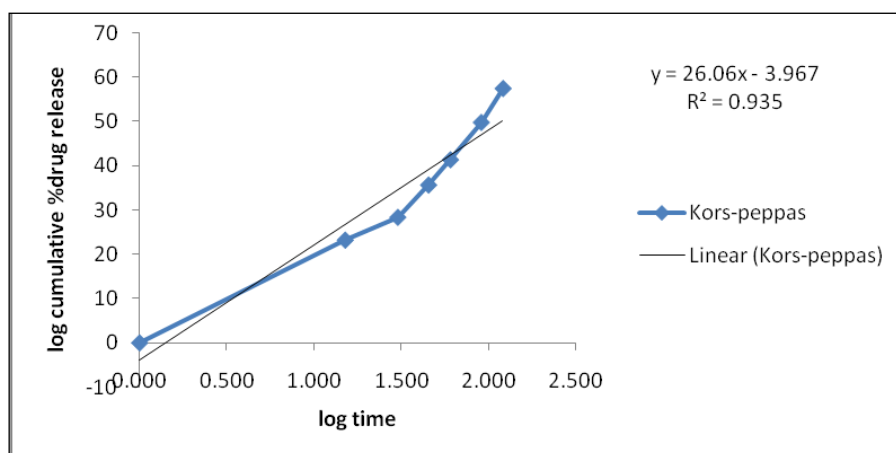


Fig.6 Kors-peppas model of formulation FA

Pharmacological evaluation[35]

Biological Evaluation

Studies on antibacterial resistance

The invitro antibacterial activity of herbal ointment was studied against Gram positive, Gram negative bacteria and fungus. The inhibition zone around each sample was used to calculate its antibacterial efficacy. When compared to the gold standard medication, the zone of inhibition produced by the herbal ointment was

significantly larger. Although the ointment was effective against both gram-positive (staphylococci) and gram-negative (*E. coli* and *pseudomonas aeruginosa*) bacteria, it was less effective at lower concentrations. The herbal ointment showed promising benefits against both bacteria and fungi when tested at a concentration of 10 ppm. Results from the ointment have been encouraging in comparison to those from the gold standard fluconazole. Tweedy's chelation theory can help explain why this ointment is so effective at preventing infection.

Activity against fungi[36]

The present investigation aimed to assess the antifungal effects of the herbal ointment. The antifungal investigations involved the utilisation of four prevalent microorganisms, namely *C. albicans*, *M. audouinii*, *A. niger*, and *T. mentagrophytes*. The chemicals' ability to inhibit fungal growth was measured using the disc-diffusion technique.

Preparation: The nutrient broth was produced in the following manner.

Composition

Peptone : 20 g.

Beef extract : 05 g.

Sodium Chloride : 05 g.

Distilled water up to :1000 ml.

Upon complete dissolution of the components and subsequent steaming for a duration of around two hours, the pH of the reaction mixture should be adjusted to approximately 7.2. Following this, autoclaving the mixture for a period of 20 minutes will yield nutritional broth. Sub-culturing the organisms from the lab stock into sterile nutrient broth and incubating them at 37°C for 24 hours prior to the testing is standard procedure. The resulting culture growth used as inoculum for the evaluation of antifungal treatment.

Preparation of test solution

The test chemical was dissolved in DMSO at a concentration of 10mg per 10ml. Ten millilitres of the resulting solution were diluted to one hundred millilitres using DMSO. As of right now, we're using a test chemical at a concentration of 100 g/ml. These sample solutions were made in correctly labelled sterilised test tubes.

Preparation of standard solution:

Flucanazole is the gold standard medication used in clinical trials. This medication can be dissolved in water, and its concentration is set to 100 g/ml.

Method of testing

Evaluation Strategy

The nutritional agar media is cooled to 45 degrees Celsius with gentle shaking to ensure even cooling. Subsequently, aseptic techniques were employed to combine the aforementioned components, followed by gentle agitation with the addition of 0.5-0.6 ml of a culture that had been incubated for a duration of 18-24 hours. Following a one-hour period of settling, the substance was subsequently transferred into the sizable petri dishes, with an estimated volume of 20-25 millilitres each dish. Subsequently, the cups were manufactured through the process of puncturing the prearranged agar using a sterilised cork borer, followed by the removal of the punched section of the agar. Each cup had a diameter of 48.6 millimetres. The test chemical, dissolved in DMSO, was added to each cup at a concentration of 100. About 45 minutes were given for the medication

solution to diffuse at room temperature after it was added. After that, the plates spent 24 hours in an incubator at 37°C. After 24 hours, we calculated the diameter of the inhibitory zone in millimetres.

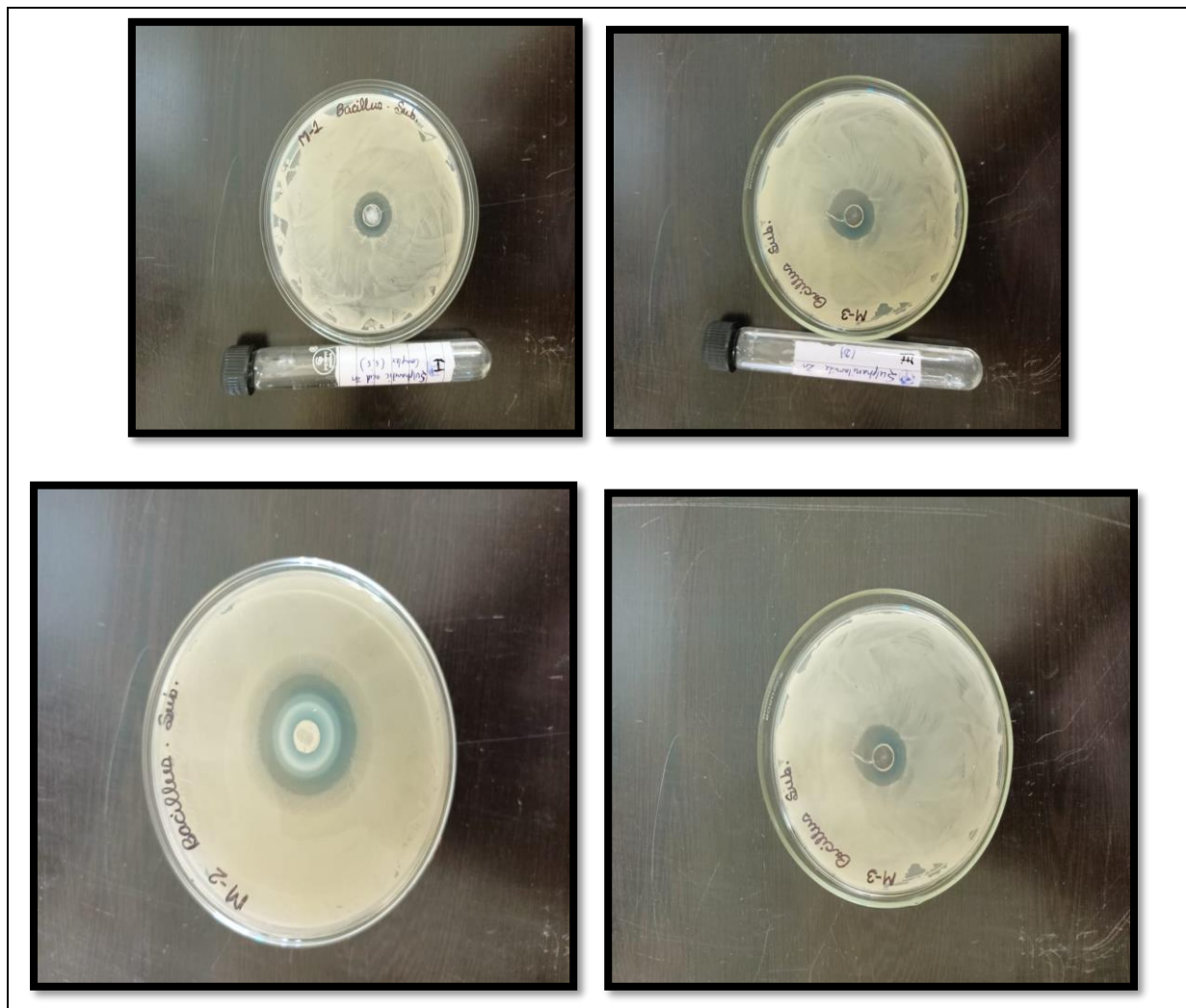


Fig.7 Systematic diagram represent the antimicrobial activity of herbal ointment

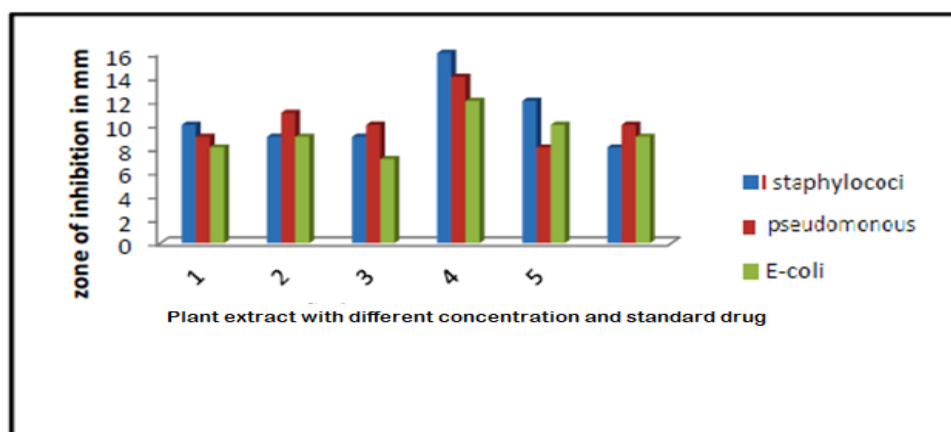


Fig.4- Bar graph represent the antibacterial activity of herbal ointment[37]

3. Result and Discussion

One key fact is exposed: its medical usefulness is enormous; all that's needed is a scientific approach. Because of the positive results found in phytochemical and pharmacological research of this plant. It demonstrates that it may be used in future studies for a wide range of other projects. Phytochemical studies have shown that this plant contains a variety of compounds, including but not limited to flavonoids, saponins, and tannins. Flavonoids, saponins, and tannins may contribute to this plant's antibacterial properties by acting as a gastro-protective barrier in addition to scavenging free radicals. According to the current study, this plant has the potential to be used in a wide range of antibacterial activities, with which it can exhibit a positive response to all free radical-generated diseases. Herbal remedies have been widely used for centuries because of its inexpensive cost, lack of adverse effects, and accessibility. Curcuma longa and piper nigrum have been used medicinally for thousands of years. Therefore, this ointment has the potential to serve as a medium for the efficient and convenient administration of these therapeutic characteristics. This study demonstrated the viability of formulating, developing, and testing a curcumin and piperine ointment. This study was done to manufacture and assess a herbal ointment. To achieve this, the Soxhlation technique was applied to the production of the herbal extract, which resulted in high extraction yields without compromising the integrity of the active chemical components. The grinding process ensured that the herbal extracts and ointment bases were thoroughly combined and would not separate while the ointment was being stored. Spreadability, extrudability, washability, solubility, loss on drying, and other physicochemical qualities were investigated and found to be adequate. The stability of the formulations was also evaluated over a period of 4 weeks at temperatures ranging from 3°C, 28°C, and 36°C. Diffusion studies, stimulation effects, and diffusion capacity all remained unchanged.

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