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Formulation and Evaluation of *Tinospora cordifolia* Stem Emulgel for Osteoarthritis

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ABSTRACT
Osteoarthritis is made up of two word osteo+ritis mean bone with inflammation so in this case inflammation of bone ,joints occur which cause pain,swelling in joints .drug delevery to the target site remains a challenge due to ineffetive drug delivery system . An attempt has been made to formulate and evaluate emulgel for suitable and ease delivery in the treatment of arthritis. This herbal emulgel contain Tinospora cordiofolia extract which used in the treatment of Osteoarthritis. This emulgel was prepared by appalling simple beaker method using carbopol 934p and hpmc as gelling agent. Emulsion was formulated by using by using liquid paraffin as oil phase, tween 80as aquous phase and span 20 as oil phase as surfactant.
For checking the compatibility study we prefer FTIR studies. Which prove the compatibility of drug and excipients. The prepared emulgel was prepared to various parameter include ph, spreadibility,rheological studies, invitro drug release etc.
The ph of preparation was near about skin ph. The viscosity and spreadibility of optimized formulation was found to be near from the invitro drug release study by using franz diffusion apparatus was found to be sustained release of formulation up to 15 hours.F1 formulation(Formulation WITH HPMC And carbopol 934) showed the highest drug release of Tinospora cordifolia (90%).F1 formulation showed the excellent physical stability.

KEYWORDS- *Osteoarthritis, Emulgel, Tinospora cordifolia Topical Gel, In Vitro Drug Release Studies.*

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I. INTRODUCTION

These days, osteoarthritis is a common condition. It is a joint degenerative condition. Pain, stiffness, and loss of function are the symptoms. (Sharma, L.2021). The knees, hips, hands, and spine are the joints that are most frequently impacted. Surgery, weight loss, exercise, and pain management are all forms of treatment. By keeping a healthy weight, engaging in regular exercise, and avoiding joint injuries, one can fend against osteoarthritis (Chow& Chin, 2020). Osteoarthritis has four distinct stages. Osteoarthritis in its pre-clinical stages is the initial stage. There are no symptoms or indications of the disease at this point. The second stage is called early osteoarthritis (Tachmazidou et al. 2019). Although there may be a few minor symptoms at this point, like pain and stiffness, the joint is still able to function largely properly. Moderate osteoarthritis is the third stage of the condition (Mehana et al 2019).

At this point, the symptoms start to worsen and start to interfere with regular tasks. Severe osteoarthritis is the name given to the fourth and last stage. The disease is in its most advanced level at this point, and the symptoms can make it very difficult for a person to lead a regular life (Kokkotis et al. 2020).

Although the cause of osteoarthritis is not entirely known, it is believed to be brought on by a number of causes. These include ageing-related changes in the body, genetics, and mechanical wear and tear on the joints. Osteoarthritis can also be brought on by joint damage or inflammation (Driban et al. 2020)

Cytokines function as signalling molecules to control the activity of other inflammatory response-related cells (Hirano, T. 2021). (TDDS) is a system where the drug is given in a controlled way to get better efficacy. The TDDS provides an easy and comfortable way of administration of drugs with minimum side effects.

A topical drug delivery system is a formulation designed to be applied to the surface of the skin. The three main types of topical delivery systems are ointments, creams and gels (Shao et al.2005). Gels have the lowest oil content of all three types of topical deliverysystems and are thus the least likely to cause irritation.

Emulgel (Minnett et al.2011)

Emulgel is a topical gel that combines an oil component with a water base. This makes it ideal for use on the skin, as it can help to lock in moisture while still providing a light, non-greasy layer of protection. Emulgel can be used alone or in conjunction with other skincare products to help maintain healthy, moisturised skin.The benefits of Emulgel as a novel formulation The combination of a medication and a polymer is advantageous in Emulgel. So that it can be absorbed by the body over an extended length of time, the medicine is released from the polymer in a regulated manner and at a steady rate. Compared to other topical painkillers, this provides more effective and long-lasting pain relief. (Zappa et al.1998),(Lang et al.2008).

Plant profile

"Tinospora cordifolia,a climbing shrub from the Menispermaceae family and an essential component of the Ayurvedic medical system, serves as a major source of numerous pharmaceutical and healthcare goods. It is known by many names in India, including Amrita, Guduchi, Giloe, and Heart Moon Leaf. Giloy is a valuable medical plant because of its therapeutic benefits and medicinal properties, as well as its phytochemicals. This essay reviews ayurvedic literature on medicinal characteristics, phytochemicals, advantages, adverse effects, and toxicity, as well as cultivation and other topics. Giloy's numerous therapeutic benefits have led to it being referred to as amrita. And it I also said to increases the lifespan of human by preventing them from many chronic disease.

II. METHODS AND METHODOLOGY

Chemicals lists.

S.No.	Chemicals	Manufacturer
1.	Carbopol 940	CDH
2.	Carbopol934	CDH
3.	Hpmc	CDH
4.	Methyl paraben	Loba chemicals
5.	Propylene glycol	Loba chemicals
6.	Liquid parafin	Loba chemicals
7.	Span 20	CDH
8.	Tween 80	CDH

Instruments List

S.No.	Instruments	
1.	Analytical Weighing Balance	Radwag
2.	Viscometer	Igene Labserve
3.	pH meter	omega Digital
4.	Soxhlet Apparatus	Borosil
5.	Franz Diffusion Cell Apparatus	Kshitiz International
6.	Magnetic stirrer	khera
7.	Heating Mental	omegA
8.	UV-VI Spectrophotometer	IGene Labserve

The stem were collected nearby area of Bidhnu, Kanpur nagar. stems of the plant were collected in the month of April 2023. The collected stems washed thoroughly with distilled water and drier under the shaded area. The stems were thengrinded using a mechanical grinder.

Fig-Tinospora cordifolia stems.

Macroscopy (Chauhan M. 2014)

For macroscopic analysis, fresh stems of plant were selected. The shape, size, color and texture of the stem have been identified. The plant was healthy and had no visible damage. The averagediameter of the stems were measured to be 2cm. The colors of the Stems were observed to be dark green with a tinge of brown. The surface of the Stem was found to be rough with small bumps. There were no visible spots or blemishes on the stems

Organoleptic Parameters (Nitish Bhatia et al.2014)

The collected stems were kept in a dry and clean place for determination of organoleptic parameters. The stems were gently crushed with the help of a pestle and mortar and their aroma was noted. Their taste was also analyzed by keeping a small quantity of the stem juice in mouth.

Physiochemical Parameters:

Ash Value Total Ash Value of crude drug is the mineral residue left on detonation of a drug.

Methodology for Ash Value (Pingali Prasuna Sundari et al. 2014)

The silica crucible was heated to red-hot temperature for 30 minutes before cooling in desiccators. In the crucible, about 1.0 g of powered material was precisely weighed anduniformly dispersed.Dried for 1 hour at 100-105^{o}C before being burned to uniform weight in a In desiccators, the crucible was made to cool.The proportion of ash was then estimated using the air dried product as a comparison (Sangeetha K et al.2014).Burn the product at muffle furnace at 600 ± 25^{o}C.

Water-soluble Ash value

Methodology for water-soluble Ash value (Sangeetha K et al.2014)

Water soluble ash is a measure of the total amount of inorganic material present in a sample that can be dissolved in water. This includes both organic and inorganic materials. The test is performed by first heating the sample to complete combustion, then dissolving the resulting ash in water.The solution is then filtered and the residue weighed. Water soluble ash is generally reported as a percentage of the original dry weight of the sample.

Ash Value= Ash weight -crucible weight *100\sample and crucible (Priani, etal.2014

Acid-insoluble Ash value

Methodology for acid-insoluble Ash value (Priani, et al.2014)

Acid insoluble ash is the inorganic residue that remains after a substance is completelyburned in acid. It consists of metals, minerals, and other inorganic materials that are not destroyed or transformed by acid. Acid insoluble ash is used to determine the purityof a substance and the presence of impurities.

Weigh out approximately 3 grams of the sample and place it in a tared crucible.Cover the sample with a lid and heat over a low flame for 5 minutes to drive off anymoisture that may be present.Raise the temperature of the furnace gradually, taking care not to overheat the sample, until white fumes are no longer evolved from the

surface of the sample.Maintain this temperature for 15 minutes.Allow the crucible and contents to cool in a desiccator before weighing.Repeat steps 1-5 until a constant weight is obtained (Manju Lata Zingare , et al.)

Loss on Drying:
Loss on drying is the weight loss of a substance when it is heated to constant temperature under specified conditions. The main purpose of this test is to determine the moisture content in the sample. The results obtained from this test can help to optimize the manufacturing process, Storage, and transportation of the product (Anarthe, et al.2017).

Procedure:
In a tarred plate, around 2 g of powdered crude material has been properly weighted and dried in oven at 100^{o}-105^{o} C.It was weighed again after cooling in a desiccator.The proportion of dried powder obtained was used to determine the loss on drying (Anarthe, et al.2017).

Preparation and Evaluation of Extracts (Mehla et al.2017),
(Rodionova et al.2017)
Soxhlet extraction is a process of separating out extract from a mixture. Soxhlet are composed of two parts: an upper part called the still head and a lower part called the extractor. The still head is where the solvent is placed and the extractor is where the material to be extracted is placed. Extraction is usually done using a Soxhlet apparatus, which consists of a glass tube with a sidearm and a thimble that fits inside it.The dried stem powder was placed in the thimble, which is then inserted into the Soxhlet apparatus. The solvent (ethanol and water) was added to the still head and heated until it begins to boil. As the solvent boils, it vaporizes and passes through the thimble containing the material to be extracted. The vapors condense on the surface of the material, causing the solvents to slowly drip down through it. This action extracts contaminants from within the material being processed

Phytochemical Tests
Phytochemical Tests was performed to analyze the presence of secondary metabolites in the plant stem. The results indicated then presence of tannins, saponins, and flavonoids. Phytochemical tests are important to determine the pharmacological activities of a plant. Tannins have astringent properties while saponins have emulsifying and foaming properties. Flavonoids are responsible for the color and taste of a plant (Varsha et al.2013)

THIN LAYER CHROMATOGRAPHIC PROFILING
Analytical or preparative procedure:
In various flask holding solvents of various polarities, dissolve a little amount of the alcoholic extract of *Tinospora cordifolia* .Put the TLC plates into the chamber with the spotted side up to lower the pencil line around the solvents . The plates should be taken out of the chamber and dry it in oven . After running and drying the plate It was put into iodine chamber and dry.UV illumination, dark blotches are seen on the plate.
Rf = Distance moved by solute /Distance moved by solvent
Where Rf is termed as retardation factor.

UV Analysis of extract:
It is an analytical method for determining how much light is absorbed by substances between 200 nm-400 nm in wavelength .using a quartz curette filled with distilled water as reference ,By using UV spectrophotometer ,a stock solution made from *Tinospora cordifolia* extract, extracted with hydro alcoholic solution were used to determine the absorbance..

FORMULATION PROCEDURE (Ashtoshkar **,** Wyman, C. E. (2004)**,** NIST, 2013)
The herbal Emulgel for wound healing has been prepared by using **Beaker Method** by taking various quantities of ingredients. For the preparation of any Emulgel, two phases were formulated i.e. gel phase and the emulsion phase.

Preparation of Gel Phase
For the preparation of gel phase, polymers with different grades in the same quantity(say 3 gm) have been used. Each polymer was dissolved in required amount of cold water along with continuousstirring.The stirring has been made in a moderate speed and hence a uniform mixture was found.

Preparation of Emulgel
For the preparation of emulsion, two phases were made.The first phase called the aqueous phase. It has been prepared by dissolving Tween 80 in distilled water.Second phase is the oil phase, which was formed by dissolving Span 20 in liquidparaffin.In a separate beaker of 50ml Methyl paraben (0.1g) has been dissolved in

Propylene glycol (0.03 ml), this solution acts as a preservative for emulsion.Again in a separate beaker (50ml) 5.0ml of extract has been taken and dissolved in a2.5ml of ethanol.The preservative and extract mixture were combined together and then this new solution was mixed in an aqueous phase.At 70^{o}C both the phases (oil phase and final prepared aqueous phase) were heated separately for 8-10 min.After heating, to the aqueous phase along with continuous stirring by homogenizer, oil phase has been added by drop-wise. The stirring lasts for 10min at 3000 rpm.The finally prepared homogenized mixture was kept at room temperature for cool down and this completed the formation of emugel.

Final Step

This was the last step of the herbal Emulgel formulation for wound healing.The finally ready gel and emulsion both were taken simultaneously and with moderate stirring gel phase has been mixed into an emulsion time.The ratio of gel and emulsion combination will be 1:1The pH of prepared mixture was checked and was adjusted to neutral i.e. 6.5- 7.0 byusing 1-2 drops (1-2%) of Triethanolamine (TEA).

Preparation of Emulgel

Evaluation of Finally Developed Emulgel:(NIST 2013, Wyman C. E. 1999)

Physical Assessment: The prepared Emulgel has been resolute for their physical tests such as color, odor, consistency and homogeneity.

Homogeneity*:* The ready wound healing Emulgel has been analyzed for homogeneity by visual examination. After transferring of gel into an proper container, rest it for 2 h and then visualized it for any clog and appearance.

Consistency: This has been determined by inspecting the ready Emulgel visually.This has been done by two methods. 1st – Checking for grittiness and 2nd – Checking for Phase separation.

Method 1st- From the ready Emulgel 1 or 2 drop has been put in the index finger and it was then rubbed with the thumb and then observes for any gritty particles.

Method 2nd- Put the prepared Emulgel into the proper container and with no disturbing it, observe its phase separation i.e, liquid part separates itself from solid partof gel.

pH Assessment (Wyman, C. E. 1996)

pH was resolute by using the digital pH meter. The evaluation was done using the 1gof formulation in use in the beaker and dissolved in the 100 mL of the water. The solution was reserved aside and by means of digital pH meter the pH was assessed.

III. RESULTS AND DISCUSSION

Approx 2 kg. of fresh *Tinospora cordifolia* stems were collected from the nearby area of Bidhnu Kanpur nagar and then stems were dried under the shaded area at 20-30 degree Celsius. After drying all dried stems were grinded with mechanical grinder and made a coarse powder. After sieving this coarse powder, approx 550 gms. of fine powder was obtained . By using this powder various physiochemical parameter like Ash Value, water soluble ash value, loss on drying were analyzed. Extraction of powder is done with Hydro alcohol (50:50 and water as solvent in Soxhlt apparatus. Various qualitative test and TLC and UV were performed by using this extract to confirm the presence of chemical constituents nurserary, and the Emulgel was ready according to the standard procedures by means of Carbapol 934, Carbapol 934+hpmc and HPMC. The

physical manifestation, pH, viscosity and spreadability of the Emulgel were evaluated. The consequences showed that the ready Emulgel was white in color with a smooth texture.

The phytochemical procedure was performed to estimate the availability of the unlike phytochemicals in the extracts. The results revealed that the stem is enriched with the saponins, tannins, flavonoids, and terpenoids in requisites of excess availability.

The pH of the Emulgel formulation-1 was bring into being to be 6.27±0.15 which showed that it is appropriate for topical application. The viscosity and spreadability of the Emulgel were surrounded by the satisfactory range. In conclusion, it can be understood that the *Tinospora cordifolia* stem based Emulgel is a capable formulation with excellent physical attributes and potential drug delivery system for topical administration of drugs.

The physical form of Emulgel was analyzed by showing its color, viscosity, spreadability and pH. The outcome obtained were within the good enough limits for all the above parameters except pH which was establish to be neutral. This formulation can still be used as a topical drug delivery system for various drugs. However, formulation 1 was found excellent in the aspects as compared to the other formulation using Carbapol 934, and HPMC.

The viscosity was observed in Emulgel formulations with formulations. The results showed that the Emulgel formulations were useful in reducing the viscosity and improving the rheological properties of the gel. The count of a small quantity of surfactant improved the efficacy of the Emulgel formulation in reducing the viscosity andimproving the rheological properties of the gel. Formulation 1 (6668.7±57.74) was establishstable and enhanced viscosity as compared to other formulations.

The spreadability was experimental in Emulgel formulations. The result was credited to theamplify in drug release from the formulation-1 due to the high thickness of the polymer which resulted in a more unvarying and sustained release of the drug with main spreadability 10.84±1.54.

The *in vitro* drug release was practical in Emulgel formulation. The outcome indicated thatEmulgel can be a probable drug delivery system for the topical application of herbal medication. The in vitro study showed that the formulation exhibit a good drugrelease profile by means of a controlled and sustained let go over 8 h. The in vitro drug free was observed in Emulgel formulation. Emulgel formulations are useful because they can provide a more homogeneous distribution of the active constituent, which leads to enhanced efficacy and safety. Formulation- 1 showed the improved drug release wit94.88 % as compared to other formulations. The extrudability was performed with the facilitate of collapsible aluminum tubes. The extrudequantity be evaluated. F2 formulation performed well as compared to other formulations.

Shape, size and Texture of *Tinospora cordifolia* stems.

S. No.	Parameters	Before Drying	After Drying
1	Shape	cylindrical	cylindrical
2	Diameter	2 cm	1.5cm
3	Texture	solid	solid

Organoleptic properties of *Tinospora cordifolia* stems.

S. No.	Parameters	Before Drying	After Drying
1	Color	Dark Green	Olive Green
2	Odor	Characteristics	Characteristics
3	Taste	Bitter	Bitter

Physiochemical property of powder *Tinospora cordifolia*

S. No	Physical Evaluation	Values Obtained (% w/w)
1	e	3.5
2	sh	0.74
3	sh	1.17
4	oss on Drying	35

Preliminary Phytochemical Tests

Sn.	Test	Solvents		
		Methanol	Ethanol	Water
1	Alkaloids	+	+	+++
2	Tannins	-	++	+
3	Saponins	++	+	++
4	Glycosides	+	++	+
5	Steroids	+	+	++
6	Phenols	+	-	++
7	Flavonoids	++	++	++

Formulae of Emulgel

Sn.	Ingredients	Formulations		
		F1	F2	F3
1	Extract	1	1	1
2	Carbopol 934+HPMC %W/V	3	NA	NA
3	Carbopol 934 %W/V	NA	3	NA
4	HPMC%W/V	NA	NA	3
5	Liquid paraffin%V/V	5	5	5
6	Propylene glycol%V/V	10	10	10
7	Methyl Parabene%W/V	0.1	0.1	0.1
8	Propyl Parabene%W/V	0.03	0.03	0.03
9	Water	Qs	qs	Qs

Physical Examination Of Emulgel :

S.no	Physical Examination	Formulation Code		
		F1	F2	F3
1	Color	Transparent	Transparent	Milky white
2	Odour	None	None	None
3	Homogeneity	fair	Excellent	good
4	Grittiness	No grittiness	Fine particle found	NO
5	Phase Separation	No	No	No

IV. Discussion

In earlier studies , many scholar attempted to formulate the various pharmaceutical dosage form by *Tinospora cordifolia* and other herbs however emulgel based on pure *Tinospora cordifolia* extract is not available so far , considering which as effort to make herbal emulgel has been made by this study

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