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Development and Evaluation of Herbal Preparation for Arthritis Treatment

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ABSTRACT

Because of higher cultural acceptance, compatibility with the human body, and fewer side effects, herbal medicines are still the backbone of around 75-80 percent of the world's population, primarily in underdeveloped nations, for basic health care. Herbal medicines are made up of plants or parts of plants that are used to cure injuries, diseases, and illnesses. They can also be used to promote health and healing. It's medicine or preparation derived from a plant or plants and used for a variety of purposes. Herbal remedies are the world's oldest method of health treatment. Cream formulations including several oils (Coconut oil, eucalyptus oil, Lemongrass oil, Wintergreen oil, Peppermint, Garlic Oil, and camphor) showed high homogeneity, stability, and anti-rheumatic arthritis action. The BHA and Chlorocresol recipe, on the other hand, proved to be the best choice since it had the largest percentage of extrudability, spreadability, and rheological qualities. Formulations F5, F6, and F7 were shown to be the most effective in terms of anti-rheumatic arthritis activity. As a result, polyherbal preparations of drugs are required for the anti-rheumatic arthritis effect.

INTRODUCTION:

Rheumatoid arthritis (RA) is an autoimmune disease that damages the joints over time. Warm, swelling, and painful joints are the most common symptoms. Rest typically makes pain and stiffness worse. The wrists and hands are the most usually affected joints, with the same joints on both sides of the body. Other regions of the body might be affected as well. Low red blood cell counts, inflammation around the lungs, and inflammation around the heart are all possible consequences. There may also be fever and decreased energy. Symptoms usually appear over weeks to months [1]. Between the mid-fourth and the final decade of life, RA develops (in about 80 percent of patients). Treatment options for RA include medications and lifestyle modifications. Nonsteroidal anti-inflammatory medicines (NSAIDs), such as salicylic acid, and steroids (usually cortisone injection) are being used to treat the condition. These medications can help with pain, but they can't help with tissue healing. Even though a variety of medications are used to manage pain and halt the course of RA, no treatment has been found to entirely cure the illness. In addition, stomach ulcers have been seen in RA patients who take NSAIDs regularly, as well as in individuals who have had their adrenals suppressed by steroids. Patients regularly seek complementary and alternative medicine as a result of these unpleasant side effects (CAM). According to a recent survey, those with RA who have chronic pain and are unsatisfied with allopathic therapy are more likely to seek alternative medicine, with 60–90% of arthritic patients using complementary and alternative medicine (CAM). As a result, finding a viable alternative to the current allopathic treatment is quite desirable. Since ancient times, natural plant compounds have been used to treat and prevent many ailments. According to a WHO survey, traditional medicine is used by nearly 80% of the world's population. Nearly 121 medicines are now prescribed in the United States, with 90 of them derived directly or indirectly from natural sources, especially plants [2, 3].

The use of herbal medicine in the treatment of RA is as old as humanity and civilization. In comparison to current allopathic medicines, herbal medicine and therapy are now commonly used by the general public due to the notion of fewer side effects and a superior safety and security profile. The goal of this study was to create a herbal oil for arthritis therapy that included coconut oil, eucalyptus oil, lemongrass oil, wintergreen oil, peppermint oil, garlic oil, and camphor. Various factors such as pH, viscosity, and others were determined and presented in this work.

MATERIALS AND METHODS:

MATERIALS: Coconut oil and Lemongrass oil were procured from Himedia (Mumbai) and Alfa remedies (Ambala), respectively. Wintergreen oil, Garlic oil, and eucalyptus oil were obtained from Modern scientific, (Gwalior) and Merck Ltd. India respectively. Diclofenac sodium, BHA, and Polysorbate 80 were purchased from Aarti Industries Limited, Vapi, Valsad, and Gujrat. Carbopol 934and Carbopol 940 were obtained from Merck Ltd. India.

METHODS:

Preparations Of Herbal Cream:

Step 1:

- Add 20ml organic extra virgin coconut oil.
- Coconut oil melts at 76°F (about 24.5°C) and it can start softening if conditions are warmer than that (especially in the summer), store coconut oil in the refrigerator.

Step 2: Whip coconut oil until it's light & fluffy (Start on low speed to soften coconut oil, and then once softened increase mixer speed to whip the coconut oil).

Step 3: Once the coconut oil is soft & fluffy, add essential oils.

Step 4: Mix the essential oils into the whipped coconut oil until everything is completely blended.

Step 5:

- (For Oil Phase): A beaker containing 120.0 g of Cetyl Alcohol, Liquid Paraffin, and Polysorbate 80 was used. The beaker was heated to 90 degrees Celsius for 60 minutes while stirring, then cooled to 60 degrees Celsius. The temperature was kept between 60 and 65 degrees Celsius.
- Step-II (for Aqueous Phase): In a beaker, purified water was heated to 90°C for 30 minutes, and subsequently dropped to 60°C. The temperature was kept between 60 and 65 degrees Celsius.

- Step-III (For Disperse Phase): With constant stirring and a temperature of 60°C, the oil phase was brought to the aqueous phase. For 5-10 minutes, homogenized at great speed. It was ultimately chilled to 40°C.

- Step-IV (Drug Phase): 25.0 g of herbal material and self-emulsifying glyceryl monostearate were combined and heated. In a beaker, heat the glyceryl monostearate to 40°C in a water bath. At a temperature of 40°C, the herbal material component was added to the dispersion phase whilst mixing.

- Step-V (Rinsing): To the dispersion phase, add chlorocresol, butylated hydroxyl anisole (BHA), and sodium metabisulphite, then mix and homogenize for 10 minutes at 40°C.

- Step-VI: While combining, the cream was chilled to 30°C. Then it was placed in a container that was shielded from direct sunlight. [4, 5]

Table No. 1: Composition of herbal material

S. No.	Ingredients	Maximum dilution ratio
1	Coconut oil	20 ml
2	Lemongrass oil	0.7%
3	Wintergreen oil	2.4%
4	Peppermint	5.4%
5	Garlic Oil	2.5%
6	Eucalyptus Oil	4.0%
7	Camphor	5%
8	Total recipe	25 ml

Optimization of composition by response variables effects (3^2 factorial designs): The effects of different concentrations of self-emulsifying agent glyceryl monostearate and emulsifier Polysorbate 80 on various characters were determined using the full 3^2 factorial designs, in which self-emulsifying agent and surfactant were two factors at three different levels (self-emulsifying agent – 2.5, 5, 7.5 percent w/w and surfactant – 2.5, 5, 7.5 percent w/w). Experimental data were acquired for comparative study, and responses to the created cream were analyzed. After comparing spreadability, viscosity, and extrudability, as well as % drug release and other parameters, the best composition was identified. [6, 7]

Characterization of Prepared Cream:

Visual Properties Inspection: Color, texture, and homogeneity were all evaluated as physical attributes of the finished compositions. The consistency of numerous compositions was assessed through visual observation, and the findings were scored as follows:

*** = Excellent, ** = Very Good, * = Good, 0 = Poor

Sensitivity: A small amount of the substance was applied to the forehead to test if it irritated it.

Color Change: The samples were kept for seven days so that colour changes could be seen.

Water washability: A little amount of testing was applied on the hand for a few minutes to test washability, and then washed with tap water.

Consistency: From a set length of 10 cm, the cone attached to the retaining rod was lowered until it landed in the center of the SSD cream-filled measuring cylinder. The cone's distance traveled was measured after 10 seconds.

Viscosity measurements: The viscosity (in cps) of the products was measured using a Brookfield viscometer (Brookfield, MA). The spindle was spun at a speed of 2.5 revolutions per minute. Before the analyses, the cream specimens were permitted to stay for 30 minutes at the specified temperature (25±1°C).

Extrudability: The mass in grams required to extrude a 0.5-cm strip of the composition in 10 seconds was estimated. Herbal cream extrusion force has been reported. [8]

Spreadability: One gram of the herbal combination was placed between two clear slides, and a weight of 500g was applied. After measuring the time it took to slip off the slides, spreadability was calculated using a formula. The spreadability was then calculated using the formula below:

$$\text{Spreadability} = m \times l / t$$

Where, m = a weight that is attached to the top slide, l = glass slide length, and t = time it took to remove the slides in seconds.

Skin irritation test: Herbal creams with varying concentrations of herbal preparation were applied to the epidermis. The sample cream and the swab carrying it has adhered to the

treated area with adhesive strips. Then any erythema was detected and assessed according to the application site's state. [9, 10]

*** = Severe erythema, ** = Moderate erythema, * = Slight erythema, 0 = No irritation

Stability analysis: Temperatures of 10°C, 30°C, and 45°C were used to keep the composition. For four weeks, the viscosity, pH, and appearance of the specimens were monitored [11, 12].

Toxicity test: The toxicological tests were carried out for a total of 28 days.

Microbiological Studies for the Herbal Creams: The proposed creams were infected on Mueller-Hinton agar plates containing, and a reference was generated by removing the cream using the streak plate technique. The plate was placed in the incubator and incubated at 37 degrees Celsius overnight. Plates were removed shortly after incubation and compared to the reference to determine microbial growth. [13-15]

RESULTS AND DISCUSSION:

Preparations of herbal cream: The herbal component containing cream preparations were made using the emulsification solvent evaporation technique; a total of nine herbal components containing cream preparations were made and evaluated for various parameters. All formulations were assessed for consistency and homogeneity. The manufactured creams were determined to be odorless, somewhat yellowish, and consistent.

Optimization of herbal material containing cream by 3^2 factorial designs: The purpose of the 3^2 factorial designs (3^2- 2 variables at three levels) was to select the stages of different independent variables (Table 2) of self-emulsifying agent glyceryl monostearate (R1) and emulsifier Polysorbate 80 (R2) with the spreadability, viscosity, and extrudability, percent drug release, and other factors.

Table No. 2: Actual unit with coded labels (3^2 factorial designs)

Factors		**Level used**	
	Level -1 (Low)	**Level 0 (Medium)**	**Level 1 (High)**
Independent variables			
R1 = Self-emulsifying agent (%w/w)	2.5	5	7.5
R2 =Surfactant (%w/w)	2.5	5	7.5
Dependent variables			
Y1 = Spreadability			
Y2 = Extrudability			
Y3 = Viscosity			
Y4 = % Drug release			

The herbal component containing preparations (HCCP) were improved using 3^2 factorial designs, and the F5 formulation was chosen as the best preparation based on response surface technique and other assessment factors (Table 3).

Table No. 3: Composition of the herbal component containing cream

Formulation	**Components (% w/w) and Water as Q.S.**						
	HCCP	**GMS (R1)**	**Surfactant (R2)**	**White soft paraffin**	**Liquid soft paraffin**	**BHA**	**Chlorocresol**
F1	25	7.5 (1)	7.5 (-1)	10	15	2.5	2.5
F2	25	7.5 (1)	2.5 (0)	10	15	2.5	2.5
F3	25	7.5 (1)	5 (1)	10	15	2.5	2.5
F4	25	5 (0)	7.5 (-1)	10	15	2.5	2.5
F5	25	5 (0)	2.5 (0)	10	15	2.5	2.5
F6	25	5 (0)	5 (1)	10	15	2.5	2.5
F7	25	2.5 (-1)	7.5 (-1)	10	15	2.5	2.5
F8	25	2.5 (-1)	2.5 (0)	10	15	2.5	2.5
F9	25	2.5 (-1)	5 (1)	10	15	2.5	2.5

Characterization of Prepared Formulations:

Physicochemical characters: Two of the new creams (F5 and F6) were off-white in colour and had a smooth, uniform texture. The texture and pH were ideal for the patients. The viscoelastic properties of the creams were good, including perceived spreadability, viscosity, and extrudability. Pre-formulation testing indicated no hazardous ingredients in the formulations. There were no allergic responses such as contact erythema dermatitis, edoema, irritation, or redness after seven days of cream therapy on rat skin. The physicochemical properties of each mix are listed in Table 4.

Table No. 4: Physicochemical Characters of Prepared Cream

Batch	Colour	Uniformity and consistency	pH	Viscosity (mPa·S)	Spreadability (S)	Extrudability (g)	Sensitivity
F1	Yellowish	Not good	5.6	27.4	30	534	Not sensitive
F2	Yellowish	Not good	5.4	27.2	32	539	Not sensitive
F3	Yellowish	Not good	5.5	27.0	34	538	Not sensitive
F4	Off white	Good	5.6	28.4	33	538	Not sensitive
F5	Off white	Excellent	5.5	27.0	35	539	Not sensitive
F6	Off white	Good	5.5	27.1	36	540	Not sensitive
F7	White	Excellent	5.6	26.6	36	537	Not sensitive
F8	White	Good	5.4	26.4	35	537	Not sensitive
F9	White	Good	5.5	26.8	37	540	Not sensitive

Skin irritation test: The table shows the results of acute skin irritation trials (repeated and loan exposure). Any place where topical formulations were administered showed no clinical

changes or signs of weight gain. Rabbits showed no signs of edoema or erythema on their skin.

Table No. 5: Scoring for skin sensitivity test

Time of film detachment	Edema	Erythema
Singled skin irritation test		
After the 1 hour of application	0	0
After the 12 hours of application	0	0
After the 18 hours of application	0	0
After the 24hour of application	0	0
Repeated skin irritation test		
After the 1 hour of application	0	0
After the 12 hours of application	0	0
After the 18 hours of application	0	0
After the 24hour of application	0	0

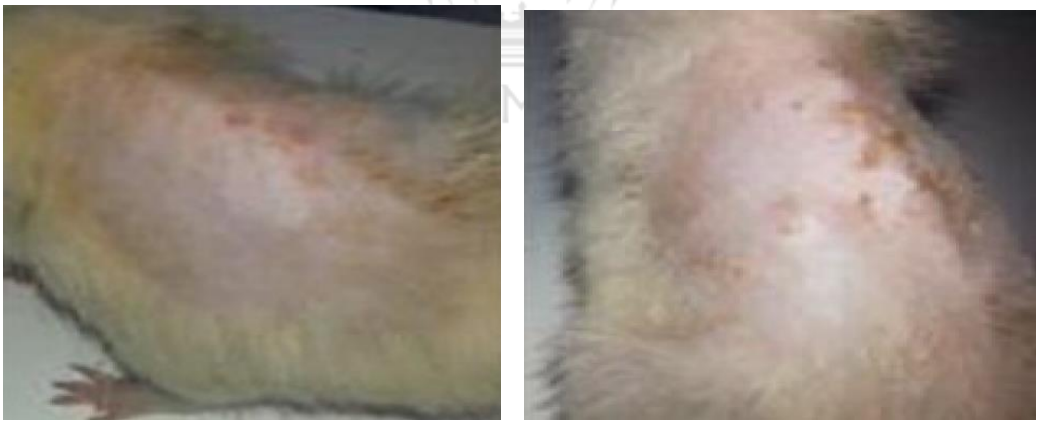

Figure No. 1: a) Control b) Cream treated

Stability analysis: Temperatures of 10°C, 30°C, and 45°C were used to keep the composition. For four weeks, the viscosity, pH, and appearance of the specimens were monitored.

Table No. 6: Stability study of prepared formulation

Stability study type	Storage criteria	Specimen time (in months)
Long term	25 °C ± 2 °C/60% RH ± 5% RH	0, 1, 2, 3, 6, 9, 12
Accelerated	40 °C ± 2 °C/75% RH ± 5% RH	0, 1, 2, 3, 6

Table No. 7: Evaluation parameters of stabilized formulations

S. No.	Batch	pH	Physical appearance	Viscosity
1	F5	5.5	Off white	27.0
2	F6	5.5	Off white	27.1
3	F7	5.6	Off white	26.6
4	Marketed	5.5	Off white	25.8

Toxicity test: The herbal extract is not harmful.

Microbiological studies for the herbal creams: In F5 and F6, there was no yeast, bacterial, or mold numbers. In compositions F5 and F6, microorganisms such as E. coli, Staphylococcus aureus, Pseudomonas aeruginosa, and Salmonella sp. were not present.

CONCLUSION:

The cream had an off-white color and a pH level that was within the prescribed range. Dermal compatibility is one of the main concerns of cream composition scientists. The lotion that was created did not induce skin irritation, sensitization, or agglomeration. Topical medications may be susceptible to microbial damage due to poor formulation or improper handling and storage. On the other hand, the upgraded F5 cream formulation exhibits medication release properties that are equivalent to a well-known branded product. An effective cream formulation for the treatment of arthritis has been developed. It satisfies all of the standard requirements. To boost therapeutic effectiveness, more studies on skin permeation and in vitro drug content augmentation may be necessary.

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