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FORMULATION OF A POLYHERBAL CREAM AND SCREENING FOR ITS ANTI-INFLAMMATORY ACTIVITY

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ABSTRACT

The present study has been undertaken with the aim to formulate and evaluate the polyherbal crem containing *Curcuma longa* Linn., and *Zingiber officinale* extract. The polyherbal formulation was designed by using methanolic extract of Rhizomes of Curcuma longa and *Zingiber officinale* in varied concentrations (2 and 4%). Topical anti-inflammatory activity of gel was also evaluated. The herbal cream was prepared by using olive oil and bees wax as cream base, The prepared herbal cream were evaluated for physical appearance, pH, spreadability, skin irritation to observe toxicity or side effects and also for anti inflammatory activity. It was inferred from the results that cream formulations were good in appearance and homogeneity. The values of spreadability indicated that these polyherbal cream were easily spread able by small amount of shear. Viscosity of polyherbal cream were determined by using Brookfield viscometer and were ranging between 4500 to 4900 centipoise. The gels showed significant inhibition in carrageenan induced paw oedema and formalin induced paw oedema in Wistar rat models.

KEYWORDS: Inflammation, Curcumin, Polyherbalcream.

INTRODUCTION

Inflammation is the reaction of living tissues to injury; it comprises systemic response and local response. Loss of function occurs depends on the site and extent of injury. Pyrexia is caused as a secondary impact of infection or other diseased states. It is the body's natural defence to create an environment where infectious agent or damaged tissue cannot survive. *Curcuma longa and Zingiber officinale* has traditionally been used in herbal medicine in the treatment of topical inflammation. curcumin, the active chemical in turmeric, that's peaked researchers' interests. Research shows that curcumin blocks certain enzymes and cytokines that lead to inflammation. This sheds light on the possibility of curcumin as a complementary treatment for RA.

Curcumin (diferuloylmethane) is one of the ingredients found in the spice, turmeric. Turmeric has been used for centuries in many Eastern countries both as a spice and as a medicine. In recent years, extensive studies have been done on the potential medicinal value of curcumin, particularly when taken orally. The effectiveness of oral curcumin, however, is hindered by poor bioavailability because the unconjugated curcumin molecule, which is hydrophobic, is poorly absorbed by the gastrointestinal tract. Very low curcumin levels are detected in blood and tissues following curcumin ingestion.[1-3] The molecule is mainly absorbed as water-soluble curcumin glucoronate or sulfate metabolites, which are largely inactive products. In contrast, topical curcumin can be formulated to be better absorbed through the skin, particularly when the skin barrier becomes defective in the presence of skin injury and disease. Largely because of the unfavorable pharmacokinetics of oral curcumin, the extensive literature on therapeutic potential of oral curcumin in clinical trials has been disappointingly negative.[4] There have been much fewer studies with topical curcumin despite the fact that the use of topical curcumin is not hindered by issues of gastrointestinal absorption.

MATERIALS AND METHODS

Plant Materials

The fresh rhizomes of *curcuma longa* and *Zingiber officinale* are collected from Tirupathi surrounding villages of Chittoor district in Andhra Pradesh. The plants were identified and authenticated by Professor of Botany, Sri Venkateswara university (SVU), located in Tirupathi (A.P). After authentification, the plants were cleaned and shade dried and milled into coarse powder by a mechanical grinder.

Preparation of Extracts

The Rhizomes of Turmeric and Ginger were shade dried and were powdered, the coarse powder was subjected to

extraction for 72 hours with petroleum ether and alcohol (70%) individually in Soxhlet apparatus and also drug powder was subjected to aqueous extraction.

The whole extract of individual plants was collected in conical flasks, filtered and the solvents were evaporated to dryness under reduced pressure. The polyherbal formulation extract was then analyzed by qualitative tests and was found to contain alkaloids, flavonoids, glycosides, sterols and tannins.

Formulation of A Polyherbal Cream

Pour all oils (except essential oil) into a jar place a water bath with 2 inches of water over medium low heat. Place a jar in electric water bath and allow contents to melt stir to combine and then add essential oils and mix well.Pour a mixture into metal tins or storage container and allow to set.

Table 1: Formulation of Poly Herbal Cream [F1]-2%.

S.NO	Formulations	Ingredients	QTY
1	F1	Olive oil	81 gm
2		Beeswax	15 gm
3		Ginger extract	2 gm
4		Turmeric extract	2 gm
5		Peppermint oil	q.s

Table 2: Formulation of Poly Herbal Cream [F2]-4%.

S.NO	Formulations	Ingredients	Quantity
1	F2	Olive oil	79gm
2		Beeswax	13gm
3		Ginger extract	4gm
4		Turmeric extract	4gm
5		Peppermint oil	q.s

Evaluation of anti-inflammatory activity of polyherbalcream

Carrageenan induced paw-oedema in rats

The inhibitory effect of polyherbal cream containing Turmeric and ginger extract on carrageenan-induced paw edema was evaluated using method described by Niemegeer and his co-workers. White Albino Rats of Wister strain of either sex, 3-4 months of age, 180-220gram of average body weight were selected. Animals were allowed to free access to feed and water before the experiment. Rats were divided into four groups each comprised of six rats. Approximately 50µl of a 1% suspension of Carrageenan in saline was prepared 1h before each experiment and was injected into the plantar surface of right hind paw of rat. 0.2g of cream containing ethanolic extract of Ginger and turmeric were applied to the plantar surface of the hind paw by gently rubbing 50 times with the index finger. Rats of the control groups received only the cream base 1% w/w Diclofenac cream are (Adva care) applied in the same way as a reference standard. 1h after the application of cream base, polyherbal formulations of Ginger and turmeric ethanolic extract and standard ; 50µl of a 1% suspension of carrageenan in saline was administered in to plantar surface of right hind paw of rat. Paw volume was measured immediately after carrageenan injection and at 1h, 2h, 3h and 4h after the administration of the noxious agent by using a plethysmometer (Model 7159, Ugo Basile arese, Italy) (Niemegeer et al., 1964). The paw volume was recorded at different time points. The percentage inhibition in paw volume is calculated by using the formula.

$$\%\,\text{Inhibition} = \frac{\text{paw volume (control)} - \text{paw volume (test)}}{\text{paw volume (control)}} \times 100$$

Statistical analysis

The results of various studies were expressed as mean ± SEM data analysis was done by one way analysis varients (ANOVA) followed by Dunnet's test using "graph pad INSTAT" version 3.00 for windows 95, graph pad software propability values of 0.05($p<0.05$) or less were considered statistically significant and results as shown in the Table no-

Croton oil Induced Ear Oedema in Mice

Weigh and number the animals. Randomize the animals into different groups according to the body weights. Anaesthetize the animals using ethyl ether as anaesthetic agent. Hold the animal gently from front paws and apply 10µ of dexamethasone solution to left inner ear of the mouse and allow it to dry at room temperature. Similarly, apply the solvent system to the right ear of the mice that serves as control for comparision with the left ear. For control group, apply the solvent system to both left and right inner ears. After two hours of the treatment, apply 10µ of croton oil solution (1% v/v) to the left inner ear of each animal. The right ear (solvent applied) (P:W:A) would serve as control. After 6 hrs of the croton oil application, sacrifise all the animals under CO2 anaesthesia and excise both the ears with the help of sharp scissor or blade. Weigh both left and right ears of each animal separately on an analytical balance. Note the different in the weights of treated (steroid) and untreated (control) ears. Calculate the % increase in ear weights of each animal in a group. Take the mean of the whole group.

$$\%\,\text{Increase in Ear Weight} = \frac{\text{Weight of Left Ear} - \text{Weight of Right Ear}}{\text{Weight of Right Ear}} \times 100$$

Calculate % decrease in ear oedema due to steroid application as compared to solvent control group as given in the Table no-

$$\%\,\text{Inhibition of earoedema} = \frac{\text{Mean \% increase in ear weight of solvent treated group} - \text{Mean \% increase in ear weight of steroid treated group}}{\text{Mean \% is increase in ear weight of solvent treated group}} \times 100$$

Physical evaluations of formulated cream

Physical assessments were carried out on the cream for the parameters such as appearance, odour, Colour, pH, Spreadability, homogeneity and viscosity measurement.

pH of the Cream
The pH meter was calibrated using standard buffer solution. About 0.5 g of the cream was weighed and dissolved in 50.0 ml of distilled water and its pH was measured.

Homogeneity
The formulations were tested for the homogeneity by visual appearance and by touch.

Appearance
The appearance of the cream was judged by its color, pearlscence, roughness and graded**.**

After feel
Emolliency, slipperiness and amount of residue left after the application of fixed amount of cream was checked**.**

Type of smear
After application of cream, the type of film or smear formed on the skin were checked.

Removal
The ease of removal of the cream applied was examined by washing the applied part with tap water**.**

Irritancy test
Mark an area (1sq.cm) on the left hand dorsal surface. The cream was applied to the specified area and time was noted. Irritancy, erythema, edema, was checked if any for regular intervals up to 24 hrs and reported.

Spreadability
Spreadability of the formulation was determined by an apparatus suggested by Mutimer *et al* with some modifications.[15] It consists of a wooden block having a pulley at one end with fixed glass slide on block. An excess of ointment (3gm) placed on ground plate. The ointment was sandwiched between this plate and another glass plate having the dimension of fixed ground plate and provided with the hook. A 1kg weight was placed on the top of the two plates for 5 min to expel air and to provide a uniform film of the ointment between the plates. Excess of ointment was scrapped off from the edges. The top plate was then subjected to pull of 240gms. With the help of string attached to the hook and time required by the top plate to cover a distance of 10cm. was noted. A shorter interval indicates better spreadability.[16] Spreadability was calculated using the following formula:

$$S = M \times L / T$$

Where, S = Spreadibility,
M = Weight in the pan (tied to the upper slide),
L = Length moved by the glass slide and
T = Time (in sec.) taken to separate the slide completely each other.

Measurement of Viscosity
Determination of viscosity of prepared ointment was carried out with Brookfield viscometer (model LV-DV-II, helipath spindle S-96) as method described by Kim JY and co-workers. The value of each formulation were done in triplicate and the viscosity values are expressed as Mean ±Standard deviation. All the above results are tabulated in Table **No-4**

RESULTS AND DISCUSSION

Phytochemical studies
The preliminary phytochemical screening of ethanolic extracts of both Ginger and Turmeric showed the presence of Alkaloids, Tannins, Resins and Flavonoids.

Physical evaluation of cream containing turmeric and ginger extracts
Polyherbal cream containing turmeric and ginger extracts were prepared and creams were evaluated for colour, odour, homogenisity, $p^{H,}$ viscocity and spreadability and results are shown in **Table No.4.**

Acute skin irritation study
Prepared polyherbal cream did not shown any signs of erythema when applied topically to the skin of animals till 7 days.

Investigation of anti-inflammatory activity of polyherbal cream formulaion
Anti-inflammatory ativity of polyherbal cream were investigated by carragenna induced paw odema and croton oil induced ear oedema in mice induced method and results obtained is shown in **Table No.6 and 7.**

Two polyherbal cream of varying concentrations of 2% and 4% were prepared using olive oil and bees wax as cream bases and they were found to be stable during the period of observation.

Polyherbal cream were subjected for investigation of anti- inflammatory activity using carrageenan- induced rat paw oedema and croton oil induced ear oedema.

The polyherbal cream containing the ethanolic extract of concentration 4% w/w showed significant reduction of oedema through the entire period of time of observation in comparision of control ($P<0.05$), although polyherbal cream containing 4% ginger and turmeric extract showed higher percentage of inhibition (41.77) of edema compare to polyherbal cream containing 2% extract for which the percentage of inhibition is 40.0.

Table 3: The Colour and % Yield of Plant Extract.

S.No.	Extracts	Colour	Yield((%w/w)
1.	Ginger	Dark brown	12%
2.	Turmeric	Yellowish some what sticky	16%

Table 4: Physical Evaluation of Polyherbal Cream.

Formulations	pH	Viscosity cps	Spreadability g.cm/sec	Homogenity
F1	6.35±0.02	27.27±0.11	9050±12.1	good
F2	6.97±0.01	20.27±0.14	9664±16.7	good

Table 5: Adverse Effect of Formulation.

S.No.	Formulation	Irritant	Erythema	Edema
1	F1	Nil	Nil	Nil
2	F2	Nil	Nil	Nil

Table 6: Evaluation of anti-inflammatory Activity of polyherbal cream Carrageenan induced paw edema in rats.

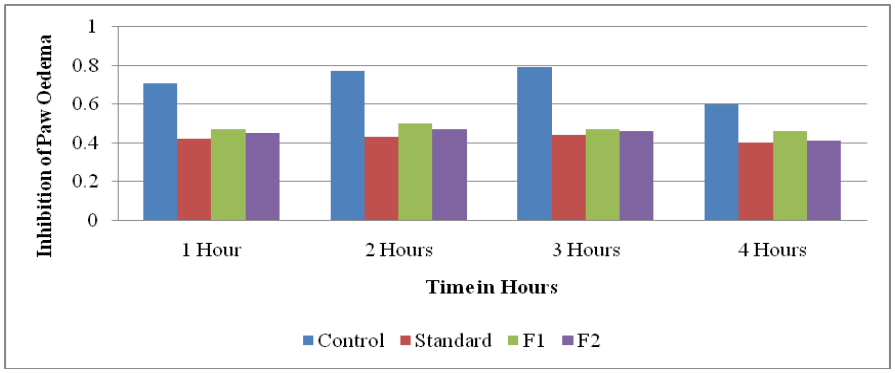
Treatment	1 hour	2 hours	3 hours	4 hours
Control Standard (1% diclofenac sodium)	0.71±0.02 0.42±0.03(41)	0.77±0.02 0.43±0.04(44.2)	0.79±0.01 0.44±0.4(44.4)	0.60±0.02 0.40±0.03(33.4)
F1	0.47±0.03(33.9)	0.50±0.04(35.1)	0.47±0.04(40.6)	0.46±0.03(33.4)
F2	0.45±0.02(36.7)	0.47±0.04(39)	0.46±0.02(42.8)	0.41±0.04(31.6)

Values are expressed as Mean±SEM, n=6 in each group values in parantheses indicate % inhibition of paw oedema

Table 7: Croton Oil Induced Ear Oedema in Mice.

Group	Dose	N	Weight(mg)	Inhibition Ear Edema (%)
Control Standard Dexamethasone	-	6	0.017±0.001 0.0054±0.0007	- 74
F1	2%	6	0.0092±0.0002	47
F2	4%	6	0.0086±0.0001	50

INHIBITION OF PAW OEDEMA



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