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Anti-inflammatory herbal gel containing *Artocarpus heterphyllus* lam. fruit extract

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Abstract
The present investigation aims at development of herbal anti-inflammatory gel using of ethanolic extract from *Artocarpus heterphyllus* Lam fruits (EAAH). Six herbal gels were prepared and all formulations were evaluated for physical appearance, pH, spreadability, viscosity, and anti-inflammatory activity using carrageenan-induced rat paw edema model on albino Wistar rats of either sex (150–200 g). Change in edema volume of the rat hind paw was measured, and percent inhibition was calculated.It is inferred from the results that gel formulations were good in appearance and homogeneity. The gels showed significant inhibition in carrageenan induced paw oedema in Wistar rat models.

Keywords: inflammation, herbal Gel, *Artocarpus heterphyllus*

Introduction
Inflammation is a complex process, which is frequently associated with pain and involves occurrences such as the increase of vascular permeability, increase of protein denaturation, and membrane alteration. It is a part of the complicated biological reaction of vascular tissues to harmful stimuli, including pathogens, damaged cells or irritants. It is characterized viaredness, swollen joints, joint pain, its stiffness and lack of joint characteristic [1].Inflammation is presently treated via NSAIDs. Unfortunately these NSAIDs motive elevated danger of blood clot ensuingin heartassaults and strokes [2].

Artocarpus heterophyllus Lam. commonly called the jackfruit tree (or Jacquier in french); is one of the widely distributed plant in tropical and sub-tropical countries such as India, Brazil, Bangladesh, Thailand, Indonesia, Philippines. *A. heterophyllus* belongs to the family Moraceae and bears large edible fruits which can reach 49 kg [3]. The *Artocarpus heterophyllus* contains various chemical constituents as several flavones colouring matters, morin, dihydromorin, cynomacurin, artocarpin, isoartocarpin, cyloartocarpin, artocarpesin, oxydihydroartocarpesin, artocarpetin, norartocarpetin, cycloartinone and artocarpanone[4] Three phenolic compounds were characterized as artocarpesin [5,7,2',4'-tetrahydroxy-6-(3- methylbut-3-enyl) flavone] (1), norartocarpetin (5,7,2',4'- tetrahydroxyflavone) (2), and oxyresveratrol [trans-2,4,3',5'- tetrahydroxystilbene] (3) by spectroscopic methods and through comparison with data reported in the literatures. The anti-inflammatory effects of the isolated compounds (1- 3) were evaluated by determining their inhibitory effects on the production of proinflammatory mediators in lipopolysaccharide (LPS)-activated RAW 264.7 murine macrophage cells. These three compounds exhibited potent anti-inflammatory activity. The results indicated that artocarpesin (1) suppressed the LPS-induced production of nitric oxide (NO) and prostaglandin E 2 (PGE 2) through the down-regulation of inducible nitric oxide synthase (iNOS) and cyclooxygenase 2 (COX-2) protein expressions. Thus, artocarpesin (1) may provide a potential therapeutic approach for inflammation-associated disorders [5].The leaves are useful in fever, boils, wounds and skin diseases. The young fruits are acrid, astringent, and carminative. The ripe fruits are sweet, cooling, laxative, aphrodisiac and also used as a brain tonic. The seeds are, diuretic, and constipating. The wood is nervine, antidiabetic, sedative and is useful in convulsions[6].The latex is useful in dysopia, ophthalmic disorders and pharyngitis and also used as antibacterial agent[7].The ash of Jackfruit leaves is used in case of ulcers. The dried latex yields artostenone, convertible to artosterone, and a compound with marked androgenic action. Mixed with vinegar, the latex promotes healing of abscesses, snakebite and glandular swellings [8].The root is a remedy for skin diseases and asthma. An extract of the root is taken in cases of fever and diarrhoea. The bark is made into poultices. Heated leaves are placed on wounds. The wood has a sedative property and its pith is said to be abortifacient. Latex is used as an anti-inflammatory agent [9].

Material and Methods
Collection and Authentication
Fruits of *Artocarpus heterophyllus* Lam. were collected from local market of Indore in the month of April, 2021. The plant was authenticated by the taxonomist Dr. Jashwinder Mehta, Career College, Bhopal(M.P.).Herbarium of plant was submitted in the Department of Botany, with voucher specimen numbers Bot/Herb/2021/37.

Extraction procedure

60.85 gram of fruits dried powdered of *Artocarpus heterophyllus* Lam. were coarsely powdered and subjected to extraction with petroleum ether by soxhlation method. The extraction was continued till the defatting of the material had taken place. Defatted dried powder of *Artocarpus heterophyllus* Lam. was then extracted with ethanol using soxhlation method for 48 hrs, filtered and dried using vacuum evaporator at 40°C [10-11].

FormulationofAnti-Inflammatory Gel

Measured quantity of Methyl paraben, glycerin, polyethylene glycol and ethanolic extract of *Artocarpus heterophyllus* Lam were dissolved in about 35 ml of water inbeaker and were stirred at high speed using mechanical stirrer (or sonicator)[12].Then Carbopol 940 was added slowly to the beaker containing above liquid whilestirring. The solution is neutralized by slowly adding triethanolamine solution with constant stirring until the gelisformed.Six formulations were prepared by using different concentration of Carbopol 940.

Table 1: Formulationofgel

Ingredients (%)	PG1	PG2	PG3	PG4	PG5	PG6
A.heterophyllus lam extract	1gm	1gm	1gm	1gm	1gm	1gm
Carbopol940	0.5mg	0.75mg	1.0mg	1.25mg	1.5mg	2.0mg
Polyethylene Glycol	0.2ml	0.2ml	0.2ml	0.2ml	0.2ml	0.2ml
Methyl Paraben	0.08mg	0.08mg	0.08mg	0.08mg	0.08mg	0.08mg
Triethanolamine	1.0ml	1.0ml	1.0ml	1.0ml	1.0ml	1.0ml
DistilledWater(q.s)	100ml	100ml	100ml	100ml	100ml	100ml

Evaluation of gel

The prepared herbal gel is evaluated for physical appearance, pH, Viscosity, Extrudability and spreadability according to standard procedures [13-16].

Drugcontent

The flavonoids content was determined by taking 1gm of gel in 10 ml volumetricflask diluted with methanol.1 ml of 2% AlCl3 solution was added to 3 ml of extract and standard and allowed to stand for 15min at room temperature; absorbancewasmeasuredat420nmusinga spectrophotometer. *In-vivo*anti-inflammatory activity of prepared gel [17].

Pharmacological Screening

Animals

Wistar rats (150–200 g) were group housed (n= 6) under a standard 12 hlight/dark cycle and controlled conditions of temperature and humidity (25±2 °C,55–65%). Rats receivedstandardrodentchow andwater*ad libitum*.Rats wereacclimatized to laboratory conditions for 7 days before carrying out the experiments.All the experiments were carried in a noise-free room between 08.00 to 15.00 h.Separate group (n=6) of rats was usedfor each set of experiments.All the experimental procedures were carried out in accordance with the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) guidelines. The study designs were approved by the Institutional Animal Ethical.

Experimental designs

Anti-inflammatoryactivitywasmeasuredusingcarrageenaninducedratpawoedemaassay. The rats were divided into three groups of six animals each.Group I was treated as control (0.1mlof1%(w/v) of was treated with carrageenan (1%w/v)in saline in the sub-planter region of the right hind paw), Group II was *Artocarpus heterophyllus* gel treated. Group III was Diclofenac sodium topical gel treated. Oedema was induced by injecting 0.1 ml. of a1% solution of carrageenan in saline into the sub plantar region of the right hind pawof the rats. The volumes of oedema of the injected and the contralateral paws were measured after the induction of inflammation using a plethysomgraph to calculate the percentage of paw oedema inhibition[18].

$$\text{Percentage Inhibition} = \frac{Vc-Vt}{Vc} \times 100$$

Where, Vc- Edema volume of control groupVt-Edema volume of test group

Statistical Analysis

Allanalysiswasperformedusinggraphpadprismfor Windows.Allstatistical analysis is expressed as mean ± standard error of the mean (SEM). Data were analyzed by oneway ANOVA, where applicable$p<0.05$was considered statistically significant, compared with vehicle followed by Dunnett'stest.

Results and Discussion

Table 2: Result of physical evaluation of formulated gels

Formulation	Physical Appearance	pH	Viscosity(cps)	Spreadabilitygm cm/sec	Extrudability	Drug content %w/w
PG1	Dark brown, Smooth, Homogeneous	6.58±0.02	3456±12	14.85±0.32	++	58.2
PG2	Dark brown, Smooth, Homogeneous	6.65±0.03	3325±11	13.25±0.25	++	54.1
PG3	Dark brown, Smooth, Homogeneous	6.69±0.01	3215±14	14.25±0.12	++	56.2
PG4	Dark brown, Smooth, Homogeneous	6.58±0.02	3165±15	14.85±0.24	++	55.8
PG5	Dark brown, Smooth, Homogeneous	6.85±0.01	3145±11	15.45±0.18	+++	59.5
PG6	Dark brown, Smooth, Homogeneous	6.81±0.02	3285±15	15.69±0.45	+++	65.5

Results of *In-vivo* anti-inflammatory activity of prepared gel

Artocarpus heterophyllus gel showed 54.5%, inhibition , as compared to 57.7 % inhibition of Diclofenac topical gels shown in Table4.

Table 3: Effect of *Artocarpus heterophyllus* gel on paw oedema induced bycarrageenaninrats

Treatment	Dose(mg/kg)	Initial	1hr	2hr	3 hr	4hr
Group-IControl	0.1mlof1%(w/v)	0.45 ± 0.05	0.49 ± 0.06	0.57 ±0.03	0.72 ±0.05	0.66 ±0.05
Group-II *Artocarpus heterophyllus* gel	2mg	0.45 ± 0.12	0.49 ± 0.05	0.55 ±0.1	0.47 ±0.25*	0.30 ±0.05*
Group-III Diclofenac sodium topical gel	10mg	0.44 ± 0.05	0.48 ± 0.05	0.56 ±0.07	0.42 ±0.04*	0.28 ± 0.06**

Values are expressed as mean ± SD.*P<0.0 significant compared to carrageenan treated group.

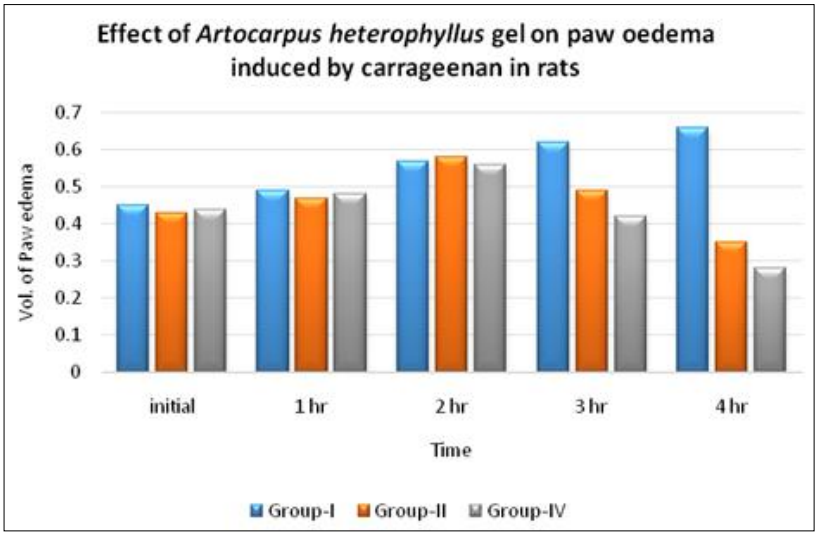

Fig 1: Effect of *Artocarpus heterophyllus* gel on paw oedema induced by carrageenan in rats

Table 4: Percentage Inhibition of *Artocarpus heterophyllus* gel on paw oedema induced bycarrageenaninrats

Treatment	Dose(mg/kg)	Meandifferences in Paw Volume (ml)	Percentageof Inhibition (%)
Group-IControl	0.1mlof1% (w/v)	0.66±0.05	--
Group-II *Artocarpus heterophyllus* gel	2mg	0.36±0.1**	54.5%**
Group-III Diclofenac Sodium topical gel	10mg	0.38±0.1**	57.7%**

Values are expressed as mean ± SD.*P<0.05-significant compared to carrageenan treated group.

Inflammationis usually abody response totissue damage andtoa numberofsystemic malfunctions including asthma, atherosclerosis, arthritis, physical injuryand infection amongst many others. Medicinal plants comprise of phytochemicalsthat improves the physiological balance of human beings and the knowledge of these healing properties has been passed down through generations. Ethanolic extract of *Artocarpus heterophyllus* Lam possess significant anti-inflammatory potential. These findings support the use of the extract in traditional system of medicine for the management of inflammatory conditions. Different formulation of ethanolic extract of *Artocarpus heterophyllus* gel were prepared and evaluated Theanti-inflammatory activity of *Artocarpus heterophyllus* gel was evaluate using the carrageenan-induced rat paw edema method. The *Artocarpus heterophyllus* gel produced 54.5%, inhibition.

Conclusion

From these results, it can be conclude that herbal gel containing 2gm of *Artocarpus heterphyllus* ethanolic extract possesses anti-inflammatory activity which can be useful for the treatment of local inflammation.

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