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INVESTIGATION AND EVALUATION OF AN ANTI-INFLAMMATORY HERBAL FORMULATION

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Abstract

This study uses methanolic extracts of Emblica officinalis (EO) and Aegle marmelos (AM) in topical gel preparations to examine and assess the anti-inflammatory properties of herbal formulations. The formulations, designated F1 through F5, were created in a Carbopol 934 gel base using different amounts of AM and EO extracts. In addition to extrudability investigations, physical criteria such as homogeneity, pH, spread ability, viscosity, and appearance were assessed to guarantee the quality of the formulation. By estimating paw volume at 1, 2, 3, and 4-hour spans after treatment, the carrageenan-instigated rodent paw edema model was utilized to assess the anti-inflammatory efficacy. The findings show that formulations F4 and F5, which have higher AM and EO extract contents, significantly reduce paw edema, with the suppression of paw edema reaching up to 65.17% after 4 hours. The extracts contained flavonoids, terpenoids, and alkaloids, which are known to have anti-inflammatory effects by modifying inflammatory pathways, according to phytochemical research. These results highlight the natural origin and lower risk of side effects of herbal formulations, which may make them viable substitutes for traditional anti-inflammatory medications. In order to determine their safety, effectiveness, and therapeutic potential in clinical settings, more investigation and clinical trials are required.

Keywords: *Anti-Inflammatory, Herbal Formulation, Topical Gel, MEEOF, MEAMF, Carbopol.*

INTRODUCTION

Research into and assessment of herbal formulations with anti-inflammatory properties as possible substitutes or supplements to traditional medications has gained traction in recent years (Balkrishna A. , 2019). This tendency is indicative of a larger cultural movement away from synthetic drugs and toward more natural and holistic approaches to healthcare, motivated by worries about the short- and long-term health risks of these synthetic medications (Bansod, 2010). The downsides of synthetic pharmaceuticals, including non-steroidal anti-inflammatory drugs (NSAIDs), which can cause gastrointestinal issues, cardiovascular risks, and liver toxicity with prolonged usage, are the driving force behind the growing interest in anti-inflammatory herbal formulations (Dadoriya, 2020). Exploring natural substitutes that might provide comparable therapeutic advantages with fewer side effects is therefore highly motivated (Giri, 2019).

Utilizing natural chemicals obtained from plants recognized for their anti-inflammatory qualities, these formulations maximize the therapeutic potential of these ingredients (Gomase, 2011). They frequently contain a wide range of plants and botanical extracts that are high in bioactive substances such saponins, terpenoids, alkaloids, and flavonoids. The potential of each of these substances to alter the body's inflammatory pathways and relieve pain, edema, and other signs and symptoms of ongoing inflammation has been investigated (Okur, 2020). Evaluating these formulations' effectiveness in lessening inflammatory ailments such as autoimmune disorders, inflammatory bowel diseases, arthritis, and other problems where chronic inflammation is a major factor is the main goal of the research (Joshi, 2020). These herbal remedies seek to improve the quality of life for those with these disorders by offering effective relief while lowering the possibility of side effects that are frequently connected to synthetic medications (Beg, 2011).

Validating the efficaciousness of herbal compositions intended to reduce inflammation requires the application of contemporary scientific approaches (Jyothi, 2016). This includes in vitro research to evaluate the effects on inflammatory markers and cytokine production, in vivo studies using animal models to comprehend pharmacokinetics and therapeutic mechanisms, and, finally, clinical trials to determine safety, dosage, and efficacy profiles in human subjects (Sekar, 2017). Phytochemical analysis is used to identify and quantify active constituents responsible for their therapeutic effects (Kabir, 2012). For herbal formulations to be safe, effective, and of high quality, it is imperative to navigate regulatory systems (Cheng, 2015). This include following Good Manufacturing Practices (GMP), carrying out thorough safety evaluations, such as toxicity tests, and securing regulatory clearances for product registration and clinical trials. Adherence to regulatory guidelines guarantees the legitimacy and dependability of these compositions and makes it easier for them to be incorporated into conventional medical procedures (Mahendra, 2019).

1.1.Objectives of the Study

- To evaluate herbal gel compositions' durability in various environmental settings in order to guarantee their continued quality and efficacy.
- To look into particular pathways and biomarkers that herbal extracts target in order to understand how they work as anti-inflammatory agents.

- To investigating the potential for herbal extracts to work in concert to improve the overall anti-inflammatory efficacy and therapeutic advantages of formulations.

2. ANTI-INFLAMMATORY HERBAL FORMULATION

A combination of organic herbs and plant extracts intended to lessen inflammation is called an anti-inflammatory herbal formulation. These mixtures make use of the therapeutic qualities of several plants that have long been recognized for their ability to heal (Kaneria, 2007).

2.1.Components and Mechanisms

a) Active Phytochemicals

An anti-inflammatory herbal formulation normally consists of a combination of herbs and plant extracts, each of which contributes its own distinct active phytochemicals that are known for their ability to reduce inflammation (Nagarkar, 2013). Included among these active chemicals are:

- **Flavonoids:** Flavonoids are polyphenolic chemicals that may be found in a wide variety of plants (Padmanabhan, 2012). They are well-known for their ability to modulate the immune system, reduce inflammation, and act as antioxidants respectively. Flavonoids, such as quercetin and kaempferol, are examples of compounds that inhibit enzymes and cytokines that contribute to inflammation (Paschapu, 2009).
- **Terpenoids:** Terpenoids are molecules that have a key role in lowering inflammation. Some examples of these compounds include curcumin, which is found in turmeric, and Boswellia acids, which are found in Boswellia serrata (Sunnetha, 2019). The NF-kB pathway, which is an important regulator of inflammation, is inhibited by curcumin, while boswellic acids inhibit 5-lipoxygenase, which is an enzyme that is involved in the process of inflammation occurring (Rai, 2019).
- **Alkaloids:** Alkaloids are nitrogen-containing chemicals that can be found in plants such as belladonna and goldenseal. They have the ability to modulate the immune response, which in turn provides a reduction in inflammation (Shaikh, 2016).
- **Saponins:** Saponins are chemicals that may be found in plants such as ginseng and licorice. They have the ability to prevent the release of inflammatory mediators, which is how they exert their anti-inflammatory effects (Suryadevara, 2018).

b) Synergistic Effects

The effectiveness of the formulation is frequently improved by the synergistic effects that result from the combination of numerous natural herbs. The term "synergy" refers to the fact that the combined action of the components is more powerful than the total of the contributions made by each of them individually (Yadav, 2018). As an illustration, a formulation that contains turmeric, ginger, and Boswellia may give more complete anti-inflammatory effects due to the combined inhibition of numerous inflammatory pathways brought about by the combination of these three ingredients (Yatoo, 2018).

c) Supporting Ingredients

It is common practice to incorporate supporting components into a formulation in order to achieve the greatest possible level of effectiveness. Additionally, these have the potential to improve the bioavailability and absorption of the active substances (Yousif, 2011). Piperine, which is derived

from black pepper, is frequently used in formulations that contain curcumin. This is done in order to enhance the absorption of curcumin within the body by inhibiting the enzymes that are responsible for its breakdown (Rajiah, 2010).

3. RESEARCH METHODOLOGY

3.1.Preparation of methanolic extracts

In Balrampur, Uttar Pradesh, fruits from E. officinalis and Aegle marmelos were gathered. Using voucher specimen numbers AMRGA012 and EOMRGA013, the Botanical Survey of Uttar Pradesh verified the authenticity of the plants.

After being cut into little pieces, the fruits of E. officinalis were dried under shade and ground into a coarse powder utilizing a machine processor. The powder was separated involving methanol as the dissolvable in a Soxhlet extractor after being gone through screen No. 40. Using a Soxhlet system, fresh A. marmelos fruit pulp was extracted using methanol. After extracting, the mixture was chilled and filtered. A residue was obtained by vacuum-evaporating the filtrate.

3.2.Formulation of topical gel

Utilizing a mechanical stirrer and the gelling specialist Carbopol 934 at a 1% w/w fixation with deionized water, herbal gel was made. Then, tri-ethanolamine was added dropwise while mixing persistently to safeguard skin pH (6.8-7). As shown in Table 1, different centralizations of 5, 10, 15, 20, and 25% w/w of the two concentrates were added to the gel and twirled for a sufficiently long timeframe to guarantee that the concentrate was uniformly blended all through the gel base. To fill the pre-arranged gel, folding cylinders were used. These blends were kept in a dry, cool climate. The following boundaries were utilized to assess the formulation.

3.3.Organoleptic assessment

Physical characteristics including look and hue were noted.

3.4.Viscosity

The Brookfield viscometer (Brookfield viscometer RVT) with shaft number 7 was utilized to gauge the thickness of the gel.

3.5.Extrudability

Standard covered folding aluminum tubes were filled with the gel pieces, and the finishes were creased closed to seal. It was noticed how much each cylinder gauged. The cylinders were braced after being situated between two glass slides. After covering the slides with 500 g, the cap was taken off. Weighing was finished on how much expelled gel that was gathered. The level of gel that was not entirely settled to be >90% (phenomenal), >80% (pleasant), and >70% (fair).

3.6.Spread ability

The gadget, which comprises of a wooden block provided by a pulley toward one side, was utilized to quantify spread ability. This approach estimated spread ability in view of the gels' slip and drag properties. On the ground slide, an abundance of the gel being scrutinized (around 2 g) was stored. After that, the gel was situated with a snare between this slide and one more glass slide that had similar aspects as a fixed ground slide. For five minutes, a one-kilogram weight was situated on every one of the two slides to force out air and make a predictable layer of gel between them. The overabundance gel was eliminated by scratching off the edges. Then, utilizing a string that was

fastened to the snare, the top plate was pulled 80 g, and how much time (estimated in a flash) required for the top slide to travel 7.5 cm was recorded. Better spread ability was shown by a more limited stretch. The following formula was utilized to decide spread ability.

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

Where,

S = Spread ability

M = Container's weight (connected to the upper slide)

L = Length that the glass slide moved

T = The amount of time (in seconds) needed to split the top and lower slides apart

3.7.Measurement of pH

Utilizing a computerized pH meter, the pH of the created gel syntheses was learned. To find any progressions over the long run, the estimation was done 1, 30, 60, and 90 days following readiness. After dissolving 1 g of gel in 100 ml of refined water, it was saved for two hours. The formulation's pH was estimated multiple times, and the typical still up in the air.

Table 1: Creation of different formulations containing MEEOF and MEAMF

Ingredients	**Quantity in %**				
	F1	**F2**	**F3**	**F4**	**F5**
MEEOF	6	11	14	22	23
MEAMF	6	11	14	22	23
Carbopol 934	2	2	2	2	2
Propylene glycol 400 (5%)	6	6	6	6	6
Triethanolamine	q.s.	q.s.	q.s.	q.s.	q.s.
Methylparaben (0.5%)	0.4	0.4	0.4	0.4	0.4
Propylparaben (0.2%)	0.2	0.2	0.2	0.2	0.2

3.8.Homogeneity

After being bundled in compartments, each created gel was outwardly assessed to guarantee uniformity. Their appearance and the presence of any totals were inspected.

3.9.Grittiness

Each formulation was inspected under a light magnifying instrument to decide if any significant molecule matter was available. Therefore, it is apparent that the gel arrangement satisfies the important rules of being free of specific material and having the imperative dirt for any topical application.

3.10. Skin irritation test

Wistar rodents of the two genders, weighing 150-200 g overall, with their skin flawless, were utilized. Three days before to the preliminary, the rodent had its hair culled. The guinea pig was

regulated arranged gel formulations, while the benchmark group got gel base. Erythema and edema on the treated skin were surveyed after the creatures had day to day medicines for seven days.

3.11. Evaluation of anti-inflammatory activity

- **Animals**

We utilized 150–200 g albino Wistar rats of both sexes on average. Every rat included in the research was kept in a conventional habitat, fed a standard rodent meal, and given unlimited access to water. Three groups, each consisting of six animals: control, test, and standard, underwent all animal procedures. The analysis convention (CPCSEA/1093) was supported by the Institutional Creature Moral Board, and the creatures used in this study were all focused on as per CPCSEA rules.

- **Carrageenan-instigated rodent paw edema**

Before the preliminary, the creatures were given water on request after a 24-hour fast. One hour preceding each trial, 0.1 ml of 1% w/v carrageenan in saline was infused into the plantar side of the rodent's right rear paw. The plantar surface of the rear paw was scoured delicately multiple times with the pointer to apply 0.2 g of herbal gel. The conventional gel base was given to the rodents in the benchmark groups. A similar method was utilized to apply 0.2 g of 1% valdecoxib gel as a norm. A medication or fake treatment was regulated one hour before to the infusion of carrageenan. Utilizing a paleothermometer, paw volume was estimated quickly following carrageenan infusion and afterward at 1, 2, 3, and 4 hour stretches following the harmful specialist's organization. The formula is utilized to get the rate restraint in paw volume.

% Inhibition = [Paw volume Control Paw volume Test] x100 Paw ( ) − × ( ) ÷ volume (Control)

3.12. Statistical analysis

Statistical analysis was conducted using the mean standard error of the mean. For this data study, we utilized GraphPad version 7, one-way analysis of variance, and Dunnett's test. When compared to the control group, statistical significance was determined as probability values of 0.05 ($p<0.05$) or below; *$p<0.05$ **$p<0.01$ 1 ***$p<0.001$.

4. DATA ANALYSIS

During the stability testing period, all five of the MEEOF and MEAMF concentrations used to generate the topical gel formulation were stable.

Table 2: Formulations F1 through F5's Anti-Inflammatory Effects Over Time Intervals

Standard	Time Interval	% Inhibition (mean±SEM)
F1	1H	17
	2H	16
	3H	16.5
	4H	10
F2	1H	18
	2H	9
	3H	26
	4H	8

F3	1H	20
	2H	44
	3H	49
	4H	50
F4	1H	19
	2H	53
	3H	60
	4H	63
F5	1H	22
	2H	58
	3H	64
	4H	62

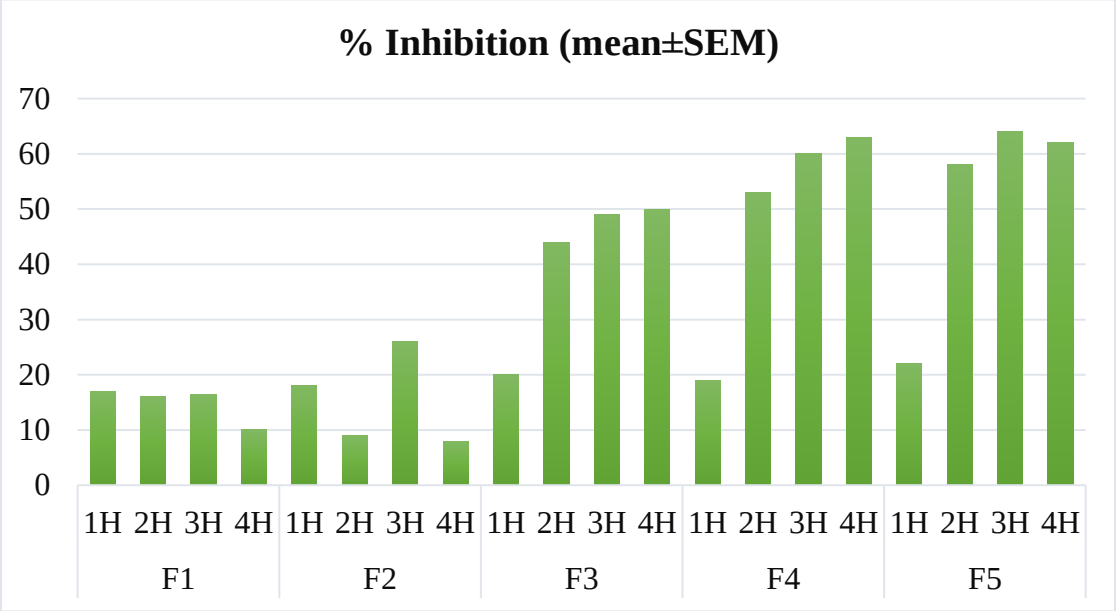

Figure 1: Formulations F1 through F5's Anti-Inflammatory Effects Over Time Intervals

The findings on the anti-inflammatory effect of formulations F1 to F5 are presented in table 2, which uses carrageenan-induced rat paw edema as a model. The data are presented at different time intervals (1H, 2H, 3H, and 4H). The fact that each formulation exhibits a different degree of percentage suppression of paw edema is evidence that they are beneficial in lowering inflammation when compared to a control group.

Both Formulation F1 and Formulation F2 have moderate inhibition percentages over all time intervals. Formulation F1 has a range of 10% to 17%, while Formulation F2 has a range of 8% to 26%. A gradual anti-inflammatory action is demonstrated by the fact that F3 demonstrates increased inhibition with time, beginning with 20% inhibition at 1H and continuing all the way up to 50% inhibition at 4H. In all time intervals, formulations F4 and F5 exhibit large and consistent

inhibition percentages. Formulation F5 demonstrates the strongest inhibition, reaching up to 64% at 3H. Formulation F4 indicates the least amount of inhibition.

Table 3: Various gel formulations are subjected to a physical examination.

Formulation	Appearance	Viscosity	Spread ability	pH	Homogeneity
F1	Light green	4520	25.35	6.3	Homogeneous
F2	Light green	4260	23.36	6.5	Homogeneous
F3	Light green	4300	23.85	6.8	Homogeneous
F4	Light green	4500	20.30	7	Homogeneous
FS	Light green	4580	20.15	6.7	Homogeneous

The physical assessment of the gel formulations (F1 to F5) in Table 3 shows consistent features across a number of criteria. The bright green color of all formulations indicates homogeneity in appearance, which is important for the aesthetics of the final product. The viscosity tests indicate different degrees of thickness that can impact the ease of application and duration of adherence on the skin. The measurements range from 4260 cP to 4580 cP, with F1 displaying the highest viscosity and F4 the lowest. All formulations exhibit sufficient spread qualities, as indicated by spread ability values ranging from 20.15 to 25.35. This is crucial for uniform coverage and user comfort. The pH levels, which vary from 6.3 to 7.0, are compatible with skin physiology and lie within the permitted range for topical applications. In general, the formulations demonstrate a uniform consistency devoid of discernible aggregates, an essential attribute for preserving product efficacy and quality in medicinal contexts.

Table 4: Extrudability analysis of different gel compositions

Formulation	Weight of formulation	Weight of gel extruded	Extrudability amount (%)	Remark
F1	14.3	14.2	85.20	Nice
F2	14.65	13.10	83.50	Nice
F3	14.96	14.40	85.15	Nice
F4	14.27	14.14	84.19	Nice
F5	14.25	13.8	85.40	Nice

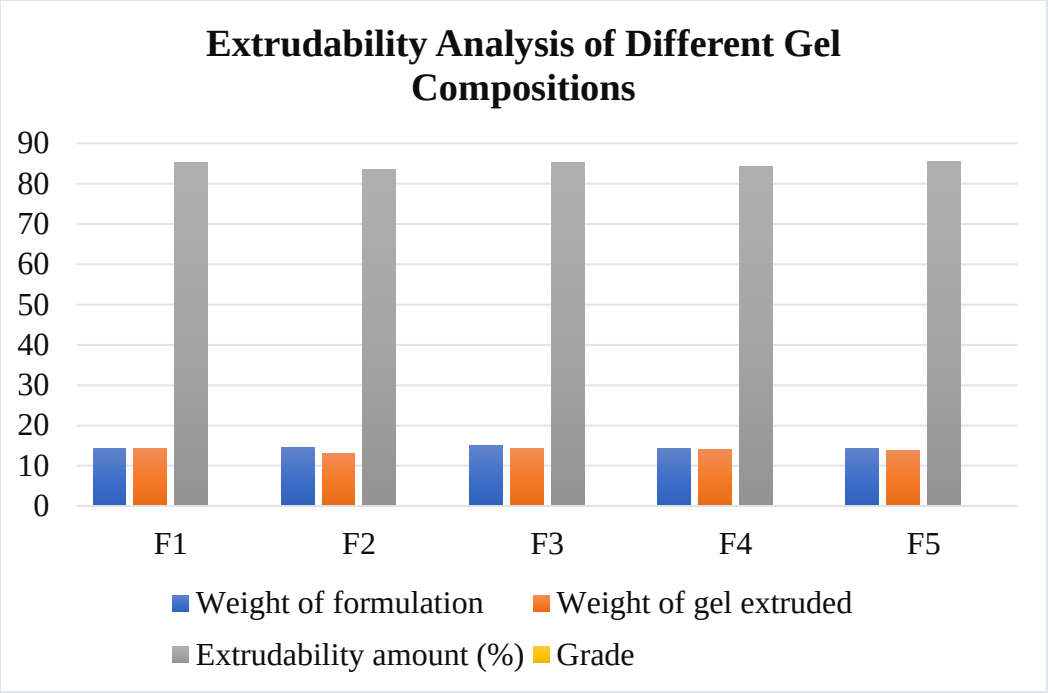

Figure 2: Extrudability analysis of different gel compositions

Table 4 presents an overview of the extrudability properties of formulations F1 through F5, with particular attention paid to weight pre- and post-extrusion, extrudability %, and grade evaluation. From F1 to F5, every formulation showed reliable and efficient extrudability, as evidenced by high percentages ranging from 83.50% to 85.40%. This measure shows how well the formulations transform their starting weight into extruded gel, which is important for preserving product quality and uniformity in pharmaceutical applications. All formulations received the same "Nice" grade, indicating that they are suitable for creating pharmaceutical gels or other formulations with consistent extrusion capabilities and that they are reliable in real-world manufacturing procedures.

Table 5: Carrageenan-induced paw edema: formulation effects

Treatm 4nt	**Paw volume (ml) upon delivery of carrageenan at different intervals**							
	1h		**2h**		**3 h**		**4h**	
	Mean± SEM	**%Inhibiti on**	**Meant ±SEM**	**%Inhibit ion**	**Mean±S EM**	**%Inhibitio n**	**Meant±S EM**	**%Inhibiti on**
Control	0.27+0. 0109	-	0.45+0. 08	-	0.8+0.01 0	-	0.74+0.0 63	-
F1	0.24+0. 0195	10.2	0.40+0. 02	13.7	0.50+0.0 45	15.35	0.73+0.0 87	7.59
F2	0.23+0. 042	13.8	0.45+0. 01	12.39	0.48+0.0 038	25.35	0.70+0.0 02	10.2
F3	0.22+0. 0091	19.49	0.29+0. 04	39.64	0.35+0.0 07*	46	0.40+0.0 12**	49.7
F4	0.22+0. 0099*	19.49	0.25+0. 02	50.09	0.27+0.0 59	58.65	0.33+0.0 085	60.2

F5	0.21+0.048*	23.2	0.19+0.07	54.23	0.25+0.008	59.65	0.29+0.009	65.17

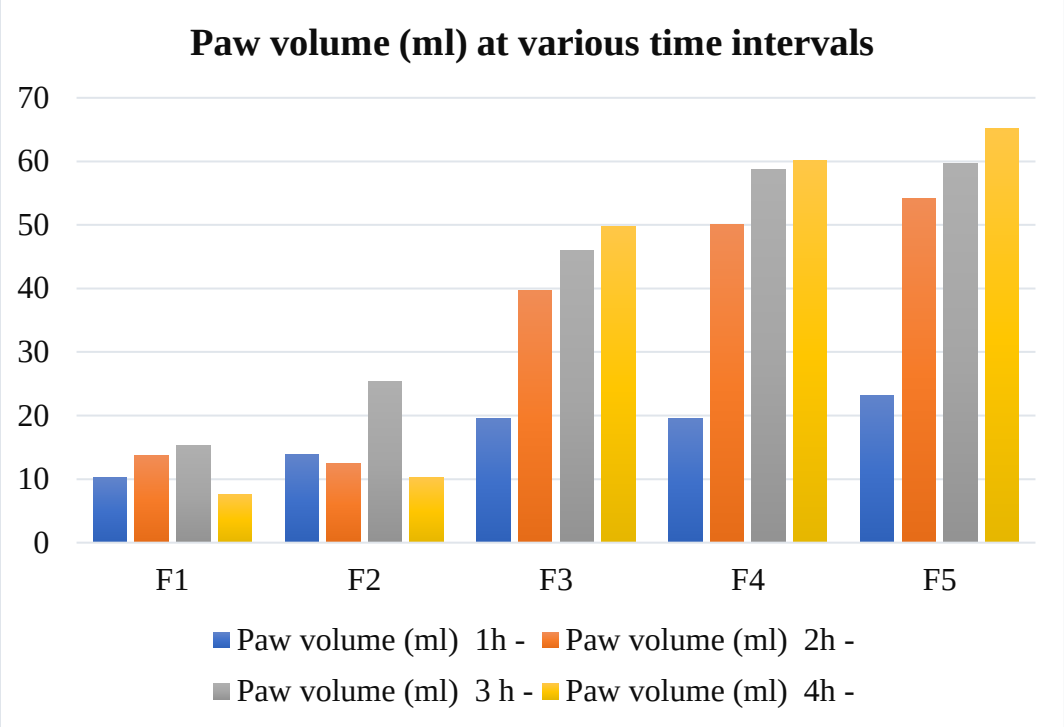

Figure 3: Paw edema caused by carrageenan: formulation effects

Data on the impact of different formulations on carrageenan-induced paw edema in rats are shown in Table 5, which shows data measured at various intervals (1, 2, 3, and 4 hours) following carrageenan administration. The mean paw volume in milliliters (ml) for each treatment (Control, F1, F2, F3, F4, F5) is displayed together with the standard error of the mean (SEM). For every formulation at every time interval, the % inhibition of edema is also provided, which shows how much anti-inflammatory action there is in comparison to the control group.

5. CONCLSUION

According to the findings of the study, the anti-inflammatory herbal gel formulations that were developed contain methanolic extracts of Emblica officinalis and Aegle marmelos. These formulations have also shown good potential. In a model of rat paw edema caused by carrageenan, formulations F3, F4, and F5 exhibited potent anti-inflammatory effects. This was established by rigorous examination. At four hours after delivery, the formulation F5 achieved the best efficacy, with a 65.17% suppression of edema. These formulations indicated significant inhibition of edema. Furthermore, the formulations exhibited desired physical features such as a great spread ability, viscosity, and pH stability, all of which are required for efficient topical application. These findings lend credence to the idea that herbal formulations should be investigated further as possible options for the management of inflammatory diseases. This opens up a viable path for natural and holistic treatment approaches in the medical field.

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