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FORMULATION AND CHARACTERIZATION OF POLYHERBAL ANTI-INFLAMMATORY GEL

Shivangi Gupta[1] and Dr. Megha[2]

1. P.G Scholar of Sirt Pharmacy, Sage University, Bhopal (Madhya Pradesh).
2. Associate Professor, Faculty of Sirt Pharmacy, Sage University, Bhopal (Madhya Pradesh).

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Abstract

According to the International Association for the Study of Pain, inflammation is the tissue's immunologic reaction to injury and is characterised by swelling, fluid buildup, and the mobilisation of white blood cells and antibodies. Natural treatments made from plants are called herbal medicines. Instead of eliciting a single molecule that interacts with a single target, they cause a coordinated pharmacological intervention of numerous compounds that interact with multiple targets. Using extracts of Curcuma amada, Piper nigrum, and Lodhra (Symplocos racemosa), menthol, and capsaicin, ten batches of polyherbal gel formulations were created. Formulations F1 through F5 were made with Carbopol 934, and Formulations F6 through F10 were made with HPMC K4M as the gelling agent. The developed formulations were assessed using a range of gel evaluation criteria, including pH determination and physical examination. Measurement of viscosity, washability, extrudability, spreadability, and in vitro diffusion studies. Spreadability of Formulation F2 was good, at 32.48±0.65 g/cm/sec. It was discovered that spreadability decreased when gelling agent concentrations (Carbopol 934 and HPMC K4M) increased. It was discovered that the extrudability of every polyherbal gel formulation ranged from 73.16% to 95.37%. The percentage of medication diffusion decreased as gelling agent concentration increased, according to the results. When compared to polyherbal formulations made with HPMC K4M, it was discovered that the components of formulations made with carbopol 934 were released more readily. The polyphenol content of the gel formulation is responsible for its in vitro anti-inflammatory effect. The stability of the F2 formulation was discovered. The developed formulation must be expanded on a pilot scale, and clinical studies are required to implement the successful introduction of a topical gel formulation including polyherbals for pain relief.

***Corresponding Author:** - **Shivangi Gupta**

Introduction: -

The traditional medical system makes use of several herbs belonging to the Zingiberaceae family. One plant in this family that has been used historically as a stomachic and carminative is curcuma amada, sometimes known as white turmeric [1]. An examination of the literature reveals that these rhizomes contain a variety of chemical

components. Nevertheless, there aren't many sources that assess the extract's pharmacological activity, which includes its carminative, stomachic, and central nervous system effects [2]. The extract demonstrated a substantial inhibitory impact on Aspergillus niger and Trichophyta rubrum, as well as a hypercholesteremic effect in rabbits. Empirical evidence supports the use of rhizomes as a domestic medicine for inflammatory diseases [3, 4]. Piper nigrum, or black pepper, is a member of the Piperaceae family. Native to India, the plants are grown in hot, humid climates [5]. In addition to being used as a spice, black pepper has medicinal properties and is sometimes combined with other well-known herbs and spices to create herbal treatments [6]. The primary physiologically active ingredient in piper nigrum is the pungent alkaloid piperine [7]. Symplocos racemosa (Symplocaceae), sometimes referred to as “Lodhra” or “Rodhra” in Sanskrit, is a tiny, evergreen tree that can grow up to six metres in height. It can be found in North and East India's plains and lower hills. [8]. The rough, dark grey bark is beneficial for liver problems, diabetes, fever, ulcers, diarrhoea, dysentery, and eye conditions [9]. According to research reports, it possesses antibacterial and anticancer properties and can be effective in treating gynaecological problems [10]. Menthol, sometimes known as "mint camphor," is a popularly accessible volatile oil extract that comes from the plant Mentha, which grows mint. Since ancient times, menthol has been applied topically to ease pain [11]. Chili peppers contain a substance called capsaicin, which gives them their fiery and irritating properties. Capsaicin causes pain in addition to the feeling of heat, which makes it a crucial tool for researching pain. One of the main ingredients in spicy peppers, capsaicin, was thought to have anti-inflammatory properties [12].

In the global health services system, these traditional medicines play a vital role. Opioids, also known as non-steroidal anti-inflammatory medicines, are commonly used to treat a variety of types of inflammation. However, they have serious adverse effects, including itching and redness. Therefore, it appears that looking for more advantageous options would be necessary. Gel formulations are preferred over other topical preparations and oral administration for drug delivery topically because they are simple to apply, extend contact time, and cause fewer side effects [13]. The goal of the current work was to create a polyherbal gel with anti-inflammatory properties in vitro.

Material And Methods:-

Materials:-

We bought dried Curcuma amada rhizomes, dried Piper nigrum fruits, and dried Lodhra (Symplocos racemosa) bark from the Nashik local market. Prof. Manohar Gulab Gavit of the Department of Botany at the MVPS KAANMS Arts, Commerce, and Science College in Nashik, Maharashtra, verified the authenticity of the plant materials. (Herbarium 3; Authentication No. KAANMS/2020-21/56). Naturite Agro Products Limited, Hyderabad, India, sent a free sample of capsaicin. We bought menthol from S. D. Fine Chemicals in Mumbai. We purchased HPMC K4M and carbopol 934 from N.R. Chem in Bombay. Analytical-grade compounds were employed for all other substances.

Methods:-

The process of making plant extract

In a prior study, the authors conducted and assessed methanolic extracts of black pepper (Piper nigrum) fruits (MEPN), white turmeric (Curcuma amada) rhizome (EECA), and lodhra (Symplocos racemosa) bark (MESR) for different phytochemical screenings. These extracts were used along with carbopol 934 and HPMC K4M as gelling agents to generate a polyherbal gel.

Formulation of Polyherbal Gel:

Preparation of gel base Schmolka et al.'s cold mechanical technique was used to create the gel base. To prevent agglomeration, carbopol 934/HPMC K4M was dissolved gradually and stirred in 60 mL of demineralized water for one hour. After that, 10 mL of demineralized water was used to dissolve triethanolamine and disodium edetate, and the mixture was agitated for ten minutes. For ten minutes, 4.83 ml of propylene glycol was stirred with 12 mL of demineralized water. Carbopol 934/HPMC K4M solution was mixed with triethanolamine solution and sodium edetate, and the mixture was stirred for ten minutes to bring the pH down to 7.4. Subsequently, a clear, uniform gel basis was created by adding propylene glycol solution and stirring for ten minutes [14].

Preparation of gel formulation

Ten formulations with varying extract concentrations (EECA, MEPN, and MESR) were made. Formulations F1 through F5 were made with Carbopol 934, and Formulations F6 through F10 were made with HPMC K4M as the gelling agent. (Table 1).

Drugs such as EECA, MEPN, MESR, menthol, and capsaicin were added to the gel base and stirred continuously until the drugs were fully dissolved. The aluminium collapsible tube was filled with the prepared gel and sealed. For the base control gel without the extract and additional active component, a similar process was used [14, 15, 16].

Evaluation of Polyherbal Topical Gel Physical Examination
After being packaged, each gel was visually inspected to ensure homogeneity. Their appearance and the existence of any aggregates were examined [17].

Determination of pH
Using a pH metre, the pH of each gel composition was determined. Before being used, the pH metre was calibrated using standard buffer solutions at pH 4, 7, and 9. The electrode was placed in the sample at room temperature for 10 minutes prior to obtaining the reading, and the pH was then recorded [18, 19, 20].

Viscosity Measurement
Using Brookfield's rheometer (R/S-CPS+ rheometer with C75-2 measurement system) at 30 rpm and room temperature (25±2°C), the viscosity of the gel formulations (0.5 g each) was measured [21].

Spreadability
The device, which was altered, is made up of a wooden block with a pulley at one end. On the block, a rectangular ground glass plate was mounted. Gel (around 2 grammes) was put on the bottom plate and sandwiched between the hook-equipped lower and upper glass plates, which were of the same size. To get a homogenous
gel film and to release any trapped air, a 500 mg weight was placed on top of each of the two plates for five minutes. Extra gel was removed with a scraper. A 50-gram pull was applied to the upper plate. The upper plate's needed time (in seconds) to travel
10 centimetres was recorded. The spreadability was determined using the subsequent formula. Spreadability is better when the time gap is shorter [22].
S = M x L/T, where M is the weight attached to the upper slide, L is the glass slide's
length, and T is the amount of time it takes for plates to travel the whole length (in seconds).

Extrudability
Standard-capped collapsible aluminium tubes were filled with the gel compositions, and the ends were crimped shut to seal. It was noted how much each tube weighed. The tubes were clamped after being positioned between two glass slides. After covering the slides with 0.5 g, the cap was taken off. Weighing was done on the amount of extruded gel that was collected. It was determined what the~~what~~ percentage of the extruded gel was [23, 24].

Grittiness
Every formulation was examined under a light microscope to determine whether any significant particle matter was present. Therefore, it is evident that the gel preparation satisfies the necessary conditions of being devoid of specific material and forming the requisite grittiness for any topical preparation [20, 24, 25, 26].

Washability
After applying formulations to the skin, the degree and simplicity of water washing were personally assessed [27].

In-vitro diffusion study
Using a traditional standard cylindrical tube that was made in the lab using a straightforward modification of a glass tube with an internal diameter of 15 mm and a height of 100 mm, the in-vitro diffusion of all polyherbal formulations and commercialised Diclofenac sodium gel 0.5% was investigated. A donor compartment was created by tying the commercial semi-permeable membrane cellophane, which had been presoaked overnight in the freshly made dissolving medium (phosphate buffer pH 6.8), to one end of an open cylinder that was open on both sides. One gramme of the polyherbal formulation was inserted into this slot. The membrane of the diffusion cell served as the corneal epithelium. All of the membrane's surface came into contact with the receptor compartment, which held 25 millilitres of phosphate buffer (pH 6.8) in a 100-milliliter beaker. A magnetic stirrer was used to continually swirl the contents of the receptor compartment, and a temperature of 37°

± 0.5°C was maintained. One millilitre of the sample (aliquot) was taken out of the receptor compartment and replaced with a new buffer solution at predetermined intervals. After making the necessary dilutions against reference using phosphate buffer pH 6.8 as a blank, the aliquot was examined for drug concentration using a UV-VIS spectrophotometer at a wavelength that was determined [14, 28].

Selection of Satisfactory Formulation of Polyherbal Gel

The selection of 10 polyherbal gel formulations was based on many factors, such as pH, viscosity, homogeneity, extrudability, washability, and homogeneity.

Evaluation of Satisfactory formulation Thixotropy Analysis

Using Brookfield's rheometer (R/S-CPS+ rheometer with C75-2 measuring system) at 30 rpm and room temperature (25±2°C), the viscosity of ordinary Lisinopril gel (0.5g) and Lisinopril ion-pair gel of the F2 formulation was evaluated [29].

Table 2:- Evaluation Of Polyherbal Gel.

Formulation	Consistency	Ph	Viscosity (Pa.S)	Spreadibility (g.cm/sec)	Homogeneity	Washability
F1	Fluid	6.22±0.13	4.86±0.89	45.58±1.56	Homogeneous	Excellent
F2	Semisolid	6.84±0.38	7.61±0.34	32.48±0.65	Homogeneous	Excellent
F3	Semisolid	6.35±0.43	8.97±0.66	24.73±1.08	Homogeneous	Good
F4	Semisolid	6.43±0.19	10.42±0.91	18.94±1.44	Homogeneous	Good
F5	Stiff	6.73±0.44	12.63±1.06	12.38±1.93	Homogeneous	Good
F6	Fluid	6.38±0.15	3.96±0.26	46.31±1.42	Homogeneous	Excellent
F7	Fluid	6.86±0.42	4.53±0.43	38.49±1.81	Homogeneous	Excellent
F8	Semisolid	6.72±0.39	6.73±1.28	31.92±1.33	Homogeneous	Good
F9	Semisolid	6.64±0.23	9.68±1.08	25.66±1.27	Homogeneous	Good
F10	Stiff	6.82±0.67	11.39±1.44	21.34±1.08	Homogeneous	Good

* All values represent mean ± standard deviation (n = 3)~~(n=3)~~

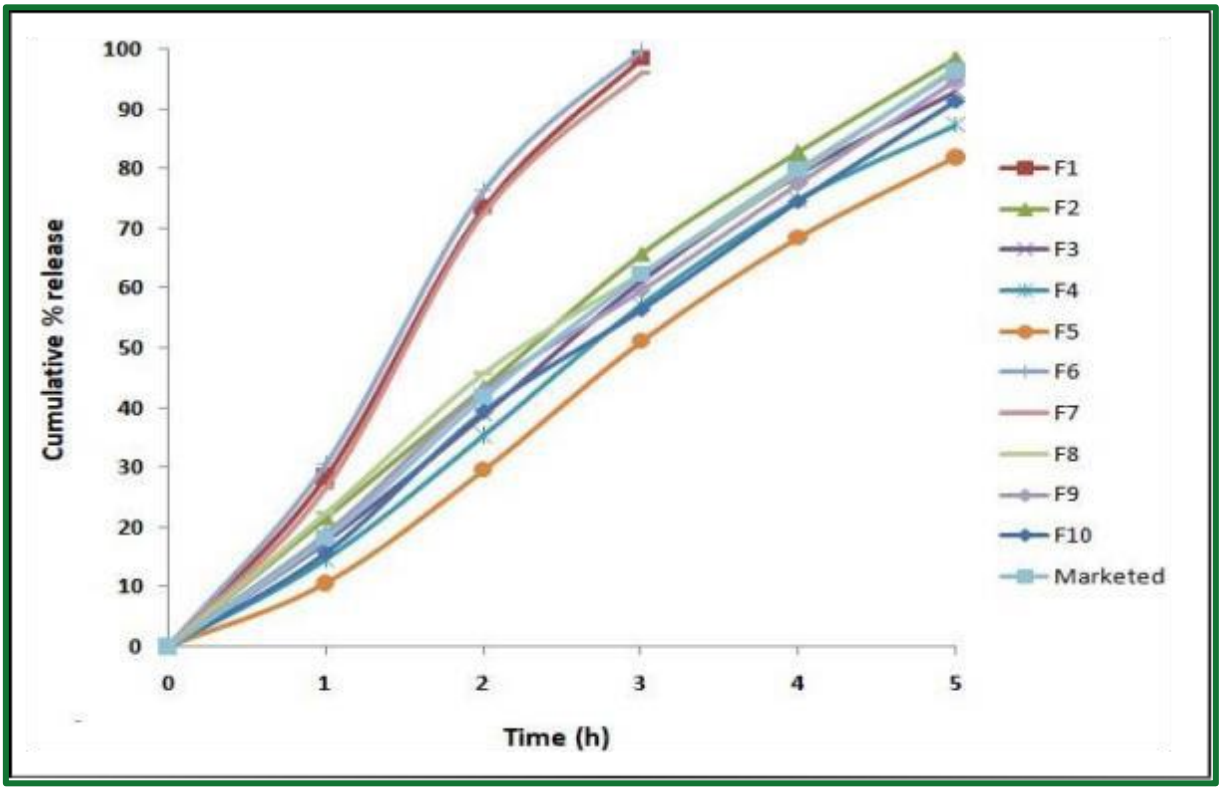

Fig. 1:- In-vitro diffusion study of polyherbal gel (F1 to F10) compared with marketed formulation Selection of Satisfactory Formulation of Polyherbal Gel.

Based on the pH, viscosity, spreadability, homogeneity, extrudability, washability, and in-vitro drug diffusion study, formulation F2, which contains 1% of carbopol 934, exhibits excellent washability, extrudability, and in-vitro diffusion, along with a homogenous formulation with pH 6.84±0.38 and viscosity 7.61±0.34 Pa.S. As a result, formulation F2 was chosen for additional assessment since it was thought to be the optimal formulation.

Evaluation of Satisfactory Formulation Thixotropy Analysis

A rheological analysis of the F2 formulation at~~in~~ 0.5 g was done. Table 3 summarises the findings. Figures 2 and 3 display the thixotropy analysis and viscosity diagram.

Skin irritation study/acute study/study/acute study/acutestudy/study/acutestudy/acutestudy/study/acutestudy/study/acutest udy/acutestudy/acuteicity

The skin-irritatingskin-irritatingskin-irritatingskin-irritatingskin-irritatingskin-irritatingskin impact of the developed polyherbal gel (F2 formulation) was assessed. The results of the skin irritation test show that the manufactured polyherbal gel was free of dermatological-dermatological reactions and ermatological reactions and did not cause irritation, redness, or edema upon application. Even after ten days of research, no erythema or edema was seen in the F2 formulations, suggesting that the polyherbal gel formulation was deemed safe.

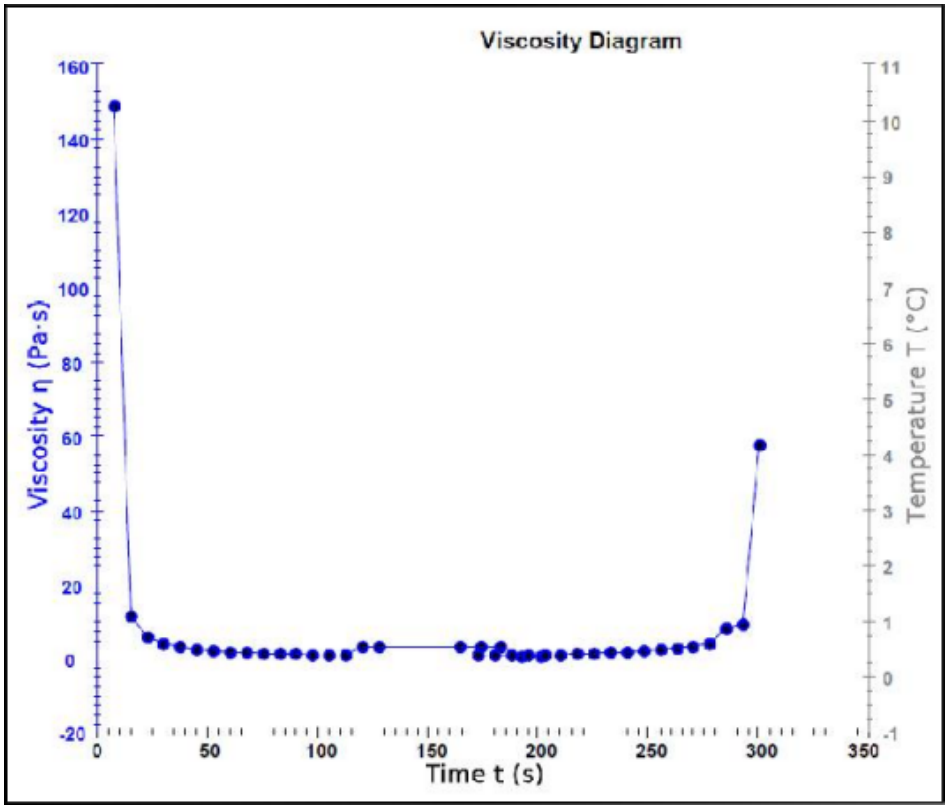

Fig. 2:- Viscosity diagram.

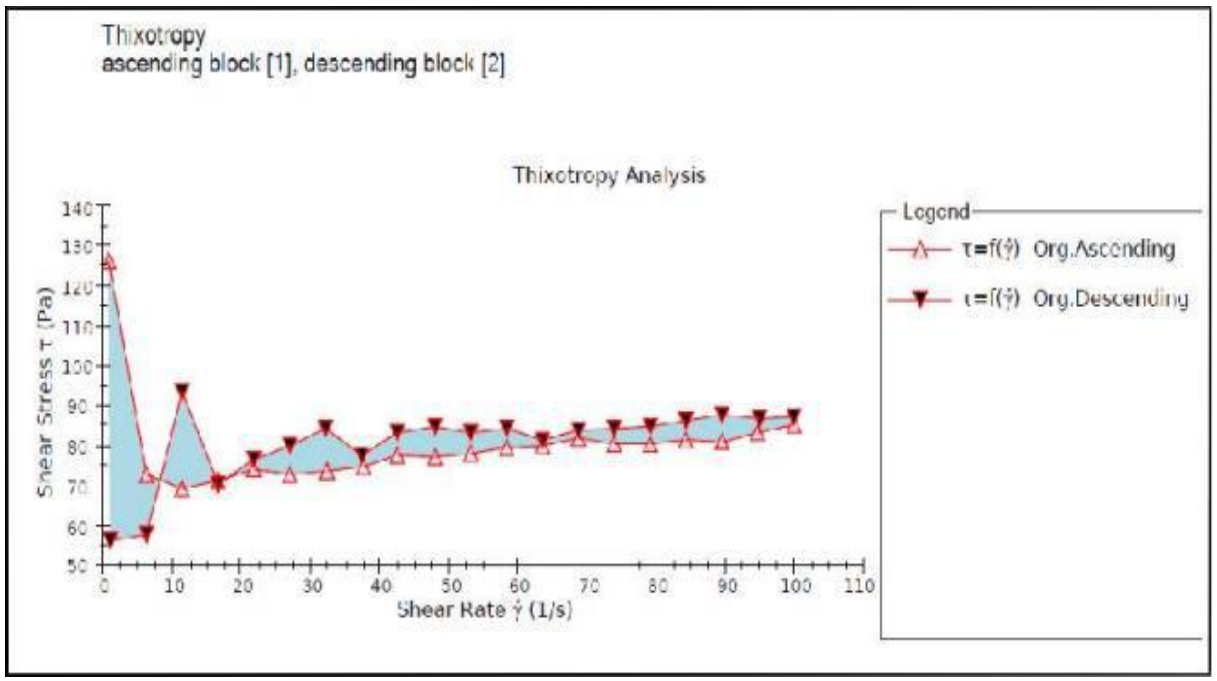

Fig. 3:- Thixotropy analysis.

Stability Studie

Stability studies were carried out in accordance with ICH recommendations on F2 formulation since it showed superior quality features in order to guarantee the quality of polyherbal gel formulation throughout its shelf life. Viscosity, pH, and homogeneity all showed negligible changes during 0, 1, 2, 3, and 6 months of stability testing. The study's findings unequivocally demonstrated the stability of the topical polyherbal gel F2.

In-vitro Anti-Inflammatory Inhibition of albumin denaturation

To explore the mechanism behind the anti-inflammatory action, the extract's capacity to prevent protein denaturation was assessed. This approach to assessing anti-inflammatory activity is easy to use and straightforward. The results of this study showed that the polyherbal gel formulation F2 and the reference drug Diclofenac sodium showed concentration-dependent suppression of protein denaturation in the range of 10–50 µg/ml. A maximum inhibition of

82.40% was noted at 50 µg/ml of the F2 formulation. At a concentration of 50 µg/ml, diclofenac sodium exhibited the highest level of inhibition, measuring 85.47%.

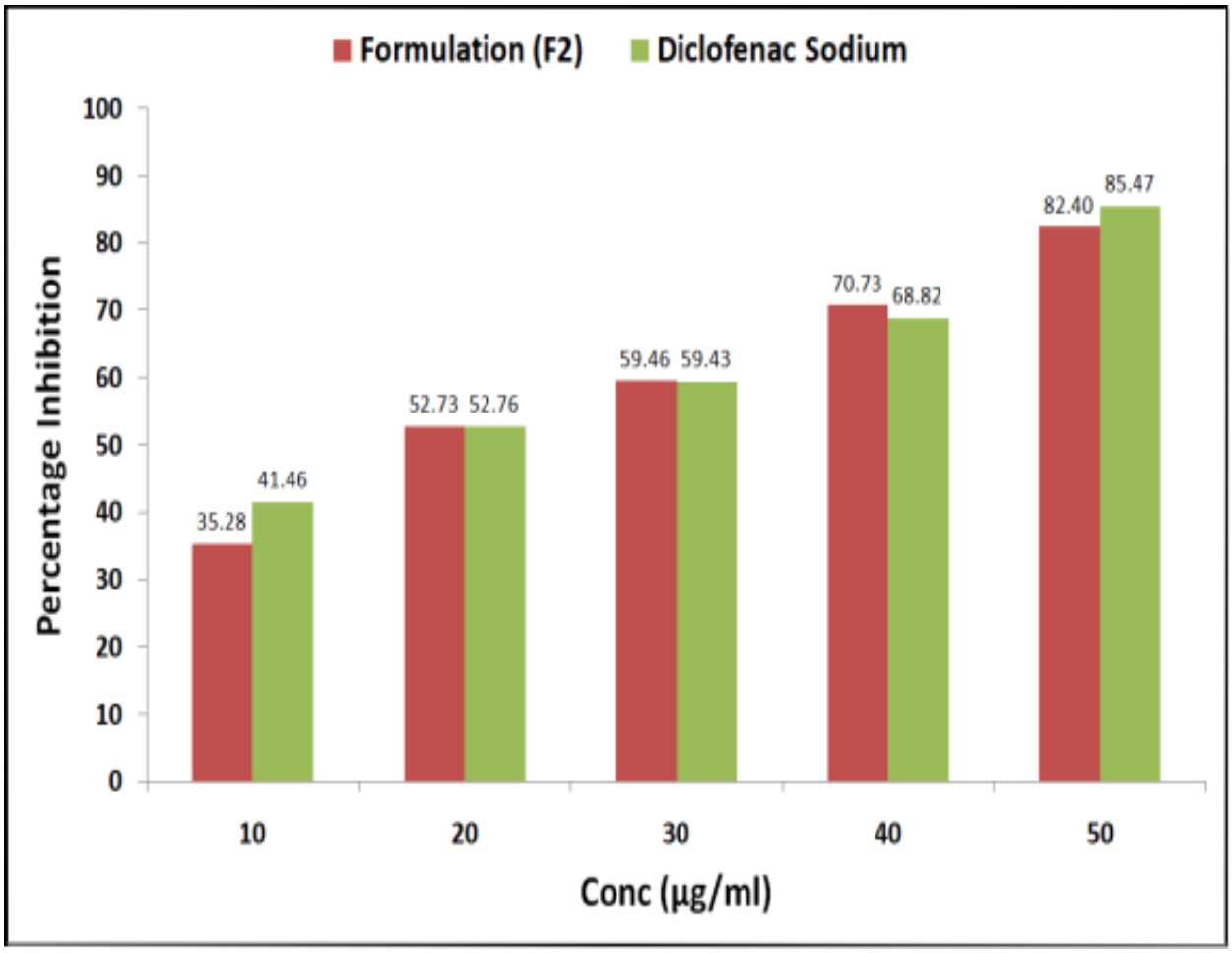

Fig. 4:- Effect of polyherbal formulation (F2) on heat-induced protein denaturation.

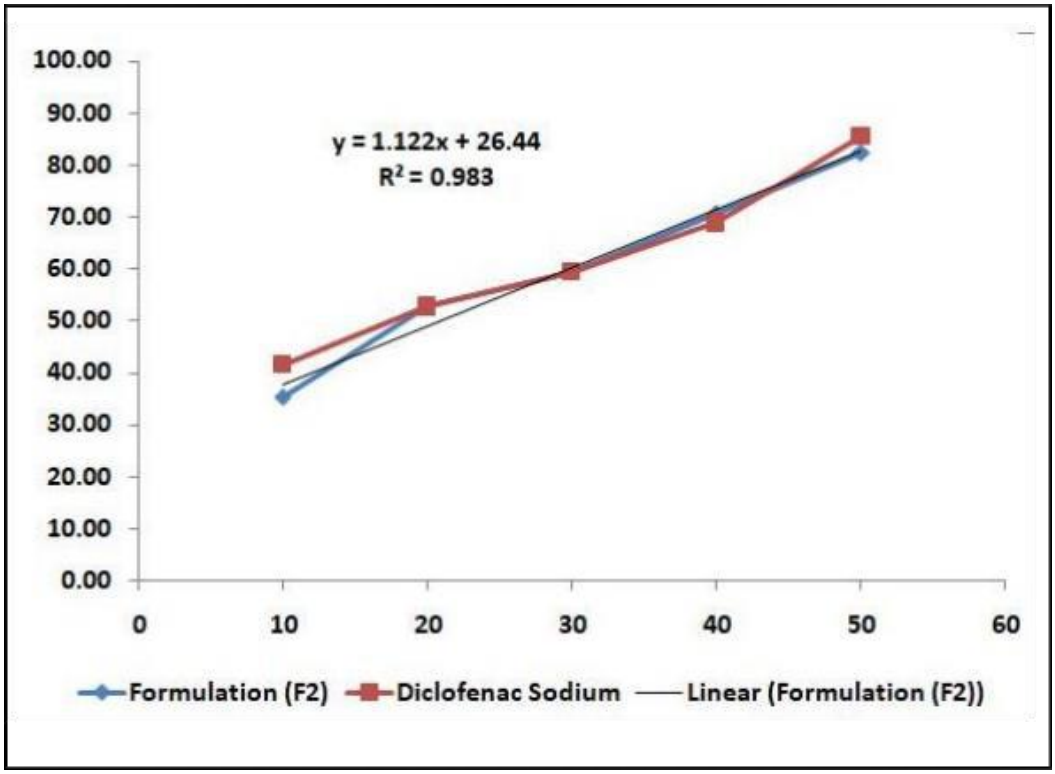

Fig. 5:- Correlation between % inhibition of formulation (F2) and Diclofenac sodium.

Conflict Of Interest

The writers affirm that there is no conflict of interest between them.

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