Research Article

Future Directions in Exploring the Synergistic Effects of *Coriandrum sativum*, *Mucuna pruriens*, and *Juglans nigra*: A Polyherbal Approach for the Treatment of Inflammation

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Abstract:

This recent study was focused to evaluate the inflammatory suppressant action of a polyherbal extract *in vivo*, isolate phytoconstituents from the most bioactive fraction, and assess their therapeutic potency. For acute inflammation, the carrageenan-induced paw edema model was employed, while chronic inflammation was assessed using the cotton pellet implantation method. A polyherbal formulation comprising *Coriandrum sativum* (stalk powder), *Mucuna pruriens* (seed powder), and *Juglans nigra* (fruit powder) was prepared to investigate its anti-inflammatory effects, highlighting on possible mechanisms of action. The anti-inflammatory effectiveness was further validated through biochemical parameters related to the inflammatory process. These plants, widely recognized in the Ayurvedic system, are well known for hepatoprotective, antimicrobial, anti-inflammatory, hypoglycemic, analgesic, and cardioprotective action. Results from the carrageenan model indicated peak anti-inflammatory activity at one- and four-hours post-injection, suggesting suppression of the early inflammatory phase mediated by histamine and serotonin. Additionally, the polyherbal extract significantly reduced granuloma formation in the cotton pellet model. Indomethacin (10 mg/kg) served as the standard drug. The methanolic polyherbal extract (PHE) at measures of 200 mg/kg and 400 mg/kg expressed significant ($p < 0.01$) antigranuloma effects, though less potent than indomethacin. The inhibition percentages were 30.8% and 37.1% for the 200 mg/kg and 400 mg/kg doses, subsequently,

approach to 66.1% for indomethacin. These findings support the anti-inflammatory potential of the formulation and highlight the need for further phytochemical investigations of the individual herbs.

Keywords: Herbal combination; Anti-inflammatory effects; Carrageenan experiment; Cotton pellets; Indomethacin; Anti-granuloma action.

1. Introduction

Inflammation is a complex systemic reaction of vascularized tissues of the entire body to harmful agents including pathogens, weakened cells, or irritants. It's a crucial component of the body's defence mechanism, aiming to extinguish the beginning cause of cell injury, discharge necrotic cells and tissues, and starts tissue repair. While fundamentally protective, uncontrolled or chronic inflammation can provide a platform for the pathogenesis of various diseases, includes arthritis, cardiovascular disorders, neurodegenerative conditions, and certain cancers. The inflammatory response involves a series of coordinated events, including vasodilation, increased vascular permeability, and the migration of leukocytes to the area of infection. Resident immune cells, such as macrophages, act as sentinels, orchestrating the activation and resolution of inflammation (Takagi, 2022). Conventional anti-inflammatory therapies, including non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids, often provide greater relief but are associated with unwanted effects upon prolonged use. As a result, there is increasing interest in exploring plant-based alternatives that offer therapeutic efficacy with improved safety profiles. Polyherbal formulations, derived from traditional medicine systems like Ayurveda, are being investigated for their synergistic potential and multi-targeted action in modulating inflammatory pathways (Havel, P. J. 2004). In the present study, a polyherbal extract composed of Coriandrum sativum (stalk), Mucuna pruriens (seeds), and Juglans nigra (fruit) was formulated and evaluated for its anti-inflammatory properties. These herbs are traditionally used for their antimicrobial, antioxidant, neuroprotective, and immunomodulatory activities. Coriandrum sativum exhibits broad-spectrum antimicrobial activity; Mucuna pruriens is rich in L-DOPA (3.2%–6%), a precursor to dopamine with known neuroprotective effects; and Juglans nigra is valued for its phytochemical richness, including essential fats, proteins, and antioxidants (Havel, P. J. 2004). This study aims to validate the preventive inflammatory potential of the formulation using both temporary and persistent inflammation models, and to support its mechanism of action through relevant biochemical and phytochemical evaluations.

Fig.1. Coriander sativum stalk.

Fig.2. Mucuna Pruriens.

Fig.3. Jugalance nigra fruit.

In the current research, a polyherbal formulation comprising *Coriandrum sativum* (stalk powder), *Mucuna pruriens* (seed powder), and *Juglans nigra* (fruit powder) was selected to evaluate its anti-inflammatory potential, with particular emphasis on its mechanism of action. The anti-inflammatory effects of the formulation were assessed in correlation with various biochemical parameters involved in the inflammatory process. These selected herbs are well-regarded in Ayurvedic system of medicine for the prevention of numerous conditions, particularly those involving inflammatory and oxidative stress pathways (Henery 1998). One of the key bioactive components contributing to the formulation's activity is L-DOPA (Levodopa)**,** known for its neuroprotective and anti-inflammatory properties. L-DOPA is notably present in significant quantities in *Mucuna pruriens* and is supported by complementary phytochemicals found in *Coriandrum sativum* and *Juglans nigra*, which further enhance the formulation's pharmacological profile. To validate inflammatory suppressants activity of the formulation, both temporary and persistent models were employed. The cotton pellet implantation model was utilized to evaluate chronic inflammation, and the results confirmed significant inhibition of granuloma formation, indicating suppression of proliferative inflammatory responses. For temporary inflammation, the carrageenan-induced paw edema model was utilized—a well-established method due to its reproducibility, sensitivity, and minimal systemic effects. Carrageenan is preferred as a phlogistic agent because it induces a biphasic inflammatory response without eliciting immune hypersensitivity, making it ideal for screening anti-inflammatory compounds. The outcomes of both models provide a comprehensive understanding of the formulation's efficacy and it is acts as a natural anti-inflammatory product (Hendrayani, S. F. et al., 2016).

2. Materials and Methods

Materials

The materials utilized for study were carefully selected to ensure the accuracy and reproducibility of the experimental procedures. The following were utilized during the investigation:

Plant Materials:

Coriandrum sativum (stalk powder), *Mucuna pruriens* (seed powder) and *Juglans nigra* (fruit powder) These plant materials were collected, authenticated, shade-dried, and powdered for formulation of the polyherbal extract (PHE).

Chemicals and Reagents:

Methanol (analytical grade) – used for extraction of phytochemicals., Carrageenan (1% w/v in normal saline) – used to induce acute inflammation., Indomethacin (standard drug, 10 mg/kg) – used as the reference anti-inflammatory agent., Normal saline – for preparation of reagents and vehicle control., Cotton pellets (20 mg each), for the chronic inflammation model., Distilled water – for reconstitution and dilution of test solutions.

Experimental Animals:

Healthy rats (wistar albino, 100–200 GM) of any sex was used, Animals were put up under suitable laboratory environment (12-hour light/dark cycle, temperature 22–25°C), with free access to food and water, and all animal procedures were executed in accordance with institutional ethical instructions. All the materials and equipment were provided by the School of Pharmacy, C.E.C., Bilaspur, and were of analytical and pharmacological grade suitable for biomedical research.

Experimental grouping of animals

- **Group I (Healthy Control):** Rats in this group received 10 mL/kg of vehicle only and served as the healthy control group.
- **Group II (Polyherbal Formulation – Low Dose):** Rats were received the polyherbal formulation at a measure of 200 mg/kg. This group was used as the initial experimental group to evaluate the formulation's effects at a lower dose.
- **Group III (Polyherbal Formulation – High Dose):** Rats received the polyherbal formulation at a measure of 400 mg/kg to assess the dose-dependent response of the formulation.
- **Group IV (Standard Control):** Rats were treated with Indomethacin at a measure of 10 mg/kg, serving as the reference standard for prevention from inflammation.

Acute Anti-Inflammatory Investigation Using Carrageenan
Principle

Inflammation is a protective tissue response to injury, infection, or external stimuli and forms a critical component of the body’s immune defence system. However, excessive or uncontrolled inflammation can lead to pathological conditions. The aging process and various chronic diseases are often linked to low-grade inflammation. Key mediators involved in inflammatory responses include histamine, bradykinin, and prostaglandins, which regulate vascular permeability and immune cell recruitment. Non-narcotic analgesics (NSAIDs) have therapeutically proven for the investigation of inflammation-related conditions just like arthritis, owing to their ability to arresting the production of these inflammatory mediators. The carrageenan-induced paw oedema model is a widely accepted and reproducible method for evaluating the acute anti-inflammatory potential of test substances. Carrageenan, a sulphated polysaccharide extracted from red algae (*Rhodophyceae*), induces inflammation through a biphasic mechanism: an initial phase mediated by histamine and serotonin, followed by a later phase involving bradykinin and prostaglandin release (Kulkarni, 1999).

Reagent Composition

- **Carrageenan Suspension:** 1% w/v carrageenan prepared in normal saline for induction of inflammation.
- **Standard Drug Solution:** Indomethacin prepared for most convenient route of administration at a measure of 10 mg/kg body weight.

Procedure

An acute anti-inflammatory effect of the polyherbal formulation was evaluated in Wistar rats (100–150 g), which were informally divided into four groups (n=6 per group). The groups received the following treatments orally:

- Group I: Vehicle (10 mL/kg) – Healthy control
- Group II: Polyherbal extract at 200 mg/kg (oral)
- Group III: Polyherbal extract at 400 mg/kg (oral)
- Group IV: Indomethacin 10 mg/kg (Standard reference drug)

Thirty minutes after oral administration, acute inflammation was induced by injecting 0.1 mL of freshly prepared 1% carrageenan suspension into the sub plantar region of the right hind paw of each rat (Winter et al., 1962). Paw thickness was measured using a digital vernier calliper at 1-, 2-, 3-, and 4-hours post-injection to assess the degree of paw oedema (Mani Vasudevan et al., 2006). The reduction in paw oedema in treated groups compared to the control group was measured as anti-inflammatory activity.

Chronic Anti-Inflammatory Investigation Utilizing Cotton Pellet Implantation in Rodents

Principle

Chronic inflammation can be experimentally modelled by inducing granuloma formation through the subcutaneous implantation of sterile cotton pellets in rats. Over time, a proliferative response occurs at the site of implantation, characterized by infiltration of inflammatory cells, formation of granulation tissue, and connective tissue development. This model enables the evaluation of the anti-proliferative phase of inflammation. The degree of inflammation is quantified by measuring the dry weight of the pellets post-extraction, which reflects the amount of newly formed connective tissue (Gerhard Vogel, 2002).

Reagent Composition

- **A. Cotton Pellets:** Sterile cotton pellets, each weighing approximately 20 mg, used for implantation.
- **B. Standard Drug:** Indomethacin, prepared for oral standard remedy at a measure of 10 mg/kg body weight.

Procedure

Wistar rats weighing between 150 and 200 grams were anesthetized for the procedure. Four sterilized cotton pellets (each ~20 mg) were subcutaneously implanted—two in the axillary region and two in the groin—following the method described by D'Arcy et al. (1960). The animals were divided into the following treatment groups (n=6 per group):

- Group I: Control group receiving vehicle (10 mL/kg)
- Group II: Polyherbal extract at 200 mg/kg (oral)
- Group III: Polyherbal extract at 400 mg/kg (oral)
- Group IV: Indomethacin at 10 mg/kg (oral standard drug)

On the designated endpoint, the implanted cotton pellets were surgically drawn out, washed superfluous tissue, and dried overnight at 60°C to constant weight. The weight of dried cotton pellets was recorded to assess the extent of granuloma formation. The percentage inhibition of granuloma tissue formation was calculated in comparison with control group. Results were tabulated and visualized using appropriate graphs and charts.

Statistical Evaluation

Data were represented as mean ± standard deviation (SD). Statistical analysis was performed using one-way Analysis of Variance (ANOVA) followed by Dunnett's multiple comparison test. A p-value of <0.05, <0.01, or <0.001 was considered statistically significant. Analysis was conducted using GraphPad Prism software (version 5.00).

3. Results

A remarkable, dose-dependent depletion in carrageenan-induced paw edema was observed, following oral regulation of the polyherbal extract at measure of 200 mg/kg and 400 mg/kg, as well as the reference drug, indomethacin, at 10 mg/kg. The anti-inflammatory response was evaluated over a 4-hour period, with results summarized in Table 1. The methanolic extract of the selected herbal formulation was found a notable reduction in the inflammation against carrageenan-induced paw oedema in rats. This model serves as a reliable and well-established method for assessing acute inflammation due to its reproducibility and clear biphasic response. Carrageenan acts as a powerful phlogistic medicament, inducing tenderness through the release of inflammatory mediators without inducing significant systemic or immunogenic side effects. The inflammatory reaction was induced by carrageenan through a biphasic mechanism. The initial phase (within the first hour) is primarily mediated by the release of histamine, serotonin, and kinins, while the late phase (after the first hour) is associated with the production of prostaglandins and other slow-reacting substances. In the present study, the extract showed maximum inhibition of oedema formation at both the 1-hour and 4-hour intervals post-carrageenan injection, indicating suppression of both early and late inflammatory mediators.

In the chronic inflammation model, results are presented in Table 2, where the inhibitory effect of the polyherbal extract on granuloma formation induced by cotton pellet implantation was assessed. The methanolic extract at doses of 200 mg/kg and 400 mg/kg significantly reduced granuloma tissue formation in rats, although its effect was comparatively lower than the standard drug indomethacin.

- The percentage inhibition of granuloma formation was:
  1. 30.8% at 200 mg/kg,

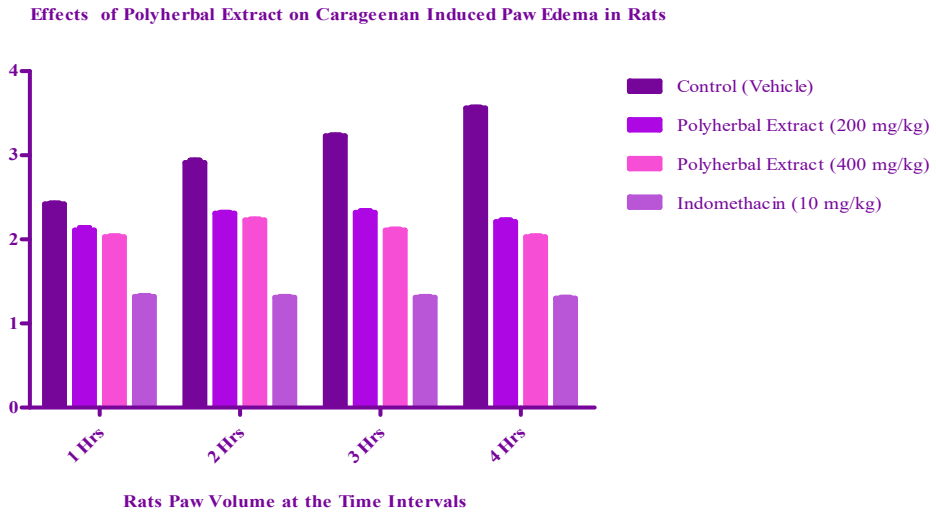
2. 37.2% at 400 mg/kg, and
3. 66.2% with indomethacin (10 mg/kg).

The data confirm that the polyherbal formulation exhibited dose-dependent anti-proliferative effects during the granulomatous phase of inflammation. This suggests that the extract plays a role in modulating the proliferative events involved in chronic inflammation, such as fibroblast proliferation, connective tissue formation, and infiltration of inflammatory cells. Chronic inflammation is typically characterized by fibroblast activation, neutrophil infiltration, and exudation of fluids, leading to granuloma formation. In the current study, the polyherbal extract effectively suppressed these processes, demonstrating its therapeutic potential in chronic inflammatory conditions. The observed anti-inflammatory activity can be attributed to the formulation's ability to inhibit cellular proliferation and reduce fibroblast activity, both of which are central to granuloma development (Selye, 1949; Gupta et al., 2003).

Table 1. Effect of PHE on Carrageenan Induced Paw Edema in Rats.

Treatment	Percentage of Inflammation at Different Time Intervals:			
	1 (HRS)	2 (HRS)	3 (HRS)	4 (HRS)
Control (Vehicle)	2.42 ± 0.01	2.91 ± 0.03	3.23 ± 0.01	3.56 ± 0.01
Polyherbal Extract (PHE) – 200 mg/kg	2.11 ± 0.03**	2.31 ± 0.01**	2.32 ± 0.02**	2.21 ± 0.02**
Polyherbal Extract (PHE) – 400 mg/kg	2.03 ± 0.01 **	2.23 ± 0.01**	2.11 ± 0.01**	2.03 ± 0.01**
Indomethacin – 10 mg/kg	1.32 ± 0.01**	1.31 ± 0.01**	1.31 ± 0.01**	1.30 ± 0.01**

The data were represented as mean ± standard deviation (SD) (n = 6). **p < 0.01** showed statistically significant differences compared to Control group.

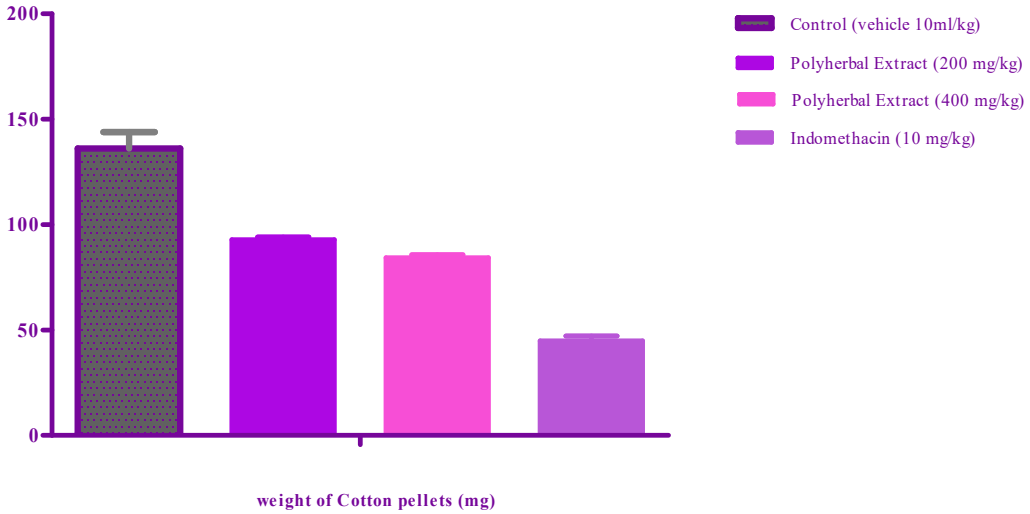


Graph 1. Effects of Polyherbal Extract on Carageenan Induced Paw Edema in Rats.

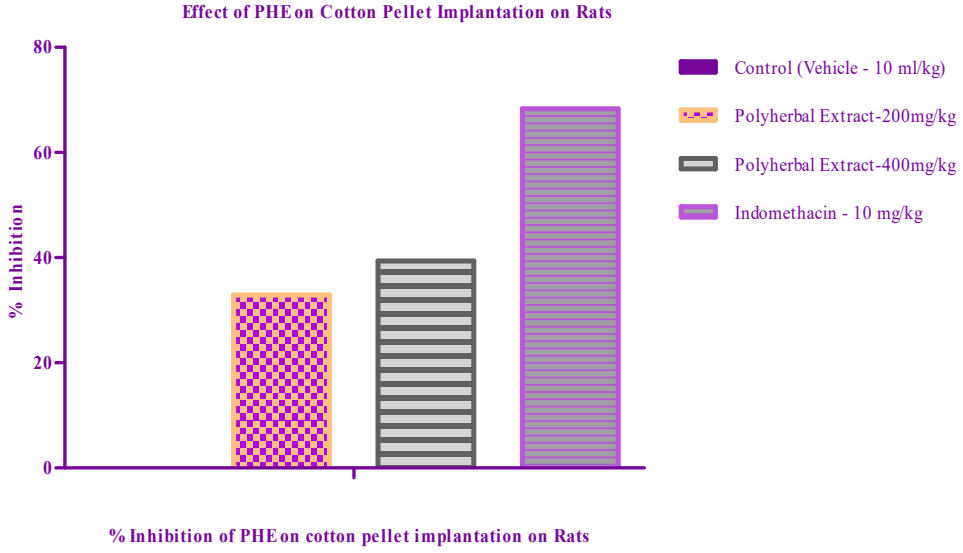
Table 2. Effect of PHE on Cotton Pellet Implantation in Rats.

Treatment group	Cotton pellet weight (mg)	Inhibition (%)
Control (Vehicle – 10 mL/kg)	135.35 ± 5.81	-
Polyherbal Extract (PHE) – 200 mg/kg	90.84 ± 2.50**	**32.88 %**
Polyherbal Extract (PHE) – 400 mg/kg	82.10 ± 4.26**	**39.34 %**
Indomethacin – 10 mg/kg	42.90 ± 2.57**	**68.30 %**

The data were represented as mean ± standard deviation (SD) (n = 6). Percentage of inflammation was statistically significant different from the Control group $p<0.01$.



Graph 2. Effect of PHE on Cotton Pellet implantation on Rats.



Graph 3. Inhibition (%) of PHE on Cotton Pellet implantation on Rats.

4. Discussion

The recent study was primarily focused on evaluating the anti-inflammatory activity of selected herbs and their polyherbal formulation (PHE), consisting of Coriandrum sativum stalk powder, Mucuna

pruriens seed powder, and Juglans nigra fruit powder. Various concentrations of the polyherbal extract were subjected to phytochemical evaluation, revealing that the methanolic extract contained a comprehensive bioactive compound, including carbohydrates, proteins, alkaloids, tannins, saponins, flavonoids, and coumarins. These phytochemicals are likely look after for the observed potency of the prepared drug in the study. During this research, two experimental models were adopted to assess the inflammatory suppressants of the polyherbal formulation. The first model, the Acute Anti-Inflammatory Investigation Using Carrageenan, involved the administration of a 1% carrageenan suspension in normal saline to induce paw edema in rats. The results indicated that polyherbal extract, at measure of 200 mg/kg and 400 mg/kg, exhibited remarkable anti-inflammatory activity, as evidenced by reduced edema formation over a four-hour period. The inflammatory suppressants action was identical to the standard drug, Indomethacin (10 mg/kg). Carrageenan-promoted paw edema is a broadly accepted model for acute inflammation studies due to its reproducibility and the fact that carrageenan is a non-antigenic agent with minimal systemic effects. The results of this model confirmed the polyherbal formulation's potential in mitigating inflammation by suppressing both early and late inflammatory mediators. The second model, the chronic anti-inflammatory investigation using cotton pellet implantation in rodents, focused to investigate the anti-inflammatory effects of the polyherbal formulation in chronic inflammation. In this model, 20 mg weighted sterilized cotton pellets were implanted subcutaneously in each rat to induce granuloma formation. Oral administration of the standard drug, Indomethacin (10 mg/kg), and the polyherbal extract at 200 mg/kg and 400 mg/kg doses resulted in a notable reduction in granuloma formation, with the polyherbal formulation showing dose-dependent inhibition. The results indicated a 30.8% inhibition at 200 mg/kg and 37.2% inhibition at 400 mg/kg, compared to a 66.2% inhibition with indomethacin. Although the polyherbal formulation was less effective than indomethacin, it still demonstrated considerable anti-granuloma activity, indicates its potential against in chronic inflammatory conditions. These findings indicate that the polyherbal formulation, particularly the methanolic extract, exhibits significant anti-inflammatory activity, which is dose-dependent. The formulation appears to be most effective during the proliferative phase of the inflammatory response, as evidenced by its inhibition of granuloma formation and fibroblast proliferation. This study highlights the potential therapeutic value of the polyherbal formulation in both acute and chronic inflammation, warranting further investigation into its clinical applications.

5. Conclusion

The investigation successfully evaluated the inflammatory suppressants effects with polyherbal formulation consisting of Coriandrum sativum stalk powder, Mucuna pruriens seed powder, and Juglans nigra fruit powder. The research highlighted the significant anti-inflammatory potential of these selected herbs, particularly their ability to modulate inflammatory pathways and mediators. Through two established experimental models—the Acute Anti-Inflammatory Investigation Using Carrageenan and the Chronic Anti-Inflammatory Investigation Utilizing Cotton Pellet Implantation in Rodents—the formulation demonstrated promising anti-inflammatory efficacy. The Acute Anti-Inflammatory

Investigation revealed that the polyherbal formulation, particularly at measure of 200 mg/kg and 400 mg/kg, exhibited a notable depletion in carrageenan-induced paw oedema, a hallmark of temporary inflammation. The results indicated a dose-dependent anti-inflammatory response, comparable to the effects of the standard drug Indomethacin. This experiment corroborates the potential of the formulation to reduce both early and late inflammatory responses, highlighting its mechanism of action in inhibiting histamine, serotonin, bradykinin, and prostaglandins. In the Chronic Anti-Inflammatory Investigation, the polyherbal formulation also demonstrated significant anti-granuloma action in the cotton pellet implantation model. The suppression of granuloma formation and the suppression of fibroblast proliferation indicated that the formulation effectively interferes with the chronic inflammatory process. Although less potent than Indomethacin, the formulation exhibited substantial suppression at measure of 200 mg/kg and 400 mg/kg, further emphasizing its potency as an effective medicament for chronic inflammatory state. This polyherbal formulation's anti-inflammatory properties can be attributed to the diverse biochemical constituents present in Coriandrum sativum, Mucuna pruriens, and Juglans nigra. These plants are eminent in the integrative medicines for their therapeutic benefits, particularly in treating inflammatory disorders. The chemical profiles of the selected herbs, including alkaloids, flavonoids, tannins, saponins, and coumarins, likely contribute to the observed effects. However, further exploration of the specific chemical constituents responsible for these activities is essential to acknowledge its mechanism of action and optimize the formulation for clinical applications. In conclusion, the polyherbal formulation of Coriandrum sativum, Mucuna pruriens, and Juglans nigra presents a promising natural alternative for the management of inflammation. The observed anti-inflammatory effects in both temporary and persistent models support its powerfulness as a therapeutic agent in the treatment of inflammatory conditions. Particular research work was based in isolation and identification of an active compounds, as well as clinical trials to confirm its potency and safety for human use.

Conflict of Interest

The researcher proclaim that they have no known competing financial conflicts of interests or bond relationships that could have shown to influence the work reported in this paper.

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