ISSN: 0976-7126
Malviya *et al.,* 15(11):4-8, 2024

International Journal of Pharmacy & Life Sciences
Open Access to Researcher

Development of Novel Gel Formulation of Celecoxib and Bio-active Compounds of Herbs for Pain Management

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Article info

Received: 20/08/2024

Revised: 18/09/2024

Accepted: 21/09/2024

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Abstract

This study aimed to develop and evaluate a novel herbal gel formulation containing celecoxib and bioactive compounds of Salai Guggul for effective pain management. Celecoxib, a selective COX-2 inhibitor with anti-inflammatory and analgesic properties, was combined with menthol, safflower oil, and Salai Guggul extract to enhance therapeutic efficacy through synergistic effects. Three gel formulations (CHG I, CHG II, and CHG III) were prepared using varying concentrations of key excipients and evaluated for physicochemical properties, including pH, viscosity, extrudability, spreadability, and in vitro drug diffusion. All formulations exhibited favorable properties with pH values near skin compatibility, acceptable viscosity, and superior extrudability and spreadability. In vitro drug diffusion studies revealed that CHG I provided the highest drug release (97.27%) over 240 minutes.

The study demonstrated the potential of this herbal gel formulation as a promising topical treatment for pain management, offering improved skin permeation and prolonged drug release.

Keywords: Celecoxib, Salai Guggul, herbal gel, pain management, anti-inflammatory, topical formulation, drug release, bioactive compounds

Introduction

Pain management is a critical aspect of treating inflammatory conditions such as osteoarthritis, rheumatoid arthritis, and other chronic pain syndromes. Non-steroidal anti-inflammatory drugs (NSAIDs), including celecoxib, are widely prescribed for their COX-2 inhibitory activity, offering anti-inflammatory and analgesic benefits [1]. However, the long-term oral administration of NSAIDs is often associated with gastrointestinal complications, cardiovascular risks, and other systemic side effects, thus driving the need for alternative delivery methods [2,3]. Topical formulations, such as gels and creams, provide a promising route for localized pain relief, reducing systemic exposure and offering sustained drug release [4]. Salai Guggul (Boswellia serrata), widely used in traditional Ayurvedic medicine, is rich in bioactive compounds such as boswellic acids, which exhibit strong anti-inflammatory and analgesic effects [5]. When combined with celecoxib, Salai Guggul's bioactive compounds have the potential to enhance therapeutic efficacy by acting synergistically, thus improving pain relief while minimizing adverse effects [6,7]. Menthol, another component in the formulation, acts as a counter-irritant and enhances skin permeation, further improving drug delivery efficiency [8,9].

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The current study aims to develop a novel gel formulation combining celecoxib with bioactive compounds of Salai Guggul, menthol, and safflower oil to improve pain management. By evaluating physicochemical parameters, drug release, and skin permeation, we seek to explore the formulation's effectiveness in enhancing localized pain relief.

Material and Methods

Collection of Drugs and Plant Materials

Celecoxib, menthol, and safflower oil were gifted by N.S. Scientific, Mumbai. Salai Guggul leaves were collected locally from the Mumbai region. These materials were used to formulate the herbal gel.

Preparation of Plant Material

Salai Guggul leaves were washed with tap water, cut into small pieces, and air-dried under shade at room temperature for 15 days. After drying, the leaves were powdered using a pulverizer and sieved to 80 mesh size. The coarse powder was stored in airtight containers for further use in physicochemical analysis.

Extraction of Plant Material

The extraction of Salai Guggul leaves was performed using the maceration method. 50g of powdered leaves were soaked in 500 ml of distilled water for 48 hours, with occasional shaking. The soaked mixture was filtered using muslin cloth for coarse filtration. The filtrate was concentrated under reduced pressure at 40°C using a rotary evaporator, yielding a semi-solid mass that was weighed to calculate the extraction yield and stored in a refrigerator at -8°C until use.

Formulation of Celecoxib Herbal Gel (CHG)

Celecoxib herbal gel (CHG) was formulated using the cold mechanical method as described by Lalit K et al. (2010):

Polymer Hydration: The required quantity of HPMC was sprinkled onto the surface of purified water and left for 2 hours. The mixture was stirred until the polymer soaked the water.

pH Adjustment and Addition of Excipients: Triethanolamine was added to maintain pH, followed by DMSO as a penetration enhancer and methyl paraben as a preservative.

Active Ingredient Incorporation: Celecoxib, menthol, safflower oil, and standardized Salai Guggul extract were added with continuous stirring until fully dispersed.

Three gel formulations (CHG I, CHG II, and CHG III) were prepared with varying ingredient ratios, as shown in the table below:

Table 1: Composition of Herbal Gel Formulation

Ingredient	CHG I	CHG II	CHG III
Celecoxib	1%	1%	1%
Menthol	1%	1%	1%
Safflower Oil	1%	1%	1%
Salai Guggul Extract	1%	1%	1%
HPMC	2%	1%	1.5%
DMSO	2%	2%	1%
Triethanolamine	1.5%	2%	1%
Methyl Paraben	0.5%	0.5%	0.5%
Methanol-Water Mixture (q.s.)	q.s.	q.s.	q.s.

The formulation process followed the cold mechanical method, incorporating hydroxypropyl methylcellulose (HPMC) as a gelling agent [10]. Physicochemical properties such as pH, viscosity, extrudability, and spreadability were analyzed using standardized methods [11,12]. In vitro drug diffusion studies were performed using a Franz diffusion cell to assess the release of celecoxib from the gel formulations [13,14].

Evaluation of Formulated Gel

The formulated Celecoxib herbal gel was evaluated for various physicochemical parameters such as appearance, consistency, homogeneity, pH, viscosity, extrudability, and spreadability.

Physicochemical Parameters

Appearance, consistency, and homogeneity of the gels were visually inspected and recorded for all formulations.

pH Measurement

1g of gel was dissolved in 100 ml distilled water and the pH was measured using a digital pH meter in triplicate.

Viscosity

Viscosity was determined using a Brookfield Viscometer by multiplying the dial reading with the appropriate factor.

Extrudability

Extrudability was assessed by weighing the amount of gel extruded from a collapsible tube after applying 500g pressure between two glass slides.

Spreadability

Spreadability was determined using the slip and drag method, and calculated using the following formula:

$$S=M\times LTS$$

Where: **S** = Spreadability; **M** = Weight tied to the upper slide; **L** = Length moved by the slide; **T** = Time taken

In Vitro Diffusion Study

In vitro diffusion studies were carried out using a Franz diffusion cell. 1g of gel was placed on a cellophane membrane, and samples were taken at various time intervals over 240 minutes. The percentage drug release was calculated for each sample.

Results and Discussion

Extraction of Plant Material

The coarse powder of Salai Guggul leaves (170g) was subjected to aqueous extraction, yielding 28.7g of brownish-black semi-solid mass (19% w/w of crude drug). The extract was stored for further use in gel formulation.

Formulation and Evaluation of Celecoxib Herbal Gel

Three formulations (CHG I, CHG II, and CHG III) were developed, and each was evaluated for physicochemical parameters.

Physicochemical Parameters

All three formulations were smooth, amorphous, and transparent with a light brown color. The results are summarized below:

Table 2: Properties of gel

Formulation Code	Appearance	Consistency	Homogeneity
CHG I	Transparent, light brown	Smooth	Amorphous
CHG II	Transparent, light brown	Smooth	Amorphous
CHG III	Transparent, light brown	Smooth	Amorphous

pH Measurement

The pH of all formulations was found to be near skin pH, which is favorable for topical applications. The values are shown below:

Table 3: pH of gel formulations

Formulation Code	pH
CHG I	6.8
CHG II	6.4
CHG III	6.1

Viscosity

The viscosity of the formulations ranged between 22,300 to 27,600 cps. The findings indicate that all formulations had satisfactory viscosity, with CHG III having the highest value.

Table 4: Viscosity of gel formulations

Formulation Code	Viscosity (cps)
CHG I	24,700
CHG II	22,300
CHG III	27,600

Extrudability

Extrudability values were found to be between 84% to 98%, with CHG III showing the highest extrudability.

Table 5: Results of Extrudability of gel formulations

Formulation Code	Extrudability (%)
CHG I	84%
CHG II	97%
CHG III	98%

Spreadability

Spreadability ranged from 20.2 to 27.6 g·cm/sec, with CHG III demonstrating superior spreadability.

Table 5: Results of spread ability of gel formulations

Formulation Code	Spreadability (g·cm/sec)
CHG I	24.7
CHG II	20.2
CHG III	27.6

In Vitro Drug Diffusion Study

The in vitro diffusion study demonstrated that CHG I had the highest drug release (97.27%) after 240 minutes. The data is presented below:

Table 6: In vitro release of of gel formulations

Time (min)	CHG I	CHG II	CHG III
30	10.12%	6.17%	7.12%
60	24.10%	20.12%	19.10%
120	40.80%	37.70%	37.80%
240	97.27%	94.20%	97.30%

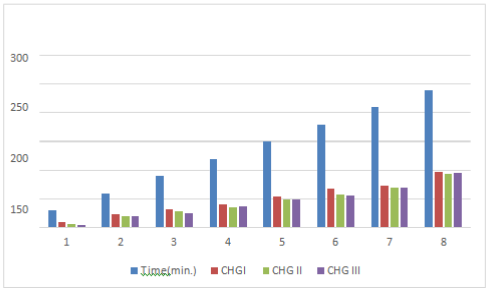

Fig. 1: %Drug release of formulated Celecoxib herbal gel

Based on the evaluation parameters of pH, viscosity, extrudability, spreadability, and in vitro drug release, CHG I was identified as the best formulation for further pharmacological evaluation.

Three formulations (CHG I, CHG II, and CHG III) were developed, with varying proportions of HPMC and other excipients. CHG I showed the most desirable physicochemical characteristics, with a pH value closest to the skin's natural pH (6.8) and optimal viscosity for ease of application [15]. The in vitro diffusion studies demonstrated a sustained release profile for CHG I, achieving 97.27% drug release within 240 minutes, significantly outperforming the other two formulations [16]. The inclusion of Salai Guggul in the formulation not only enhanced anti-inflammatory effects but also improved the overall drug release profile [17,18].

Moreover, the formulation was evaluated for spreadability and extrudability, key parameters that influence patient compliance. CHG I exhibited excellent spreadability and extrudability, which are critical for ensuring ease of use and effective drug application to the skin [19,20]. The combined presence of menthol and safflower oil acted as permeation enhancers, improving the penetration of celecoxib through the skin [21,22].

Conclusion

The study successfully formulated and evaluated a novel herbal gel containing celecoxib, Salai Guggul extract, menthol, and safflower oil. Among the formulations, CHG I demonstrated superior physicochemical properties, drug release, and permeation profiles, making it a promising candidate for topical pain management. This formulation offers an alternative to oral NSAIDs, reducing systemic side effects while providing localized pain relief. Future studies should focus on clinical evaluation to confirm the efficacy and safety of this formulation in human subjects.

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Cite this article as:
Mudgade S. C., Dharashivkar S., Malviya R. and Singh M. M. (2024). Development of Novel Gel Formulation of Celecoxib and Bio-active Compounds of Herbs for Pain Management. *Int. J. of Pharm. & Life Sci*., 15(11): 4-8.

Source of Support: Nil
Conflict of Interest: Not declared
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