RESEARCH ARTICLE

Development and Evaluation of Polyherbal Gel for Treatment of Diabetic Neuropathy

Mahaveer Singh[1], Desu Brahma Srinivasa Rao[2], Varinder Soni[3], PS Minhas[4], S Amudha[5*]

[1]*Department of Pharmaceutics, DR Karigowda College of Pharmacy, Hassan, Karnataka, India.*
[2]*Department of Pharmacology, Hindu College of Pharmacy, Guntur, Andhra Pradesh, India.*
[3]*Khalsa College of Pharmacy, Amritsar, Punjab, India.*
[4]*Priyadarshini College of Pharmacy, Koratagere Tumkur, Karnataka, India.*
[5]*School of Pharmacy, Sathyabama Institute of Science and Technology, Chennai, Tamil Nadu, India.*

Received: 26th September, 2023; Revised: 30th October, 2023; Accepted: 14th January, 2024; Available Online: 25th March, 2024

ABSTRACT

Diabetic neuropathy is a prevalent and painful issue of diabetes mellitus, impacting a large number of people with both type 1 and 2 diabetes. Herbal formulations are found to be effective and have fewer side effects. The study aimed to create a topical polyherbal gel using ethanolic extracts and to evaluate polyherbal gel. Ethanolic extract of *Curcuma longa* rhizomes and *Gingko biloba* leaves were obtained and used to prepare different formulations of polyherbal gels using Carbopol 940 and other excipients. The developed compositions were assessed using a range of gel evaluation standards, including physical examination pH, viscosity measurement, spreadability. The *in-vitro* permeation study is derived from the Franz diffusion. The evaluation shows ideal results for polyherbal gel. The pH of the polyherbal gel was observed to be between 6.22 and 6.51, which is considered suitable for topical application. The polyherbal gel formulations showed ideal viscosity range and spreadability. Among the four formulations, the PG_3 formulation was found to be stable.

Keywords: Diabetic neuropathy, Hyperglycaemia, Polyherbal gel.

International Journal of Drug Delivery Technology (2024); DOI: 10.25258/ijddt.14.1.23

How to cite this article: Singh M, Rao DBS, Soni V, Minhas PS, Amudha S. Development and Evaluation of Polyherbal Gel for Treatment of Diabetic Neuropathy. International Journal of Drug Delivery Technology. 2024;14(1):165-168.

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

The most prevalent root of neuropathy globally is diabetes mellitus, which is increasingly more prevalent in developing nations due to rising rates of obesity and type 2 diabetes. One common and severely incapacitating consequence of diabetes mellitus is diabetic neuropathy.[1] Two-thirds of diabetic patients are thought to have either subclinical or clinical neuropathy. A substantial portion of the global population is afflicted with diabetic neuropathy, a dangerous and prevalent consequence of diabetes mellitus. This disorder is brought on by extended exposure to high blood sugar, which damages nerves all over the body. About 10% or so of diabetic patients have ongoing trauma. This pain can be severe or unmanageable, stimulus-generated or spontaneous. Pain symptoms may include burning, needle-like sensations, shooting, discomfort, jabbing, sharp cramps, tingling, freezing or allodynia. It is usually worse at night. About 25 to 50% of patients with diabetic autonomic neuropathy die within five to ten years of the condition, which is the cause of silent myocardial infarction. Diabetic neuropathy affects sensory abnormalities, motor function, and autonomic regulation.[2-4] The condition's systemic nature is highlighted by the presence of muscular weakness, impaired coordination, and complications related to the cardiovascular, gastrointestinal, and genitourinary systems. The aforementioned clinical challenges mandate a multidisciplinary approach to care, wherein endocrinologists, neurologists, and pain specialists collaborate. Herbal products are safe and effective in treating diabetes and its complications, according to several studies. The polyherbal gel may be effective in treating painful diabetic neuropathy along with routine standard care. However, it is crucial to note that patients with diabetes who receive intensive hyperglycaemic control also experience a reduction in neuropathic pain. These have made varying degrees of success in their attempts to use natural products to encourage wound closure, particularly in the early stages of the healing cascade. The physician faces a challenge in managing diabetic painful neuropathy. Various strategies are employed to address this condition, such as controlling hyperglycemia, pharmacotherapy with anticonvulsants to reduce pain intensity, electrical spinal cord stimulation, and

**Author for Correspondence: amudhakrishnakumar@gmail.com*

other topical and physical treatments involving the use of medicinal gels and creams. Several studies have demonstrated the advantages and effectiveness of herbal formulations in the treatment of diabetic foot ulcers.[5]

A polyherbal formulation refers to a medicinal preparation that contains a combination of multiple herbs or plant extracts. The theory behind combining different plant compounds in a formulation to create synergistic effects that may enhance therapeutic benefits and minimize side effects is often the basis for using multiple herbs. Since ancient times, traditional medicine has been a significant source of novel compounds with potential applications for developing chemotherapeutic agents.[6] Additionally, nature has contributed a significant number of compounds from which numerous modern drugs have been isolated. The drugs selected for this work were *Curcuma longa* rhizomes, *Gingko biloba* leaves, and Aloe vera gel. These three important herbs are stated to possess crucial antibacterial, neuroprotective effects, immune-modulating and anti-inflammatory characteristics that aid in wound recovery and managing diabetic neuropathy.[7]

MATERIAL AND METHODS

Rhizomes of *C. longa* and leaves of *G. biloba* were collected from local herbal drug store. Aloe vera gel was purchased from urban Botanics.

Extracts

The dried ethanolic extract of *C. longa* rhizomes and *G. biloba* leaves were taken after extraction and stored in desiccators for preparation of polyherbal gel.

Formulation of Polyherbal Gel

Carbopol 940 was dissolved in water and was left to expand, then stirred some more to create a gel. The preparation of gel was divided in two phases, in the first phase, methylparaben was dissolved in distilled water using a water bath and heat. After the mixture cooled down, propylene glycol was mixed to it.[8-10] For the second phase, ethanolic extract of *C. longa, G. biloba* and aloe vera gel, and glycerine were mixed and to it Carbopol gel base was combined while constantly stirred. Last are mixed in a triethanolamine. Triethanolamine was gradually added to the mixture to regulate the skin's pH to between 6.8 and 7 and create a gel with the necessary uniformity.[11] The formulation is given in Table 1.

Table 1: Formulation of polyherbal gel including alcoholic extract of traditional Indian herbs

Ingredients	PG_1	PG_2	PG_3	PG_4
Curcumin extract (mg)	500	500	500	500
G. biloba extract (mg)	100	100	100	100
Aloe vera (mg)	300	300	300	300
Carbopol 940 (mg)	0.25	0.50	0.75	1.00
Methyl paraben (mg)	0.02	0.02	0.02	0.02
Propylene glycol (mL)	2	4	2	4
Glycerine (mL)	10	10	10	10
Triethanolamine (mL)	1	1	1	1
Distilled water (mL)	q.s	q.s	q.s	q.s

Evaluation of Polyherbal Gels

Physical evaluation

The polyherbal gel's physical appearance was visually evaluated to assess its transparency and clarity.

Determination of pH

A precisely weighed 1-gram of gel was distributed throughout 100 mL of distilled water. A digital pH meter was used to determine the dispersion's pH.

Gelling capacity

A visual approach was used to determine the gelling capacity. A 100 µL sample was put into a vial with two mL of recently made artificial tear fluid that had been equilibrated at 35°C. The gel formation was eventually visually assessed, and the amount of time it took to form was noted.[12]

Viscosity

The gels' viscosity measurements were observed with DV-I Brookfield viscometer and the corresponding reading was noted.

Spreadability

An adequate amount of sample is taken between two glass slides and a weight of 1-gm is applied on the slides for 5 minutes to observe the spreadability.[13]

The following formula can measure spreadability:

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

Where, S: Spreadability, M: Weight tide the upper slide, L: Length of a glass slide, T: The amount of time needed to divide the slides

In-vitro drug release

A 1-mL gel sample was placed into a 7 cm-long dialysis membrane. After that, the bags were suspended in a shaking water bath with 50 mL of a 1:1 ethanol-to-water mixture that had been heated to 37 ± 0.5°C and 25 strokes per minute. One mL sample was taken out at pre-arranged intervals and changed with an equivalent volume of the brand-new medium. During the course of the release studies, which lasted up to a week, the entire set of release media was swapped out and replaced with new daily (24 hours). After diluting the samples, the concentration of tannins at wavelength 263 nm was measured using a UV spectrophotometer.[14,15]

RESULTS AND DISCUSSION

According to the observed results, the formulated polyherbal gel has excellent clarity and transparency. For most of the preparation intended for use, the pH obtained fell within the acceptable range. Each formulation's pH value fell within a narrow range of neutral pH, indicating that they are not meant to irritate the skin. Both the gelation temperature and the gelling capacity were observed to be in the limit. The pH of

Table 2: Evaluation parameters of polyherbal gel

Evaluation parameter	*PG_1*	*PG_2*	*PG_3*	*PG_4*
Consistency	Fluid	Semi-solid	Semi-solid	Semi-solid
Odor	Characteristic	Characteristic	Characteristic	Characteristic
Color	Yellow-orange	Yellow-orange	Yellow-orange	Yellow-orange
Transparency	T	T	T	T
pH	6.22	6.75	6.37	6.51
Viscosity (Pa.S)	5.23	6.04	8.98	11.04
Spreadability (gcm/sec)	38.64	35.8	27.04	18.81
Drug content (%)	95.8	98.34	94.9	98.76

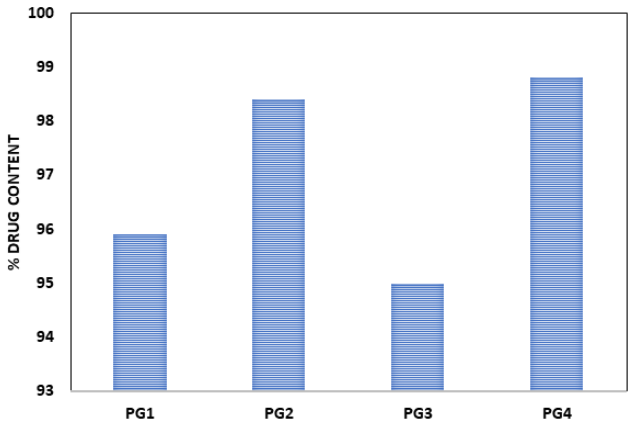

Figure 1: Drug content of polyherbal gels

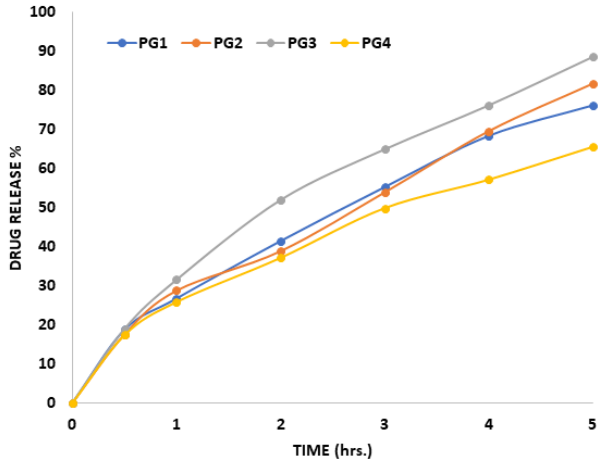

Figure 2: Drug release (%) of polyherbal gels

the polyherbal gel was measured by utilizing a pH meter. The pH of the polyherbal gel was found to be between 6.22 to 6.51. The viscosity of gels increases as the amount of the carbopol increases. PG_3 shows excellent viscosity. The spreadability was found in between 18.81 to 38.64 gcm/sec. The spreadability decreases as the amount of Carbopol 940 increases (Table 2). The amount of medication in the polyherbal gel suggested that the system was suitable for high trapping in the internal phase (Figure 1).

In-vitro Drug Release Study

The *in-vitro* diffusion of all polyherbal formulations were studied. Results showed that, as the concentration of the gelling agent increases, %drug diffusion increases. PG_3 was found to have maximum drug release and PG_4 was found to have minimum drug release (Figure 2).

CONCLUSION

Based on the outcomes of drug content and drug release, formulation code PG3 was determined to be the most effective and appropriate in contrast to other evaluated polyherbal gels, and it is regarded as effective. It was determined by the current study that polyherbal gel prepared from *C. longa* extract, *G. biloba* extract, Aloe vera and Carbopol 940 found to be a potent and effective formulation in treatment of diabetic neuropathy. A more thorough clinical trial may also be conducted concerning its protection and effectiveness profile.

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