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Formulation and evaluation of herbal gel containing *biophytum sensitivum* for the treatment of wound healing

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ABSTRACT

Non curative wounds are one of the major problems often encountered in health care system. The resumption of interest to use of Traditional System of Medicine especially plant-based medicines is rapidly growing. Herbs are more potent healers and promote the repair mechanisms in a scientific way without causing any side effects. *Biophytum sensitivum* is used as traditional medicine to cure variety of diseases. The plant *Biophytum sensitivum* is also useful in the management of wound healing. Gels are a more recent class of dosage forms that are made by trapping a large volume of aqueous or hydro alcoholic liquid in a network of colloidal solid particles. In comparison to ointments and creams, gel formulations typically include quicker drug release. These are superior in terms of patient acceptability and ease of use. In this study we are going to prepare herbal gel containing *biophytum sensitivum* for the treatment of wound healing. The plant is collected from Calicut district, Kerala, India. The plant material was identified and authenticated from Botanical survey of India, southern regional centre, Coimbatore, Tamilnadu. Plant extract were taken by cold maceration technique using ethanol. After the preformulation studies Gel was formulated as per the procedure. Then evaluation test like homogeneity, Ph, drug content, viscosity, spreadability, extrudability, washability, *in-vitro* diffusion study and anti-bacterial activity was carried out after the formulation. From these formulations F5 (95.65±0.42) F6 (96.72±0.31) was selected as best formulation based on the *in-vitro* release and it was incorporated into a gel by using Carbopol 940 as a polymer.

Keywords: *Biophytum sensitivum,* Carbopol 940, Gel, Wound healing

INTRODUCTION

In everyday pathology, wounds remain a challenging clinical problem, with early and late complications presenting a frequent cause of morbidity and mortality. In an attempt to reduce the wound burden, much effort has focused on understanding the physiology of healing and wound care with an emphasis on new therapeutic approaches and the continuing development of technologies for acute and long-term wound management.[1]

A wound is defined as damage or disruption to the normal anatomical structure and function. This can range from a simple break in the epithelial integrity of the skin or it can be deeper, extending into subcutaneous tissue with damage to other structures such as tendons, muscles, vessels, nerves, parenchymal organs and even bone.

Herbal medicine (HM) is the fulcrum of complementary and alternative medicine, which in recent times is increasingly gaining widespread popularity all over the world and gradually streaming toward integration into the mainstream healthcare systems. The use of HM cuts across gender, social and racial classes in both developing and developed countries of the world. Due to the increasing popularity of HM, stakes in the world markets (local and international) are also rapidly increasing and the annual sale is rapidly approaching US $62 billion. An important driver in this upsurge in patronage and use includes low cost, the wide acceptance due to its status of being a natural product with the acclaim of low toxicity,

efficacy in certain challenging diseases, flexibility in its accessibility, preparation and use.[2]

The skin is the largest organ of the body, accounting for about 15% of the total adult body weight. It performs many vital functions, including protection against external physical, chemical, and biologic assailants, as well as prevention of excess water loss from the body and a role in thermoregulation. The skin is continuous, with the mucous membranes lining the body's surface.[2]

Topical drug administration is a localized drug delivery system anywhere in the body through ophthalmic, rectal, vaginal and skin as topical routes. Skin is one of the most readily accessible organs on human body for topical administration and is main route of topical drug delivery system. This review is concern with all detail information regarding rational approach to topical formulations, principles of topical permeation and basic components of topical drug delivery systems. Overall, the clinical evidence indicates that topical gel is a safe and effective treatment option for use in the management of skin related disease.

Gels are a more recent class of dosage forms that are made by trapping a large volume of aqueous or hydro alcoholic liquid in a network of colloidal solid particles. In comparison to ointments and creams, gel formulations typically include quicker drug release. These are superior in terms of patient acceptability and ease of use.

In the late 1800s, the word "Gel" was coined to describe certain semisolid materials based on physiological properties rather than molecular composition. Gels are a highly dilute cross-linked network that does not flow in its steady-state. They are made up of a two-part semi-solid structure with a lot of liquid. One of their distinguishing characteristics is the existence of a continuous structure with solid-like properties. Due to the biocompatibility, network structure, and molecular stability of the integrated bioactive agent, gels have become a preferred material for drug delivery formulations. The majority of topical gels are made with organic polymers like carbomers, which give the products an aesthetically pleasing, clear, sparkling appearance and are easily washed off the skin with water.

MATERIALS AND METHODS

MATERIALS

The medicinal plant *Biophytum sensitivum* were collected locally from Calicut district, Kerala, India. The plant material was identified and authenticated from Botanical survey of India, southern regional centre, Coimbatore, Tamilnadu.carbopol 940 and methyl paraben were obtained from nice chemicals. Ethanol is obtained from loba chemicals, Mumbai. Propyl paraben and propylene glycol obtained from isochem laboratories

Preparation of plant extract

The Freshly collected leaves of *Biophytum sensitivum* Were cleaned and air dried under shade for 48 hours. Then dried leaves were then grounded into powder using an electrical grinder. Powder was extracted using ethanol. The mixture was allowed to stand for 24 hours to ensure that all solvents and samples were completely homogenized. The macerated mixture was then filtered using filtered using filter paper and Buchner funnel

Preparation of gel

Accurately weighed Carbopol 940 was taken in a beaker and dispersed in 50 ml of distilled water. Kept the beaker aside to swell the Carbopol for half an hour and then stirring should be done using mechanical/lab stirrer at 1200 rpm for 30 min. Take 10 ml of propylene glycol and required quantity of Extract. Take 10 ml propylene glycol in another beaker and add weighed quantity of propyl paraben and methyl paraben to it and stirred properly. After all Carbopol dispersed, extract and preservatives solutions were added with constant stirring. Triethanolamine was added drop wise to the formulations for adjustment of required skin pH (6.8-7) and to obtain the gel at required consistency.

Table 1: Composition of gel formulation

Gel code	F1	F2	F3	F4	F5	F6
Plant aqueous extract (gm)	-	-	5	-	-	5
Plant ethanolic extract (gm)	5	5	-	5	5	-
Carbopol 940(gm)	1.5	1	0.5	0.5	0.5	0.5
Propylene glycol (ml)	5	10	10	10	10	10
Methyl paraben (gm)	0.08	-	-	-	0.08	0.08
Propyl paraben (gm)	0.02	-	-	-	0.02	0.02
Triethanolamine (ml)	1	1	1	1	1	1
Water (ml)	Upto 100	Upto 100	Upto 100	Upto 100	Upto 100	Upto 100

EVALUATION OF GEL

Homogeneity: The optimized gel was tested for homogeneity by visual inspection. It was tested for their appearance and presence of any aggregates.

Measurement of pH: The pH of various gel formulations was determined by using digital pH meter. One gram of gel was dissolved in 100 ml distilled water and stored for two hours The measurement of pH of each formulation was determined.[32]

Drug content: 1g of the prepared gel was mixed with 100ml of suitable solvent. Aliquots of different concentration were prepared by suitable dilutions; the stock solution and absorbance were measured by using UV spectrophotometer.

Viscosity: Viscosity of herbal gel was determined by using Brookfield viscometer at 5 rpm using spindle no.6. Each reading was taken after equilibrium of the sample at the end of two minutes.

Spreadability: Spreadability refers to the extent of area to which gel readily spreads on application. Spreadability was

measured on the basis of slip and drag characteristics of gels. Two sets of glass slides of standard dimensions were taken. The herbal gel formulation was placed over one of the slides. The other slide was placed on the top of the gel, such that the gel was sandwiched between the two slides in an area occupied by a distance of 7.5 cm along the slides. An excess of gel (about 2 g) under study was placed on this ground slide. The gel was then sandwiched between this slide and another glass slide having the dimension of fixed ground slide and provided. Weight of 1 kg was placed on the top of the slide for 5 minutes to expel air and to provide a uniform film of the gel between the slides. Excess of the gel was scrapped off from the edges. The top plate was then subjected to pull and the time (in seconds) required by the top slide to cover a distance of 7.5 cm be noted. A shorter interval indicates better Spreadability. [32]

Extrudability

The gel formulation were filled in standard capped collapsible aluminium tubes and sealed by crimping to the end. The weight of tubes were recorded and the tubes were placed between two glass slides and were clamped. 500gm was placed over the slides and then the cap was removed. The amount of extruded gel was collected and weighed. The percent of extruded gel was calculated as

1.When it is greater than 90% then extrudability is excellent.
2. When it is greater than 80% then extrudability is good.
3. When it is 70% then extrudability is fair

Formulation was applied on the skin and then ease extends periods of washing with water was checked.

In vitro diffusion study

The diffusion studies of the prepared gels can be carried out by using cellophane membrane. Gel sample was taken in cellophane membrane and the diffusion studies were carried out at 37 ± 1° using 250 ml of phosphate buffer (pH 7.2) as the dissolution medium. Five milliliters of each sample was withdrawn periodically at 1, 2, 3, 4, 5, 6, 7 and 8 h and each sample was replaced with equal volume of fresh dissolution medium. Then the samples were analyzed for the drug content by using phosphate buffer as blank.

Anti-Bacterial Activity

The optimized formulation was tested *in-vitro* for its antibacterial activities against S.aureus and E.coli by Well Diffusion method and Line Streak Test and inhibition zone of anti-bacterial activity was critically examined.

Inoculum preparation: - Sterile nutrient broth (pH 7.4) was prepared and used for inoculums preparation. One loop of bacterial culture was transferred from mother stock and inoculated into the sterile nutrient medium. The content was incubated in a rotary shaker for overnight at 37 °C and then used for the antimicrobial study

Stability studies

The stability studies were conducted for the optimized formulation as per ICH guidelines. Samples were stored at 30ºC±2ºC/65% RH±5%RH and the sample were withdrawn at initial, 20th and 30th day and to analyze the physical appearance, drug content and percentage cumulative drug release.

RESULT

Pre-formulation studies

Organoleptic properties of drug

Physical state	: Solid powder
Colour	: greenish
Taste	: slightly bitter
Odour	: Unpleasant

UV-Vis Spectroscopy

DETERMINATION OF λmax

The *Biophytum sensitivum* extract absorption spectrum was scanned between 200-800nm in phosphate buffer. The peak was shown

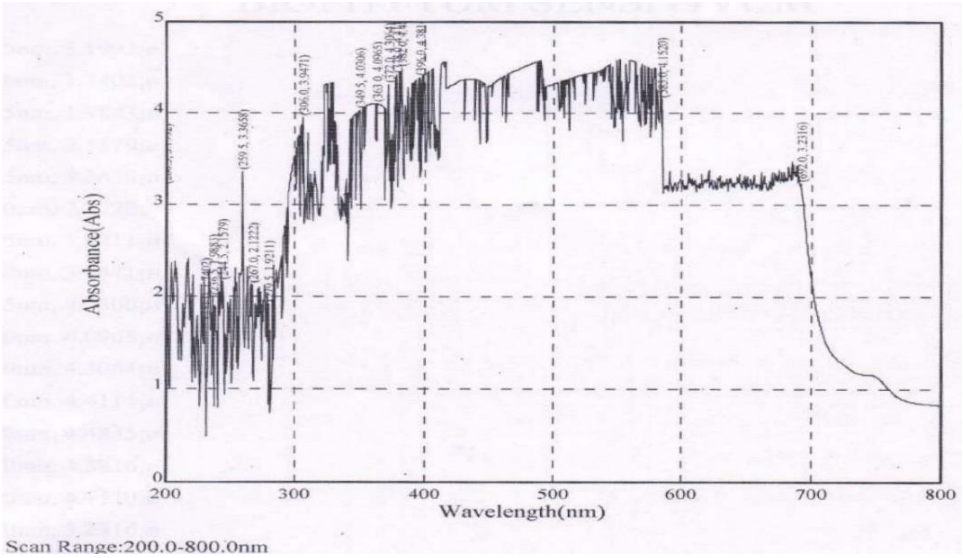

Fig 1

Calibration curve of extract

The λmax *biophytum sensitivum* of extract was determined by scanning the prepared solution in the wavelength range of 200-400 nm. The maximum wavelength was found to be 382nm. The calibration curve of *Biophytum sensitivum* extract was constructed by dissolving the drug in pH 7.2 phosphate buffer.

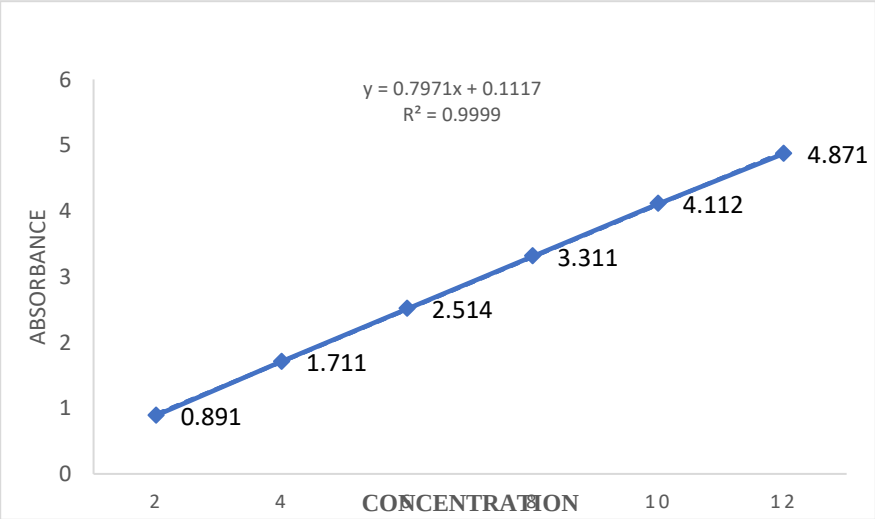

Fig 2: Calibration Curve of *Biophytum sensitivum*

Measurement of pH

Table 2: Result of pH of Gel Formulation

FORMULATION	pH
F1	7.2±0.15
F2	7.1±0.13
F3	7±0.06
F4	6.9±0.12
F5	7.1±0.06
F6	6.9±0.09

Drug content

Table 3: Result of Drug Content of Gel Formulation

FORMULATION	DRUG CONTENT (%)
F1	97.1±1.26
F2	96.1±1.52
F3	97.4±1.21
F4	96.9±1.92
F5	98.5±1.45
F6	98.9±1.39

Viscosity

Table 4: Result of Viscosity of Gel Formulation

FORMULATION	VISCOSITY (cps)
F1	74300±1.01
F2	69200±1.62
F3	62100±0.92
F4	61300±0.52
F5	61200±0.32
F6	61300±0.15

Spreadability

Table 5: Result of Spreadability of Gel Formulation

FORMULATION	SPREADABILITY (gm.cm/sec)
F1	20.21±0.041
F2	19.23±0.013

F3	18.97±0.023
F4	18.12±0.012
F5	17.83±0.01
F6	17.01±0.010

Extrudability

Table 6: Result of Extrudability of Gel Formulation

FORMULATION	EXTRUDABILITY (gm/cm2)
F1	++
F2	++
F3	+++
F4	+++
F5	+++
F6	+++

*+++ -excellent, ++ - good, + - fair

Good washability for all formulations.

In-vitro drug release of herbal gel containing *biophytum sensitivum*

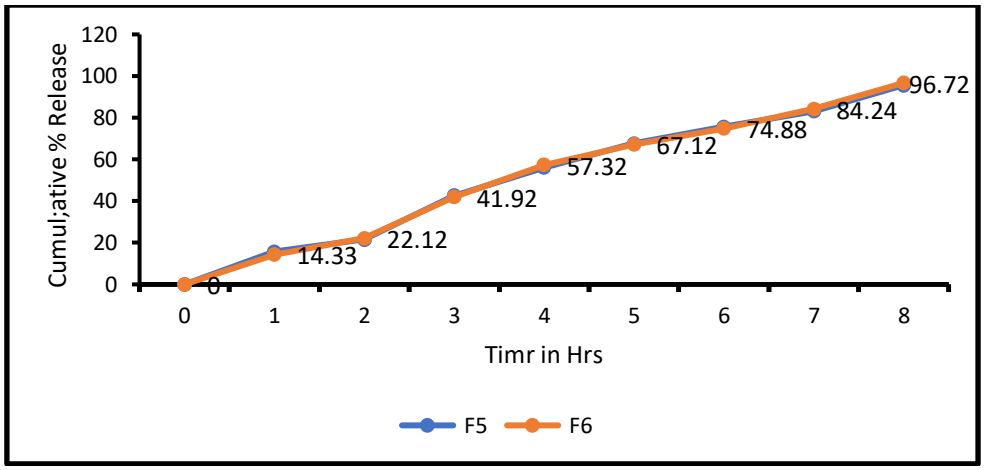

Fig 3: *In-Vitro* Drug Drug Release Profile

Anti-bacterial activity

From the obtained results, it was confirmed that all the given samples (1 & 2) show antibacterial activity towards both the *E. coli* and *S. aureus* strains in line streak test. But in well diffusion method, the obtained zone of lysis was slight due to the difficulty in diffusion of gel.

Samples : Sample 1 – Aqueous plant extract gel
Sample 2 – Ethanolic plant extract gel

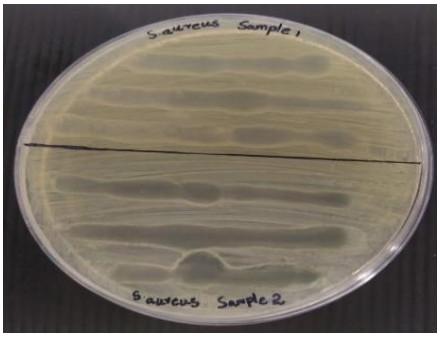

Fig 4: Line streak test in *Staphylococcus aureus*

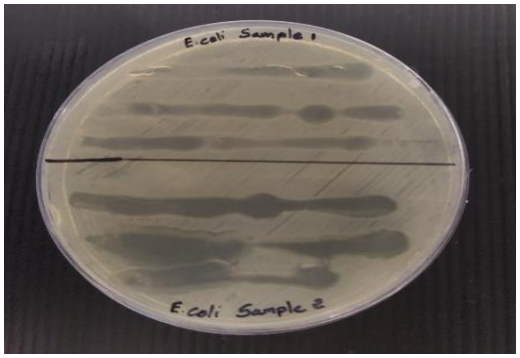

Fig 5: Line streak test in - *Escherichia coli*

Stability studies

Table 7: Result of Stability Studies

PARAMETERS	Initial		20th day		30th day	
	F5	F6	F5	F6	F5	F6
Homogeneity	Good	good	Good	good	good	good
pH	7.1	6.9	7.1	6.9	7.1	6.9
Drug content	98.5	98.9	98.1	98.7	97.8	98.4
viscosity	61200	61300	61200	61300	61100	61300
Spreadability	17.83	17.01	17.81	17.01	17.81	17
Extrudability	+++	+++	+++	+++	+++	+++
% Cumulative Release	95.65	96.72	95.59	96.68	95.38	96.44

**Storage condition: - 30ºC±2ºC/65%, RH±5%RH*

For the optimized gel formulation i.e stability study was carried out as per ICH guideline. There were no marked charges in the optimized gel formulation. The results of homogeneity, drug content, pH, spreadability, extrudability, viscosity, % cumulative drug release of the formulation was related to that of initial reference. The results were shown in Table 15 and it showed that the formulated gel was stable during the stability studies

CONCLUSION

Biophytum sensitivum gel were prepared and a total of 6 formulation were prepared. All the formulations were evaluated for homogeneity, pH, drug content, viscosity, spreadability, extrudability and *in-vitro* drug diffusion study. The optimized formulation showed excellent antimicrobial activity. From these formulations F5 (95.65±0.42) F6 (96.72±0.31) was selected as best formulation based on the *in-vitro* release and it was incorporated into a gel by using Carbopol 940 as a polymer.

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