Development and Quality Evaluation of a Salvia verbenaca Herbal Cream for Anticandidal Application

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Abstract:

Candidiasis is a prevalent opportunistic fungal infection predominantly caused by Candida species, impacting mucosal and cutaneous tissues, with rising incidence attributed to immunosuppression, antibiotic misuse, and hormonal imbalance. Traditional antifungal treatments, although efficacious, often entail unpleasant effects, recurrence, and the development of drug resistance, prompting the investigation of safer and more effective alternative medicines. Herbal preparations developed from medicinal plants provide a viable strategy due to their bioactive phytoconstituents and few adverse effects. Salvia verbenaca (family: Lamiaceae), historically recognised for its antibacterial, anti-inflammatory, and wound-healing qualities, has garnered interest as a prospective antifungal agent.

This research focusses on the creation and assessment of a herbal cream using an extract of Salvia verbenaca for the treatment of candidiasis. The plant material underwent extraction with appropriate solvents, followed by first phytochemical screening to discover active compounds including flavonoids, phenolics, terpenoids, and essential oils recognised for their antifungal properties. A topical herbal cream was developed with suitable excipients and optimised for consistency, stability, and patient acceptance.

The prepared cream was assessed for physicochemical characteristics such as appearance, pH, viscosity, spreadability, homogeneity, and stability under various storage settings. The in-vitro antifungal efficacy against Candida albicans was evaluated using conventional microbiological techniques, and the findings were juxtaposed with a commercial antifungal formulation. The herbal cream demonstrated acceptable physicochemical properties, robust durability, and notable antifungal efficacy, suggesting its medicinal potential.

This study's results indicate that Salvia verbenaca-based herbal cream may be a safe, effective, and cost-efficient option for treating candidiasis. Additional in-vivo research and clinical trials are advised to confirm its effectiveness and safety for clinical use.

Keywords: *Candida albicans, Salvia verbenaca,* Herbal Cream,Candidiasis, Antifungal

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Introduction:

Candidiasis is a prevalent opportunistic fungal infection mostly caused by Candida species, particularly Candida albicans. These organisms are typical commensals of human mucosal surfaces; but, under conducive situations such as immunosuppression, hormone imbalance, extended antibiotic medication, inadequate hygiene, and metabolic abnormalities, they may multiply excessively and induce infection. Candidiasis often impacts the skin, oral cavity, gastrointestinal system, and vaginal mucosa, resulting in considerable pain and persistent health complications, especially in women. The rising prevalence of candidiasis and the development of antifungal resistance have emerged as significant issues in clinical practice [1,2]. Presently available antifungal drugs, such as azoles and polyenes, demonstrate efficacy; nevertheless, they often entail limitations like adverse drug responses, elevated recurrence rates, extended treatment durations, and the emergence of resistant fungus strains. Synthetic antifungal formulations may induce cutaneous discomfort, hypersensitivity responses, and disturbance of natural microbial flora with extended usage. These issues underscore the need for alternative treatment

strategies that are safe, effective, cost-efficient, and appropriate for prolonged usage [3,4]. Herbal remedies have been used since antiquity in traditional medical systems for the treatment of infectious disorders. Medicinal plants are abundant in bioactive phytoconstituents, including flavonoids, phenolic compounds, terpenoids, alkaloids, and essential oils, many of which have significant antifungal and anti-inflammatory activities. Herbal preparations are often well tolerated and have fewer adverse effects, making them appealing options for topical antifungal treatment [5-7].

Salvia verbenaca L., referred to as wild sage and classified under the Lamiaceae family, is a fragrant medicinal herb historically used for the management of skin infections, wounds, inflammation, and microbiological ailments. Phytochemical investigations of Salvia verbenaca have identified essential oils, flavonoids, phenolic acids, diterpenes, and triterpenoids, which enhance its antibacterial and antifungal properties. Numerous species under the genus Salvia are well documented for their efficacy against fungal infections, including Candida species, hence endorsing the medicinal potential of Salvia verbenaca. Topical drug delivery solutions, such as creams, are favoured for treating cutaneous and mucocutaneous candidiasis because of their simplicity of administration, localised impact, improved patient adherence, and less systemic adverse effects. Herbal creams effectively deliver plant-derived antifungal drugs directly to the infection site while ensuring formulation stability and patient acceptance [9].

This research is to create, develop, and assess a herbal cream including Salvia verbenaca extract for the treatment of candidiasis. The research focusses on refining the formulation, analysing physicochemical and stability properties, and testing in vitro antifungal efficacy. This study aims to develop a scientifically confirmed herbal topical formulation that might function as a safe and effective alternative to traditional antifungal treatments [8].

Materials and Methods

Selection of Plant Material

The leaves of *Salvia verbenaca* have been traditionally used for medicinal purposes across Mediterranean, Middle Eastern, and South Asian regions. Their therapeutic value is largely attributed to the presence of phenolic compounds, flavonoids, terpenoids, and essential oils. The leaves are known to possess antimicrobial, anti-inflammatory, antioxidant, wound-healing, antifungal, analgesic, and antipyretic properties. In traditional practices, leaf infusions are commonly used to relieve digestive disorders such as indigestion, abdominal cramps, and diarrhoea, thereby supporting gastrointestinal health. They are also employed in the management of respiratory conditions and gynaecological ailments.

Although *Salvia verbenaca* is widely used in folk medicine for its antimicrobial, antifungal, anti-inflammatory, and wound-healing effects, comprehensive scientific studies evaluating its toxicity are limited. Therefore, the present study was undertaken to investigate the acute toxicity profile of this medicinal plant.

Procurement and Authentication of Plant Samples

Leaves of *Salvia verbenaca* were collected during the months of June and July from different locations in the Malwa region of M. P, India. The plant material was identified and authenticated by Dr. Saba Naaz, Professor and HoD of Botany, Safia College of Science, Bhopal (M.P.). A voucher specimen (No. Safia/159/Bot) was preserved in the laboratory for future reference.

Extraction of Plant Material

A total of 250 g of air-dried *Salvia verbenaca* leaves were coarsely powdered and subjected to Soxhlet extraction using a hydro-alcoholic solvent system comprising ethanol and water (90:10). The extraction process was continued until complete exhaustion of the plant material. The resulting filtrate was concentrated by evaporation to obtain the crude extract.

Preparation of Plant Extract

The hydro-alcoholic extract of dried *Salvia verbenaca* leaves was used for the formulation of the herbal cream.

Formulation of Herbal Cream

The herbal cream was prepared using the following steps:

Preparation of Oil Phase

Stearic acid, cetyl alcohol, and almond oil were accurately weighed and melted together in a porcelain dish at a temperature of 70°C.

Preparation of Aqueous Phase

The hydro-alcoholic extract of *Salvia verbenaca* leaves, glycerol, methyl paraben, triethanolamine, and distilled

water were combined in a separate porcelain dish and heated to 70°C.

Incorporation of the Aqueous Phase into the Oil Phase

The aqueous phase was slowly introduced into the oil phase under constant stirring at room temperature. The fragrance was incorporated at the final step, after which the prepared cream was transferred into an appropriate container.

Evaluation Parameters of Herbal Cream

The prepared herbal cream formulations were evaluated using the following parameters:

Physical Evaluation

The physical appearance of the cream, including clarity and transparency, was examined visually by observing the samples under proper illumination against a white background.

Estimation of pH

The pH meter was calibrated prior to analysis. Samples were placed in a beaker, and pH measurements were recorded using a calibrated electrode. The procedure was repeated three times, and the average value was calculated.

Estimation of Viscosity

Viscosity measurements were performed using a Brookfield viscometer equipped with spindle number 01 at 20 rpm. Approximately 15 ml of the cream was placed in a beaker, and the spindle was immersed in the sample. Readings were taken at temperatures of 4°C and 37°C. Each measurement was performed three times, and the average value was recorded.

Estimation of Homogeneity

All formulations were visually inspected to assess homogeneity and to detect the presence of any lumps or aggregates.

Estimation of Spreadability

Spreadability was evaluated by placing a fixed quantity of cream between two glass slides. The slides were adjusted to a distance of 7.5 cm and compressed to obtain a uniform thin layer. Excess cream was removed, and a weight of 20 ± 0.5 g was placed on the upper slide. The time required for the slides to separate to the original distance of 7.5 cm was recorded. The test was performed in triplicate, and the mean value was calculated. Spreadability was determined using the standard formula.

S= mX l/t

l represents the length of the slide (7.5 cm), m denotes the mass attached to the slide, and t is the time measured in seconds.

Evaluation of Wetness

The moisture characteristics of the prepared herbal cream were assessed by applying a small quantity to the skin surface and observing the wetness produced [20].

Evaluation of Smear Type

The herbal cream was spread on the skin, and the nature of the film or smear formed after application was visually examined and recorded [21].

Evaluation of Emollient Properties

The formulated herbal cream was tested for its emollient behavior by assessing smoothness, slipperiness, and any residual film left on the skin after application [22].

Determination of Emulsion Type (Dilution Test)

To identify the nature of the emulsion, the herbal cream was separately diluted with water and oil. The miscibility behavior of the formulation with each phase was observed to determine whether the emulsion was oil-in-water (o/w) or water-in-oil (w/o). The results were recorded accordingly [23].

Dye Solubility Test

The emulsion type was further confirmed using a dye solubility method. The formulation was blended with a water-soluble dye (amaranth) and observed under a microscope. The distribution pattern of the dye within the formulation was examined to ascertain the continuous phase of the emulsion [24].

Determination of Drug Content

The amount of drug present in the herbal cream was determined using UV–Visible spectrophotometric analysis. An accurately weighed 1 g sample of the formulation was transferred into a 50 mL volumetric flask and made up to volume with methanol. The mixture was shaken well to ensure complete dispersion and then filtered using Whatman filter paper. From the clear filtrate, 0.1 mL was withdrawn, further diluted to 10 mL with methanol, and analyzed at the selected wavelength.

In Vitro Drug Release Study

The in vitro release behavior of the herbal cream was assessed using a semi-permeable dialysis membrane bag measuring approximately 7 cm in length. The formulation was enclosed within the membrane and suspended in 50 mL of an ethanol–water (1:1) release medium. The system was maintained at 37 ± 0.5 °C using a thermostatically controlled water bath. At predetermined time intervals, 1 mL of the dissolution medium was withdrawn and immediately replaced with an equal volume of fresh medium to maintain constant

volume and sink conditions. After a study period of one week, the collected samples were appropriately diluted and analyzed using a UV–Visible spectrophotometer at the corresponding λmax. All experiments were performed in triplicate, and the cumulative percentage of drug released was calculated.

Anti-candidal Activity

The anti-candidal activity was assessed according to the approach outlined by Shriwas et al., [12]

Table 1:Composition of herbal cream of *Salvia verbenaca* extract

Ingredients	FormulationCode							
	HCS1	HCS2	HCS3	HCS4	HCS5	HCS6	HCS7	HCS8
HAESV	0.5	0.75	1.0	1.5	0.5	0.75	1.0	1.5
Stearicacid	5.0	5.0	5.0	5.0	10	10	10	10
Cetyl alcohol	10	10	10	10	5.0	5.0	5.0	5.0
Almondoil	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0
Glycerol	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
Methylparaben	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
Triethanolamine	qs	qs	qs	qs	qs	qs	qs	qs
Water(100ml)	qs	qs	qs	qs	qs	qs	qs	qs
Totalweight	100	100	100	100	100	100	100	100

Note:All values are taken in gm

Result and Discussion

Many investigations have evaluated the effects of plant-derived extracts and their formulations on systemic infections, particularly in the management of fungal diseases such as vaginal candidiasis.. It was also disclosed that there are already many herbal preparations available in the market for vaginal infections, which show promising efficacy with few or no adverse effects. This study aimed to manufacture and assess a herbal cream comprising a hydro-alcoholic extract of Salvia verbenaca leaves.The developed herbal cream was assessed according to recognised methods. The findings are shown in Table 2. The drug concentration was highest in HCS7, measuring 97.25 (Table 3). The medication release profile data reveal that formulation HCS7 achieved a release of 95.24% (Table 4).

Table 2: Evaluation parameters of herbal cream

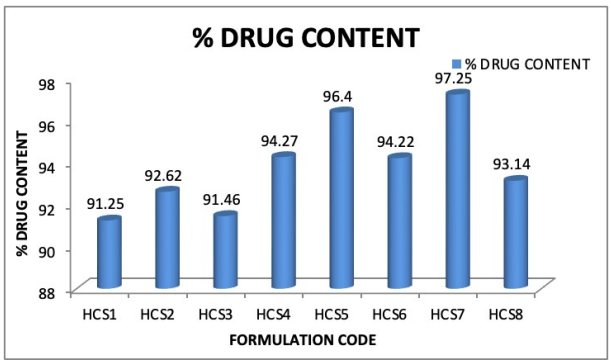
FC	Parameters								
	Appearance	pH	Viscosity (cP)	Homogeneity	Spreadability	Wetness	Type of smear	Emolliency	Type of Emulsion
HCS1	Pale white & Clear	6.8	27265	Homogenous	64.25	+++	Non Greasy	No residue left	o/w type
HCS2	Pale white & Clear	7.0	27698	Homogenous	65.38	+	Non Greasy	No residue left	o/w type
HCS3	Pale white & Clear	6.9	27462	Homogenous	67.56	++	Non Greasy	No residue left	o/w type
HCS4	Pale white & Clear	6.8	27123	Homogenous	61.36	++	Non Greasy	No residue left	o/w type
HCS5	Pale white & Clear	6.9	27585	Homogenous	62.85	++	Non Greasy	No residue left	o/w type
HCS6	Pale white & Clear	6.8	27689	Homogenous	61.74	++	Non Greasy	No residue left	o/w type
HCS7	Pale white & Clear	7.0	27754	Homogenous	68.68	+++	Non Greasy	No residue left	o/w type
HCS8	Pale white & Clear	7.0	27812	Homogenous	61.27	+	Non Greasy	No residue left	o/w type

(Note:+=Good,++=Better,+++=Best)

Table3:Drugcontentofherbal cream

FormulationCode	%Drug Content
HCS1	91.25
HCS2	92.62
HCS3	91.46
HCS4	94.27
HCS5	96.40

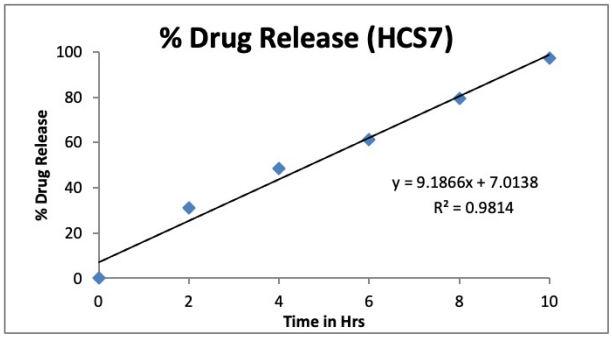
HCS6	94.22
HCS7	97.25
HCS8	93.14



Graph1: Drugcontentof herbalcream in percent

Table4:%Drugreleaseofherbalcream

Time (Hrs)	%Drug Release (HCR5)
0	00.00
2	29.33
4	47.38
6	59.14
8	83.47
10	95.24



Graph1:%Drugreleaseofoptimizedherbalcream

The optimized herbal cream, HCS7, was assessed for its antifungal activity using a selected fungal strain to establish the efficacy of the formulation. The results were compared with those of a commercially available standard product, which demonstrated that HCS7 exhibited significant effectiveness (Table 5).

Table5:Anti-*Candidal*Activityofherbalcream

S/No.	Test	Zoneof Inhibition(mm)
1.	Negative Control	4.78±0.02
2.	Marketed Cream	22.15±0.004**
3.	HCS7	19.24±0.012*

Note: All values are expressed as Mean (X) ±SEM, (n=3). One way ANOVA followed by student test, values are statistically significance *P<0.01,**P<0.001 when compared with control and standard.

Conclusion

The results demonstrate that the herbal cream formulated with a hydro-alcoholic extract of Salvia verbenaca leaves shows strong anti-Candida activity, indicating its potential usefulness in managing gynaecological conditions. In addition, there is a need to establish thorough pharmacological assessments and clinical protocols to ensure the development of safe and effective therapeutic products. Among the tested formulations, HCS7 displayed favorable drug composition and release properties. Therefore, the study concludes that the selected herbal formulation, particularly the herbal cream HCS7, has a notable therapeutic effect against vaginal candidiasis, although extensive clinical investigations are required to confirm its safety and clinical efficacy.

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