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Formulation and Evaluation of Antifungal Herbal Gel Containing Ethanolic Extract of *Senna Alata, Murraya Koenigii* and *Aloe Vera*

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ABSTRACT

Herbal medicines is still the mainstay of about 75-80% of the world's population, mainly in developing countries, for primary health care because of better cultural acceptability, better compatibility with human body and lesser side effects. Herbal medicines consist of plant or its part to treat injuries, disease or illnesses and are used to prevent and treat diseases and ailments or to promote health and healing. it is a drug or preparation made from a plant or plants and used for any to such purpose. The aim of present study was to prepare herbal gel formulation containing ethanolic extract ofantifungal herbal gel containing ethanolic extract of senna alata, murraya koenigi iand aloevera. Topical gel formulation was designed by using ethanolic extract antifungal herbal gel containing ethanolic extract of senna alata, murraya koenigii and aloevera in varied concentrations. The gel was prepared by using carbopol 940(1%w/v),ethanol,propylene glycol, methyl paraben, propyl paraben, edta disodium, tri-ethanolamine and required amount of distilled water. the prepared gels were evaluated for physical appearance, ph, spread ability, drug content, swelling index, diffusion study, viscosity, homogeneity and grittiness. it was inferred from results that gel formulations were good in appearance and homogeneity. Antifungal herbal gel containing ethanolic extract of senna alata, murraya koenigii and aloevera based gel proved to the formula of choice, since it showed the highest percentage of extrudability, good spreadability and rheological properties.

Keywords: Ethanolic extract, Optimization, Rheological properties, Anti fumgal activity.

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INTRODUCTION

Most of the time, the human species live in peaceful coexistence with the microorganisms that surround them and only when the defense system is damaged or the concentration of pathogens reach an exceptionally high density, an infection may emerge. Most infections pass by unrecognized but sometimes the infecting agents do elicit a response of the body, which leads to clinically manifest signs and symptoms, a condition known as infectious disease. As strategies to control bacterial infections in patients improved, fungi be the most hazardous pathogens. Yeasts and moulds now rank amongst the 10 most frequently isolated pathogens among patients in Intensive Care Units. On the contrary, modern treatment modalities may even facilitate the growth of fungi through negative interference with the remaining components of the immune system. Let's have a closer look at these peculiar infective agents, called fungi or mycoses.

In India, drugs of herbal origin have been used in traditional systems of medicines such asAyurveda, Unani, Siddha and Folk (tribal) medicines since ancient times. Among these systems, Ayurveda is most practiced and widely accepted alternative system of medicine in India.

The most noticeable change towards herbal medicine in the developed countries of this century has been because of the interest shown by the ordinary people. From being regarded as **"old fashioned"** and **distrusted,** herbs such as ginseng and guarana which are now hailed as wonder drugs. The change in attitude began in the 1960s, when the 'hippie' movement advocated a nature living, initiating "alternative"' medicine and therapies. The growth of the conservation movement and the founding of companies using only natural products in an environmentally friendly way were also major factors. As a result, increasingly wide ranges of herbs are now available as fresh, dried, as ingredients of cosmetics, perfumes, and over-the-counter medicines.

Besides the advances and advantages of conventional medicine, or biomedicine as it is also known, it is clear that herbal medicine has much to offer. We tend to forget that in all but the last fifty years or so, humans have relied almost

entirely on plants to treat all types of illnesses, from minor problems such as coughs and colds to life threatening diseases such as tuberculosis and malaria. Today, herbal remedies are coming back into prominence because the efficacy of conventional medicines such as antibiotics, which once had near-universal Tectiveness against serious infections, is on the wane.

MATERIAL AND METHODS

Collection and Authentication

The senna alata leaves were collected from out cuts State Forest Research Institute Jabalpur, Madhya Pradesh region, India in January 2019, the collected leaves were shade dried for 1 week then powder by mechanical manner and packed in air tight manner. Murraya koenigii and aloe vera leaves collected local garden in Bhopal, Madhya Pradesh region, India in January 2019, the collected leaves were shade dried for 1 week then powder by mechanical manner and packed in air tight manner. The samples were identified and authentication by State Forest Research Institute, Jabalpur, MP, India.

Preparation of extraction

About200g of powdered leaves were weighed and extract with ethanol by using maceration process. The powdered leaves were soaked for 24 hrs in 1.5 L of ethanol with stirring by placing on a magnetic stirrer. After 24 hrs, the mixture was filtered to collect the ethanolic extraction. Then the extraction was poured into evaporating dishes and placed on a water bath at 45-50 ^{0}C to speed up the rate of evaporation.

Method of preparation of gel

Firstly carbopol 934 was dispersed in distilled water and purified water kept the beaker aside to swell the carbopol 934 for half an hour and then stirring should be done to mix the carbopol 934 to form gel. In another beaker weight and transfer the required quantity of extracted drug powder and dissolved in polyethylene glycol 400 and go for sonication for 10 mint sand the solution was added and mixed to the first solution. 5ml of distilled water was taken and required quantity of methyl paraben and propyl paraben were dissolved by heating on water bath and solution was cooled. Finally full mixed ingredients were mixed properly to the carbopol 934 gel with continuous stirring and lastly triethanolamine was added drop wise to the formulation for adjustment of required skin pH (6.8 - 7) and to obtain the gel at required consistency. By using this method we prepared 4 formulations with 4 different concentration of carbopol i.e 1% 1.5% 2% 2.5% respectively.

Preparation of Gel base

Table No. 1:- Formula for 50gm of 1 % Herbal Gel Formulation

Ingredients	Quantity In gm/ml
Extract of senna alata	1 gm
Extract of aloe vera	1 gm
Extract of murrya kaoinigii	1 gm
Carbopol	1 gm
Poly ethylene glycol	5 ml
Methyl paraben	0.5 ml
Propyl paraben	0.05 ml
Triethanolamine	1.5 ml
Water	Q. S.

Carbopol 934 was used as gelling agent in the preparation. Gel was prepared by dispersing Carbopol 934 in purified water with constant stirring at a moderate speed then the pH of gel was adjusted to 6 to 6.5 using Triethanolamine (TEA).

Table No. 2:-Formula for 50 gm of 1.5 % Herbal Gel Formulation

Ingredients	Quantity In gm/ml
Extract of senna alata	1gm
Extract of aloe vera	1gm
Extract of murrya kaoinigii	1gm
Carbopol	1.5gm
Poly ethylene glycol	5 ml
Methyl paraben	0.5 ml
Propyl paraben	0.05 ml
Triethanolamine	1.5 ml
Water	Q. S.

Table No. 3:- Formula for 50 gm of 2 % Herbal Gel Formulation

Ingredients	Quantity In gm/ml
Extract of senna alata	1gm
Extract of aloe vera	1gm
Extract of murrya kaoinigii	1gm
Carbopol	2 gm
Poly ethylene glycol	5 ml
Methyl paraben	0.5 ml
Propyl paraben	0.05 ml
Triethanolamine	1.5 ml
Water	Q. S.

Table No. 4:- Formula for 50 gm of 2.5 % Herbal Gel Formulation

Ingredients	Quantity In gm/ml
Extract of senna alata	1gm
Extract of aloe vera	1gm
Extract of murrya kaoinigii	1gm
Carbopol	2.5gm
Poly ethylene glycol	5ml
Methyl paraben	0.5 ml
Propyl paraben	0.05 ml
Triethanolamine	1.5 ml
Water	Q. S.

Evaluation tests

Physical appearance

The physical appearance of the formulation was checked visually.

- **Color**: The color of the formulations was checked out against white & blackbackgrounds.
- **Consistency**: The consistency was checked by applying the gel on to theskin.
- **Greasiness:** The greasiness was assessed by the application on to theskin.
- **Odor**: The odor of the gels was checked by mixing a little amount of gel in water and by taking smell.

Batch Code	Colour	Homogeneity	Consistency	Phase separation
HG 1	brown	Excellent	Excellent	None
HG 2	brown	Excellent	Excellent	None
HG3	brown	Excellent	Excellent	None
HG4	brown	Excellent	Excellent	None

Determination of pH

The pH values of 1% aqueous solutions of the optimized gel was measured at 25^{0}C using a pH meter (Systronic digital pH meter 335, India).

S. No.	Formulation code	pH value
1	HG 1	6.9
2	HG 2	6.7
3	HG 3	6.8
4	HG 4	6.8

Rheological study

The viscosity of the formulated batches was determined using a Cone and Plate Viscometer with spindle 7 (Brookfield Engineering Laboratories). The assembly was connected to a thermostatically controlled circulating water bath maintained at 25^{0}C. A definite quantity of gel was added to a beaker covered with thermostatic jacket. The gel was rotated at 100 rotations per minute with spindle 7.

Spreading Coefficient

Spreading coefficient was determined by apparatus suggested by Mutimer. It consists of a wooden block, which is attached to a pulley at one end. Spreading coefficient was measured on the basis of 'Slip' and 'Drag' characteristics of gels. A ground glass slide was fixed on the wooden block. 2 gm of gel under study was placed on this ground slide. The gel preparation was then sandwiched between this slide and second glass slide having same dimension as that of the fixed ground slide. The second glass slide is provided with the hook. Weight of 500 mg was placed on the top of the two slides for 5 min to expel air and to provide a uniform film of the gel between the two slides. Measured quantity of weight was placed in the pan attached to the pulley with the help of hook. The time (in sec) required by the top slide to cover a distance of 5 cm was noted.

Table 5: Spreading Coefficient value of Gel Vs Marketed Gel

S. No.	Formulation	Spreading(g.cm/sec)
1	HG 1	18.58±0.78
2	HG 2	17.67±0.54
3	HG 3	15.78±0.69
4	HG 4	14.98±0.87
5	Marketed Gel	14.35±0.92

Extrudability Study

It is a useful empirical test to measure the force required to extrude the material from a tube. For determination of extrudability the gel formulation was filled in standard plastic caped collapsible tube. The initial weight of tube was recorded. The tube was placed between two glass slides and clamped. 1 g weight was placed over the glass slide and then cap was opened. The amount of gel extruded was collected and weighed. The % of gel extruded was calculated and compared with the marketed gel.

Table 6: % Extrudability of Gel Vs Marketed Gel

S. No.	Formulation	% Extrudability
1	HG 1	88%
2	HG2	85%
3	HG 3	88%
4	HG 4	86%
5	Marketed Gel	84%

Skin irritation studies

The Wistar rats of either sex weighing 150-200 g were used for this test. The intact skin was used. The hair was removed from the rat 3 days before the experiment. The extracts containing gels were used on test animal. Gel base was applied on the back of animal taken as control. The animals were treated daily up to seven days and finally the treated skin was examined visually for erythema and edema.

Antimicrobial Susceptibility test of gel

Herbal gel were tested for antimicrobial activity against *E. coli* using the disk diffusion method with slight modification (bansal et al). The *E.coli* were preserved at department of microbiology. Muller Hinton agar (MHA) plates were prepared by pouring 15ml of molten media into sterile petri plates. A drop of 10µl vehicle formulation was placed on surface of medium and incubated at 37^{0}C for 24 hrs. at the incubation, inhibition zone were measured around drop with transparent ruler in mm. this study was performed in triplicate.

Stability Studies

Stability studies were performed to all the four formulations in four different timings that is on day-0, 15th day and on 30th day. On these time intervals all the evaluation studies and skin irritation studies were performed to check the stability of the topical herbal gel formulations.

RESULTS & DISCUSSION

The development of formulation preformulation studies are performed on repotedmethods.The drug was found to be of white crystalline powder, which smooth texture. The melting point was found to be Senna alata , Murraya koenigii and Aleo vera 150^{0}C,208^{0}C,223^{0}C, which was similar to be the reported melting point found in literature.

Solubility of Senna alata, Murraya koenigii and Aleo vera was determination is various polar and non-polar solvent and resilt are reported as describe in pharmacopoeia of India. The solubility of Sennaalata , Murraya koenigii and Aleo vera was found to be methanol 1mg/1000 ml.Gel have the potential to be efficient, viable, safe and cost effective system for administration of herbal on account of their biodegradability, biocompatibility, and suitability for topical applications and low immunogenicity.Herbalgel was

prepared by emulsification technique and optimized for various formulation variables.

It was observed that on increasing the gelling agent concentration from 1.0 gm to 2.5 gm the viscosity increase from 1900 to 2490 cp.The increase in viscosity with an increase in concentration of gelling agent can be attributed due to greater quantity of gelling agent available which enhanced the viscosity of the formulation. The Drug content increased from 91.85±1.35 to 97.30±1.6 on increasing the concentration of Carbopol (gelling agent) from 0.5 gm to 2.0 gm which may be due to increase in viscosity of the solution which prevented the drug crystals from leaving the droplets.

However on further increasing the concentration of gelling agent the drug content was found to be decreased as highly viscous solution was prepared, which was difficult to process. The highest drug content was found in the formulation HG 3 and the viscosity was also sufficient, therefore this concentration of gelling agent was selected.

Varying concentration of oil was used for preparation of Gel. With an increase in oil concentration, the viscosity of Gel was found to increase from 1720 cp to 1900 cp. It ma1y be because of the quantity of emulsifier present in the formulation which was not sufficient to adsorb at the interface, which caused the oil droplets to coalesce, and resulted in increase in viscosity. As the concentration of Carbopol increased drug content was found to decrease because highly viscous solution was prepared, which was difficult to process and this resulted in loss of drug content. The highest drug content was found in formulation HG3 i.e., 92.9±3.42%, therefore this concentration of oil was selected. The highest drug content found in formulation HG3 i.e., 95.11±4.88%. Due to highest drug content this concentration of emulsifier was selected.

Finally the gel was prepared 2 % herbal gel using extract 3gm of herbal product, 2 gm of Carbopol, methy paraben 0.5 ml, propyl paraben 0.05 ml, 1.5ml triehtenolamine and water characterized for its physical appearance, pH, spreadability, extrudability, drug content and *in vitro* drug release. The prepared herbal Gel formulation was brown coloured viscous creamy preparation with a smooth and homogenous appearance. The pH value of the optimized formulation was found to be 6.8 which was near the pH value of the skin, so it does not give any adverse effect. The pH value of formulation was found to be suitable for topical delivery. The values of spreadability indicate that the gel is easily spreadable by small amount of shear. Spreadability of marketed product was 14.62±0.85 gm cm/sec while that of formulated gel was found to be 18.48±0.82 gm cm/sec, which indicates that spreadability of prepared gel containing herbal was good as compared to the marketed gel.

The % extrudability of prepared gel and marketed cream was found to be 89% and 85% respectively, which indicate that herbal gel possess better extrudability as compared to marketed gel .Skin irritation test was performed on healthy Wistar rats. No allergic symptoms like inflammation, redness, irritation appeared on rats of group 4 receiving herbal gel after 72 hrs. Severe erythma was observed in animals of group 2 recieving 0.8% Formalin solution .From the skin irritation study it can be concluded that herbal Gel does not produce any irritation or erythma and hence can be used as a safe and efficient drug delivery system.Herbal gel are formulated for use a bacterial infection . The optimized formulation HG3 was evaluated for antibacterial activity against *E.Coli* bacterial strain as compared to drug suspension. In this study, during 5 hrs gel of drug actively inhibit bacterial zone but after 24 hrs its effectiveness was constant while during 5 hrs medicated gel slowely inhibit bacterial zone but after 5 hrs its effectiveness was controlled because it give antibacterial activity for longer period of time.This study revealed that medicated gel showed larger or controlled zone of inhibition (1.53 ±0.04) as compared to drug suspension (0.89 ±0.21) after 24 hrs.

Table 7: *In-vitro* antibacterial activity of optimized formulation and pure drug

S. No.	Name of Extract	Name of Culture	Concentration	Zone Of Inhibition In (Cm)
1	Herbal leaf extract	E. coli	HG 1	0.72 ± 0.31
			HG 2	0.02 ± 0.23
			HG 3	1.53 ±0.4
			HG 4	1.49 ± 0.41
2	Standard (Neomycin)	E. coli	25 µg/ml	0.53 ±0.12
			50 µg/ml	0.56 ± 0.15
			75 µg/ml	0.89 ±0.21
			100 µg/ml	0.87 ± 0. 19

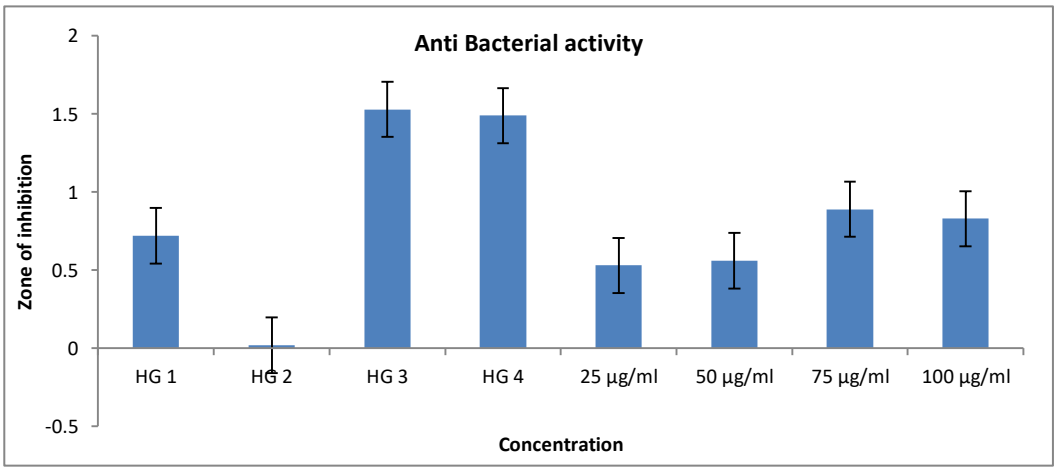

Fig:1: Graphical representation of Anti-microbial activity of herbal gel Formulations and the standard drug.

CONCLUSION

As many traditional healers are using this *sennaalata, aloe vera and murrya kaunigii* for treating number of fungal and bacterial infections, we made a formulation by using the senna *alata ,aloe vera and murry kainigii* extractions. No change was observed in its pH and other physical parameters and skin irritation studies were observed with all the four formulations. Along with the above the gel formulation is also have good antimicrobial activity. The antimicrobial activity of the *sennaalata, aloe vera and murrya kaunigii herbal* gel formulations shows dose dependent zone of inhibitions in exponential manner i.e HG3 formulations shows 1.53±0.4 cm zone of inhibition it is very much greater than the remaining three formulations and the standard Neomycin. When compared with the standard drug our formulation gels are showing better antimicrobial activity.

By this study results we are concluding that all these four formulations are best in their stability and anti-microbial activity so we can use this formulation for treating microbial infections. Antifungal activity of the herbal gel formulation was also planned to perform by using the isolated fungal strains as early as possible.

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Abbreviations

HG1 : Formulation1
HG2 : Formulation2
HG3 : Formulation3
HG4 : Formulation4
g :Gram
ml : Milliliter
µg : Microgram
L :Liter
^{0}C : degreecentigrade
h :Hour
q.s : Quantitysufficient
mm :Millimeter
TEA : triethanloamine
% :Percentage

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