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Development and Characterization of Anti-Fungal Emulgel Containing Volatile Oil of Sphaeranthus Indicus Linn.

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ABSTRACT

In the present study, the active chemical constituents responsible for the anti-fungal activity in the plant Sphaeranthus indicus i.e. Eudesmanolides and sphaeranthanolides were evaluated and studied. The use of emulgel has been known and can be used to entrap hydrophobic drug, so here volatile oil of S.indicus is used. Thus, the aim of the present study was to design a novel drug delivery system i.e. emulgel which can be directly applied to topically. It bypasses first pass metabolism and gives immediate action by getting absorbed into the skin in a fast manner. The main categories of essential oil are terpenes and terpenoids. These terpenes and terpenoids due to their high lipophilic nature can even disrupt fungal cell membrane causing cell death or inhibiting sporulation and germination of fungus such a Candida albicans. Essential oil also acts by inhibiting the ergosterol biosynthesis.

Different formulations of emulgel having varying quantities of polymer and volatile oil were prepared by optimizing their concentrations and its behavior was studied by performing various evaluation parameters. **SE1, SE4** and **SE7**formulation was found out to be suitable for its used as a anti-fungal emulgel. These formulations was considered as best because the consistency was similar to marketed formulations. And the viscosity of it was 4007±2.87, 4021± 3.20 and 4068± 2.87 cps of 10 RPM and 2413± 5.70, 2404± 2.00 and 2397± 2.36 cps of 50 RPM while spreadability 10± 0.03, 10.34± 0.56 and 9.37± 0.84g.cm/sec.

I. INTRODUCTION

The topical drug delivery system can be used when other system of drug administration fails. The study is also preferred to avoid risks of intravenous therapy. [1] Topical drug delivery can be defined as the application of a drug containing formulation to the skin to treat cutaneous disorder. The most commonly used drug delivery system is topical. Topical route of drug administration is the simplest and easiest route of localized drug delivery anywhere in the body by routes such as ophthalmic, rectal, vaginal and skin. These can be usually applied as a wide spectrum of preparations in case of both cosmetic and dermatological, to the healthy or a diseased skin [2].Drugs can be administered topically for their action at the site of application or for systemic effects. Drug absorption increases through the skin if the drug is in solution, only if it has a favourable lipid/water partition coefficient and it is an non-electrolyte. Emulgel(gellified emulsions) are topical drug delivery system which are generally used whereas other systems of drug administration fail to directly treat skin disorders such as fungal infections, acne, psoriasis etc. [3].As the name itself suggests that, they are the combination of emulsion and gel. Both oil-in-water and water-in-oil type of emulsion can be used as a vehicles to deliver drugs to the skin. They have high ability to penetration the skin. The presence of gelling agent in water phase converts the classical emulsion into an emulgel. Emulgel has got several properties for dermatological use such as being thixotropy, greaseless, easily spreadable, easily removable, emollient, non-staining, water- soluble, long self-life, bio-friendly, transparent and pleasing appearance. [4]

II. MATERIAL AND METHODS

EXTRACTION OF S.INDICUS LINN. OIL

The most common Clevenger apparatus is used to extract oil, specific glassware can be use as the round bottom flask. The flask, of variable size, contains water which is boiled as well as the plant to be extracted. The steam rises in the assembly to a condenser, and the condensate falls into the small burette on the right. Oil floats on the water, which for its part is gradually returned to the heated flask through the diagonal conduit. After 2 hours of

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extraction, the oil volume collected in the burette can be directly measured.
The quantity of S.indicusLinn oil obtained was less as the flowers were of dried form. So the S.indicus oil was purchased from the market.

OPTIMIZATION OF HPMC 15cps

- Polymer of different grades were used to check its efficacy.
- HPMC 15cps was taken in different concentration (4g, 5g, 6g, 7g) was added to 100ml distilled water.Keep the solution covered and undisturbed for one night.
- **Next day low viscous solution was formed.**
- This viscosity solution was not suitable for formulation of emulgel.
- Because of its low viscosity the formulation will not adhere on to the skin properly and will flow from the skin due to its liquid nature.

TABLE 1: Optimization of HPMC 15cps

S.NO.	QUANTITY OF HPMC 15cps(g)	QUANTITY OF WATER(ml)
H1	4	100
H2	5	100
H3	6	100
H4	7	100

OPTIMIZATION OF CARBOPOL-934

- Carbopol 934 in different concentrations were taken (0.5%, 0.75%,1%, 1.25%, 1.5%,) was slowly added to 100ml distilled water while stirring it under a mechanical stirrer for approximately 1 hr.
- After uniformly dispersing it, stirring was stopped.
- Carbopol is acidic in nature so it is necessary to adjust its pH to neutral which does not lead to irritation on skin.
- 25ml of this solution was taken and Triethanolamine was added drop wise stirring gently till a pH of 7-8 was obtained.
- **0.5%, 0.75%, were low viscose solution are formed.**

TABLE 2: Optimization of Carbopol-934

S.NO.	QUANTITY OF CARBOPOL 934(100%)	QUANTITY OF WATER(ml)
C1	0.5	100
C2	0.75	100
C3	1.0	100
C4	1.25	100
C5	1.5	100

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STEP-I GEL PREPARATION

STEP 1 Carbopol 934 (1%, 1.25%, 1.5%,) was slowly added to 100ml distilled water while stirring it under a mechanical stirrer for approximately 1 hr.
STEP 2 After uniformly dispersing it, stirring was stopped
STEP 3 25ml of this solution was taken and Triethanolamine was added drop wise stirring gently till a pH of 7-8 was obtained.

STEP-II EMULSION PREPARATION

STEP 1 (Oily phase):- S.indicus oil
STEP 2 (Aqueous phase):- Tween 80, purified water were mixed.
STEP 3:- Methyl paraben and Propyl paraben were mixed in propylene glycol.

- The solution obtained in Step 3 was mixed with the aqueous phase obtained in Step 2.
- After this both the resulting solutions were mixed and kept under stirrer for homogenous emulsion.

STEP-III PREPARATION OF EMULGEL

The composition of emulgel formulations is shown in table 2. The obtained emulsion was mixed with the gel in 1:1 ratio with gentle stirring to obtain the S.indicus emulgel. Finally pH of emulgel was adjusted by using Triethanolamine [14].

TABLE 3: Formulation of S.indicus Gel and Emultion

Ingredients(%)w/w	CF1*	CF2	CF3	CF4*	CF5	CF6	CF7*	CF8	CF9
Formulation of gel									
Carbopol 934	1.0	1.25	1.5	1.0	1.25	1.5	1.0	1.25	1.5
Triethanolamine	1.65	1.65	1.65	1.65	1.65	1.65	1.65	1.65	1.65
Water	100	100	100	100	100	100	100	100	100
Ingredients(%)w/w	EF1	EF2	EF3	EF4	EF5	EF6	EF7	EF8	EF9
Formulation of emulsion									
S.indicus(oil)	0.5	0.5	0.5	1.0	1.0	1.0	1.5	1.5	1.5
Propylene glycol	10	10	10	10	10	10	10	10	10
Tween 80	6	6	6	6	6	6	6	6	6
Methylparaben	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
Propylparaben	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Water	83	83	83	82.5	82.5	82.5	82	82	82

***This formulations was considered as best because the consistency was similar to marketed formulations. CF and EF formulation was added in the ratio 1:1 to form SE(S.indicus emulgel)**

III. RESULT AND DISCUSSION

EFFECT OF POLYMER

Two polymers were taken in order to compare its texture and viscosity. HPMC 15cps was taken in different concentrations, but the viscosity of the gel obtained was very low. Usually in emulgel formulation HPMC 2910 is used, which was not available in the lab.

So Carbopol 934 was taken in order to form gel, so different concentrations were taken out of which 0.5% and 0.75% gave low viscosity gels, while 2% were highly viscous. Three gel concentrations were taken i.e. 1%, 1.25% and 1.5%.

CHARACTERIZATION OF OIL

Pre-examination of the oil was done by the lab from where we purchased.S.indicus is a volatile oil which gets readily absorbed from the skin as soon as it is applied. So the quantity of oil taken in formulation does not lead to toxicity. Propylene glycol decreases the evaporation rate of volatile oil from the skin. And small globule size acts as a carrier for the drug molecule.
The quantity of S.indicus oil obtained was less as the flowers were of dried form. So the S.indicus oil was purchased from the market.

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Physical Examination

Batch no.	SE1*	SE2	SE3	SE4*	SE5	SE6	SE7*	SE8	SE9
Colour	White creamy	White creamy	White creamy	White creamy	White creamy	White creamy	White creamy	White creamy	White creamy
Phase separation	None	None	None	None	None	None	None	None	None

TABLE4: Physical parameters of final formulation

pH

The pH values of all prepared S.indicus emulgel formulation ranged from 6.2 to 6.8 which are considered acceptable to avoid the risk of irritation upon application to the skin because adult skin pH is 5.5. pH of the S.indicus emulgel formulation were determined by using Digital pH meter. pH meter electrode was washed by distilled water and then dipped into the formulation to measure pH and this process was repeated 3times.

EFFECT OF VISCOSITY

The experiment done it was observed that an optimum viscosity is essential for the formulation to be effective. Rheological properties such as viscosity and thixotropy of semi-solid dosage forms can influence the delivery of drug. Viscosity can directly influence the rate of diffusion of drug. If the viscosity of the formulation is higher, then the release of the volatile oil from emulgel becomes difficult. And if the viscosity of the emulgel is low then the emulgel does not adhere to the skin properly and flows form the skin without giving any effect.

Viscosity decreases with increase in shear rate, while the original viscosity is regained after shearing stops. Most of the topically applied semi-solids show Non-Newtonian behavior. The structures formed within semi-solid drug products during manufacture can show a wide range of behaviours, including shear thinning, viscosity, thixotropy and irreversible or reversible structure damage.

TABLE 5: Viscosity study emulgel formulation (mean± SD, n =3)

Viscosity (cps)									
RPM	**SE1**	**SE2**	**SE3**	**SE4**	**SE5**	**SE6**	**SE7**	**SE8**	**SE9**
10	4007±2.87	4911±5.44	5817±6.60	4021±3.20	4856±3.94	5793±4.89	4068±2.87	4938±1.41	5781±2.39
50	2413±5.705	3503±2.30	4291±2.83	2404±2.00	3482±1.89	4263±5.22	2397±2.36	3490±5.35	4248±4.26

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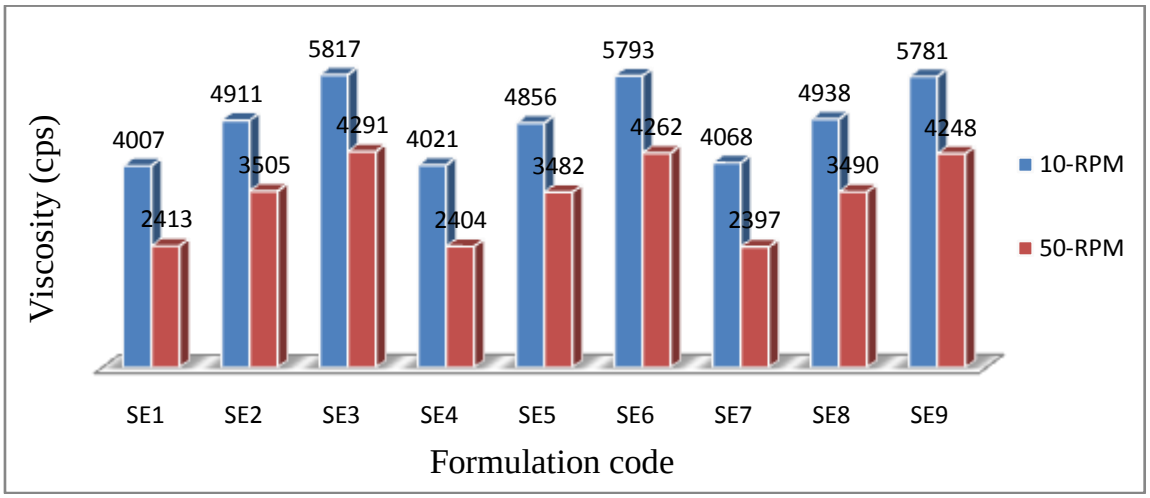

Fig. 6: Viscosity of emulgel formulation (min± SD; n=3)

SPREADABILITY

Viscosity is inversely proportional to spreadability. If the viscosity is higher then it will be difficult to spread the formulation onto the skin properly. The correct formulation of this emulgel allows it to easily flow out of the container (yield stress), should have no stability issue and rather have good spreadability (shear-thinning) on the surface. This helps in uniform coating of emulgel on the skin surface.

Spreadability of emulgel formulation (mean± S.D,n=3)

Batch no	SE1	SE2	SE3	SE4	SE5	SE6	SE7	SE8	SE9
Spreadability (gm.cm/sec)	10±0.34	7.31±0.29	6.25±0.43	10.34±0.56	6.97±0.53	6.39±0.45	9.37±0.84	7.14±0.28	6.12±0.32

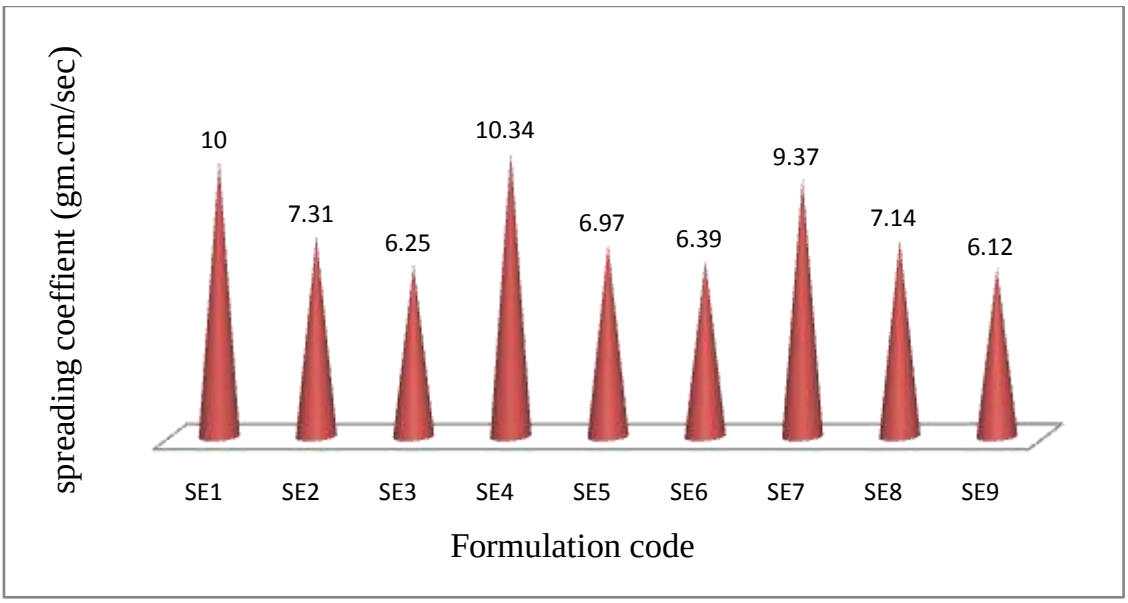

Fig. 7: Spreadability of emulgel formulation (mine± SD; n=3)

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ACCELERATED STABILITY STUDY

Till 1 month the product was stable and there was no phase separation observed. So the quantity of surfactant plays an important role in making the formulation stable.

IV. CONCLUSION

Different formulations of emulgel having varying quantities of polymer and volatile oil were prepared by optimizing their concentrations and its behavior was studied by performing various evaluation parameters. **SE1, SE4** and **SE7**formulation was found out to be suitable for its used as a anti-fungal emulgel. These formulations was considered as best because the consistency was similar to marketed formulations. And the viscosity of it was 4007±2.87, 4021± 3.20 and 4068± 2.87 cps of 10 RPM and 2413± 5.70, 2404± 2.00 and 2397± 2.36 cps of 50 RPM while spreadability 10± 0.03, 10.34± 0.56 and 9.37± 0.84g.cm/sec.

There is a growing public concern due to the increased health and environmental hazard associated with synthetic molecules. For this very reason which is an alternative, safe and natural method was studied in order to develop new anti-fungal dosage form. Essential oils can be a promising natural product which can be mixed with a polymer and made into a new dosage form for fungal inhibition.

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