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Formulation Development and Evaluation of Niosomes Containing Extract of *Tecoma stans* (L.) Juss. Ex Kunth

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Abstract

Niosomes are becoming increasingly relevant in medication administration because they can lower toxicity and alter pharmacokinetics and bioavailability. Topically applied niosomes can improve drug residence duration in the stratum corneum and epidermis while decreasing systemic absorption. It can function as a drug reservoir, and changing the vesicular compositions or surface features can alter the drug release rate and affinity for the target site. Ketoconazole is an imidazole derivative with a broad spectrum of action that can be used to treat both superficial and systemic fungal infections. *Tecoma stans* (L.) Juss. Ex Kunth. Commonly known as Piliya (H), Yellow trumpet busy, Yello bell (E) belongs to family Bignoniaceae is an evergreen ornamental garden and street plant present in wild state. Almost every part of the plant is used medicinally for the treatment of various diseases. The flowers of the plant are used in the treatment of fungal infection, inflammations, stomach pain, diabetes and many others disorders of human being. In the present work ethanolic extract of flowers of plant was taken in consideration to formulate Niosomes and was further evaluated. The results indicate that most promising formulation was F8, which contained Tween 40 as surfactant at ratio of 2:1 with cholesterol.

Key words: *Tecoma stans* (L.) Juss. Ex Kunth., Niosomes, Fungal infection

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Introduction

Fungal infections have surpassed bacteria as the primary cause of infection worldwide. Resistance against human pathogenic organisms has been widely documented in recent years from all over the world. However, the situation in both poor and industrialised countries is concerning due to the indiscriminate use of antibiotics. The treatment of infectious diseases in immunocompromised persons has gotten more difficult due to bacterial and fungal pathogen resistance. Most prevalent fungal infections, such as candidiasis (caused by the yeast-like fungus Candida albicans), aspergillosis (caused by Aspergillus), blastomycosis (caused by Blastomyces), and others, are becoming more widespread in humans and are responsible for the majority of disorders. These species develop quickly at temperatures ranging from 25 to 370 degrees Celsius. [1]

Topical formulations are designed to treat local infections on the uppermost layer of the skin by effectively penetrating the medications into the stratum corneum, thereby eliminating the fungi or organism responsible. The benefits of topical preparations include reduced systemic bioavailability, which minimises systemic side effects, potential self-medication, increased patient compliance, and targeted or localised therapy. However, topical preparations have drawbacks such as poor dermal bioavailability, poor penetration into the stratum corneum, variable drug levels at the site of infection, ointment and cream greasiness or stickiness, skin irritation, allergic reactions, and uncontrolled evaporation of drugs from the preparation. [2] Therefore, there is a need for novel topical formulations to address the problems associated with the current existing formulations. Recently, formulation scientists have explored

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nanoparticle-based drug delivery systems to improve topical formulations. This is done by delivering active drugs precisely to the infection site while enhancing skin penetration, reducing irritation, and increasing the sustained effect. Several novel drug delivery systems have been formulated to encapsulate antifungal agents and improve their efficacy. Some of them include microemulsions, nanoemulsions, niosomes, dendrimers, solid lipid nanoparticles, liposomes, ethosomes, lipid nanoparticles, and polymeric nanoparticles. Keeping the above facts in view the present work was undertaken to develop an effective and safe antifungal formulation using novel approach indented for the treatment of fungal infection.

Materials and Methods

Plant Material Collection

The plant part (Flowers) was collected from the Malwa region of Madhya Pradesh in the month of December-2018. The plant sample was authenticated as by Botanist and Voucher specimen was assigned.

Extraction

The crude drug material (flowers) was prepared by dehydrating and pulverizing. The extraction process was accomplished in a hot continuous mode utilizing methanol as the solvent. The rotary vacuum evaporator was used for absolute remotion of leftover dissolvent after collecting the methanol dissoluble components in the receiver. The finished product was moved to a light-resistant container and hermetically sealed. [3]

Preparation of niosomes

Selection of surfactants for niosomes formation

The different nonionic surfactants viz., span 20, span 60, tween 40 & tween 60 grades were selected for present study.

Preparation of Drug Loaded Niosome

EETSF (Ethanolic extract of *Tecoma stans flower*) loaded niosomes were formulated by using thin film hydration technique and the different nonionic surfactants (span 20, span 60, tween 40 & tween 60) grades in different drug:surfactant:Cholesterol ratios as 1:1:1, 1:2:1, 1:1:2. Accurately weighted quantities of surfactant and Cholesterol were dissolved in 5 ml chloroform using a 100 ml round bottom flask. The lipid solution was evaporated by rotary shaker. The flask was rotated at 135 rpm until a smooth and dry lipid film was obtained. The film was hydrated with 5 ml phosphate buffer saline (PBS) of pH 7.4 containing drug for 3 hours with gentle shaking. The niosomal suspension was further stabilized by keeping at 2-8ºC for 24 hours. [4-5]

Preparation of Niosomal gel

Formulation of 2.5% EETSF gel

Gel was prepared using carbopol-934 as gelling agent. Required quantity of gelling agent was weighed and dispersed in sufficient quantity of distilled water. This dispersion was neutralized by drop wise addition of triethanolamine till a clear gel was obtained. A 2.5% w/w gel was obtained by dissolving EETSF in propylene glycol, and treated in the same way as explained above. [6-7]

Incorporation of niosomes of EETSF to gel base

Selected niosomal formula equivalent of 2.5% w/w EETSF was incorporated into gel base by gentle mechanical mixing at 25 rpm for 15 min.

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Table 1: Formulation and Composition of Niosomal

Formulation Code	Surfactant used	Drug (MELN): Surfactant:Cholesterol Ratio	Solvent	Weight taken (mg)
F1	Span 20	1:1:1	Chloroform	100:100:100
F2		1:2:1	Chloroform	100:200:100
F3		1:1:2	Chloroform	100:100:200
F4	Span 60	1:1:1	Chloroform	100:100:100
F5		1:2:1	Chloroform	100:200:100
F6		1:1:2	Chloroform	100:100:200
F7	Tween 40	1:1:1	Chloroform	100:100:100
F8		1:2:1	Chloroform	100:200:100
F9		1:1:2	Chloroform	100:100:200
F10	Tween 60	1:1:1	Chloroform	100:100:100
F11		1:2:1	Chloroform	100:200:100
F12		1:1:2	Chloroform	100:100:200

Table 2: Formulation of 2.5 % EETSF gel

Ingredients	Quantity (100 gm)
EETSF (2.5%)	2.5 gm
Carbopol 934 (2%)	2 gm
Propylene glycol (10%	9.6 ml
Triethanol amine	qs
Distilled water	qs

Characterization of niosomes

Niosomes formulations were characterized using standard procedures. [4-5]

Vesicle shape and morphology

Shape and morphology of niosomal formulations were determined by optical microscopy and Scanning Electron Microscopy (SEM).

Particle size

The particle size of the niosomal suspension was determined by optical microscopy. A drop of niosomal suspension was placed on a glass slide. A cover slip was placed over the niosomes suspension and evaluated the average vesicle size by an ordinary optical microscope using a pre calibrated ocular eye piece micrometer.

Entrapment Efficiency

Entrapment efficiency of niosomal formulations was determined by centrifugation method. 10mL niosomal suspension was poured into a stopper test tube and centrifuged by using cooling centrifuge at 10,000 rpm maintained at 4^0Cfor 90minutes and then filtered by using Whatman filter paper to obtain clear fraction. The clear fraction was used for the determination of free drug by using UV spectrophotometer at 335 nm respectively. The encapsulation efficiency was calculated using the formula

$$\mathbf{EE\ (\%) = [(Ct\text{-}Cf)/Ct] \times 100}$$

Where, Ct is concentration of total drug; Cf is concentration of unentrapped drug.

Drug Content

Drug content was determined by disrupting the niosomal formulation by propane-1-ol, diluted suitably using phosphate buffer pH 6.8 and analysed for the drug content spectrophotometrically at 335 nm respectively.

Evaluation of niosomal gel and plain gel

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The niosomal gel and plain topical gel were characterized with respect to pH, viscosity, and spreadability. [6-7]

Physical examination

The plain gel and niosomal gel was visually examined for color and texture.

pH Measurements

The pH of the gel formulations was delivered by using digital pH meter.

Viscosity Measurement

The viscosity of gel formulations was determined by Brookfield viscometer. 25.0 g gel was taken in beaker and spindle number 4 was rotated at 50 rpm and viscosity of the sample was determined.

Spreadability

The spreadability of gel formulations was determined by using spreadability apparatus. 1.0 g of gel sample was placed on the lower slide and upper slide was placed on the top of the sample.The spreadability was determined by the formula

$$S = m \times l / t$$

Where, S is spreadability, m is weight tied to upper slide, l is length travel by upper slide and t is time.

Results and Discussion

Developed niosomal formulations were characterized with respect to particle size, shape, entrapment efficiency, and *in vitro* drug release profile. It was clearly observed that niosomes are spherical in shape for all prepared batches. Mean particle size of the niosomal formulation was found to be in the range of 1.50μm to 5.92 μm. It was clearly depicted from Figure that particle size of niosomal formulations was increased on increasing the cholesterol content. The entrapment efficiency of the niosomal formulation was increased on increasing the cholesterol ratio from t to 2. The drug content by thin film hydration method f was in the range of 96.23 to 98.28 %. Drug content of niosomal formulations was also influenced by varying the amount of surfactant. As the amount of surfactant in niosomal formulation increased, the drug content was also increased and this may be due to the decrease in leakage of drug results in enhancement of entrapment efficiency and drug content.

Table 3: Evaluation Parameters of Niosomal formulation containing EETSF

Formulation Code	Particle size (µm)	EE(%)	Drug content (%)
F1	5.80±1.11	65.22±0.11	96.23±0.09
F2	4.84±1.02	70.29±0.18	97.32±0.11
F3	5.92±0.43	70.02±0.02	97.42±0.14
F4	2.15±0.04	69.21±0.11	96.89±0.29
F5	3.11±1.03	72.09±0.32	97.22±0.04
F6	4.32±1.14	78.11±0.12	97.69±0.29
F7	1.56±0.22	80.03±0.18	97.90±0.08
F8	2.82±1.09	84.84±0.36	98.28±0.11
F9	3.98±0.11	78.12±0.32	97.61±0.06
F10	1.05±1.30	71.21±0.21	96.20±0.02
F11	2.12±0.19	70.29±0.20	97.09±0.05
F12	2.18±0.02	77.35±0.10	97.29±0.03

All reading are expressed as mean ± S.D. (n = 3)

On the basis of results obtained of entrapment efficient and drug content and *in vitro* diffusion studies of niosomal formulation it was found that the formulation code F8, was found to have

highest entrapment efficiency and drug content, therefore these three formulation were taken and was incorporated to form niosomal gel. A plain gel was also prepared as per methods described in methodology. All the prepared formulations were evaluated. The results were presented below.

Table 4: Physical examination and other characterization of plain and niosomal gel formulation containing MELN

Formulation Code	Color	Homogenity	Texture	pH	Viscosity (cps)	Spreadability (gmcmsec)	Drug Content
PG EETSF	White	Homogeneous	Smooth	7.10	6078	15.89	97.02±0.01
F8	White	Homogeneous	Smooth	7.00	6220	16.12	98.11±0.06

Conclusion

It is clear from the data that the most promising formulation was F8, which contained Tween 40 as surfactant at ratio of 2:1 with cholesterol.

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