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Research Article

Formulation and Evaluation of antifungal emulgel loaded with Econazole nitrate for topical use

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Abstract

The current study was to formulate and evaluate Econazole nitrate emulgel. The main goal of this formulation was to treat fungal infection of skin. Nine emulgel formulations were prepared by emulsion gel method by using econazole nitrate, Sessame oil, Carbopol 934, surfactant and excipients. The developed formulations were assessed for their appearance, pH, spread-ability, extrudability and the release characteristics of the drug were assessed through in-vitro diffusion study by using goat membrane and Franz diffusion cell. The compatability between Drug-excipient was evaluated by FTIR while anti- fungal efficacy assessed against *Aspergillus niger* using agar diffusion method. All developed formulations exhibited acceptable physicochemical characteristics, including uniform appearance, good homogeneity, skin-compatible pH, satisfactory spread-ability, adequate extrudability, and consistent drug content. FTIR spectra confirmed the absence of significant interactions between Econazole nitrate and the formulation excipients. Among the tested formulations, F3 demonstrated the most desirable sustained drug release profile in 8 Hrs and exhibited the greatest antifungal activity, as evidenced by the largest zone of inhibition. The selected Econazole nitrate emulgel formulation showed excellent physicochemical stability, sustained drug release, and enhanced antifungal efficacy.

Keywords: Econazole Nitrate, Emulgel, Anti-fungal Activity, Goat Membrane.

INTRODUCTION

Topical drug delivery systems (TDDS) involve the application of drug-loaded formulations directly onto the skin to manage localized skin disorders or alleviate cutaneous symptoms related to systemic diseases. These systems are particularly useful when conventional routes of drug administration are less effective or undesirable. Topical formulations are widely employed used to treat various dermatological conditions, including fungal infections, acne, and inflammatory skin disorders. (1)

The skin, being the largest organ of the human body, serves as a protective barrier between the internal environment and external surroundings. It consists of three major layers: the epidermis, dermis, and subcutaneous tissue. Despite its barrier function, the skin offers an accessible route for local drug delivery, enabling therapeutic agents to act directly at the site of infection while minimizing systemic side effects. (2)

Dermal drug delivery offers several advantages, such as ease of application, improved patient adherence, avoidance of first-pass metabolism, and reduced risk of systemic adverse effects. Among the various topical dosage forms, gels have become increasingly popular due to their non-greasy nature, patient acceptability, and ability to enhance drug penetration through the skin. Furthermore, emulgels, which combine the properties of emulsions and gels, have emerged as effective carriers for hydrophobic drugs, providing enhanced stability, drug release, and therapeutic efficacy for the treatment of skin infections. (2,3)

Fungal infections are diseases caused by pathogenic fungi that can affect the hair, nails, skin, mucous membranes, and internal organs. These infections occur when fungi invade body tissues and multiply under favorable conditions such as warm and moist environments. Dermatophytosis represents a common type of fungal infections which include (ringworm), candidiasis, and aspergillosis. While superficial fungal infections mainly affect the outer layers of the body, systemic fungal infections can involve deeper tissues and organs, particularly in immunocompromised individuals. Factors such as poor hygiene, prolonged antibiotic use, diabetes, and weakened immunity increase the risk of fungal infections. Treatment

typically involves the use of antifungal agents administered topically or systemically, depending on the severity and location of the infection. Effective management is important to prevent recurrence, reduce discomfort, and improve the patient's quality of life. (3)

Econazole is a recently introduced imidazole antifungal agent which is very closely related structurally to another imidazole derivative, miconazole. For local application the nitrate salt of Econazole is used, while in preliminary investigations of systemic use in a few patients Econazole base has been administered orally or intravenously. (4) This classification of antifungal drug can be used to treat skin infections like athlete's foot, ringworm, jock itch, pityriasis versicolor. Econazole nitrate exhibits strong anti-feeding properties against the keratin-digesting common clothes moth *Tineola bisselliella*. Econazole nitrate drug shows poor bioavailability for oral use because of poor and variable gastrointestinal absorption and extensive first-pass metabolism. It is mainly used as a topical antifungal and having Log P value of 5.5 which shows it is highly lipophilic. Econazole nitrate is a weakly basic, poorly water-soluble drug. In the acidic stomach it dissolves better than at intestinal pH. Overall oral absorption remains poor because of low aqueous solubility and significant first-pass metabolism hence suitable for topical route of administration. (4)

Emulgel is an innovative and stable semisolid dosage form that combines the properties of both emulsions and gels, enabling it to incorporate water-soluble (hydrophilic) as well as oil-soluble (lipophilic) drugs within a single formulation. It is essentially an emulsion that has been developed into a gel through the incorporation of a suitable gelling agent into either the aqueous or non-aqueous phase, resulting in a system that can be formulated as oil-in-water (o/w) or water-in-oil (w/o) types depending on therapeutic requirements. The major advantage of emulgel lies in its superior skin penetration ability, related to the presence of both phases, which improves the passage of drug molecules across the skin via three primary routes:

1. Through the intact stratum corneum,

2. Via sweat ducts, and

3. Through sebaceous follicles

The stratum corneum accounts for >99% of the skin surface area available for percutaneous drug absorption. The inclusion of a gelling agent not only transforms the classical emulsion into a structured, elegant formulation but also enhances patient compliance through improved spread-ability and a non-greasy feel, (5) ease of application and removal, thixotropic behavior, emollient properties, aesthetic appearance, transparency, and prolonged shelf life. Along with improving drug bioavailability at the affected site, emulgels offer better viscosity, adhesiveness, and stability, leading to enhanced therapeutic outcomes. Owing to these favorable attributes, emulgels have gained signicant interest in the pharmaceutical field for the topical delivery of various therapeutic agents such as analgesic, anti-inflammatory, anti-arthritis, anti-acne, and antifungal drugs. (6) These advantages make emulgels a promising and widely accepted transdermal drug delivery platform in dermatological and pharmaceutical applications. (7)

In the this work the emulgels of Econazole nitrate are prepared using sesame oil and loaded in to gelling agent and evaluated.

MATERIALS AND METHOD

MATERIALS

Econazole nitrate (Yarrow Chem. products Mumbai), Tween 80 (Merck specialities Pvt Lt, Mumbai), Span20 (SDFCL Mumbai), Propyl paraben (Merck Specialities Pvt Lt, Mumbai), Methyl paraben (Merck Specialities Pvt Lt, Mumbai), Carbopol 934 (Sd fine chem Ltd, Mumbai), Triethanolamine (Sd fine chem Ltd, Mumbai), Sesame oil (Research-lab fine chem industries, Mumbai) and Propylene glycol (Merck specialities Pvt Lt, Mumbai).

METHOD

Preparation of standard curve of Econazole nitrate

Weigh 50mg of drug dissolve in methanol to get stock A, from stock A pipette out 10ml and make up with phosphate buffer to get stock B. Appropriate aliquots were then withdrawn and diluted to obtain concentration ranging from 4-40µg/ml, the samples were analysed using UV spectroscopy (UV-1601,Shimadzu, Japan) at 271nm. All measurements were carried out in triplicate and result expressed as mean ± standard deviation (SD, n = 3). (8)

Compatibility study by FTIR Spectra:

Fourier Transform Infrared (FTIR) spectroscopy was used to evaluated the compatibility of the drug, and the selected formulation. Approximately 1–2 mg of each sample was accurately weighed and blended thoroughly with 100–150 mg of dry potassium bromide (KBr) using a mortar and pestle to achieve a fine and homogeneous mixture. The resulting blend was pressed into a transparent pellet using high pressure for infrared spectroscopy. Each pellet was then placed in the sample holder of the FTIR spectrophotometer, (Bruker Alpha E) and the spectra were captured over the wavelength range of 4000–400 cm^{-1}. The same protocol was performed out separately for Econazole nitrate, rice bran wax, and the developed emulgel formulation. The obtained spectra were analyzed to identify characteristic functional groups and to assess any potential intermolecular interactions involving the drug and formulation components. (9)

Preparation of Emulsion

The oleaginous phase was prepared by dispersing Span 20 in a mixture of liquid paraffin and sesame oil. Econazole nitrate was then incorporated into the oil phase with continuous stirring until completely dissolved. Separately, the aqueous phase was prepared by dissolving Tween 80 in purified water. Propyl paraben was dissolved in propylene glycol and added to the aqueous phase. Both phases were heated to

approximately 70°C and mixed gradually under constant stirring to obtain a uniform emulsion. (10)

Preparation of Gel Base

The gel base was prepared by dispersing Carbopol 934 in distilled water with constant mechanical stirring until a homogeneous gel was formed. further distilled water was added to achieve the desired consistency. The pH of the gel was adjusted to 6.0–7.0 using triethanolamine (TEA). (11)

Preparation of Econazole Nitrate Emulgel

The prepared emulsion and gel base were allowed to cool to room temperature. The emulsion was then combined into the gel base in a 1:1 ratio with gentle stirring to obtain a smooth and homogeneous. Econazole Nitrate emulgel formulation. The final product was stored in suitable containers for further evaluation studies. (12)

Table 1: Econazole Nitrate Emulgel formulations

Ingredients	Formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Econazole nitrate(mg)	50	50	50	50	50	50	50	50	50
Sessame oil(ml)	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Span 80(ml)	0.25	0.50	0.75	1.0	1.25	1.50	1.75	2.0	2.5
Tween80(ml)	0.50	0.75	1.0	1.25	1.50	1.75	2.0	2.5	2.75
Carbopol 934(mg)	100	100	100	100	100	100	100	100	100
Propylene glycol(ml)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Methyl paraben(mg)	10	10	10	10	10	10	10	10	10
Propyl paraben(mg)	5	5	5	5	5	5	5	5	5
Triethanolamine	pH was adjusted								

EVALUATION OF EMULGEL

Physical appearance

The formulations were examined visually for their homogenity, color, phase separation and consistency.

Determination of pH

Initially, the electrodes were rinsed with distilled water to provide accurate results. 1g of prepared formulation was dissolved in required quantity of distilled water, then electrode was immersed in it and pH value was measured. All estimations were carried out in triplicate, and the values were reported as mean ± standard deviation (SD, n = 3). (13)

Spreadability

1g of prepared emulgel was placed in between the glass slides. These slides were fixed on the wooden block where, one end of wooden block attached to pulley and allow to laden with gel. The gel spreading diameter was noted and the study was performed in triplicate and the results are expressed as mean ± standard deviation (SD, n = 3). (14)

$$S=\frac{ML}{T}$$

Where,

S=Spreadability

M=Mass

L=Length

T=Time

Drug content

Weigh 1g of each formulation and transferred into a 100 ml volumetric flask. Then dissolved it in methanol and allowed to stir continuously for 2-3 hrs and the volume was then adjusted to 100ml with methanol. The resulting solution was filtered and measured using UV spectrophotometer (UV-1601,Shimadzu, Japan) at 271nm. The measurements were carried out in triplicate, and the results were expressed as mean ± standard deviation (SD, n = 3). (15)

Extrudability

Aluminium collapsible tubes were filled with emulgel formulations. The formulation was extruded by the external force (weight of 500 gm) and the extrudability of the formulation was checked. The measurements were carried out in triplicate and the results were expressed as mean ± standard deviation. (+++ Excellent, ++Very Good, +Good) (SD, n = 3). (16)

In vitro drug release by using dialysis membrane:

The in vitro drug release study of the Econazole nitrate emulgel was examined using a modified Franz diffusion cell. A diffusion tube with an internal diameter of 2 cm was fitted with a cellophane membrane at one end and filled with one gram of the developed emulgel formulation. The diffusion tube was then subsequently

immersed in a beaker containing 150 ml of phosphate buffer solution (pH 7.4), which served as the receptor medium. The system was regulated at 37 ± 0.5°C using a thermostatically controlled magnetic stirrer, and continuous stirring was provided at 120 rpm with a Teflon-coated magnetic bead to ensure uniform distribution of the drug. At predetermined time intervals of 0.25, 0.5, 0.75, 1, 2, 3, 4, 5, 6, and 8 hours, 5 ml aliquot were withdrawn from the diffusion medium and immediately replaced with an equal volume of fresh phosphate buffer (pH 7.4) to maintain sink conditions. The samples were examined using a UV–Visible spectrophotometer (UV-1601,Shimadzu, Japan) to determine the amount of drug released from the formulation. All measurements were carried out in triplicate, and the results were expressed as mean ± standard deviation (SD, n = 3). (17)

In vitro drug release by using goat membrane:

The in vitro diffusion study of the Econazole nitrate emulgel was performed by means of modified Franz diffusion cell with a goat membrane as the diffusion barrier. Approximately 1 g of the emulgel formulation was applied uniformly spread over the membrane. The membrane was positioned between the donor and receptor compartments, and the receptor medium consisted of 150 ml phosphate buffer solution (pH 7.4). The entire assembly was maintained at 37 ± 0.5°C using a thermostatically controlled magnetic stirrer, while continuous agitation was provided at 120 rpm with a Teflon-coated magnetic bead to ensure proper mixing of the receptor medium. At predetermined intervals of 0.25, 0.5, 0.75, 1, 2, 3, 4, 5, 6, and 8 hours, 5 mL samples were collected from the diffusion receptor chamber and replaced with an equal volume of fresh phosphate buffer (pH 7.4) to maintain sink conditions throughout the experiment. The amount of Econazole nitrate diffused through the membrane was quantified by measuring the absorbance of the collected samples using a UV–Visible spectrophotometer (UV-1601,Shimadzu, Japan). All measurements were carried out in triplicate, and the results were expressed as mean ± standard deviation (SD, n = 3). (18)

Drug release kinetics:

For Econazole nitrate emulgel formulation drug-release kinetics was fitted in four kinetic models, zero-order, firstorder, Higuchi and Korsmeyer–Peppas kinetics models

Zero Order:

Zero order was calculated by following equation

$$Q_t = Q_0 - K_0 t$$

Where,

Q_t= release at time 't'

Q_0= drug concentration

K_0= zero order rate constant(h^{-1})

First order Kinetics:

First-order was calculated by the following equation

$$\text{Log } C = \text{Log } C_0 - \frac{Kt}{2.303}$$

Where,

C = Amount of drug remained at time 't'.

C_0= Initial amount of drug

K = Frist order rate constant (h^{-1})

Higuchi's model:

Drug release from the matrix devices by diffusion has been described by following Higuchi's classical diffusion equation

$$Q = K_H t^{1/2}$$

Where,

Q= cumulative amount of drug release

K_H= higuchi constant

t= time in hours

Korsmeyer - Peppa's Model:

Korsmeyer-Peppa's Model indicates the study mechanism of drug release from the matrix tablets which also describes the drug behavior from polymeric systems.

$$M_t / M_\infty = Kt^n$$

Where,

M_t / M_∞ = Fraction of drug released at time t

K = Release constant (h^{-1})

n = release exponent.

Antifungal activity

The selected Econazole nitrate emulgel was assessed against *Aspergillus niger* using the agar well diffusion technique. Potato Dextrose Agar (PDA) medium was prepared according to standard procedures, sterilized, and introduced to sterile microbiological plates. Once the medium solidified, it was inoculated with a freshly prepared fungal suspension of *Aspergillus niger* to ensure uniform microbial growth. Sterile wells of 10 mm diameter were then holed in the agar using a cork borer, and a measured quantity of the emulgel formulation, blank emulgel, pure drug solution was delivered to every well. The inoculated plates were allowed to incubate at 37 ± 2°C for 48–72 hours to allow fungal growth and release of the drug into the surrounding medium. After the incubation period, the antifungal efficacy of the emulgel was estimated by calculating the diameter of the clear zone of inhibition formed around each well. The results were reported as the mean zone of inhibition expressed in millimeters (mm). (19)

Stability studies:

The Econazole nitrate emulgel formulation was subjected to stability testing under the selected storage conditions. The formulation was evaluated for In-vitro drug release. The drug-release profile obtained after stability testing was compared with the initial drug-release profile.

RESULTS

Preparation of standard curve of Econazole

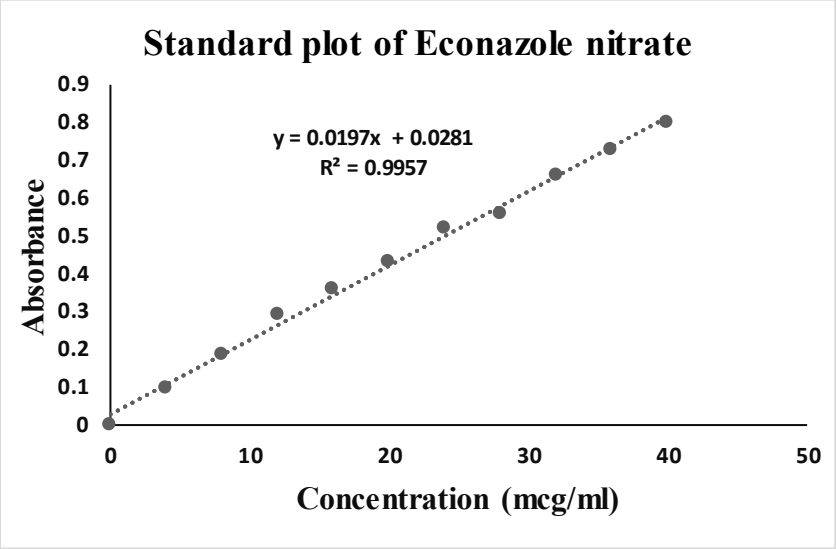

Figure 1: Standard plot of Econazole nitrate

Compatibility study by FTIR:

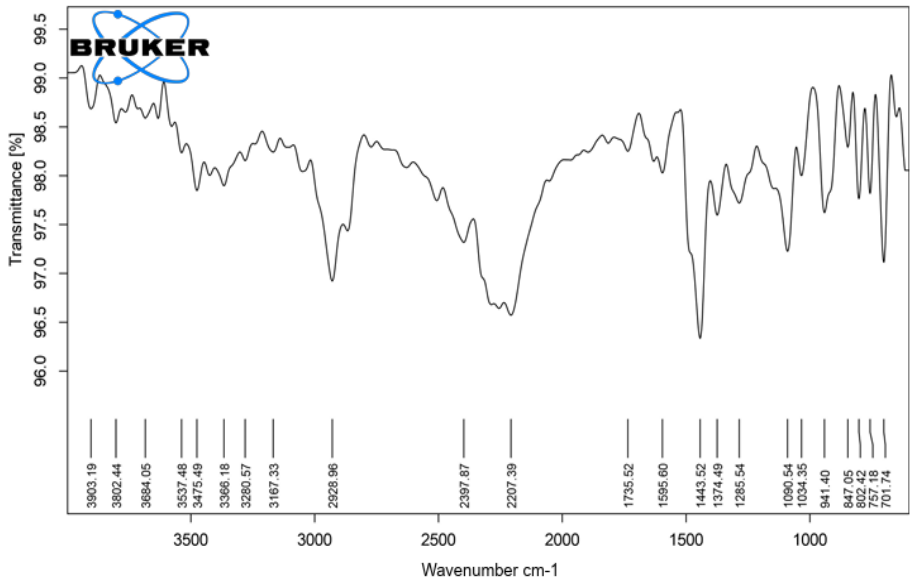

Figure 2: FTIR spectra of Econazole nitrate

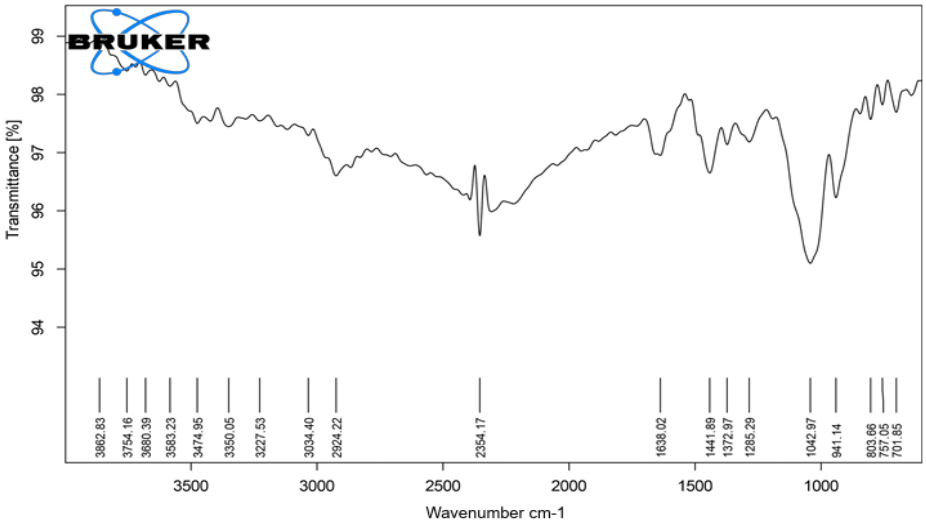

Figure 3: FTIR spectra of formulation F3

Physical Appearance:

Photo 1: Econazole nitrate emulgel formulations

Emulgel formulations were smooth homogeneous and has white creamy viscous texture and glossy appearance. The findings of different formulations were shown in table 2

Table 2: Physical Appearance of formulations

Formulations	Color	Phase separation	homogeneity	Consistency
F1	Milky white	None	Excellent	Excellent
F2	Milky white	None	Excellent	Excellent
F3	Milky white	None	Excellent	Excellent
F4	Milky white	None	Good	Good
F5	Milky white	None	Excellent	Excellent
F6	Milky white	None	Good	Excellent
F7	Milky white	None	Excellent	Excellent
F8	Milky white	None	Excellent	Excellent
F9	Milky white	None	Excellent	Good

Determination of pH

The emulgel formulations shows pH ranges from 7.0-7.6, which is suitable for topical drug delivery. So, the formulations have good skin compatibility.

Spread-ability

All the formulations showed ease of application with good spread-ability. Formulation F3 showed the highest and F7 shows lowest spread-ability.

Table 3: Determination of pH

Formulation	pH *
F1	7.6±0.2
F2	7.5±0.5
F3	7.5±0.1
F4	7.7±0.2
F5	7.6±0.3
F6	7.4±0.5
F7	7.3±0.1
F8	7.0±0.1
F9	7.4±0.4

*Values are mean ± standard deviation (SD, n = 3)

Table 4: Determination of Spread-ability

Formulation	Spread-ability(cm)
F1	0.388±0.028
F2	0.175±0.014
F3	1.25±0.01
F4	0.166±0.013
F5	0.3±0.022
F6	0.625±0.015
F7	0.119±0.025
F8	1±0.02
F9	0.315±0.013

Values are mean ± standard deviation (SD, n = 3)

Extrudability

Extrudabilty of the Econazole nitrate emulgel formulations are reported in table 5. The formulations F3, F5 and F8 showed excellent extrdudability. (+++ Excellent, ++Very Good, +Good)

Table 5: Estimation of Extrudability

Formulation	Extrudability
F1	++
F2	++
F3	++++
F4	+++
F5	++++
F6	+++
F7	+++
F8	++++
F9	++

Photo 2: Extrudability of Econazole nitrate emulgel formulations

Drug content

The drug content of prepared Econazole nitrate emulgel formulations are reported in table 6. The drug content values ranged between 92.2±0.03 to 98±0.10%. Formulation F3 showed the highest drug content (98.3±0.10%), whereas F1 showed the lowest (92.2±0.03%) The relatively narrow variation among the formulations indicates good uniformity of drug distribution in the prepared emulgels.

Table 6: Estimation of Drug content

Formulation	Drug content (%)
F1	92.2±0.03
F2	95.5±0.01
F3	98.3±0.10
F4	94.4±0.13
F5	96.2±0.04
F6	93.3±0.08
F7	95.1±0.15
F8	97.2±0.2
F9	93.3±0.05

Values are mean ± standard deviation (SD, n = 3)

In vitro drug release studies:

In vitro drug release by using dialysis membrane:

The in vitro drug release study shows lowest for the formulation F1 (27.99%) and highest for the formulation F3 (60.02%) for 8hrs. The results were tabulated in table 7.

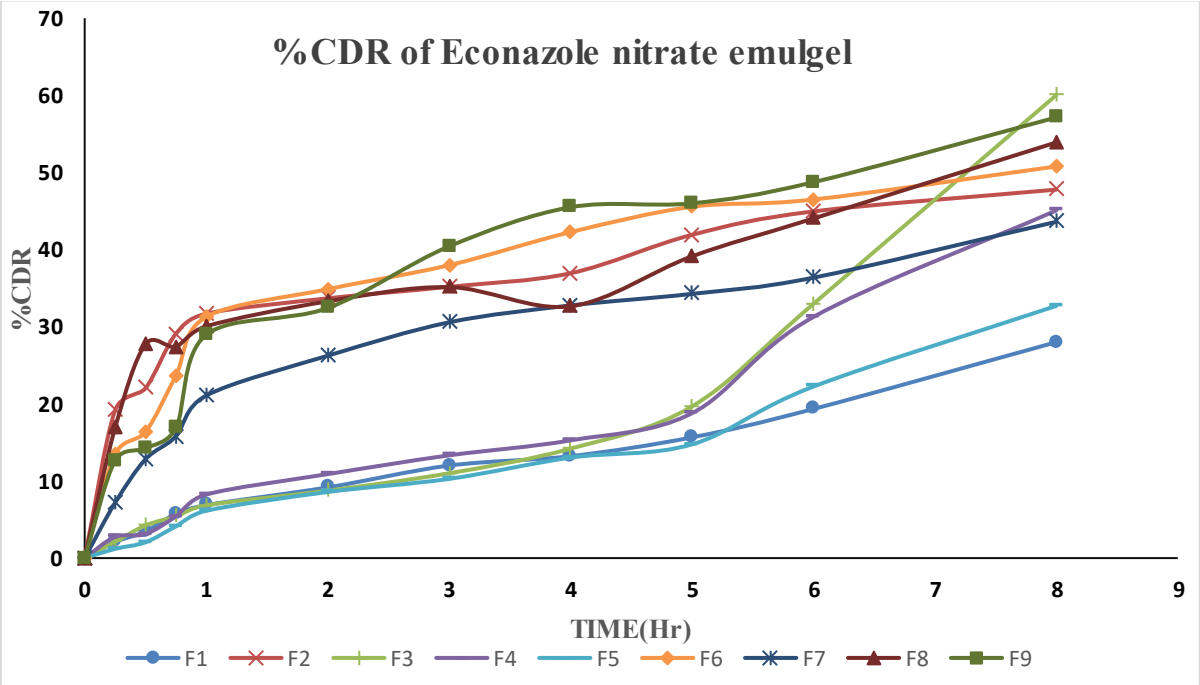

Figure 4: In vitro drug release from Econazole nitrate emulgel formulations by using dialysis membrane

Table 7: In vitro drug release by dialysis membrane

Time (hrs)	Cumulative % drug release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.25	2.09±0.06	19.11±0.07	2.10±0.05	2.74±0.07	1.19±0.05	13.45±0.07	7.15±0.06	16.89±0.05	12.61±0.07
0.5	3.46±0.04	22.01±0.08	4.22±0.03	3.11±0.08	2.04±0.05	16.34±0.05	12.74±0.06	27.72±0.06	14.22±0.04
0.75	5.77±0.05	29.05±0.06	5.41±0.05	5.39±0.06	4.10±0.04	23.62±0.05	15.77±0.04	27.39±0.04	16.84±0.05
1	6.81±0.06	31.69±0.06	6.84±0.04	8.23±0.06	6.13±0.03	31.26±0.06	21.06±0.05	30.05±0.05	28.94±0.06
2	9.15±0.07	33.67±0.08	8.75±0.05	10.88±0.07	8.56±0.05	34.85±0.07	26.22±0.03	33.28±0.06	32.41±0.04
3	11.19±0.05	35.15±0.07	10.99±0.03	13.30±0.07	10.26±0.03	37.97±0.05	30.56±0.04	35.13±0.02	40.40±0.05
4	13.21±0.04	36.93±0.06	14.18±0.04	15.26±0.08	13.02±0.05	42.26±0.07	32.75±0.05	32.64±0.02	45.48±0.05
5	15.65±0.06	41.91±0.05	19.65±0.04	18.77±0.06	14.74±0.05	45.54±0.07	34.25±0.07	39.12±0.05	45.99±0.06
6	19.33±0.07	44.94±0.07	32.95±0.05	31.26±0.07	22.23±0.04	46.48±0.06	36.35±0.07	44.05±0.05	48.73±0.03
8	27.99±0.05	47.77±0.07	60.02±0.06	45.07±0.06	32.699±0.05	50.774±0.05	43.60±0.06	53.88±0.06	57.13±0.06

In vitro drug release by using goat membrane:

The in vitro drug release study shows lowest for the formulation F9 (15.09%) and highest for the formulation F2 (47.08%) for 8hrs. The results were tabulated in table 8.

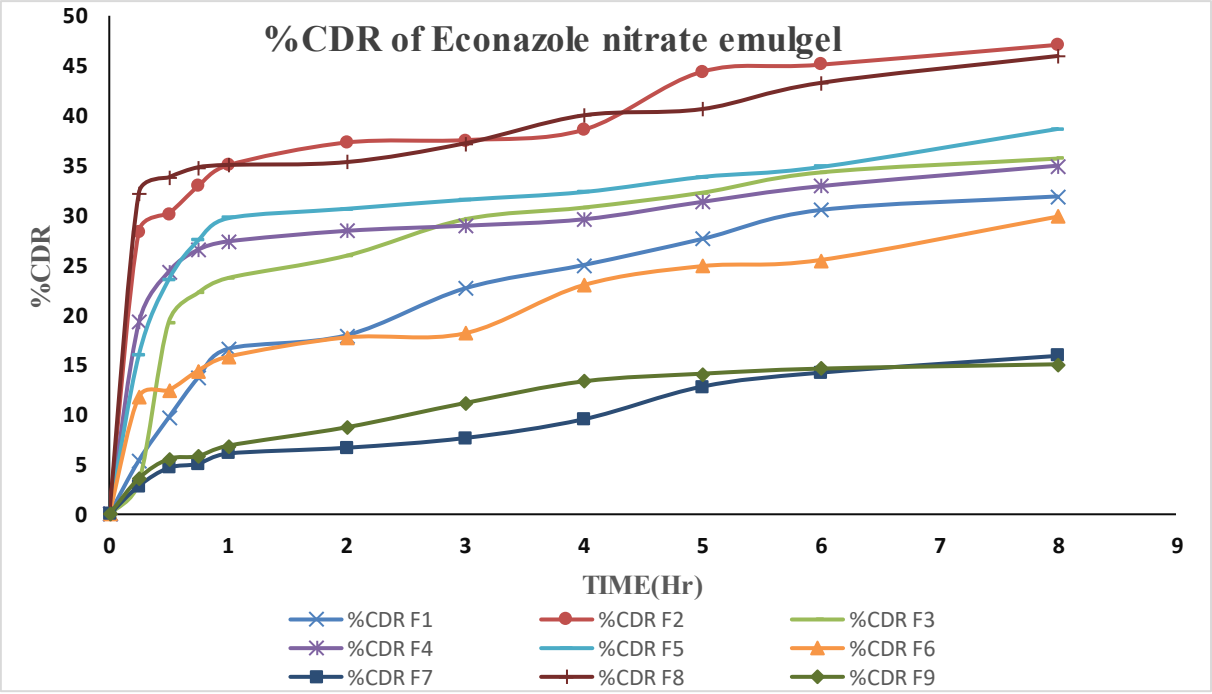

Figure 5: In vitro drug release from Econazole nitrate emulgel formulations by using goat membrane.

Table 8: In vitro drug release by using goat membrane

Time (hrs)	Cumulative % drug release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.25	5.41±0.21	28.38±0.18	3.22±0.24	19.2±0.21	16.01±0.22	11.77±0.19	2.85±0.16	32.24±0.23	3.60±0.17
0.5	9.68±0.21	30.1±0.17	19.23±0.24	24.35±0.2	23.51±0.23	12.45±0.18	4.65±0.18	33.79±0.24	5.54±0.18
0.75	13.76±0.22	32.90±0.17	22.21±0.22	26.53±0.2	27.46±0.21	14.41±0.19	5.05±0.19	34.80±0.22	5.81±0.17
1	16.58±0.21	35.00±0.18	23.69±0.24	27.3±0.21	29.68±0.23	15.80±0.17	6.08±0.17	35.04±0.21	6.86±0.19
2	17.95±0.23	37.28±0.17	25.92±0.23	28.4±0.23	30.63±0.21	17.73±0.18	6.67±0.16	35.31±0.23	8.72±0.19
3	22.65±0.21	37.52±0.17	29.57±0.22	28.9±0.23	31.54±0.21	18.14±0.19	7.64±0.17	37.20±0.24	11.15±0.18
4	24.99±0.23	38.55±0.16	30.75±0.24	29.5±0.22	32.31±0.22	22.97±0.18	9.52±0.19	40.00±0.25	13.32±0.19
5	27.60±0.2	44.38±0.17	32.24±0.23	31.3±0.22	33.82±0.21	24.88±0.18	12.79±0.17	40.6±.0.24	14.09±0.17
6	30.51±0.2	45.08±0.16	34.2±0.23	32.90±0.2	34.82±0.21	25.50±0.19	14.20±0.19	43.26±0.21	14.60±0.18
8	31.8±0.22	47.08±0.16	35.7±0.22	34.96±0.2	38.64±0.22	29.84±0.18	15.88±0.18	45.96±0.23	15.04±0.19

Drug release kinetics

Drug release kinetics of Econazole nitrate emulgel by dialysis membrane

The formulations exhibited different degrees of correlation with the applied kinetic models. F1 and F3 showed the highest correlation with the zero-order model, whereas F2, F6, F7, F8 and F9 showed better correlation with the Higuchi model. F4 and F5 showed comparatively higher correlation with the zero-order model. The Korsmeyer–Peppas exponent (n) values ranged from 0.0756 to 0.2192, indicating Fickian diffusion as the predominant mechanism of drug release.

Table 9: Drug release kinetics of Econazole nitrate emulgel by dialysis membrane**:**

Formulation code	Correlation co-efficient (r^2)			Korsmeyer peppa's model (n value)
	Zero order equation	First order equation	Higuchi equation	
F1	0.9506	0.9391	0.9101	0.0756
F2	0.7169	0.8017	0.8854	0.1349
F3	0.8128	0.7077	0.6761	0.1704
F4	0.904	0.8429	0.8017	0.1325
F5	0.9304	0.9036	0.842	0.088
F6	0.8006	0.8714	0.948	0.1829
F7	0.8633	0.9009	0.9724	0.1449
F8	0.7204	0.7899	0.8484	0.1382
F9	0.8752	0.9233	0.9723	0.2192

Drug release kinetics of Econazole nitrate emulgel by goat membrane

The first-order model showed a higher R^2 value than the zero-order model for all formulations (F1–F9), with R^2 values ranging from 0.5422 to 0.9521. Formulation F7 showed the first-order correlation (R^2 = 0.9521).

Table 10: Drug release kinetics of Econazole nitrate emulgel by goat membrane:

Formulation code	Correlation co-efficient (r^2)			Korsmeyer peppa's model (n value)
	Zero order equation	First order equation	Higuchi equation	
F1	0.865	0.9097	0.9795	0.103
F2	0.5461	0.6491	0.7438	0.1042
F3	0.6695	0.784	0.8448	0.4172
F4	0.4813	0.5422	0.6936	0.065
F5	0.548	0.6113	0.7605	0.087
F6	0.8163	0.8556	0.9317	0.0707
F7	0.946	0.9521	0.9564	0.0418
F8	0.4306	0.5406	0.623	0.0833
F9	0.8816	0.894	0.9857	0.0442

Anti-fungal activity:

The anti-fungal activity of selected Econazole nitrate emulgel formulation and pure drug solution was performed.

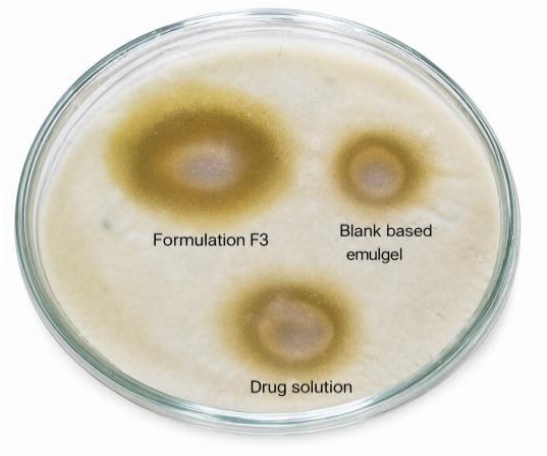

Figure 6: Concentration of drug used 20µg/ml

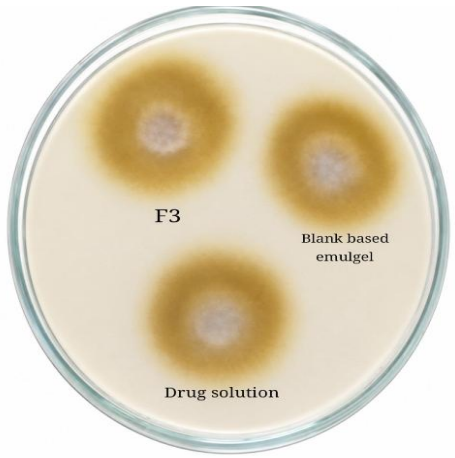

Figure 7: Concentration of drug used 40µg/ml

Table 11: Anti- fungal activity of Econazole nitrate emulgel formulation F3 and pure drug

Parameters	Concentrations tested	
	20 µg/ml	40 µg/ml
Formulation F3	18 mm	25 mm
Blank emulgel	8 mm	12 mm
Drug solution	13 mm	15 mm

Stability study

The minor variations in drug release were observed after storage, indicating that the formulation maintained its drug-release characteristics and remained stable during the study period.

Table 12: Cumulative % Drug Release of Formulation F3 after stability study

Time	Cumulative % drug release of formulation F3	
	At room temperature	At 40 ^{0}C ± 0.5 ^{0}C Temperature and 75% ± 5% after 6 weeks
	F3	F3
0	0	0
0.25	2.10±0.05	1.5±0.04
0.5	4.22±0.03	3.31±0.05
0.75	5.41±0.05	5.13±0.04
1	6.84±0.04	6.47±0.05
2	8.75±0.05	7.49±0.04
3	10.99±0.03	10.55±0.04
4	14.18±0.04	12.22±0.05
5	19.65±0.04	17.98±0.05
6	32.95±0.05	30.55±0.04
8	60.02±0.06	58.42±0.05

Values are mean ± standard deviation (SD, n = 3)

CONCLUSION

The Econazole nitrate emulgel formulations were successfully developed as a modern topical drug delivery system for the treatment of fungal infections. The formulated emulgel exhibited desirable physicochemical properties, including good homogeneity, acceptable pH, excellent spreadability, suitable extrudability, and satisfactory drug content. The FTIR analysis confirmed the compatibility of the drug with the selected excipients. In vitro drug release demonstrated prolonged and effective and sustained drug diffusion. The selected formulation also showed significant antifungal activity, indicating its potential therapeutic effectiveness. Overall, the results suggest that Econazole Nitrate emulgel is a stable, effective, and patient-friendly formulation that combines the advantages of both emulsions and gels, making it a promising alternative to conventional topical antifungal preparations.

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