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FORMULATION AND EVALUATION OF KETOCONAZOLE LOADED TRANSFERSOMAL GEL

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Abstract

Objective: The present study aims to investigate the potential of a transfersomal gel formulation loaded with ketoconazole as an innovative approach for treating fungal infections, offering a viable alternative to conventional dosage forms. Through optimization, the developed formulation exhibits the ability to augment the bioavailability and skin permeation of ketoconazole, thereby enhancingits therapeutic efficacy.
Materials and method: ketoconazole-loaded transfersomal gel were prepared by the film-hydration method using carbopol, Tween 80, distilled water, Span 80, phosphatidylcholine, propylene glycol, soya phosphatidyl choline.
Results and discussion: The optimized ketoconazole-loaded transfersom was used to prepare ketoconazole-loaded transfersomal gel with the aid of Carbopol 940 as the gelling agent. The Optimized ketoconazole-loaded transfersomal gel had a spherical shape with the particle size of, polydispersity index, the zeta potential, encapsulation efficiency, and release efficiency. In-vivo release studies showed that the cumulative amount of ketoconazole-loaded transfersomal gel was significantly higher and good bioavailability.
Keywords: ketoconazole, transfersomal gel, transfersome, topical drug delivery

1. Introduction

Fungal infections represent a prevalent and widespread health concern impacting a substantial number of individuals globally. Notably, dermatophytosis, candidiasis, and pityriasis versicolor are recognized as the most frequently encountered types of fungal infections. To combat these infections, ketoconazole, an imidazole derivative, has gained substantial usage as an antifungal drug. Nevertheless, the therapeutic effectiveness of ketoconazole is hindered by its limited water solubility and inadequate bioavailability. Traditional formulations of ketoconazole, such as tablets, capsules, and creams, exhibit various limitations, including suboptimal bioavailability, inadequate dermal penetration, and systemic adverse effects.[1]
Transfersomes, an innovative pharmaceutical delivery system, represent a class of deformable vesicles comprising phospholipids and surfactants capable of encapsulating both hydrophilic and lipophilic therapeutic agents. These vesicles possess a distinctive capacity to traverse the stratum corneum, the outermost epidermal layer, facilitating drug diffusion into the underlying tissues. Extensive studies have demonstrated that transfersomal formulations exhibit remarkable improvements in drug bioavailability and skin permeability, exemplified by the enhanced delivery of ketoconazole and other therapeutic compounds.[2]
Gels represent semi-solid pharmaceutical formulations with notable applicability for topical

administration, making them an advantageous option for the targeted delivery of drugs. Their distinctive properties, including controlled release, prolonged duration of action, and enhanced patient adherence, render them highly favorable. Consequently, the formulation of a transfersomal gel loaded with ketoconazole could present a promising strategy for the efficient topical administration of the drug, resulting in enhanced therapeutic efficacy.[3]

In recent years, a substantial research focus has emerged concerning the advancement of transfersomal gels as a drug delivery system. Numerous investigations have documented the efficacious encapsulation of diverse drugs within transfersomes, which are subsequently incorporated into gels. Nonetheless, limited attention has been directed towards the development and assessment of transfersomal gels loaded with ketoconazole.[4]

The formulation optimization process involved the systematic manipulation of various parameters including the concentrations of phospholipids, surfactants, and drug, as well as the duration and temperature of sonication. The resultant optimized formulation was subjected to characterization using diverse parameters including particle size, zeta potential, entrapment efficiency, and in vitro drug release. Additionally, the effectiveness of the transfersomal gel was assessed through in vitro antifungal activity assays and ex vivo skin permeation studies. [5, 6]

Multiple investigations have elucidated the application of transfersomes as a vehicle for administering diverse pharmaceutical agents, encompassing antifungal compounds like ketoconazole. In a study conducted by Patel and Vavia in 2007, elastic liposomes containing ketoconazole were formulated and subjected to an assessment of their in vitro efficacy. The findingsindicated that the elastic liposomes exhibited a notably augmented rate of permeation through the skin and greater deposition of the drug compared to conventional liposomes.[7]

Similarly, El-Kamel et al. (2016) prepared transfersomal ketoconazole gel for the topical treatment of fungal infections. The transfersomal gel showed a significantly higher antifungal activity and skin permeation rate than the conventional gel. The authors attributed the improved performance to the transfersomes' ability to enhance the drug's skin penetration and retention.[8]

Cevher et al. (2018) formulated ketoconazole transfersomes and conducted an in vitro assessment of their efficacy. The researchers observed that the transfersomes exhibited a considerably elevated rate of skin permeation and drug deposition compared to conventional liposomes. They further attributed the enhanced performance of the transfersomes to their capacity to penetrate the stratum corneum and facilitate drug delivery to the underlying tissues.[9]

Numerous investigations have additionally investigated the utilization of gels as a means of administering pharmaceutical substances, including antifungal agents like ketoconazole. Patel et al. (2010) conducted a study revealing that ketoconazole gel exhibited superior effectiveness in the treatment of fungal infections when compared to conventional cream formulations. The authors ascribed this enhanced performance to the gel's capacity for sustaining drug release and facilitating improved cutaneous penetration.[10]

In recent years, there has been a notable surge in the scientific community's focus on the advancement of transfersomal gels as a means of drug delivery. Notably, Kalepu and Nekkanti (2015) conducted a study that demonstrated the successful formulation of a transfersomal gel containing curcumin, with the specific aim of treating skin cancer. Their findings revealed that the transfersomal gel exhibited a substantially augmented rate of skin permeation and drug deposition when compared to conventional gel formulations. This enhanced performance was attributed to the inherent capability of transfersomes to effectively penetrate the skin and transport the drug to the underlying tissues.[11]

The present study aims to investigate the potential of a transfersomal gel formulation loaded

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with ketoconazole as an innovative approach for treating fungal infections, offering a viable alternative to conventional dosage forms. Through optimization, the developed formulation exhibits the ability to augment the bioavailability and skin permeation of ketoconazole, thereby enhancing its therapeutic efficacy.

2. Material and Methodology

In the present study, the drug ketoconazole, distilled alcohol, phosphate buffer, carbopol, Tween 80, distilled water, Span 80, phosphatidylcholine, propylene glycol, soya phosphatidyl choline, methanol, chloroform, and saline phosphate buffer were obtained from an unknown supplier, while distilled alcohol was sourced from Changshu Yangyuan Chemical China. All the others chemical and reagents were used analytical grade

3. Preformulation studies:

3.1 Organoleptic Properties

Organoleptic evaluation means the study of drugs using organs of senses. It refers to the methods of analysis like colour, odour, taste, size, shape and special features, such as touch, texture, etc.

3.2 Fourier transforms infrared study

Fourier transform infrared was used for the identification of drug polymer interaction.

3.3 Standard Curve of ketoconazole

Standard Curve of ketoconazole was prepare a standard curve a series of standard solutions with known concentrations of the drug can be prepared using UV spectroscopy. Prepared standard solution of ketoconazole was scanned over uv range 200 to 400nm and determined the λ max of ketoconazole.

3.4 Solubility of ketoconazole

An excessive amount of a drug was introduced into a 250 mL conical flask containing an appropriate volume of solvent. Both buffer solutions were subjected to agitation in an orbital shakerfor duration of 48 hours. Subsequently, a 100 µL portion of the resulting clear supernatant was extracted and diluted to a final volume of 20 mL. The diluted samples were then subjected to analysis using a UV spectrophotometer:

3.5 Melting point of ketoconazole

The melting point of an organic solid was successfully determined using a melting point apparatus. The experimental procedure involved the insertion of a capillary sample, adjustment of the heating rate, continuous monitoring through the viewfinder, and subsequent cooling down of the apparatus. The obtained melting point provided crucial information about the compound's physical properties, facilitating its identification and assessment of purity.

3.6 Evaluation of powder blend

Angle of repose

The angle of repose of a powder blend was ascertained using the funnel method. Precisely measuredquantities of the powder blend were introduced into a funnel. The funnel's height was adjusted to ensure that its tip made contact with the apex of the powder blend. Subsequently, the powder blend was allowed to flow unhindered through the funnel, settling onto the underlying surface. The diameter of the resulting cone formed by the powder was measured, and the angle of repose was determined by applying the following equation.

$\tan \theta = h/r$

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Where, h and r are the height and radius of the powder cone respectively.

3.7 Bulk density and tapped density

A standardized procedure was followed to evaluate the physical properties of powdered blends. Each formula consisted of a precise quantity of 2 grams of powder blend, which had been adequately shaken to disperse any agglomerates that had formed. The powder blend was carefully introduced into a 10 ml measuring cylinder. The initial volume of the powder blend in the cylinder was recorded. Subsequently, the measuring cylinder was allowed to fall freely from a height of 2.5 cm onto a rigid surface at two-second intervals. This tapping process was repeated until no further change in volume was observed.
The bulk density (ρB) and tapped density (ρT) of the powder blend were determined using the following mathematical equations, respectively:
Bulk Density (ρB) = Mass of Powder Blend / Initial Volume of Powder Blend
Tapped Density (ρT) = Mass of Powder Blend / Tapped Volume of Powder Blend
By applying these equations, the bulk density and tapped density of the powder blend could be calculated, providing valuable information about its physical characteristics

3.8 Compressibility Index

The Compressibility Index (CI) of the powder blend was assessed employing Carr's compressibility index formula, given by.
Carr's index (%) = $(\rho T - \rho B)/\rho T \times 100$

3.9 Hausner's ratio

The Hausner's ratio is a number that is correlated to the flowability of a powder or granular material. The ratio of tapped density to bulk density of the powders is called the Hausner's ratio. It was calculated by the following equation.
H = $\frac{\rho T}{\rho B}$

4. Formulation of Ketoconazole-Loaded Transfersomes

Ketoconazole-loaded transfersomes were synthesized using the thin film hydration technique. In summary, a mixture containing Ketoconazole (1 to 2%w/v), varying quantities of Phospholipid (2to 3.5%w/v), Cholesterol (1 to 1.5% w/v), and Tween80 (0.5 to 1.5% w/v) was dissolved in 5 mL ofchloroform. The solvent was then removed by vacuum evaporation using a rotary evaporator, resulting in the formation of a thin lipid film. Subsequently, the lipid film deposited on the inner surface of a round-bottom flask was hydrated with 10 mL of phosphate buffer solution at pH 7.4. The hydration process was carried out by rotating the flask at 60 revolutions per minute for 30 minutes. The resulting vesicles were allowed to swell at room temperature for 1 hour. Finally, the vesicles were sonicated using a bath sonicator for 30 minutes to achieve a uniform suspension.

5. Formulation of Transfersomal Gel

Carbopol-940, a polymer, was dispersed in distilled water to form an aqueous dispersion. The dispersion was subjected to stirring until it exhibited increased viscosity, indicating thickening. Once complete dispersion was achieved, 10 ml of propylene glycol was slowly added to the Carbopol-940 dispersion, along with additional ingredients including 10 ml of isopropyl alcohol and 5 ml of triethanolamine. Furthermore, 10 ml of transfersomes dispersion was incorporated into the Carbopol gel with continuous stirring. To achieve a final volume of 100 g of gel, an

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appropriate quantity of distilled water was added.

Table 1 Transfersomal gel formulation chart for ketoconazole:

Ingredient	Formulation-1 Concentration %	Formulation-2 Concentration %	Formulation-3 Concentration %	Formulation-4 Concentration %
Ketoconazole	1	1.5	2	1
Phospholipid	2	2.5	3	3.5
Cholesterol	1	1	1.5	1
Tween 80	0.5	1	1.5	0.5
Carbopol 934P	0.5	1	1.5	2
Triethanolamine	0.1	.25	0.35	0.45
Purified water	q.s.	q.s.	q.s.	q.s.

Note: q.s. means quantity sufficient to obtain desired volume

6.1 Characterization of Transfersomal Gel Formulation

Characterization of transfersomal gel formulation is important to ensure the stability, drug release, and efficacy of the product. Some of the key parameters that are commonly used for characterization include:

6.1.1 Size and Shape Analysis

The average size of the gel was determined through microscopic analysis. A sample of Transfersome gel was appropriately diluted with purified water, and a drop of the diluted suspension was examined under a microscope at magnifications of 15x and 45x. To measure the vesicle size, a matched eyepiece micrometer and a stage micrometer were employed. One hundred and fifty vesicle diameters were randomly selected and measured. The average diameter wassubsequently determined using formula. The formula is shown in below [12-15].

Average diameter (d_{ave}) =
$\frac{\sum nd}{\sum n}$ n = number of vesicles
d = diameter of the vesicles

6.1.2 Drug entrapment studies (% Entrapment Efficiency studies)

Ultracentrifugation was employed to evaluate the encapsulation efficiency of drugs within

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Transfersome gel. A 1% Triton X-100 solution (1 ml) was combined with Transfersome gel formulation (10 ml). The resulting mixture underwent vortexing for two 5-minute cycles, with 2minutes of rest between each cycle. Subsequently, 1.5 ml of each vortexed sample and untreated Transfersome gel formulation were transferred into separate centrifugal tubes. These samples were then subjected to centrifugation at 20,000 rpm for duration of 3 hours. The supernatant layer was isolated and appropriately diluted with water. The drug concentration in both the vortex and un vortex samples was determined, yielding values of 260.2 nm and 222.4 nm, respectively. [16-18] The effectiveness of the trap was determined as follows:

Entrapment Efficiency = $\frac{t-c}{t}$ X 100

'T' is total amount of drug detected from supernatant layer of vortex sample. 'C' is the amount of drug unentrapped and detected from supernatant layer of unvortex sample.

6.1.3 Stability Studies

To conduct the stability study, a solution containing transferosomes (TFs) gel formulation optimized for the delivery of ketoconazole was prepared. The samples were subjected to varying storage conditions in order to evaluate their long-term and accelerated stability. Specifically, the samples were stored at a temperature of 25°C with a relative humidity (RH) of 60% to simulate long-term storage conditions. For accelerated stability testing, the samples were stored at a higher temperature of 40°C with an RH of 75%. Additionally, a refrigerator condition was simulated by storing the samples at a controlled temperature of 5±3°C. The stability studies were conducted over a period of three months to assess the changes in the formulation over time [19-23].

7. Result & Discussion

7.1 Organoleptic properties

The oranoleptic properties of drug was studied and found to be suitable as official method. The physical properties of ketoconazole are shown in Table 5.1. The physical appearance of the powder gave satisfactory result. The prepared patches were flexible, homogenous, opaque, non-sticky and smooth natured

Table 2: Physical properties of Ketoconazole

Parameters	Remarks
General appearance	Crystalline powder
Colour	White to slightly beige-colored
Odour	Odorless crystalline powder
Taste	Slightly bitter

7.2 FTIR study

The FTIR study of drug and excipents mixture was studied and found to be no any other peaks. The results of FTIR peaks revealed that drug and excipents mixture was not show any interaction and suitable for the formulation and development. The FTIR spectra of ketoconazole are shown in figure 5.

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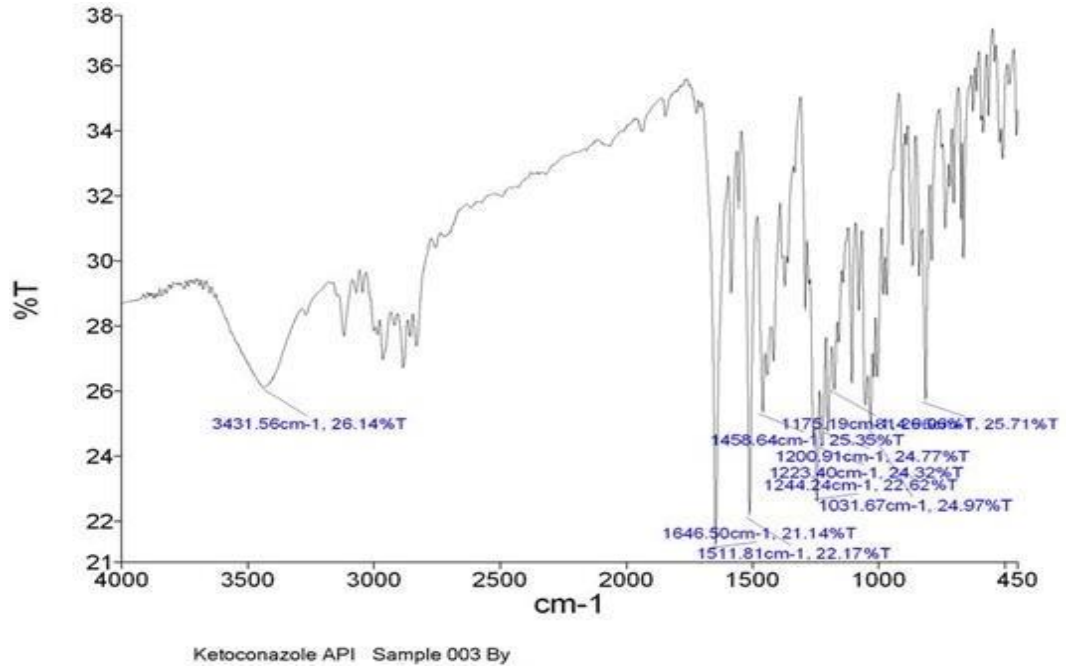

Fig. 1. FTIR spectrum of ketoconazole

7.3 Standard curve

The standard curve of ketoconazole was determined and found to be λ-max 239nm.

7.4 Solubility of ketoconazole

Solubility of ketoconazole was determined using in various solvents which is shown in tabulated form below. Highest solubility was found to be in ethanol. It is indicated that drug was suitable forthe development of transferosome gel.

Table 3: Solubility Study

S. No.	**Surfactant**	**Wavelength (nm)**	Solubility
1.	Water	237 nm	Sparingly soluble
2.	Methanol	237nm	Sparingly soluble
3.	Ethanol	237 nm	Slightly more soluble in ethanol than in methanol
4.	Chloroform	237 nm	Insoluble

7.5 Melting point

The melting point of ketoconazole was found to be 148-152^{0}C. The melting point of ketoconazole was indicated that drug is pure and suitable for the formulation.

7.6 Flow properties of ketoconazole

Micromeritic properties of powder blends of batches F1-F5 were determined. The results are shown in Table 5.4. The data presented in the table 5.4 represented the micromeritic properties

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of powder blends from five different batches labeled F-1 through F-4 was under satisfactory.

Table 4: Micromeritic properties of powder blends of batches F1-F4.

Powder Blend	Angle of Repose (°)	Bulk density (g/cc)	Tapped density (g/cc)	Carr's index (%)	Hausner's Ratio
F-1	28.6	0.61	0.70	12.85	1.14
F-2	32.4	0.63	0.75	16	1.19
F-3	33.6	0.65	0.79	17.72	1.2
F-4	29.5	0.62	0.72	13.88	1.16

7.7 The angle of repose

The angle of repose, as a fundamental parameter in the study of powder flowability, serves as an indicator of the flow characteristics of powdered substances. It is established through the measurement of the angle formed by a heap of powder upon deposition onto a level horizontal plane. In the case of the examined powder blends, the observed values for the angle of repose rangebetween 28 and 34 degrees, which implies that these particular blends possess a favorable to moderately favorable flowability trait. The results was indicated that F1 to F4 all optimized formulation showed satisfactory as per official guideline.

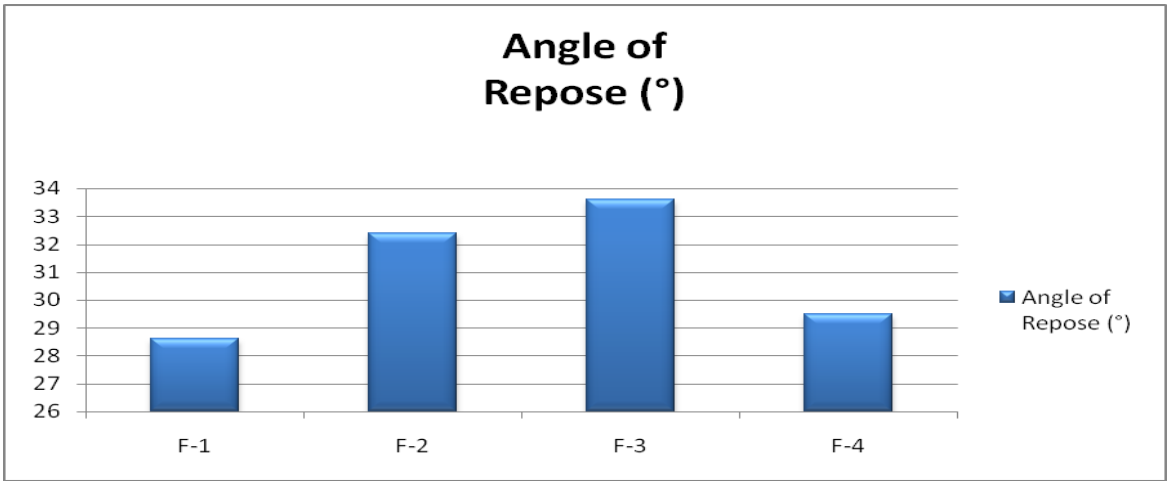

Fig 2. The angle of repose of powder blends of batches F1-F4

7.8 Bulk density

The bulk density, which refers to the density of a powder blend in its loose state, and tapped density, which represents the density of the powder blend after undergoing tapping to settle the particles, was measured in this study. The bulk density values ranged from 0.60 to 0.65 g/cc, while the tapped density values ranged from 0.71 to 0.80 g/cc. The discrepancy between the bulk and tapped density serves as an indication of the powder's settling ability, with a smaller difference indicating superior settling properties. The results demonstrated that all optimized formulations (F1 to F4) exhibited satisfactory performance in accordance with the official

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guidelines.

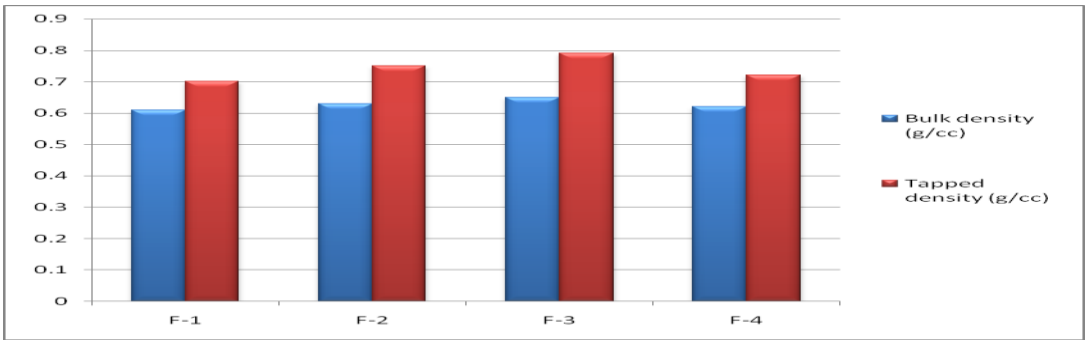

Fig. 3. The Bulk density and tapped density of powder blends of batches F1-F4

7.9 Carr's index

The Carr's index, denoted as CI, serves as a quantitative indicator for evaluating the compressibility characteristics of powdered substances. It is derived by employing the formula (tapped density - bulk density) divided by tapped density, multiplied by 100. The obtained values for Carr's index fall within the range of 13.46% to 19.6%, signifying a moderate level of compressibility for the investigated powders. The experimental findings unequivocally demonstrated that all meticulously optimized formulations, denoted as F1 through F4, showcased commendable performance, adhering to the stipulations prescribed by the authoritative guidelines.

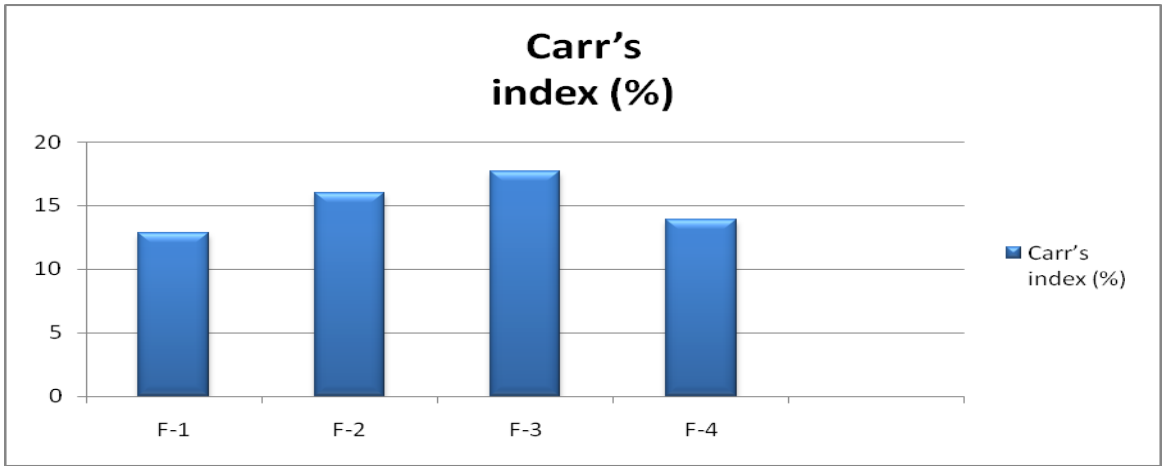

Fig. 4. The Carr's index of powder blends of batches F1-F4

7.10 Hausner's ratio

The Hausner's ratio, denoted as HR, is determined through the division of tapped density by bulk density. This ratio serves as a quantitative measure of the cohesiveness and interparticulate friction within a powder. Hausner's ratio values typically fall within the range of 1.15 to 1.24. Higher values of HR signify greater cohesiveness and reduced flowability of the powder. The experimental outcomes revealed that all optimized formulations (F1 to F4) exhibited commendableperformance in compliance with the established regulatory guidelines.

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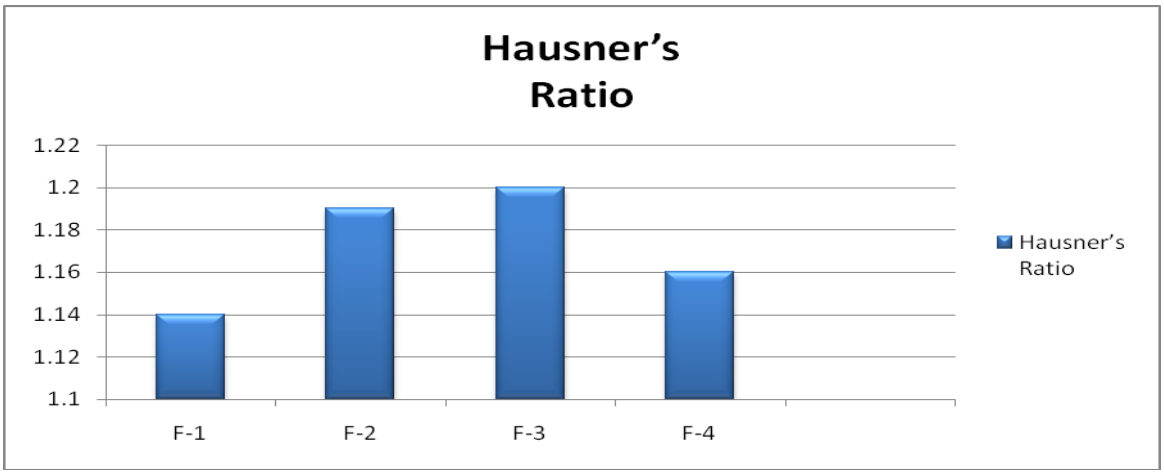

Fig. 5. The Hausner's ratio of powder blends of batches F1-F4

7.11 Characterization

Since the physical characterization of prepared transfersomal formulations and their similarities was determined [19-23].

7.12.1 Size & Shape Analysis

The size distribution analysis of Ketoconazole Transfersomal gel formulation was conducted to determine the characteristics of the vesicles present. Vesicles, being lipid-based structures utilized for targeted drug delivery within the body, play a significant role in this formulation. The presented data encompasses the size range of the vesicles, the average size (d) of vesicles within each range, the number of vesicles (n) in each size range, the percentage of vesicles in each size range, as well as the product of (n) and (d). These findings collectively indicated that Formulation-1 of ketoconazole transfersomal gel exhibited a relatively homogeneous size distribution of vesicles. Such uniformity holds potential implications for drug delivery efficiency and therapeutic efficacy.

Average diameter (d_{ave}) = $= \frac{560}{123} = 4.5528$ µm

Table 5: Size distribution of Ketoconazole Transfersomal gel of Formulation-1

S.NO	SIZE RANGE	AVERAGE SIZE (D)	NO. OF VESICLES (N)	% VESICLES	(N) X (D)
1.	0.0-3.4	1.5	40	30.5	60
2.	3.5-6.5	4.2	50	34.0	210
3.	6.5-9.5	7.6	20	18.0	152
4.	9.5-12.5	10.50	10	4.0	105.2
5.	12.5-15.5	11.25	03	2	33.75

7.12.2 Size distribution of Ketoconazole Transfersomal gel of Formulation-2

The data provided describes the size distribution of the vesicles in Formulation-2 of ketoconazole transfersomal gel. Similar to Formulation-1, vesicles in Formulation-2 are used to deliver drugs to

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specific sites in the body. The table shows the size range of the vesicles, the average size (d) of the vesicles within each size range, the number of vesicles (n) in each size range, the percentage of vesicles in each size range, and the product of (n) and (d). Overall, the data indicates that Formulation-2 of ketoconazole transfersomal gel has a relatively uniform size distribution of vesicles, which may have implications for drug delivery and efficacy.

Table 6: Size distribution of Ketoconazole Transfersomal gel of Formulation-2

s.no	Size range	Averagesize (d)	No.of vesicles(n)*	% vesicles	(n) x(d)
1.	0.0-3.5	1.5	65	39.16	97.5
2.	3.5-6.5	4.2	69	41.57	310.5
3.	6.5-9.5	7.6	25	15.06	32.5
4.	9.5-12.5	10.50	04	2.41	42
5.	12.5-15.5	11.25	03	1.81	25.5

Average diameter (dave) = $\frac{\sum nd}{\sum n} = \frac{508}{166}$ = 3.0602 µm

7.12.3 Size distribution of Ketoconazole Transfersomal gel of Formulation-3

The data provided describes the size distribution of the vesicles in Formulation-3 of ketoconazole transfersomal gel. The vesicles in Formulation-3 are used to deliver drugs to specific sites in the body. The table shows the size range of the vesicles, the average size (d) of the vesicles within each size range, the number of vesicles (n) in each size range, the percentage of vesicles in each size range, and the product of (n) and (d). The average size of the vesicles in Formulation-3 is smaller than those in Formulation-1 and Formulation-2.

Table 7: **Size distribution of Ketoconazole Transfersomal gel of Formulation-3**

S.NO	SIZE RANGE	AVERAGE SIZE (D)	NO.OF VESICLES (N)*	% VESICLES	(N) X (D)
1.	0.0-3.5	1.5	85	60.28	127.5
2.	3.5-6.5	4.2	44	31.21	184.8
3.	6.5-9.5	7.6	06	4.26	45.6
4.	9.5-12.5	10.50	04	2.84	42
5.	12.5-15.5	11.25	02	1.42	22.5

Average diameter (dave) = $\frac{\sum nd}{\sum n} = \frac{422.4}{141}$ = 2.99 µm

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7.12.4 Size distribution of Ketoconazole Transfersomal gel of Formulation-4

The data shows the size distribution of Ketoconazole Transfersomal gel for four different formulations (Formulation-1 to Formulation-4). Each formulation has five size ranges (0.0-3.4 µm, 3.5-6.5 µm, 6.5-
9.5 µm, 9.5-12.5 µm, and 12.5-15.5 µm) and the corresponding average size (d), number of vesicles (n), % vesicles, and (n) x (d) values are given for each size range. Overall, this data provides information on the size distribution of Ketoconazole Transfersomal gel in different formulations, which can be useful for optimizing and evaluating the effectiveness of the formulation for drug delivery.

Table 8: Size distribution of Ketoconazole Transfersomal gel of Formulation-4

S.NO	SIZE RANGE	AVERAGE SIZE (D)	NO. OF VESICLES (N)*	% VESICLES	(N) X (D)
1.	0.0-3.5	1.5	76	57.58	114
2.	3.5-6.5	4.2	46	34.85	193.2
3.	6.5-9.5	7.6	06	4.55	45.6
4.	9.5-12.5	10.50	03	2.27	31.5
5.	12.5-15.5	11.25	01	0.76	11.25

Average diameter (dave) = $\frac{\sum nd}{\sum n} = \frac{602.65}{132}$ = 4.56 µm

7.13 Entrapment Efficiency

Size and trapping efficiency are commonly considered as parameters for optimizing vesicular formulations. Once the presence of vesicle bilayers in the transfersomes system has been confirmed, the drug-capturing ability of vesicles was investigated through ultracentrifugation. The entrapment efficacies of drugs within ethosomal vesicles, as well as the presence of untrapped or free drugs, were assessed by employing the ultracentrifugation technique. The resulting data are presented in the table below.

Table 9: Entrapment Efficiency of Ketoconazole Transfersomal gel

S.No	Name of formulation	Entrapment Efficiency %
1.	FORMULATION-1	63.06
2.	FORMULATION-2	55.54
3.	FORMULATION-3	70.56
4	FORMULATION-4	68.54

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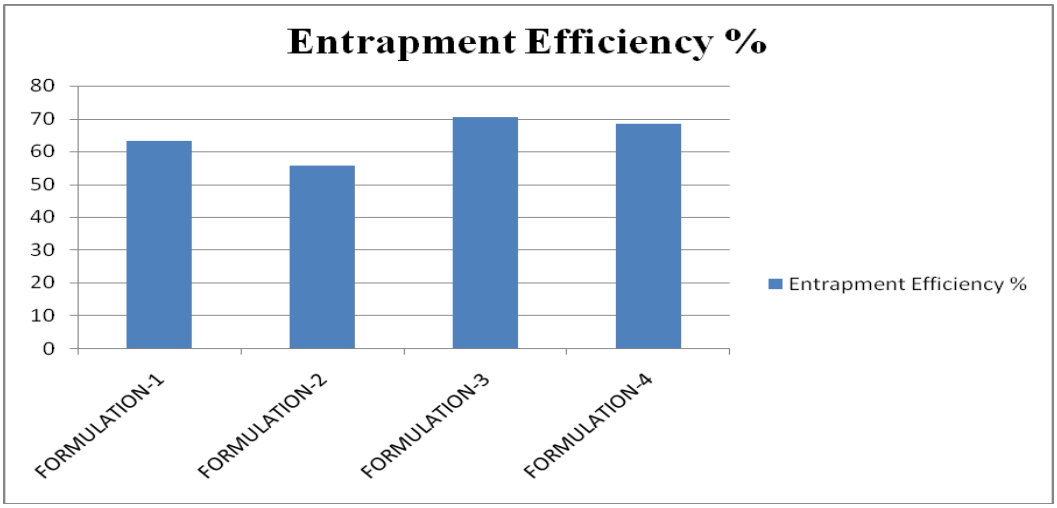

Fig.6. Entrapment efficiency (EE) of ketoconazole in four different formulations

Formulation 3 was showed highest entrapment efficiency at 70.56%, and was indicated that it can be the most effective formulation for delivering ketoconazole. Conversely, formulation 2 has the lowest entrapment efficiency at 55.54% respectively.

Stability Studies:

Stability assessment was conducted over a span of 3 months under various storage conditions, namely room temperature (25°C ± 2°C), refrigerated temperature (2°C - 8°C), and accelerated stability conditions (40°C ± 2°C/75% ± 5% RH), in accordance with the guidelines set forth by the InternationalCouncil for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). Theevaluation encompassed the monitoring of the following parameters:

Physical stability: The transferosomal formulation underwent visual inspection to detect any alterationsin color, consistency, and phase separation. No discernible physical modifications were observed throughout the duration of the study. Chemical stability: The drug content within the tested formulations remained within the acceptable range of ± 5% deviation from the initial concentration over the entire 3-month period. Based on the obtained results, it can be concluded that the transferosomal formulation of ketoconazole exhibited physical and chemical stability for a minimum of3 months, irrespective of the storage conditions employed.

Conclusion:

Based on these results, it can be inferred that the ketoconazole transferosomal formulation remained physically and chemically stable for a minimum of 3 months under various storage conditions. This data can be utilized to determine the formulation's shelf life, ensuring its safety and efficacy for administration to patients.

Conflict of interest:

The Authors declare no conflict of interest.

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Nil

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