CODEN: WJAPAC Impact Factor: 3.87 ISSN: 3049-3013

World Journal of Advance Pharmaceutical Sciences

Volume 2, Issue 4. Page: 118-125 Research Article www.wjaps.com

FORMULATION AND EVALUATION OF KETOCONAZOLE SPANLASTICS GEL

Sayan Das*[1], Pritam Kundu[1], Subhashini B. Hawaldar[1], Anju K. P.[2]

[1]Department of Pharmaceutics, Spurthy College of Pharmacy, Rajiv Gandhi University of Health Sciences, Bengaluru, Karnataka.

[2]Assistant Professor, Department of Pharmaceutics, Spurthy College of Pharmacy, Rajiv Gandhi University of Health Sciences, Bengaluru, Karnataka.

How to cite this Article Sayan Das*, Pritam Kundu, Subhashini B. Hawaldar, Anju K. P. (2025). FORMULATION AND EVALUATION OF KETOCONAZOLE SPANLASTICS GEL, 2(4), 118-125.

Article Info

Article Received: 03 October 2025,

Article Revised: 23 October 2025,

Article Accepted: 13 November 2025.

DOI: https://doi.org/10.5281/zenodo.17624038

***Corresponding author:**

***Sayan Das**

Department of Pharmaceutics, Spurthy College of Pharmacy, Rajiv Gandhi University of Health Sciences, Bengaluru, Karnataka.

ABSTRACT

Ketoconazole is administered to treat fungal infections. It has a restricted pharmacological purpose due to its low aqueous solubility, which lowers the drug's bioavailability. Also, oral ketoconazole causes major systemic side effects on the human body. As a result, topical ketoconazole treatment is favored over oral ketoconazole. The current study was carried out to develop and assess a ketoconazole-loaded spanlastic gel. Spanlastic was created utilizing the ethanol injection process, utilizing Span 60 and Tween 80 serving as non-ionic surfactants and edge activators, respectively. The formulation was examined for several parameters, including particle size, entrapment efficiency, and surface charge. The formulation demonstrated lower particle size and a higher entrapment efficiency of 99.90±0.02%. The Zeta potential of spanlastics was found to be -23mv. The spanlastic formulation was mixed into a gel made with 1% w/w Carbopol 934 and tested for various parameters. The produced gel was homogeneous and contained 92.64±0.02 mg/ml. Stability investigations revealed that ketoconazole-loaded spanlastic gel was stable. As a result, we can infer that the proposed formulation is a potential delivery strategy with improved efficacy, controlled release, and patient compliance.

KEYWORDS: Spanlastics, Elastic vesicle, Edge activator, Penetration enhancer.

INTRODUCTION

Spanlastics: Drug delivery via the skin has been challenging due to its natural barrier, particularly the stratum corneum. Scientists have developed ways to circumvent the barrier without inflicting injury or inconvenience. In the 1990s, Paul Enrilch developed targeted medication delivery by identifying a technique that directly targets sick cells. The term Spanlastic (Span + Elastic) was first used in 2011. Spanlastics are a promising way for improving transdermal medication delivery. These are unique drug delivery device that traps the drug in a bilayer-like core cavity.[1]

Spanlastics are flexible, nanoscale vesicles designed to improve drug administration through the skin. These products are made up of non-ionic surfactants (such as Span 60) and edge activators (such Tween 80 or sodium cholate). The edge activator increases the elasticity and deformability of the vesicle membrane, allowing it to pass through narrow skin gaps without losing structure. Unlike liposomes or niosomes, spanlastics are intended for deep skin penetration and increased medicine absorption. Their composition makes them suitable for delivering both water- and fat-soluble medications.[2]

Structure: Spanlastics are bilayered spheroid structures consisting of amphiphilic molecules as suitable matrices for Bio-encapsulation.[1]

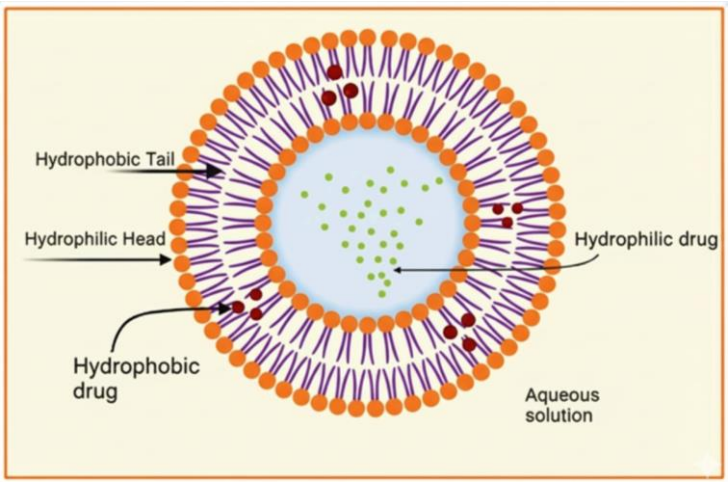

Fig no 1: Structure of Spanlastic vesicle.

Ketoconazole (KTZ): KTZ is a broad-spectrum imidazole anti-fungal medication. It is effective against many fungal infections like dermatophytosis, seborrhoeic dermatitis, leishmaniasis, tinea pedis, tinea cruris and pityriasis versicolor, many more. Oral KTZ has many severe systemic side effects including hepatotoxicity, adrenal insufficiency, and cardiac related issues. Hence, topical KTZ is currently preferred than oral KTZ.

KTZ is available in different topical preparations such as cream, shampoo, gel, foam etc. In several studies, it has been found that topical KTZ has the cure rate of 80-90% against fungal infections.[3,4]

By formulating KTZ spanlastics, we can increase the bioavailability and efficiency of the drug by providing localized and targeted anti-fungal action.

MATERIALS AND METHOD

Materials: Ketoconazole was supplied from Chemsworth, Span 60 was supplied from INR chem, Mumbai. Tween 80 & Carbopol 934 were supplied from Molychem, Mumbai. Other excipients used were of analytical grade.

Methods

Pre-formulation studies of drug

Organoleptic properties[5]

Organoleptic properties like colour, odour, and its crystalline property were determined visually. From the studies, it was observed that Ketoconazole is white to slightly off-white in colour, odourless and is crystalline in nature.

Determination of solubility[6]

The solubility of ketoconazole showed that it is soluble in methanol, ethanol, 0.1N HCl, chloroform, dichloromethane and insoluble in water, ether and 0.1 NaOH.

Determination of Standard Calibration curve of Ketoconazole[7]

10 mg ketoconazole was added to 10 ml volumetric flask. Then add methanol to dissolve the drug completely. The volume was made up to 10ml (Stock I). 1 ml from Stock I was transferred to another 10 ml volumetric flask and diluted with methanol (Stock II). The prepared sample was 100 µg/ml. Finally, 10 ml methanol and 1 ml Stock II solution were added to a 10 ml volumetric flask. This will give the solution of 10 µg/ml. Now scan sample between 200 – 400 nm using UV Spectrophotometer to identify the λ max of ketoconazole. And the calibration curve was plotted between the concentration and absorbance. The calibration curve of 2-22 µg/ml was carried out in Methanol. The standard curves of ketoconazole were prepared in Methanol solution, at λ max 241 nm. The data were regressed to obtain the straight line.

Drug – Excipient Compatibility Study[8]

Drug – Excipient compatibility study done by FT-IR spectroscopy. The presence of characteristic peaks associated with specific structural characteristics of the drug molecule was noted. The compatibility of Ketoconazole with polymers/excipients was studied using FTIR spectroscopy. About 1 mg of the sample and 100 mg of KBr (1:100 ratio) were finely ground using mortar and pestle. The mixture was compressed into a transparent pellet under a hydraulic press (7 kg/cm²) and scanned in the range of 4000–400 cm^{-1} using FTIR spectrophotometer. The spectra of pure drug, polymer, and their physical mixtures were obtained and compared for the presence or absence of characteristic functional group peaks.

Preparation of ketoconazole spanlastic by Ethanol injection method[9]

Preparation of Organic Phase (Lipid Phase): Take 500mg of ketoconazole, 300 mg of Span 60, and 300 mg of Tween 80 in a 250 mL beaker. Using a hot plate

magnetic stirrer, add 9 mL of absolute ethanol to the mixture and stir vigorously, until all the components are completely dissolved, forming a clear and transparent solution.

Preparation of Aqueous Phase: Take 91 mL of distilled water in a 250 mL beaker. Heat the water on a hot plate magnetic stirrer to a temperature of about 70-80°C to prepare the aqueous solution and maintain the same temperature.

Ethanol Injection (Vesicle Formation): Draw the entire organic phase solution into a 10 mL syringe using a 25-gauge needle. Position the needle of the syringe just above the surface of the continuously stirring hot aqueous phase. Slowly and steadily inject the organic phase solution into the hot aqueous phase at a controlled rate (1ml per minute). The rapid dilution of ethanol in the aqueous phase causes the self-assembly of surfactants and drug molecules into spanlastics.

Maturation and Solvent Evaporation: After injecting all of the organic phase, continue stirring the mixture at an elevated temperature of 70-80°C for about 30-60 minutes. This step is crucial for the complete evaporation of ethanol and for the stabilization of the formed spanlastic vesicles. A milky or opalescent spanlastics suspension will appear. Remove the beaker from hot plate magnetic stirrer and allow the spanlastics suspension to cool down to room temperature.

Concentration of spanlastics suspension: Once cooled, Take the target volume of 100 mL suspension and centrifuge it at high speed to get the concentrated quantity of spanlastics. Once the concentrated spanlastic is completely obtained, re-disperse it in exactly 10 mL of fresh distilled water or phosphate-buffered saline (PBS). Carefully decant and discard the supernatant. Store the spanlastic suspension in a tightly sealed container and keep it at a temperature between 2-8°c.

Table 1: Formula for ketoconazole spanlastics.

Ingredients	Quantity
Ketoconazole (mg)	500
Span 60 (mg)	300
Tween 80(mg)	300
Ethanol (ml)	9
Distilled water (ml)	91

Preparation of Ketoconazole (KTZ) loaded spanlastic gel[10]

To prepare the Ketoconazole-loaded spanlastic gel, slowly Carbopol 934 was added first and dissolved in an appropriate amount of deionized water with constant stirring. The mixture was kept stirring continuously for about 1.5 to 2 hours to ensure complete dissolution and obtain a homogeneous gel base. The prepared Carbopol gel base was kept for 24 hours for hydration. After that, the required amount of triethanolamine was added to neutralize and to adjust the pH of the gel base. Further, required quantity of KTZ-loaded concentrated spanlastics suspension was added to the Carbopol gel base, and the mixture was stirred for an additional 30 minutes to achieve a uniform dispersion.

Propylene glycol was incorporated as a penetration enhancer, and methyl paraben was added as a preservative. The final product was a smooth, homogeneous Ketoconazole-loaded spanlastic gel suitable for further characterization and use.

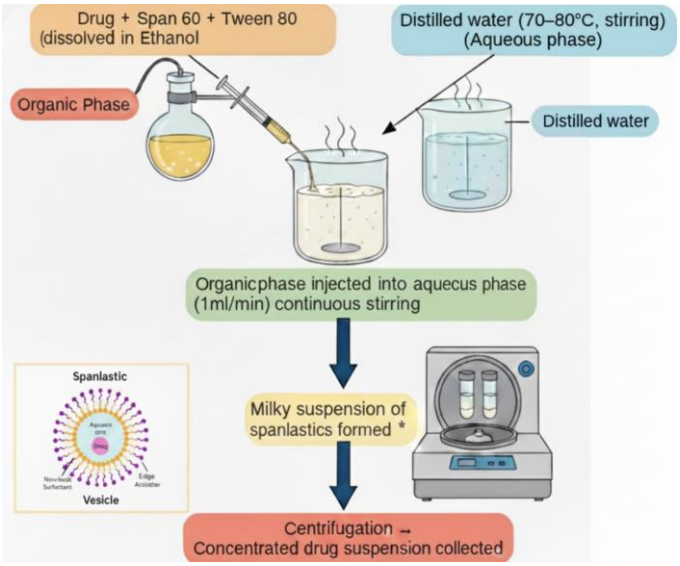

Fig no 2: Ethanol injection method.

Characterization of ketoconazole spanlastics

1. Vesicle Size[11]

The size of spanlastic vesicles is a critical parameter that influences drug release, stability, and cellular uptake. Dynamic Light Scattering (DLS) is typically used to measure vesicle size by analysing the scattering patterns of light as it interacts with the particles. This method is especially useful in detecting variations in vesicle behaviour caused by Brownian motion. Instruments like the Zetasizer are widely employed in this analysis.

2. Polydispersity Index (PDI)[12]

PDI is used to assess the uniformity of the vesicle population in a spanlastic formulation. A lower PDI value indicates a more homogeneous distribution of vesicle sizes, which is preferable for consistent drug delivery and predictable release profiles. Like vesicle size, PDI is also determined using the DLS technique with the help of a Zetasizer.

3. Zeta Potential[13]

Zeta potential measures the surface charge of the vesicles, which reflects their electrostatic stability in suspension. A higher magnitude of zeta potential—whether positive or negative—typically means the vesicles are less likely to aggregate over time. This parameter is measured using a Zetasizer, which operates based on the principle of electrophoretic mobility in an electric field.

4. Elasticity Measurement[14]

The flexibility or deformability of spanlastic vesicles is evaluated using the Deformability Index (DI). This test involves forcing the vesicles through a polycarbonate membrane with defined pore sizes under controlled pressure. The degree to which the vesicles deform and pass through the pores gives insight into their ability to navigate biological barriers like mucosal membranes. A higher deformability index suggests better penetration potential. The DI is calculated using the formula.

$$\mathrm{DI} = J\left(\frac{rv}{rp}\right)^2$$

Where,

- J = amount of vesicle suspension extruded in 10 minutes
- rv = size of spanlastic vesicles after extrusion
- rp = pore size of the membrane

Characterization of ketoconazole spanlastic gel

1. Physical appearance[15]

The prepared ketoconazole spanlastic gel examined for physical appearance as clarity, color, homogeneity, and presence of foreign particles.

2. PH test[16]

pH of various spanlastic gel formulations is determined by using digital pH meter. 1 gm of gel was dissolved in 100 ml of distilled water and pH was measured. The measurement of formulation is done in triplicate to avoid error.

3. Viscosity measurement[17]

Viscosity of Spanlastic gel was determined by using Brookfield viscometer. 20 ml of gel is filled in a 25 ml beaker and the viscosity was measured using spindle number 6 at 10 rpm.

4. Spreadability test[18]

One of the criteria for a dermatological preparation was to meet the ideal qualities is that it should possess good Spreadability. Spreadability is the term expressed to denote the extent of area to the gel readily spreads on application to skin or the affected area. The therapeutic efficiency of the formulation also depends on its Spreadability values. So, determination of Spreadability is important in evaluating gel characteristics. Spreadability is measured as: S=ML/T. The Spreadability of each sample was evaluated in triplicate by using parallel plate method. 1 g of sample was sandwiched between two glass plates and force was applied on top glass plate with 45g of standard weight. Each sample was tested at least three times at constant temperature and exerted weight and the mean values of spread surface area on the lower plate were calculated using the above formula.

7. Drug Content[19]

Determining the total drug content involves disrupting the spanlastic vesicles to release the encapsulated drug. Isopropyl alcohol is commonly used to rupture the vesicles. The released drug is then quantified using UV-visible spectrophotometry. This test ensures that the correct dosage has been incorporated into the system.

8. Entrapment Efficiency (%EE)[20]

Entrapment efficiency refers to the percentage of drug successfully encapsulated within the vesicles compared to the total drug used. After centrifuging the formulation to separate unencapsulated drug, the supernatant is analysed. The amount of drug retained in the vesicles is then calculated using the formula.

$$EE\% = \left(\frac{Encapsulated\ drug}{Total\ drug\ added}\right) x\ 100$$

This parameter is crucial for optimizing drug loading and therapeutic efficacy.

9. Thermodynamic stability[21]

The selected formulation is subjected to different Thermodynamic stability tests.

Heating cooling cycle: The temperature of refrigerators between 4° and 45° of six Cycles with storage at each temperature of not less than 48 Hr is studied. Those formulations, which are stable at these Temperatures, are subjected to centrifugation.

Centrifugation: Distilled water was used to dilute nano emulsions. The nano emulsions were centrifuged at 200rpm for 15minutes at 30°C to check for changes in homogeneity.

RESULT AND DISCUSSION

Determination of Standard Calibration curve of Ketoconazole

Ketoconazole calibration curve was obtained at a wavelength of 241 nm in the concentration of 2µg-22µg/ml. It exhibits high linearity, as illustrated in the fig no.03, with a regression coefficient of 0.999 (R2).

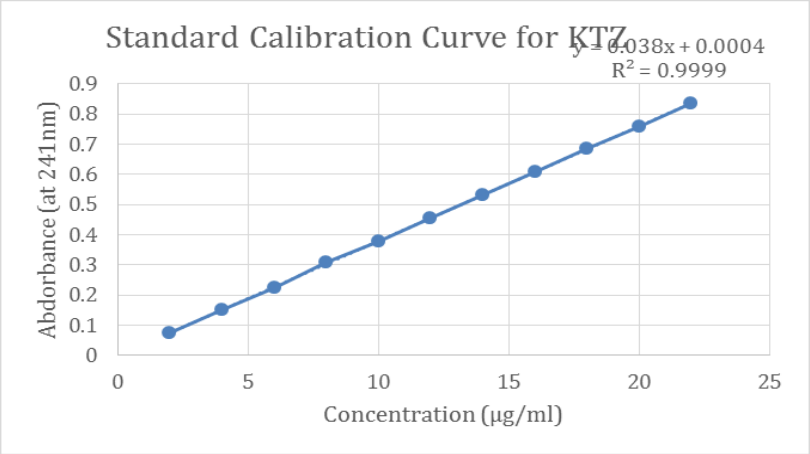

Fig no 03: Standard Calibration curve of Ketoconazole in methanol.

Drug – Polymer, Excipients compatibility study

The IR spectra of the drug-polymer and drug-excipient combinations were compared to the standard spectrum of the pure medication Ketoconazole, and the distinctive peaks associated with particular functional groups and the bonds of the molecules. The peak ranges from O-H/N-H stretch 3380-3385 cm^{-1}, C-H aliphatic 2923-2926 cm^{-1}, C-H aromatic 3050-3053 cm^{-1}, C=O (span ester) 1735 cm^{-1}, C=C (aromatic ring) 1590-1591 cm^{-1}, C-N imidazole 1450 cm^{-1}, C-O stretch 1225-1226 cm^{-1}, C-Cl bending 748-755 cm^{-1}. All major functional peaks of KTZ were retained in the presence of polymer and excipients. No disappearance or formation of new peaks was detected, confirming the absence of chemical interaction.

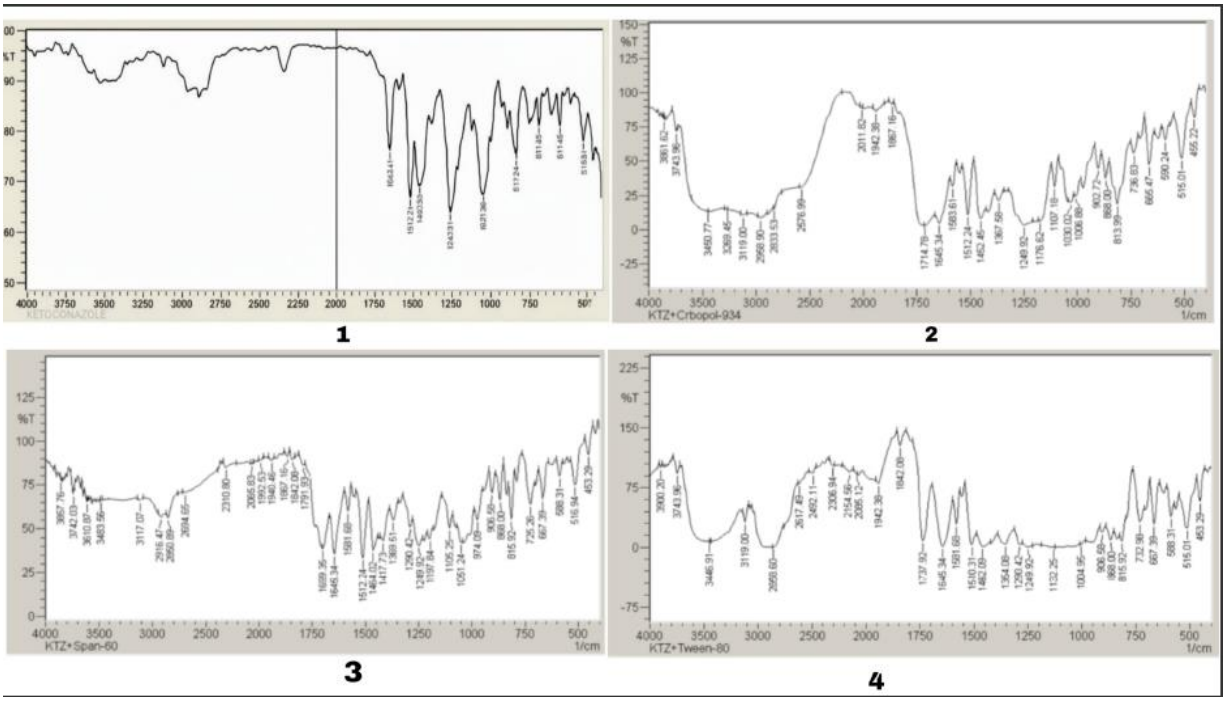

Fig no 04: FT-IR spectrum of ketoconazole with excipients and polymer.

Evaluation of Spanlastics

1. Particle size and PDI

The mean particle size of spanlastics was determined to be 186.1 nm, which is within the literature limits.

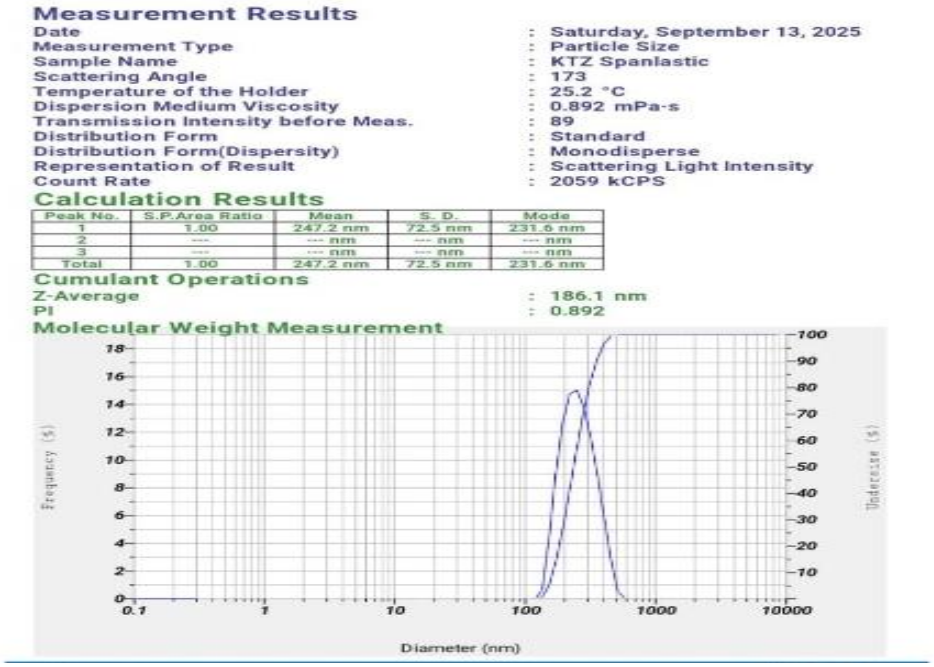

Fig no 05: Particle size & PDI of ketoconazole spanlastics.

2. Zeta potential

Zeta potential was determined to be -23mv. The negative zeta potential means that the spanlastics have no charge and that the system is stable since there is no aggregation.

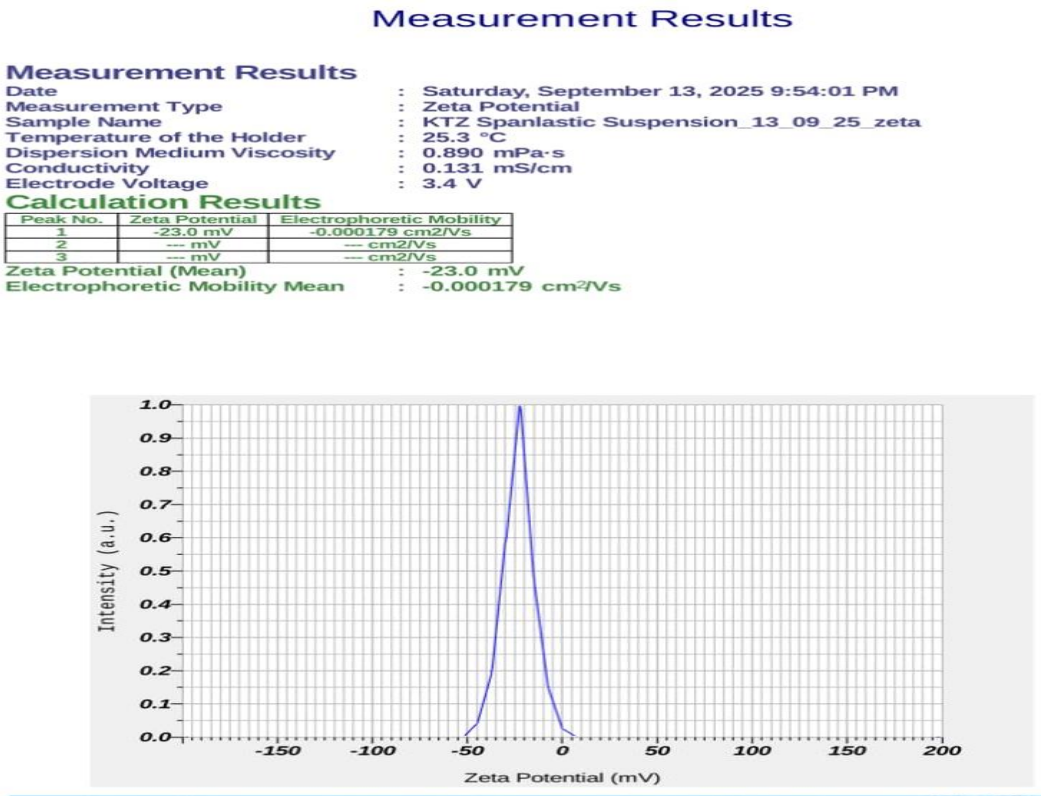

Fig no 06: zeta potential of ketoconazole spanlastic.

Evaluation of Spanlastic gel

1. Physical examination

Ketoconazole spanlastic gel were produced in a milky colour with a smooth, homogeneous appearance and outstanding consistency. The formulations showed no signs of phase separation.

2. pH

The pH of the formulation was measured by using the digital pH meter. The pH of the spanlastic gel is found to be 5.71±0.01.

3. Viscosity

Viscosity of the spanlastic gel is measured by using Brookfield viscometer. The viscosity of the spanlastic gel was measured as 10,299 mPas.

4. Spreadability

The Spreadability of the formulation was found to be 7.2 g.cm/s of ketoconazole spanlastic gel.

5. Drug content

The drug content of spanlastics was determined by spectrophotometrically at 241nm, with drug content of 92.64±0.02 µg/ml.

6. Entrapment Efficacy

The entrapment efficacy of ketoconazole spanlastics was found to be 99.90±0.02 %.

7. Thermodynamic stability

There was no phase separation, indicating that all of the produced spanlastics were stable.

CONCLUSION

The present research investigation was successful in its attempt to develop spanlastic gel for the controlled topical administration of ketoconazole employing span 60 as an anionic surfactant, tween 80 as an edge activator, and ethanol as a solvent. The results of the experiments show that ketoconazole-loaded spanlastic gel has the potential to enhance topical delivery of ketoconazole and improve patient compliance when treating fungal infections, compared to conventional formulations.

REFERENCE

1. Sharma A, Pahwa S, Bhati S, Kudesia P. Spanlastics: a modern approach for nanovesicular drug delivery system. Int J Pharm Sci Res., 2020; 11(3): 1057-65.
2. Mousa SAA, Qelliny MR, Ibrahem RA, Hadiya S, Sarhan HA, Mady FM. Spanlastics: A unique formulation strategy in the delivery of pharmaceuticals Carbapenems as a model. J Adv Biomed Pharm Sci., 2024; 7: 117–125.
3. Choi FD, Juhasz MLW, Mesinkovska NA. Topical ketoconazole: a systematic review of current dermatological applications and future developments. J Dermatolog Treat., 2019; 30(8): 801–9.
4. Udhan N, Waghmare V, Tidke P, Vidhate N, Mundada S. Formulation and evaluation of 2% ketoconazole cream. World J Pharm Pharm Sci., 2024; 13(5): 2038–45.
5. Agustin E, Sari GD. Formulation and evaluation of ketoconazole nano-suspension. J Food Pharm Sci., 2024; 12(1): 1-7.
6. Vasoya JM, Shah AV, Serajuddin ATM. Investigation of possible solubility and dissolution advantages of co-crystals. I: Aqueous solubility and dissolution rates of ketoconazole and its cocrystals as functions of pH. ADMET DMPK., 2019; 7(2): 106-30.
7. Dhumal PG, Karande DP, Chaugule RR, Padwal PN. Analytical method development and validation of ketoconazole by UV spectroscopy. Asian J Res Chem Pharm Sci., 2020; 8(1): Article 02.
8. Ansari MD, Khan I, Solanki P, J Pandit J, Jahan RS, Mohd Aqil, Yasmin S. Fabrication and optimization of Raloxifene loaded spanlastics vesicle for transdermal delivery. J Drug Deliv Scie Tech., 2022; 68: 1-12.
9. Dubey V, Paswan SK, Soni PK. Formulation Designing and optimization of Loteprednol-loaded Spanlastic Nanocarriers for Treatment of Ocular Inflammation. Asian J Pharm., 2023; 17(2): 233-44.
10. El-Nabarawi MA, Shamma RN, Farouk F, Nasralla SM. Design, formulation and evaluation of ketoconazole-loaded spanlastics for topical delivery. J Liposome Res., 2019; 29(2): 189-200.
11. Ahmed OAA, Khorasani S, Mozafari MR. Impact of particle size and polydispersity index on the clinical applications of lipidic nanocarrier systems. Pharmaceutics, 2018; 10(2): 57.
12. Almohamady HI, Mortagi Y, Gad S, Zaitone SA, Alshaman R, Alattar A. Spanlastic Nano-Vesicles: A Novel Approach to Improve the Dissolution, Bioavailability, and Pharmacokinetic Behaviour of Famotidine. Pharmaceutics, 2023; 15(12): 1614.
13. Albash R, El Mahdy MM, Al-Sanea MM, Alruwaili NK, Alsharif KF, Mostafa SM. Development and optimization of pH-sensitive spanlastics for enhanced cytotoxicity and apoptotic activity in breast cancer. Int J Nanomedicine, 2021; 16: 1025–1043.
14. Balasubramaniam J, Srinivas P, Sudhakar Y. Spanlastics-A novel nanovesicular carrier system for ocular delivery. Int J Pharm., 2011 Jul 30; 413(1-2): 202–10.
15. Kaur S, Kaur G, Garg R, Jain S. Formulation and In Vitro Characterization of Ketoconazole Span 80 Based Transfersomes Gel, Its Comparison with Liposomal Gel and Evaluation of Antimicrobial Activity. Res J Pharm Technol, 2016; 9(10): 1711–9.
16. Anju K P, Shripathy D, Shabaraya A R. Antifungal topical nanoemulgel containing miconazole nitrate,

International Journal of Health Sciences and Research, 2021; 11(11): 208-229.
17. S B Kute, R B Saudager. Emulsified gel A Novel approach for delivery of Hydrophobic drugs: An overview. J Adv pharm Edu & Res., 2013; 3(4): 368-76.
18. Kumar JR, Muralidharan S, Parasuraman S. In vitro and in vivo evaluation of microspheres loaded topical gel delivery system of ketoconazole in male rats against candida glabrata. J Pharma Scie Res., 2014; 6(11): 376-83.
19. Ruckmani K, Sankar V. Formulation and optimization of zidovudine niosomes. AAPS PharmSciTech, 2010; 11(3): 1119–1127.
20. Nawal A. Rajab and Mohammad S. Jawad. Formulation and In Vitro Evaluation of Piroxicam Microsponge as a Tablet. International Journal of Pharmacy and Pharmaceutical Sciences, 2016; 8(2): 104–114.
21. Shaikh Neha M., Vijayendra Swamy S. M, Nagoba Shivappa N, Kulkarni K. B. Formulation and Evaluation of Nanoemulsion for Topical Application, Journal of Drug Delivery & Therapeutics, 2019; 9(4-s): 370-375.