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"Enhancing the solubility of ketoconazole: formulation, development of melt-spun dispersions using sucrose and lactose as carriers"

Mangesh Machhindra Raut[1], Meghana Hiraman Raykar*[1], Ramesh Vithoba Shinde[1], Srushti Subhash Bhosale[1]
[1]Department of Pharmaceutics, Hon. Shri. Babanrao Pachpute Vichardhara Trust's, Group of Institutions, Faculty of Pharmacy, At Post- Kashti, Tal.-Shrigonda, Dist.-Ahilyanagar, State- Maharashtra, India, Pin Code - 414701

***Corresponding Author:**
Email ID: drmeghanaraykar17@gmail.com

Abstract:
Ketoconazole is a poorly water-soluble antifungal agent with limited bioavailability, which poses challenges in attaining effective therapeutic levels. This study focused on enhancing the solubility of ketoconazole using centrifugal melt spinning, a novel formulation technique. During this process, ketoconazole was exposed to centrifugal forces in its molten state, resulting in the formation of amorphous solid dispersions. In this formulation approach, ketoconazole was incorporated into amorphous solid dispersions using centrifugal melt spinning. The process involved subjecting the drug to centrifugal forces during melting, facilitating its dispersion within a hydrophilic matrix. Microfibers containing 10% w/w ketoconazole were successfully prepared using sucrose as the carrier, enabling the formation of stable amorphous fibers potentially enhancing solubility and dissolution rate. n comparison, the drug-loaded microfibers prepared with sucrose and lactose exhibited markedly faster release rates, achieving 94.98 ± 0.61% and 91.47 ± 0.52% respectively, within the same time period. This enhanced release is attributed to the increased surface area of the fibers relative to that of conventional tablet formulations.
Keyword: *centrifugal melt spinning method, Microfiber, solubility.*

INTRODUCTION:

Antifungal agents' chemistry and biology: Human health and life are continuously and seriously threatened by fungal infections. Exposure to fungal toxins can cause toxic effects, while fungal proteins may trigger allergic responses in susceptible individuals, and infections (mycoses) are the three categories into which these fungal infections in humans fall [1]. Even healthy individuals can develop various fungal infections, including superficial, cutaneous, and subcutaneous forms, and in some cases systemic infections. These may range from mild conditions such as athlete's foot and nail infections to severe, life-threatening disseminated diseases like histoplasmosis [2].Numerous fungal diseases are brought on by opportunistic pathogens, which can be either endogenous (Candida infections) or environmental (Aspergillus, Cryptococcus infections) [3].Apart from patients with acquired immunodeficiency syndrome (AIDS), Another category of fungal infections includes invasive fungal infections and dermatomycoses, which are caused by different pathogenic fungal species people who are more susceptible, such as newborns, cancer patients undergoing chemotherapy, organ transplant recipients, and burn patients. Additional risk factors include the use of corticosteroids and antibiotics, diabetes, skin and dermal diseases, malnourishment, neutropenia, and surgery [4]. Fungal illnesses have become more common and severe in recent years, especially in people with weakened immune systems. There is There has been a consistent rise in the incidence of fungal infections associated with sepsis. The background of ketoconazole.

Researchers did not become interested in the antifungal action of azole compounds until after topical chlormidazole was introduced in 1958, despite Woolley having previously reported the antifungal activity of benzimidazole in 1944. In the 1980s, the triazole antifungal drug itraconazole was created. With the goal of achieving more antifungal efficacy and improved safety profiles, it was developed as an advancement over previous azole antifungals such as ketoconazole. Itraconazole was created by Johnson & Johnson subsidiary Janssen Pharmaceuticals. During the late 1980s and early 1990s, itraconazole received its first medical approval. In 1992, It has been approved by the U.S. Food and Drug Administration (FDA) [5]. Derived from itraconazole (ITZ), Ketoconazole (PSZ, SCH 56592) is a novel class of oral active triazole antifungal drug having a tetrahydrofuran core. In comparison to triazoles based on dioxolanes, this medication has a wider range of activity.[6] Ketoconazole was the first azole introduced for oral administration in the treatment of systemic fungal infections [7]. Itraconazole has taken its position because to its hepatotoxicity, unless the cheaper cost of ketoconazole outweighs the latter's advantages. Because of its historical significance, ketoconazole can be regarded as the imidazole class's prototype. It has the chemical formula C26H28Cl2N4O4 and is formally known Ketoconazole, chemically described as *cis-1-acetyl-4-[4-[2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl] methoxyphenyl] piperazine oxide*. [7] Introduced in 1977, ketoconazole is an imidazole antifungal agent with broad-spectrum activity, which received FDA approval in 1981. Since ketoconazole coupled the oral absorption of ketoconazole with the efficacy of miconazole, its broad-spectrum activity offered distinct advantages over well-established antimycotics at the time of licensure. By inhibiting a P450-dependent enzyme, ketoconazole, like other imidazole drugs, disrupts the formation of ergosterol and ultimately modifies the structure and function of the cell wall. Ketoconazole's effectiveness against dermatophytes, yeasts, Molds, dimorphic fungi, and some bacteria was shown in early in vitro investigations. Additionally, ketoconazole showed in vivo action in animal models of systemic, cutaneous, and oral and vaginal candidosis. [8] Ketoconazole may be hazardous to fungus because it inhibits 14-demethylation, which stops lanosterol from being converted to ergosterol. A significant part of the fungal cell membrane contains ergosterol. The organism may suffer from changes in cell membrane permeability brought on by its absence or an excess of 14-methylated sterols. It has also been demonstrated that ketoconazole prevents mammalian cells from converting lanosterol to cholesterol. The impact on mammalian cells, however, had seemed to be far less strong in vitro.[9]. Oral administration is the most common, convenient, and cost-effective route of drug delivery. The small intestine serves as the primary site for drug absorption, and the extent of absorption across the intestinal epithelium significantly influences the bioavailability of the medication [10]. For orally administered drugs, the first-pass effect is an important consideration. This refers to the substantial reduction in drug concentration before reaching systemic circulation, primarily due to metabolic processes in the liver. The peak medication level in plasma is comparatively low when oral dosing is used compared to other parenteral administration methods. Furthermore, the period at which the maximum plasma level is reached is more unknown since it varies more widely for various medications following oral administration than following parenteral administration [11]. In particular studies, the maintenance of a pseudo-plateau level over an extended period of time may partially offset this. Oral administration is one of the most widely used drug administration techniques, despite these disadvantages. It's likely considered that there aren't many restrictions on the medicine formulation. Furthermore, it appears that rodents can tolerate the dosage process quite well. It is sometimes overlooked that a wide range of biopharmaceutical parameters may influence both the rate and extent of drug absorption., and that an animal's health might also have an impact on drug transport. In theory, the entire length of the gastrointestinal system is where gastrointestinal absorption occurs. Since the mucosal lining of the gastrointestinal tract is nearly impermeable to ionized molecules, the majority of chemicals are absorbed via diffusion of their nonionized forms. Therefore, depending on the ionic nature of the chemical, drug absorption will be improved in the acidic stomach or in the nearly neutral intestine. However, intestinal absorption is typically dominating due to the intestinal villi's significantly higher surface area [12]. Oral

administration is recommended for patients who can swallow and tolerate medications, as it offers convenience. Drugs with short half-lives are often formulated as sustained-release or timed-release preparations, allowing gradual absorption over several hours Nanofibers are classified as nanostructured vehicles since their individual fiber diameter is less than 100 nm. While created fibers with a diameter between 100 and 1000 nm are also classified as nanofibers, they are often produced via a process called electrospinning [17,18]. For creating nanofibers, centrifugal spinning—also referred to as force spinning-is thought to be a safer, quicker, and more efficient method than electrospinning. This method's basic idea is comparable to that of making cotton candy [25]. A variety of nanofibers, including metal, carbon, ceramic, and polymer nanofibers, can be produced more quickly and safely using centrifugal spinning, which uses centrifugal force. The polymer solution injected in the spinneret with two or more orifices is first ejected by centrifugal force. Then, the polymer material's surface area is increased by the jet stretching process, which deposits it onto the collector. When the polymer solution evaporates, the jet will solidify and compress, eventually producing the nanofibers [26]. Especially in the fiberglass sector, centrifugal spinning is a well-known technique for creating glass fibers, often known as "glass wool," with an average diameter larger than 1 μm. Despite having many uses in the fiberglass sector, this method is relatively new for creating polymeric fibers, particularly polymeric nanofibers. It is noteworthy that Hooper invented the centrifugal spinning technique in 1924 in order to create artificial silk fiber from viscose by subjecting a viscous substance to centrifugal forces. Consequently, since Hooper developed this technique, it has been applied to the manufacture of fiber. Since 2010, Badrosamay et al. have proposed rotary jet spinning (RJS), a centrifugal spinning method for micro/nanofiber fabrication, as an alternate method for forming nanofibers that is inspired by the cotton-candy production principle. Lozano et al. filed the first patent pertaining to this method in 2012. FibRio® Technology Co. launched the company's first commercial machine under the ForcespinningTM trademark. Some of the drawbacks of electrospinning, including its low production rate and the requirement for a high voltage for industrial applications, can be addressed by this technology. Centrifugal spinning has been regarded as one of the most promising methods for creating nanofibers because of the aforementioned advantages. In essence, centrifugal forces are used in this approach to create nanofibers. Typically, a polymer melt or solution would be poured into a revolving chamber with several orifices. The centrifugal force created by rotation pushes the solution or melt toward the chamber's inner surfaces, guiding it towards the orifices. As soon as the centrifugal force overcomes the solution's or melt's surface tension and viscosity, the polymer jet leaves the orifices. The jet is then sufficiently stretched as it travels toward the collector, causing the solvent to evaporate or the melt to cool, forming dried and nanoscale fibers [27, 28].

MATERIALS AND METHODS

Ketoconazole was gifted by Cipla Pharmaceuticals Goa. Sucrose was purchased from Sigma Aldrich Mumbai.

Preparation of microfibers by centrifugal melts pinning:

Material Preparation

Two types of microfibers were developed, one incorporating sucrose and the other lactose. For each type, physical mixtures were prepared by combining 70%, 80%, and 90% (w/w) of the selected sugar with 30%, 20%, and 10% (w/w) of ketoconazole (KTZ), respectively. The components were thoroughly blended using the components were triturated using a mortar and pestle for about 5 minutes to achieve uniform mixing.

Microfiber Preparation:

Exactly 10 grams of each physical mixture (PM) was weighed and introduced into a custom-built apparatus modeled after a cotton candy machine. This device likely functions by heating the PM to a specific, though unspecified, temperature before spinning it into microfibers. The spinning process was conducted at a speed of 2400 rpm under ambient conditions, with the room temperature maintained at approximately 27 ± 5°C.

Formulation Code	KTZ%	Sucrose%	Lactose%	% Yield
S blank	0	100	0	92 ±2
L blank	0	0	100	89 ±3
DS10	10	90	0	89 ±2
DS20	20	80	0	88 ±2
DS30	30	70	0	85 ±2
DL10	10	0	90	87 ±1
DL20	20	0	80	86 ±2
DL30	30	0	70	84 ±2

Table 1: Preparation of Optimized Microfibers

Percentage Yield and drug loading capacity

$$\textbf{Yield}\ \left(\%\frac{w}{w}\right) = \frac{weight\ of\ prepared\ solid\ dispersion}{weight\ of\ drug+carrier} \times 100$$

Drug loading capacity was estimated using an equation

$$\textbf{DLE}\left(\%\frac{w}{w}\right) = \frac{Amount\ of\ drug\ measured}{Therotical\ anount\ of\ of\ drug\ based\ on\ drug\ loading} \times 100$$

Drug loading capacity for both KTZ loaded sucrose and lactose fibres was Quantified by dissolving 10mg of fibres in 10 mL of phosphate buffer (pH 6.8) in which both drug and carrier are soluble, The UV absorbance was taken at 245 nm. The amount of drug was Estimated using the calibration curve.

Microscopic analysis of lactose and sucrose fibers encapsulated in KTZ

Freshly made sucrose and lactose fiber loaded with KTZ were examined using a Scientific research microscope (motic-B1 advanced series 223). The diameter of the tiny fiber was measured at 5x magnification using image analysis software (Moti soft). Assessment of Moisture Uptake Evaluating these fibers' ability to absorb moisture is essential because they contain hydrophilic chemicals. Following Lee and Bismarck (2011), the methodology used in this investigation comprised determining the weight gain of samples exposed to different relative humidity (RH) values after they had a known initial weight. These samples were kept at room temperature in conditions with regulated relative humidity levels of 22 ± 2%, 52 ± 2%, and 75 ± 2%. The fibers were exposed for a maximum of 24 hours or until they began to exhibit indications of structural breakdown. After calculating the weight difference before and after each time period, the moisture content (MC) was found using the following formula:

$MC= (m-m_0)/ m_0 \times 100\%$

MC represents the moisture content

m_0 is the initial mass of the samples

m is the mass of the fibers after exposure to moisture

Scanning Electron Microscopy (SEM)

Electron microscopic analysis (SEM)) research was used to comprehend the microscopic structure and surface properties of the newly made KTZ-loaded lactose and sucrose microfibers. High-resolution magnification provided by this potent imaging method enables researchers to see details at the micro and nanoscale. The FEI Nova NANOSEM 450, a flexible SEM platform renowned for its outstanding picture quality and cutting-edge features, was selected as the tool for this investigation It makes use of a concentrated electron beam that moves over the sample's surface to produce comprehensive data regarding its composition and topography.

The KTZ-loaded microfibers were meticulously prepared for visualization during the SEM investigation. To avoid electrostatic charge during the analysis, this usually entails mounting the samples on a conductive stub and sometimes covering them with a small layer of conductive material, such as gold. The sample surface is subsequently subjected to an electron beam bombardment by the SEM apparatus. A variety of signals are produced by the interaction between the electrons and the sample, including secondary electrons that reveal details about the topography of the sample.

Saturation Solubility of KTZ, KTZ Encapsulated Sucrose and lactose Microfibers

It was examined how microfibers affected KTZ's solubility. Erlenmeyer flasks were containing 10 mL of phosphate buffer (pH 6.8), excess pure KTZ, and KTZ-loaded lactose and sucrose microfibers. The flasks were placed on a shaking platform (Remi CIS-18 Plus) and incubated for 72 hours at 37°C. After filtering, UV spectroscopy at 240 nm was used to measure each sample's KTZ concentration. Following that, saturation solubilities for both carriers' pure KTZ and microfibre-loaded forms were computed and contrasted.

Powder X-ray Diffraction analysis (PXRD)

X-ray scattering measurements were used to examine the crystallinity of pure KTZ, KTZ-loaded lactose, and sucrose microfibers. To differentiate between crystalline and amorphous states, samples were scanned across a 2θ range of 10-80° by wide-angle X-ray diffraction with a Rigaku Ultima IV instrument diffractometer.

Differential Scanning Calorimetry (DSC) Analysis

The thermal melting behavior of ketoconazole, ketoconazole-loaded lactose microfibers made by centrifugal melt spinning, and ketoconazole-loaded sucrose microfibers was examined using differential scanning calorimetry (DSC). Using Mettler Toledo Instruments, a thermal analysis was conducted on pure ketoconazole and ketoconazole-encapsulated lactose and sucrose microfibers (3-5 mg each) at 50 mL min-1 N_2 flow and 10°C min-1 heating.

Fourier transform infrared (FTIR) Spectroscopy

An attenuated total reflectance infrared spectrophotometer was employed for examining the chemical structure and physical form of microfibers (KTZ, KYZ-loaded sucrose, and KTZ-loaded lactose) in order to look into the effects of high-temperature centrifugal melt spinning on possible drug-carrier interactions. (Shimadzu ATR-FTIR)

***In-vitro* Dissolution Studies**

KTZ release Pure KTZ, non-fibrillated physical mixes, and freshly made KTZ-encapsulated microfibers (lactose and sucrose) were compared in vitro using a USP II paddle dissolution equipment. The dissolution medium consisted of phosphate buffer (pH 6.8)., and it was run at 50 rpm and 37°C±0.2 °C. Microfibers (100 mg drug equivalent) were distributed, and fresh phosphate buffer (pH 6.8) medium was added to 5 mL aliquots at regular intervals of 3, 5, 10, 20, 30, 40, 50, and 60 minutes to keep the dissolution media at a consistent volume. In order to compare the release characteristics of the various formulations, the amount of KTZ that was released from the fiber was measured at 240 nm using a UV-VIS spectrophotometer.

Preparation of tablets from microfibers

The fibers were compressed using a rotatory tablet machine (CIP 12 STN). A die was filled with fibers that had been carefully weighed up to 460 mg (laden with sugar) and 480 mg (loaded with lactose). Punches and dies on both sides were made using the D tooling without any embossing. The turret the rotation speed was adjusted to 15 RPM, and the compaction force was kept low.

Result

KTZ-Loaded sucrose microfibers yielded a significantly higher percentage (88.88 ± 1.07%) compared to KTZ-loaded lactose microfibers (83.35 ± 1.15%). Similarly, KTZ-Loaded sucrose microfibers exhibited a higher drug loading efficiency (95.86 ± 0.68%) than KTZ- Loaded lactose microfibers (84.25 ± 0.6%).

Table 2: Average diameter of drug-loaded sucrose and lactose fibres

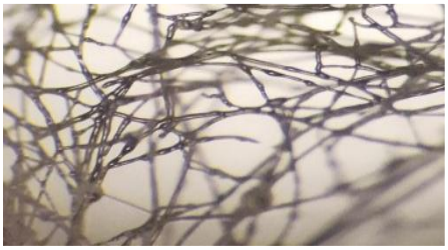
Sr. No.	Diameter(µm)for drug- loaded sucrose microfibres	Diameter(µm) for drug- loaded lactose microfibres

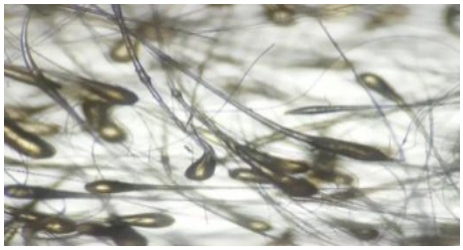
D1	7.74	20.51
D2	14.34	25.69
D3	9.98	23.09
D4	12.19	24.01
D5	11.56	40.99
D6	9.92	38.66
D7	8.17	22.59
D8	13.22	25.44
D9	18.44	34.35
D10	17.88	32.22
Average Diameter	**12.34 ±3.7(µm)**	**28.75±7.24(µm)**

Scanning Electron Microscopy (SEM)

Both ketoconazole-loaded sucrose and lactose microfibers exhibited a uniform structure, smooth surface morphology, and irregular fiber orientation, suggesting that the drug was molecularly dispersed consistently throughout both types of microfibers.

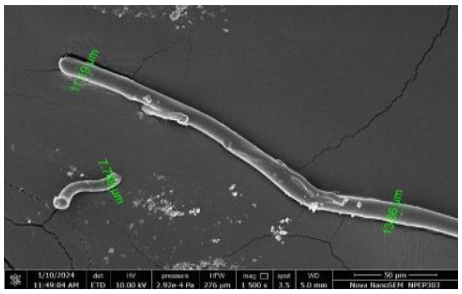
Figure 1: a) KTZ-loaded sucrose microfibers under motic microscope b) KTZ-loaded lactose microfibers

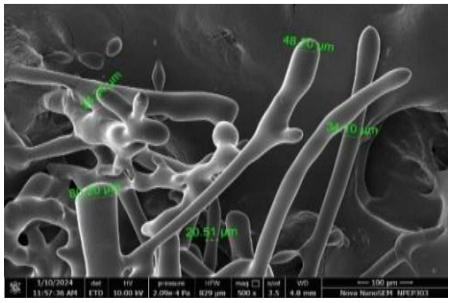




under motic microscope

Figure 2 : a)SEM image of KTZ encapsulated sucrose microfibers b) SEM image of KTZ encapsulated





lactose microfibers

Powder X-ray Diffraction (PXRD)

The major X-ray diffraction peaks of ketoconazole were observed at 2θ values of 10.76°, 13.22°, 16.52°, 22.56°, and 23.83°. The API ketoconazole exhibited distinct peaks at 2θ = 10.76° (intensity 3850), 2θ = 13.22° (intensity 3683), 2θ = 16.52° (intensity 7258.33), 2θ = 22.56° (intensity 5641.67), and 2θ = 23.86° (intensity 3450)., also the angles with moderate intensities occurred at2θof10.78°,13.20°,16.54°,22.58°,22.62°,and23.86°.Whenexamining the X-ray diffraction pattern, the API Ketoconazole displays peaks at 2θ = 10.78° with an intensity of 3741.67, 2θ = 13.20° with an intensity of 3675, 2θ = 16.54° with an intensity of 6900, 2θ = 22.58° with an intensity of 3416.67°, 2θ = 22.62° with an

intensity of 2900, and 2θ = 23.86° with an intensity of 5641.41 all this indicates indicate the crystalline structure of Ketoconazole. The clear peaks of KTZ were no longer visible in the diffractogram of KTZ-encapsulated sucrose and lactose microfibers. Instead, the characteristic peaks of KTZ that could still be detected showed decreased intensity, suggesting that KTZ exists in an amorphous state within the fibers.

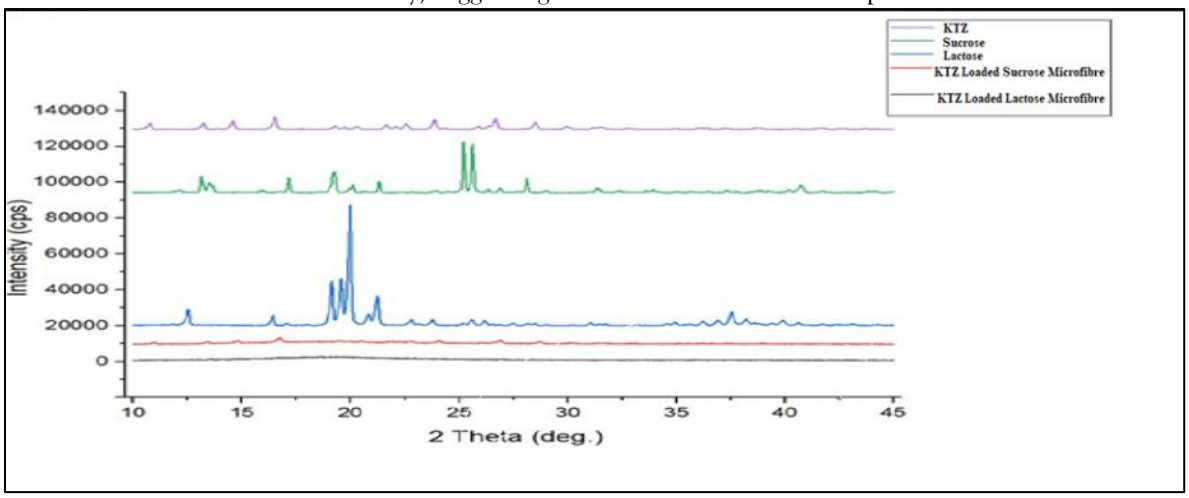


Figure 3: XRD overlay of KTZ, sucrose, lactose, KTZ-loaded sucrose microfibers and KTZ-loaded lactose microfibers

Saturation Solubility of KTZ, KTZ-loaded Sucrose And lactose Microfibers

This study compared the saturation solubility of pure KTZ and KTZ incorporated into sucroseand lactose microfibers within a phosphate buffer (pH6.8). As illustrated in Figure 4, the pure KTZ demonstrated a solubility of 0.02573 mg/mL, while the KTZ-encapsulated sucrose microfibers displayed a significantly higher solubility of 0.0827 mg/ml. Notably, the solubility of Ketoconazole experienced a 3.21-fold increase when compared to pure KTZ in sucrose microfibres. Additionally, the solubility of the drug-encapsulated lactose microfibers showed a solubility of 0.0614 mg/mL and a 2.38-fold increase compared to pure KTZ. This suggests that drug-loaded sucrose microfibres have a higher solubility than that of drug- loaded lactose microfibres.

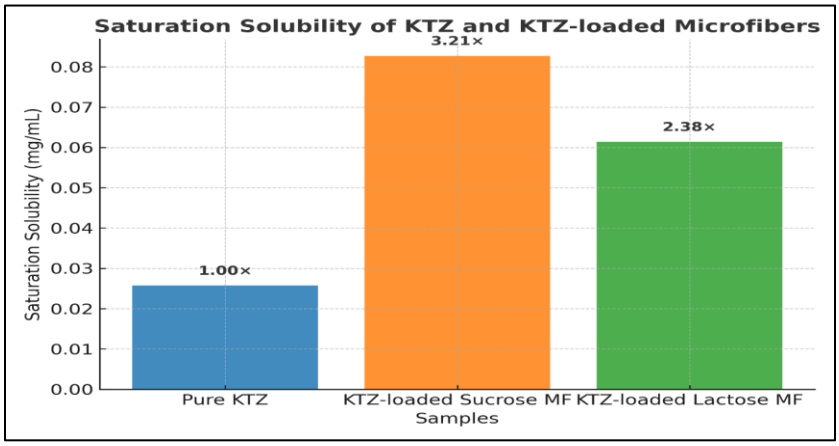


Figure 4: The relative solubility of Ketoconazole inapH6.8phosphatebuffer

FT-IR analysis:

The FTIR spectrum was obtained using an FTIR spectrophotometer (IR Affinity-1, Shimadzu, Japan), showing a broad absorption band near 3400 cm^{-1} attributed to O–H/N–H stretching vibrations stretching,

peaks in the 2950–2850 cm^{-1} region due to aliphatic C–H stretching, and a strong absorption at approximately 1645 cm^{-1} attributed to C=O stretching. Additional bands were observed near 1510 cm^{-1} (aromatic C=C and/or C=N stretching), 1106 cm^{-1} (C–O stretching), and 1077 cm^{-1} (C–N stretching). A distinct peak at ~867 cm^{-1} was assigned to C–Cl stretching. These peaks confirm the presence of the principal functional groups of the compound, and no significant peak shifts or disappearance were observed in comparison with the individual components, indicating the absence of chemical interactions.

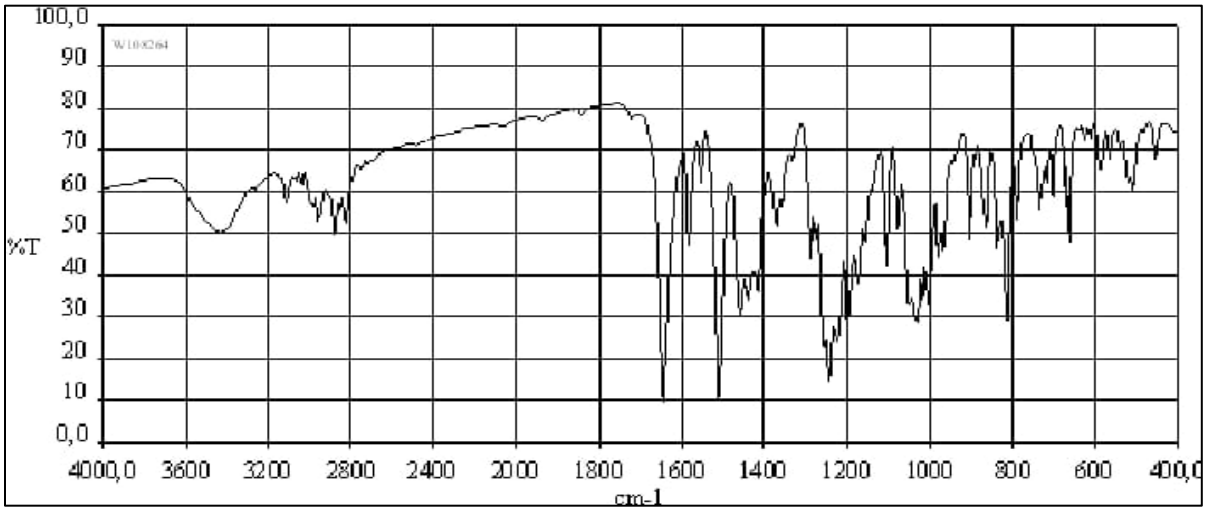


Figure 5: IR spectrum

Table 3: Comparative cumulative percentage release of KTZ, KTZ+SucrosePM ,KTZ loaded sucrose microfibres, KTZ loaded lactose microfibres, KTZ S 30, KTZ L 30

Time (Min)	KTZ	KTZ+ Sucrose PM	KTZ+ Lactose PM	KTZ loaded sucrose microfibres	KTZ-loaded lactose microfibres	KTZ S 30	KTZ S30	KTZ125
0	0	0	0	0	0	0	0	0
3	42.38	49.83	48.32	85.04	80	71.4	69.2	12.3
5	48.17	60.17	58.95	94.98	91.47	75.9	73.2	28.7
10	57.11	69.6	68.02	96.4	94.53	81.8	77.35	39.4
20	67.4	81.83	79.55	97.49	96.2	86.7	83	47.3
30	86.69	88.03	86.07	98.44	97.53	91.4	87.22	56.2
40	94.44	95.95	94.14	99.16	98.06	94.3	91.33	67.2
50	97.1	98.11	98.21	99.5	99.3	98.2	97	74.9
60	100	100	100	100	100	100	100	81.1

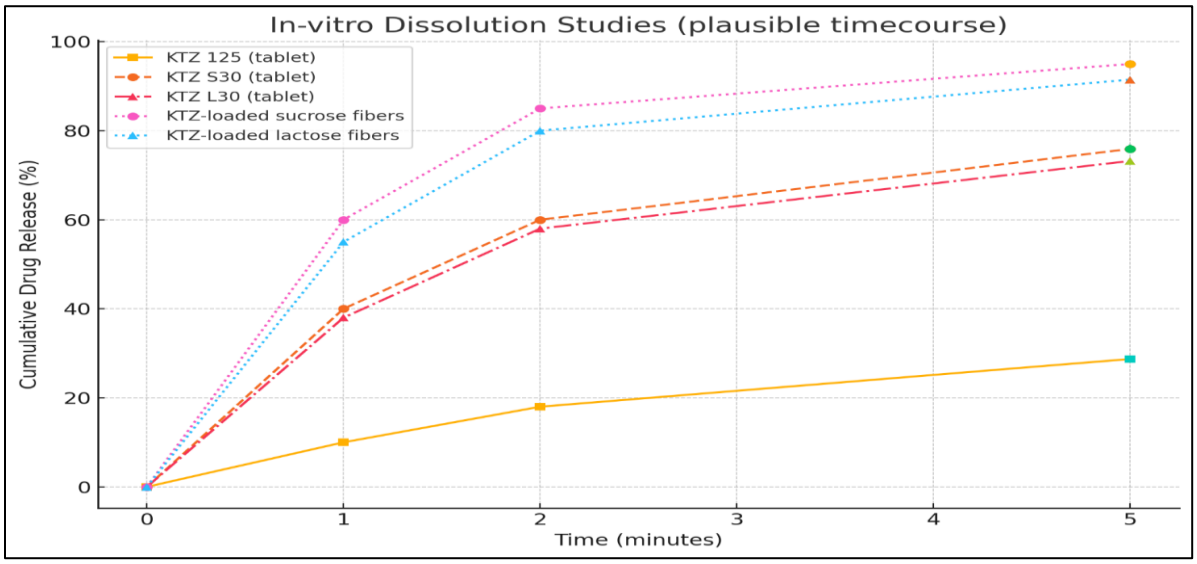


Figure 6: Dissolution profile of KTZ-Loaded Sucrose Microfibres KTZ-Loaded Lactose Microfibres KTZ S 30, KTZ L 30 &KTZ 125

The comparative release profiles of KTZ-loaded sucrose and KTZ-loaded lactose microfibres (figure 9). Notably, KTZ 125 displayed the lowest dissolution rate, releasing only 28.71 ± 0.6% within 5 minutes. While tablet KTZ S 30 and KTZ L 30 exhibited dissolution of 75.9 ± 0.90% and 73.2± 049% respectively. In contrast, both the drug-loaded sucrose and drug- loaded lactose microfibers demonstrated significantly faster release rates, reaching 94.98 ± 0.61% and 91.47 ± 0.52% respectively, within the same time frame this is due to the higher surface area of the fibers comparing with to that of the tablet

CONCLUSION:

This study explored the use of centrifugal melt spinning, a rapid technique, to create *microfibres* solid dispersions loaded with poorly soluble drugs. These dispersions aimed to offer improved dissolution properties. The produced fibres exhibited a Consistent Configuration, smooth covering and Irregular orientation, indicating successful production. Specifically, the researchers focused on creating sucrose and lactose microfibers containing 10% w/w Ketoconazole. They achieved high yield and loading efficiency, demonstrated by scanning electron microscopy (SEM) images showing a homogeneous fibre structure, suggesting successful drug incorporation. Further analysis using DSC (Differential Scanning Calorimetry), FTIR (Fourier-Transform Infrared Spectroscopy), and XRD (X-ray Diffraction)") confirmed the conversion of Ketoconazole into an amorphous state within both the microfibers. These drug-loaded sucrose fibre displayed impressive drug release, with 94.98 ± 0.61% released within 5 min, Also the lactose loaded microfibres showed 91.47 ± 0.52%drug release within 5 min, and have increased solubility up to 3.4 and 2.7 folds respectively Compared pure Ketoconazole The solubility and dissolution rate of drug-loaded sucrose microfibers were higher compared to those of lactose. This indicates that sucrose microfibers may enhance drug release at the absorption site, thereby improving oral bioavailability. The study also suggest that the sucrose is the superior carrier than lactose for producing solid dispersions using centrifugal melt spinning.

REFERENCES

1) Finkelstein, E., Amichai, B. and Grunwald, M.H. (1996b) 'Ketoconazole and its uses, International Journal of Antimicrobial Agents, 6(4), pp. 189–194. https://doi.org/10.1016/0924-8579(95)00037-2.

2) Kathiravan MK, Salake AB, Chothe AS, Dudhe PB, Watode RP, Mukta MS, et al. The biology and chemistry of antifungal agents: A review. Bioorganic & MedicinalChemistry [Internet]. 2012 Oct 1;20(19):5678–98. Available from: https://doi.org/10.1016/j.bmc.2012.04.045

3) Elewski, B.E. (1999c) 'Treatment of tinea capitis: beyond Ketoconazole,' Journal of the American Academy of Dermatology, 40(6), pp. S27–S30. https://doi.org/10.1016/s0190- 9622(99)70394-4.
4) Fujioka, Y. et al. (2008b) 'Evaluation of in vivo dissolution behavior and GI transit of Ketoconazole, a BCS class II drug,' International Journal of Pharmaceutics, 352(1–2), pp. 36–43. https://doi.org/10.1016/j.ijpharm.2007.10.008.
5) Ketoconazole(2024b).https://pubmed.ncbi.nlm.nih.gov/30726008
6) Bennett, M.L. et al. (2000b) 'Oral Ketoconazole remains the treatment of choice for tinea capitis in children,' Pediatric Dermatology, 17(4), pp. 304–309. https://doi.org/10.1046/j.1525-1470.2000.01784.x.
7) Araujo GA, Silva EP, Sanabio RG, Pinheiro JA, Albuquerque MB, Castro RR, Marinho MM, Lima FK, Marinho ES. Characterization in silico of the structural parameters of the antifungal agent Ketoconazole. Sci. Signpost Publ. 2016 May.
8) Gupta AK, Lyons DC. The rise and fall of oral ketoconazole. Journal of cutaneous medicine and surgery. 2015 Jul;19(4):352-7.
9) Pont A, Williams PL, Azhar S, Reitz RE, Bochra C, Smith ER, Stevens DA. Ketoconazole blocks testosterone synthesis. Archives of internal medicine. 1982 Nov 1;142(12):2137-40.
10) AbuhelwaAY,WilliamsDB,UptonRN,FosterDJR.Food,gastrointestinalpH,andmodels of oral drug absorption. European Journal of Pharmaceutics and Biopharmaceutics [Internet]. 2017 Mar 1;112:234–48. Available from: https://doi.org/10.1016/j.ejpb.2016.11.034
11) Oral drug administration. In: Techniques in the behavioral and neural sciences [Internet]. 1994. p. 59–115. Available from: https://doi.org/10.1016/b978-0-444-81871-3.50011
12) Lou J, Duan H, Qin Q, Teng Z, Gan F, Zhou X, et al. Advances in oral Drug Delivery Systems: Challenges and opportunities. Pharmaceutics [Internet]. 2023 Feb 1;15(2):484.
Availablefrom: https://doi.org/10.3390/pharmaceutics15020484
13) Nayak R, Padhye R, Kyratzis IL, Truong YB, Arnold L. Recent advances in nanofibre fabricationtechniques.TextileResearchJournal[Internet].2011Oct19;82(2):129–47.Availablefrom: https://doi.org/10.1177/0040517511424524
14) SongJ,KimM,LeeH.Recentadvancesonnanofiberfabrications:unconventionalState-of- the-Art spinning techniques. Polymers [Internet]. 2020 Jun 20;12(6):1386. Available from: https://doi.org/10.3390/polym12061386
15) Gunther J, Lengaigne J, Girard M, Toupin-Guay V, Teasdale JT, Dubé M, et al. A versatile hot melt centrifugal spinning apparatus for thermoplastic microfibres production. HardwareX [Internet]. 2023 Sep 1;15:e00454. Available from: https://doi.org/10.1016/j.ohx.2023.e00454
16) Molina A, Vyas P, Khlystov N, Kumar S, Kothari A, Deriso D, et al. Low cost centrifugal melt spinning for distributed manufacturing of non-woven media. PloS One [Internet]. 2022 Apr 19;17(4):e0264933. Available from: https://doi.org/10.1371/journal.pone.0264933
17) Zhang Z, Sun J. Research on the development of the centrifugal spinning. MATEC Web of Conferences [Internet]. 2017 Jan 1;95:07003. Available from: https://doi.org/10.1051/matecconf/20179507003
18) Chen HS, Miller CE. Centrifugal spinning of metallic glass filaments. Materials Research Bulletin [Internet]. 1976 Jan 1;11(1):49–54. Available from:https://doi.org/10.1016/0025-5408(76)90213-0