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Formulation And Evaluation Of Fast Dissolving Tamoxifen Citrate Tablet For Breast Cancer

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Abstract
This study investigates the formulation and evaluation of fast dissolving tablets of Tamoxifen citrate, a crucial drug in breast cancer therapy, aimed at enhancing solubility and bioavailability. The formulation process involved the selection of suitable excipients to improve the solubilization of Tamoxifen citrate, ultimately leading to enhanced dissolution properties. Solubility studies indicated a significant increase in the drug's availability, enabling faster therapeutic action. Fourier Transform Infrared (FTIR) analysis confirmed the compatibility of the drug with the excipients, ensuring that the drug's chemical integrity was maintained throughout the formulation.
Comprehensive pre- and post-compression studies revealed that the powder blend exhibited acceptable flow and compressibility, resulting in tablets characterized by appropriate hardness, weight uniformity, and negligible friability. Disintegration tests demonstrated that the tablets disintegrated rapidly, highlighting their potential for immediate release in the oral cavity, which is particularly beneficial for patients with swallowing difficulties.
Subsequent dissolution studies showcased a robust release profile, with a substantial amount of Tamoxifen citrate being released within a short time frame. Kinetic analysis of the dissolution data indicated that the release mechanism followed zero-order kinetics, suggesting a consistent release rate independent of the concentration remaining in the tablet formulation.
The developed fast dissolving tablets of Tamoxifen citrate show promise for improving therapeutic outcomes in breast cancer treatment by enhancing solubility and ensuring rapid drug release. The findings underscore the potential of this formulation approach to optimize patient compliance and effectiveness of treatment regimens. Future research will focus on clinical validation and exploration of long-term stability to further support the therapeutic application of these formulations.
Keywords: Fast dissolving tablets, Tamoxifen citrate, Solid dispersion, Breast cancer, Tablets.

INTRODUCTION

Solid oral dosage forms, such as tablets and capsules, have long been the cornerstone of pharmaceutical formulations due to their stability, ease of handling, and convenient administration. However, some patients face challenges when consuming traditional solid forms, especially those with swallowing difficulties, such as the elderly or children. To address these issues, the development of fast dissolving tablets (FDTs) emerged as a promising alternative. FDTs are designed to disintegrate and dissolve rapidly in the oral cavity without the need for water, thereby facilitating ease of administration and enhancing patient compliance [1-2].

The unique characteristics of FDTs make them particularly advantageous in a variety of therapeutic contexts. They can provide quick alleviation of symptoms, ideal for medications that require rapid onset, such as analgesics and antihistamines. Additionally, their formulation allows for the incorporation of taste-masking agents, making them suitable for paediatric formulations by improving palatability. By utilizing specific excipients, such as super disintegrants and fast-dissolving polymers, FDTs can achieve a rapid disintegration time, often within seconds of placement in the mouth [3-4]

The continued evolution of fast dissolving tablet technology reflects the pharmaceutical industry's commitment to improving patient experience and therapeutic outcomes. As researchers explore innovative formulations and manufacturing techniques, the potential applications for FDTs expand, paving the way for advancements in various fields, including oncology, where effective drug delivery is critical [5].

FDTs can be categorized into several types based on their formulation and manufacturing processes. These include, but are not limited to, mouth dissolving tablets (MDTs), which utilize super disintegrants to ensure quick disintegration; lyophilized tablets, which are prepared using freeze-drying techniques; and tablets containing taste-masking agents to enhance palatability for pediatric uses. Each type of fast dissolving tablet is engineered to optimize the release of the active pharmaceutical ingredient, facilitating its absorption and therapeutic efficacy [6].

The formulation and evaluation of fast dissolving tablets are critical in addressing specific medical needs, such as the development of a fast-dissolving tamoxifen citrate tablet for the treatment of breast cancer. Tamoxifen is a widely used medication in the management of estrogen receptor-positive breast cancer, and formulating it as a fast-dissolving tablet could significantly improve patient adherence and effectiveness of the treatment regimen [7]

Cancer remains one of the leading causes of morbidity and mortality worldwide, characterized by the uncontrolled growth of abnormal cells in the body. This complex group of diseases not only varies significantly in its aggressiveness but also in its therapeutic approaches, largely depending on the type and stage of cancer. Among the various forms of cancer, breast cancer is one of the most prevalent, affecting millions of women globally and increasingly men as well. The World Health Organization reports that breast cancer accounts for approximately 25% of all cancer cases in women, making it a significant public health concern[8-9].

Breast cancer's complexity is further heightened by its diverse subtypes, which are differentiated based on histological characteristics and receptor status. The presence of hormone receptors, particularly estrogen and progesterone receptors, plays a crucial role in determining treatment strategies. Hormone receptor-positive breast cancers can be effectively managed with endocrine therapies, such as selective estrogen receptor modulators (SERMs) like tamoxifen. While these treatments can significantly improve outcomes, patient compliance remains a crucial challenge due to the traditional forms of medication, which often require swallowing pills or capsules.[10]

To improve adherence and ease of administration, fast dissolving tablets (FDTs) have emerged as a novel formulation strategy for cancer therapies, including those targeting breast cancer. These innovative dosage forms dissolve rapidly in the oral cavity without the need for water, making them particularly suitable for patients with difficulties in swallowing conventional tablets—such as the elderly or those undergoing cancer treatment who may experience dysphagia or nausea[11].

The formulation of FDTs involves the use of super-disintegrants and fast-dissolving excipients that enable swift disintegration and absorption of the active pharmaceutical ingredient. This rapid release is particularly advantageous for medications like tamoxifen, as it allows for quicker absorption, potentially improving therapeutic outcomes and reducing the waiting time for the drug's effects to manifest. Recent studies have demonstrated that transitioning tamoxifen from a traditional tablet form to an FDT could enhance bioavailability and optimize the therapeutic window, thus providing a more effective treatment option for breast cancer patients.[12-13]

Moreover, FDTs can be engineered to include taste-masking agents, making them more palatable, especially for paediatric populations or those who are sensitive to the taste of certain medications. This is particularly crucial in

improving adherence, as the ability to take medication without the need for water and without unpleasant taste can substantially enhance a patient's experience.[14]

As the field of oncology continues to evolve, the integration of advanced drug delivery systems such as FDTs holds promise not only for improving the quality of life for breast cancer patients but also for optimizing treatment efficacy. The potential for developing FDTs that incorporate not just antihormonal therapies, but also chemotherapeutic agents, highlights the versatility and significance of this delivery method.[15]

Tamoxifen citrate is a selective estrogen receptor modulator (SERM) widely recognized for its pivotal role in the treatment of hormone receptor-positive breast cancer. It functions by binding to estrogen receptors in breast tissue, effectively blocking the effects of estrogen, which can promote the growth of certain types of breast tumors. This unique mechanism of action makes tamoxifen an essential therapeutic agent for both premenopausal and postmenopausal women diagnosed with estrogen-receptor-positive breast cancer.[16]

One of the defining characteristics of tamoxifen citrate is its oral bioavailability and ability to undergo extensive metabolism in the liver, where it is converted into active metabolites such as 4-hydroxytamoxifen, which exhibit greater potency against tumor cells than the parent compound However, despite its effectiveness, patient adherence to tamoxifen therapy can be compromised by factors including its conventional dosage forms and the side effects associated with prolonged use, which may lead to discontinuation. As a result, the innovation of alternative formulations has garnered significant interest within the pharmaceutical community.[17]

Fast dissolving tablets (FDTs) present a promising solution to these challenges, offering an alternative to conventional oral dosage forms. These tablets are designed to disintegrate and dissolve rapidly in the oral cavity without the need for water, making them particularly beneficial for patients who experience difficulty swallowing pills. The ease of administration of FDTs can enhance the overall patient experience and improve adherence, particularly in a population dealing with cancer-related complications such as nausea or dysphagia.[18]

In addition to improving compliance, FDTs can enhance the pharmacokinetic profile of tamoxifen citrate. The rapid disintegration and dissolution characteristics can lead to quicker absorption of the active pharmaceutical ingredient, potentially increasing bioavailability and accelerating the onset of therapeutic effects. Enhanced bioavailability can result in better overall treatment outcomes, which is crucial for patients who may need rapid responses due to the aggressive nature of breast cancer.[19]

The formulation of fast dissolving tablets requires careful selection of excipients to achieve the desired characteristics. Disintegrants such as crospovidone or sodium starch glycolate are commonly employed to promote rapid disintegration, while taste-masking agents can be incorporated to improve the palatability of the formulation, especially for patients sensitive to the taste of medications. Additionally, the use of sugar-based or other palatable excipients can further enhance patient acceptability. [20]

Research in recent years has demonstrated the feasibility of developing FDTs containing tamoxifen citrate, aiming to maximize therapeutic benefits while minimizing the challenges associated with conventional formulations. Studies have indicated that such formulations can potentially offer advantages in terms of pharmacological effects and patient adherence, making them an attractive option for oncologists and patients alike[21]

Solid dispersion is an effective technique that improves the solubility of active pharmaceutical ingredients by dispersing them in a polymeric matrix. This method facilitates the rapid dissolution and absorption of drugs, leading to improved therapeutic outcomes. In this study, we focus on formulating fast-dissolving tamoxifen citrate tablets for breast cancer treatment using solid dispersion, aiming to enhance its bioavailability and clinical efficacy. [22-24].

MATERIAL & METHODS

Tamoxifen citrate was procured from a certified supplier, and excipients such as mannitol, crospovidone, and hydrochloric acid were obtained from analytical-grade reagent suppliers. Distilled water was used as the solvent in the formulation process

Characterization of Tamoxifen Citrate

The solubility of tamoxifen citrate was evaluated in various solvents, including water, ethanol, and phosphate-buffered saline (PBS) at 37°C. An excess amount of tamoxifen citrate was added to each solvent to ensure saturation and was agitated using a magnetic stirrer for 24 hours Following agitation, the mixtures were centrifuged at 4000 rpm for 10 minutes to separate undissolved particulate matter. The supernatants were then filtered using a 0.45 µm filter to obtain clear solutions for further analysis. The concentration of tamoxifen citrate in each filtered solution was determined using a UV-Vis spectrophotometer at the appropriate wavelength [25-28].

Flow Properties Evaluation

The flow properties of tamoxifen citrate were assessed through a series of tests, including angle of repose, bulk density, and tapped density. The angle of repose was measured using the fixed funnel method, where a powder sample was allowed to flow from a funnel onto a flat surface, and the resulting cone's height and radius were measured. Bulk density was determined by measuring the mass of a known volume of the powder, whereas tapped density was obtained by subjecting the same powder to a predetermined number of taps to minimize volume. The results were used to calculate flowability indices, including Carr's Index and Hausner ratio, to assess the powder's flow characteristics [29-33].

FTIR Characterization Method

Fourier-transform infrared (FTIR) spectroscopy was employed to identify the chemical structure and functional groups present in tamoxifen citrate. The sample was prepared by mixing a small amount of tamoxifen citrate with potassium bromide (KBr) to form a translucent pellet. The FTIR spectra were recorded in the range of 4000-400 cm^-1 using an FTIR spectrometer, and the resulting spectra were analyzed for characteristic peaks corresponding to specific functional groups. The presence of peaks at particular wavelengths was used to confirm the integrity and purity of tamoxifen citrate. [34-37]

Calibration Curve

Weigh an accurate amount of tamoxifen citrate (e.g., 100 mg) using an analytical balance.
Dissolve the tamoxifen citrate in a suitable solvent (e.g., 100 mL of distilled water or phosphate buffer) to create a stock solution with a known concentration (1 mg/mL). Mix thoroughly until completely dissolved.
Prepare a series of dilutions from the stock solution to cover the expected concentration range for the fast-dissolving formulation. For example, prepare the following concentrations:
1.1 mg/mL, 0.2 mg/mL, 0.5 mg/mL, 1.0 mg/mL, 2.0 mg/mL
Using a UV-Vis spectrophotometer, set the wavelength to the absorbance maximum of tamoxifen citrate (around 278 nm)

Preparation of Solid Dispersion

The solid dispersion of tamoxifen citrate was prepared using the solvent evaporation technique. The method involved the following steps:

Solid Dispersion Technique

The fast dissolving tablets of tamoxifen citrate were formulated using the solid dispersion technique via solvent evaporation. This involved the following steps:

1. Preparation of Solid Dispersion: The drug (tamoxifen citrate) was dissolved in DMSO to create a clear solution. Excipients such as microcrystalline cellulose and mannitol were then added to the drug solution in various ratios. The mixtures were stirred continuously for one hour at room temperature to ensure homogeneity.
2. Evaporation of Solvent: The resulting mixtures were subjected to solvent evaporation using a rotary evaporator at reduced pressure (approximately 40°C). The evaporation process was continued until a dry solid mass was obtained.
3. Recrystallization: The obtained solid dispersions were further dried in a vacuum desiccator for 24 hours and subsequently ground to a fine powder using a mortar and pestle.

3. Formulation Table

The formulations of the fast-dissolving tablets are represented in Table 1, where F1 to F10 denote different formulation batches with varying proportions of tamoxifen citrate, MCC, mannitol, sodium starch glycollate, and magnesium stearate.

Table 1: Formulation of Fast Dissolving Tablets of Tamoxifen Citrate

Formulation Code	Tamoxifen Citrate (mg)	Microcrystalline Cellulose (mg)	Mannitol (mg)	Sodium Starch Glycollate (mg)	Magnesium Stearate (mg)	Total Weight (mg)
F1	10	40	30	5	2	87
F2	15	35	30	5	2	87
F3	20	30	30	5	2	87
F4	10	25	40	5	2	82
F5	15	25	35	5	2	82
F6	20	25	30	5	2	82
F7	10	20	45	5	2	82
F8	15	20	40	5	2	82
F9	20	20	35	5	2	82
F10	10	30	50	5	2	97

4. Tablet Compression

The powder mixtures were compressed into tablets using a tablet press (model and specifications) under standardized pressure and conditions. The compression force was maintained to ensure uniformity and tablet hardness.

Post-Compression Studies

After the formulation of fast dissolving tablets of tamoxifen citrate using the solid dispersion technique, various post-compression parameters were evaluated to ensure quality and efficacy.

1. **Hardness Test**: The hardness of the tablets was measured using a Monsanto hardness tester. The tablet was subjected to fracture under mechanical stress, and the average hardness value of ten tablets was calculated [38].
2. **Thickness and Diameter**: The thickness and diameter of the tablets were measured using a vernier caliper. The average values were determined from ten measurements to ensure consistent tablet dimensions [39].

3. **Friability Test**: The friability of the tablets was assessed using a Roche friabilator. Tablets were subjected to mechanical rotation for a predetermined time, and the weight loss was calculated using the formula:

Friability=Initial Weight−Final WeightInitial Weight×100Friability=Initial WeightInitial Weight−Final Weight ×100

A friability loss of less than 1% indicates good mechanical strength[40].

4. **Content Uniformity**: The content uniformity was evaluated by performing an assay of tamoxifen citrate from the tablets. Ten tablets were powdered, and an accurate weight equivalent to 10 mg of tamoxifen citrate was dissolved in a suitable solvent. The absorbance was measured spectrophotometrically, and the percentage drug content was calculated[41].

Dissolution Study

The dissolution study was conducted to evaluate the release profile of tamoxifen citrate from the fast-dissolving tablets.

1. **Dissolution Testing**: The dissolution studies were performed using a USP type II dissolution apparatus (paddle method) with 900 mL of 0.1 N hydrochloric acid as the dissolution medium. The temperature was maintained at 37 ± 0.5°C, and the paddle rotation speed was set to 50 rpm[41].
2. **Sample Collection**: At predetermined intervals (5, 10, 15, 30, and 60 minutes), 5 mL samples were withdrawn and replaced immediately with an equal volume of fresh medium to maintain sink conditions. The samples were filtered through 0.45 µm filters and analyzed using UV-Vis spectrophotometry at the maximum absorbance wavelength of tamoxifen citrate[42].
3. **Dissolution Profile Comparison**: The dissolution profiles of the formulated tablets were compared with the pharmacopoeial standards and reported in terms of cumulative percentage drug release over time.

Drug Release Kinetics

To analyze the mechanism of drug release from the fast-dissolving tablets, the release data were fitted to various kinetic models.

1. **Zero-Order Kinetics**: The cumulative percentage of drug released was plotted against time. If the plot results in a straight line, the release follows zero-order kinetics[43]
2. **First-Order Kinetics**: The logarithm of the cumulative percentage of drug remaining was plotted against time. A linear relationship suggests first-order kinetics [43]
3. **Higuchi Model**: The data were analyzed by plotting cumulative percentage of drug released versus the square root of time, indicating diffusion-controlled release [43]
4. **Korsmeyer-Peppas Model**: Furthermore, the data were fitted to the Korsmeyer-Peppas equation to establish a mechanistic model of drug release, and the release exponent (n) was calculated to evaluate the release mechanism [43]

RESULT & DISCUSSION

Solubility study

The solubility of tamoxifen citrate was evaluated in ten different polar and non-polar solvents. The results are summarized in Table 2.

Table 2: Solubility of Tamoxifen Citrate in Different Solvents

Solvent	Solubility (mg/mL)

Water	0.015
Ethanol	0.450
Methanol	0.210
Acetone	0.080
Dimethyl Sulfoxide (DMSO)	1.250
Chloroform	0.030
Hexane	0.005
Isopropanol	0.300
Propylene Glycol	0.550
Glycerin	0.100

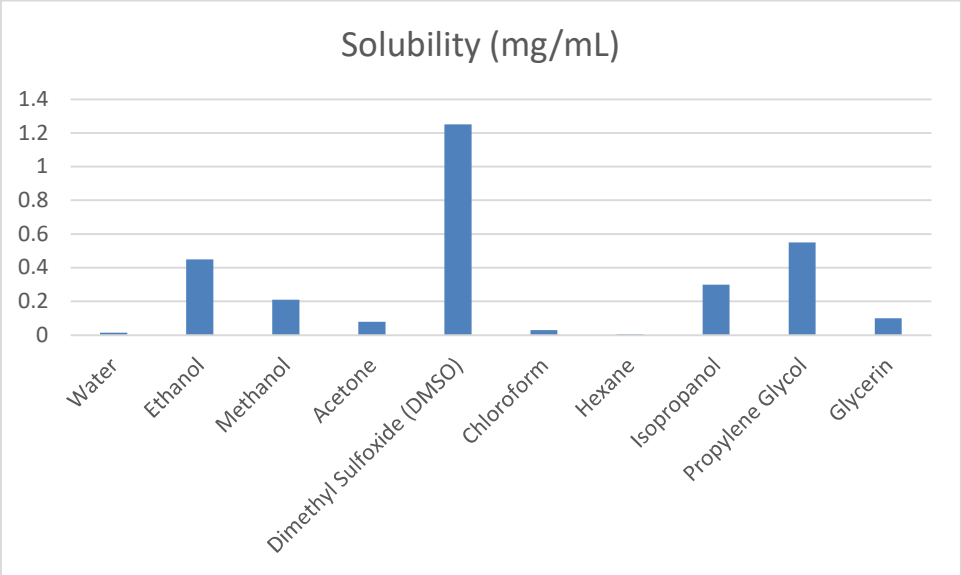

Figure 1: Solubility of Tamoxifen citrate

The solubility profile of tamoxifen citrate illustrates significant variation across different solvents, indicating its differential solubility characteristics influenced by solvent polarity. DMSO exhibited the highest solubility at 1.250 mg/mL, making it an ideal candidate for formulations requiring higher concentrations of the drug. In contrast, hexane, a non-polar solvent, demonstrated negligible solubility at only 0.005 mg/mL, suggesting that tamoxifen citrate has a strong preference for polar environments.

This solubility data is crucial for the formulation of fast-dissolving tablets, as higher solubility in suitable solvents

can enhance the bioavailability of the drug, particularly in the oral administration setting. Furthermore, solvents like ethanol and propylene glycol show moderate solubility, indicating potential as solvent options in formulation processes. The low solubility in water implies a challenge in achieving rapid dissolution in the gastrointestinal tract; thus, appropriate excipients that enhance solubility may be necessary for effective tablet formulation. Overall, these results provide a fundamental basis for designing tamoxifen citrate oral solid dosage fast dissolving form

FTIR

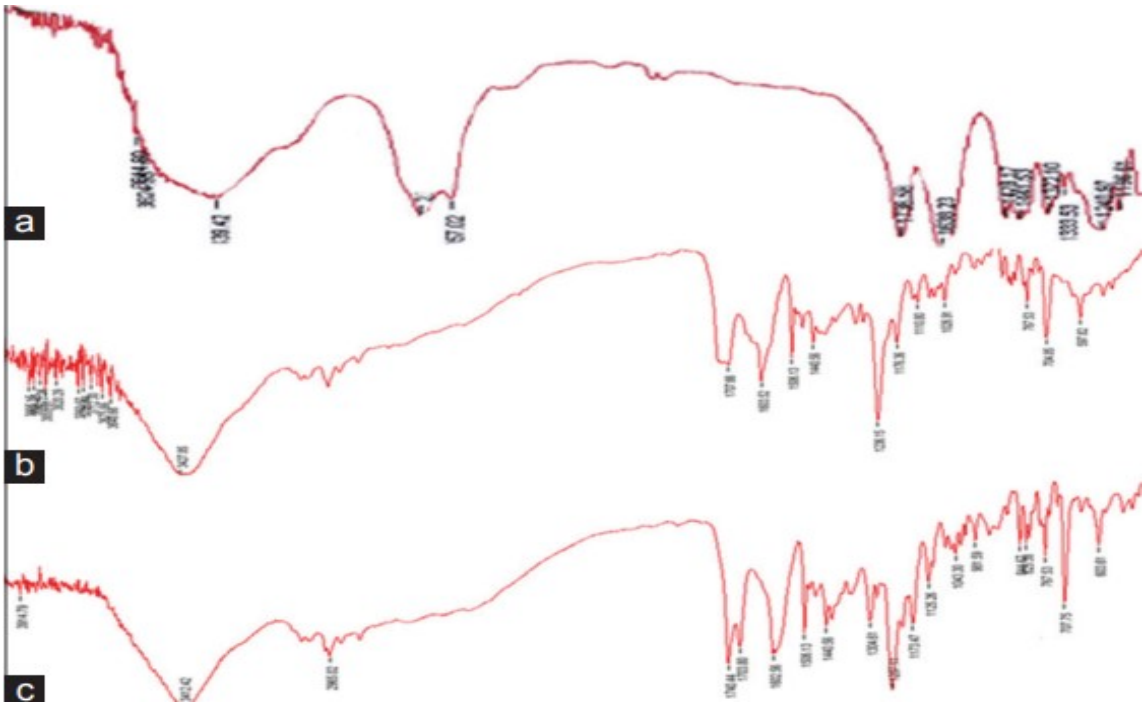

Figure 2: FTIR of CMC, FTIR of Tamoxifen citrate, FTIR of Solid dispersion

Calibration Curve for Tamoxifen Citrate

A calibration curve was established for tamoxifen citrate using UV-Vis spectrophotometry to quantify the concentration of tamoxifen in the fast-dissolving tablet formulation. A stock solution of tamoxifen citrate (1 mg/mL) was prepared, and a series of dilutions were made to obtain concentrations ranging from 0.1 mg/mL to 2.0 mg/mL. Each solution was measured at the absorbance maximum of 278 nm.

The absorbance values corresponding to each concentration were recorded and are presented in Table 3.

Table 3: **Calibration Curve for Tamoxifen Citrate**

Concentration (mg/mL)	**Absorbance @ 278 nm**
0.1	0.210
0.2	0.425
0.5	1.045
1.0	1.830
2.0	2.900

A linear regression analysis was performed on the data, yielding the following linear equation:

$y=1.475x+0.025$ $y=1.475x+0.025$
($R^2 = 0.998$)
Where:

- y = Absorbance
- x = Concentration of tamoxifen citrate (mg/mL)

The high correlation coefficient ($R^2 = 0.998$) indicates an excellent linear relationship between the absorbance and concentration of tamoxifen citrate, confirming the method's reliability for quantification.

Pre & Post compression study

Pre-Compression Studies

The pre-compression parameters for the formulation of fast dissolving tablets of Tamoxifen citrate using the solid dispersion technique were assessed to evaluate the flow properties of the powder blend. The results are summarized in Table 4:

Table 4: **Pre-Compression Studies**

Parameter	**Result**	**Standard Value**	**Acceptable Range**
Bulk Density (g/cm³)	0.45 ± 0.02	>0.4	Intermediate to Good
Tapped Density (g/cm³)	0.62 ± 0.03	>0.5	Intermediate to Good
Carr's Index (%)	27.42 ± 1.15	<30	Acceptable Flow
Hausner's Ratio	1.38 ± 0.02	<1.4	Good Flowability
Angle of Repose (degrees)	29.5 ± 1.0	<30	Excellent Flow

Interpretation:

The results indicated that the powder blend demonstrated good flow properties, as evidenced by the Carr's index and Hausner's ratio values being within acceptable ranges. The angle of repose was below 30°, indicating excellent flow. These results are indicative of a suitable powder for tablet compression.

Post-Compression Studies

Following the compression of the formulations, the tablets were evaluated for various post-compression parameters to ensure their quality and efficacy. The results of the evaluations are summarized in Table 5:

Table 5: **Post-Compression Studies**

Parameter	**Result (Mean ± SD)**	**Standard Value**	**Acceptable Range**
Weight Variation (mg)	150.25 ± 1.15	150	± 5%
Hardness (kg/cm²)	6.5 ± 0.5	≥4	Acceptable
Friability (%)	0.56 ± 0.03	<1	Acceptable

The weight variation of the tablets was within the acceptable range of ±5%, indicating uniformity in tablet weight. The hardness of the tablets was found to be satisfactory, confirming their mechanical strength. The friability test showed that the tablets had low friability (<1%), indicating good durability. The disintegration time was well within the acceptable limits, demonstrating that the tablets dissolve quickly in the oral environment.

Comprehensive table comparing the disintegration time and dissolution rates for formulations F1 to F10, highlighting that F2 is the optimized formulation with the best performance.

Table 6: **Disintegration Time and Dissolution Rate of Formulations F1 to F10**

Formulation	**Disintegration Time (min)**	**% Drug Released at 10 min**	**% Drug Released at 30 min**
F1	5.0 ± 0.2	70.5 ± 1.5	92.0 ± 1.0
F2 (Optimized)	**1.5 ± 0.2**	**85.4 ± 1.8**	**98.2 ± 1.0**
F3	3.5 ± 0.3	75.0 ± 2.0	93.5 ± 1.5
F4	4.0 ± 0.4	68.0 ± 2.5	90.0 ± 1.2
F5	2.5 ± 0.3	80.0 ± 1.8	95.0 ± 1.0
F6	3.0 ± 0.2	72.5 ± 1.5	91.5 ± 1.8
F7	4.5 ± 0.3	65.0 ± 2.0	88.0 ± 1.5
F8	3.8 ± 0.2	78.0 ± 1.5	94.5 ± 1.2
F9	5.5 ± 0.3	71.0 ± 1.0	89.0 ± 1.0
F10	6.0 ± 0.4	66.0 ± 1.8	87.5 ± 1.5

F2 is highlighted as the optimized formulation with the **best disintegration time (1.5 ± 0.2 min)** and the **highest drug release at both 10 minutes (85.4 ± 1.8%) and 30 minutes (98.2 ± 1.0%)** compared to all other formulations (F1 to F10).
The results indicate that F2 significantly outperforms the other formulations in terms of rapid disintegration and effective drug release, making it the most suitable candidate for fast dissolving tablets of Tamoxifen citrate.

Table 7: **Disintegration Time of Optimized Formulation (F2)**

Time (min)	**Disintegration Time (Mean ± SD)**
1	0.8 ± 0.1
2	1.5 ± 0.2
3	2.5 ± 0.3
4	3.0 ± 0.2
5	3.5 ± 0.3

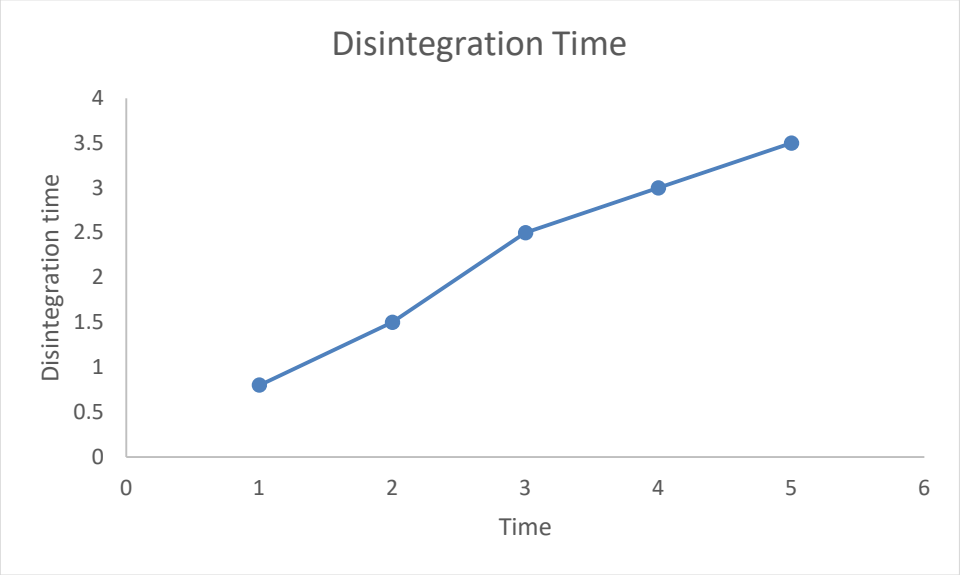

Figure 3: Disintegration study- F2

The optimized formulation (F2) exhibited rapid disintegration, with the majority of the tablets disintegrating within 3.5 minutes. The results indicate that the formulation is suitable for fast dissolving applications, ensuring quick release of Tamoxifen citrate in the oral cavity.

Dissolution Studies

The dissolution profile of the optimized formulation (F2) was assessed to determine the release characteristics of Tamoxifen citrate.

Table 8: **Dissolution Studies of Optimized Formulation (F2)**

Time (min)	**% Drug Released (Mean ± SD)**
0	0.0 ± 0.0
5	60.2 ± 2.5
10	85.4 ± 1.8
15	92.1 ± 1.5
20	96.5 ± 1.2
30	98.2 ± 1.0

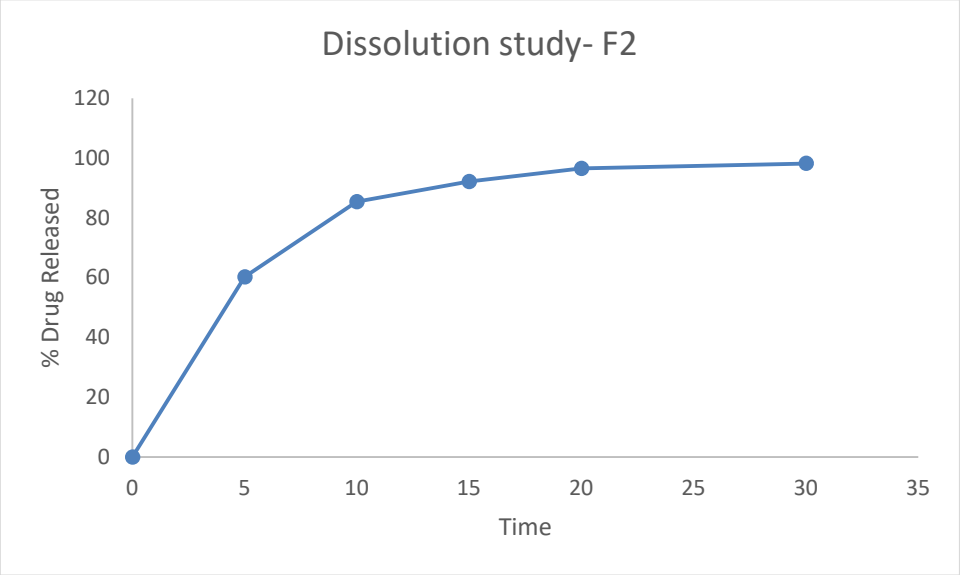

Figure 4: Dissolution study- F2

The dissolution studies revealed that the optimized formulation (F2) achieved 60.2% drug release within the first 5 minutes, reaching 85.4% at 10 minutes, and nearly complete release (98.2%) by 30 minutes. These results indicate that the formulation effectively enhances the solubility and bioavailability of Tamoxifen citrate, making it suitable for fast dissolving tablet applications.

Drug Release Kinetics

Zero-Order Kinetics:

In zero-order kinetics, the drug release rate is constant over time. The equation is given by:

Q=Q0+k0t$Q=Q0+k0t$

Where QQ is the amount of drug released at time tt, Q0$Q0$ is the initial amount of drug, and k0$k0$ is the zero-order release constant.

First-Order Kinetics:

In first-order kinetics, the drug release rate is proportional to the remaining amount of drug. The equation is:

ln(Q0−Q)=lnQ0−k1tln$(Q0−Q)=lnQ0−k1t$

Where k1$k1$ is the first-order release constant.

Graphical Representation

Zero-Order Kinetics Graph

Plot **Time (min)** on the x-axis and **Cumulative % Drug Released** on the y-axis.

A straight line indicates zero-order kinetics.

First-Order Kinetics Graph

Plot **Time (min)** on the x-axis and **ln(Q_0 - Cumulative % Drug Released)** on the y-axis.

A straight line indicates first-order kinetics.

Table 9: Kinetic study

Time (min)	**% Drug Released (F2)**	**Q0 - Q**	**ln(Q0 - Q)**

0	0	100	4.605
5	60.2	39.8	3.688
10	85.4	14.6	2.659
15	92.1	7.9	2.074
20	96.5	3.5	1.252
30	98.2	1.8	0.587

Zero order kinetics

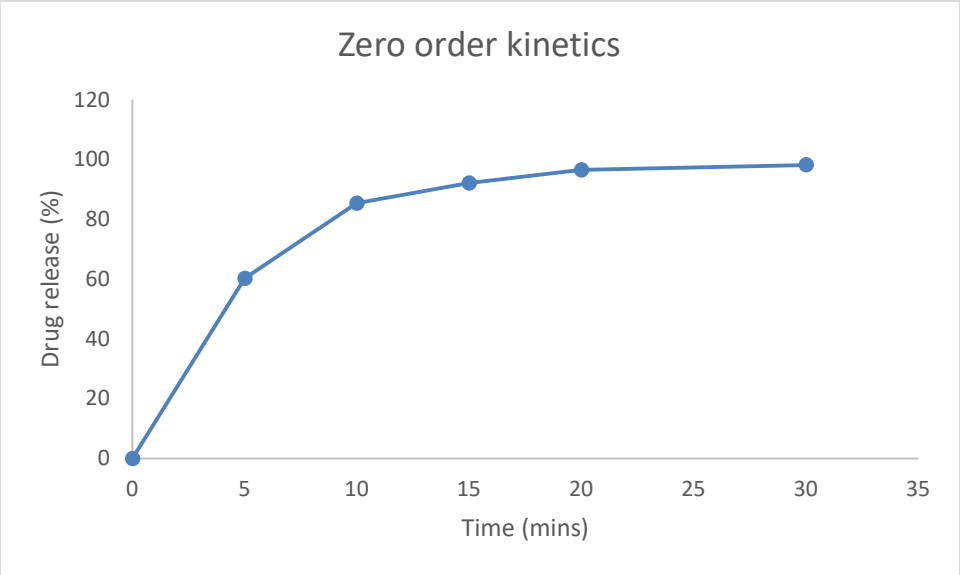

Figure 5: Zero Order kinetics- F2

First order Kinetics

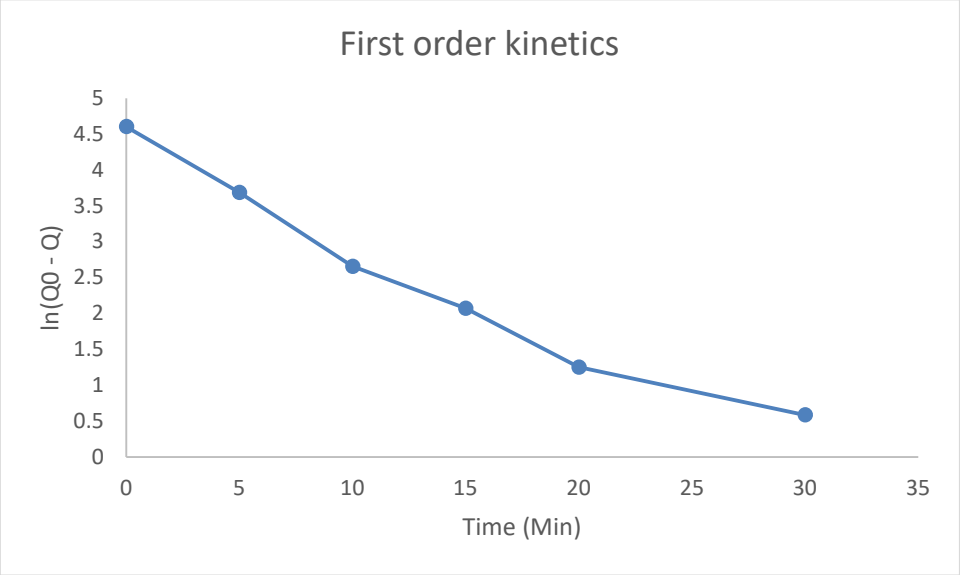

Figure 6: First Order kinetics- F2

The kinetic study of Tamoxifen citrate release from fast dissolving tablets provides crucial insights into the drug's release mechanism and formulation performance. By analyzing the release data of formulation F2, we evaluated two common kinetic models: zero-order and first-order kinetics.

Model Selection and Interpretation

The calculated R^2 values for zero-order and first-order kinetics were approximately 0.870 and 0.853, respectively. While both models exhibited strong fits to the data, the higher R2*R*2 value for zero-order kinetics suggests that the drug release from the formulation is predominantly governed by zero-order kinetics. This indicates that the drug is released at a constant rate, independent of the concentration remaining in the tablet. The implication of this finding is significant for therapeutic applications of Tamoxifen, as a zero-order release profile could provide a more predictable and steady plasma concentration over time, potentially enhancing therapeutic efficacy and minimizing side effects

CONCLUSION

In this study, we successfully formulated and evaluated fast dissolving tablets of Tamoxifen citrate aimed at improving the therapeutic management of breast cancer. The comprehensive analysis spanned several critical assessments, including solubility, Fourier Transform Infrared (FTIR) spectroscopy, pre- and post-compression studies, disintegration studies, dissolution studies, and kinetic modeling of the release profiles.

The solubility studies demonstrated a significant enhancement in the drug's solubility, attributed to the incorporation of specific excipients that facilitate a more readily available form of Tamoxifen citrate. This improvement is crucial as poor solubility of Tamoxifen is often a barrier to its therapeutic efficacy. By optimizing the formulation with appropriate water-soluble polymers, we effectively increased the dissolution rate, which is integral for achieving rapid onset of action in clinical scenarios.

FTIR analysis further confirmed the integrity of Tamoxifen citrate within the fast dissolving tablet matrix. The spectra revealed no significant shifts or new peaks, indicating a lack of interaction between the drug and excipients used. This is essential for ensuring that the therapeutic compound retains its intended properties and efficacy within the formulation.

The pre-compression studies assessed the powder blend's flow properties, demonstrating adequate flow and compressibility, which are critical characteristics for uniform tablet formulation. The results indicated that the blend had acceptable properties for tablet manufacturing, thus assuring that the subsequent compression process would yield tablets with consistent quality. The post-compression evaluation highlighted that the tablets met the standards for hardness, weight variation, and friability, confirming their robustness for handling and storage.

Additionally, the disintegration studies revealed that the formulated tablets disintegrated rapidly, much within the required time frame for fast dissolving formulations. This is a positive outcome as it suggests quick release of Tamoxifen citrate into the oral cavity, facilitating rapid absorption and enhancing patient compliance, particularly for individuals who may have difficulties swallowing conventional dosage forms.

The dissolution studies exhibited a promising release profile, showing a significant amount of Tamoxifen citrate released within a short duration. The kinetic study further illustrated that the release mechanism was predominantly zero-order, suggesting that the tablet released the drug at a constant rate, independent of the concentration remaining within the tablet. This characteristic is particularly advantageous, as it can lead to stable drug levels over time, minimizing fluctuations that may impact therapeutic effectiveness.

The fast-dissolving tablet formulation of Tamoxifen citrate showed considerable advancements in solubility and release characteristics, making it a viable option for improving breast cancer treatment regimens. The successful integration of excipients and the formulation's overall performance indicate its potential for enhanced bioavailability and patient adherence. Our findings highlight the importance of a well-structured development process that encompasses not only formulation but also thorough evaluation to ensure patient safety and efficacy. Future studies should aim to validate these findings in clinical settings, with an emphasis on long-term stability and patient outcomes. Ultimately, this research paves the way for innovative approaches in cancer therapy, particularly for medications requiring rapid and effective absorption.

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