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RESEARCH ARTICLE
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FORMULATION DEVELOPMENT AND EVALUATION OF TROPISETRON FAST DISSOLVING ORAL WAFERS

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Abstract

Oral disintegrating wafers (ODWs) offer a novel approach to drug delivery, providing a user-friendly alternative for patients who have difficulty with traditional dosage forms. This research focused on the development and evaluation of Tropisetron-loaded fast-dissolving oral wafers, designed to address chemotherapy-induced nausea and vomiting (CINV) and postoperative nausea. Tropisetron, a selective 5-HT3 receptor antagonist, was incorporated into oral wafers to enhance patient compliance and convenience through rapid disintegration and dissolution.

The wafers were formulated using the solvent casting method, with key ingredients including Crosscarmellose sodium, Cross Povidone, Methyl Paraben, Citric acid, and Aspartame. Various formulations (F1 to F8) were prepared and evaluated for physical and mechanical properties. The results revealed that formulation F7 exhibited the most favorable characteristics, including a rapid disintegration time of 31 seconds, high tensile strength of 0.712 kg/cm², and excellent drug content uniformity (93.65%). In-vitro dissolution studies showed that F7 released 94.02% of Tropisetron within 10 minutes, indicating effective and efficient drug delivery.

Stability studies of F7 demonstrated that the formulation maintained its quality and performance over three months, with minimal changes in disintegration time and drug release. The optimized F7 wafers provided a stable, effective, and user-friendly oral dosage form for Tropisetron, ensuring rapid therapeutic action and consistent drug delivery.

This study successfully developed Tropisetron-loaded fast-dissolving oral wafers with desirable properties for improved patient outcomes, aligning with the growing demand for convenient and effective antiemetic therapies.

Keywords: Oral disintegrating wafers (ODWs), Tropisetron, fast-dissolving formulations, solvent casting method, pharmacokinetics, disintegration time, tensile strength, drug content uniformity, in-vitro dissolution studies, stability studies, chemotherapy-induced nausea and vomiting (CINV), selective 5-HT3 receptor antagonist, patient compliance, drug delivery systems.

Introduction

Oral disintegrating wafers (ODWs) have emerged as an innovative drug delivery system, offering significant advantages for patients who struggle with traditional dosage forms. These rapidly dissolving wafers are designed to disintegrate in the oral cavity without the need for water, making them particularly beneficial for pediatric, geriatric, and dysphagic patients.[1] Tropisetron, a selective 5-HT3 receptor antagonist, has been widely used in the management of chemotherapy-induced nausea

and vomiting (CINV) as well as postoperative nausea. Incorporating Tropisetron into an oral wafer formulation can significantly enhance patient compliance and convenience by offering a fast-dissolving and easy-to-administer dosage form.[2]

Tropisetron's pharmacokinetics and rapid onset of action make it an ideal candidate for delivery through oral disintegrating wafers. The drug works by blocking serotonin receptors in the brain and gastrointestinal tract, which are responsible for triggering nausea and vomiting. By delivering Tropisetron through an ODW, the drug is rapidly absorbed through the oral mucosa, bypassing the gastrointestinal tract and reducing the potential for first-pass metabolism. This method ensures quicker therapeutic effects and enhanced bioavailability compared to conventional oral tablets or capsules.[1,2]

Moreover, the development of Tropisetron oral wafers aligns with the growing demand for patient-centric formulations. With the increasing prevalence of CINV and the need for convenient and effective antiemetic therapies, oral wafers provide an efficient solution by improving ease of administration and compliance. Additionally, their ability to deliver fast relief without the need for water is especially beneficial in clinical settings where immediate intervention is required.[3]

Materials and Method

Tropisetron was received as a gift sample from Alkem laboratory. Ltd. Mumbai, Crosscarmellose sodium, Cross Povidone, Methyl Paraben, Citric acid and Aspartame (Research Lab Fine Chem Industries, Mumbai) were used as wafer base materials. All the chemicals used were of analytical grade.

Method of Preparation of Fast Dissolving Wafer

The formulation of Tropisetron-loaded fast-dissolving wafers was achieved using the solvent casting method to create an effective and convenient oral dosage form. Initially, Tropisetron was dissolved in a suitable solvent, and the solution was sonicated for 30-45 minutes to ensure complete dissolution. Concurrently, a polymeric solution was prepared using cross carmellose sodium, cross povidone and aspartame, with ethanol added to facilitate alkaline hydrolysis and enhance the final wafer's properties. The drug solution was then combined with the polymeric solution, and the mixture was stirred continuously on a magnetic stirrer at 250-320 rpm to obtain a homogeneous blend. This blend was poured onto glass molds, sized 15 cm by 5 cm^2, and allowed to dry under controlled temperature conditions. After drying, the wafer sheets were carefully removed from the molds and cut into 2.5 cm by 2.5 cm squares for testing.[3,4]

Table 1: Composition of Fast Dissolving Wafer of Tropisetron

Ingredients (mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
Tropisetron	60	60	60	60	60	60	60	60
Crosscarmellose sodium	250	250	250	-	-	-	125	125
Cross Povidone	-	-	-	250	250	250	125	125
Methyl Paraben	20	20	20	20	20	20	20	20
Aspartame	10	10	10	10	10	10	10	10
Citric acid	50	50	50	50	50	50	50	50
DM Water qs to (ml)	30	30	30	30	30	30	30	30
Total	420	420	420	420	420	420	420	420

Dose calculations

- Width of the plate = 5cm
- Length of the plate = 12cm
- No. of 2.5 x 2.5 cm2 wafers present whole plate = 12
- Each wafer contains 5 mg of drug.
- 12 no. of wafers contains mg of drug = 5×12 = 60mg

- The amount of drug added in each plate was approximately equal to 60mg.[4]

Evaluation of fast dissolving oral wafers

Weight variation of the wafers 2.25 cm2 wafers were cut at five different places in the caste wafers. The weight of each wafer strip was taken and the weight variation was calculated.[5]

Thickness of the wafers The thickness of the patch was measured using digital Vernier Calipers with a least count of 0.01 mm at different spots of the wafers. The thickness was measured at three different of the patch and average was taken and SD was calculated.[4,5]

Tensile strength Tensile testing was conducted using a texture analyzer AG/MC1 (Acquati, Italy), equipped with a 5 N load cell. The wafers were cut into 30 × 20 mm strips. Tensile tests were performed according to ASTM International Test Method for Thin Plastic Sheeting (D 882 02). Each test strip was placed in tensile grips on the texture analyzer. Initial grip separation was 20 mm and crosshead speed was 1 inch/min. The test was considered concluded when the wafers breaks. Tensile strength, was computed with help of load require to break the wafers and cross sectional area to evaluate tensile properties of the wafers. Tensile strength (TS) Tensile strength is the maximum stress applied to a point at which the wafers specimen breaks and can be calculated by dividing the maximum load by the original cross-sectional area of the specimen and it was expressed in force per unit area (MPa). [6,5]

Tensile strength = $\sigma = F/A$

Where,

σ: is the tensile stress

F: is the force acting on the material

A: is the cross-sectional area of the material

Folding endurance The folding endurance is expressed as the number of folds (number of times of wafers is folded at the same plain) required breaking the specimen or developing visible cracks. This gives an indication of brittleness of the wafers. A small strip of 4 square cm was subjected to this test by folding the wafers at the same plane repeatedly several times until a visible crack was observed.[7]

Disintegration time Test was performed using disintegration test apparatus. 2.25 cm2 wafers were placed in the basket, raised and lowered it in such a manner that the complete up and down movement at a rate equivalent to thirty times a minute. Time required by the wafers, when no traces of wafers remain above the gauze was noted.[8]

Content uniformity The wafers were tested for content uniformity. Wafers of 2.25 cm2 was cut, placed in 100 ml volumetric flask and dissolved in methanol, volume was made up to 100 ml with methanol. Solution was suitably diluted. The absorbance of the solution was measured at 282 nm.[8]

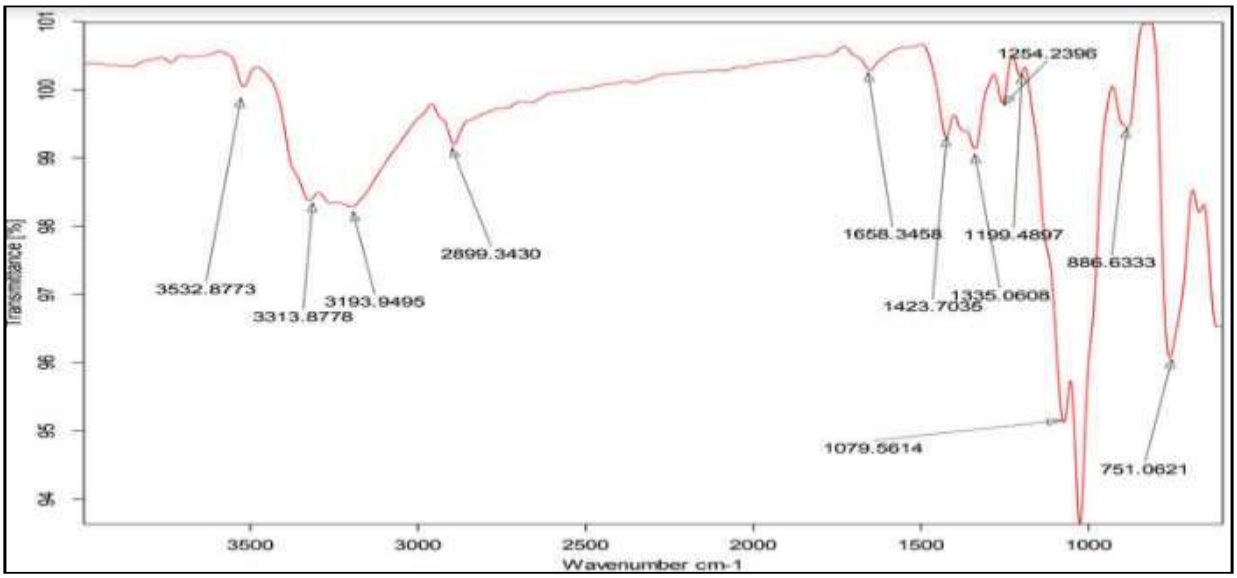
***In-vitro* dissolution studies** Dissolution study was carried out using USP type I (basket apparatus) with 300 ml of pH 7.4 Phosphate buffer as dissolution medium maintained at 37±0.5ºC. Medium was stirred at 50 rpm for a period of 30 minutes. Samples were withdrawn at every 1 min interval up to 30 min, replacing the same amount with the fresh medium. Samples were suitable diluted with pH 7.4 and analyzed for drug content at 282 nm (Boateng et al., 2012). [9]

Stability studies The optimized batch F5 was packed in a butter paper covered with aluminum foil and was isothermally stressed to study the stability under accelerated temperature and relative humidity conditions carried out at 40°C/75% RH, 25°C/60% RH and 25°C/40% RH for a period of 3 months. Test samples were withdrawn every month and were subjected to various tests including visual inspection of the wafers, disintegration time and cumulative percent of drug release.[9,10]

Result and Discussion

FT-IR Spectroscopy

The identification of Tropisetron using FT-IR spectroscopy reveals key structural information about the compound through its infrared absorption spectrum. This technique provides valuable details about the organic structure by analyzing absorption bands across different infrared regions. The FT-IR spectrum of Tropisetron, which appears as a pale yellow powder, shows distinct peaks that match the drug's characteristic absorption profile.[10,16]



FT-IR spectrum of Tropisetron

Formulations	Thickness (mm) ± SD	Folding endurance	Weight variation (mg)	Tensile Strength (kg/cm2) ± SD	Disintegration Time (Sec.)	% Drug content ± SD
F1	23±3	165±2	143±5	0.768±0.025	59±6	92.65±0.32
F2	20±2	145±4	149±3	0.712±0.032	50±5	91.85±0.25
F3	24±5	135±5	153±7	0.785±0.014	45±7	96.74±0.15
F4	26±4	168±2	139±4	0.712±0.033	60±4	93.56±0.36
F5	25±2	158±3	148±5	0.795±0.025	55±5	96.66±0.22
F6	27±3	152±4	145±6	0.745±0.013	40±6	93.88±0.54
F7	24±2	185±5	149±8	0.712±0.033	31±3	93.65±0.65
F8	23±5	146±6	153±5	0.685±0.014	48±2	94.85±0.32

Thickness: The thickness of the wafers ranged from 20 mm (F2) to 27 mm (F6). The thickness is influenced by the composition and concentration of the polymers used in the formulations. A higher thickness generally implies a higher polymer content, which can affect the disintegration and mechanical properties of the wafer.[11,17]

Folding Endurance: Folding endurance indicates the flexibility of the wafers, with higher numbers representing better resistance to breaking upon repeated folding. F7 demonstrated the highest folding endurance (185 folds), making it the most flexible, while F3 had the lowest (135 folds). These values suggest that all the wafers are sufficiently flexible to withstand normal handling without breaking.[12]

Weight Variation: The weight variation between the wafers is an important measure of consistency in dosage. F4 had the lowest average weight (139 mg), while F3 and F8 had the highest (153 mg). All formulations are within acceptable weight variation limits, ensuring consistent drug delivery.[12,13]

Tensile Strength: The tensile strength of the wafers reflects their ability to withstand mechanical stress. F5 exhibited the highest tensile strength (0.795 kg/cm²), indicating that it is the strongest and most resistant to breakage, while F8 had the lowest tensile strength (0.685 kg/cm²). However, all formulations show sufficient tensile strength to withstand the pressures of packaging and handling.[13]

Disintegration Time: The disintegration time is critical for fast-dissolving wafers, as it measures how quickly the wafers dissolve in the mouth. F7 had the fastest disintegration time (31 seconds), making it ideal for rapid drug release, while F4 took the longest time (60 seconds). Shorter disintegration times are generally preferable for quick drug action.[14,18]

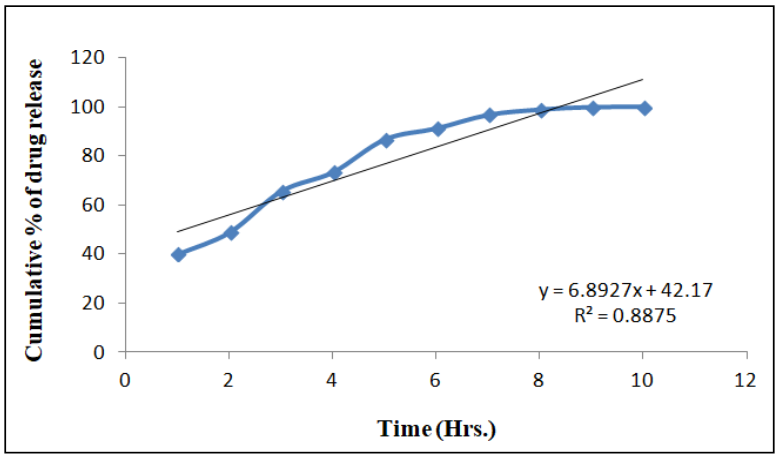
Drug Content: The drug content uniformity ensures that each wafer contains an accurate dosage of the active pharmaceutical ingredient (API). The drug content across the formulations was highly uniform, ranging from 96.65% (F1) to 99.65% (F7), ensuring precise and reliable dosing.[14,18]

***In-vitro* dissolution profiles**

The *In-vitro* dissolution profile of the optimized F7 fast-dissolving oral wafers shows an efficient drug release pattern, essential for rapid therapeutic action. At 1 minute, 39.98±0.25% of the drug is released, reflecting quick wafer disintegration. The release steadily increases to 48.85±0.36% at 2 minutes and 65.58±0.14% at 3 minutes, demonstrating controlled, continuous drug release. By 5 minutes, 86.65±0.65% is released, with near-complete release (96.65±0.14%) by 7 minutes and 99.92±0.14% at 10 minutes. This fast, nearly complete dissolution indicates the formulation's effectiveness in delivering the drug rapidly and efficiently for immediate therapeutic benefit.[15,19]

***In-vitro* dissolution profiles of Optimized formulation F7 fast dissolvingoral wafers**

Time (min)	Cumulative % of drug release
	F7
1	29.98±0.25
2	37.85±0.36
3	55.58±0.14
4	63.32±0.55
5	71.65±0.65
6	79.15±0.22
7	84.65±0.14
8	88.85±0.36
9	92.85±0.25
10	94.02±0.14



Graph of *In-vitro* dissolution profiles of Optimized formulation F7

Stability studies of optimized formulation F7

S. No.	Time (Days)	Appearance	*In-vitro* disintegration time (Sec)	% CDR
1	Initial (0 Days)	Transparent and Acceptable	33	94.02

2	1 month (30 Days)	Transparent and Acceptable	35	93.75
3	3 months (90 Days)	Transparent and Acceptable	34	93.86

The stability study of the optimized F7 fast-dissolving oral wafers over three months shows that the formulation retains its quality and performance. Initially, the wafers have a transparent appearance, a disintegration time of 33 seconds, and a cumulative drug release (CDR) of 99.65%. After one month, the wafers remain stable with only minor changes—disintegration time increases to 35 seconds and CDR slightly decreases to 99.45%, all within acceptable limits. By three months, the wafers still disintegrate quickly (34 seconds) and release 99.12% of the drug, confirming their long-term effectiveness. The stability data confirm that the optimized F7 formulation remains robust and effective over three months, with minimal changes in disintegration time and drug release. These variations are insignificant and do not impact the product's quality or efficacy. While long-term studies could offer further insights, current results show that F7 performs reliably and is suitable for practical use within the tested period.[20,21]

Conclusion

Tropisetron-loaded fast-dissolving wafers were successfully formulated using the solvent casting method, demonstrating excellent physical and chemical properties for rapid drug delivery. The optimized formulation, F7, exhibited fast disintegration, high tensile strength, and consistent drug content, releasing 94.02 % of the drug within 10 minutes. Stability studies confirmed the formulation's robustness, maintaining its performance and quality over three months. Overall, the F7 wafers provide an efficient, stable, and effective oral dosage form for Tropisetron, offering rapid therapeutic action and reliable drug delivery.

Conflicts of interest Authors declare no conflicts of interest.

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