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Original Research Article

FORMULATION AND CHARACTERIZATION OF DEXLANSOPRAZOLE FAST DISSOLVING ORAL WAFERS

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ABSTRACT

GERD a chronic gastrointestinal illness with a prevalence of 20%, often diagnosed digestive illnesses. As an alternative to capsules, tablets, and syrups for elderly and young patients who have difficulty swallowing, rapid disintegrating drug delivery systems were created in the late 1970s. Fast dissolving wafers which are more convenient and simple to use than other dosage forms like orally disintegrating tablets. Therefore, the creation of fast-dissolving oral wafer formulations will be aim of this project. The formulation & evaluation of wafer was performed as per protocol. Results showed that the weight variation among the eight formulations ranged from 122±2mg to 139±5mg. The thickness also varied between 0.23±0.02 to 0.28±0.03 mm. The tensile strength spans from 1.68±0.15 MPa for F8 formulation to maximum of 3.25±0.25 MPa for F1 formulation. The folding endurance was found to be highest for F7 formulation which is 185±5. Further, the least disintegration time observed was 31±3 which is also the attribute of F7 formulation. Additionally the drug content was found to be maximum for F7 again with the value of 99.45±0.47 %. The cumulative % drug release was observed to be 99.92 % in 10 minutes for F7. The stability studies of optimized formulation F7 indicated that formulation remained stable for 3 months. It can be concluded that fast-releasing sublingual wafers of Dexlansaprazole is developed for the rapid and effective drug delivery with increased bioavailability.

Keywords: GERD, Fast dissolving drug delivery system, Oral Wafers, Bioavailbility, Dexlansaprazole

INTRODUCTION

The regurgitation of stomach contents into the esophagus is a defining feature of gastroesophageal reflux disease (GERD), a chronic gastrointestinal illness. With a prevalence of 20%, it is one of the most often diagnosed digestive illnesses. It has a negative impact on quality of life and imposes a heavy financial burden in the form of direct and indirect expenditures. The esophagogastric junction barrier is disrupted in GERD due to a variety of causes that might be intrinsic, structural, or both. As a result, the esophagus is exposed to acidic gastric contents. Clinically, GERD frequently presents with symptoms of regurgitation and heartburn. Additionally, it may exhibit unusual extra-esophageal symptoms as chest pain, tooth erosions, a persistent cough, laryngitis, or asthma (Clarrett and Hachem,. 2018; Eslick and Talley, 2009; Patrick, 2011).

As an alternative to capsules, tablets, and syrups for elderly and young patients who have difficulty swallowing, rapid disintegrating drug delivery systems were created in the late 1970s. Many orally disintegrating tablets that dissolve in the mouth without chewing or drinking water

were commercialized to address the demand. Later, oral drug delivery technology had advanced from conventional dosage form to modified release dosage form, and recently rapid disintegrating films had been produced in place of oral disintegrating tablets (Habib *et al*., 2000; Parkash *et al*., 2011).

The industry recently saw the introduction of orally fast dissolving wafers which are more convenient and simple to use than other dosage forms like orally disintegrating tablets. A huge variety of pharmaceutical industries are becoming interested in OFDFs as this technology has developed over the past few years from the confection and oral care markets in the form of breath strips into a novel and well appreciated form by consumers. The type of medication delivery device known as an orally fast dissolving wafers dissolves or disintegrates when placed in the oral cavity in a matter of seconds without the need for water.

Fast dissolving wafers resemble postal stamps in terms of their thickness, size, and shape. Through intragastric, sublingual, or buccal routes of administration, these wafers have the potential to deliver the medication systemically. They have also been utilized for local action (Bhyan *et al*., 2011; Garsuch and Breitkreutz *et al*., 2009). This kind of technology provides a comfortable method of administering medication not only to certain demographic groups including children, the elderly, patients who are bedridden, and patients who are mentally ill, but also to the entire public. Some businesses unveiled more durable fast-dissolving drug delivery methods. The tongue's floor or top is where the wafer is deposited. This wafers instantly dissolves when placed on the tongue, releasing the medication, which dissolves in the saliva. As saliva descends into the stomach, some medications are absorbed from the mouth, pharynx, and esophagus. Enhancing medicine bioavailability in this situation ensures no choking danger and a pleasant mouthfeel.

When there is too much acid in the stomach, several conditions are treated with dexlansoprazole. It is used to treat gastroesophageal reflux disease (GERD), a disorder where the acid in the stomach washes back up into the esophagus, which causes erosive esophagitis or "heartburn." Therefore, the creation of fast-dissolving oral wafer formulations will be beneficial for GERD patients (Sushmitha *et al*., 2014; Behm and Peura, 2011).

MATERIALS & METHODS

Chemicals & Reagents

API, Cross carmellose sodium, Methyl Paraben, Aspartame, Citric acid, DM water were obtained from S.D. Fine chemicals Mumbai.

Formulation development of wafers of Dexlansoprazole

Drug **(**Dexlansoprazole) containing fast dissolving wafers were fabricated by the solvent casting method. Cross carmellose sodium, Aspartame by solvent casting technique with ice cold distilled water and sublingual wafers were prepared. Drug solution was sonicated for 30-45 min to solubilize the drug completely in the solvent. Drug solution was poured into polymeric solution and ethanol was added for alkaline hydrolysis. Both solutions are uniformly mixed to get a homogeneous solution on magnetic stirrer at 250-320 rpm. Then this solution was spread on film former by adjusting the desired temperature on glass

moulds of 15cm*5 cm^2. Once the wafer sheet was ready, it was cut into desired size of 2.5*2.5 cm^2 cm was dried and The dried wafers were carefully removed from the glass plates and was cut into size required for testing (Costa *et al*., 2019).

Table 1: Selection and optimization of wafers forming agents

Name of ingredients (mg for 12 strips)	F1	F2	F3	F4	F5	F6	F7	F8
API	720	720	720	720	720	720	720	720
Cross carmellose sodium	250	500	250	500	250	500	250	500
Methyl Paraben	20	20	20	20	20	20	20	20
Aspartame	20	20	20	20	20	20	20	20
Citric acid	50	50	50	50	50	50	50	50
DM water qs to (ml)	30	30	30	30	30	30	30	30

Dose calculations

- Width of the plate = 5cm
- Length of the plate = 12cm
- No. of 2.5 x 2.5 cm^2 wafers present whole plate = 12
- Each wafer contains 60 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 720mg.

Evaluation of fast dissolving oral wafers

Weight variation of the wafers

2.25 cm^2 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 (Mandeep *et al*., 2013).

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 spots of the patch and average was taken and SD was calculated.

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).

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 (Vaidya *et al*., 2013).

Disintegration time

Test was performed using disintegration test apparatus. 2.25 cm^2 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.

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.

***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.

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.

RESULTS AND DISCUSSION

The weight variation among the eight formulations ranged from 122±2mg to 139±5mg. The thickness also varied between 0.23±0.02 to 0.28±0.03 mm. Since the uniformity of the film's thickness directly affects the precision of the dose applied to the film, doing so is crucial.

The tensile strength spans from 1.68±0.15 MPa for F8 formulation to maximum of 3.25±0.25 MPa for F1 formulation. The folding endurance was found to be highest for F7 formulation which is 185±5.

Brittleness of the film is shown by folding endurance. Cross carmellose sodium concentration rose along with folding endurance, which affected the overall flexibility of the dexlansaprazole loaded wafer. The films were strong enough to endure handling if the folding endurance for FDF had a higher value.

Further, the least disintegration time observed was 31±3 which is also the attribute of F7 formulation. An indication of the drug's start of action is provided by an in vitro disintegration study. According to the findings, the disintegration time decreased as plasticizer concentration increased.

Additionally the drug content was found to be maximum for F7 again with the value of 99.45±0.47 %.

The cumulative % drug release was observed to be 99.92 % in 10 minutes. The ideal proportion of the wafer-forming polymers utilized, which have both features of gelation and fast melt, can be attributed to the drug's quicker release. Due to the fact that a significantly bigger sink condition was maintained during the drug release trials, which resulted in a much faster release of the

drug into the media, the drug release was found to be substantially faster than that of the permeation for the identical formulations.

The stability studies of optimized formulation F7 indicated that formulation remained stable for 3 months.

Table 2: Weight variation (mg) parameters of fast dissolving oral wafers

Formulation code	Weight variation (mg)
F1	132±5
F2	130±3
F3	125±2
F4	136±4
F5	128±5
F6	122±2
F7	145±3
F8	139±5

Table 3: Thickness (mm) of fast dissolving oral wafers

Formulation code	Thickness (mm)
F1	0.23±0.02
F2	0.25±0.03
F3	0.26±0.02
F4	0.25±0.01
F5	0.24±0.03
F6	0.28±0.02
F7	0.27±0.05
F8	0.28±0.03

Table 4: Tensile strength (MPa) of fast dissolving oral wafers

Formulation code	Tensile strength (MPa)
F1	3.25±0.25
F2	2.45±0.32
F3	1.85±0.15
F4	2.98±0.16
F5	2.32±0.32
F6	1.85±0.22
F7	1.78±0.14
F8	1.68±0.15

Table 5: Folding endurance (No. of folds) of fast dissolving oral wafers

Formulation code	Folding endurance (No. of folds)
F1	165±2
F2	145±4
F3	135±5
F4	168±2
F5	158±3
F6	152±4
F7	185±5
F8	146±6

Table 6: Disintegration time (Sec) of fast dissolving oral wafers

Formulation code	Disintegration time (Sec.)
F1	59±6
F2	50±5
F3	45±7
F4	60±4
F5	55±5
F6	40±6
F7	31±3
F8	48±2

Table 7: Drug content (%) of fast dissolving oral wafers

Formulation code	Drug content (%)
F1	98.85±0.15
F2	96.65±0.25
F3	97.45±0.36
F4	98.12±0.32
F5	98.65±0.45
F6	98.12±0.36
F7	99.45±0.47
F8	98.74±0.32

Table 8: *In-vitro* dissolution profiles of Optimized formulation F7 fast dissolving oral wafers

Time in min	Cumulative % of drug release
	F7
1	32.25
2	45.65
3	55.85
4	69.98
5	74.65
6	88.98
7	92.25
8	99.92
9	99.85
10	99.92

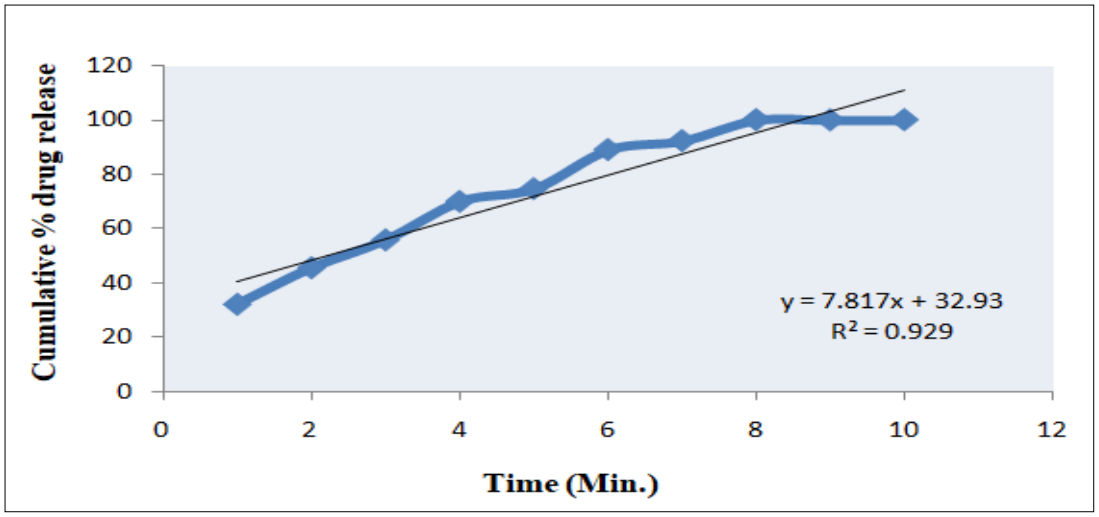

Figure 1: Graph of *In-vitro* dissolution profiles of Optimized formulation F7

Table 9: Stability studies of optimized formulation F7

S. No.	Time (Days)	Appearance	*In-vitro* disintegration time (Sec)	% CDR
1	Initial (0 Days)	Transparent and Acceptable	31	99.45
2	1 month (30 Days)	Transparent and Acceptable	32	99.12
3	3 months (90 Days)	Transparent and Acceptable	34	98.85

CONCLUSION

Dexlansaprazole has a 25% systemic oral bioavailability, making it an effective antiemetic. The primary goal of the experiments discussed was to create Dexlansaprazole sublingual wafers that dissolve quickly and have improved oral bioavailability for the treatment of motion sickness. As a result, it was successful in developing fast-releasing sublingual wafers of Dexlansaprazole for the rapid and effective drug delivery with increased bioavailability

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

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