



Formulation and Characterization of Fast Dissolving Strips of an Antiemetic Drug

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ABSTRACT

The creation and characterisation of oral meclizine hydrochloride wafers that dissolve quickly is the goal of the current study. Solvent casting was used to create fast-dissolving wafers containing meclizine hydrochloride. At 232 nm, a UV-visible spectrophotometer was used to assess the drug content. The Meclizine hydrochloride wafers showed consistent drug distribution, with a percentage drug content ranging from $95.65 \pm 0.23\%$ to $99.12 \pm 0.61\%$. Every preparation quickly absorbs moisture and breaks down when it comes into touch with water. The disintegration time of the prepared Meclizine hydrochloride wafers was between 6 ± 1 and 15 ± 1 seconds. At 6 ± 1 seconds, formulation F7 had the quickest disintegration time. Formulations using only xanthan gum, gelatin, and gum acacia had the fastest disintegration time, at 15 ± 1 seconds. Meclizine hydrochloride wafer formulation F7 was used for the in vitro drug release investigations. According to the drug release statistics, the drug release at 60, 120, 180, 240, 300, and 360 seconds was 36.65%, 48.89%, 64.56%, 72.32%, 85.65%, and 98.15%, respectively. The ideal ratio of the wafer-forming polymers utilized, which have both gelation and rapid melt capabilities, may be attributed to this quicker drug release. Because of the considerably greater sink condition maintained during the drug release trials, which results in a much quicker release of the drug into the medium, the drug release was shown to be much faster than the permeation for the identical formulations. **Keywords:** gum acacia, xanthan gum, gelatin, fast-dissolving oral wafers, and meclizine hydrochloride.

INTRODUCTION

Buccal drug delivery is the primary and most widely accepted drug delivery method among the novel drug delivery systems. There are oral disintegrating pills on the market that dissolve in one to two minutes.

Pediatric and elderly patients who have trouble swallowing conventional oral solid dose forms might use the oral flash release wafer drug delivery system, one of the rapid dissolving drug delivery options, as an

alternative to tablets, capsules, and syrups 1. Local action, quick product release, and direct systemic circulation in the mouth cavity have all been facilitated by this technique. Additionally, this administration enhances solubility and shields the medication from first-pass metabolism.

Solid dose forms known as oral thin wafer medication delivery methods dissolve quickly in the mouth when taken without chewing or drinking water. Another name for this is rapid dissolving buccal films, oral wafers, and oral strips 2.

The systemic administration of both novel and current medicinal medications is made easier by the permeability of mucosal membranes. By bypassing the hepatic metabolism, several mucosal areas, such as the nasal, rectal, vaginal, ocular, and oral mucosa, may enhance bioavailability. For both novel and old therapeutic molecules, some of which are now exclusively accessible by parenteral distribution, transmucosal drug delivery is being studied as an appealing delivery method. Because of their physiological characteristics, the buccal mucosa and the sublingual region are the most appropriate locations for both local and systemic drug administration among the several transmucosal drug delivery sites. 3–4.

Patients all throughout the globe utilize fast-dissolving wafers, a recently developed oral dose form. 5. Fast dissolving wafers have garnered a lot of interest on the market because to their many benefits and a two to three year shelf life. These dosage forms may be utilized even in acute conditions for immediate treatment. 6. These oral sublingual wafers are just a thin oral strip that dissolves instantly in the sublingual cavity because saliva is present in the mouth, releasing medication in a little period of time⁷. Since sublingual wafers don't need water for engulfment, they seem to be a very useful dose form for travel. Because this dose form is so effective at avoiding first pass metabolism, even a quick beginning of action is accomplished. Wafers are applied sublingually to improve the medication's onset of action, reduce dosage, and increase efficacy.⁹ They are more stable, long-lasting, and dissolve more quickly than other traditional dosage forms.¹⁰ An oral wafer also helps to increase the drug's bioavailability, improves dosing accuracy (i.e., single unit dosage form¹¹), may enable the use of bitter-tasting drugs in formulations, and increases patient compliance 12–13. A disease known as benign prostatic hyperplasia occurs when the prostate gland enlarges without developing cancer. The wall of the bladder thickens and becomes incapable of emptying entirely. The creation and characterisation of oral meclizine hydrochloride wafers that dissolve quickly is

the goal of the current study.

MATERIAL AND METHODS

Material

Meclizine was obtained as a gift sample from pharmaceutical company. All other chemical were purchased from Hi Media, Mumbai. Double distilled water was prepared freshly and used whenever required. All the chemicals used in this work were of analytical grade.

Methods

Formulation development of oral wafers of Meclizine hydrochloride

Drug (Meclizine hydrochloride) containing fast dissolving wafers were fabricated by the solvent casting method. The optimized amount of polymers was dissolved in 5ml of water and stirred continuously for 1 hour, optimized amount of Plasticizer and drug were dissolved in 95% ethanol and then added to the polymeric solution, the optimized amount of drug was dissolved in 2ml of water and kept on sonication for proper dispersion. Polymeric solution was stirred for 30 min using magnetic stirrer and was kept in undisturbed condition till the entrapped air bubbles were removed. The aqueous solution was casted in a glass moulds having 2.5 x 2.5 cm * 10 wafers area and was dried at controlled room temperature (25°-30°C, 45 %RH) as well as at increased temperature (microwave oven). The wafers took approximately 48 hr to dry at controlled room temperature. The dried wafers were carefully removed from the glass plates and were cut into size required for testing. The wafers were stored in air tight plastic bags till further use.

Table 1: Formulation of oral wafers of Meclizine hydrochloride

Name of ingredients (mg for 12 strips)	F1	F2	F3	F4	F5	F6	F7	F8	F9
API	120	120	120	120	120	120	120	120	120
Xanthan gum	100	200	300	100	200	300	100	200	300
Gelatin	50	100	150	50	100	150	-	-	-
Gum acacia	25	50	75	-	-	-	25	50	75
Pullulan	-	-	-	25	50	75	25	50	75
Methyl Paraben	20	20	20	20	20	20	20	20	20
Aspartame	20	20	20	20	20	20	20	20	20
Citric acid	50	50	50	50	50	50	50	50	50

DM water qs to (ml)	30	30	30	30	30	30	30	30	30
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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 wafers contains 10 mg of drug.
- 12 no. of wafers contains mg of drug? = $10 \times 12 = 120\text{mg}$
- The amount of drug added in each plate was approximately equal to 120mg.

Evaluation of prepared wafers**Thickness**

Three random wafers were selected from each batch and the thickness was measured at three different places using a vernier caliper ¹⁴.

Weight uniformity

For each formulation, three randomly selected patches were used. For weight variation test, 10 wafers from each batch were weighed individually by digital electronic balance and the average weight and relative standard deviation was calculated.

Surface pH determination

The surface pH of fast dissolving wafers was determined in order to investigate the possibility of any side effects in vivo¹⁵⁻¹⁶. As an acidic or alkaline pH may cause irritation to the oral mucosa, it is important to keep the surface pH as close to neutral as possible. The wafer to be tested was placed in a petridish and was moistened with 0.2 ml of distilled water. The electrode of pH meter (Electronic India) was placed on the surface of wafer to determine the surface pH.

Folding endurance

This was determined by repeatedly folding one wafers at the same place until it broke. The number of times the wafers could be folded at the same place without breaking cracking gave the value of folding endurance¹⁷.

Percentage of moisture content

The wafers were weighed individually and kept in desiccators containing activated silica at room

temperature for 24 hrs. Individual wafers were weighed repeatedly until they showed a constant weight. The percentage of moisture content was calculated as the difference between initial and final weight with respect to final weight ¹⁸⁻¹⁹

$$\text{Percentage of Moisture Content} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Drug content analysis

The patches (n=3) of specified area were taken into a 10 ml volumetric flask and dissolved in methanol and volume was made up with 10 ml methanol. Subsequent dilutions were made and analyzed by UV spectrophotometer at 232nm²⁰.

Disintegrating time

The most important criteria of present work are to that dosage form should be dissolved within few seconds²¹. The incorporation of polymers to minimizes the disintegrating time. *In vitro* disintegration time was determined by placing the wafer in a petridish containing 10ml distilled water with swirling every 10 sec. The time at which the wafer disintegrated was noted.

In vitro dissolution study

The *in vitro* dissolution test was performed using the USPXXX dissolution apparatus II (Paddle type)²². The dissolution studies were carried out at 37±0.5°C; with stirring speed of 50 rpm in 900 ml phosphate buffer (pH 6.8). Wafers size required for dose delivery (2.5×2.5 cm²) was used. Five ml aliquot of dissolution media was collected at time intervals of 1, 2, 5, 10 and 15 minutes and replaced with equal volumes of phosphate buffer (pH 6.8). The collected samples were filtered through 0.45 µm membrane filter and the concentration of the dissolved Meclizine hydrochloride was determined using UV-Visible spectrophotometer at 232nm. The results were presented as an average of three such concentrations.

RESULTS AND DISCUSSION

Due to the varying amounts of polymers utilized in the formulation development process, the thickness of the produced meclizine hydrochloride ranged from 75±4 µm to 86±3 µm. After undergoing a weight variation test, the prepared Meclizine hydrochloride wafers showed a weight variation ranging from 98±6 mg to 124±3 mg (Table 2). One wafer was folded repeatedly in the same spot until it broke in order to ascertain this. The value of folding endurance was determined by how many times the wafers could be folded in the same spot without breaking or cracking. The formulation's elasticity is indicated by the maximal folding endurance. The formulation is readily broken because to its rigidity. The greatest value of Meclizine hydrochloride wafers was observed in formulation F7 (220±6), while the folding endurance value was more than 100 in all of the formulations.

Since an acidic or alkaline pH is certain to irritate the oral mucosa, the surface pH of each formulation was measured in order to look into the potential for any negative effects on the oral cavity. It was discovered that the formed wafers' pH ranged from 6.4±0.2 to 6.9±0.2. Therefore, table 3 suggests that the meclizine

hydrochloride wafers won't irritate the oral cavity.

After being individually weighed, the wafers were stored for 24 hours at room temperature in desiccators with active silica. Wafers were weighed one after the other until their weight remained consistent. It was discovered that the prepared wafers had a moisture level between 1.05 ± 0.14 and 1.35 ± 0.15 . Therefore, it can be concluded that, out of all the formulations, the meclizine hydrochloride formulation F7 had the lowest moisture content.

At 232 nm, a UV-visible spectrophotometer was used to assess the drug content. As shown in Table 3, the percentage drug content ranged from $95.65 \pm 0.23\%$ to $99.12 \pm 0.61\%$, demonstrating consistent drug distribution throughout the Meclizine hydrochloride wafers. Every preparation quickly absorbs moisture and breaks down when it comes into touch with water. According to Table 3, the disintegration time of the prepared Meclizine hydrochloride wafers ranged from 6 ± 1 to 15 ± 1 seconds. At 6 ± 1 seconds, formulation F7 had the quickest disintegration time. Formulations using only xanthan gum, gelatin, and gum acacia had the fastest disintegration time, at 15 ± 1 seconds. Meclizine hydrochloride wafer formulation F7 was used for the in vitro drug release investigations. According to the drug release statistics, the drug release at 60, 120, 180, 240, 300, and 360 seconds was 36.65%, 48.89%, 64.56%, 72.32%, 85.65%, and 98.15%, respectively. The ideal ratio of the wafer-forming polymers utilized, which have both gelation and rapid melt capabilities, may be attributed to this quicker drug release. For the identical formulations, the drug release was shown to be much quicker than the permeation because the drug release tests maintained a considerably bigger sink condition, which resulted in a much faster release of the drug into the medium (table 4).

Table 2: Results of evaluation of prepared wafers

Formulation code	General Appearance	Thickness* in μm	Weight* mg
F1	Translucent	80 ± 2	110 ± 5
F2	Translucent	84 ± 1	115 ± 3
F3	Translucent	86 ± 3	119 ± 4
F4	Translucent	78 ± 2	112 ± 2
F5	Translucent	80 ± 3	118 ± 4
F6	Translucent	82 ± 1	124 ± 3
F7	Translucent	75 ± 4	98 ± 6
F8	Translucent	78 ± 2	102 ± 2
F9	Translucent	81 ± 3	105 ± 4

*Average of three determinations (N=3)

Table 3: Result of surface pH determination, folding endurance, percentage of moisture content

Formulation code	Folding endurance* (Times)	Surface pH Determination	Percentage of Moisture Content*
F1	110±5	6.4±0.1	1.21±0.23
F2	125±4	6.5±0.2	1.12±0.14
F3	142±3	6.4±0.2	1.14±0.25
F4	133±4	6.7±0.3	1.32±0.14
F5	148±5	6.4±0.2	1.14±0.32
F6	165±8	6.5±0.1	1.16±0.14
F7	220±6	6.8±0.4	1.05±0.14
F8	185±5	6.9±0.2	1.22±0.22
F9	192±4	6.7±0.1	1.35±0.15

Table 4: Drug content analysis and disintegrating time

Formulation code	Drug content analysis (%)	Disintegrating time (Sec.)
F1	98.65±0.45	12±2
F2	95.65±0.23	15±1
F3	98.78±0.14	14±2
F4	97.96±0.56	8±2
F5	97.45±0.65	9±2
F6	98.85±0.74	9±2
F7	99.12±0.61	6±1
F8	98.78±0.41	10±2
F9	99.05±0.32	12±2

Table 5: Results of *In-Vitro* release study of optimized formulation F7

S. No.	Time (Sec.)	Percentage cumulative drug release
1.	60	36.65
2.	120	48.89
3.	180	64.56
4.	240	72.32
5.	300	85.65
6.	360	98.15

Conclusion

An antiemetic medication with a 25% systemic oral bioavailability is meclizine hydrochloride. The primary goal of the experiments discussed was to create meclizine hydrochloride sublingual wafers that dissolve quickly and have improved oral bioavailability for the treatment of motion sickness. Meclizine

hydrochloride fast-releasing sublingual wafers were therefore successfully created for quick and efficient medication administration with enhanced bioavailability.

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