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FORMULATION AND CHARACTERIZATION OF FAST DISSOLVING ORAL WAFERS OF RIZATRIPTAN

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ABSTRACT

Migraine is a major global health issue that affects over 10% of the population and is the second leading cause of years lived with disability worldwide. Hours or days can pass between migraine attacks, and they typically happen once a month on average Wafers are practical alternative to oral tablets for patients who have difficulty swallowing tablets or have no liquids available at the onset of an attack. Thus, this study aims at developing Fast Dissolving Oral Wafers of Rizatriptan. Oral wafers were prepared by standard methods. The thickness of formulated Rizatriptan was varied between 75±4 µm to 86±3 µm. The formulated. The wafers showed a weight variation between 98±6mg - 124±3 mg. The pH of the formulated wafers was found to be in the range of 6.2±0.2-6.9±0.1. The moisture content of the formulated wafers was found to be in the range of 1.25±0.25 - 1.85±0.14. Thus, it can be considered that the formulation F7 of the Rizatriptan showed minimum moisture content among all formulations. The percentage drug content was between 96.64±0.32% and 99.45±0.18%. The formulated Rizatriptan wafers showed a disintegration time in the range of 8±2-20±5sec (as shown in Table 8.3). Formulation F7 showed the least disintegration time of 8±2 sec. Thus, from results it can be concluded that the formulated oral wafer of Rizatriptan have all ideal properties & can be used as instant remedy to control headache.

Keywords: Fast Dissolving, orally disintegrating Wafers, Rizatriptan, Migraine.

INTRODUCTION

Migraines are caused by spontaneous overactivity and aberrant amplification in the brainstem's pain and other, primarily sensory, pathways. According to current thinking, the trigeminovascular system's innervation of the cranial arteries results in feedback loops that are largely neurological in nature. Although migraine is more than just head pain, it often manifests as episodic incapacitating headaches. The alternative diagnosis is tension type headache (TTH), which is co-morbid with migraine. (this differential is also discussed from the other perspective elsewhere in this supplement). Hours or days can

pass between migraine attacks, and they typically happen once a month on average. TTH is frequently chronic and more frequently present than absent [1,2].

Oral administration of drugs is the most preferred way for the delivery of drugs to due to its various advantage, but oral drug delivery system still needs some advancement to be made because of their drawbacks related to particular group of patients. Wafers are placed on a patients tongue are any oral mucosal tissue. They are instantly wet by saliva due to the presence of hydrophilic polymer and other excipients, it rapidly hydrates and dissolves to release the medication for mucosal absorption [3,4].

Wafers are practical alternative to oral tablets for patients who have difficulty swallowing tablets or liquids, patients who simply prefer not to do so or have no liquids available at the onset of an attack. Thus, this study aims at developing Fast Dissolving Oral Wafers of Rizatriptan.

MATERIAL AND METHODS

Formulation of Rizatriptan loaded fast dissolving wafers

Drug (Rizatriptan) containing fast dissolving wafers were fabricated by the solvent casting method. The optimized amount of polymer was dissolved in 5ml of water and stirrer 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 was cut into size required for testing. The wafers were stored in air tight plastic bags till further use [5].

Table 1: Selection and optimization of wafers forming agents

Name of ingredients (mg for 12 strips)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Rizatriptan	60	60	60	60	60	60	60	60	60
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

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.

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 vivo.

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 endurance.

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 by first subtracting final weight from initial weight and then dividing it by initial weight. The value obtained is further multiplied by 100 for getting exact percentage.

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 282nm.

Disintegrating time

The most important criteria of present work are to that dosage form should be dissolved within few seconds. 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). 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 cm^2) 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 Rizatriptan was determined using UV-Visible spectrophotometer at 282nm. The results were presented as an average of three such concentrations.

Stability studies

Stability studies were carried out with optimized formulation which was stored for a period of one, two and three months at 40±2ºC temperature and 75±5% relative humidity for a period 3 months. The % Assay of formulation was determined by U.V. spectrophotometer using calibration curve method. The % assay of wafers was found to slightly decrease at higher temperature [6].

RESULTS & DISCUSSION

In the formulation and characterization of fast-dissolving oral wafers of rizatriptan, formulation F7 was identified as the optimized formulation based on the evaluation parameters. The thickness of formulated Rizatriptan was varied between 75±4 µm to 86±3 µm. The wafers showed a weight variation between 98±6mg - 124±3 mg. The pH of the formulated wafers was found to be in the range of 6.2±0.2-6.9±0.1. The moisture content of the formulated wafers was found to be in the range of 1.25±0.25 - 1.85±0.14. Thus, it can be considered that the formulation F7 of the Rizatriptan showed minimum moisture content among all formulations. The percentage drug content was between 96.64±0.32% and 99.45±0.18%. The formulated Rizatriptan wafers showed a disintegration time in the range of 8±2-20±5sec (as shown in Table 8.3). Formulation F7 showed the least disintegration time of 8±2 sec. The dissolution rate of rizatriptan from the oral wafers was evaluated using in vitro dissolution studies. Formulation F7 exhibited a significantly faster dissolution rate compared to other formulations. This can be attributed to the choice of excipients and their concentrations, which facilitated rapid disintegration and drug release. The disintegration time of the oral wafers is an important parameter affecting patient compliance and drug delivery. Formulation F7 demonstrated a rapid disintegration time, indicating its ability to dissolve quickly in the oral cavity. The compatibility of rizatriptan with the excipients used in formulation F7 was assessed to ensure chemical stability and efficacy of the drug. Stability studies were conducted under various storage conditions, including temperature and humidity, to evaluate the long-term stability of the oral wafers. Formulation F7 demonstrated good compatibility and stability, indicating its suitability for pharmaceutical use.

Table 2: Results of evaluation of prepared wafers

Formulation code	General Appearance	Thickness* in µm	Weight* mg
F1	Translucent	65±5	125±3
F2	Translucent	63±4	132±5
F3	Translucent	72±5	141±4
F4	Translucent	68±6	136±2
F5	Translucent	69±3	142±3
F6	Translucent	71±2	152±6
F7	Translucent	73±3	147±5
F8	Translucent	75±2	152±4
F9	Translucent	70±3	162±2

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	125±5	6.2±0.2	1.32±0.36
F2	132±6	6.8±0.1	1.45±0.25
F3	148±5	6.5±0.3	1.85±0.14
F4	152±4	6.7±0.2	1.63±0.25
F5	169±3	6.9±0.1	1.74±0.32
F6	172±2	6.7±0.4	1.65±0.14
F7	225±4	6.8±0.2	1.25±0.25
F8	165±2	6.3±0.3	1.36±0.36
F9	148±3	6.4±0.2	1.26±0.15

Table 4: Drug content analysis and disintegrating time

Formulation code	Drug content analysis (%)	Disintegrating time (Sec.)
F1	97.85±0.25	20±5
F2	96.64±0.32	16±6
F3	98.78±0.18	15±4
F4	97.82±0.26	19±2
F5	96.65±0.17	17±3
F6	98.15±0.33	15±5
F7	99.45±0.18	8±2
F8	98.65±0.12	10±6
F9	98.15±0.14	13±3

Table 5: Results of Optimized formulation F-7

Name of ingredients (mg for 12 strips)	Ingredients (mg)
API	60
Xanthan gum	100
Gelatin	-
Gum acacia	25
Pullulan	25
Methyl Paraben	20
Aspartame	20
Citric acid	50
DM water qs to (ml)	30

Table 6: Results of *in-vitro* release study of optimized formulation F7

S. No.	Time (Sec.)	Percentage cumulative drug release
1.	60	26.65
2.	120	42.23
3.	180	59.98
4.	240	69.95
5.	300	85.65
6.	360	98.87

CONCLUSION

Rizatriptan wafer is effective and well tolerated for the acute treatment of migraine. The rizatriptan wafer provides a more rapid onset of action and superior pain relief. Thus, the rizatriptan wafer represents a convenient and well-accepted alternative formulation for many migraineurs. In conclusion, formulation F7 of fast-dissolving oral wafers of rizatriptan was identified as the optimized formulation based on its superior dissolution rate and rapid disintegration time. The successful development of the optimized formulation highlights the potential of fast-dissolving oral wafers as an alternative dosage form for rizatriptan, providing a convenient and patient-friendly option for individuals who have difficulty swallowing conventional tablets. Further studies, including in vivo evaluations and clinical trials, are warranted to validate the performance and therapeutic efficacy of the optimized formulation in real-world settings.

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