Available online on 25.04.2019 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Research Article

Formulation and Evaluation of fast dissolving films of Granisetron Hydrochloride

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ABSTRACT

Granisetron hydrochloride is a novel serotonin 5-HT3 receptor antagonist used as an antiemetic to treat nausea and vomiting following chemotherapy. It is well absorbed from the gastrointestinal tract, but its oral bioavailability is low (60%) due to extensive first-pass metabolism which makes it an ideal candidate for rapid release drug delivery system. In the present work we have prepared and evaluated fast dissolving oral films of Granisetron hydrochloride by solvent casting method using different concentrations polymers HPMC, PVA and their combinations. Mannitol was used as a disintegrating agent and Propylene glycol as a plasticizer. The prepared oral films were evaluated for Physical appearance, texture, Weight uniformity, thickness uniformity, percentage moisture absorption, disintegration time, drug content uniformity, folding endurance, tensile strength, in-vitro drug release, and stability studies. In-vitro release rate of Granisetron hydrochloride was studied in phosphate buffer pH 6.8. F1, F5 and F7 showed maximum release rate about 94.95%, 95.98% and 96.29% in 180 seconds respectively, whereas F3 showed 60.98%. Short term stability studies of selected films indicated that there is no significant change with respect to physical appearance, disintegration time, drug content and in-vitro drug release.

Keywords: oral films, granisetron hydrochloride, HPMC, PVA, fast dissolving.

Article Info: Received 25 Feb 2019; Review Completed 30 March 2019; Accepted 21 April 2019; Available online 25 April 2019

Cite this article as:

Rathore R, Gupta AK, Parashar AK, Formulation and Evaluation of fast dissolving films of Granisetron Hydrochloride, Journal of Drug Delivery and Therapeutics. 2019; 9(2-A):36-38

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INTRODUCTION

Drug delivery may be defined as the method or process of administering an active pharmaceutical ingredients and delivering to the desired site inside the body to elicit its therapeutic effect. Oral route is one of the most popular, preferable and convenient route for drug administration. It possesses certain advantages like ease of administration, self medication, patient compliance and flexibility with a wide range of dosage form [1]. However researchers are seeking to incorporate various technologies in oral formulations to make them more efficacious [2].

Recently, fast-dissolving drug delivery systems have started gaining popularity and acceptance as new drug delivery systems, which aim to enhance safety and efficacy of a drug molecule by formulating it into a convenient dosage form for administration and to achieve better patient compliance. It improves the efficacy of APIs by dissolving within minute in oral cavity after the contact with saliva without chewing and no need of water for administration. It gives quick absorption and instant bioavailability of drugs due to high blood flow and permeability of oral mucosa is many times greater than that of skin [3-4]. Along with the local action these oral films are useful in patients such as pediatric, geriatrics, bedridden, emetic patients, diarrhea, sudden episode of allergic attacks, or coughing for those who have an active life style [5].

Granisetron hydrochloride is a novel serotonin 5-HT_3 receptor antagonist used as an antiemetic to treat nausea and vomiting following chemotherapy [6]. It is well absorbed from the gastrointestinal tract, but its oral bioavailability is low (60%) due to extensive first-pass metabolism which makes it an ideal candidate for rapid release drug delivery system [7]. Hence, an attempt was made to prepare and evaluate fast dissolving oral films containing Granisetron hydrochloride as a model drug by solvent casting method using natural and synthetic polymers.

MATERIALS AND METHODS

Materials

Granisetron HCl was obtained as gift sample from Salvavidas Pharmaceutical Pvt. Ltd, Surat. Polvinyl alcohol, HPMC K15 and Propylene glycol were purchased from SD–Fine chemicals, Mumbai. All other chemicals and reagents were of analytical reagent grade.

Methods

Formulation of fast-dissolving films

In the present study, fast-dissolving films of Granisetron HCl were prepared by a solvent casting technique. Flat, square-shaped, aluminum foil-coated glass molds having a surface area of 25 cm were fabricated for casting the films. The weighed quantities of polymers were kept for swelling overnight in distilled water and dissolved. The drug and aspartame were dissolved in distilled water and added to the above mentioned polymer solution along with propylene glycol as a plasticizer, mixed thoroughly to form a homogenous mixture. The volume was made up to 10 ml with distilled water. Entrapped air bubbles were removed by applying vacuum.

The casting solution (10 ml) was poured into glass molds and dried at 40°C in a vacuum oven for 24 h for solvent evaporation. The films were removed by peeling and cut into a square dimension of 2.5 cm × 2.5 cm (6.25 cm^2). It was dried for 24 hours at room temperature. The film was removed from the Petri dish very carefully and observed for any imperfections. Film that was clear and bubble free was selected for further studies. Composition of various formulations is shown in table-1, where fast-dissolving films were prepared with different polymers and ratios by maintaining the concentration of the plasticizer and sweetener constant.

Table-1 Formulation of Fast dissolving films

Code	HPMC (mg)	PVP K-30 (mg)	Granisetron HCl (mg)	Propylene Glycol (ml)	Aspartame (mg)	Distilled Water (ml)
F1	100	-	20	0.1	40	10
F2	-	100	20	0.1	40	10
F3	50	50	20	0.1	40	10

Thickness of the film

The thickness of the patch was measured using digital Vernier Calipers with a least count of 0.01 mm at different spots of the film. The thickness was measured at three different spots of the patch and average was taken and SD was calculated (table-2).

Drug content uniformity

Prepared fast-dissolving film was dissolved in 100 ml of distilled water and filtered. After suitable dilutions with distilled water, the concentration of the drug was determined by measuring the absorbance at 230 nm against the distilled water as blank [11].

Disintegration time

Test was performed using disintegration test apparatus. 6.25 cm^2 film was 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 film, when no traces of film remain above the gauze was noted (table-2).

Folding endurance

The folding endurance is expressed as the number of folds (number of times the film is folded at the same place) required to break the specimen or to develop visible cracks. This also gives an indication of brittleness of the film. A strip of 5 cm × 5 cm was subjected to folding endurance by folding the film at the same place repeatedly several times until a visible crack was observed, and the values were reported [11].

Table-2 Physicochemical properties of prepared patches

Code	Thickness (mm)	Flexibility	Drug Content (%)	Disintegration time (s)
F1	0.144±0.018	Flexible	95.45±1.09	10
F2	0.168±0.016	Flexible	98.59±1.04	8
F3	0.165±0.025	Flexible	94.25±1.15	11

In vitro dissolution studies

The simulated salivary fluid was taken as the dissolution medium to determine the drug release.

The dissolution profile of quick release films of Granisetron HCl was carried out in a beaker containing 30 ml of the simulated salivary fluid (pH 6.8) as a dissolution medium, maintained at 37 ± 0.5°C. The medium was stirred at 100 rpm. Aliquots (5ml) of the dissolution medium were withdrawn at 15, 30, 60, 90and 120 s time intervals and samples were assayed spectrophotometerically at 230 nm. The percentage of the drug dissolved at various time intervals was calculated and plotted against time (Figure 1).

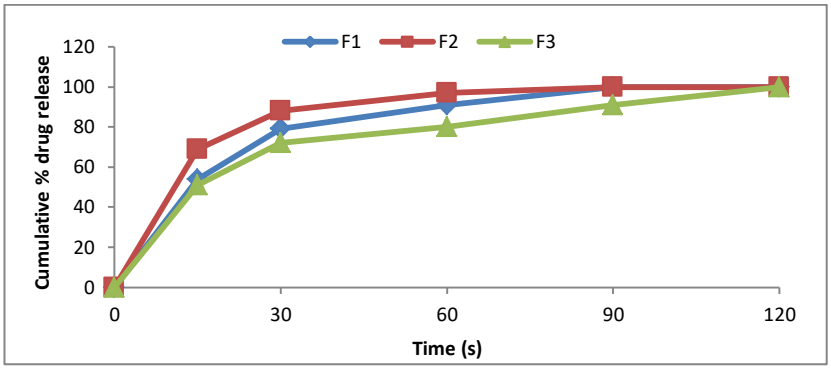

Figure 1 Comparison of in vitro percentage drug release of all formulations

Stability studies

The stability study of the formulated fast-dissolving films was carried out under different environmental conditions of 2-8°C (45% RH), 25-30°C (60% RH), and 45-50°C (75% RH) for a period of 45 days. The films were characterized for the drug content and other parameters during the stability study period [11].

RESULTS AND DISCUSSION

Fast-dissolving films of Granisetron HCl were prepared by the solvent casting method on glass molds, using HPMC K15 and PVA as polymers, Propylene glycol as plasticizer and aspartame as sweetener and Distilled water as a solvent. The effect of the nature of polymers was studied by preparing various formulations of fast-dissolving films. In all these formulations, a constant amount of drug (20 mg) was maintained. The characterization of prepared fast dissolving films were done for various parameters like thickness of the films, Drug content uniformity, Folding endurance of the films, Disintegration time, In-vitro dissolution and stability studies. It was observed that there was no significant difference in the thickness among the films, which indicated that the films were uniform. Drug content of F1, F2 and F3 formulations was found to be 95.45±1.09, 98.59±1.04 and 94.25±1.15% (table-2).

From the *in vitro* drug release, it was observed that in formulations containing a single polymer, the drug release was found to be faster and films formed of PVA polymer resulted in a fastest release of drug. The drug release was found to be in the following order: F2 > F1 > F3. Stability study for the prepared film was carried out for 45 days at different temperature and humidity conditions. Fast-dissolving films were found to be physically and chemically stable as they showed no significant change in terms of physical characteristics and drug content at a lower temperature and room temperature. However, when stored at 45-50°C for 45 days, films became brittle.

CONCLUSIONS

The aim of the present study was design formulation and evaluation of fast dissolving films of Granisetron HCl using various polymers. Fast-dissolving films were developed by solvent casting method and evaluated for different physicochemical properties. All formulations showed good results for thickness, drug content, disintegration time and folding endurance. In vitro release profile of the prepared films showed the effect of type of different polymers. Based on physicochemical parameters and in vitro release profile formulation F2 can be considered as the best formulation. The conclusion from all encouraging results reaches that fast-dissolving films of Granisetron HCl may be more suitable for clinical use in the treatment of severe vomiting conditions during chemotherapy, where a quicker onset of action for a dosage form is desirable.

ACKNOWLEDGMENT

The authors would like to thank Chameli Devi institute of Pharmacy, Indore for the financial support and providing all facilities to perform the above research work.

CONFLICTS OF INTEREST

There are no conflicts of interest.

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