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DEVELOPMENT OF MOUTH DISSOLVING TABLETS USING DIFFERENT TECHNIQUES

Dr. Bharat V. Jain[1]*
[1]*Professor, Smt. Sharadchandrika Suresh Patil College of Pharmacy, Chopda-425107, M.S

***Corresponding Authors:** - Dr. Bharat V. Jain,
*Professor, Smt. Sharadchandrika Suresh Patil College of Pharmacy, Chopda-425107, M.S
E-mail:- bharatjain2006@gmail.com

Abstract:
Mouth dissolving tablets constitute an innovative dosage form that overcomes the problems of swallowing and provides a quick onset of action. In view of enhancing bioavailability an attempt has been made to study three different methods direct compression, effvercent and sublimation in formulation of mouth dissolving tablets of Granisteron HCl. Total Six formulations using various super disintegrants, subliming agents and different ratio of sodium bicarbonate: citric acid were prepared. All prepared formulations were evaluated for physico- chemical parameters. The formulations exhibited good disintegration properties with total disintegration time in the range of 20 to 35 s. Comparative evaluation of three methods showed direct compression method is a better than effervescent method than sublimation method as its formulations rapidly disintegrate in oral cavity. *In vitro* cumulative percentage drug release for formulations prepared by directcompression with explotab super disintegrants shows 98.79%, effervescent method with 12:6 ratios of sodium bicarbonate: citric acid shows 95.05% while sublimation method using camphor shows 92.13% releases in 12 min. Kinetic studies indicated that all the formulations followed first order release with diffusion mechanism.

Keywords: Mouth dissolving tablets, Granisteron HCl, effervescentmethod, diffusion mechanism

INTRODUCTION:

The oral route of administration is considered as the most widely accepted route. But the most evident drawback of the commonly used oral dosage forms like tablets and capsules is difficulty in swallowing, leading to patient's incompliance particularly in case of pediatric and geriatric patients[1]. Recently fast dissolving drug delivery systems have started gaining popularity and acceptance as one such example with increased consumer choice, for the reason of rapid disintegration or dissolution, self-administration even without water or chewing.

Granisetron is an anti emetic, generally prescribed in cancer chemotherapy to control nausea and vomiting. It is selective 5 HT-3 antagonists and binds to receptor and stops vomiting.

Cancer chemotherapy causes lot of adverse effects, of which nausea and vomiting is prime one. This can be clearly seen with model anticancer drug cisplatin, which is first line drug in many types of cancers. Hence anti emetic drugs like ondansetron, granisetron are administered one hour prior to the administration of anticancer drug [1]. But this becomes a major patient non compliance in the case of children, elderly and bed ridden patients for whom swallowing tablets causes inconvenience [2].

MATERIAL AND METHODS:

Materials:

Granisetron was obtained as a gift sample fromHealth biotech India pvt ltd, Chandigarh. Excipients for tablet were gifted by Signet chemical corporation, Mumbai. All solvents used were of analytical grade and were purchased from S.D. Fine chemicals, ltd, Mumbai.

Preparation of Mouth Dissolving Tablets:

In the present study, an attempt has been made to develop mouth-dissolving tablets of Granisteron Hydrochloride by direct compression, effervescent approach and sublimation methods using suitable super disintegrants and subliming agents. Granisteron Hydrochloride tablets each containing 1.0 mg drug was prepared as per the formulae given in Table 1. The formulations F1 and F2 were prepared by the direct compression (DC) method, formulations F3 and F4 were prepared by sublimation method (SBM) and formulations F5 and F6 were prepared by effervescent method (EFT).

In direct compression method all the ingredients were passed through # 60 sieve. Granisteron Hydrochloride, mannitol, microcrystalline cellulose and sodium saccharin were triturated in a glass mortar. Super disintegrants were incorporated in the powder mixture and finally magnesium stearate and talc were added as lubricant. The powder mix was weighedindividually and compressed with 10 mm flat face surface punches using hydraulic press.

In sublimation method accurately weighed quantities of Granisteron Hydrochloride, volatile component, mannitol and sodium saccharine were mixed and passed through # 45 sieves. Finally, magnesium stearate and talc were added and then subjected to compression. After compression tablets were heated in hot air oven at 60^0 Cuntil constant weight was obtained to ensure thecomplete removal of volatile component.

In the effervescent method, sodium bicarbonate and anhydrous citric acid were pre-heated at a temperature of 80º to remove absorbed/residual moisture (10:8 and 12:6 concentrations), mannitol, microcrystalline cellulose and sodium saccharin accurately weighed and sifted through # 44 mesh separately, and was thoroughly mixed in a mortar to get a uniform powder and then add magnesium stearate and talc. The ingredients after sifting through sieve No. 44 were thoroughly mixed and directly compressed into tablets on a 10-station rotary machine using 10 mm round flat punches.

TABLE 1: COMPOSITION OF MOUTH DISSOLVING TABLET OF GRANISTERON HCl

INGREDIENTS	F1 (mg) DC	F2 (mg) DC	F3 (mg) SM	F4 (mg) SM	F5 (mg) EM 10:8	F6 (mg) EM 12:6
Granisteron HCl	01	01	01	01	01	01
Avicel PH-102	40	40	--	--	20	20
Mannitol	110	110	128	128	132	132
Sodium saccharine	5	5	5	5	5	5
Kolliodon CL	38	--	--	--	--	--
Explotab	--	38	--	--	--	--
Camphor	--	--	60	--	--	--
Ammonium Bicarbonate	--	--	--	60	--	--
Sodium Bicarbonate	--	--	--	--	20	24
Citric Acid	--	--	--	--	16	12
Magnesium Stearate	3	3	3	3	3	3
Talc	3	3	3	3	3	3

Formulation F1 and F2 uses direct compression method (DC), formulation F3 and F4 (SM) uses sublimationmethod and formulation F5 and F6 uses effervescent method (EM).

Evaluation of Tablet characteristics:

The tablets were evaluated for hardness, friability, weight variation, wetting time and disintegration time. Percent drug content were analyzed using UV Spectrophotometer 1601 (Shimadzu) at 210 nm.

Dissolution studies of all tablets were performed using automated dissolution tester (Type II, Lab India).Tablets were added to the 900 ml of Phosphate buffer pH6.8 at 37˚C±0.˚C,whichwas stirred with a rotating paddle at 75 rpm.

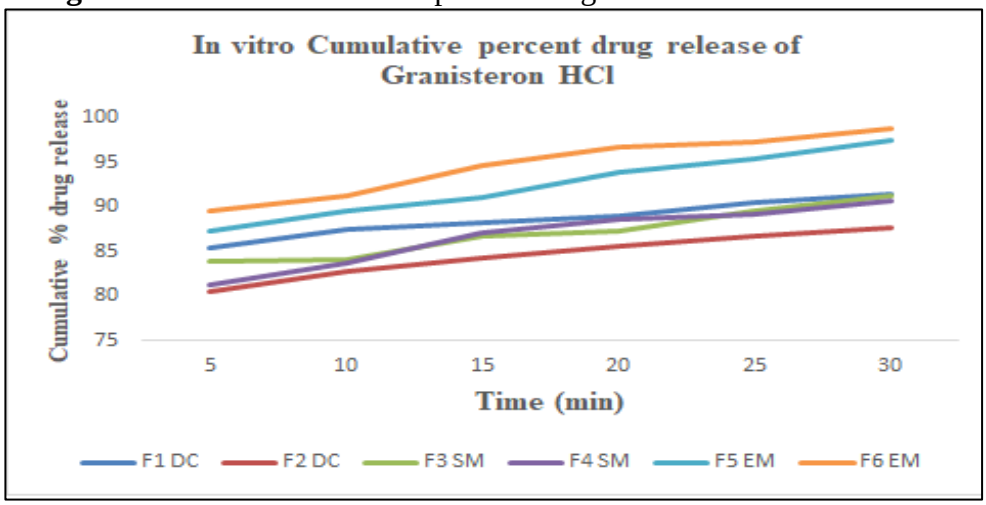
TABLE 2: EVALUATION OF MOUTH DISSOLVING TABLETS

Parameters	F1 DC	F2 DC	F3 SM	F4 SM	F5 EM 10:8	F6 EM 12:6
Diameter (mm)	10	10	10	10	10	10
Hardness (kg/ sq.cm)	3.7±0.30	3.5±0.27	3.3±0.11	3.2±0.11	3.9±0.41	4.0±0.22
Friability (%)	0.7±0.10	0.4±0.16	0.2±0.05	0.2±0.0.06	0.7±0.11	0.2±0.09
Wetting time (sec)	25±1.09	27±0.65	30±0.1	36±0.15	24±0.2	18±0.14
Disintegration time (sec)	37	41	32	36	27	25
% Drug content	99.20	98.58	99.35	99.13	99.87	99.97
%Drug released in 5min	85.37	80.48	83.87	81.29	87.25	89.55
%Drug released in 30min	91.46	87.64	91.20	90.58	97.54	98.80

TABLE 3: IN VITRO DISSOLUTION PARAMETERS IN pH 6.8 PHOSPHATE BUFFER

Time (Min)	Percent drug Released					
	F1 DC	F2 DC	F3 SM	F4 SM	F5 EM 10:8	F6 EM 12:6
5	85.37	80.48	83.87	81.29	87.25	89.55
10	87.50	82.70	84.15	83.74	89.45	91.25
15	88.23	84.35	86.65	87.12	91.05	94.68
20	89.06	85.58	87.25	88.63	93.85	96.77
25	90.45	86.76	89.46	89.10	95.47	97.20
30	91.46	87.64	91.20	90.58	97.54	98.80

Figure 1: In vitro Cumulative percent drug release of Granisteron HCl



RESULT:

All the tablets showed smooth texture. Weight variation and friability was within limits. Hardness of all tablets was between 3-4 kg/cm ^{2}. Due to addition of sodium saccharine, all tablets showed non bittertaste. *In vitro* disintegration time of all the tablets was within 60 seconds. Drug content of all theformulations was within limits and drug release was more than 80% within 30 min. The release profile of granisetron from different formulations in phosphate buffer (pH 6.8) are shown in Fig 1

DISCUSSION:

From the study, it can be concluded that effervescent method showed better disintegration and drug release as compared to direct compression and sublimation method. The main aim of formulating

mouth dissolve tablets was to achieve instantaneous dispersion without the aid of water. By seeing in vitro dispersion time and disintegration, it can be clearly stated that, the objective has been achieved. Above all, most of the formulation showed 80% drug release within 30 min, hence decreasing the lag time for absorption. By seeing this, it can be clearly seen that there is more chance for pre gastric absorption, thereby reducing first pass metabolism. Therefore overall oral bioavailability can be increased. As the target patients are children and elderly, the addition of sweeteners increased the appeal and patient compliance.

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