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Research Article

FORMULATION AND EVALUATION OF BUCCOADHESIVE TABLET OF GRANISETRON HYDROCHLORIDE USING NATURAL POLYMER

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Abstract

The objective of this study was to formulate and evaluate buccoadhesive tablet of Granisetron hydrochloride using natural polymers like chitosan, guar gum and xanthan gum by direct compression technique. Granisetron hydrochloride is an antiemetic drug used to redused emesis. In the present study, an attempt was made to prepare buccoadhesive tablet of granisetron Hydrochloride (anti-emetic drug), in order to overcome bioavailability problems, to redused dose depandant side effects and frequency of administrations. Buccoadhesive tablets containing the drug were prepared by direct compression method using combination of polymers (natural polymers used such as Chitosan, guar gum, xantun gum). Estimation of granisetron hydrochloride was carried out spectrophotomatrically at 305 nm. The buccoadhesive tablet were evaluated for various physical and biological parameters, buccoadhesive strength, drug content uniformity, in vitro drug release, drug-excipient interactions (FTIR) .The IR spectroscopic studies indicated that there are no drug-excipient interactions. The formulations F1 (containing Chitosan as polymer) was found to be promising, which showed 93.21% drug realesed in 8 h. These formulations have displayed good bioadhesion strength (4.90gm to 3.90gm respectively).

Keywords: Granisetron hydrochloride, buccal tablet, chitosan, guar gum, xanthun gum.

Introduction

Drug delivery by the transmucosal routes has gained significant attention over the last decades particularly for the delivery of therapeutic proteins and peptides because the oral bioavailability of these drugs is usually negligible due to their poor absorption, enzymatic degradation and extensive first pass metabolism and there is a need for alternatives to the conventional parental route (injections) for administrating them. The non-parental transmucosal routes commonly used include buccal, sublingual, rectal, nasal and vagina. While each of these routes of drug

administration has its associated advantages and disadvantages, buccal routes have its unique benefits. Lower enzymatic activity of saliva, easy removal of formulation, better patient acceptance and compliance or some of the prominent features of buccal route.

Buccoadhesive drug delivery system have gained considerable interest with regard to systemic drug delivery especially proteins and peptides which undergo extensive hepatic first pass metabolism thus results in premature drug degradation within the gut. Examples of some proteins and peptides delivered by buccal route include thyrotropine releasing hormone, calcitonin, buserdin, and oxytocin[1].

The buccal region of the oral cavity is an attractive target for administration of the drug of choice. Buccal delivery involves the administration of the desired drug through the buccal mucosal membrane lining of the oral cavity. Mucosal lining of the oral cavity is richly vascularized and more accessible for the administration and removal of dosage form. Additionally buccal drug delivery has a high patient acceptability compared to other non-oral routes of drug administration and also harsh environmental factors that exist in oral delivery of a drug are circumvented by buccal delivery[2].

The buccal mucosa has been investigated for local and systemic delivery of therapeutic peptides and other drugs that are subjected to first-pass metabolism or are unstable within the rest of the gastrointestinal tract. Buccal delivery offers a safer mode of drug utilization, since drug absorption can be promptly terminated in cases of toxicity by removing the dosage form from the buccal cavity. A suitable buccal drug delivery system should possess good bioadhesive properties, so that it can be retained in the oral cavity for the desired duration. In addition, it should release the drug in a unidirectional way toward the mucosa in a controlled and predictable manner, to elicit the required therapeutic response.[3]

Materials

Granisetron Hydrochloride was obtained from Wockhard Ankleshwar gujarat as a gift sample. All other excipients were obtained from S.D. Fine Chemicals Mumbai.

Method

Characterization of Granisetron Hydrochloride

1. FT- IR Spectral Analysis

IR sperctral analysis of pure Granisetron hydrochloride, and granisetron complexes with Chitosan, guar gum, xanthun gum was carried out by KBr disc method.

2. Drug content uniformity

Five tablets were powdered in a glass mortar and the powder equivalent to 1 mg of drug is placed in a stoppered 100 ml conical flask. The drug is extracted with 25 ml water with vigorous shaking on a mechanical gyratory shaker (100 rpm) for 2 h and filtered into 50 ml volumetric flask through Whatmann filter paper (Mean pore diameter 1.5 μm) and more solvent is passed through the filter to produce 50 ml. Aliquots of the solution are filtered through 0.22 μm membrane filter and analyzed for drug content by measuring the absorbance at 305 nm against solvent blank. The drug content was calculated using the standard calibration curve. The mean percent drug content was determined as an average of three determinations.

3. Swelling index

$$\textbf{Swelling index} = 100\ (w_2 - w_1) / w_1.$$

4. Mucoadhesion strength

Mucoadhesion strength of the tablet was measured on a modified physical balance employing the method by goat cheek pouch from slotter house as model mucosal membrane. A physical balance was taken and the left pan was removed so as to hang a thick thread of suitable length. To this thread a glass stopper with uniform surface was tied. A clean glass mortar was placed below hanging glass stopper. In this mortar a clean 500 ml glass beaker was placed in which one more 50 ml glass beaker in inverted position was placed and 50 gm weight was added to prevent floating. The temperature was maintained by adding hot water in outer mortar. The balance was so adjusted that right hand-side was exactly 5 gm heavier than the left. The goat cheek pouch, excised and washed was tied tightly with mucosal side upward using thread over the base of inverted 50 ml glass beaker. This beaker suitably weighted was lowered into 500 ml beaker that the buffer reaches the surface of mucosal membrane and keeps it moist. This was then kept below left hand side of balance. The oral buccoadhesive tablet was then stuck to glass stopper through its backing membrane using an adhesive (Feviquick). The 5gm on right hand side is removed; this causes application of 5 gm of pressure on oral buccoadhesive tablet overlying moist mucosa. The balance was kept in this position for 3 minutes and then slowly weights were increased on the right pan, till tablet separates from mucosal membrane. The total weight on right pan minus 5 gm gives the force required to separate tablet from mucosa. This gives bioadhesive strength in grams.


Figure No 1: Muccoadhesive strength

Preparation of tablets containing Granisetron hydrochloride by direct compression method

All the ingredients including drug, polymers and excipients were weighed accurately according to the batch formula. The drug is thoroughly mixed with mannitol on a butter paper with the help of a stainless steel spatula. Then all the ingredients except lubricants were mixed in the order of ascending weights and blended for 10 min in an inflated polyethylene pouch. After uniform mixing of ingredients, lubricant was added and again mixed for 2 min. Then tablets were prepared using drug and excepient mixture by direct compression. The formula is showed in table No.1.

EVALUATION OF GRANISETRON HYDROCHLORIDE BUCCOADHESIVE TABLETS

All the prepared tablets were evaluated for weight variation, thickness, friability, hardness, assay, muccoadhesive strength, swelling index, in vitro dissolution studies, surface pH and IR spectroscopy. The result of evaluation parameters is given in Table No.2 and 3.

Table No-1: Composition of Granisetron Hydrochloride buccoadhesive tablet.

Ingredient	Formulation code								
Mg/tablet	F1	F2	F3	F4	F5	F6	F7	F8	F9
Granisetron HCL	1	1	1	1	1	1	1	1	1
Chitosan	46	42	44	--	--	--	--	--	---
Xanthun gum	--	--	--	46	50	42	--	--	--
Guar gum	--	--	--	--	--	---	46	44	46
Sodium alginate	6	4	2	6	-	2	-	2	6
PVP K-30	5	5	5	5	5	5	5	5	5

Mannitol	**36**	**42**	**42**	**36**	**38**	**40**	**42**	**42**	**36**
PEG 4000	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**
Aspartame	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**
Magnesium stearate	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**
Talc	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**

(All quantities in mg)

Table No-2: Evaluation of buccoadhesive tablet of Granisetron hydrochloride.

Sr. No.	Batch No.	Thickness (mm)	Weight variation(mg)	Friability (%)	Hardness (kg/cm2)
1	**F1**	**2.30**	**100 ± 5%**	**0.82**	**3.6**
2	**F2**	**2.31**	**99 ± 5%**	**0.63**	**4.4**
3	**F3**	**2.42**	**102 ± 5%**	**0.66**	**4.5**
4	**F4**	**2.37**	**105 ± 5%**	**0.65**	**4.7**
5	**F5**	**2.36**	**98± 5%**	**0.75**	**3.4**
6	**F6**	**2.41**	**97± 5%**	**0.79**	**4.4**
7	**F7**	**2.44**	**96± 5%**	**0.70**	**4.6**
8	**F8**	**2.40**	**101± 5%**	**0.66**	**4.2**
9	**F9**	**2.32**	**103± 5%**	**0.66**	**3.8**

Complies as per USP specification.

Table No. 3

Sr. No.	Batch No.	Surface pH	Swelling index (after 8 hr)	Drug Content (%)	Muccoadhesive Strength (gm)
1	F1	6.78	21.33	97.89	4.90
2	F2	6.53	21.62	95.43	4.60
3	F3	5.97	21.71	93.47	3.90
4	F4	6.68	25.49	91.01	4.83
5	F5	5.83	24.84	86.94	4.30
6	F6	5.63	30.65	92.21	4.22
7	F7	5.79	30.20	96.51	4.51
8	F8	5.88	27.92	97.26	4.69
9	F9	6.30	36.07	97.44	4.86

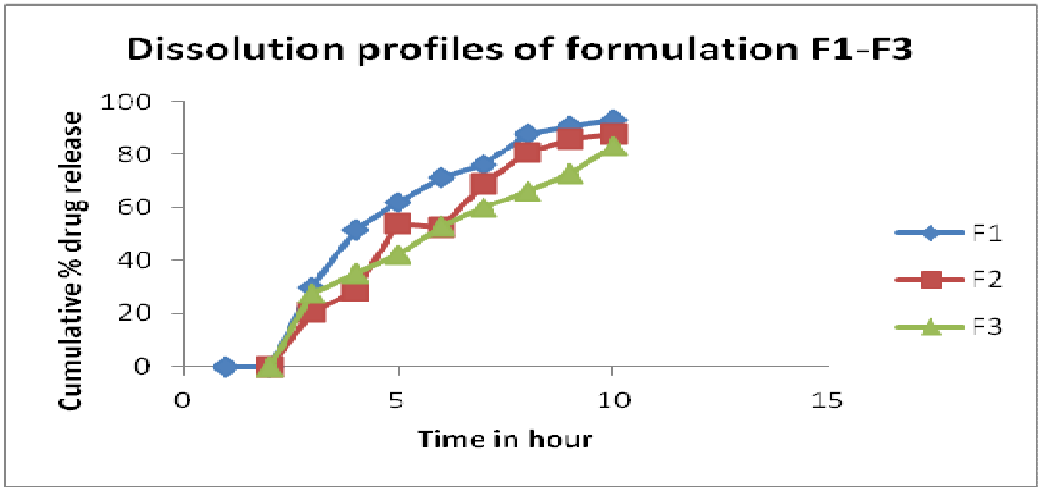
In-vitro Dissolution studies

This was carried out in USP XXIII tablet dissolution test apparatus, employing paddle stirrer at 50 rpm and 900 ml of pH 6.8 phosphate buffer as dissolution medium. The release study was performed at 37 ± 0.5o C. The backing layer of the oral buccoadhesive tablet is attached to glass disk with cyanoacrylate adhesive. The disk was placed at the bottom of the dissolution vessel. Samples of 5 ml are withdrawn at predetermined time intervals and replaced with fresh medium. The samples were filtered through 0.22 nm membrane filter disc (Millipore Corporation) and analyzed for Granisetron hydrochloride after appropriate dilution by measuring the absorbance at 305nm

Table No-4: In vitro Drug dissolution profile formulation F1-F9.

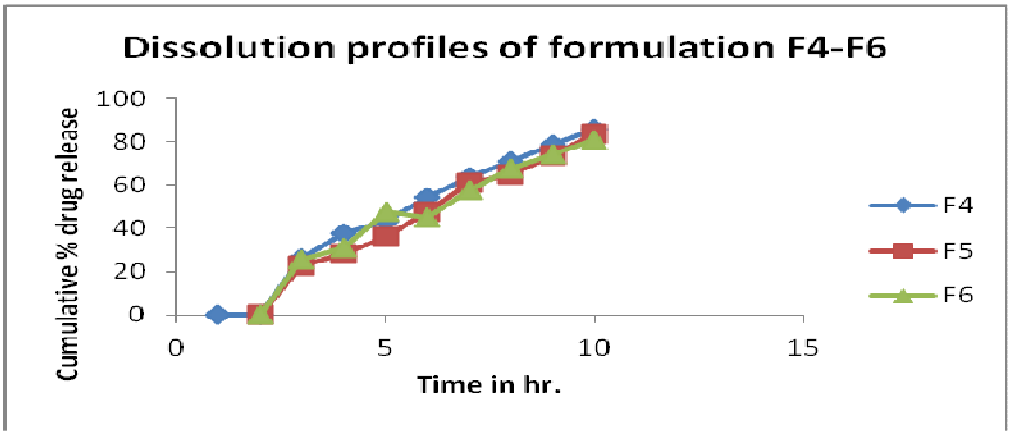
Sr. no	Time in hour	% of Drug Release								
		Formulation No.								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	0	0	0	0	0	0	0	0	0	0
2	1	30.20	20.75	27.41	25.90	22.90	25.69	28.05	20.53	22.90
3	2	51.85	28.60	35.08	37.86	28.61	31.20	40.24	27.95	30.76
4	3	61.85	54.20	42.21	43.30	35.94	47.99	48.25	37.87	42.18
5	4	71.35	52.41	52.34	54.28	48.01	44.86	59.89	50.82	50.62
6	5	76.35	68.94	59.92	63.58	61.18	57.51	67.69	59.91	61.84
7	6	87.76	81.06	66.19	71.15	64.91	67.46	78.26	65.97	65.98
8	7	90.83	85.85	72.67	78.71	73.95	74.18	83.47	71.59	72.02
9	8	93.21	88.03	83.44	85.62	83.66	80.66	88.87	87.95	85.59

Fig. No-2: In Vitro Dissolution profiles formulation F1-F3.



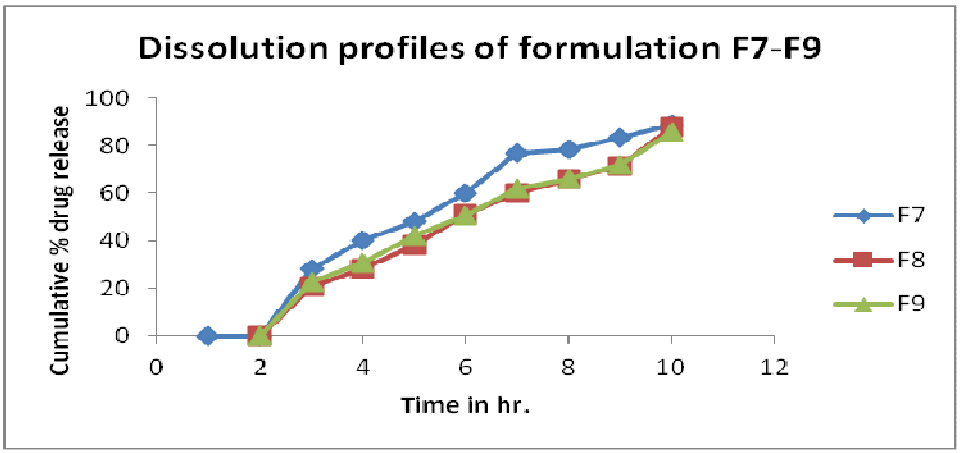
Showing relationship between Time Vs % Drugs Release.

Fig. No-3: In Vitro Dissolution profiles of formulation F4-F6.



Showing relationship between Time Vs % drug release

Fig. No-4: In Vitro Dissolution profiles of formulation F7-F9.



Showing relationship between Time Vs % drug release

Result and Discussion

It could be observed that all the prepared tablets fulfill the IP requirements for physicochemical properties and results are given in Table 2. The hardness of prepared buccal tablets was found to be in the range of 3.4 to 4.7kg/cm^2 and shown in Fig. 2.The thickness and weight of the prepared buccal tablet were found to be in the range of 2.30 to 2.44 mm and 96 to 105 mg respectively. Friability values of all tablets were less than 1 % indicate good mechanical strength to with stand the rigorous of handling and transportation. The average drug content of the buccal tablets was found to be within the range of 86.94 to 97.89 %. The surface pH of all the formulations was found to be in the range of 5.63 to 6.68.Hence it is assume that these formulations cause no any irritation in the oral cavity. The swelling profile of different batches of tablets. The swelling indices of the tablets increased with increasing amount of chitosan, guar gum and xanthun gum.

The mucoadhesivity of tablets was found to be maximum in case of formulation F1 i.e. 4.90 gm. This may be due to fact that the combination and higher concentration of chitosan and sodium alginate. The results are given in Table 3. In vitro drug release data of the all the buccal tablet formulations of Granisetron hydrochloride was subjected to goodness-of-fit test by linear regration analysis according to zero order, first order kinetics and according to Higuchi's and Korsmeyer-Peppas equations to assertion mechanism of drug release are shown in Table 4 and in Fig. 2 to 4. The formulations F1, and F8 shows drug release 93.21%, and 88.87% within 8 h are shown in Table 4 and Fig.2- 4. The FTIR studies revealed that there was no physicochemical interaction between Granisetron hydrochloride.

Conclusion

It can be concluded that the mucoadhesive buccal tablets of Granisetron hydrochloride can be prepared by using natural polymers to control the drug release and also to avoid the first pass metabolism. The formulations F1and F8 were found to be promising, which shows an in vitro drug release of 93.21 and 88.87 in 8 h along with satisfactory mucoadhesion strength.

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