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Formulation and Evaluation of Pantoprazole Sodium SesquihydrateIR Buccal Films.

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ABSTRACT

Pantoprazole sodiumsesquihydrate is a proton pump inhibitor(PPI).Pantoprazole gets degraded at gastric P^H, so most of the formulations are developed as enteric coated or delayed release formulations. Amount of the drug in the dosage form is not made available to the systemic circulation due to hepatic first pass effect. Buccal route can bypass hepatic first pass metabolism.The study is intended to formulate and evaluate Pantoprazole sodium sesquihydrate IR buccal films using solvent castingat various viscosity grades of HPMC (5cps,100K,K5M).The best formulation was found to be F2which is formulated using HPMC 100K(100mg) as water solublepolymer,PEG 400 and glycerol. The cumulative drug release was found to be 89.6% for 30min and 99% within 60min.FTIR studies were carried out which showed no drug – excipient incompatibility.

Keywords: Pantoprazole sodium sesquihydrate,buccalfilms,transmucosal delivery, Solvent casting, HPMC.

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INTRODUCTION

The mucosa is relatively permeable with a rich blood supply. The oral transmucosal drug delivery bypasses liver and avoids pre-systemic elimination in the GI tract and liver. Mouth dissolving films, a new drug delivery system for the oral delivery of the drugs, was developed based on the technology of the transdermal patch. The delivery system consists of a very thin oral strip, which is simply placed on the patient's tongue or any oral mucosal tissue, instantly wet by saliva the film rapidly hydrates and adheres onto the site of application. It then rapidly disintegrates and dissolves to release the medication for oromucosal absorption or with formula modifications, will maintain the quick-dissolving aspects allow for gastrointestinal absorption to be achieved when swallowed. In contrast to otherexisting, rapid dissolving dosage forms, which consist of liophylisates, the rapid films can be produced with a manufacturing process that is competitive with the manufacturing costs of conventional tablets.[1] Pharmaceutical companies and consumers alike have embraced OTFs as a practical and accepted alternative to traditional OTC medicine forms such as liquids, tablets, and capsules. OTFs offer fast, accurate dosing in a safe, efficacious format that is convenient and portable, without the need for water or measuring devices. OTFs are typically the size of a postage stamp and disintegrate on a patient's tongue in a matterof seconds for the rapid release of one or more APIs.[2]

Pantoprazole is in a class of drugs called proton pump inhibitors (PPI) which block the production of acid by the stomach. . Proton pump inhibitors are used for the treatment of conditions such as ulcers, gastroesophageal reflux disease (GERD) and Zollinger-Ellison syndrome that are caused by stomach acid. Pantoprazole, like other proton-pump inhibitors, blocks the enzyme in the wall of the stomach that produces acid. By blocking the enzyme, the production of acid is decreased, and this allows the stomach and esophagus to heal.[3]

Pantoprazole gets degraded to the acidic pH in the stomach, so they are usually formulated as enteric coated or delayed release tablets and also as IV infusions.[4] So the objective of the study is to formulate an immediate release buccal films using different viscosity grades of HPMC(5cps,100K,K15M) .[5] The drug gets released in the oral mucosal cavity and absorbed into the systemic circulation avoiding hepatic first-pass metabolism. [6]

MATERIALS AND METHODS

Chemicals

Patoprazole sodium sesquihydrate,Hydroxypropyl methyl cellulose 5cps,HPMC K100,HPMC K15 M, Polyethylene glycol,Propyleneglycol,Ethanol,Glycerine.

Preparation of buccalmucoadhesive films

The solvent evaporation method was used for the preparation of films.[7] About 10 films were prepared using different composition of polymers and the films were observed for dispersion of drug, flexibility, and glossy structure. Among these four formulations were selected and used for further analysis. [8]

Buccal films of Pantoprazole sodium were prepared by solvent evaporation method using film forming polymers.Required amount of HPMC K4M was weighed accurately and soaked in water and kept aside for 10min for swelling of polymer. [9]Required amount of water was added to the above polymer solution and dispersion was stirred. Simultaneously required amount of Pantoprazole sodium was weighed accurately and dissolved in 5ml of distilled water in another beaker. Then drug solution was added to the polymer solution and 1ml of glycerol as plasticizer was added and mixed thoroughly with the help of magnetic stirrer. The above solution was sonicated for 20min for the removal of air bubbles. The glass mould (petridish) having diameter 8.6cm was placed over a flat surface and the resulting 30 ml solution was transferred into petridish slowly drop by drop and the solution was spread uniformly. Funnel was inverted and it is placed over the petridish to get uniform evaporation. The petridish containing polymeric solution of drug was kept at room temperature for 24hours. The patch was removed carefully and circular films of 1.5 cm2 were punched out so that each film contained 20mg of the drug. And films were packed with aluminium foil and preserved in desiccators till evaluation tests were performed. Similarly formulations F2, F3, F4 were prepared. [10][11][12] as shown in table 1.

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RESULTS

Evaluation parameters were carried out for different formulations and the results are shown in table 2.

Diffusion studies

The diffusion studies were carried out for different experimental trials using Franz diffusion cell apparatus. The %cummulative drug release for different formulations are obtained are shown in table 2. As Diffusion studies are carried out in the following media. [13][14][15]. Figure 1 represents % cummulative drug release of different formulations F1 to F5.

Buffer Stage: (pH 6.8)

- Apparatus: Franz diffusion cell apparatus
- Dissolution medium:pH 6.8 phosphate buffer
- RPM: 50
- Temperature: 37 ± 0.5°C
- Time: 5,10,15,20,30,45 and 60 minutes

FTIR studies

IR spectra was obtained by using the FTIR spectrophotometer (H400-84100, Shimadzu, Japan) using KBR pellets and scanning range was 4400 to 400 cm-1 at a scan period of 1 min. The FTIR spectra of pure drug, drug with excipients and only excipients are shown. From this it is clear that the characteristic peaks at O- H and C- H absorption bands from 3000 to 3500 cm−1; C C, C N absorption bands from 1800 to 1500 cm−1(Badwan et al., 2002). Sesquihydrate has an absorption band at 815 cm−1 shows the presence of the drug are present in both the pure drug, formulation without any change in their positions, indicating no chemical interaction between drug and excipients, as confirmed by the FTIR studies. Figure 2 shows FTIR graph of Pantoprazole sodium sesquihydrate.

Table 1: Composition of Pantoprazole sodium IR buccal films F1 to F5

S.No	INGREDIENTS	FORMULATIONS				
		F1	F2	F3	F4	F5
1	Pantoprazole sodium sesquihydrate	388mg	388mg	388mg	388mg	388mg
2	HPMC 5cps	100mg	_	_	_	_
3	HPMC K 100	_	100mg	200mg	_	_
4	HPMC K15 M	_	_	_	100mg	200mg
5	PEG	_	0.4ml	0.4ml	0.4ml	0.4ml
6	Propylene glycol	0.48ml	_	_	_	_
7	Ethanol	20ml	_	_	_	_
8	Glycerine	_	0.2ml	0.2ml	0.2ml	0.2ml
9	Water	_	10ml	10ml	10ml	10ml

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Table 2: It shows various evaluation parameters of different formulations.

S.NO	Evaluation parameters	F1	F2	F3	F4	F5
1	Content uniformity(mg)	23	20	19	24	23
2	Thickness (mm)	0.693	0.827	0.42	0.76	0.72
3	Tensile strength	1.889	1.963	1.534	1.654	1.865
4	Folding endurance	222	226	207	213	217
5	Dissolving time (sec)	190	245	225	258	264
6	Disintegration time (sec)	32	20	28	28	24
7	Surface pH	6.48	6.14	6.24	6.32	6.29
8	Drug content (%)	94.04	96.34	93.13	95.04	94.9
9	Swelling index (%)	109	112	98	105	99

Table 3: It shows % cummulative drug release profile of different formulations F1 to F5

TIME (min)	F 1(%)	F2 (%)	F3 (%)	F4 (%)	F5(%)
0	0	0	0	0	0
5	25.09	35.8	15.9	28.05	35
10	35.3	49.1	26.3	39.8	49.2
15	47.6	61.8	39.4	49	59.4
20	59.7	75.9	43.4	58.3	68.6
30	74.6	89.6	58.9	72.9	84.5
45	83.7	96.4	61.9	79.3	92.1
60	89.8	99	66.5	82	96.2

Figure 1: It shows % Cummulative drug release of different formulations F1 to F5

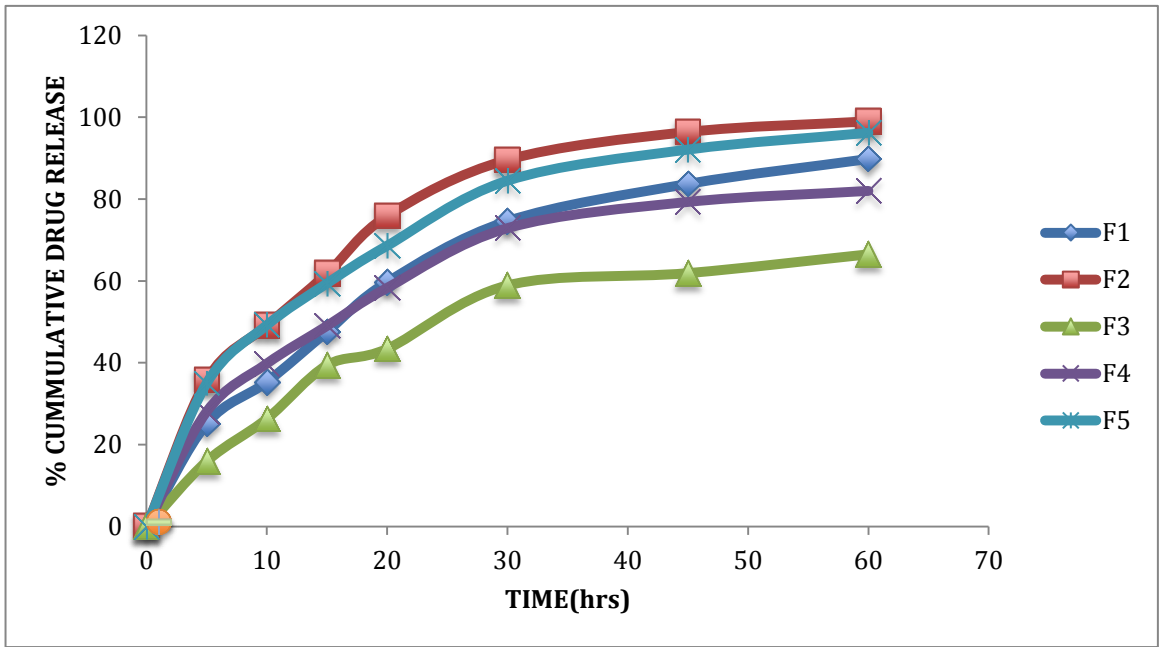

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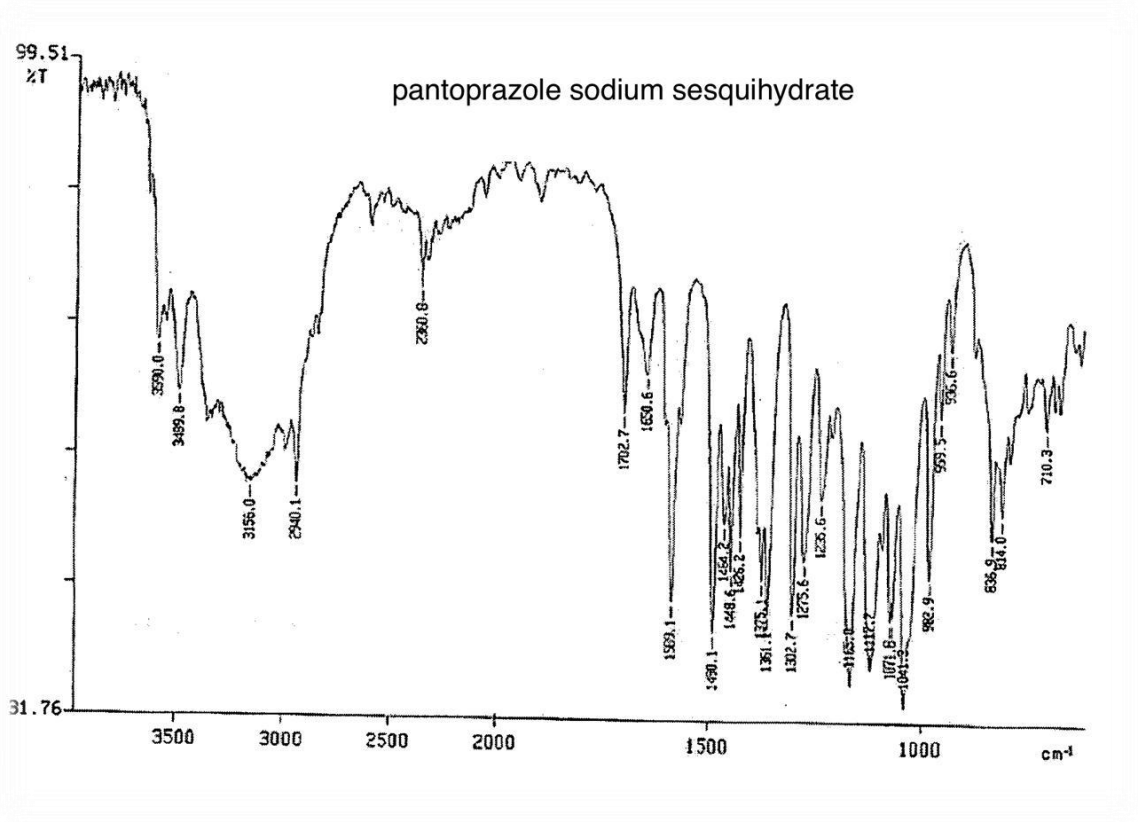
Figure 2: FTIR graph showing pantoprazole sodium sesquihydrate peaks



DISCUSSION

The objective of the study is to formulate and evaluate Pantoprazole sodium oral fast dissolving films. Pantoprazole is in a class of drug called proton pump inhibitor (PPI)which blocks acid secretion from the gastric parietal cells.

During the drug-excipient interaction study, it was observed that there was no significant physical change in the drug when mixed with excipients and kept under stressed conditions for three months.

The Calibration curve of the drug constructed by using UV-Spectrophotometer was found to be linear over a concentration range of 2 to 12 µg/ml. (r^2=0.999)

The initial batches F1 formulated using Hydroxypropyl methyl cellulose (5cps) may be useful in preparation of IR buccal films. Cumulative drug release for formulation F1 was found to be 89.8% within 1 hr.

In Formulation F2 and F3, an increase in concentration of HPMC K 100 resulted in decrease in cumulative release of 66.5% within 1 hr and maximum drug release of 99% was obtained for formulation F2.

Formulations F4 and F5 which was formulated using HPMC K15 M. Formulation F4 released 82% of drug within 1 hour. In Formulation F5 an increase in concentration of HPMC K15 Machieved better results as the drug release was found to be 96.2%.

F2 is the optimized formulation and the maximum drug release of 89.6% was released within 30minutes and a total of 99% release was achieved which is the highest among all the batches prepared.

CONCLUSION

Among five formulations of immediate release buccal films of pantoprazole sodium sesquihydrate was formulated and formulation F2 was found to have the best release of 99% within 1 hour.

Stability study is carried out for 3 months at 25°C; 60% RH: and 40°C; 75%RH, according to ICH guidelines. The films were tested for drug release and percentage label claim during the stability period and confirmed that the results were found within the limits. The identified formula shall be utilized for the formulation development and other studies.

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