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FORMULATION DEVELOPMENT AND EVALUATION OF BUCCAL TABLETS OF PANTOPRAZOLE

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Abstract :
The aim of present work is to formulate and evaluate buccal tablets of protonix (pantoprazole sodium) which is subjected to first pass effect and having short half life. To increase the bio availability of a protonix by delivering through the buccal mucosa, as it is a potential site for direct delivery of drugs into systemic circulation. To control the drug release from the tablets by using matrix forming bioadhesive polymers, as the half life of drug is very low. To study the effect of drug : polymer ratio on drug release and other bioadhesive properties.

Key words: ***Buccal, Protonix, Bioadhesive, Systemic circulation, Half life***

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INTRODUCTION:

Buccal drug delivery is a type of bioadhesive drug delivery; especially it is a mucoadhesive drug delivery in which drug delivery system is adhered to buccal mucosa. Buccal delivery involves the administration of desired drug through the buccal mucosal membrane which is the lining of the oral activity.

OVERVIEW OF THE BUCCAL MUCOSA

- Buccal mucosa structure and its suitability:
- Buccal mucosa present as a lining of the buccal region which is a part of the mouth bounded anteriorly and laterally by lips and cheeks, posteriorly and medially by the teeth and gums, and above and below by the reflections of the mucosa from the lips and cheeks to the gums.

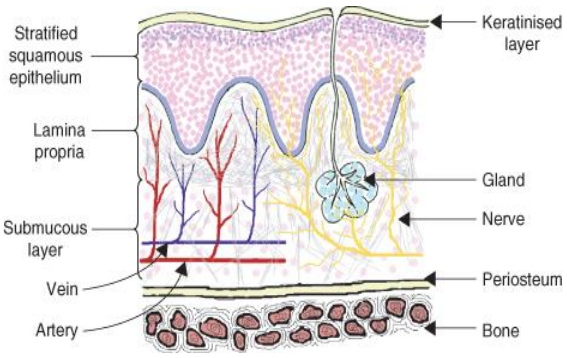


Fig.1: Cross section of buccal mucosa

ADVANTAGES OF BUCCOADHESIVE DRUG DELIVERY:

Drug administration via the buccoadhesive drug delivery offers several advantages such as:

- Drug is easily administered and extinction of therapy in emergency can be facilitated.
- The buccal mucosa is easily accessible, so dosage forms can be easily administered and even removed from the site of application.
- It is a passive system and does not require activation.
- Enzymatic activity is very low as compared to stomach.
- It can be easily removed in case of emergency [1].

LIMITATIONS OF BUCCOADHESIVE DRUG DELIVERY:

There are some limitations of buccal drug delivery system such as :

- Drugs which are unstable at buccal pH cannot be administered.
- Drugs which have a bitter taste or unpleasant taste or an obnoxious odour or irritate the mucosa cannot be administered by this route.
- Drug required with small dose can only be administered.
- Those drugs which are absorbed by passive diffusion can only be administered by this route.
- Eating and drinking may become restricted [2].

Various mucoadhesive polymers can broadly be categorized as follow:

(I) Synthetic polymers:

1. Cellulose derivatives (Methylcellulose (MC), Ethyl cellulose (EC), Hydroxy ethyl cellulose (HEC), Hydroxyl propyl cellulose (HPC), Hydroxy propyl methylcellulose (HPMC), Sodium carboxy methylcellulose (NaCMC), Poly hydroxyl ethyl methylacrylate, Poly (Acrylic acid) polymers (Carbomers, Polycarbophil), Poly ethylene oxide, Poly vinyl pyrrolidone, Poly vinyl alcohol.

(II) Natural polymers:

Tragacanth, Sodium alginate, Guar gum, Xanthan gum, Soluble starch, Gelatin, Chitosan

MECHANISM OF BIOADHESION:

For bioadhesion to occur, three stages are involved:

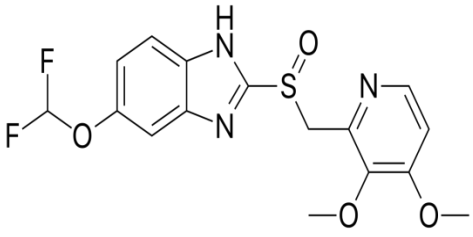
1. An intimate contact between a bioadhesive and a membrane either from a good wetting of the bioadhesive and a membrane or from the swelling of bioadhesive.
2. Penetration of the bio-adhesive into the tissue takes place.
3. Inter penetration of the chains of the bioadhesive with mucous takes place. Low chemical bonds can then settle.

The bonding between the mucus and the biological substance occurs chiefly through both physical and chemical interactions results from enlargement of the adhesive material and chemical bonds due to electrostatic interaction, hydrophobic interactions, hydrogen bonding and dispersion forces. [3]

DRUG PROFILE

PROTONIX (Pantoprazole sodium) :

1. **Drug class:** Proton pump inhibitor.
2. **Brand name :** panprazol**,** panrazole
3. **Structure :**



4. **Molecular weight :** 383.37 g / mol
5. **Molecular formula : $C_{16}H_{15}F_2N_3O_4S$**

6. **Chemical name :** protonix
7. **Properties :**

- Pantoprazole sodium is a white to off - white crystalline powder and is recemic.
- Pantoprazole has weekly basic and acidic properties.
- Pantoprazole sodium is a freely soluble in water, very slightly soluble in phosphate buffer at pH 7.4 and practically insoluble in n-hexane

8. **Mechanism of action**: Pantoprazole is a proton pump inhibitor (PPI) that suppresses the final step in gastric acid. Gastric acid production by forming a covalent bond to two sites of the (H, K) – ATPase enzyme system at the secretary surface of the gastric parietal cell. This effects is dose related and leads to inhibition of both basal and stimulated gastric acid secretion irrespective of the stimulus. The binding to the (H, K) – ATPase result in a duration of antisecretaary effect that persists longer than 24 hrs.
9. **Pharmacokinetics :**
PROTONIX is prepared as an enteric-coated tablet so that absorption of pantoprazole begins only after the tablet leaves the stomach. Peak serum concentration (Cmax) and area under the serum concentration time curve (AUC) increase in a manner proportional to oral and intravenous doses from 10 mg to 80 mg. Pantoprazole does not accumulate and its pharmacokinetics are unaltered with multiple daily dosing. Following oral or intravenous administration, the serum concentration of pantoprazole declines biexponentially with a terminal elimination half-life of approximately one hour. In extensive metabolizers (see Metabolism section) with normal liver function receiving an oral dose of the entericcoated 40 mg pantoprazole tablet, the peak concentration (Cmax) is 2.4 :g/mL, the time to reach the peak concentration (tmax) is 2.4 h and the total area under the plasma concentration versus time curve (AUC) is 4.8 mg hr/ml. When pantoprazole is given with food, its tmax is highly variable and may increase significantly. Following intravenous administration of pantoprazole to extensive metabolizers, its total clearance is 7.6-14.0 L/h and its apparent volume of distribution is 11.0-23.6L [3].

Absorption:
The absorption of pantoprazole is rapid, with a Cmax of 2.5 g/mL that occurs approximately fluid. The serum protein binding of pantoprazole is about 98%, primarily to albumin [5].

Metabolism:
Pantoprazole is extensively metabolized in the liver through the cytochrome P450 (CYP) system. Pantoprazole metabolism is independent of the route of administration (intravenous or oral). The main metabolic pathway is demethylation, by CYP2C19, with subsequent sulfation; other metabolic pathways include oxidation by CYP3A4. There is no evidence that any of the pantoprazole metabolites have significant pharmacologic activity. CYP2C19 displays a PROTONIX (pantoprazole sodium) Delayed-Release Tablets known genetic polymorphism due to its deficiency in some sub-populations (e.g. 3% of Caucasians and African, Americans and 17-23% of Asians). Although these sub-populations of slow pantoprazole metabolizers have elimination half-life values of 3.5 to 10.0 hours, they still have minimal accumulation (£ 23%) with once daily dosing [6].

Elimination:
After a single oral or intravenous dose of 14C-labeled pantoprazole to healthy, normal metabolizer volunteers, approximately 71% of the dose was excreted in the urine with 18% excreted in the feces through biliary excretion. There was no renal excretion of unchanged pantoprazole. [7]

Renal Impairment:
In patients with severe renal impairment, pharmacokinetic parameters for pantoprazole were similar to those of healthy subjects. No dosage adjustment is necessary in patients with renal impairment or in patients undergoing hemodialysis. [8]

Hepatic Impairment:
In patients with mild to moderate hepatic impairment, maximum pantoprazole concentrations increased only slightly (1.5-fold) relative to healthy subjects. Although serum half-life values increased to 7-9 hours and AUC values increased by 5- to 7-fold in hepatic-impaired patients, these increases were no greater than those observed in slow CYP2C19 metabolizers, where no dosage frequency adjustment is warranted. These pharmacokinetic changes in hepatic-impaired patients result in minimal drug accumulation following once daily multiple-dose administration. No dosage adjustment is PROTONIX (pantoprazole sodium) Delayed-Release Tablets needed in patients with mild or moderate hepatic impairment. The pharmacokinetics of pantoprazole has not yet been well characterized in patients with severe hepatic impairment. Therefore, the potential for modest drug accumulation (£ 21%) when dosed

once daily needs to be weighed against the potential for reduced acid control when dosed every other day in these patients [9].

MATERIALS AND METHOD:

MATERIALS :

Pantoprazole, HPMC, Carbopol, Micro crystalline cellulose, Mannitol, Magnesium stearate, Talc, Potassium dihydrogen ortho phosphate, Sodium hydroxide, Agar Agar powder [10].

FORMULATION:

Buccoadhesive Tablets Preparation:

RESULTS AND DISCUSSION:

Pantoprazole was mixed manually in poly bags with different ratios of HPMC (Or) Carbopol as mucoadhesive polymers and Mannitol, microcrystalline cellulose as diluents for 10 mins.The blend was then compressed into tablets by direct compression method using 9 mm flat faced punches on a single station tablet punching machine [11].

EVALUATION OF BUCCAL TABLETS:

A) Characterization of tablets for physiochemical parameters

Weight variation, Tablet thickness, Tablet hardness, Friability, In- vitro release studies, Surface pH , Moisture absorption.

Table 1: Weight variation, Thickness, Hardness

Formulation	Mass(mg) Mean ± SD	Thickness(mm) Mean ± SD	Hardness (Kgs)
F1	1.08	2.24± 0.02	6.1± 0.3
F2	0.60	2.29± 0.03	5.8 ±0.3
F3	0.59	2.36 ±0.03	5.6± 0.2
F4	0.80	2.40 ±0.04	5.4 ±0.2
F5	1.05	2.19± 0.02	5.1±0.6

Table 2: Friability:

Formulation	Friability
F1	0.69
F2	0.98
F3	0.57
F4	0.61
F5	0.73

Table 3: -Vitro drug release:

Time (hrs)	F1	F2	F3	F4	F5
0.00	0.00	0.00	0.00	0.00	0.00
1	13.27± 0.83	40.07± 0.56	35.15 2.70	34.45 0.35	47.14 ±0.88
2	23.06± 0.25	57.05 ±1.65	54.90 1.35	51.23 0.56	57.33± 0.56
4	41.95 ±0.58	80.30 ±1.45	70.50 0.24	81.04 2.47	80.05± 2.49
6	60.86 ±0.65	90.25± 2.34	85.26 1.25	89.54 1.27	95.60 ±1.25
8	77.30± 0.53	96.68 ±1.25	97.68 1.28	111.42 1.50	113.82 ±1.45

Table 4: Moisture absorption of buccal tablets :

Formulation	Moisture absorption (%) Mean± SD
F1	12.23 ±1.22
F2	12.40± 1.70
F3	53.81± 1.62
F4	56.43 ±1.45
F5	89.94± 1.36

Table 5: Surface ph value (Mean±SD) of formulation F1 TO F5:

Time (hrs)	F1	F2	F3	F4	F5
0.25	6.86±0.02	6.01± 0.05	6.32± 0.10	7.34± 0.03	6.98± 0.03
0.5	7.01±0.03	6.65± 0.02	6.59± 0.04	7.44± 0.01	6.46 ±0.03
0.75	6.25± 0.04	7.01± 0.04	7.09 ±0.02	7.23± 0.04	6.25± 0.02
1	6.98± 0.02	6.25 ±0.05	6.79 ±0.06	7.09± 0.03	6.03± 0.03
2	6.06 ±0.03	7.12± 0.05	6.04±0.05	6.05 ±0.03	6.00 ±0.02
3	6.98± 0.03	7.05 ±0.05	6.89± 0.06	6.09± 0.02	6.45± 0.01
4	6.09 ±0.02	7.09± 0.04	6.98± 0.07	6.99± 0.03	6.61± 0.03
5	6.08± 0.03	7.40± 0.05	6.25± 0.07	6.06 ±0.03	6.79 ±0.04
6	6.79± 0.02	7.29 ±0.07	6.79 ±0.06	6.91± 0.02	6.22 ±0.02
7	6.52 ±0.08	7.11 ±0.03	6.48 ±0.04	6.69± 0.04	6.99± 0.03
8	6.48± 0.05	7.44±0.05	6.99 ±0.05	6.79± 0.05	6.73± 0.02

a) **Weight variation, hardness, thickness** :
The weight variation and the thickness of the tablets were within the limits of uniformity. The mass ranged from 196.54 to 199.58 mg with SD values 0.59-1.08. thickness ranged between 2.19 and 2.40mm with SD values of 0.02 to 0.04. the mass and thickness of all compressed tablets were within the limits as per USP. The hardness of all prepared tablets was in the range of 5.1 to 6.1 kgs.

b) Friability :
The drug content ranged from 107.5 ±0.39 % in formulation F1 to 108.80± 0.58 % in the formulation F5 and the friability was ranged from 0.57 to 0.73. friability of all compressed tablets were within the limits as per USP.

c) In- vitro drug release:
The release of pantoprazole from buccoadhesive tablets varied according to the type and ratio of matrix forming polymers. The drug release was governed by the amount of matrix forming polymers and microcrystalline cellulose. Formulation F1 showed good controlled release upto 10hrs, it has given 77.30± 0.53% drug release at the end of 10hrs. Formulations F2 and F3 given almost same drug release pattern within 10 hrs. F4 and F5 had given maximum drug release with 8 hrs. Formulations F4 and F5 given burst release after 4 hrs.

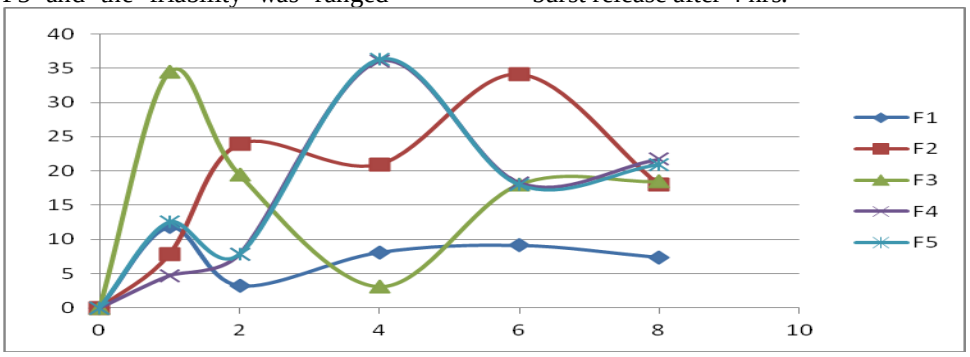


Fig.2: Standard graph of in vitro drug release

d) Moisture absorption :

The moisture absorption studies give an indication of the relative moisture absorption capacities of polymers and wether the formulations maintain their integrity after moisture absorption. Moisture absorption increased from F1 to F5. The possible reason may be the increased concentrations of polymer from formulations F1 to F5. The moisture absorption was more in formulations containing HPMC when compared to formulations containing Carbopol. This may be due to more hydrophilic nature of HPMC.

e) Surface pH :

The surface ph of the tablets remained fairly constant at a pH of approximately 6.12-7.5 over the 8 hrs test period confirming that the surface pH of the tablets was within the neutral conditions of the saliva(pH 6.0-7.5) and that no extremes in pH occurred throughout the test period. These results suggested that the polymeric blend used in the formulation is suitable for buccal application owing to the acceptable pH measurement.

CONCLUSION:

Pantoprazole sodium was formulated as buccal tablets to improve its bioavailability by avoiding first pass metabolism. HPMC, and carbopol were selected as polymers. Mucoadhesive drug delivery system utilize the properties of bioadhesion of certain water soluble polymer which become adhesive on hydration and hence can be used for targeting a drug to a particular region of the body for a controlled period of time. It can be concluded that the bioadhesive controlled release tablets can overcome the disadvantage of poor and erratic bioavailability of pantoprazole associated with currently marketed oral formulations.

REFERENCES:

1. Jain NK. Controlled and Novel Drug Delivery, 1st edition, published by CBS Publishers and Distributors, New Delhi. 1997; 52-81.
2. Patel KV, Patel ND, Dodiya HD, Shelat PK. Buccal bioadhesive drug delivery system: an overview. Ind. J. of Pharma. & Bio. Arch. 2011; 2(2): 600-609.
3. Shojaei AH. A systemic drug delivery via the buccal mucosal route. Pharm. Tech. 2001: 70-81.
4. Verma S, Kaul M, Rawat A, Saini S. An overview on buccal drug delivery system Ind. J .Pharm. Sci. Res. 2011; 2(6): 1303-1321.
5. Patel RS, and Poddar SS. Development and characterization of mucoadhesive buccal patches of salbutamol sulphate, Curr. Drug Deliv., 2009, 6, 140-144.
6. Angela A, Federica B, Teresa C, Federica C, Beatrice V and Barbara L. Mucoadhesive chitosan/gelatin films for buccal delivery of Propranolol hydrochloride, Carbohydrate Polymers xxx (2011) xxx–xxx.
7. Shammi Goyal, Jitendra Kumar Rai, R.K.Narang, Rajesh K.S. Sulfonyl ureas for antidiabetic therapy, an overview for glipizide. International journal of pharmacy and pharmaceutical sciences, 2010; 2(2): 1-6.
8. V.Tamassia. The pharmacokinetics and bioavailability of glipizide. Current Medical Research & Opinion, 1975; 3(1): 20-30.
9. D. Mahalaxmi, A. Senthil, V. Prasad, B. Sudhakar, S. Mohideen. Formulation and Evaluation of mucoadhesive buccal tablets of Glipizide. International Journal of Biopharmaceutics, 2010; 1(2): 100-107.
10. Sellappan Velmurugan and Kiran Kumar, Raghavarapu. Formulation and invitro evaluation of Glipizide mucoadhesive Buccal Tablets. International Journal of Pharma and biosciences, 2013; 4(2): 594-607.
11. Suvakanta Dash, Padala narasimha Murthy, Lilakantha Nath and Prasanta Chowdhury. Kinetic modeling on drug release from controlled drug delivery systems- A review. Acta Poloniae Pharmaceutical- Drug Research, 2010; 67(3): 217-23.