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FORMULATION, DEVELOPMENT AND EVALUATION OF BUCCAL MUCOADHESIVE TABLETS OF NARATRIPTAN

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Abstract

Naratriptan completely absorbed following oral administration. The mean oral absolute bioavailability of the tablet is about 60%. This clearly indicates that Naratriptan have first pass metabolism problem. The aim of present work to formulate and characterize buccal mucoadhesive tablets of Naratriptan. Buccal tablets of Naratriptan using HPMC K4, Carbopol 934 and Na Alginate prepared by direct compression method were found to be good without chipping, capping and sticking. The drug content was uniform in all the formulations of tablets prepared. Low values of standard deviations indicate uniform distribution of drugs within the matrices. The drug polymer ration influenced the release of drug from the formulations. An increase in polymer decreased the drug release. Formulation F4 with drug polymer (HPMC K4, carbopol and Na Alginate) has shown promising results as per USP test II requirements.

Key words: Naratriptan, Buccal mucoadhesive tablets, Formulation, Evaluation

Introduction

The outermost layer of stratified epithelium makes up the oral mucosa. A basement membrane, a lamina propia, and the submucosa as the innermost layer are found below. The epithelium is close to the remainder of the body's stratified squamous epithelia.It has a mitotically active basal cell layer that progresses through a series of differentiating intermediate layers to the superficial layers, where cells are shed from the epithelium's surface. The buccal mucosa epithelium has about 40-50 cell layers, while the sublingual epithelium has less[1]. When they progress from the basal to the superficial layers, epithelial cells grow in size and become flatter. The buccal epithelium turnover cycle has been measured to be 5-6 days, which is likely indicative of the oral mucosa as a whole. The buccal mucosa is 500-800m thick, while the rough and soft palates, the floor of the jaw, the ventral tongue, and the gingiva are 100-200m thick[2].

The oral mucosa is a leaky epithelia that lies somewhere between the epidermis and the intestinal mucosa. The permeability of the buccal mucosa is measured to be 4-4000 times greater than that of the flesh. The oral mucosa's permiabilities decrease in order of sublingual greater than buccal, buccal greater than palatal, and buccal greater than palatal. The sublingual mucosa is comparatively thin and non-keratinized, the buccal mucosa is thicker and non-keratinized, and the palatal mucosa is intermediate in thickness but keratinized, so this rank order is dependent on the relative thickness and degree of keratinization of these tissues.The permeability barrier in the oral mucosa is thought to be made up of intercellular content extracted from so-called "membrane coating granules'" (MCG)[3]. MCGs form as cells divide, fusing with the plasma membrane at the apical cell surface and releasing their contents into the intercellular spaces of the epithelium's upper one-third.This barrier can be seen in the superficial layer's outermost 200 meters. A variety of very large molecular weight tracers, such as horseradish peroxides11 and lanthanum nitrate, have been used in permeation experiments[4-5].

Localized drug distribution to oral cavity tissues has been explored for the treatment of periodontal disease, bacterial and fungal infection, among the different routes of administration attempted so far in novel drug delivery systems.Mucoadhesion has gained popularity over the years due to its ability to improve localized drug distribution

by maintaining a dosage product at the site of action (e.g., within the gastrointestinal tract) or systemic drug delivery by retaining the formulation in close proximity to the absorption site (e.g. buccal cavity)[6]. The tendency of a polymer (synthetic or organic) to bind to biological tissue for a prolonged period of time is known as bioadhesion. The biological surface may be epithelial tissue or the mucus layer on a tissue's surface. Mucoadhesion is the term used to describe adhesion to a mucous coat.

The buccal route of drug delivery allows drugs to enter the systemic circulation directly via the jugular vein, bypassing first-pass hepatic metabolism and resulting in high bioavailability.Other benefits include simple accessibility, low enzymatic activity, suitability for drugs or excipients that moderately and reversibly affect or irritate the mucosa, painless administration, the ability to include permeation enhancers, enzyme inhibitors, or pH modifiers in the formulation, and flexibility in designing as a multidirectional or unidirectional release device for local or systemic intervention[7].

Naratriptan completely absorbed following oral administration. The mean oral absolute bioavailability of the tablet is about 60%. This clearly indicates that Naratriptan have first pass metabolism problem. The metabolic pathway of Naratriptan included primarily hepatic. In vitro, Naratriptan is metabolized by a wide range of cytochrome P450 isoenzymes into a number of methods may not always be convenient for the patient.

In addition, the thin sublingual mucosa (about 190 um compared to 500-800 um of the buccal mucosa) and the abundance of blood supply at the sublingual region allow excellent drug penetration (absorption) to achieve high plasma drug concentration with a rapid onset of action. The aim of present work to formulate and characterize buccal mucoadhesive tablets of Naratriptan.

Material and Methods

Method for preparation of Naratriptan buccal tablet

Direct compression was taken after to manufacture the buccal tablets of Naratriptan[8]. Six different formulations (F1, F2, F3, F4, F5, and F6) were set up by direct compression. Every one of the polymers chose, drug and excipients were gone through strainer no. 40 preceding utilizing into plan. The sum and proportion of drug and polymers were

weighed according to given in table No. 7.1 and all the definition were utilized for encourage assessments parameters. Polymers selected for tablets are:

- HPMC K4
- Carbopol 934
- Na Alginate

Table 1: Various formulations of Naratriptan buccal tablets

Excipients (mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
Simvastatin	2.5	2.5	2.5	2.5	2.5	2.5
HPMC K 4	25	50	75	12.5	25	37.5
Carbopol	-	-	.	12.5	25	37.5
Na Alginate	-	-	-	10	20	30
$Mg(C_{18}H_{35}O_2)_2$	10	10	10	10	10	10
Talc	10	10	10	10	10	10
Lactose	102.5	77.5	52.5	92.5	57.5	22.5
Total Weight	150	150	150	150	150	150

Evaluation of tablets[9-10]

All the tablets were evaluated for following various parameters which includes;

General Appearance

Five tablets from various batches were randomly selected and organoleptic properties such as color, odor, taste, shape, were evaluated. Appearance was judged visually. Very good (+++), good (++), fair (+) poor (-), very poor (- -).

Thickness and diameter

Thickness and diameter of tablets were determined using Vernier caliper. Five tablets from each batch were used, and an average value was calculated.

Drug content

Twenty tablets were taken and amount of drug present in each tablet was determined. The tablets were crushed in a mortar and the powder equivalent to 10mg of drug was transferred to 10ml standard flask. The powder was dissolved in 5 ml of phosphate

buffer pH 6.8 and made up to volume with of phosphate buffer pH 6.8. The sample was mixed thoroughly and filtered through a 0.45µ membrane filter. The filtered solution was diluted suitably and for drug content by UV spectrophotometer at λ max of 226nm using of phosphate buffer pH 6.8 as blank.

Hardness

For each formulation the hardness of five tablets was resolved utilizing the Monsanto hardness tester (Cadmach).

Friability

The friability of sample of 10 tablets was estimated utilizing a Friability tester (Electro Lab). Ten tablets were weighed, rotated at 25 rpm for 4 minutes. Tablets were reweighed after removal of fines (dedusted) and the percentage of weight loss was calculated.

Uniformity of weight

Twenty tablets were randomly selected from each batch individually weighed, the average weight and standard deviation of 20 tablets was calculated.

Swelling Index

Swelling study of individual polymers and combinations was carried out using eight-stage USP type 1 (basket) Dissolution Test Apparatus (Lab India, DS 8000) at 50 rpm, and phosphate buffer pH 6.8 was used as medium, and the temperature was maintained at 37 ± 0.5°C. Weight of individual tablet was taken prior to the swelling study (W_1). The tablet was kept in a basket. The weight of tablet was taken at time interval of 2, 4, 8, 12 hours (W_2). Percent hydration (swelling index) was calculated as shown in Table 7.4 using the following formula:

Swelling index = $(W_2 - W_1) \times 100/W_2$,

Where W_1 is the initial weight of tablet and W_2 is the weight of hydrated tablet

Dissolution rate studies[11]

In vitro drug release of the sample was done using USP-type II dissolution apparatus (Paddle type). The dissolution medium, 900 ml phosphate buffer pH 6.8 was set into the dissolution flask maintaining the temperature of 37±0.5^{0}C and rpm of 75. One Naratriptan tablet was set in every container of dissolution apparatus. The mechanical

assembly was permitted to keep running for 10 hours. Sample measuring 5 ml were pulled back after each 1 hour up to 2 hours using 10ml pipette. The new disintegration medium (37^0C) was supplanted each time with a similar amount of the sample and takes the absorbance at 226.0 nm using spectroscopy.

Results and Discussion

Naratriptan completely absorbed following oral administration. The mean oral absolute bioavailability of the tablet is about 60%. This clearly indicates that Naratriptan have first pass metabolism problem. The metabolic pathway of Naratriptan included primarily hepatic. In vitro, Naratriptan is metabolized by a wide range of cytochrome P450 isoenzymes into a number of methods may not always be convenient for the patient.

Therefore, there is growing interest in developing new, non-parenteral, reliable and convenient dosage forms using administration routes where a rapidly dissolved drug is immediately absorbed into the systemic circulation. The advantage of the buccal drug delivery is that the drug can be directly absorbed into systemic circulation bypassing enzyme degradation in the gut and liver. In addition, the thin sublingual mucosa (about 190 um compared to 500-800 um of the buccal mucosa) and the abundance of blood supply at the sublingual region allow excellent drug penetration (absorption) to achieve high plasma drug concentration with a rapid onset of action. The aim of present work to formulate and characterize buccal mucoadhesive tablets of Naratriptan.

Buccal tablets of Naratriptan using HPMC K4, Carbopol 934 and Na Alginate prepared by direct compression method were found to be good without chipping, capping and sticking. The drug content was uniform in all the formulations of tablets prepared. Low values of standard deviations indicate uniform distribution of drugs within the matrices. The drug polymer ration influenced the release of drug from the formulations. An increase in polymer decreased the drug release. Formulation F4 with drug polymer (HPMC K4, carbopol and Na Alginate) has shown promising results as per USP test II requirements.

Table 2: Results of post compression properties of Naratriptan buccal tablets

Formulation code	Thickness (mm)	Hardness (kg/cm2) n=3	Weight variation (mg) n=3	Friability (%) n=3	Drug content (%) n=3
F1	2.89±0.32	4.2±0.3	155±5	0.856±0.025	99.12±0.25
F2	2.85±0.25	4.3±0.2	152±4	0.785±0.035	99.25±0.36
F3	2.83±0.35	4.4±0.5	149±6	0.882±0.014	99.05±0.45
F4	2.84±0.15	4.5±0.4	153±5	0.745±0.036	98.89±0.15
F5	2.83±0.25	4.3±0.2	154±2	0.956±0.025	99.45±0.25
F6	2.83±0.36	4.2±0.3	150±3	0.855±0.014	98.96±0.35

Table 3: Results of Swelling Index of Naratriptan buccal tablets

Formulation Code	% Swelling Index			
	2 hrs.	**4 hrs.**	**8hrs.**	**12hrs.**
F1	15.65	36.65	59.98	75.65
F2	23.36	45.58	63.32	78.85
F3	28.85	48.85	72.23	80.95
F4	32.25	54.45	63.32	75.65
F5	27.74	58.89	65.45	89.32
F6	29.95	57.45	69.98	79.85

Table 4: *In-vitro* drug release study of buccal tablets

Time	% Cumulative Drug Release					
(hr)	F1	F2	F3	F4	F5	F6
0.5	33.25	32.25	30.14	25.56	20.36	18.56
1	45.56	40.23	39.98	32.25	26.65	22.25
1.5	65.56	60.58	59.88	46.69	40.23	39.98
2	88.89	79.98	78.89	58.89	51.12	49.98
3	98.89	87.52	85.56	69.98	60.23	55.56
4	-	93.32	92.23	76.12	71.45	69.78
6	-	98.85	99.12	88.56	79.98	78.89
8	-	-	-	92.23	86.65	83.32
12	-	-	-	98.78	90.12	89.98

Table 5: *In-vitro* drug release data for optimized formulation F4

Time (h)	Square Root of Time(h)$^{1/2}$	Log Time	Cumulative* % Drug Release	Log Cumulative % Drug Release	Cumulative % Drug Remaining	Log Cumulative % Drug Remaining
0.5	0.707	-0.301	25.56	1.408	74.44	1.872
1	1.000	0.000	32.25	1.509	67.75	1.831
1.5	1.225	0.176	46.69	1.669	53.31	1.727
2	1.414	0.301	58.89	1.770	41.11	1.614
3	1.732	0.477	69.98	1.845	30.02	1.477
4	2.000	0.602	76.12	1.881	23.88	1.378
6	2.449	0.778	88.56	1.947	11.44	1.058
8	2.828	0.903	92.23	1.965	7.77	0.890
12	3.464	1.079	98.78	1.995	1.22	0.086

Table 6: Regression analysis data of Naratriptan buccal Tablets

Batch	Zero Order	First Order	Higuchi	Korsmeyer-Peppas
	r^2	r^2	r^2	r^2
F4	0.788	0.989	0.916	0.946

Conclusion

Among these formulations F4 is acceptable for further pharmacodynamic and pharmacokinetic evaluation. When the regression coefficient values of were compared, it was observed that 'r' values of first order was maximum i.e. 0.989 hence indicating drug release from formulations was found to follow first order kinetics.

References

1. Amir H Shojaei. Buccal Mucosa as a Route for Systemic Drug Delivery. Journal of Pharmacy and Pharmaceutical Sciences. 1998; 1(1): 15-30.
2. Salamat-Miller N, Chittchang M, Johnston TP. The use of mucoadhesive polymers in buccal drug delivery. Advance Drug Delivery Review. 2005; 57(11): 1666-1691.
3. Squier, C.A. and Hall, B.K., The permeability of mammalian non-keratinized oral epithelia to horseraddish peroxidase applied in vivo and in vitro, Arch. Oral Biol., 29:45-50, 1984.
4. Hill, M.W. and Squier, C.A., The permeability of oral palatal mucosa maintained in organ culture, J. Anat., 1979;128:169-178.
5. Gandhi, R.B. and Robinson, J.R., Oral cavity as a site for bioadhesive drug delivery, Adv. Drug Del. Rev., 1994;13:43-74.
6. Giradkar KP, et al, Design development and in vitro evaluation of bioadhesive dosage form for buccal route, International journal of pharma research & development, 2010, 2.
7. Shidhaye SS, et al, Mucoadhesive bilayered patches for administration of sumatriptan, AAPS pharm sci tech, 2009, 9(3).

8. Grover I, Agarwal G, Formulation and Evaluation of Sublingual Tablets of Lisinopril, Journal of Scientific & Industrial Research, 2012; 71: 413-417.
9. Bhanj SB, Ellaiah HK, Formulation and Evaluation of Perindopril Sublingual Tablets, International Journal of Research in Pharmaceutical and Biomedical Sciences, 2011; 2(3):1193-1198.
10. Chaudhari P, Formulation and evaluation of Rizatriptan Benzoate Fast Disintegrating Tablet, Research Journal of Pharmaceutical, Biological and Chemical Sciences, 2011;482-488.
11. Bharbwaj V,Formulation and evaluation of fast disintegrating sublingual tablets of amlodipine besylate using different superdisintegrants, International Journal of Pharmacy and Pharmaceutical Sciences,2010; 2(3).