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FORMULATION DEVELOPMENT AND EVALUATION OF GABAPENTIN BUCCAL TABLETS

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Abstract

The aim of present work is to prepare and characterize buccal tablets of Gabapentin using different super disintegrants such as Cross povidon, PVP K30, Micro crystalline cellulose. This formulation were prepared by using factorial design 3×3 by using the various disintegrants and various bioadhesive polymers. PVP K30 and micro crystalline cellulose were used in different concentration in each formulation. The tablet were prepared by direct compression method & were evaluated and based on disintegration & dissolution studies F1 is considered as best formulation of improving solubility of drug. Prepared Gabapentin buccal tablet were evaluated for weight variation, thickness, hardness, drug content, bioadhesive strength, disintegration rate and dissolution rate studies. The Gabapentin buccal tablet F1 formulation was found to be 7 sec of disintegration time and 12 min of dissolution time. The devloped buccal drug delivery of Gabapentin tablets was one of the alternative route of administration to avoid first pass metabolism and to improve bioavailability through buccal mucosa and improve patient compliance.

Keywords: Gabapentin, buccal tablet, Formulation, Evaluation.

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INTRODUCTION

Buccal drug delivery is a favorable route compare to parenterals, injectable and adds a several advantages over other routes1. The parenteral route offers excellent bioavailability, similarly having poor patient compliance, anaphylaxis, and some other infections. Peroral route posses some inconvenience to patients. Hence for the immediate release of medication and for instant release at desire location in which the drug is absorbed distributer and easily metabolized. This limitation leads to the development of alternative routes of administration. Buccal mucosa has absorptive function and offers many benefits like avoidance of first pass effect, which is a non invasive route, increase in bioavailability, a rapid action is possible and reduce side effects. Buccal, sublingual, palatal and gingival regions shows effective drug delivery in oral cavity.

Buccal and sublingual route of drug delivery are most widely in which local and systemic effects are treated. The permeability of oral mucosa denotes the physical nature the tissues. The permeable part is sublingual mucosa and buccal mucosa is thinner part and in which there is a high blood flow and surface area; it is a feasible site when a rapid onset of action is desired. For the treatment of acute disorders sublingual route is a preferred one; however its surface washed with saliva which makes formulations in the oral cavity hard in nature.

Buccal drug delivery system is well accepted because it is having several advantages. Buccal areas offer a control release system which is having immobile surface. The buccal layer is tolerate to potential allergens and has capability of preventing damage compare to other mucosal tissue. In treatment of the local or systemic therapies, buccal mucosa favors a useful measure by overcoming drawbacks and as convenient route for the administration. This type of route is well vascularized draining to the heart unswervingly via the internal jugular vein. In chronic systemic therapies, buccal drug delivery acts as potential site and chemical modification due to salivary production and its composition.

There is a chance of drug loss at site of absorption in case of the oral route and for some dosage form salivary scavenging is constant with in oral cavity which make difficult for retaining to an extensive duration at the site to enhance the absorption. Bioadhesive polymers have prolonged contact time with the tissues and can notably maintain the performance of several drugs. The controlled drug delivery products have high patient compliance and a low cost with enhanced bioavailability [1-9].

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MATERIALS AND METHODS

Gabapentin was obtained from Sun pharmaceutical ltd, Ahmadnagar. Cross povidon, polyvinyl pyrrolidon, Micro crystalline cellulose, Hydroxy propyl methyl cellulose, Mannitol, Magnesium stearate, Sodium Saccharin are obtained from S.D. Fine chemicals, Mumbai.

FORMULATION OF GABAPENTIN BUCCAL TABLET [10-12]

Gabapentin buccal tablet were prepared by using different super disintegrants like Cross povidon, polyvinyl pyrrolidon K30 and Micro crystalline cellulose with the help of direct compression method. Binder like hydroxy propyl methyl cellulose, Diluent like Mannitol, Lubricant like Magnesium stearate, Sweetner like Sodium saccharin were used for preparation of tablets. The composition of all nine formulation was made by using 3×3 factorial design. All the ingredient except magnesium stearate were uniformly blended, mixed and passes through #44 to get fine particles. Then finally add magnesium stearate. Mix it very well. The resultant mixture was compressed into tablets by using multitooling tablet compression machine. All the formulation F1-F9 containing 100 mg tablet were prepared.

EVALUATION OF GABAPENTINE TABLETS [13-18]

1) Weight variation

Twenty tablets were randomly selected from each batch and individually weighted. The avarage weight and standard deviation of 20 tablets was calculated. The batch passes the test for weight variation test if not more than two of the indivisual tablet weight deviate from the avarage weight.

2) Thickness uniformity

Three tablets were selected randomly from each batch and thickness were measured by using vernier caliper.

3) Hardness

Hardness or tablet crushing strength (F_o) the force required to break a tablet in a diametric compression was measured using Monsanto Harness tester.

4) Friability

Friability of the tablets was determined using friability apparatus. This device subjects the tablets to the combined effect of abrasions and shock in a plastic chember revolving at 25 rpm and dropping the tablets at a height of 6 inches in each revoluation. Preweighted sample of tablets was placed in the friabilator and were subjected to 100 revolutions. Tablets were dedusted using a sift muslin cloth and reweighted, the friability (F) is given by formula.

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F = (1- Wo/W) ×100

Where Wo is weight of the tablets before the test and W is the weight of the tablets after the best.

5) Content uniformity

The Gabapentin content in the tablet was estimated as follows.

Assay:

Standard preparation

Weigh accurately about 8 mg std Gabapentin USP working standard in 100 ml volumetric flask. Dissolve the drug in the 0.1 N Hcl. Make up volume with the 0.1 N Hcl and shake well.

Sample preparation

For this 100 mg tablet of each batch is taken which is equivalent to 8 mg std gabapentin. Triturate it very well with the help of morter and pestle one by one and then add it separately in 10 ml volumetric flask. Make up the volume with the 0.1 N Hcl. And assayed individually.

(LIMIT: NLT 95%, NMT 110%)

6) Disintegration test

The disintegration time of the tablet was determined as per Indian Pharmacopoeia monograph. The test was carried out using tablet disintegration test machine, IP standard. Tablets were placed in the test apparatus and distilled water was used as the disintegration medium. The time required to obtain complete disintegration of the tablet was noted. The electrolab disintegration apparatus was used for this test.

Temperature…… 37^oC

Std time required for buccal tablet…….. within 3 min

7) Percent water absorption

The water uptake characteristics of the loose disintegration powder allows and evaluation of both the intrinsic swelling and the wettability of the superdisintegrants water uptake and performed at room temperature. A piece of tissue paper folded twice was placed in small petridish containing 6 ml water. A tablet was put on the paper and time required for completing wetting qas0.5-2min.thw weighted tablet was weighted. Water absorption ratio was determined using following equation. % water absorptoion = $(W_b- W_a/ W_b).100$

Where, W_b is the weight after water absorption, W_a is the weight before water absorption.

8) *In-vitro* release study

The in-vitro dissolution studies were performed using type II dissolution apparatus at 100 rpm. The dissolution medium consisted of o.1 N HCl(900 ml) , maintained at 37^o C. an aliquot (5 ml)

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was withdrawn at specific time intervals and drug content was determined by UV-visible spectrophotometer at 222 nm for Gabpentin. At each time of withdrawal, 5 ml of fresh corresponding dissolution medium was replaced into the dissolution flask. It was made clear that none of the ingredients used in the buccal formulations interfered with the assay. The release studies were conducted in triplicate. The parameters of dissolution studies are given followings.

USP dissolution apparatus……. Type II (Paddle)

9) Bioadhesive strength

A modified physical balance used for the determination of the ex vivo bioadhesion strength. Fresh sheep buccal mucosa obtained from local slaughterhouse was cut into pieces, washed with distilled water followed by phosphate buffer pH 6.8. A piece of buccal mucosa was fixed to the apparatus with instant adhesive. The tablet was fixed on the sheep buccal mucosa using few drops of phosphate pH 6.8. the other side of tablet attached to a pulley. To the pulley a pan was fixed which is used to keep the weights. A beaker was weighted initially and placed to balance the weight of physical balance on the both sides. Water was poured drop wise on the other side of balance until the tablet detachment the weight o the beaker was noted and from this weight of the water is calculated. This detachment force gave the bioadhesion strength of the bucoadhesive tablet in grams.

Table 1: Composition of Gabapentin buccal tablets

Drug/Excipient	F1	F2	F3	F4	F4	F6	F7	F8	F9
Gabapentin	8	8	8	8	8	8	8	8	8
Cross providon	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
PVP K30	2	6	10	2	6	10	2	6	10
Microcrystalline cellulose	4	8	12	4	8	12	4	8	12
Hydroxy propyl methyl cellulose	6	6	6	6	6	6	6	6	6
Magnesium stearate	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Sodium saccharin	2	2	2	2	2	2	2	2	2
Mannitol	73	65	57	69	61	65	65	69	61

RESULT & DISCUSSION

In the present study, an attempt has been made to formulate and evaluate bucc tablet of Gabapentin by direct compression technique. Those tablet were evaluated for pre-compression parameters such as bulk density, tapped density, Carr's index, Hausner's Ratio and angle of repose and for post compression parameters such as hardness, weight variation, water absortion ratio disintegration time, invitro dissolution and bioadhesion studies.

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Precompression parameters of blends

The bulk density of pre-compression blends was found to be in the range of 0.626 to 0.636 g/ml, Tapped density in the range of 0.675 to 0.689 g/ml, Carr's index values were in the range of 5.5% to 7.8%. Housner's ratio in the range of 1.058 to 1.083 and Angle of repose between 31.92° to 40.43°. All the values were found to be within the prescribed limits according to the IP, thus ensuring good flow.

Post compression parameters

Thickness, Hardness and Friability The hardness of the tablet formulation was found to be in the range of 2.2 to 3.2 kg/cm^2. Thickness values were found to be in the range of 3.04 to 3.35 mm and friability values were found to be in the range of 0.53% to 0.83% which was found to be according to the I.P. limits and thus ensuring good mechanical strength to all the formulations.

Uniformity of weight

All the prepared buccal tablets of gabapentin were evaluated for weight variation. The weight of all the tablets was found to be uniform with low values of standard deviation and within the prescribed I.P. limits.

Uniformity of drug content

The values indicates uniform drug content within the tablets. The percent drug content of all the tablets was found to be in the range of 98.37% to 99.37%.

Disintegration time, water absorption study

The percent water absorption was found to be in the range of 41.57% to 53.92% which is in the I.P limits. Among the tablets prepared F1 formulation was found to be promising and has shown disintegration time 7 sec.

***In vitro* dissolution study**

In vitro dissolution studies were performed in 0.1 N Hcl buffer maintained at a temperature of 37°c at RPM of 100 in a USP II apparatus the absorbance's noted at 222 nm. The dissolution results showed gradient increases with the the increase in the concentration of the super disintegrants. Among all the formulation F1 was found to show best results with 99.98% release within 12 mins.

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Table 2: Physical Parameters of powder blend

Formulation code	Bulk Density (g/m)	Tapped Density (g/m)	Carr's Index (%)	Hausner's Ratio	Angle of Respose
F1	0.635 ± 0.0052	0.689 ± 0.005	7.8 ± 1.015	1.062 ± 0.049	36.50 ± 0.43
F2	0.630 ± 0.0023	0.678 ± 0.0029	7 ± 0.058	1.076 ± 0.006	40.43 ± 0.24
F3	0.629 ± 0.0023	0.676 ± 0.0029	6.9 ± 0.058	1.075 ± 0.006	34.37 ± 0.45
F4	0.636 ± 0.0045	0.685 ± 0.0029	7.1 ± 0.081	1.077 ± 0.009	34.19 ± 0.56
F5	0.626 ± 0.0061	0.679 ± 0.0029	7.7 ± 1.504	1.075 ± 0.007	34.07 ± 0.3
F6	0.634 ± 0.0023	0.687 ± 0.0045	7.6 ± 1.09	1.083 ± 0.005	31.92 ± 0.54
F7	0.633 ± 0.0046	0.686 ± 0.0052	7.6 ± 1.09	1.083 ± 0	33.94 ± 0.82
F8	0.633 ± 0.0075	0.680 ± 0.008	7.6 ± 1.09	1.083 ± 0	35.05 ± 0.28
F9	0.642 ± 0.0052	0.675 ± 0.008	5.5 ± 1.34	1.058 ± 0.015	32.2 ± 0.53

Table 3: Physical parameters of Gabapentin Buccal Tablet

Formulation code	Thickness (mm)	Hardness (kg/cm2)	Friability (%)	Weight Variation	% Drugs Content	Disintegration Time(sec)	Water absorption(%)
F1	3.06 ± 0.011	2.2 ± 0.03	0.67 ± 1.05	1.922 ± 0.056	99.12	7	50.41
F2	3.09 ±0.013	2.4 ± 0.02	0.62 ± 0.66	1.918 ± 0.062	98.87	19	53.92
F3	3.04 ± 0.025	3.2 ± 0.03	0.53 ± 0.61	1.986 ± 0.0046	98.87	25	49.25
F4	3.21 ± 0.028	2.8 ± 0.02	0.54 ± 0.72	2.103 ± 0.064	99.12	10	42.25
F5	3.16 ± 0.021	2.8 ± 0.02	0.83 ± 0.83	1.919 ± 0.067	99.37	10	41.57
F6	3.18 ± 0.008	2.6 ± 0.03	0.67 ± 0.75	1.893 ± 0.025	99.15	21	42.8
F7	3.35 ± 0.008	3.2 ± 0.01	0.65 ± 0.85	1.891 ± 0.0085	98.87	10	42.94
F8	3.30 ± 0.02	2.4 ± 0.01	0.68 ± 0.69	1.886 ± 0.18	99.37	19	50.76
F9	3.32 ± 0.01	2.2 ± 0.02	0.59 ± 0.61	2.028 ± 0.06	98.37	27	51.58

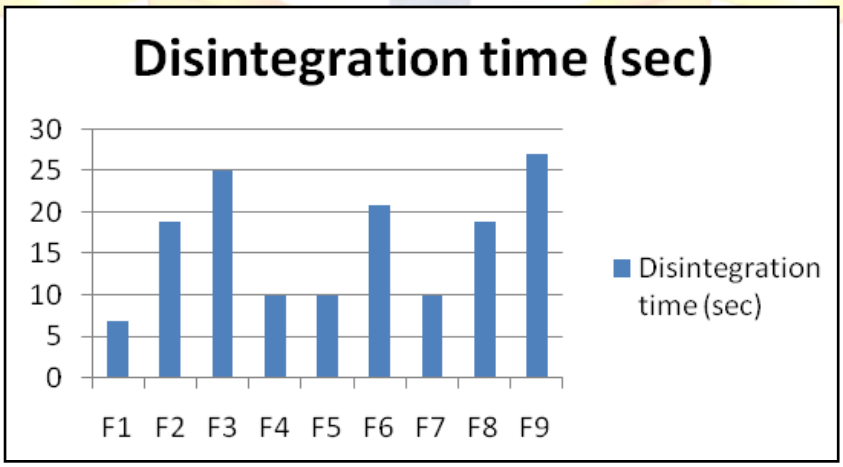

Fig. 1: Disintegration time of Gabapentin buccal tablet

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Table 3: Comparative dissolution data Gabapentin tablets

Formulation code/Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
3	39%	27.27%	21.90%	40.01%	41.34%	27.01%	41.06%	22.75%	29.1%
6	64.8%	43.63%	31.36%	61.03%	62.74%	33.21%	63.09%	36.55%	41.21%
9	89.21%	64.72%	57.07%	76.37%	74.07%	62.43%	72.22%	54.01%	54.76%
12	99.98%	87.09%	66.81%	87.43%	84.23%	70.02%	86.88%	62.61%	62.55%
15	-	91%	74.18%	100.01%	94.81%	79.27%	99.19%	76.66%	69.60%
18	-	98.99%	82.63%	-	-	86.86%	-	87.25%	76.66%
21	-	-	89.36	-	-	96.97%	-	97.67%	81.67%

Table 4: Ex-vivo Bioadhesion strength for prepared tablets

Formulation code	Bioadhesive Strength(g)	Force Of Adhesion (N)
F1	26.68 ± 0.014	2.519 ± 0.0001
F2	21.74 ± 0.028	2.508 ± 0.0007
F3	27.32 ± 0.007	2.375 ± 0
F4	26.57 ± 0.14	1.993 ± 0.02
F5	23.28 ± 0.28	2.370 ± 0.001
F6	25.21 ± 0.14	1.971 ± 0.007
F7	27.02 ± 0.28	1.993 ± 0.002
F8	24.10 ± 0.17	2.525 ± 0.001
F9	25.16 ± 0.007	2.620 ± 0.001

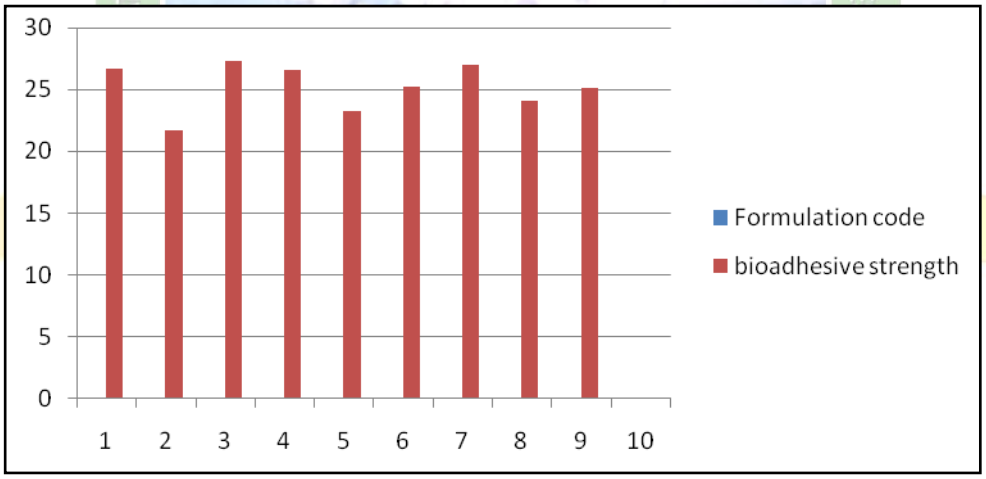

Fig. 2: Bioadhesive strength of gabapentin buccal tablet

CONCLUSION

Buccal tablets of Gabapentin were prepared by direct compression method. It was shown that with the devloped formulations, the Gabapentin release and bioadhesion properties of buccal tablet can be changed by changing the polymer concentration. The formulation F1 consist of Gabapentin (8 mg), Cross povidon (2.5mg), polyvinyl pyrrolidon K30 (2mg), Micro crystalline cellulose (4mg), hydroxy propyl methyl cellulose (6mg), Magnesium stearate (2mg), sodium

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saccharin (2.5mg) and Mannitol (quantinty required to fullfill 100 mg) were selected. Various physiochemical parameters tested for this F1 formulation showed good results. It having the disintegration time 7 sec and dissolution time is 12 min and also good bioadhesion property. It was conclude that devlopment of buccal drug delivery of Gabapentin tablets was one of the alternative routes of administration to avoid first pass effect and to improve the bioavailability of Gabapentin through buccal mucosa. In addition, these formulation reduce the need of frequent administration and improve patient complience. This finding suggested that the Gabapentin tablets have a strong potential for use as a buccal drug delivery system.

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