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ORIGINAL ARTICLE **OPEN ACCESS**

Formulation and Evaluation of Muco-Adhesive Buccal Tablets of Carvedilol

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ABSTRACT
Oral route of administration have several types. The oral route of administration having different disadvantages like hepatic first pass metabolism, degradation in GIT due to enzymes and prohibition of certain class of drug such as protein and peptides. Amongst the various routes of drug delivery buccal drug delivery is good alternative. The buccal region offers an attractive route of administration for systemic drug delivery. In the present investigation, the drug Carvedilol was selected for the design of Mucoadhesive Buccal Drug delivery System. Carvedilol is used alone or together with other medicines to treat high blood pressure (hypertension). High blood pressure adds to the workload of the heart and arteries. If it continues for a long time, the heart and arteries may not function properly. Using different concentration of drug and polymers mucoadhesive Buccal Tablet compress by direct compressional method. Different formulation (MF1 to MF9) with different concentration of polymer were prepared. All buccal tablet formulation were evaluated for different parameters like friability, weight variation, disintegration and dissolution. It was observed that formulation MF7 optimum result and also showed 99.11% drug release in 01 hour. On the basis of present work it was concluded that the drug release rate decreased with an increase the concentration of PVP K-30, HPC and Magnesium Stearate mucoadhesion property increased with increase concentration of PVP K-30.
Keywords: *Mucoadhesive, Buccal tablets, Formulation and Evaluation, Carvedilol.*

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INTRODUCTION

Amongst the various routes of drug delivery, oral route is mostly preferred by the patient. Based on our current understandings of biochemical and physiological aspects of absorption and metabolism many drugs, cannot be delivered effectively through the conventional oral route, because after administration are subjected to pre-systemic clearance extensively in liver, which often leads to a lack of significant correlation between membrane permeability, absorption and bioavailability. Buccal delivery is defined as drug administration through the mucosal membranes lining the cheeks (buccal mucosa) [1]. The oral route of drug administration is divided into several types. But this route also have some disadvantages such as hepatic first pass metabolism and enzymatic degradation within the GI tract, that prohibit oral administration of certain classes of drugs especially peptides and proteins, and buccal drug delivery is one of the a good alternative amongst the various routes of drug delivery. Within the oral mucosal cavity, the buccal region offers an attractive route of administration for systemic drug delivery [2].Buccal routes of drug delivery offer a large number of advantages over the other route of drug administration for systemic drug delivery such as bypass of first pass effect and drug directly delivered to systemic circulation, avoidance of pre-systemic elimination within the GI tract. These factors make the buccal drug delivery a very attractive and feasible site for systemic drug delivery [3].

Mucoadhesive Buccal Dosages Forms

Although the buccal mucosa as a novel drug delivery route is being widely explored recently, its potential as a route for drug delivery was known to mankind centuries ago. Modern day researchers are therefore exploring the various routes available for drug delivery, especially through the oral mucosa, and coming up with novel drug delivery systems.

Tablets

Tablets are small, flat, and oval, with a diameter of approximately 5-8 mm. Unlike conventional tablets, mucoadhesive tablets allow for drinking and speaking without major discomfort. These are placed directly onto the mucosal surface for local or systemic drug delivery. These soften, adhere to the mucosa, and are retained in position until dissolution and or release is complete. Mucoadhesive tablets, in general, have the potential to be used for controlled release drug delivery, but coupling of mucoadhesive properties to tablet has additional advantages. For example, it offers efficient absorption and enhanced bioavailability of the drugs due to a high surface-to-volume ratio and facilitates a much more intimate contact with the mucous layer. Mucoadhesive tablets can be tailored to adhere to any mucosal tissue, including those found in the stomach, thus offering the possibilities of localized as well as systemic controlled release of drugs [4, 5].

Films/Patches

Mucoadhesive films may be preferred over adhesive tablets in terms of flexibility and comfort. In addition, they can circumvent the relatively short residence time of oral gels on the mucosa, which are easily washed away and removed by saliva. Moreover, in the case of local delivery for oral diseases, the films also help protect the wound surface, thus helping to reduce pain, and treat the disease more effectively. An ideal film should be flexible, elastic, and soft, yet adequately strong to withstand breakage due to stress from mouth movements. It must also possess good mucoadhesive strength in order to be retained in the mouth for the desired duration of action [6-10].

Gels and Ointments

Semisolid dosage forms, such as gels and ointments, have the advantage of easy dispersion throughout the oral mucosa. However, drug dosing from semisolid dosage forms may not be as accurate as from tablets, patches, or films. Poor retention of the gels at the site of application has been overcome by using mucoadhesive formulations. Certain mucoadhesive polymers, for example, sodium carboxy methyl cellulose, carbopol, hyaluronic acid, and xanthan gum, undergo a phase change from liquid to semisolid. This change enhances the viscosity, which results in sustained and controlled release of drugs. Hydrogels are also a promising dosage form for buccal drug delivery [11-19].

MATERIALS AND METHOD

Carvedilol was purchased from Flagship Biotech International PVT., LTD. Thane, Maharashtra. PVP K 30 and Magnesium stearate were purchased from Doshion Pharma-polymer Division, Ahmedabad, India. HPC and Mannitol were purchased from Canton Laboratories, Mumbai, India.

Preparation of Mucoadhesive Buccal Tablet

Mucoadhesive tablets were prepared by adopting a previously established method with slight modification. Direct compression technique was applied for the tablet compression, using varying proportions of different grades of polymer. All the powders in pure form were accurately weighed. Carvedilol was then mixed with PVP K30. The remaining polymers were mixed with talc in a separate pouch. These two mixtures were then mixed for 5 min after passing through a 40 mesh sieve. HPC and Mannitol were mixed in a separate pouch for 2 min. Then it was mixed with the previous mixture for 5 min. Finally, magnesium stearate and Talc was added and the resultant mixtures were mixed and the blend was then compressed into tablets having an average weight of 100 mg, using a ten station tablet punch.

Table No.1:Table of Drug and Excipient in mg Tablet Formulation

Content	MF1	MF2	MF3	MF4	MF5	MF6	MF7	MF8	MF9
Drug	12.5	12.5	12.5	12.5	12.5	12.5	**12.5**	12.5	12.5
PVP K-30	32.5	37.5	42.5	32.5	27.5	27.5	**-**	-	-
HPC	-	-	-	-	10	20	**32.5**	37.5	32.5
Mannitol	10	10	10	10	10	10	**10**	10	10
Magnesium Stearate	30	25	20	30	25	15	**25**	20	20
Talc	15	15	15	15	15	15	**20**	20	25

Evaluation of Tablet

Pre compressional Evaluation of Blend

Melting Point

Melting point method is prime confirmation of drug. In this method temperature was noted at which point sample start melt to finish. For this drug whose analysis to be carried out was filled into capillary tube and tied in such a way that it remain dipped in liquid paraffin bath and temperature was noted.

Solubility Analyze

Solubility is the property of a solid, liquid, or gaseous chemical substance called solute to dissolve in a

solid, liquid, or gaseous solvent to form a homogeneous solution of the solute in the solvent. The solubility of a substance fundamentally depends on the solvent used as well as on temperature and pressure.

UV Spectroscopy.

Accurately weighed 10 mg of carvedilol was solubilized by 10 ml of methanol in a 100 ml volumetric flask, and phosphate buffer pH 6.8 was added to make up the volume so as to give stock solution of concentration 100 µg/ml. The standard solutions were diluted with phosphate buffer pH 6.8 to obtain various dilutions (10, 15, 20, 25, 30, 35µg/ml) in standard volumetric flasks (10 ml). The dilutions were scanned in the wavelength range of 200-400 nm. The λmax of carvedilol was found at 284 nm. The linear relationship was observed over the range of 10-35 µg/ml. Absorbances were noted at 284 nm against pH 6.8 phosphate buffer as a blank. A calibration graph of the absorbance versus the concentration of the drug was plotted and represented.

Fourier Transform Infrared (FTIR) Spectroscopy

The combination of attenuated total reflectance-FTIR imaging and nano-FTIR accompanied by chemo metrics is a potent tool to overcome the deficiency of conventional infrared detection. FTIR shows an enormous potential in drug characterization, drug quality control, and bio-sample detection.

Angle of Repose

The frictional forces in a loose powder or granules can be measured by the angle of repose. This is the maximum angle possible between the surfaces of a pile of powder or granules and the horizontal plane. Different ranges of flow ability in terms of angle of repose shown in Table 2.

Table No. 2:Predicated Flow Property of Angle of Repose

Angle of repose ,θ	Predicted flow property
25-30	Excellent
31-35	Good
36-40	Fair (Aid not needed)
41-45	Passable (May hang up)
46-55	Poor (Must agitate or vibrate)
56-65	Very poor
>66	Very very poor

Angle of Repose is calculated by given formula,

$$\mathbf{Tan\ \theta = h/r}$$

Where; h = Height of pile in cm.

r = Radius of pile in cm.

Bulk Density (pb)

Bulk density is defined as the mass of a powder divided by the bulk volume. The bulk density of a powder depends primarily on particle size distribution, particle shape and the tendency of the particles to adhere to one another.

Bulk density is calculated by given Formula

$$\mathbf{\rho b = m/\ vb}$$

Where,

ρb = Bulk density, m = Mass of powder, vb = Bulk Volume

Tapped Density (TP)

The tapped density is an increased bulk density attained after mechanically tapping a container containing the powder sample. The tapped densityis obtained bymechanically tapping a graduated measuring cylinder or vessel containing the powder sample.

Tapped Density is calculated by given Formula

Where,

$$\mathbf{\rho t = m/\ vt}$$

ρt = Tapped density , m = Mass of powder , vt = Tapped volume

Carr's Index (CI)

Compressibility is indirectly related to the relative flow rate, cohesiveness and particle size distribution of the powder. Tapped density (ρt) and bulk density (ρb) of powder material were used to measure compressibility of a powder material. It is a measure used to describe compression capability of the powder material.

Table No. 3: Table of Compressibility Index of Flow

Sr. No.	Compressibility index	Flow
1.	5-45	Excellent
2.	12-16	Good
3.	18-21	Fair to possible
4.	23-35	Poor
5.	33-38	Very poor
6.	>40	Very poor

Hausner's Ratio

It is the ratio of bulk volume to tapped volume or tapped density to bulk density. It is a measure used to describe compressibility of powder. Tapped density (ρt) and bulk density (ρb) of powder material were used to measure Hausner's Ratio of a powder material.

Hausner's Ratio is calculated by given Formula

$$\textbf{Hausner's Ratio} = \rho t/\rho b$$

Where, ρb =Bulk density, ρt = Tapped density

Post Compressional Evaluation of Tablet

Weight Variation

The test for uniformity of weight is performed by weighing individually 20 tablets randomly selected from a tablet batch and determining their individual weights. The individual weights are compared with the average weight.

Hardness

Tablets should not be too hard or too soft. An extremely hard tablet could indicate excessive bonding potential between active ingredients and excipients, which can prevent proper dissolution of the tablet needed for an accurate dosage.

Friability

Friability (the condition of being Friable) testing is a method, which is employed to determine physical strength of compressed and uncoated tablets upon exposure to mechanical shock and attrition.

Percentage Drug Content

Content uniformity testing is an important assessment for oral solid dosage (OSD) forms. Content uniformity testing sets a limit on the variance of API within each tablet

Swelling Index

From Successful batch, three tablets were individually weighed (W1) and placed separately in petri dishes with 5mL phosphate buffer of pH 6.8. At the time interval of 1, 2, 4, and 8 h, they were taken out from the petri dish and excess water was removed by using filter paper. The swollen tablets were reweighed (W2) and the percentage of hydration was calculated for each tablet.

Disintegration Time

Disintegration time was performed by apparatus specified in USP, 900 ml of 0.1 N HCl was used as disintegration medium, and the temperature was maintained at 37±2°C and the time in seconds taken for complete disintegration of the tablet, with no palpable mass remaining in the apparatus, was measured in seconds.

***In vitro* Drug Releases Studies**

An *in vitro* Drug Releases of Carvidelol from its ODT was performed by using Dissolution Rate Test Apparatus with a paddle stirrer (USP type II) at 50 rpm. 900 ml of 0.1 N HCl was used as dissolution medium which was maintained at 37±0.50C. Aliquots of dissolution medium (5 ml) were withdrawn at different time intervals of 5, 10, 15, 20, 25, 30, 40, 50 and 60 minutes and filtered through Whatmann filter paper. The sample of dissolution fluid withdrawn at each time was replaced with fresh dissolution fluid. Filtered sample solution was suitably diluted with 0.1 N HCl and the amount of drug dissolved were determined by UV spectrophotometer, by measuring the absorbance of the sample at 284 nm.

Stability studies of Carvedilol buccal tablets

The design of the formal stability studies for the drug product should be based on knowledge of the behavior and properties of the drug substance and from stability studies on the drug substance and on experience gained from clinical formulation studies. The likely changes in storage and the rationale for the selection of attributes to be tested in the formal stability studies should be stated.

Stability testing of formulation batch was carried out to determine the stability of drug and carrier and

also to determine the physical stability of formulation under accelerated storage condition at 45°C/70 % RH. The prepared tablets were placed in borosilicate screw-capped glass containers. The samples were kept at the condition of 45°C/70% RH and were analyzed at 30th and 50th days for drug content, hardness and in-vitro dissolution study.

RESULT AND DISCUSSION

Melting Point: Melting Point of Carvedilol was found in performance 113 °C

Solubility Analysis

Table No. 4:Solubility Analysis of Drug

Sr. No.	Test	Observation
1.	Methanol	Soluble
2.	Isopropanol	Sparingly soluble
3.	pH (1.2)	High Soluble
4.	pH (7.5)	Low Soluble

UV- Spectroscopy of Carvedilol

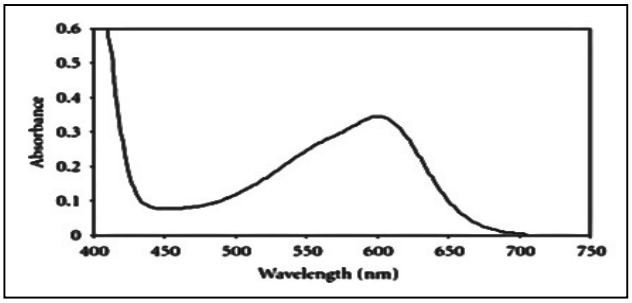

Fig. No. 1: UV-Spectra of Carvedilol

Calibration Curve of Carvedilol

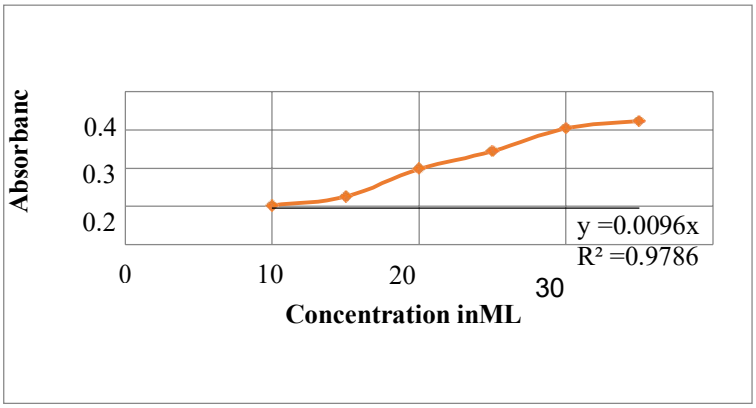

Fig. No. 2: Calibration Curve of Carvedilol

Preparation of standard calibration curve of Carvedilol

Table No. 5: Concentration and Absorbance of Calibration Curve Carvedilol

Concentration(ml)	Absorbance
10	0.103
15	0.125
20	0.198
25	0.244
30	0.304
35	0.323

FTIR Spectra of Carvedilol

Fig. No. 3: Figure of FTIR Spectra of Carvedilol

Precompression Evaluation of Powder Blend

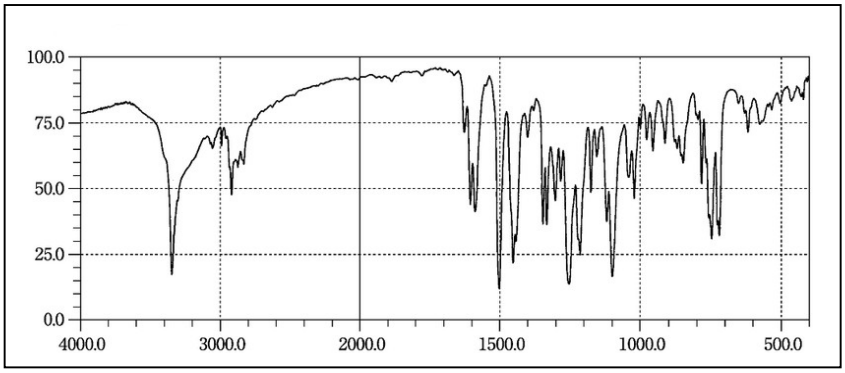

Table No. 6: Table of Pre compression Evaluation of Powder Blend

Formulation	Angle of Repose	Bulk Density (g/ml)	Tapped Density (g/ml)	Compressibility Index (%)	Hausner Ratio
MF1	22.64±0.24	0.315±0.36	0.414±0.28	34.60	1.314
MF2	23.67±0.21	0.314±0.35	0.416±0.29	24.51	1.324
MF3	25.12±0.25	0.311±0.37	0.417±0.30	74.16	1.340
MF4	21.74±0.24	0.317±0.34	0.412±0.27	76.52	1.299
MF5	20.55±0.26	0.315±0.40	0.418±0.25	33.55	1.326
MF6	23.30±0.28	0.321±0.36	0.422±0.28	33.86	1.314
MF7	26.62±0.30	0.325±0.41	0.415±0.31	78.31	1.276
MF8	21.57±0.29	0.317±0.38	0.414±0.26	76.15	1.305
MF9	20.69±0.27	0.314±0.36	0.419±0.27	74.52	1.334

Post Compressional Evaluation of Tablet

Table No. 7: Table of Post compressional Evaluation of Tablet

Formulation	Weight riation (mg)	Hardness (kg/cm)	Friability (%)	Drug Content (%)
MF1	99±2	5.54±0.18	0.34±0.10	99.43±0.24
MF2	99±2	5.82±0.25	0.32±0.15	99.24±0.34
MF3	97±3	5.26±0.20	0.17±0.05	9004±0.44
MF4	105±2	5.10±0.12	0.17±0.08	98.32±0.26
MF5	100±4	5.98±0.15	0.17±0.05	100.02±0.25
MF6	90±3	5.79±0.20	0.12±0.15	100.29±0.37
MF7	102±2	6.01±0.14	0.19±0.12	99.86±0.19
MF8	98±2	6.08±0.17	0.28±0.05	98.94±0.34
MF9	100±3	6.21±.0.18	0.12±0.15	99.72±0.55

Swelling Index

Swelling Index of successful Formulation MF7

Table No. 8: Table of swelling index of Mucoadhesive Buccal Tablet of Carvedilol

Time (h)	Percentage Swelling
	F7
0	0
1	40.21±0.08
2	49.46±0.12
4	51.43±0.06
8	52.21±0.05

Disintegration Time

Table No. 9: Table of disintegration time of Mucoadhesive Buccal tablet of Carvedilol

Formulation	Disintegration Time (min)
MF1	3.5
MF2	4.2
MF3	3.0
MF4	2.4
MF5	3.4
MF6	3.9
MF7	3.5
MF8	4.6
MF9	4.0

***In vitro* Drug Release Studies**

Table No. 10: Table of *In vitro* Drug Release Studies

Time (min)	MF1	MF2	MF3	MF4	MF5	MF6	MF7	MF8	MF9
10	26.84	31.98	33.45	23.67	33.12	32.13	37.77	30.12	32.35
20	38.83	37.13	47.98	38.43	45.56	39.27	44.32	41.56	46.48
30	57.54	59.11	65.55	59.88	61.19	45.50	52.89	58.23	70.35
40	82.43	76.98	79.12	79.91	76.37	65.20	78.98	80.45	81.12
50	92.44	88.17	91.78	86.55	89.94	89.10	92.98	90	91.78
60	96.02	98.12	99.23	98.76	99.94	90.25	99.11	93.78	97.67

***In vitro* Drug Release**

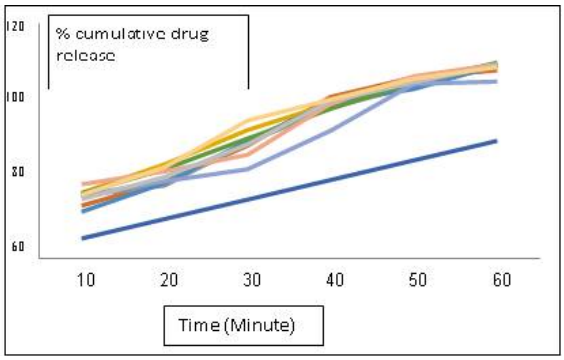

Fig. No. 4: Curve of Mucoadhesive Buccal Tablet of Carvedilol

Buccal Tablet of Carvedilol Stability Study

Table No. 11: Stability study of optimized formulation (MF7)

Time (hrs)	Appearance	Cumulative% drug release in 15 min	Drug content
Initial	White	100.10±0.22	99.21±1.17
30 days	White	99.11±0.10	95.24±1.60
60 days	White	97.88±0.25	90.10±1.11
90 days	White	96.21±0.22	88.17±1.13

DISCUSSION AND CONCLUSION

The results of the present study indicate that muco adhesive buccal tablets of Carvedilol with controlled drug release can be successfully prepared by direct compression method using PVP K-30 and HPC as Thickening Agent as mucoadhesive polymers. It exhibited well controlled and delayed release pattern. The pH of the proposed of formulation is friendly to the skin and other physicochemical properties of formulation. The Formulation F7 shows better result to compare other formulation batches. The prepared Muco adhesive Buccal Tablet was evaluated for various parameters like hardness, friability, weight Disintegration and dissolution. F7 formulation sowed 99.11 % drug release at the end 1 hrs. The Stability Study of F7 Formulation is 90 Day stable. This study concludes that, the addition of HPC increases the viscosity and swelling of tablets there by controls the release of drug and improves the muco adhesive properties.

REFERENCES

1. Mamatha, Y., Selvi, A., Prasanth, V. V., Sipai, M. A. B., & Yadav, V. (2012). Buccal drug delivery: a technical approach. Journal of Drug Delivery and Therapeutics, 2(2).26-33
2. Reddy, P. C., Chaitanya, K. S. C., & Rao, Y. M. (2011). A review on bioadhesive buccal drug delivery systems: current status of formulation and evaluation methods. DARU Journal of Pharmaceutical Sciences, 19(6), 385.
3. Shojaei, A. H., Chang, R. K., Guo, X.. (2007). Systemic drug delivery via the buccal mucosal route. Pharma Portal 25(6), 70-81.
4. Gandhi, P. A., Patel, M. R., Patel, K. R., & Patel, N. M. (2011). A review article on mucoadhesive buccal drug delivery system. International journal of pharmaceutical research and development, 3(5), 159-173.
5. Andrews, G. P., Laverty, T. P., & Jones, D. S. (2009). Mucoadhesive polymeric platforms for controlled drug delivery. European journal of pharmaceutics and biopharmaceutics, 71(3), 505-518.
6. Boddupalli, B. M., Mohammed, Z. N., Nath, R. A., & Banji, D. (2010). Mucoadhesive drug delivery system: An overview. Journal of advanced pharmaceutical technology & research, 1(4), 381.
7. Salamat-Miller, N., Chittchang, M., & Johnston, T. P. (2005). The use of mucoadhesive polymers in buccal drug delivery. Advanced drug delivery reviews, 57(11), 1666-1691.
8. Robinson, J. R., & Gandhi, R. B. (1988). Bioadhesion in drug delivery. Indian Journal of Pharmaceutical Sciences, 50(3), 145-152.
9. Gandhi, S. D., Pandya, P. R., Umbarkar, R., Tambawala, T., & Shah, M. A. (2010). Mucoadhesive drug delivery systems-An unusual maneuver for site specific drug delivery system. Int J Pharm Sci, 851-871.
10. Madhav, N. S., Shakya, A. K., Shakya, P., & Singh, K. (2009). Orotransmucosal drug delivery systems: a review. Journal of controlled release, 140(1), 2-11.
11. Vanessa Hearnden. (2011). New developments and opportunities in oral mucosal drug delivery for local and systemic disease. 2(3), 15-13
12. Shojaei A H. Buccal mucosa as a route for systemic drug delivery: a review Journal of Pharm Sci. 1998; 1(1):15-30.
13. Nazila Salamat-Miller.(2005). The use of mucoadhesive polymers in buccal drug delivery Advanced Drug Delivery Review. 3:57(11):1666-91.
14. Ahmed S, El-Setouhy DA, El-Latif Badawi AA and El-Nabarawi MA. (2010). Provesiculargranisetron hydrochloride buccal formulations. *In vitro* evaluation and preliminary investigation of in vivo performance. European Journal of Pharm. Sci. 60:10-23.
15. MILLER NS, Chittchang M, Johnston TP. (2005). The Use of Mucoadhesive Polymers in Buccal Drug Delivery. Advanced Drug Delivery. Review. 57, 1666 –1691.
16. Swarbrick James and Boylan C. Encyclopedia of Pharmaceutical Technology. IInd Edition, Vol. 2, Marcel Dekker, Inc., New York, 1990; 189-210.
17. Chien, Y. W. (1992). Novel Drug Delivery Systems, IInd edition, Revised and expanded. Marcel Dekker, Inc.,New York, Vol. 50: 8-9,197-228,
18. Rathbone, M. J. (Ed.). (1992). Oral mucosal drug delivery . Drug and Pharmaceutical sciences. II nd Edition Marcel Dekker. Inc., New York 456-457
19. Pharmacogenetics, pharmacogenomics, and personalized medicine. Introduction to Basics of Pharmacology and Toxicology: Volume 1: General and Molecular Pharmacology: Principles of Drug Action, 235-259.

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