IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

DEVELOPMENT AND EVALUATION OF A BUCCAL DRUG DELIVERY SYSTEM FOR THE ANTI-ANGINAL DRUG-NICORANDIL

[1]Sunil Firangi*, [2]Mashkura Sultana, [3]R.B.Sangoligi, [4]Dr Syed Sanaullah
[1]Associate Professor, [2]PG Student, [3]Assistant Professor, [4]Principal & HOD
Dept. of Pharmaceutics.
Luqman college of Pharmacy, Gulbarga, Karnataka, India

Abstract:
The aim of the present study was to develop buccal formulation of Nicorandil to maintain constant therapeutic levels of the drug for over period of 8hrs. Nicorandil dose was fixed as 3mg & total weight of the tablet was kept constant as 100mg.various bioadhesive polymers such as Carbopol 934 (CP), Polyvinylpyrrolidone (PVP), Polyvinylalcohol (PVA) and Ethylcellulose (EC), are used. All the formulations were passed by various physicochemical evaluation parameters and they were found to be within limits. Whereas from the dissolution studies it was evident that the formulation (F3) showed better and desired release pattern i.e.,87.83 in 8hrs and maximum drug release due to high wettability of the polymer PVP and PVA. It followed zero order release kinetics mechanism.

Index terms: **Nicorandil, Buccal tablet, Bio adhesive polymers, Zero order release kinetics.**

I. INTRODUCTION:

Buccal administration refers to an enteral route of administration by which drugs diffuse through the oral mucosa and enter directly into the bloodstream[1]. It is one of the alternate oral routes of drug administration, particularly to those drugs that undergo first-pass effect[2]. The mucoadhesive drug delivery systems uses bioadhesion property of certain polymers which on hydration become adhesive, therefore it is used as targeted drug for specific area of the body for prolonged duration of time[3].
The classifications of mucoadhesive delivery system on the basis of route of application[4]:

1. Ocular drug delivery system
2. Buccal drug delivery system
3. Gastro-intestinal drug delivery system
4. Nasal drug delivery system
5. Vaginal drug delivery system and
6. Rectal drug delivery system

Buccal administration may provide better bioavailability of some drugs and a more rapid onset of action compared to oral administration because the medication does not pass through the digestive system and thereby avoids first pass metabolism. Oral mucosal cavity is classified into three categories

1) Sublingual delivery: which is systemic delivery of drugs through the mucosal membranes lining the floor of the mouth.

2) Buccal delivery: which is drug administration through the mucosal membranes lining the buccal mucosa (cheeks), and

3) Local delivery: which is oral cavity (mouth).

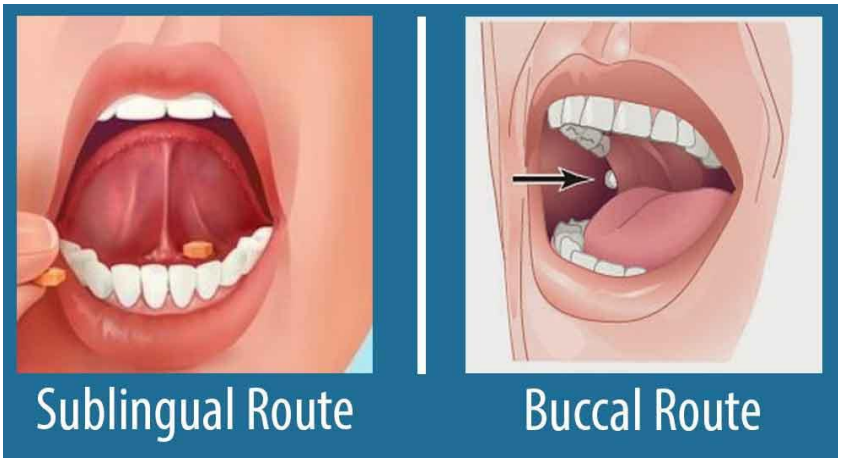

Fig 1: Sublingual & Buccal routes

Advantages of Buccal drug delivery system[5,6,7]:
1) It is richly vascularized and more accessible for the administration and removal of a dosage form.
2) It has a high patient acceptability compared to other non-oral routes of drug administration.
3) Harsh environmental factors that exist in oral delivery of a drug are circumvented by buccal delivery.
4) Avoids acid hydrolysis in the gastrointestinal (GI) tract and by passing the first-pass effect.
5) Rapid cellular recovery and achievement of a localized site on the smooth surface of the buccal mucosa.

Disadvantages of Buccal drug delivery system[5]:
1) Low permeability of the buccal membrane: specifically when compared to the sublingual membrane.
2) Smaller surface area. The total surface area of the membranes of the oral cavity available for drug absorption is 170 cm2 of which ~50 cm^2 represents non-keratinized tissues, including the buccal membrane.
3) The continuous secretion of saliva (0.5–2 l/day) leads to subsequent dilution of the drug.
4) Swallowing of saliva can also potentially lead to the loss of dissolved or suspended drug and, ultimately, the involuntary removal of the dosage form.

Limitations of Buccal drug delivery system[5,6,7]:
1) Drugs which are unstable at buccal pH cannot be administered.
2) Eating and drinking may become restricted.
3) There is an ever present possibility of the patient swallowing the dosage form.
4) Over hydration may leads to slippery surface and structural integrity of the formulation may get disrupted by this swelling and hydration of the bioadhesive polymers.
5) Drugs which irritate the mucosa or have a bitter or unpleasant taste or an obnoxious odor cannot be administered by this route.
6) Only drug with small dose requirement can be administered.
7) Only those drugs which are absorbed by passive diffusion can be administered by this route.
8) Drugs contained in the swallowed saliva follow the pre-oral and advantages of buccal route are lost.

Nicorandil is hydrophilic with a short half-life of 3-8hr. Its major side effect is ulceration with other side effects as headache & dizziness. Nicorandil is one of the emerging molecules in the case of hypertension and angina, maintenance the blood pressure at a normal physiological level, for which a constant and uniform supply of drug is desired[8,9].

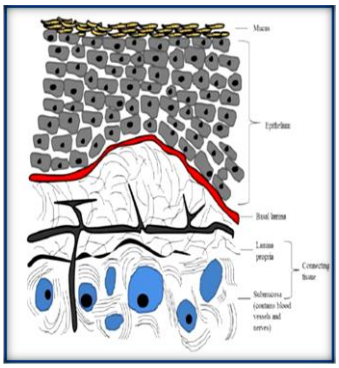

Fig 2: Structure of buccal mucosa[10]

II. Materials and Method:

Nicorandil was obtained as gift sample from Natco labs, Mumbai., Carbopol 934 & β- Cyclodextrin from Merck Specialities Pvt Ltd, Mumbai. Other excipients used in preparation were of IP grades, all other chemicals were of analytical grade and were provided by the college.

2.1 METHODOLOGY:

Analytical method development:

Procedure for standard graph of nicorandil[11]: 100mg pure drug was dissolved in pH 6.8 buffer solution and made up to 100ml in a standard flask, from this 10 ml of solution is withdrawn and made up to 100ml with to give the stock solution100 µg/ml, from this 1ml, 2ml, 3ml, 4ml and 5ml are withdrawn & transferred into a series of 10 ml volumetric flasks and final volume was made up to 10ml to get concentrations of 10, 20, 30, 40, 50 µg/ml. A blank was also prepared and the absorbance was measured at 262nm and the standard graph was plotted concentration (µg/ml) Vs Absorbance. The results are given in table 1 and figure 3.

Table 1: Standard calibration data in pH 6.8

Concentration (mcg/ml)	pH 6.8
0 mcg/ml	0.000
10 mcg/ml	0.161
20 mcg/ml	0.333
30 mcg/ml	0.503
40 mcg/ml	0.662
50 mcg/ml	0.828

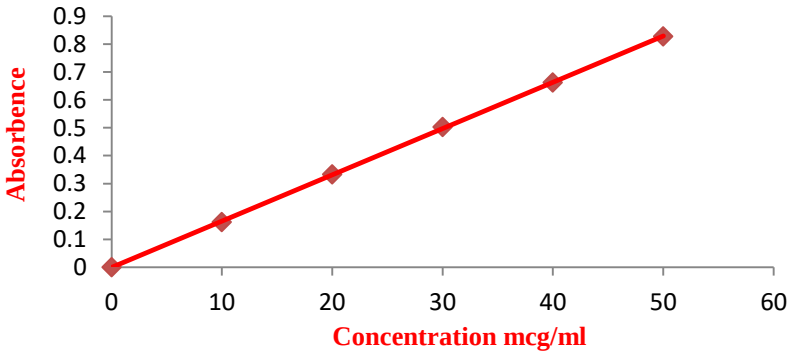

Fig 3: Standard calibration curve in pH 7.4.

Formulation of Tablets[12]

All the formulations were prepared by direct compression. The compositions of different formulations are given in the table no 2.

Table 2. Different Formulations of Nicorandil

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
Nicorandil	3 mg	3 mg	3 mg	3 mg	3 mg	3 mg	3 mg	3 mg
Carbopol-934	40 mg	30 mg	25 mg	50 mg	-	-	40 mg	-
β-Cyclodextrin	2 mg	2 mg	2 mg	2 mg	2 mg	2 mg	2 mg	2 mg
Ethyl Cellulose	30 mg	30 mg	30 mg	30 mg	30 mg	30 mg	30 mg	30 mg
PVP	20 mg	30 mg	30 mg	50 mg	-	-	40 mg	30 mg
PVA	5 mg	5 mg	10 mg	5 mg	-	10 mg	5 mg	5 mg
Mag. Stearate	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Mannitol	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Total weight	**100 mg**	**100 mg**	**100 mg**	**140 mg**	**35 mg**	**45 mg**	**120 mg**	**70 mg**

III. RESULTS AND DISCUSSION:

3.1 Pre-Compressional Parameters:

The properties/characteristics of powder blend plays an important in formulations. Table 3 shows the powder blend properties of prepared granules. Bulk density depends on particle size, shape and tendency of particles to adhere together, may influence compressibility, porosity, dissolution and other properties.

Table 3: Precompressional parameters of all the Formulations

Formulations	Angle of repose (θ)	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Carr's Index	Hausner Ratio
F1	25.11±0.02	0.49±0.04	0.54±0.04	16.21±0.06	0.86±0.06
F2	25.67±0.04	0.52±0.09	0.52±0.04	16.87±0.05	0.98±0.05
F3	25.54±0.06	0.50±0.05	0.58±0.05	17.11±0.01	0.64±0.03
F4	25.43±0.03	0.51±0.06	0.54±0.07	17.67±0.08	1.12±0.04
F5	25.34±0.07	0.52±0.03	0.57±0.03	16.92±0.04	1.2±0.08
F6	24.22±0.05	0.53±0.04	0.56±0.06	17.65±0.09	1.06±0.09
F7	25.18±0.06	0.54±0.06	0.59±0.04	16.43±0.05	0.76±0.03
F8	24.22±0.09	0.58±0.04	0.67±0.02	17.97±0.02	1.15±0.09

3.2 Post-compressional parameters:

Tablet Weight, Hardness, Friability, Drug content, Invitro drug release & Stability studies[13,14]:

All the formulations were evaluated for various parameters like Weight variation, Hardness and Friability. All the prepared tablets formulations F1 to F8 shown in Table 4, it was found that there was no much variation in thickness of tablets; it showed that powder blends was consistent in particle size and uniform behavior during tablet compression. The hardness of tablets was measured by Pfizer hardness tester. The hardness was in range of 4.4 to 4.9 Kg/cm^2. Tablet hardness reflects differences in tablet density and porosity, which showed results in difference release patterns of the drug by affecting the rate of penetration in the dissolution medium at the surface of the tablet.

Weight Variation: The weight (mg) of each of 20 individual tablets was determined by dusting each tablet off and placing it in an electronic balance. The weight data from the tablets were analyzed for sample mean and percent deviation. The results are showed in table 4.

Friability: The present study of tablets is within the limit and the slight variation in seen in friability because of the variation in compression force applied and its total weight. The friability of tablets also depends on type of filler and moisture contents present in it. The friability was found to be in the range of 0.42 to 0.60 shown in Table 4.

Drug Content: Drug content was in range of 98.34 to 99.76, which reflects good drug content uniformity in all the prepared formulations. The reading complies as per I P. which indicates drug was uniformly distributed throughout the tablet compressed shown in Table 4.

Table 4: Post-Compressional properties prepared tablets

Formulations	Average weight (mg)	Hardness (kg/cm^2)	Friability (%)	Thickness (mm)	Drug content (%)
F1	98.5	4.7	0.48	2.2	99.45
F2	101.4	4.6	0.43	2.3	99.34
F3	98.6	4.4	0.42	2.3	99.65
F4	100.6	4.8	0.45	2.2	99.76
F5	99.4	4.7	0.60	2.6	99.42
F6	100.7	4.5	0.52	2.3	98.34
F7	102.3	4.4	0.54	2.5	98.54
F8	101.2	4.9	0.52	2.3	99.62

Table 5: *In vitro* release data of formulations F1, F2, F3 & F4

Time (Hrs)	F1	F2	F3	F4
	Cumulative* percent drug released ± SD	Cumulative* percent drug released ± SD	Cumulative* percent drug released ± SD	Cumulative* percent drug released ± SD
01	28.17±0.02	18.3±0.06	28.1±0.04	29.0±0.04
02	32.0±0.04	32.0±0.02	35.6±0.02	31.0±0.05
03	40.0±0.06	34.0±0.02	42.2±0.01	39.0±0.08
04	42.0±0.02	37.6±0.04	58.2±0.06	49.1±0.06
05	44.1±0.01	44.6±0.09	59.3±0.09	55.5±0.05
06	46.8±0.04	47.0±0.05	62.2±0.05	64.5±0.02
07	52.8±0.02	53.8±0.02	78.8±0.04	71.5±0.04
08	64.8±0.06	69.3±0.06	87.8±0.02	79.0±0.08

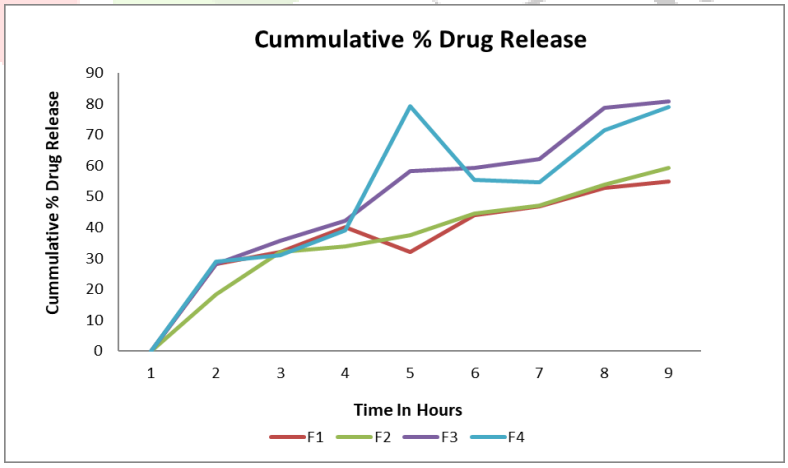

Fig 4: *In vitro* release curves of formulations F1, F2, F3 & F4

Table 6: *In vitro* release data of formulations F5, F6, F7 & F8

Time (Hrs)	F5	F6	F7	F8
	Cumulative* percent drug released ± SD	Cumulative* percent drug released ± SD	Cumulative* percent drug released ± SD	Cumulative* percent drug released ± SD
01	18.31±0.02	18.61±0.06	9.31±0.04	18.3±0.04
02	20.82±0.04	24.78±0.02	15.61±0.02	26.0±0.05
03	31.63±0.06	38.8±0.02	22.7±0.01	40.0±0.08
04	38.16±0.02	42.6±0.04	34.7±0.06	46.5±0.06
05	42.5±0.01	49.9±0.09	43.1±0.09	56.6±0.05
06	51.8±0.04	53.9±0.05	55.7±0.05	65.0±0.02
07	62.5±0.02	65.4±0.02	62.8±0.04	71.6±0.04
08	67.1 ±0.06	70.18±0.06	68.6±0.02	75.8±0.08

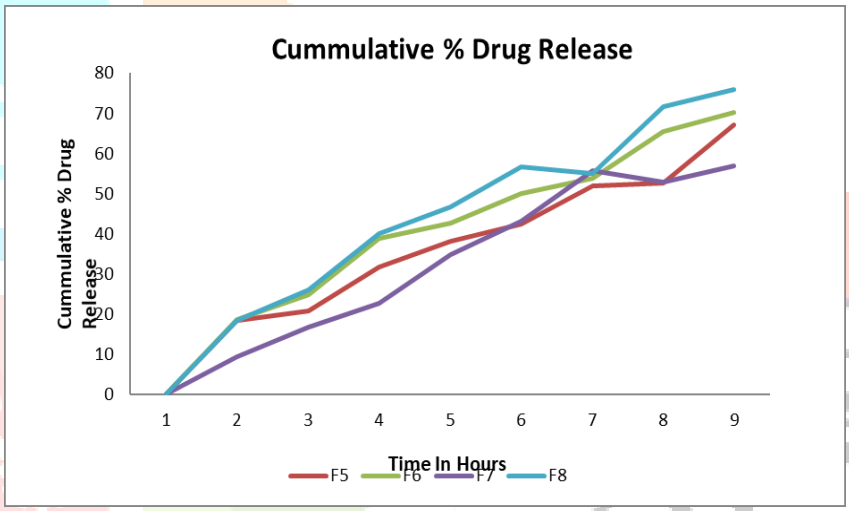

Fig 5: *In vitro* release curves of formulations F5, F6, F7 & F8

Dissolution t_{50} and t_{70} values: The dissolution t_{50} and t_{85} values for all the tablets formulations are given in table 7 & in figure 6. The comparative effect of the release profiles of drug from the tablets in terms of dissolution t_{50} and t_{70} values are shown in figure 6.

Table 7: Dissolution t_{50} and t_{70} values of various formulations of prepared tablets

Formulations	t_{50} (hr)	t_{70} (hr)
F1	7	-
F2	7	8
F3	4	7
F4	4	7
F5	6	-
F6	5	8
F7	6	7
F8	8	7

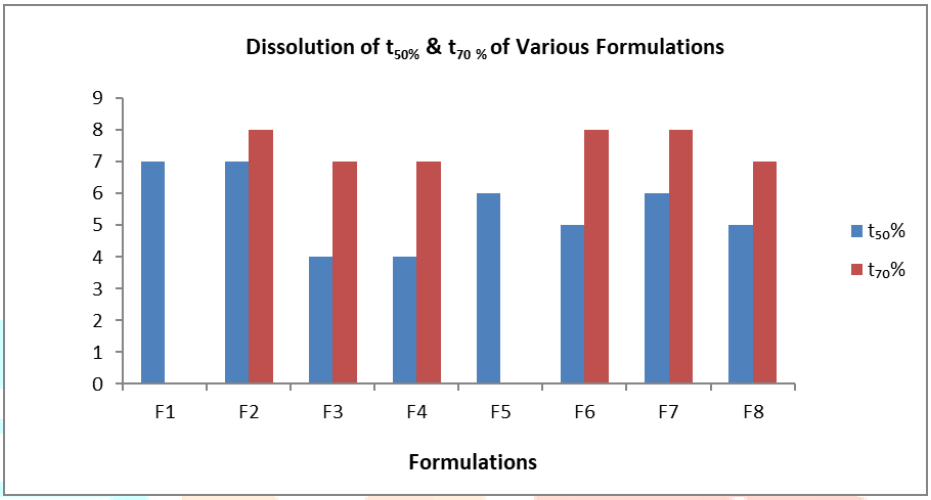

Fig 6: Dissolution t_{50} and t_{70} graph of various formulations of prepared tablets

IV. Stability Studies: Short term stability studies were performed for formulation F3 at 45^0c ± 1^0c for 3 weeks (21 days). The sample were analyzed for percent drug content and invitro drug release studies. The results are given in table 8, no appreciable difference was observed for the above parameters.

Table 8: Stability studies of Formulation F3

Sl no	Time in days	Physical changes	Mean ± SD (45° C)
1.	01	--	87.80±0.74
2.	07	No Change	87.18±0.12
3.	14	No Change	86.05±0.28
4.	21	No Change	86.04±1.10

Table-10: In Vitro release data of formulation F3

Time (Hrs)	Cumulative*percent drug released ± SD	
	45 ± 1^0 C	45 ± 1^0 C
	1st Day	21st Day
01	18.79±0.91	17.09±0.07
02	27.03±1.56	26.00±0.54
03	33.01±2.17	32.74±1.20
04	46.12±0.86	45.52±1.60
05	59.10±1.86	57.08±0.99
06	65.54±2.28	63.93±1.02
07	71.45±0.63	70.10±0.84
08	87.17±1.44	86.22±0.81

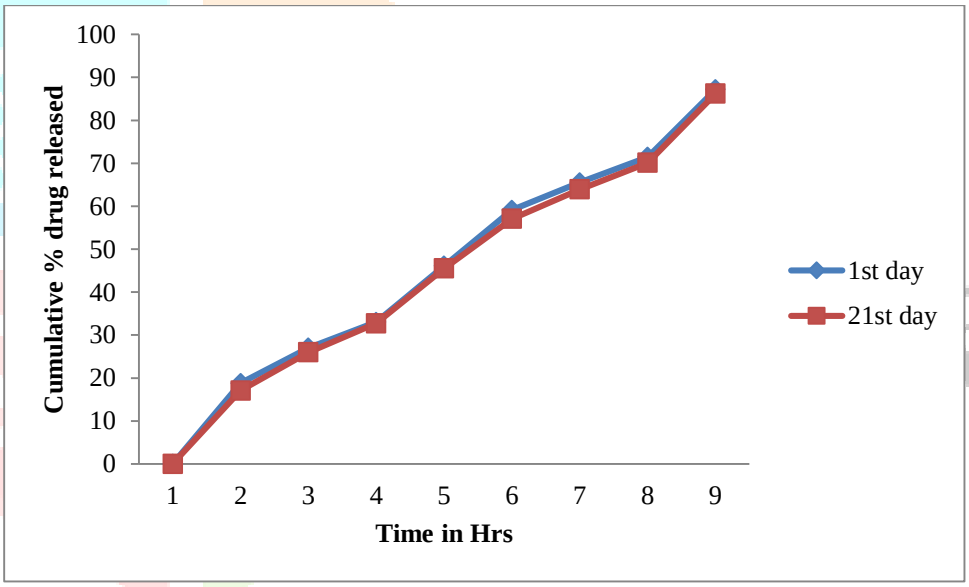

Fig 7: In Vitro release data of formulation F3

V. CONCLUSION: From study it is evident that, buccal tablets of Nicorandil can be developed using various bioadhesive polymers such as Carbopol 934, Polyvinylpyrrolidone (PVP), Polyvinyl alcohol(PVA) and Ethylcellulose (EC), for the prolonged release of the drugnicorandil to maintain constant therapeutic levels of the drug for over 8 hrs. All the prepared tablet formulations were found to be good without capping and chipping. Formulated tablets gave satisfactory results for various post-compressional parameters like hardness, friability, thickness, weight variation and content uniformity and they were found to be within limits. Whereas from the dissolution studies it was evident that the formulation (F3) showed better and desired drug release pattern i.e.,87.86 % in 8 hours and maximum drug release due to high wettability of the polymer PVP and PVA. It followed zero order release kinetics mechanism.
Short term stability studies of formulation F3 indicates there are no significant changes in the drug content and dissolution parameter value at stable at 45^0C and 75% RH for a period of 21 days.

VI. ACKNOLEDGEMENTS:

I would like to express my sincere thank to my guide Mr Sunil Firangi, Principal Dr Syed Sanaullah & Management for valuable guidance & support.

VII. REFERENCES:

[1] A.B.Sudheer, A.V.Saikishore, A.M.Sandeep, A.K.Srikanth, B.M.TejaKrishna, 2013. Design And Development Of Muco adhesive Buccal Tablets Of Metoprolol Succinate By Using Moringa Oleifera Gum: An International Journal of Advances in Pharmaceutical Sciences, 4(6): 1186-1196.
[2] Gazzi Shanker, Chegonda K. Kumar, Chandra Sekhara Rao Gonugunta, B. Vijaya Kumar and Prabhakar Reddy Veerareddy, 2009. Formulation and Evaluation of Bioadhesive Buccal Drug Delivery of Tizanidine Hydrochloride Tablets. AAPS PharmSciTech, 10, (2).
[3] LokhandeS.S, Lahoti S.S, 2012. Buccoadhesive drug delivery system: need, Asian Journal of Biomedical and Pharmaceutical Sciences, 2(14): 29-36.
[4] AsaneG.S, NirmalS.A, RasalK.B, NaikA.A, Mahadik M.S, 2008. Polymers for mucoadhesive drug delivery system: a current status. Drug Development and Industrial Pharmacy, 34:1246-1266.
[5] Parth S. Patel, Ashish M. Parmar, Nilang S. Doshi, Hardik V. Patel, Raxit R. Patel, Chetan Nayee, 2013. Buccal Drug Delivery System: A Review, Int. J. Drug Dev. & Res., 5(3): 35-48
[6] Puratchikody A, Prasanth V.V, Mathew S.T., Kumar B.A, 2011. Buccal drug delivery past, present and future: A Review, Inter J of Drug Delivery, 3, 171-184.
[7] Gandhi Pankil A, Patel K.R, Patel M.R, Patel N.M, 2011. A review article on muccoadhesive buccal drug delivery system, Inter. J. of Pharm. Res. Development, 3(5), 159-173.
[8] Leonetti G, Fruscio M, Gradnik R, Chianca R, Bolla GB, Prandi P, Zanchetti A, 1989. Nicorandil, a new vasodilator drug, in patients with essential hypertension. J Hypertens. 1989;7: S292-S293.
[9] Camm AJ, Maltz MB, 1989. A controlled single-dose study of the efficacy, dose response and duration of action of nicorandil in angina pectoris. Am J Cardiol, 20(63):61J-65J.
[10] Rao N.G, Shravani B, Reddy M.S, 2013. Overview on buccal drug delivery system. Journal of Pharmaceutical Sciences and Research, 5(4):80-88.
[11] Ishida M, Nambu N, Nagai T, 1983. Highly viscous gel ointment containing Carbopol for application to the oral mucosa. Chem Pharm Bull (Tokyo), vol 31:4561-4564.
[12] Dortunc B, Ozer L, Uyanik N, 1998. Development and in vitro evaluation of a bucco adhesive pindolol tablet formulation. Drug Dev Ind Pharm, vol 24: 281-288.
[13] Guda Aditya, Ganesh Kumar Gudas, Manasa Bingi, Subal Debnath, V.V.Rajesham, 2010. Design And Evaluation Of Controlled Release Mucoadhesive Buccal Tablets Of Lisinopril, International Journal of Current Pharmaceutical Research, Vol 2 (4): 876-920.
[14] Sunil Firangi, Ananth Rao Kulkarni, R. B. Sangoligi, Dr. S. N. Hiremath and Dr Syed Sanaullah, 2023. Formulation and In-vitro Evaluation of Controlled Release Matrix Tablets of Anti-Hypertensive Drug: Verapamil Hydrochloride, International Journal in Pharmaceutical Sciences, vol 1 (10): 1-12.