**International Journal of Pharmacy and Natural Medicines**

Journal Home Page: www.pharmaresearchlibrary.com/ijpnm

**RESEARCH ARTICLE**

# Formulation and Evaluation of Fast Dissolving Buccal Tablets of a Model Non-Dihydropyridine Calcium Channel Blocking Drug

**Mithun Bhowmick*, Nilesh Soni, Ghanshyam Sahu, Vivek Asati, Vaishali Rathi, Jagdish Rathi**

*NRI Institute of Pharmaceutical Sciences, 3, Sajjan Nagar, Raisen road, Bhopal, MP, India*

**ABSTRACT**

Hypertension is a major cause of concern not just in the elderly but also in the youngsters. In today's research of oral drug delivery systems for hypertension, tablet dosage forms are supplanted by new drug delivery system because of problems like hepatic metabolism, GI toxicity and enzymatic degradation which leads to non-compliance and ineffective therapy. These problems can be overcome by formulating the drug into fast dissolving buccal tablets for oromucosal absorption with fast onset of action and improved bioavailability. The aim of the present study was to prepare and characterize mouth dissolving tablet of Diltiazem hydrochloride using super disintegrants like (sodium starch glycolate, crosscarmellose and crosspovidone)and developing a suitable dosage form, exhibiting a maximum disintegration in the mouth in order to provide good or dispersible formulation for rapid dissolution of drug and absorption which may produce the rapid onset of action.

**Keywords:** Buccal tablets, sodium starch glycolate, crosscarmellose and crosspovidone

**ARTICLE INFO**

***Corresponding Author**
Mithun Bhowmick
NRI Institute of Pharmaceutical Sciences, Sajjan Nagar
Raisen road, Bhopal, M.P, India
MS-ID: IJPNM3627

**PAPER QR-CODE**

**ARTICLE HISTORY: Received** 15 Oct 2018, **Accepted** 24 Nov 2018, **Available Online** 15 December 2018



**Citation:** *Mithun Bhowmick, et al.* Formulation and Evaluation of Fast Dissolving Buccal Tablets of a Model Non-Dihydropyridine Calcium Channel Blocking Drug. *Int. J. Pharm. Natural Med.*, 2018, 6(2): 109-115.

**CONTENTS**



## 1. Introduction

Antihypertensive drugs like Propranolol, Metoprolol, Oxprenolol, Diltiazem hydrochloride have the oral problems like difficulty in swallowing, less oral bioavailability, first pass metabolism in conventional tablet dosage forms. To overcome such problems the antihypertensive drugs can be formulated in the form of fast disintegrating tablets where the drug is rapidly disintegrated in mouth within fraction of seconds and improves the oral

drug bioavailability. Fast disintegrating tablets can be prepared by methods like direct compression, wet granulation, sublimation, effervescent methods along with superdisintegrants to increase *in vitro* dispersion time. Some of the newer methods to formulate quick release dosage forms include Zydis, Orasolv, Flashtab, Wowtab, oraquick, Ziplet, Diltiazem hydrochloride is a Antihypertensive drug, which undergoes extensive hepatic degradation, which have poor bioavailability (40%) for overcoming this problem fast disintegrating tablets of Diltiazem hydrochloride can be formulated which avoids extensive first pass metabolism and improvement in dissolution efficacy, disintegration time which results in improvement in bioavailability. This formulation can be effectively used in case of hypertensive patients as it can be administered without the intake of water. Therefore the main objective of the present work is to develop fast disintegrating tablets for Diltiazem hydrochloride to improve bioavailability, disintegration time, dissolution efficacy and patient compliance. Hence, in the present study an attempt has been made to formulate fast disintegrating tablets of Diltiazem HCl by direct compression method using three superdisintegrants sodium starch glycolate, (SSG) crosscarmellose sodium and crospovidone, microcrystalline cellulose (MCC) as diluent with other excipients like sweetener and flavour with a view to develop a convenient means of administration to those patients suffering from difficulties in swallowing.

## 2. Materials and Methods

**Materials:** Diltiazem hydrochloride was obtained as a gift sample from Nicholas Piramal Ltd., Mumbai. Sodium starch glycolate, crosscarmellose and Crospovidone were obtained as gift sample from Signet Chemicals Ltd, Mumbai. All other chemicals and reagents used were of analytical grade.

**Methods**

**Preformulation studies:**

Preformulation testing is the first step in the rationale development of dosage forms of a drug substance. It can be defined as an investigation of physical and chemical properties of a drug substance alone and when combined with excipients. It gives extensive information to bring out good quality at high standard at which optimal dosage desired. Preformulation studies were performed on the drug (API), which included melting point determination, solubility and determination of λmax. The following preformulation studies were performed:

**1. Determination of solubility**:

Solubility of Diltiazem HCl was performed in solvents water and methanol.

**2. Determination of melting point**: Melting point of pure Diltiazem HCl was determined by open capillary method. The capillary tube was closed at one end by fusion and was filled with Diltiazem hydrochloride by repeated tapings. The capillary tube was placed in a digital melting point apparatus. The instrument was set to automatically increase the temperature of the heating bath at a rate of 100ºC min rise of temperature per minute. The rise in temperature was viewed through magnifying lens. The temperature at which the drug started melting was recorded. This was performed thrice and the average value was calculated.

**3. Determination of λmax**

A solution of Diltiazem HCl containing conc. 10µg/ml was prepared in phosphate buffer pH 6.8 and UV spectrum was taken using Shimadzu (UV-1800) spectrophotometer. The solution was scanned in the range of 200-400nm.

**Formulation development**

In this work, direct compression method with the aid of superdisintegrants was attempted for the formulation development of fast disintegrating tablets of Diltiazem HCl. The Diltiazem HCl tablets are available in 30mg, 60mg and 120mg doses in the market. Dose of 30 mg is selected for the present study. Development of the formulation in the present study was mainly based on the type and concentration of polymers and the properties of the drug. Various polymers in different concentrations were used so as to get tablets with good physical properties.

**Manufacture of Diltiazem HCl fast disintegrating Tablets**

Diltiazem HCl fast disintegrating tablets were manufactured in nine formulations DF1 to DF9 using the ingredients mentioned in the Table 4.3 keeping the total weight (200 mg) of the tablet constant in all the formulations. The drug and the excipients were passed through #60-sieve. Weighed amount of drug and excipients except magnesium stearate were mixed in a polybag by geometric addition method for 20 minutes manually. The blend was then lubricated by further mixing with magnesium sterate (#60-sieve). The mixture blend was subjected for drying to remove the moisture content at 40 to 45ºC, the mixture was blended with flavor and the powder blend was then compressed on 10-station rotary punching machine using flat faced punches. Round punches measuring 8 mm diameter were used for compression of tablets.

**Evaluation of Diltiazem HCl tablets**.

**Pre-compression parameters**

**Angle of Repose (θ)**:

The frictional force in a loose powder or granules can be measured by angle of repose. Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and horizontal plane. $\theta = \tan^{-1}(h/r)$ Where, θ is the angle of repose h is height of pile r is radius of the base of pile

**Method:**

A funnel was filled to the brim and the test sample was allowed to flow smoothly through the orifice under gravity. From the cone formed on a graph sheet was taken to measure the area of pile, thereby evaluating the flowability of the granules. Height of the pile was also measured.

**Bulk Density:**

Loose bulk density (LBD) and tapped bulk density (TBD) of Diltiazem HCl and the tablet blends were determined using bulk density apparatus. The pure drug was passed through #18 sieve to break the clumps, if any. Accurately weighed 5 g of the drug or 25 g of polymers was placed in a 100 ml graduated measuring cylinder. Initial volume was

observed. The cylinder was tapped initially 200 times from a distance of 14 ± 2 mm. The tapped volume was measured to the nearest graduated unit. The tapping was repeated additional 200 times. Again the tapped volume was measured to the nearest graduated unit. The same thing was done for powder blends of the tablets. The LBD and TBD were calculated in g per ml using following formula.

LBD = weight of the powder / volume of the packing
TBD = weight of the powder / tapped volume of the packing

**Compressibility Index (Carr's Index):**
The compressibility index of the granules was determined by carr's compressibility index.

**Hausner ratio**
The hausner ratio of the powder was determined by the following equation. Hausner ratio = TBD / LBD Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25).

**Post-compression parameters:**
The tablets after punching of every batch were evaluated for in-process and finished product quality control tests i.e. thickness, weight uniformity test, hardness, friability, drug content, *in vitro* dispersion time, water absorption ratio, wetting time and *in vitro* drug release studies.

**Thickness:**
Thickness of tablets indicates the strength to withstand compression force applied during manufacturing process. Thickness of tablets was measured by digital caliper.

**Hardness Test:**
Hardness (diametric crushing strength) is a force required to break a tablet across the diameter. The hardness of a tablet is an indication of its strength. The tablet should be stable to mechanical stress during handling and transportation. The degree of hardness varies with the different manufactures and with the different types of tablets. The hardness was tested using Monsanto tester. "Hardness factor", the average of the six determinations, was determined and reported. The force was measured in kilograms per centimeter square.

**Friability Test:** Friability is the loss of weight of tablet in the container/package, due to removal of fine particles from the surface. This in process quality control test is performed to ensure the ability of tablets to withstand the shocks during processing, handling, transportation, and shipment. Permitted friability limit is 1.0 %. Roche friabilator (Electrolab, Mumbai) was used to measure the friability of the tablets. Ten tablets were weighed collectively and placed in the chamber of the friabilator. In the friabilator, the tablets were exposed to rolling, resulting free fall of tablets (6 inches) within the chamber of the friabilator. It was rotated at a rate of 25 rpm. After 100 rotations (4 minutes), the tablets were taken out from the friabilator and intact tablets were again weighed collectively.

**Weight Uniformity Test:**
Twenty tablets were weighed individually and all together. Average weight was calculated from the total weight of all tablets. The individual weights were compared with the average weight. The percentage difference in the weight variation should be within the permissible limits (±7.5%). The total weight of tablets formulated was 200 mg.

***In vitro* dispersion Time:**
*In vitro* dispersion time was measured by dropping a tablet into a petridish containing 10 ml of phosphate buffer pH 6.8 solution (simulated saliva fluid). Three tablets from each formulation were randomly selected and tested. *In vitro* dispersion time was found and expressed in seconds.

**Wetting time and Water absorption ratio:**
Wetting time of dosage form is related with the contact angle. Wetting time of the fast disintegrating tablets is another important parameter, which needs to beassessed to give an insight into the disintegration properties of the tablets; a lower wetting time implies a quicker disintegration of the tablet. The wetting time of the tablet can be measured using a simple procedure. Two circular tissue papers of 10 cm diameter are placed in a petridish having the same inner diameter. Ten ml of phosphate buffer solution, 6.8 pH containing Eosin, a water soluble dye, is added to petridish. A tablet is carefully placed on the surface of the tissue paper so that complete tablet was not immersed in the solution. Then, the time required for buffer to reach upper surface of the tablet is noted as wetting time.

**Drug content determination:**
Calibration of Diltiazem HCl in phosphate buffer (pH6.8) solution at λmax 236

**Preparation of Buffers and Reagents**

**Sodium hydroxide solution (0.2 M):**
Eight grams of sodium hydroxide was taken in 1000 ml volumetric flask containing about 700 ml distilled water and volume was made up to the mark with distilled water.

**Potassium dihydrogen phosphate solution (0.2 M):**
27.218 g of Potassium dihydrogen phosphate was added in 1000 ml volumetric flask containing about700 ml distilled water and volume was made up to the mark with distilled water.

**Procedure for calibration of Diltiazem HCl in phosphate buffer (pH6.8) solution*:***
From stock solution, appropriate aliquots were pippetted into different volumetric flasks and volumes were made up to 10 ml with phosphate buffer (pH 6.8) solution, so as to get drug concentrations of 2, 4, 6, 8 and 10 µg/ml. The data are given in the Table 5.7 and calibration curve constructed is shown in the Fig.5.8.

**Procedure of determining drug content:** Three uncoated tablets were selected randomly and average weight was calculated. Tablets were crushed in a mortar and accurately weighed amount of tablet powder was taken from the crushed blend. Then the samples were transferred to three 100 ml volumetric flasks and were diluted up to the mark with phosphate buffer (pH 6.8) solution. The contents were shaken periodically and kept for 24 hours for solvation of drug completely. The mixtures were filtered, appropriately diluted, and absorbences were measured at λmax 236 nm against blank reference. The drug content in each tablet was calculated using the standard calibration curve of Diltiazem HCl in phosphate buffer pH 6.8 solution.

**In vitro drug release**

**Calibration of Diltiazem** HCl in phosphate buffer (pH6.8) solution at λmax 236 nm. The procedure for the calibration curve of Diltiazem HCl is same as mentioned under Drug content determination section.

**Procedure for determining In vitro drug release studies**

In vitro drug release of the samples was carried out using USP – type II dissolution apparatus (paddle type). The dissolution medium, 900 ml of phosphate buffer (pH 6.8) solution, was placed into the dissolution flask maintaining the temperature of 37±0.5ºC and rpm of 50. One tablet was placed in each flask of dissolution apparatus. The apparatus was allowed to run for 10 min. Samples measuring 5 ml were withdrawn after every 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10 min. Samples were filtered through 10 µm filter. The fresh dissolution medium was replaced every time to maintain sink condition. The collected samples were analyzed at 236 nm using dissolution medium as blank. The cumulative percentage drug release was calculated.

## 3. Results and Discussion

**Preformulation Studies**

**Determination of solubility**: Diltiazem HCl was found to be freely soluble in water and methanol.

**Determination of melting point**

The melting point of Diltiazem HCl was found to be in the range of 215ºC.

**Determination of λmax**

Wavelength of maximum absorption of Diltiazem HCl in phosphate buffer pH6.8 was found to be 236 nm**.**

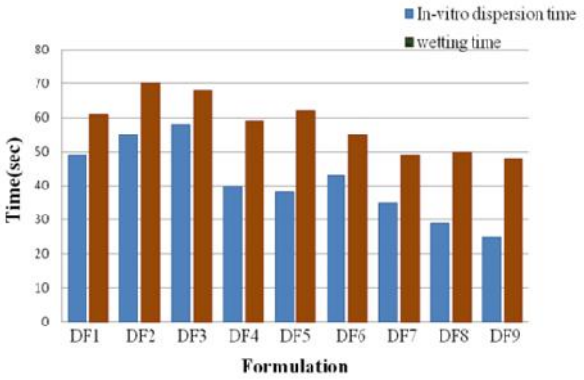


**Figure 1:** Comparison between *in vitro* dispersion time and wetting time of Diltiazem HCl tablets

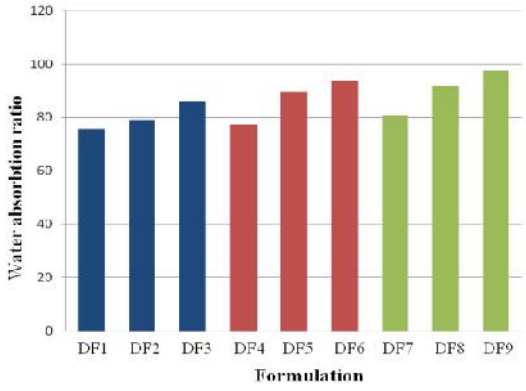


**Figure 2:** Water absorption ratio of Diltiazem HCl tablets

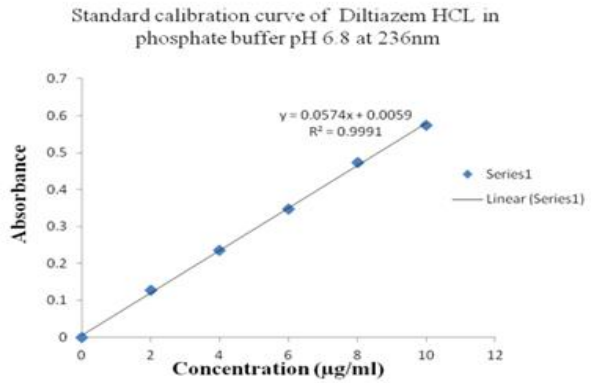


**Figure 3:** Standard calibration curve of Diltiazem HCl in phosphate buffer pH 6.8 at 236nm

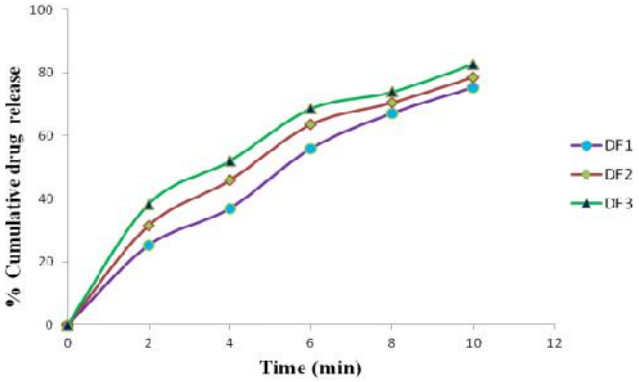


**Figure 4:** *In vitro* drug release profile of Diltiazem HCl tablets containing SSG

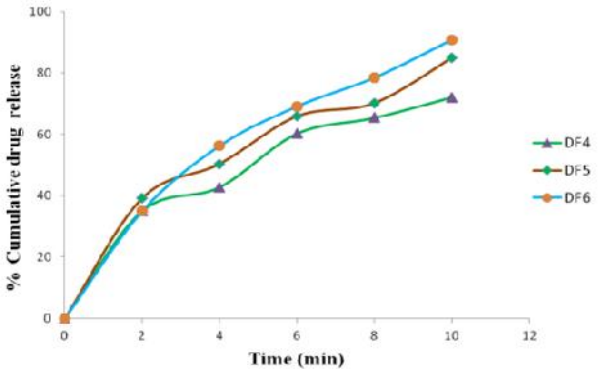


**Figure 5:** *In vitro* drug release profile of Diltiazem HCl tablets containing Crosscarmellose sodium

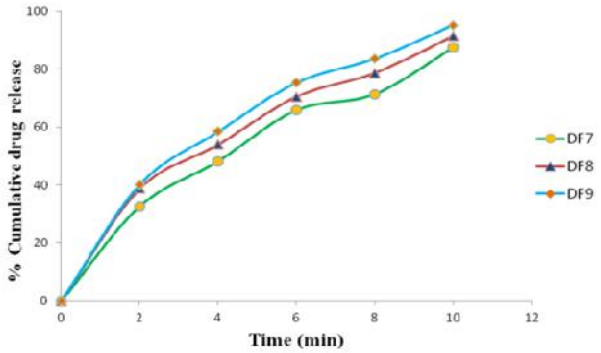


**Figure 6:** *In-vitro* drug release profile of Diltiazem HCl tablets containing Crospovidone

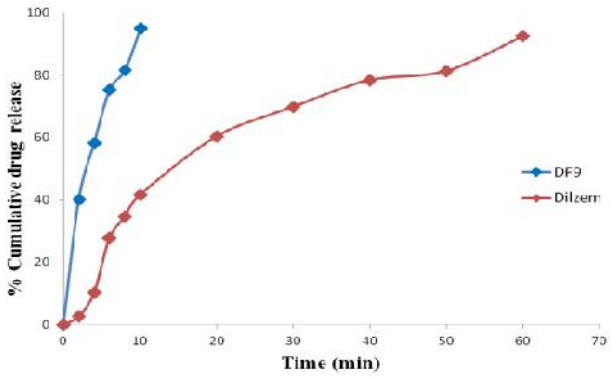


**Figure 7:** Comparison of *in vitro* drug release profile of Diltiazem HCl tablet formulation DF9 with marketed product (Dilzem)

**Discussion**

In the present study, an attempt was made to develop and evaluate fast disintegrating tablets of Diltiazem HCl (30mg) for better treatment of hypertension especially for angina pectoris condition. In general Diltiazem HCl having only 40% oral bioavailability because of high first pass metabolism rate. Thus, formulated fast disintegrating tablets of Diltiazem HCl prevents or avoids first pass metabolism and their absorption directly takes place into the saliva which results in better oral bioavailability compared to conventional Diltiazem HCl tablets.

**A. Preformulation Studies**

The solubility of Diltiazem HCl reveals that it was soluble in water and alcohol.¬ The melting point of Diltiazem HCl was found to be 215ºC, which complied with¬ BP standards thus indicating purity of obtained drug sample. In Preformulation studies, it was found that, the λmax of Diltiazem HCl by UV spectroscopic method was found at 236 nm in pH6.8 buffer. A standard calibration curve of Diltiazem HCl was made in phosphate buffer pH 6.8 by taking absorbance V/S concentration between 2-12µg/ml ranges, This complied with BP standards thus indicating purity of obtained drug.

**B. Evaluation of Diltiazem HCl fast disintegrating tablets**

**Pre-compression parameters:** Precompression parameters play an important role in improving the flow properties of pharmaceuticals especially in tablet formulation. These include angle of repose, bulk density, tapped density, carr's index and haunser ratio. Before formulation of tablets the drug and superdisintegrants were evaluated for all the above said parameters and it was found that all the observations were within the prescribed limits of IP, indicating compressibility of the tablet granules is good.

**Post-compression parameters**

**Tablet thickness and hardness**

The thickness of the tablet indicates that die fill was uniform. The thickness depends upon the size of the punch (8 mm) and the weight of the tablet (200 mg).

**Friability**

Friability is needed for tablets to withstand force of compression applied during the manufacture of tablets. The friability of all the formulated tablets of Diltiazem HCl was found to be within the official limits.(i.e. not more than 1%) of % friability.

**Weight variation**

Prepared tablets were evaluated for weight variation and percentage deviation from the average weight are reported and was found to be within (±7.5) the prescribed official limits.

***In vitro* dispersion time**

All the formulated tablets (DF1-DF9) have shown *in vitro* dispersion time of less than 60 seconds, showing that formulated Diltiazem HCl tablets were better and effective for the treatment of hypertension than conventional tablets. Among all the formulations, tablets prepared with crospovidone were shown less than 40 sec of dispersion time.

**Wetting time**

The wetting time of all the formulations (DF1-DF9) were found to be within 48- 70 seconds, which complies with the official specifications. A comparison of *in vitro* dispersion time and wetting time was shown.

**Water absorption ratio**

The water absorption ratio of all the formulated batches was found to be 75-97 % which was satisfactory in giving effective and better formulations of fast disintegrating tablets.

**Drug content**

The drug content of all the nine formulations of Diltiazem HCl tablets were found to be more than 90 % which were within the limits of BP specifications.

***In vitro* dissolution study**

Total nine formulations were formulated DF1 to DF9 by using three different superdisinegrants in varying concentrations. The formulations DF7-DF9 containing crospovidone showed more than 80% drug release. Among those three the formulation DF9 showed highest drug release of 95.72%. A comparision of optimized formulation (DF9) was made with marketed tablets (Dilzem) to show that formulated Diltiazem HCl tablets were effective and suitable than conventional tablets. The comparison of *in-vitro* drug release profile of optimized formulation (DF9) and marketed product (Dilzem) was given in results.

## 4. Conclusion

The conclusion drawn from the present investigation is given below.

- Nine batches of fast disintegrating tablets of Diltiazem HCl were successfully prepared using sodium starch glycolate, crosscarmellose and crospovidone by direct compression method.
- The tablets were evaluated for parameters like thickness, hardness, friability, in
- Vitro dispersion time, wetting time, water absorption ratio, % drug content and in- vitro drug release studies.
- Based on the results, DF9 was identified as ideal and better formulation among all formulations developed for Diltiazem HCL tablets.

- In vitro release of optimized formulation of Diltiazem HCl fast disintegrating tablets of DF9 was found to be 96.72% drug release within 10 min. with in vitro dispersion time being 25 sec.
- The final optimized formulation (DF9) was compared with marketed product of Diltiazem HCl tablets (Dilzem) which shows 91.53% drug release in 1 hr. From this observation it was concluded that the formulated tablets of Diltiazem HCl (DF9) were superior and effective in achieving patient compliance.

## 5. Reference


[1] Edwards LD, Fletcher AJ, Fox AW. Principles and practice of pharmaceutical medicine. 2nd ed. London: JohnWiley & Sons; 2007: p.7-61.

[2] Lachman L, Liberman HA, Kaing JL. The theory and practice of industrial pharmacy. 3rd ed. Bombay: Varghese publishing house; 1987: p.293-335.

[3] Liberman HA, Lachman L, Schwartz JB. Pharmaceutical dosage forms tablet volume 1. 2nd ed. New York: Marcel dekker inc; 2005 p. 75-7.

[4] Ghosh TK, Pfister WR. Drug delivery to the oral cavity molecules to market. U.S.A: Taylor and Francis group; 2005: p. 261-89.

[5] Shukla D, Chakraborty S, Singh S, Mishra B. Mouth dissolving tablets I: An overview of formunation technology. Sci Pharm 2009; 77: 309-26.

[6] Bhowmik D, Krishnakanth CB, Chandira RM. Fast dissolving tablet: An overview. J. Chem. Pharm. Res. 2009;1 (1): 163-77.

[7] Kumaresan C. Orally disintegrating tablet-rapid disintegration, sweet taste, and target release profile 2008; 6 (5).

[8] Bhaskaran S, Narmada GV. Orally disintegrating tablets. Indian Pharmacist 2002; 1 (2): 9-12.

[9] Swarbrick, J, Boylan J. Encyclopedia of Pharmaceutical technology, 2nd ed. New York (NY): Marcel Dekker; 2002: p. 2623-38.

[10] Mishra DN, Bindal M, Singh SK, Kumar SGV. Rapidly disintegrating tablets of Valdecoxib. Indian Drugs 2005; 42: 685-7.

[11] http://www.pharmpedia.com

[12] Hirwaiker AA, Ramesh M, Fast disintegrating tablets of Atenolol by dry granulation method. Indian J. Pharm. Sci 2004; 66: 422-6.

[13] Devi VK, Asha AN, *et al.* Oral dispersible Fluconazole tablets - preparation and evaluation. Indian drugs 2006; 43 (7): 548-52.

[14] Mahajan HS, Kuchekar BS, *et al.* Mouth dissolve tablets of Sumatriptan Succinate. Ind. J. Pharm. Sci. 2004; 238- 40.

[15] Gandhi BR, Mundada AS, Gandhi KR. Evaluation of kyron T-314 as a novel super disintegrants.Int. J.Drug Delivery 3(2011) 109 – 114.

[16] Patel NV, Chotai NP, Patel MP. Formulation designs of oxcarbazepine fast release tablets prepare by melt granulation technique. Asian J Pharm.2008: 22-5.

[17] Udhav S, Bagul et al. Manufacturing Technologies for Mouth Dissolving Tablets. Phrmainfo. net.2006:1-7

[18] Chaudhari PD, Chaudhari SP, Lanke SD, Patel N. Formulation and in-vitro evaluation of taste masked Orodispersible dosage form of lavocetirizine dihydrochloride. Ind J Pharm Educ Res. 2007; 42(4): 319-27.

[19] Abdelbary G, Prinderre.P, Eouani C, Joachim J, Reynier JP. Determination of in vitro disintegration profile of rapidly disintegrated tablet and correlation with oral disintegration. Int J Pharm. 2005; 292: 29-41.

[20] Prabhu NB, Rao L, Amin PD. Studies of taste masking drotaverine hydrochloride and its formulation. Ind Drugs. 2007; 44(11): 848-51.

[21] Chakraboty S, Khandai M, Singh PS. Comparative study of effect of natural and synthetic superdisintegrants in formulation of fast dissolve tablets. Int J Green Pharmacy. 2008; 2(1): 22-5.

[22] Devi VK, Asha AN, Pal RS, Reddy MCH. Orodispersible fluconazole tablets – preparation and evaluation. Ind Drugs. 2006; 43(7): 548-52.

[23] Debjit B, Jayakar B, Sampath KK. Design and characterization of fast dissolving tablets of Telmisartan. Int. J. Pharma Recent Res. 2009,1(1),31-40.

[24] Mulla JA, Dasankoppa FS, Villas GJ, Sholapur HP. Fast dissolving tablet of promethazine: A novel oral formulation for the treatment of fractionated radiotherapy – induced nausea and emesis. Ind Drugs. 2008; 45(4): 314-7.

[25] Jacob S, Shirwalkar AA, Joseph A, Srinivasan KK. Novel co-processed excipients and microcrystalline cellulose for preparing fast dissolving tablets of Glipizide. Ind J Pharm Sci. 2008; 69(5): 633-9.

[26] Lalla JK, Mamania HM, Fast dissolving Rofecoxib tablet. Ind J Pharm Sci. 2004; 66(3): 350-3.

[27] Chaudhari PD, Chaudhari SP, Kolhes R, Dave KV and More DM. Formulation and evaluation fast dissolving tablets of famotidine. Ind Drugs. 2005; 42(10): 641-9.

[28] Zhao NA, Larry LA. Studied functionality comparison of three classes of superdisintegrants in promoting aspirin tablet disintegration and dissolution. AAPS Pharm Sci Tech. 2005; 6(4): 634-40.

[29] Patel DM, Patel MM. Optimization of fast dissolving tablets prepare by sublimation technique. Ind J Pharm Sci. 2008; 70(1): 71-6.

[30] Mishra DN, Bindal M, Singh SK, Kumar SGV. Rapidly disintegrating oral tablets of valdecoxib. Ind Drugs. 2005; 42(10): 685-91.

[31] Nandgude TD, Saifee M, Bhise KS. Formulation and evaluation of fast disintegrating tablets of diphenhydramine tannate. Asian. J. Pharm. 2006; 1(1): 41-5.

[32] Raghavendra Rao NG, Upendra Kulkarni. Development of fast dissolving tablets of Carbamazepine by solid dispersion technique. Asian J of Pharma and Clinical Res (AJPCR). Vol.3 Issue 2, April -June 2010, Page No, 114 - 117.

[33] Shetty CM, Prasad DV, Gupta RM. Development of fast dispersible aceclofenac tablets: Effect of functionality of superdisintegrants. Ind J Pharm Sci. 2008; 70 (2): 180-5.

[34] Adamo F, Valentina B, Ceschel GC, Celestino R. Fast dispersible / slow releasing ibuprofen tablets. Eur J Pharm Bio. 2008; 69: 335-41.

[35] Sharma S, Gupta GD, Jain CP, Naruka PS. Development and evaluation of carvedilol fast dissolving tablets using superdisintegrants and solid dispersion technique. The Pharma Review. 2007: 159-62.

[36] Shishu, Bhatti A, Singh T. Preparation of tablets rapidly disintegrating in saliva containing bitter taste-asked granules by compression method. Ind J Pharm. sci. 2007; 69 (1): 80-4.

[37] Swamy PV, Prashant A. Borgaonkar, Shrisand SB. Effect of dispersants on the dissolution of amoxicillin trihydrate from capsule formulation. The Pharma Review. 2008: 135-8.

[38] Patil JS, Pandya NR, Marapur SC, Shirla shetty SS. Preparation of nimodipine inclusion complexes; a comparative study. Int. J. Pharmacy and pharmaceutical sciences. 2010; 2 (1): 71- 81.

[39] Rao TV, Vidhyadhara S. Formulation and evaluation of mouth dispersible tablets of simvastatin by direct compression technique. The Pharma Review. 2008: 137-9.

[40] Takao M, Yoshinori M, Takeshi Y, Katsuhide T. Formulation design of novel fast-disintegrating tablets. Int J Pharm. 2005; 306: 83-90.

[41] Patel DM, Patel NM, Shah RR, Jogani PD and Balapatel A. Studies in formulation of Orodispersible tablets of rofecoxib. Ind J Pharm Sci. 2004; 66(5): 621-5.

[42] Swamy PV, Areefulla SH, Shirand SB, Gandra S, Prashant B. Orodispersible tablets of meloxicam using disintegrant blend for improved efficacy. Ind J Pharm Sci. 2007; 69(6): 836-40.

[43] Seong Hoon Jeong, Park K. Development of sustain release fast-disintegrating tablets using various polymer coated ion-exchange resin complexes. Int j Pharm. 2008; 353: 195-204.

[44] Desai SA, Kharade SV, Petkar KC and Kuchekar BS. orodissolving tablets of promethazine hydrochloride. Ind J Pharm Educ Res. 2006; 40(3): 172-4.

[45] Rampure MV, Raju SA, Shirsand SB, Swamy PV and Nagendrakumar. Rapidly disintegrating oral tablets of alfuzosin. The Pharma Review. 2008: 140-2.

[46] Kuchekar BS, Badhan AC, Mahajan HS, Mouth dissolving tablets of salbutamol sulphate: A novel drug delivery system. Ind drugs.2004 41.

[47] Cirri M, Righi FM, Francesca Maestrelli, Paola Mura, Maurizia Valleri. Development of glyburide fast dissolving tablets based on the combined use of cyclodextrins and polymers. Drug Develop Ind Pharmacy 2009; 35(1): 73-82.

[48] Raghavendra Rao NG, Patel T, Gandhi S. Development and evaluation of carbamazepine fast dissolving tablets prepared with complexes by direct compression technique. Asian J Pharm. 2009; 3(3): 97-103.

[49] Jacob S, Shirwalkar A. Preparation and evaluation of microencapsulated fast melt tablets of ambroxol hydrochloride. Ind J Pharm Sci. 2009; 71(3): 276-84.

[50] Deshmukh SS, Potnis VV, Mahaparale PR, Kasture PV and Gharge VS. Development and evaluation of ziprasidone hydrochloride fast disintegrating/ dissolving tablets using complexation techniques. Ind J Pharm Educ Res. 2009; 43(3): 300-7.

[51] Sheeba FR, Gilesh DA. Formulation and evaluation of Nifedipine sublingual tablets. Asian J Pharm. and Clinical Res. 2009; 2(3): 44-48.

[52] http:// www.rxlist.com. Accessed on June 2007.

[53] Tripathi KD. Esssential of medical pharmacology. 5th ed. New Delhi: Jaype Brothers Medical Publishers (P) Ltd; 2004 p.334-3.