AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

Formulation and Evaluation of Pantoprazole and Domperidone Mouth Dissolving Tablet Using Different Superdisintegrants

T.Mallamma*[1], Snehalatha[1], T.S.Nagaraja[1], T.Vyjayanthimala[1].

1. S.J.M.College of Pharmacy,Chitradurga, Karnataka.

ABSTRACT

The purpose of this research was to develop mouth dissolve tablets ofdomperidone andpantoprazole, were prepared by direct compression technique. Pantoprazole inhabits gastric acid formation and thereby it is very efficient for the treatment of gastric and duodenum ulcers. Domperidone, an antiemetic drug, has been used as an add-on treatment in adults and children. The tablets were prepared using microcrystalline cellulose as diluent and aspartames as sweetening agent along with three different levels of disintegrant. The superdisintegrant used in this study were CCS and SSG. The tablets were evaluated for weight variation, hardness, friability, wetting time, water absorption ratio, disintegration time (DT) and dissolution study. formulation prepared with 30% of CCS showed Disintegration time of 20seconds in vitro. Also the hardness, friability, dissolution rate of prepared tablets (batch F6) were found to be acceptable according to standard limits.

Keywords: pantoprazole, Domperidone, Superdisintegrants, melt in mouth tablet, Direct compression.

*Corresponding Author Email: mallammareddy89@gmail.com

Received 1 April 2013, Accepted 15 April 2013

Please cite this article in press as: Mallamma T. *et al.*, Formulation and Evaluation of Pantoprazole and Domperidone Mouth Dissolving Tablet Using Different Superdisintegrants. American Journal of PharmTech Research 2013.

INTRODUCTION

Orally disintegrating tablets contain a wide variety of pharmaceutical actives covering many therapeutic categories and can be particularly good applications for paediatric and geriatric treatments. The time for disintegration of orally disintegrating tablets is generally considered to be less than one minute, although patients can experience actual oral disintegration times that typically range from 5-30 seconds. Orally disintegrating tablets are characterized by high porosity, low density, and low hardness[1]..

Fast dissolve, quick dissolve, rapid melt, quick disintegrating, mouth dissolving, orally disintegrating, orodispersible, melt-in-mouth, tablets etc are some of the terms which are used to refer to this unique form of drug delivery, which has many advantages over the conventional oral solid dosage forms.[2]

FDTs can be prepared by different methods as direct compression, freeze-drying, spray drying, sublimation and wet granulation method[3].

The mouth dissolving tablets (MDT) or ODTs by overcoming the drawback associated with conventional tablets. These tablets disintegrate/dissolve/ disperse in saliva within few seconds.[4]USFDA has defined ODTs tablet as ―A solid dosage form containing medicinal substances, which disintegrate rapidly, usually within a matter of seconds, when placed upon the tongue".

To obviate the problems associated with conventional dosage forms, orally fast disintegrating tablets have been developed, which combine hardness, dosage uniformity, stability and other parameters, with extremely easy administration, since no water is required for swallowing the tablets and they are thus suitable for geriatric, pediatric and travelling patients.[5].

Domperidone is widely used anti-emetic drug acting by an inhibition of the dopaminergic receptor. Domperidone does not cross blood brain barrier. Domperidone is also effective in gastroparesis, paediatric gastroesophageal reflux (infant vomiting). Domperidone after oral dosing undergoes extensive gastric and hepatic first pass metabolism resulting in low bioavaibility (15%) which therefore, may not minimize the rate of vomiting[6].Domperidone facilitates gastric emptying and decreases small bowel transit time by increasing esophageal and gastric peristalsis and by lowering esophageal sphincter pressure.[7]*.

Attempts were made to enhance dissolution rate along with faster disintegration using superdisintegrants like, Sodium starch glycolate (SSG) and Crosscarmellose Sodium in the formulation of tablets. Two model drugs, with poor aqueous solubility pentaprazole and

Domperidone were selected for the studies. pantaprazole (a proton pump inhibitor) is used in treatment of ulcers and reflux oseophagitis and Domperidone (prokinetic and antiemetic properties) is used for relief on nausea and vomiting of any cause, uremia and reflux oesophagitis.[8]

MATERIALS AND METHODS

Pantoprazole and Domperidone BP were obtained as gift sample by Torrent Pharmaceutical Ltd., Ahmadabad, India. Microcrystalline Cellulose, Crosscarmellose Sodium and Sodium starch glycolate were also obtained from man pharmaceuticals Ltd. Mehsana. All other chemicals used were of suitable analytical grade.

METHODS:

Pantopraozle sodium & Domperidone ODT where prepared by Direct Compression method. All the formulations contained 20 mg of pantoprazole and 30 mg of Domperidone and by using different superdisintegrants in different concentrations ranging from 10% to 30% and 4% of Aspartames. Various batches prepared shown in (Table 1).

All the ingredients were passed through 60-mesh sieve separately and collected, finally compressed into tablets after lubrication with magnesium stearate (1.5%) and talc (2.5%) by using 8 mm flat bivel edged punch using RIMEK 8 station tablet compression machine. The mixture was compressed into 200-mg tablets. **The prepared tablets were evaluated for various parameters like hardness, friability, wetting time, uniformity of dispersion, disintegration time, dissolution study.[9 10]**

Table 1: It shows the batches prepared using different concentration of each disintegrant.

Ingredients(mg)	F1	F2	F3	F4	F5	F6
Pantoprazole	20	20	20	20	20	20
Domperidone	30	30	30	30	30	30
MCC	114	94	74	114	94	74
SSG	20	40	60	_	_	-
CCS	_	_	_	20	40	60
Aspartamate	8	8	8	8	8	8
Talc	5	5	5	5	5	5
Magnesium stearate	3	3	3	3	3	3

Evaluation of the granules:[11]

Angle of repose:[12]

The angle of repose of granules was determined by the funnel method. The accurately weighed granules were taken in a funnel. The height of the funnel was adjusted in such away that the tip of the funnel just touched the apex of the heap of the granules. The granules were allowed to

flow through the funnel freely onto the surface. The diameter of the powder cone was measured & angle of repose was calculated using the following equation:

$$\tan\varphi = h/r$$

where, h & r are the height & radius of the powder cone.

Bulk density:[13]

Both loose bulk density (LBD) & tapped bulk density (TBD) were determined. A quantity of 2 g of powder from each formula, previously lightly shaken to break any agglomerates formed, was introduced into a 10 ml measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2 second intervals. The tapping was continued until no further change in the volume was noted. LBD & TBD

were calculated using the following formulas:

LBD = weight of the powder / volume of the packing

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

Compressibility Index:[14]

The compressibility index of the granules was determined by Carr's compressibility Index:

Carr's index (%) = [(TBD – LBD) * 100] / TBD

Where: LBD = weight of the powder / volume of the packing

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

Evaluation of the prepared tablets [15,16]

Weight uniformity

Twenty randomly selected tablets were weighed individually and the average weight and the standard deviation were calculated.

Hardness

Hardness of the tablets was measured using Monsanto hardness tester.

Friability

Friability of the tablets was determined using Roche friabilitor at 25 rpm/min for 4 min. Twenty tablets were weighed and loss in weight (%) was calculated.

Wetting time and water absorption ratio [17]

Procedures similar to those used by Bi Y. *et al*. were used to measure tablet wetting time and water absorption ratio. A piece of tissue paper folded twice was placed in a small culture dish (i.d. = 6.5 cm) containing 6 ml of water. A tablet was placed on the paper, and the time for complete wetting was measured. The wetted tablet was again weighed. Water absorption ratio, *R*,

was calculated using the formula;

$$R = 100(W_a - W_b)/W_b$$

Where, Wa and W b are the weight after and before water absorption, respectively.

Disintegration time (*in vitro*)

The disintegration time for six tablets was measured, and the average time and standard deviation were calculated for each. Three batches for each disintegrant SSG, CCS with varying concentration were prepared and analyzed..

Dissolution studies [18]

For the dissolution studies, dissolution apparatus USP type II used for drug pantoprazole and drug Domperidone. One tablet was placed in each basket, Paddles rotated at 100 rpm in 900 ml o the dissolution medium (0.1 N HCl at37+0.5^0 C). The samples were withdrawn at suitable time interval. Samples were assayed by HPLC.

RESULTS AND DISCUSSION

Physical properties of the formulation

The prepared tablets were evaluated for physical parameters such as, hardness was 2-4 kg/cm^{2}and friability was observed between 0.36-0.81%, which was below 1% indicating the sufficient mechanical integrity and strength of the prepared tablets. (Table 2). Percent weight variation was observed between 1.8 and 3.6,well within the acceptable limit as per USP Wetting time and water absorption ratio was determined using the method described by Bi *et al.* (Table 2). The results obtained by evaluating the powder blends of drug and excipients is shown in (Table 3). Values for angle of repose were found in the range of 24 to 27° showing that the blend of powder was free flowing and can be used for direct compression. The value for Carr's index was less than 1, indicating that all the batches of powder blends were having good compressibility. Lower HR(<1.25) indicates better flow properties than higher ones(>1.25).The result of in vitro disintegration of all the tablets were found to be within prescribed limit a satisfy the criteria of Fast Dissolving Tablet. All the formulated tablets have shown in vitro dispersion time of less than 60sec,Among all the formulations, F6 formulation prepared with Crosscarmellose were shows20sec. of dispersion time. The drug release profile of pantoprazole and Domperidone with SSG & CCS shows peppas model fitting(figure:1) and matrix model fitting (figure :3)also its dissolution profile is shown in(figure:2) and (figure:4).The comparison between the wetting time & disintegration time of all the formulation is showed in (figure:5). There was no significant variation in the physicochemical parameters, in vitro

disintegration time, and in vitro dissolution profiles after 1.5 months stability (table 4) study as per ICH guidelines Q1C.It was observed that formulations F1, F2 and F3 containing sodium starch glycolate had higher water absorption ratio and take more time for wetting of tablets (Table 2). crosscarmelose had less wetting time and minimum water absorption ratio for hydrophilic combination of pantoprazole and Domperidone. The disintegration times for formulation F1-F6 was compared (Table 2), that indicates the formulation (F6) containing crosscarmelose (60 mg) disintegrated the fastest with no mass left and had good hardness.

Table 2 - It shows the physical parameters of prepared formulation:

Formulation	Hardness Test (Kg/cm2)	Friability Test(%)	Weight Variation Test	Drug Content uniformity	Disintegration Time Sec	Wetting Time sec	Water Absorption ratio
F1	3.2	0.42±0.13	1.8±0.3	107.34	34	58	35±0.56
F2	3.1	0.51±0.33	2.1±0.4	84.69	28	60	45±0.49
F3	2.8	0.72±0.45	3.1±0.1	104.5	32	56	39±0.78
F4	3.3	0.36±0.43	1.9±0.9	92.45	29	54	46±0.67
F5	2.8	0.49±0.21	3.2±0.4	89.67	24	58	49±0.89
F6	2.7	0.33±0.78	3.1±0.5	96.08	20	50	36±0.98

***mean**±SD, n=3(all the values are the average of three determinations)

Table 3 :**Pre compression evaluation parameters**

Formulation code	Angle of repose	LBD	TBD	Carrs index	HR	Test for dispersion
F1	26.71	0.57	0.65	12.30	1.14	Passes
F2	29.35	0.60	0.70	14.28	1.16	Passes
F3	24.89	0.58	0.67	13.43	1.15	Passes
F4	25.23	0.61	0.71	14.08	1.16	Passes
F5	23.32	0.59	0.67	11.94	1.13	Passes
F6	29.51	0.62	0.73	13.69	1.17	Passes

mean±SD,n=3(all the values are the average of three determinations)

Table 4: stability data of selected formulation (F6).

Formulation code	Time (Days)	parameters					
		Hardness $(Kg/cm)^2$	Friability	Disintegration Time (sec)	Drug content	wetting time	Dissolution studies
F6	15 days	2.73	0.39	19.3	97	56.9	95.6
F6	30 days	2.84	0.45	18.5	97.4	51.2	94.3
F6	45 days	2.92	0.53	18	96.5	50.5	91.8

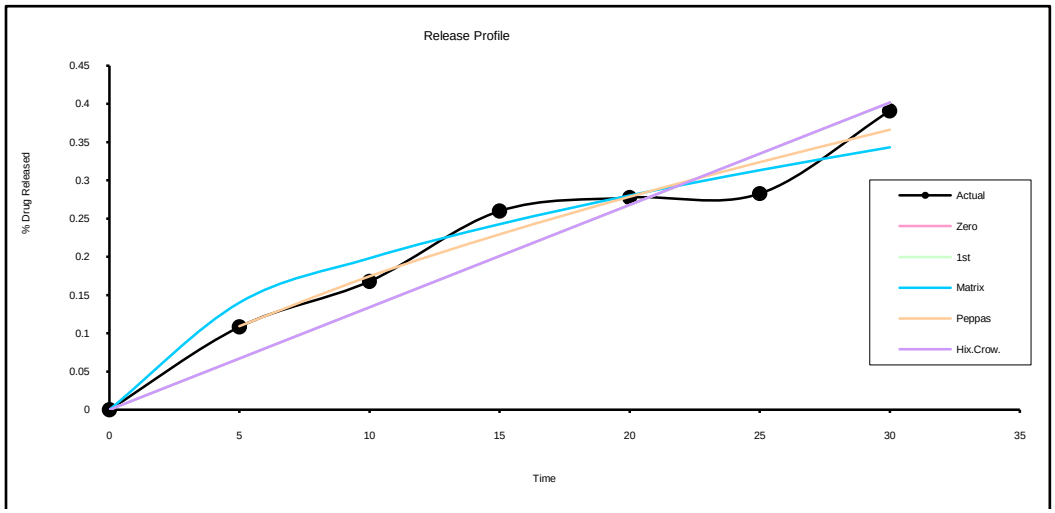

Figure 1:Drug release profile for pantoprazole with SSG and CCS (peppas model)

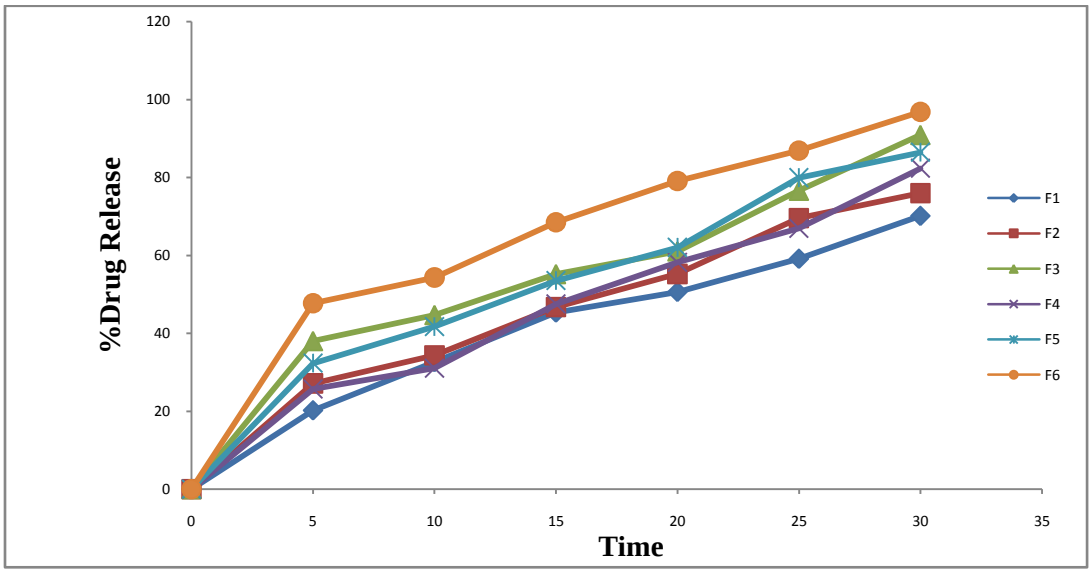

Figure 2:Dissolution profile for pantoprazole using CCS and SSG.

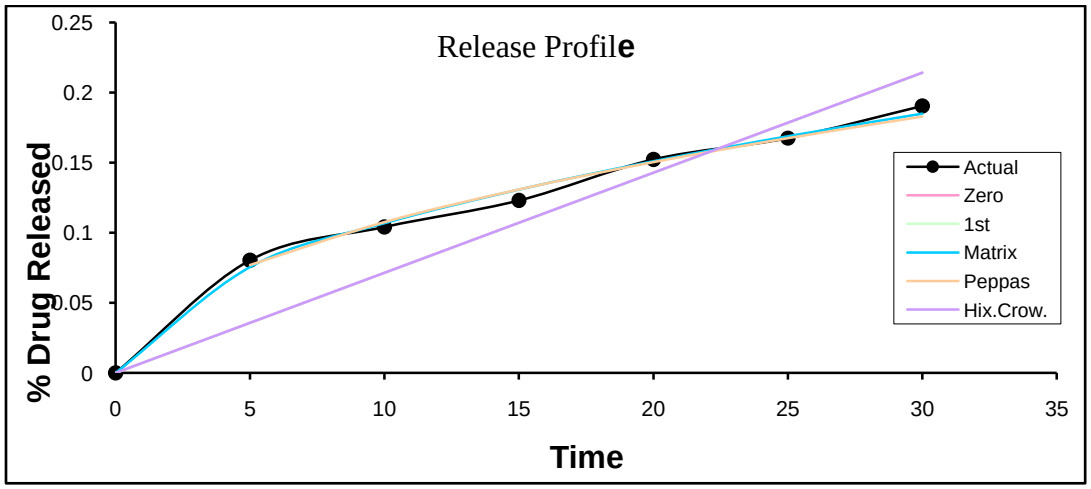

Figure 3:Drug Release profile for Domperidone using CCS and SSG(Martix model)

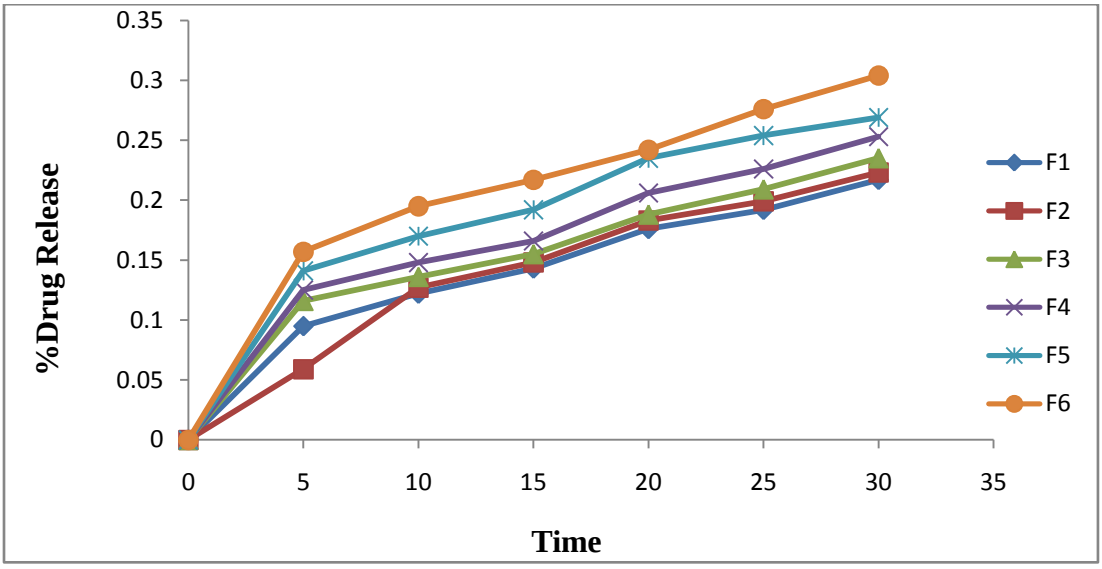

Figure 4: Dissolution profile for Domperidone using SSG and CCS:

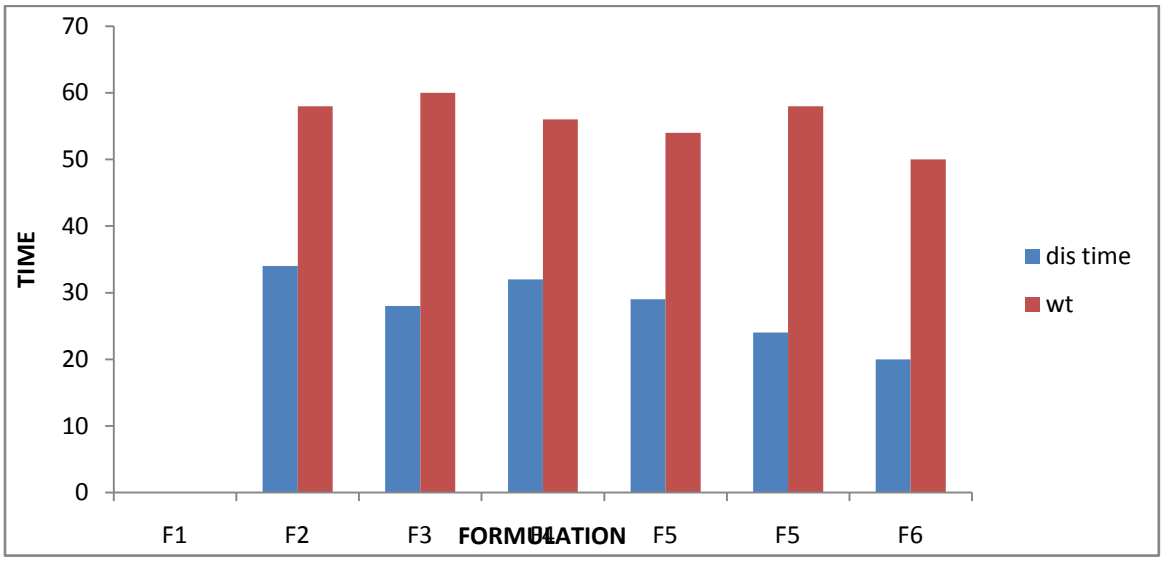

Figure 5: Comparison of Wetting Time and Disintegration Time

CONCLUSION :

Direct compression method can be considered as an important method for the formulation of fast dissolving..Various percentage of the superdisintegrant were also used to get best formulations with high bioavailability. Formulation having the better superdisintegrant will have better in vitro disintegration time and dissolution along with lesser friability and weight variation..The use of superdisintegrants for preparation of fast-dissolving tablet is to get dispersed in the mouth quickly and releases the drug early as compared to its formulated conventional tablet. figure 2 & 4 show the cumulative percentage of pantoprazole and Domperidone tablet with different concentration of CCS and SSG released from formulation. It is clear that the dissolution has improved considerably in formulation F6 as compared to formulation F1, F2, F3,F4 and

F5.Thus, it may be concluded that the fast dissolving tablets of Domperidone and pantoprazole can be successfully prepared and undoubtedly the availability of various technologies and manifold advantages of fast dissolving tablets will surely enhance patient compliance and its popularity in the near future.

AKNOWLEDGEMENT:

The authors are thankful to Dr. Shivamurthy Murugha Sharanaru, President, S.J.M VidyaPeetha for providing all necessary facilities through the Principal, S.J.M college of Pharmacy, Chitradurga and also thankful to for providing the gift sample of Torrent Pharmaceutical Ltd., Ahmadabad, India.

REFERENCES:

1) Anantha Lakshmi Pallikonda, RavindarBairam, M. Motilal, MekalaShubashKumar. Formulation and Evaluation of Mouth Dissolving Tablets, Der Pharmacia Lettre, 2010: 2 (1), 342-46 .
2) Kumaresan C. Orally disintegrating tablet-rapid disintegration, sweet taste, and target release profile Pharma Reviews.2008; 6 (5).
3) Brown D., Drug Delivery Technol., 2004;1-7.
4) Shukla D, Chakraborty S, Singh S, Mishra B. Mouth dissolving tablets I: An overview of formulation technology. Sci Pharm 2009; 77: 309-26.
5) Mini Adamo, Valentina Bergamante ,Gian Carlo Ceschel , Celestino Ronchi ,Carlos Alberto Fonseca de Moraes, Fast dispersible/slow releasing ibuprofen tablets, Eur J Pharma and Biopharma, 2007; 335-341.
6) Tripathi KD, Essential of Medical Pharmacology, 7 thed, Jaypee Publisher Ltd. Delhi.2008:639
7) Sharma Shailesh, Singh Gurjeet and Gupta GD. Formulation Design and Optimisation of Mouth Dissolving Tablets Of Domperidone Using Sublimation Technique, 2010;1(1).
8) Shailendrakumar Singh, DinaNathMishra, Rishab Jassal, Pankaj Soni. Fast Disintegrating Combination Tablets of Omeprazole and Domperidone. Asian J Pharm Clin Res 2009;2 (4).
9) TejveerKaur, Bhawandeep Gill, Sandeep Kumar, G.D. Gupta. Mouth Dissolving Tablets: A Novel Approach to Drug delivery. Int J Curr Pharm Res. 2011;3(1):1-7.
10) P.S.Mohanchandran, P.G. Sindhumol ,T.S. Kiran. Superdisintegrants: an overview. IJPSRR. 2011;6(1):105-9.

11) Reddy K R, Mutalik S, Reddy S., " APPS PharmSciTech", 2003: 4 (4), 61.
12) Cooper J, Gunn C. powder flow and compaction. In: Carter SJ, eds. Tutorial Pharmacy, New Delhi, India: CBS Publisher and distributors; 1986; 211-233.
13) Shah D, Shah Y, Rampradhan M. Development and evaluation of controlled release diltiazem micro particles using crosslinked poly (vinly alcohol). Drug Dev Ind Pharm. 1997; 23 (6): 567-574.
14) Aulton ME, Wells TI. Pharmaceutics: The Science of Dosage Form design. London, England: Churchill Livingstone;1988.
15) Pue M A. Pharmaco kinetics of Pantoprazol flowing oral administration the healthy mail subjects. Eur J Clin Pharma , 1993 ; 44, 575- 8
16) Judmaier G, Comparison of Pantroprazole and Ranitidine in the treatment of acute Duodenal ulcer. Aliment PharmaTher, 1994,8 ,81-6
17) Bi Y., Sunada H., Yonezawa Y., Danjo K., Otsuka A., Iida K., Preparation and evaluation of compressed tablet rapidly disintegrating in oral cavity. Chem. Pharm. Bull. 1996;44, 2121-27.
18) Prasanna Reddy. Battu. Simultaneous HPLC Estimation of Pantoprazole & Domperidone from Tablets .Int J Chem Tech Res 2009;1(2), 275-77).