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RESEARCH ARTICLE
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DESIGN AND DEVELOPMENT OF ORODISPERSIBLE TABLETS USING NOVEL SUPERDISINTEGRANTS

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ABSTRACT

The present work aimed at preparing oro-dispersible tablets of Tadalafil with the purpose of developing a dosage form for a very quick onset of action, which is very convenient for administration, without the problem of swallowing and using water. The tablets of tadalafil was prepared by using superdisintegrants like sodium starch glycolate, Indion 234s, Indion 234 as an ion exchange resins by direct compression method. The formulated fast dissolving tablets were evaluated for physical characteristics such as Hardness, thickness, uniformity of weight, drug content uniformity, Invitro disintegration and invitro dissolution .The formulations were subjected to disintegration, In-vitro drug release tests. The FTIR and DSC studies revealed that no physicochemical interaction between excipients and drug. Fast dissolving tablets of tadalafil containing combination ofSSG and Indion 234s as superdisintegrant showed (94.33%) drug release within 10min.Percentage content uniformity (99.20%). Fast dissolving tablets of Tadalafil can beconsidered suitable for clinical use in the treatment of Erectile Dysfunctioning.

Keyword: Tadalafil, Indion 234, Indion 234s, Direct compression method.

INTRODUCTION

Oral routes of drug administration have wide acceptance up to 50-60% of total dosage forms.Solid dosage forms are popular because of ease of administration, accurate dosage, self medication, pain avoidance and most importantly the patient compliance. Fast dissolving tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people. The faster the drug into solution, quicker the absorption and and onset of clinical effect.[1] Recently fast dissolving drug delivery systems have started gaining popularity and acceptance as one such example with increased consumer choice, for the reason of rapid disintegration or dissolution, self-administration even without water or chewing.

Recent market studies indicate that more than half of the patient population prefer ODTs to other dosage forms. Most consumers would ask their doctors for ODTS(70%), purchase ODTs(70%), or prefer ODTs over regular tablets of liquids (>80%).[3,17] Tadalafil is a potent and selective inhibitor of cGMP specific phosphodiesterase type 5 (PDE5) which is responsible for degradation of cGMP in the corpus cavernosum. Tadalafil is the orally administered drug for used to treat male erectile dysfunction. Tadalafil have very low aqueous solubility and hence has low bioavailability. A unique attempt has made to design and evaluate the orodispersible tablets (ODTs) of Tadalafil using ion

exchange resins like indion 234, indion 234s as superdisintegrants with the objective of enhancing the solubility and bioavailability of tadalafil.[4, 5] Indion 234s and Indion 234 is high purity pharmaceutical grade weak acid cation exchange resin. Used for tablet disintegration and taste masking of bitter drugs. Indion 234s based on crosslinked polyacrylic acid. It is a white to off white free flowing powder.[6,7,8.]

MATERIALS

Tadalafil was obtained as a gift sample from Ajanta pharma, Aurangabad. Indion 234 and Indion 234s was obtained as a gift sample Ion Exchange India Ltd, Mumbai. Sodium Starch Glycolate was procured as a gift sample from Glenmark Pharma, Sinner, Nashik . Allmaterials and solvents used were of analytical grade.

METHOD

Preparation of Mouth Dissolving Tablets

Orodispersible tablets of Tadalafil were prepared by direct compression method using ion exchange resins. Required amount of Tadalafil, Sodium starch glycolate, Indion 234, Indion 234s, according to the formulation table was weighed accurately. Simultaneously all the excipients were weighed accurately. Powder of drug were mixed / blended with superdisintegrants, lactose as diluent, aspartame as sweetner, talc as glidant & magnesium stearate as lubricant. All ingredients were passed through mesh #60. Before compression, hardness was adjusted. 20mg of Tadalafil were compressed on 10 station rotary punching machine (RIMEK INDIA) to get tablets, each weighing 200mg.

EVALUATION OF POWDER BLEND[6]

1. Evaluation of Powder Flow Properties

The Indion 234 and Indion 234s were evaluated for flow properties including bulk density, angle of repose, Carrs compressibility index, and Hausner ratio.

2. Swelling Index

The study was carried out using 100 ml stoppered graduated cylinder. The initial bulk volumeof 1 gm Indion 234 and Indion 234s was noted saperately. Water was added in sufficient quantity to produce 100 ml of a uniform dispersion. The sediment volume of the swollen mass was measured after 24 hour, stored at room temperature.

The swelling index was calculated as :

$$\text{Swelling Index} = \frac{V2-V1}{V1} \times 100$$

Where, V1 and V2 are initial volume of material before hydration and volume of hydrated material, respectively.

Pre formulation Evaluation parameters Micromeritic properties[5,9,10,11]

Micromeritic properties5,9,10,11

A. Angle of Repose

Angle of repose of different formulations was measured according to fixed funnel method, Completely dried granules were weighed and passed through the funnel, which was kept at height ‘h’ above the horizontal surface and the diameter of the pile was measured and the angle of repose was determined for all the formulations using the formula

$$\tan \theta = h / r$$

$$\text{Angle of repose } (\theta) = \tan^{-1} (h / r)$$

Where, h- height of pile, r- radius

B. Bulk density and Tapped density

The loose bulk density (LBD) and tapped bulk density (TBD) of granules were determined. The prepared granules was poured into calibrated measuring cylinder (10ml) then noted initial volume.

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

C. Compressibility index

The compressibility index (Carrs index) of the all formulations were determined by using the below mentioned equation:

$$\textbf{Carrs Index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

D. Hausners ratio

Hausners ratio is an indirect index of ease of powder flow. It is calculated by the following formula,

$$\textbf{Hausners Ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

Lower Hausner's ratio (<1.25) indicates better
Flow properties than higher ones (>1.25)

Evaluation of Tablet Characteristics [5,12-14,16]

A. Hardness

The crushing load which is the force required to break the tablet in radial direction was measured using a Monsanto hardness tester. Ten tablets from each formulation batch were tested randomly and average hardness was calculated. It is given in kp or kg/cm2.

B. Thickness and Diameter

The thickness and diameter of tablets was determined using a Vernier caliper. Five tablets from each type of formulation were used and average values were calculated.

C. Weight Variation

Weight variation was calculated as per method described in Indian Pharmacopoeia 1996. 20 tablets were weighed individually and the average weight is calculated. The requirements are met if the weights of not more than 2 of tablets differ by more than the percentage listed in table no tablet differ in weight by more than double that percentage.

D. Friability

Roche friabilator was used for the purpose, 10 tablets were weighed and placed in the Roche friabilator test apparatus, the tablets were exposed to rolling and repeated shocks, resulting from free falls within the apparatus. After 100 revolutions the tablet were de-dusted and weighed again. The friability was determined as,

$$\textbf{\%Friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

E. Drug content uniformity

For this purpose five tablets were weighed and crushed with pestle in a small glass morter. The fine powder was weighed to get 200mg (equivalent to 60mg of Tadalafil), and transferred to 250ml conical flask containing 100ml of phosphate buffer PH 6.8 stirred for 45min in ultra sonicator then solution was filtered and the filtrate obtained was analysed by UV spectrophotometrically at 284nm ,& drug content was determined.

F. Wetting time

A piece of tissue paper (12cm x 10.75cm) folded twice was placed in Petri dish (6.5cm internal diameter) containing 6ml of phosphate buffer ph 6.8. A tablet was carefully placed on the surface of tissue paper and allowed to wet completely. The time required for complete wetting of the tablet was measured as a wetting time.

G. Water absorption ratio

A piece of tissue paper folded twice was placed in small petri dish (10cm diameter) containing 6ml of Phosphate buffer ph 6.8. A tablet was put on the tissue paper and allowed to wet completely. The wetted tablet was then reweighed. Water absorption ratio, R was determined using following equation

$$\mathbf{R} = \frac{(Wa-Wb)}{Wb} 100\ \mathbf{x}$$

Where, Wa= weight of tablet after absorption
Wb= weight of tablet before absorption

H. Disintegration test

Test was performed using disintegration test apparatus. Tablets were placed in the disintegration tubes and time required for complete disintegration, that is without leaving any residues on the screen was recorded as disintegration time.

I. Invitro dispersion time

Tablets were added to 10ml buffer solution (PH 6.8) and time required for complete dispersion was measured. Three tablets from each formulation were randomly selected and in vitro dispersion time was performed.

J. Invitro dissolution

Dissolution type 2 model was used for carried out in-vitro drug release studies on the prepared batches of the tablets. 900ml of phosphate buffer is used having ph 6.8, 370 C±0.50C , 900ml, 50 rpm and 5ml aliquots were taken out after every minute. And the volume was replaced with 5ml of aliquots of fresh dissolution medium. The samples withdrawn were analysed UV spectrophotometrically at 284nm. Cumulative percent drug release was calculated by using an equation obtained from a standard curve.

RESULT AND DISCUSSION

Table 1 : Formulation of Orodispersible tablets of Tadalafil

Ingredients	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
Tadalafil	20	20	20	20	20	20	20	20
SSG	05	15	-	-	-	-	15	15
Indion 234		-	05	15	-	-	15	-
Indion 234s	-	-	-	-	05	15	-	15
B-cyclodextrine	05	15	05	15	05	15	15	15
Mannitol	10	10	10	10	10	10	10	10
Talc	10	10	10	10	10	10	10	10

Magnesium Stearate	10	10	10	10	10	10	10	10
Lactose	140	120	140	120	140	120	105	105
Total	200	200	200	200	200	200	200	200

Table 2: Characterization of Granules

F. code	Angle of Repose	Bulk density	Tapped density	Carr's index	Hausners Ratio
F1	28.1±0.09	0.559±0.01	0.666±0.02	18.59±1.56	1.23±0.009
F2	25.8±0.06	0.585±0.05	0.646±0.03	21.73±1.64	1.25±0.002
F3	24.8±0.32	0.58±0.04	0.796±0.02	20.64±3.04	1.23±0.009
F4	29.8±0.15	0.564±0.04	0.693±0.01	20.51±2.82	1.23±0.002
F5	28.4±0.21	0.552±0.01	0.746±0.03	17.28±0.53	1.13±0.003
F6	27.5±0.09	0.585±0.05	0.646±0.03	17.05±0.68	1.13±0.02
F7	25.8±0.01	0.559±0.02	0.733±0.02	21.73±1.64	1.25±0.002
F8	25.8±0.15	0.561±0.03	0.71±0.02	20.51±2.82	1.23±0.002

Table 3: Post compression parameters

F. code	Avg. weight(mg)	Diameter(mm)	Thickness	Hardness(kg/cm^2) ±SD
F1	198.79	8.0	3.25	3.13±0.005
F2	199.20	8.1	3.05	3.76±0.005
F3	198.90	8.2	3.18	3.96±0.01
F4	197.90	8.0	3.28	4.00±0.01
F5	199.20	8.0	3.02	4.03±0.01
F6	198.42	8.1	3.00	3.1±0.005
F7	199.72	8.0	3.27	3.4±0.01
F8	199.94	8.2	3.18	3.36±0.01

Table 4: Post compression parameters

F. code	% Friability	Wetting time(sec)	Disintegration time (sec)	Invitro- dispersion time(sec)	Drug content (%)
F1	0.6±0.8%	25.66	52.33±0.01	62.66±0.02	99.20
F2	0.4±0.2%	30±0.04	48.00±0.02	74.12±0.02	95.35
F3	0.2±0.4%	24±0.02	40.22±0.01	52±0.02	98.58
F4	0.2±0.2%	19.33±0.01	38.05±0.01	56.66±0.02	99.10
F5	0.2±0.2%	22±0.04	49.66±0.00	72.05±0.01	95.35
F6	0.6±0.7%	21.33±0.02	52.22±0.01	62.22±0.01	99.10
F7	0.7±0.2%	27.42	42.00±0.01	58.04±0.02	98.58
F8	0.4±0.8%	32.04±0.04	48.66±0.00	75.04±0.02	99.20

Table 5: In-vitro dissolution parameters in pH 6.8 phosphate buffer

Time (min)	Percent drug released							
	F1(%)	F2(%)	F3(%)	F4(%)	F5(%)	F6(%)	F7(%)	F8(%)
1	12	12.41	8.83	12.66	12.16	24.91	12.41	20.91
2	19.33	19	12.5	30.75	29.16	35.83	14.66	26
3	27.41	25.75	27.25	32.16	44.16	40.16	28.25	34.33
4	52.33	40.08	43.75	35.08	66.25	44.33	44	39.33
5	65	59.08	45.83	56.25	73	46	66.66	49.33
6	67.33	65	56.66	62.5	77.5	62.66	71.33	62.66
7	70.83	73.25	73.25	73.1	79.16	75.16	81.58	73.1
8	72.66	80.33	81.41	80.18	86.5	81	86.75	80.18
9	75.16	83.66	83.41	86.85	86.83	86.66	89.33	86.85
10	77.25	87.58	89.33	91	90.08	92.66	92.66	94.33

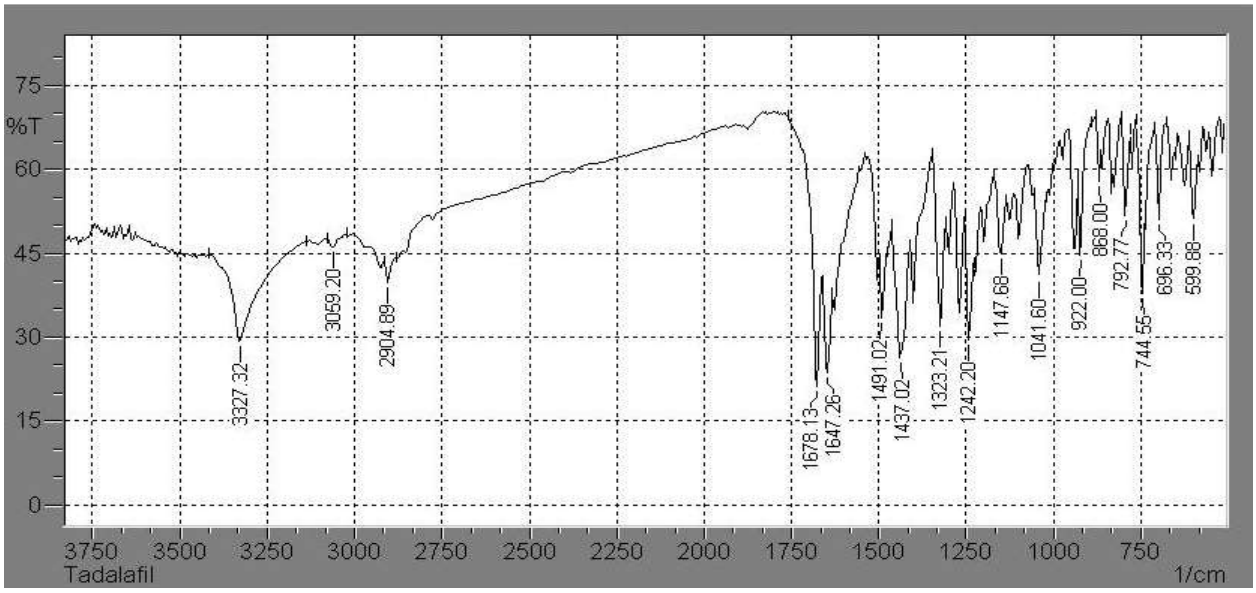

Figure 1 : FTIR of pure drug TadalafilDifferential scanning calorimetry (D SC) of Tadalafil

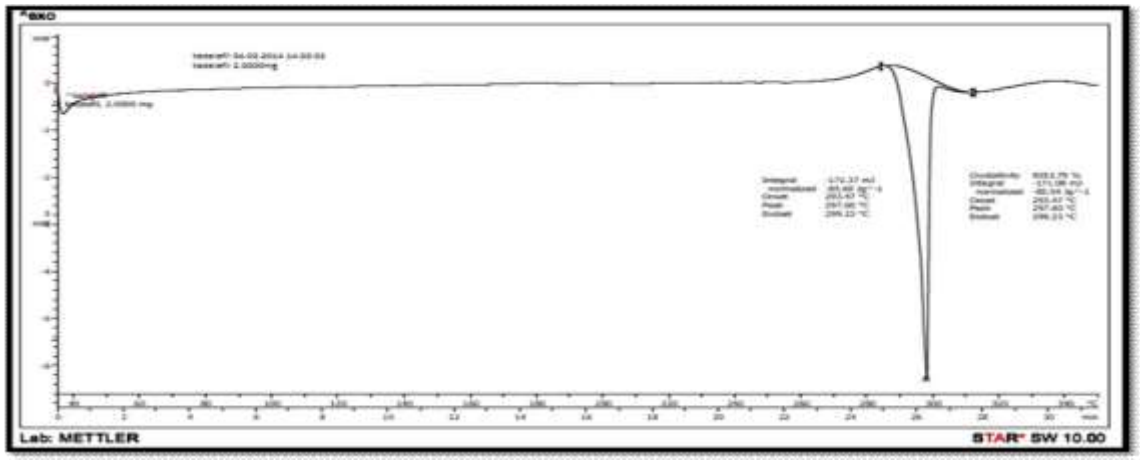

Figure 2 : DSC of Tadalafil

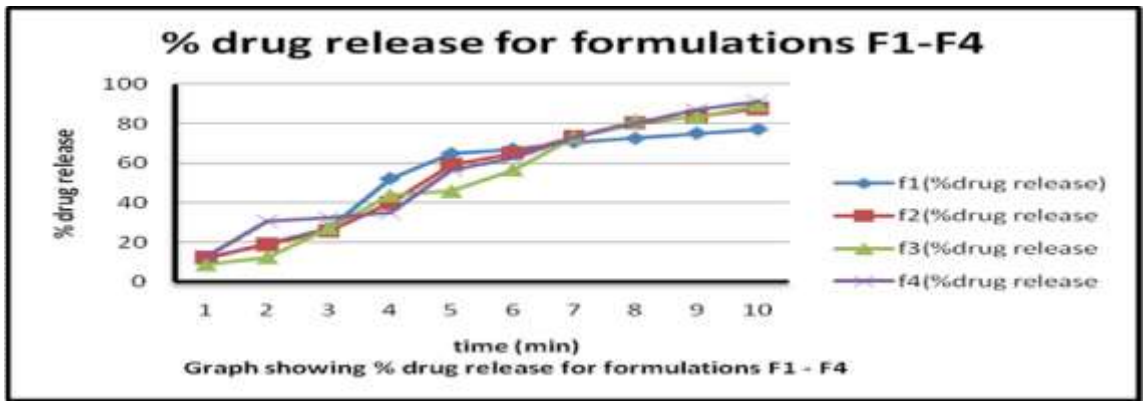

Figure 3: Drug release profile F1-F4

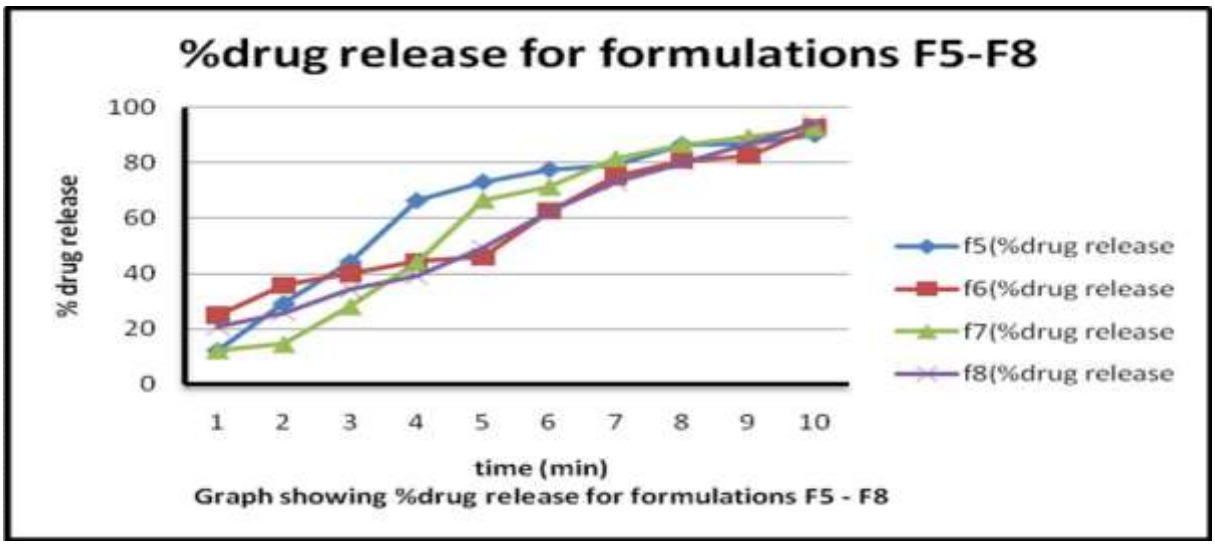

Figure 4: Drug release profile F5-F8

CONCLUSION

Oral disintegrating tablets (ODT) of Tadalafil is successfully prepared by using direct compression method. The aim of the present work is to introduce ion exchange resins like indion 234 and indion 234s which are showing better disintegrant properties so we can used ion exchange resins for the formulation of orodispersible tablets. They are showing better release as compared to SSG and other disintegrants. From the formulations conclude that formulation F8 as the best formulations according to their release rate. Formulation f4 and f6 containing indion 234 and indion 234s 7.5% respectively. Formulation f7 containing two disintegrants SSG and indion 234 7.5%, and formulation f8 containing SSG and indion 234s7.5%.

REFERENCES

1. Debjit Bhowmik, Chiranjib B, Krishnakanth, Pankaj R., Margret Chandira; Fast dissolvingtablet: An overview; Journal of chemical and pharmaceutical research, 2009,1(1): 163- 177.
2. Bharat V. Jain, Rupali R. Patil, Sonali S. Wankhede, Dipak R.Patil, Dr.Shashikant D. Barhate; Development of Mouth Dissolving Tablets of Grenisetron Hydrochloride using three different techniques; International Journal of Pharmaceutical Research and Development; 2011; Vol.3(3),May. 2011(23-26).
3. Kumara Swamy S., Narendra D. and Agaiah Goud B; Formulation and Evaluation of Orodispersible Tablet of Theophylline using different super disintegtants; Journal of Advance Pharmaceutical Sciences; Vol.2 , 2012: 260-264.
4. Drug Bank / Drug Data: online.
5. K. Mallikarjuna Rao, V. Sreenivasulu, M. Gobinath, C. Thejaswi,J.Radha Rani; Formulation and invitro characterization of orodispersible tablets of Tadalafil by using Dry Granulation Method with Superdisintegrants; Journal of research and development; June 2012/ Vol.1(2): 36-
6. Bharat Jain, Shashikant Barhate; Indion 234s as a disintegrant: Formulation and Evaluationof Grenisetron Hydrochloride Orodispersible Tablets; Iventy Impact :Novel Excipients ; Vol. 2013, issue 2, 81-83.
7. Indion 234s Description : Ion Exchange India Limited. www.ion india.com
8. Indion 234 Description : Ion Exchange India Limited. www.ion india.com
9. C. V. S Subrahmanyam "Text Book of Physical Pharmacy", 2nd edition , Delhi: Vallabh Prakashan, 2004, 210-228.
10. Aulton M E. Eds: Pharmaceutics: The science of dosage form and design, 2nd ed., Churchill Livingstone, USA , 1998, pp.223-253.
11. Martin A, Swarbrick J, Cammarata A, "Physical Pharmacy", 3rd edition, Verghese publishing company Bombay, 1991, pp. 492-520.

12. Hareesha Chamarthi, Ramesh Kannuri, Senthil Kumar M., Gargeyi pavuluri, Swathi Krishna. K. V.; Formulation and evaluation of orodispersible tablet of Escitalopram Oxalte by superdisintegrants addition method; International Journal of Pharmaceutical Research and Development; 2011; Vol 3(8): November 2011 (65-72).
13. Mahajan Yogesh Y, Tekade Bharat W., Thakre Vinod M., Patil Vijay R., Jagdale Sunil; Formulation and Evaluation of Orally Disintegrating Tablet of Ondensetron Hydrochloride; International Journal of Drug Delivery 4 (2012): 09-19.
14. The Indian Pharmacopoeia.(2010). Govt of India, Ministry of Family Welfare, the Indian Pharmacopoeial commission, Gaziabad page 1815-1817.
15. Lachman L, Lieberman HA, Kanig J L. The theory and practice of industrial pharmacy,3rd edn, Varghese publishing house, Bombay, 1986, pp. 297-300.
16. Suryakant B. Jadhav, Dinesh M. Sakarkar, Datta R. Kaudewar, Girish S. Kaminwar, and Rajesh V. Kshirsagar; Formulation and Evaluation of Mouth Dissolving Tablets of Diltiazem Hydrochloride; Pelgia research library : Der Pharmacia Sinica; 2011, 2(6): 23- 31.
17. K.B.Deshpande; Orodispersible Tablet: An Overview of Formulation and Technology ; International Journal of Pharma and Biosciences, 2(1) : 2011; 0975-6299.