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DESIGN, OPTIMISATION AND EVALUATION OF ATENOLOL FAST DISSOLVING TABLETS EMPLOYING STARCH GLUTAMATE-A NEW SUPERDISINTEGRANT

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ABSTRACT

The purpose of the present study is to evaluate starch glutamate as a superdisintegrant in the formulation of fast dissolving tablets of poorly soluble drugs. Starch glutamate was synthesized by gelatinization process. The synthesized starch glutamate was subjected to physical and micromeritic evaluation. To establish as starch glutamate as a superdisintegrant, fast dissolving tablet of atenolol was prepared employing starch glutamate in different proportions in each case by direct compression method employing 2^3 factorial design. All fast dissolving tablets prepared were evaluated for drug content, hardness, friability, disintegration time and other dissolution characteristics like percent dissolved in 5 min (PD_5), Dissolution efficiency in 5 minutes (DE_5) and first order rate constant ($K_{1)}$.The starch glutamate prepared was found to be fine, free flowing slightly crystalline powder. Starch glutamate exhibited good swelling in water. The swelling index was 50% all micrometric properties indicated good flow and compressibility needed for solid dosage from manufacturing. All the fast dissolving tablets formulated employing starch glutamate were of good quality with regard to drug content, hardness and friability and fulfilled the official (IP/USP) requirements of compressed tablets with regard to the above mentioned physical properties. Starch glutamate was found to be a superdisintegrant which enhanced the dissolution efficiency when combined with sodium starch glycolate, crosscarmellose sodium, with the atenolol and hence it could be used in the formulation of fast dissolving tablets to provide immediate release of the contained drug within 5minutes.

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INTRODUCTION

The concept of fast dissolving drug delivery system emerged from the desire to provide patient with conventional means of taking their medication[1].Fast dissolving tablets are solid dosage form containing indicated substances which disintegrate rapidly, usually within few seconds when placed upon tongue requiring additional water to facilitate swallowing. Fast dissolving tablets offer great advantages for the patients having difficulty in swallowing. It has been reported that dysphasia (difficulty in swallowing) is usual among all groups and more specific with pediatric, geriatric population along with patients have nausea, retching, and motion sickness complications [1]. Fast dissolving tablets overcome this problem and provide the advantages for pediatrics, geriatric [2-3], bedridden, disabled patients and also for who may have difficulty in swallowing tablets, capsules and liquid orals. Fast dissolving tablets (FDT) will rapidly disintegrate in the mouth without the need of water [4-5]. Fast dissolving tablet formulation provides sufficient strength, quick disintegration/ dissolution in the mouth without water [6], rapid dissolution and absorption of the drug, which will produce the quick onset of action. Pre gastric absorption of FDT can result in improved bioavailability and as a consequence of reduced dose [7]. Various techniques can be used to formulate fast dissolving tablets. Direct compression one of the techniques which require the incorporation of superdisintegrant or highly water soluble excipients into the formulation to achieve fast tablet disintegration. Direct compression does not require the use of water or heat during the formulation procedure and is the ideal method for moisture and heat-liable medication. The aim of the work was to formulate and characterize fast-dissolving tablets of atenolol by utilizing optimization techniques for rapid dissolution of drug and absorption employing a new superdisintegrant i.e., starch glutamate.

Optimization technique provide both a depth of understanding and an ability to explore and define ranges for formulation and processing factors with a rational approach to the selection of several experimental and manufacturing step for a given product, to quantitatively select a formulation. It is at this point that optimization can become a useful tool to quantitative a formulation that has been qualitatively determined.

The present investigation deals with an attempt of systematic formulation approach for optimization of atenolol fast dissolving tablets employing starch glutamate, sodium starch glycolate, crosscarmellose sodium as superdisintegrants. A 2^3 factorial design was applied to investigation the main and interaction effects of the three formulation variables i.e., starch glutamate (A), sodium starch glycolate (B), crosscarmellose sodium (C) in each case to find the formula with less disintegration time and more dissolution efficiency 5 min and to permit arbitrary selection of tablets with immediate release of drug with in 5 min.

MATERIALS AND METHODS:

Materials:

1) Starch glutamate(prepared in the laboratory)
2) Sodium hydroxide (Finar chemicals Ltd. Ahmadabad)
3) Potato starch (Yarrows Chemicals, Mumbai.)
4) Glutamic acid (Finar chemicals Ltd. Ahmadabad)
5) Distilled water (prepared in the laboratory)
6) Atenolol (Yarrow chemicals, Mumbai).
7) Sodium starch glycolate (Yarrow chemicals, Mumbai).
8) Crospovidone (Yarrow chemicals, Mumbai)
9) Mannitol. (Yarrow chemicals, Mumbai)
10) Microcrystalline cellulose (Qualigens fine chemicals, Mumbai).
11) Talc (Molychem, Mumbai)
12) Magnesium stearate (Molychem, Mumbai)

Preparation of Starch Glutamate (a novel superdisintegrant):

Initially10 grams of glutamic acid were dissolved in distilled water and the p^H was adjusted to 3.5 using 10M NAOH and finally made up to 25 ml. To the above mixture 25 grams potato starch was added and conditioned for 16 hrs at room temperature, later the product was kept in oven at 60^0C for 6 hrs, the mass is washed and removed un reacted glutamic acid, and dried at 60^0C until it gets dried. The product obtained was ground and sized.

Characterization of starch glutamate:

The starch glutamate prepared was evaluated for the following

Solubility:

Solubility of starch glutamate was tested in water, aqueous buffer of pH 1,2,3,4, and 7.4 and organic solvents such as alcohol, dichloromethane, chloroform, acetone and petroleum ether.

pH:

The pH of 1% w/v slurry was measured by pH meter.

Melting point:

Melting point was determined by using melting point apparatus.

Viscosity:
Viscosity of 1% dispersion in water was measured using ostwald viscometer.

Swelling Index:
Starch glutamate (200 mg) was added to 10 ml of water and light liquid paraffin taken in two different graduated test tubes and mixed. The dispersion in the tubes was allowed to stand for 12 h. The volumes of the sediment in the tubes were recorded. The swelling index o the material was calculated as follows.

S.I (%) = Volume of sediment in water – volume of sediment in light liquid paraffin/ Volume of sediment in light liquid paraffin X 100

Property:
The gelling property (gelatinization) of the starch and starch glutamate prepared was evaluated by heating a 7% w/v dispersion of each in water at 100^0C for 30 min.

Particle size:
Particle size analysis was done by sieving using optical microscopy method.

Density:
Density (g/cc) was determined by liquid displacement method using benzene as liquid.

Bulk density [8]:
Both loose bulk density (LBD) and tapped bulk density (TBD) were determined by transferring the accurate weighed amount of sample in 50 ml measuring cylinder, the granules without any agglomerates and measured the volume of packing and tapped 50 times on a plane surface and tapped volume of packing recorded and LBD and TBD calculated by following formula.

LBD =Mass of powder/Volume of packing

TBD= Mass of powder/Tapped volume of packing.

Percentage compressibility index [9]
Percentage compressibility of powder mix was determined by Carr's compressibility index calculated by the following formula.

% Carr's Index= (TBD-LBD)×100/TBD; Where, TBD= Tapped bulk density; LBD= Loose bulk density.

Angle of repose
The frictional forces in loose powder or granules can be measured by the angle of repose. This is the maximum angle possible between the surface of a mass of powder or granules and the horizontal plane. Angle of repose is calculated by applying the next equation;

$$\tan \theta = h/r;\ \theta = \tan^{-1}(h/r)$$, where θ=angle of repose; h=height; r=radius

Fourier Transform Infrared (FTIR) Spectroscopy:
FTIR spectra of starch lactate were recorded on samples prepared in potassium bromide (KBr) disks using a BRUKER FT – IR, (Tokyo, Japan). Samples were prepared in (KBr) disks by means of a hydrostatic press at 6-8 tons pressure. The scanning range was 500 to 4000 cm^{-1}.

X – Ray diffraction:
Diffraction pattern of starch glutamate was recorded with an x-ray diffractometer (analytical spectra's Pvt. Ltd., Singapore). X-ray diffraction was performed at room temperature (30^0C) with a diffractometer; target, Cu(λ1.54 A), filter, Ni; voltage,40 kV; current 30mA; time constant 10mm/s ; scanning rate 2^0/min; measured from 2.5-50^0 at full scale 200.

Drug – Excipients compatibility studies:
The compatibility of starch glutamate with the selected drug (atenolol) was evaluated FTIR studies.

Infrared spectroscopy:
Fourier transform infra red (FTIR) spectra of atenolol, and their mixtures (1: 1) with starch glutamate were recorded on a Perkin Elmer, IR Spectrophotometer model: spectrum RXI, using KBr disc as reference.

Preparation of atenolol fast dissolving tablets:

The tablets were prepared by direct compression method employing 2^3 factorial design in which 3 independent variables {superdisintegrants i.e.,sStarch glutamate (A), sodium starch glycolate (B), crosscarmellose sodium (C)} and 1 dependent variable (dissolution efficiency in 5 min) were selected. The composition of different formulation of atenolol fast dissolving tablets is shown in Table no 1 in which the levels of superdisintegrants were selected at 2 levels i.e., lower and higher level concentrations. For starch glutamate (A), the lower level i.e., 5% concentration and upper level i.e., 10% concentration. For sodium starch glycolate (B) and crosscarmellose sodium (C), the lower level is zero concentration and higher level i.e., 5% concentration. For uniformity in particle size each ingredient was passed through # 100 mesh sized screen before mixing. Starch glutamate, sodium starch glycolate, crosscarmellose sodium, mannitol and microcrystalline cellulose were accurately weighed and mixed using mortar and pestle, and the added to atenolol. Finally talc and magnesium stearate were added to the powder mixture. Finally mixed blend was compressed by using eight station rotator press Karnawathi Machineries Pvt, Ltd., Ahmedabad, India).

Table 1: Formulae of atenolol fast dissolving tablets employing starch glutamate prepared by direct compression method involving mannitol as diluent.

Ingredients (mg/tablet)	F1	F2	F3	F4	F5	F6	F7	F8
Atenolol	25	25	25	25	25	25	25	25
Starch glutamate	15	30	15	30	15	30	15	30
Sodium starch glycolate	-	-	15	15	-	-	15	15
Crospovidone	-	-	-	-	15	15	15	15
Mannitol	98	83	83	68	83	68	68	53
Micro crystalline cellulose	150	150	150	150	150	150	150	150
Talc	6	6	6	6	6	6	6	6
Magnesium stearate	6	6	6	6	6	6	6	6
Total weight	300	300	300	300	300	300	300	300

Evaluation of atenolol fast dissolving tablets:

Hardness test [10]

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablet was determined using Monsanto hardness tester and expressed in kg/cm²

Uniformity of weight:

Weight variation test was done with 20 tablets. It is the individual variation of tablet weighed from the average weight of 20 tablets.

Friability:

The friability of tablets was measured using a Roche fribilator. Tablets were rotated at 25 rpm for 4 minutes or up to 100 revolutions. The tablets were then reweighed after removal of fines and the percentage of weight loss was calculated.

$$F = 100 \text{ X } W \text{ (initial)} - W \text{ (final)} / W \text{ (initial)}$$

Drug content uniformity [11]:

For content uniformity test, ten tablets were weighed and powdered a quality of powder equivalent to 10 mg of atenolol was extracted into 7.4 phosphate buffer and filtered. The atenolol content was determined by measuring the absorbance spectrophotometrically at 360 nm after appropriate dilution with 7.4 phosphate buffer. The drug content was calculated using the standard calibration curve. The mean percentage drug content was calculated as an average of three determinations.

Wetting time[12,13]:

The wetting of the tablets was measured using a very simple process. Five circular tissue paper cm diameters were placed in a petridis with a 10 cm diameter. Ten milliliters of water containing soluble dye (Amaranth) was added to the petridish. A tablet was carefully placed on the surface of paper. The time required for water to reach the upper surface of the tablet was noted as the wetting time.

Water absorption ratio:

A piece of tissue paper folded twice in a small petri dish containing 6 ml of water. A tablet was put in the tissue paper allowed to completely wet. The wetted tablet was then weighed. Water absorption ration R was determined using following equation.

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

Where,

W_a = weight of tablet after water absorption.

W_b = weight of tablet before water absorption.

***In – vitro* disintegration time[14]:**

Disintegration time for FDTs was determined using USP disintegration apparatus with pH 7.4 phosphate buffer. The volume of medium was 900 ml and temperature was 37±0.2^{0}C. The time in seconds taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured.

***In – vitro* dissolution studies[5]:**

The *in vitro* dissolution rate study of atenolol fast dissolving was performed using 8 station dissolution test apparatus (Electro lab TDT- 08L) fitted with paddles (50 ppm) at 37 ± 0.5^0 C, using pH 7.4 phosphate buffer (900 ml) as a dissolution media. At the predetermined time intervals 5 ml sample were withdrawn, filtered through 0.45 µ membrane filter, diluted and assayed at 360 nm using a analytical technology T360 UV/Visible Double beam spectrophotometer. Cumulative percentage drug release was calculated using standard absorbance from the calibration curve. All the dissolution experiment were conducted in triplicate (n=3).

RESULTS AND DISCUSSION

The starch glutamate prepared was found to be fine, smooth and free flowing amorphous powder. The physical and micromeritic properties of the starch glutamate are summarized in table 2. It was insoluble in aqueous solvents and insoluble in organic solvent tested (methanol ether, dichloromethane, and chloroform) the p^H of 1% aqueous dispersion was 2.88.

Starch glutamate exhibited good swelling in water. The swelling index was 1200. All micromeritic properties indicated good flow and compressibility needed for solid dosage form manufacturing. The density of starch glutamate was found to be 0.584g/cc.

Table 2: Physical and micromeritic properties of the starch glutamate prepared.

Parameters	Observation
Solubility	Insoluble in all aqueous and organic solvents Tested
PH (1% aqueous dispersion)	2.88
Melting point	Charred at 325^{0}C
Viscosity (1%w/v aqueous dispersion)	1.08cps
Sweelling index	1200
Gelling property	No gelling and the swollen particles of starch glutamate separated from water. Where as in the case of starch, it was gelatinized and formed gel.
Moisture absorption	4.4%
Particle size	158µm (80/120 mesh)
Density	0.584g/cc
Bulk density	0.562g/cc
Angle of repose	27.47^0
Compressibility Index	14.23%

The FTIR spectrum of starch and starch glutamate is shown in fig: 1,2. The presence of peaks of absorption of 1619.29 cm^{-1} characteristic peak of esters. So from FTIR studies it was concluded that starch glutamate (ester) was formed when starch was allowed to react with glutamate anhydride. The X-ray diffraction pattern (Fig:3) of starch glutamate did not show any characteristic peak, which indicates that the structure is completely amorphous. The disappearance of pink colour in the ester test confirmed the presence of ester. i.e starch glutamate.

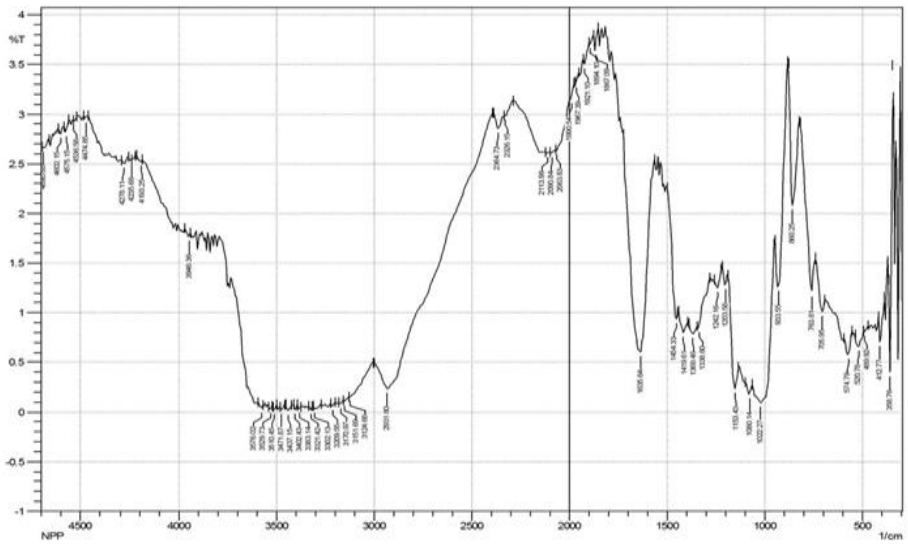
As the starch glutamate was amorphous, smooth and free flowing powder and it had got all the characteristics of super disintegrants it was concluded that starch glutamate can be used as novel superdisintegrant in the formulation of fast dissolving tablets.

The compatibility of starch glutamate with the selected drug (atenolol) was evaluated by DSC, FTIR, and TLC studies. The DSC thermo gra of atenolol (AT) and atenolol-starch glutamate (AT-SG) are shown in Figs.5. and 6. The DSC thermo grams of AT and AT-SG exhibited endothermic peaks at 220.16^{0}C and 220.11^{0}C respectively. These melting peaks of AT and AT-SG correspond 152- 154^{0}C melting point of atenolol and atenolol-SG mixtures correspond to the melting points of the respective drug indicating no interactions between the selected drug and starch glutamate polymer . The DSE study, thus, indicated no interaction no between starch glutamate and selected drug.

The FTIR spectral of AT and AT-SG shown in Figs.2 and 3 The characteristic FTIR bands of atenolol at 3290.56,cm^{-1} (C-H), 1620.21 cm^{-1} (N-H)were all observed in the FTIR spectral of both AT and AT-SG. This FTIR spectral observation also indicated no interaction between starch glutamate and the drug selected.

In the TLC study, single spots were observed in the case of pure drug as well as its mixture with starch glutamate. The close agreement of the R_f value of the drug and its mixture with starch glutamate (Table.3) indicated no interaction between the drug and starch glutamate.

Thus the results of DSC, FTIR, and TLC indicated no interaction between the selected drug and starch glutamate, the new superdisintegrant. Hence, starch glutamate could be used as a superdisintegrant in the design of fast dissolving tablet of the selected drug.



FTIR Spectra of Potato Starch.

Fig:1 . FTIR Spectra of Potato Starch.

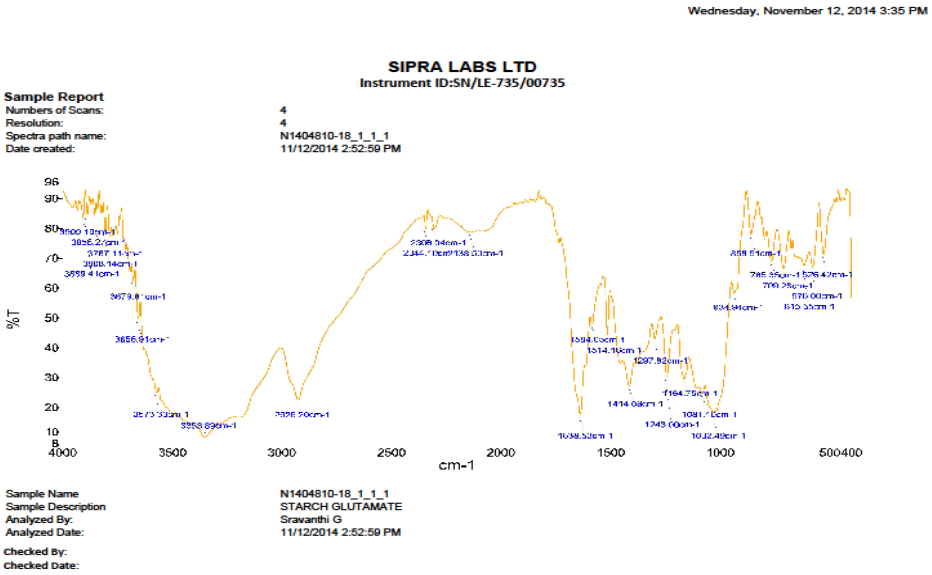


Fig: 2. FTIR Spectra of Starch Glutamate.

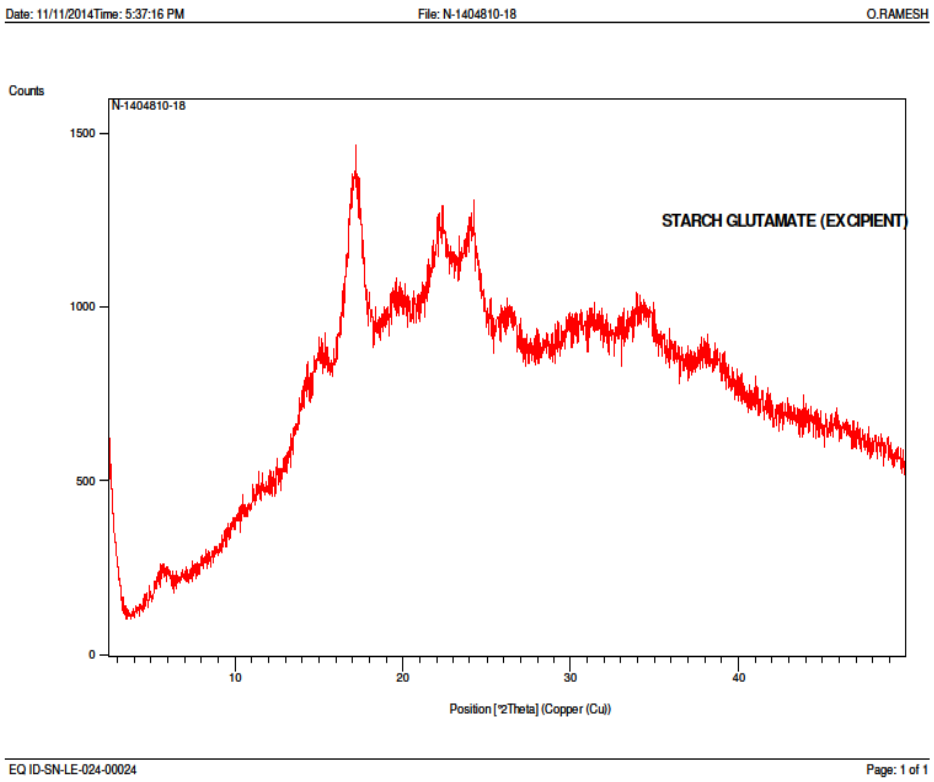


Fig: 3.X-Ray diffraction pattern of starch glutamate.

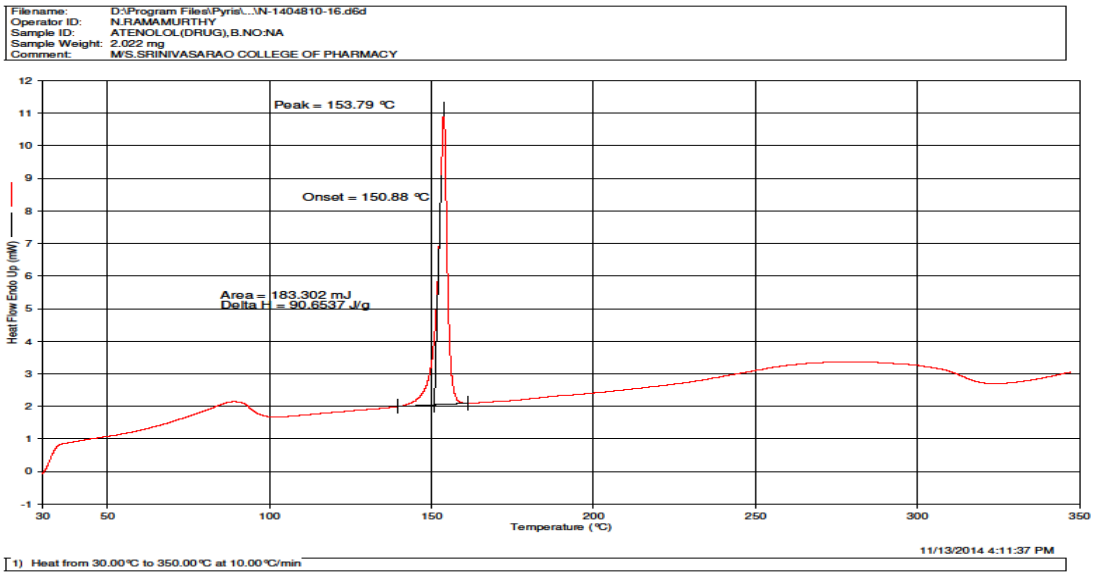


Fig: 4. DSC Theramogram pure drug.

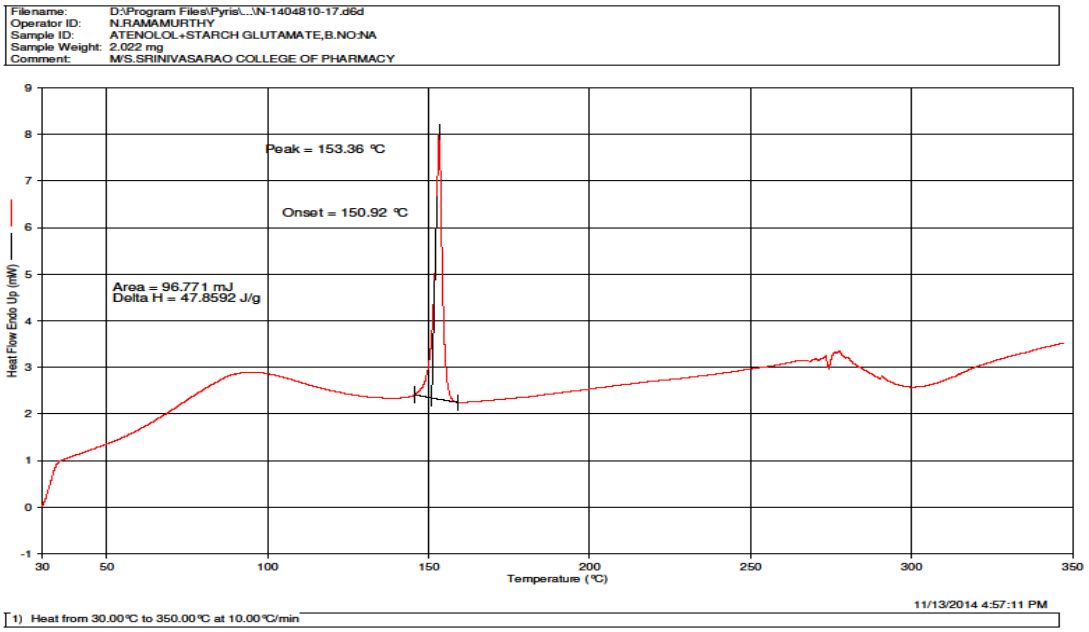


Fig: 5. DSC Theramogram of Atenolol with Starch glutamate.

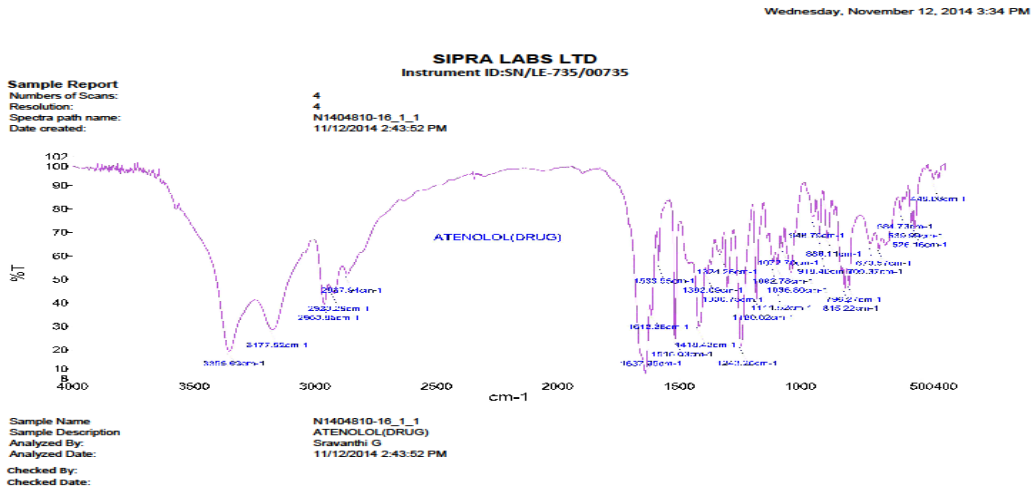


Fig: 6. FTIR Spectra of atenolol pure drug.

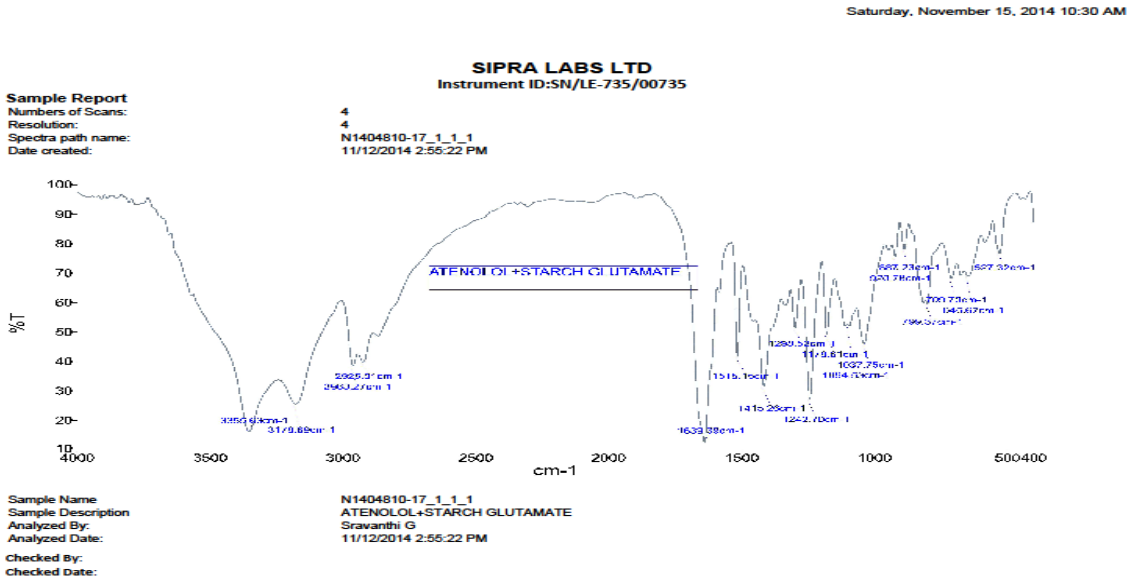


Fig: 7. FTIR Spectra of atenolol pure drug with starch glutamate.

Fig 6. FTIR spectra of atenolol.

Sample	Frequency of peak	Functional group
Atenolol	3617.25	(-COOH)

Fig 7. FTIR spectra of atenolol with starch glutamate.

Sample	Frequency of peak	Functional group
Atenolol + Starch glutamate	3317.01	(-COOH)

Table: 3. R_f values of selected drug and the mixtures (1:1) with starch glutamate.

S. No	Product	R_f value
1.	Atenolol	0.75
2.	Atenolol - Starch glutamate	0.73

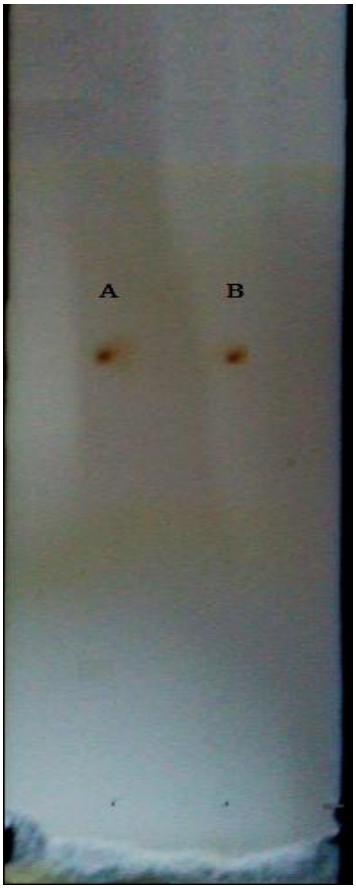
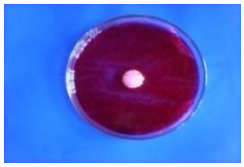
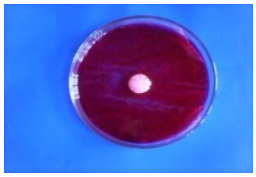
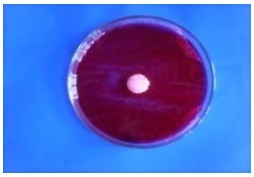


Fig:8. TLC plates showing (A) atenolol pure drug (B) atenolol and starch glutamate.

Fast dissolving tablets each containing 25 mg of atenolol could be prepared by employing starch glutamate by direct compression method. Hardness of the tablets was in range of 3.6-4.0kg/sq.cm. It indicates good strength with a capability to resist physical and pre functionary stress condition during handling. Weight loss on the friability test was less than 0.16% in all case. All the fast dissolving tablets prepared containg atenolol with in 100±5% of the labeled claim. As such the prepared were of good quality with to drug content, hardness and friability. The disintegration time of all formulated tablets was found to be in the range of 20±0.3 to 36±0.6 seconds as indicated in the table: 4

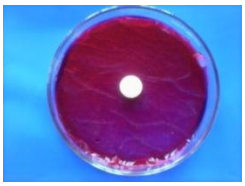
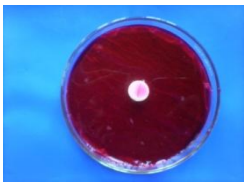
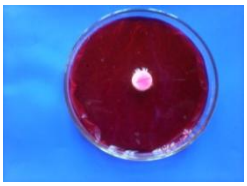
The result *in-vitro* wetting time and water absorption ratio were found to be within prescribed limits and satisfy the criteria of fast dissolving tablets (Fig.9). The in-*vitro* wetting time was decreased when the superdisintegrant was used. In the case of formulation F1 starch glutamate, the wetting item found to be 39±0.6sec.

F1 Atenolol Fast Dissolving Tablets.

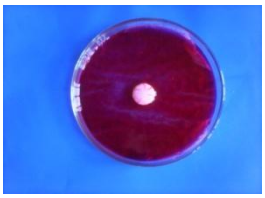
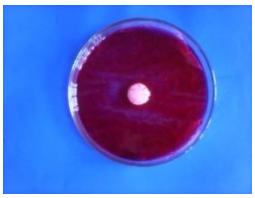
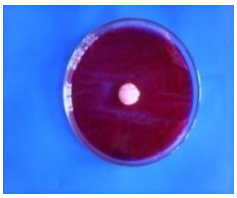
At T=0 **At T=28 sec** **At T= 39 sec**

F2 Atenolol Fast Dissolving Tablets.

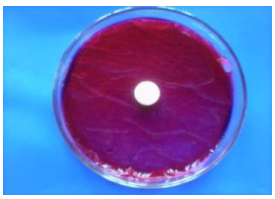
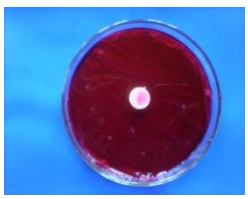
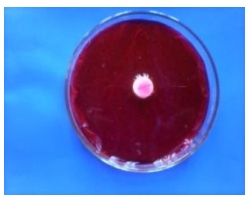
At T=0 **At T=28 sec** **At T= 39 sec**

F3 Atenolol Fast Dissolving Tablets.

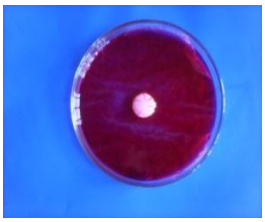
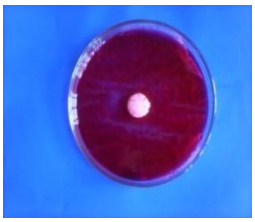
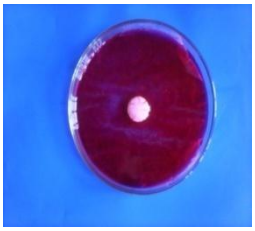
At T=0 **At T=15 sec** **At T= 34 sec.**

F4 Atenolol Fast Dissolving Tablets.

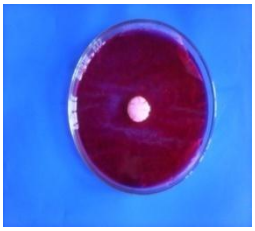
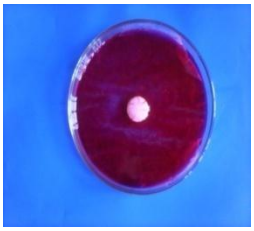
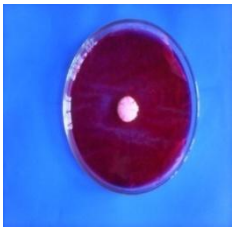
At T=0 **At T=17 sec** **At T= 36 sec.**

F5 Atenolol Fast Dissolving Tablets.

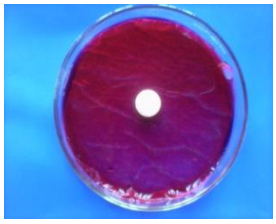
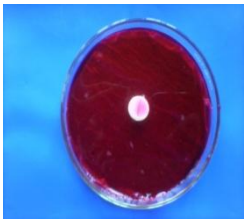
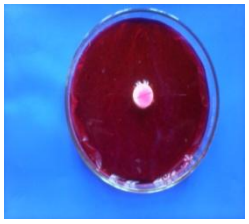
At T=0sec **At T=21sec** **At T= 48 sec**

F6 Atenolol Fast Dissolving Tablets.

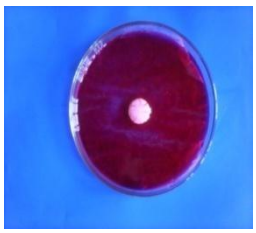
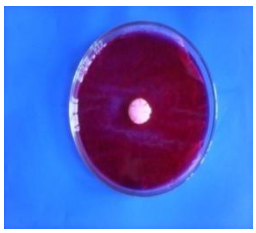
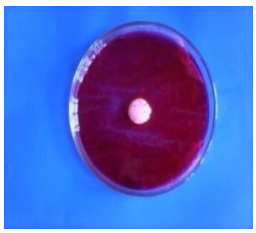
At T=0 **At T=16 sec** **At T= 31 sec**

F7 Atenolol Fast Dissolving Tablets.

At T=0 **At T=25 sec** **At T= 34 sec**

F8 Atenolol Fast Dissolving Tablets.

At T=0 **At T=19 sec** **At T=33sec** **A**

Table 4: Physical properties: hardness, friability drug content of atenolol fast dissolving tablets prepared by direct compression method involving mannitol as diluent.

Formul-ation code	Hardness (Kg/Cm^2) ±S.D	Friability (%)±S.D	Drug Content ± S.D	Disintegration Time (S)±S.D	Wetting Time (sec)±S.D	Water Absorption Ratio (%) ±S.D
F1	3.9±0.01	0.12±0.012	24.11±0.12	36±0.6	39	59.34
F2	4.0±0.01	0.13±0.013	24.32±0.54	35±0.5	21	60.87
F3	3.8±0.04	0.15±0.015	24.61±0.12	33±0.3	31	61.64
F4	3.9±0.06	0.14±0.014	24.42±0.36	30±0.4	29	60.78
F5	4.0±0.01	0.12±0.013	24.22±0.45	28±0.9	33	59.79
F6	3.6±0.03	0.14±0.012	24.62±0.73	25±0.5	32	58.63
F7	3.7±0.02	0.12±0.014	24.82±0.92	22±0.8	22	55.41
F8	4.0±0.01	0.15±0.012	24.27±0.34	20± 0.3	19	53.61

Table 5: Atenolol percent dissolved from dissolving tablets employing starch glutamate prepared by direct compression method involving mannitol as diluent.

Cumulative percent drug atenolol dissolved								
Time (Min)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
1	15.6±0.23	69.2±0.23	63.1±0.78	66.5±0.13	65.8±0.65	52.9±0.12	51.98±0.43	75.39±0.26
2	25.8±0.31	83.5±0.45	66.5±0.67	82.1±0.25	86.9±0.78	67.2±0.34	66.56±0.52	82.18±0.34
3	31.9±0.12	88.9±0.67	86.2±0.34	86.9±0.56	92.3±0.56	82.1±0.54	82.18±0.18	86.26±0.67
4	42.7±0.15	93.7±0.18	89.6±0.56	90.3±0.65	93.7±0.28	86.9±0.23	87.62±0.31	91.69±0.42
5	52.9±0.34	99.1±0.65	95.7±0.21	94.4±0.76	95.7±0.67	89.6±0.31	91.69±0.29	99.84±0.57
6	57.7±0.31	-	97.1±0.89	99.1±0.87	99.1±0.54	93.7±0.36	99.16±0.35	-
7	61.1±0.14	-	99.1±0.56	-	-	98.4±0.45	-	-
8	63.8±0.16	-	-	-	-	-	-	-
9	66.5±0.24	-	-	-	-	-	-	-
10	65.6±0.18	-	-	-	-	-	-	-
15	69.9±0.36	-	-	-	-	-	-	-
20	72.6±0.31	-	-	-	-	-	-	-
25	76.7±0.13	-	-	-	-	-	-	-
30	80.8±0.17	-	-	-	-	-	-	-
45	83.5±0.32	-	-	-	-	-	-	-
60	86.2±0.38	-	-	-	-	-	-	-
90	93.7±0.14	-	-	-	-	-	-	-
120	98.4±0.78	-	-	-	-	-	-	-

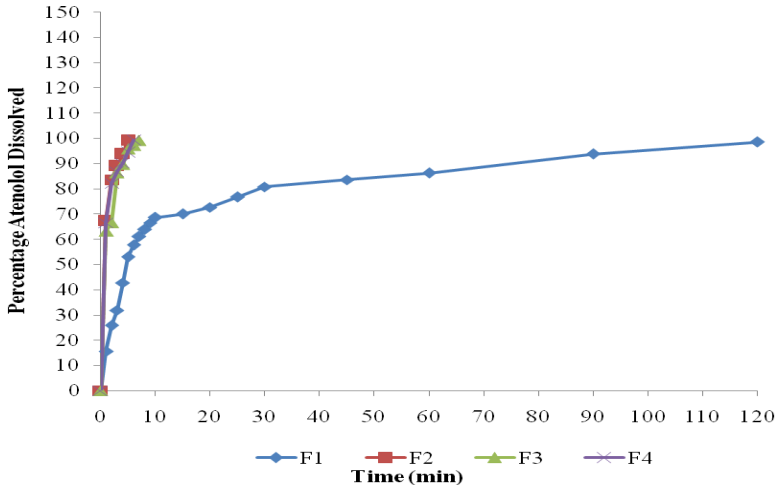


Fig. 10: Dissolution profiles of atenolol fast dissolving tablets employing starch glutamte prepared by direct compression method. (F1, F2, F3 and F4).

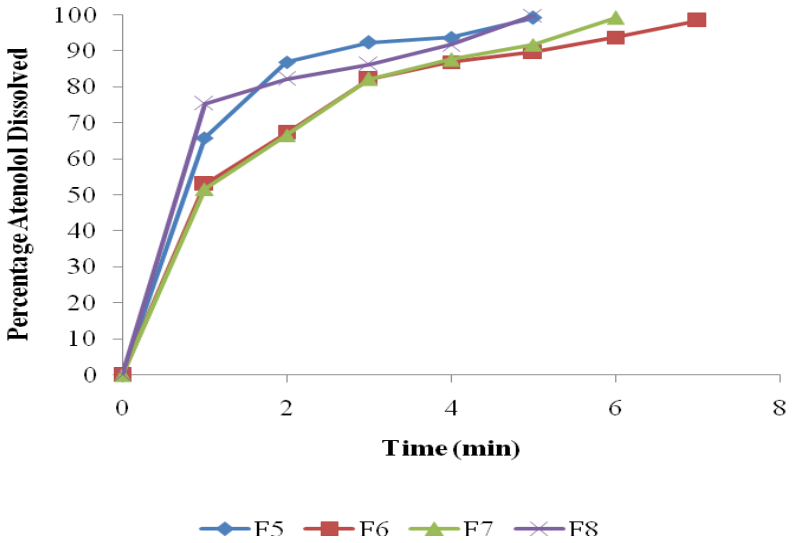


Fig11: Dissolution profiles of atenolol fast dissolving tablets employing starch glutamate prepared by direct compression method. (F5 to F8).

Table 6: Dissolution parameters of atenolol fast dissolving tablets formulated employing Starch Glutamate and other known superdisintegrants prepared by direct compression involving mannitol as diluents.

Parameters	F1	F2	F3	F4	F5	F6	F7	F8
PD_5	2.2	11.9	68.8	66.2	70.4	67.2	75.0	83.9
DE_5 (%)	3.2	9.1	66.13	49.5	49.0	59.8	56.6	64.7
Increase in DE_5 (%) No. of folds	-	2.8	20.6	15.4	15.3	18.6	17.6	20.2
K_1 (min^{-1})	0.0019	0.0099	0.1584	0.0100	0.0004	0.0142	0.1150	0.1829
Increase in K_1 (min^{-1}) No. of folds	-	5.0	80.4	5.0	0.2	7.2	58.5	92.8

To evaluate the individual and combined effects of the factors involved, fast dissolving tablets were formulated employing selected combination of the factors as per 2^3- factorial design. The fast dissolving time and release parameters (percent drug released in 24 h) of the fast dissolving tablets formulated were analyzed as per ANOVA of 2^3- factorial time (table 7) indicated that the individual, effects of starch glutamate (A), sodium starch glycolate (B), and Crospovidone(C) as well as the combined effect of AB, AC, BC and (ABC) factors were significant on disintegration time and dissolution efficiency in 5 min of atenolol for dissolving tablets.

Table 7: ANOVA of dissolution efficiency in 5 min of atenolol fast dissolving tablets formulated employing starch glutamate involving mannitol as diluents.

Source of variation	d. f	S.S	M.S.S	Variance ratio	Result
Replicates	2	0.265	0.132	0.05	P > 0.05
Treatments	7	36442.96	5206.13	2253.73	P < 0.05
Starch Glutamate (A)	1	2212.04	2212.04	957.59	P < 0.05
Sodium Starch Glycolate (B)	1	1731.37	1731.37	749.51	P < 0.05
Starch Glutamate X Sodium Starch Glycolate (AB)	1	340.37	340.37	147.34	P < 0.05
Crospovidone (C)	1	8214.04	8214.04	3555.86	P < 0.05
Starch Glutamte X Crospovidone (AC)	1	7123.00	7123.00	3083.54	P < 0.05
Sodium Starch Glycolate X Crospovidone (BC)	1	652.04	652.04	282.26	P < 0.05
Starch Glutamate X Sodium Starch Glycolate X Crospovidone (ABC)	1	11.04	11.04	13.35	P < 0.05
Error	14	32.415	2.31	---	---
Total	23	---	---	---	---

P<0.05 indicate significance; p>0.05 indicate non-significance.

∗ d.f – Degree of Freedom * S.S – Sum of Square * M.S.S – Mean Sum of Squares.

CONCLUSION

Starch glutamate is an efficient superdisintegrant for fast dissolving tablets. The disintegration and dissolution efficiency of the fast dissolving tablets of atenolol was good and depended on the concentration of superdisintegrant employed i.e., Starch glutamate(10%), and crosscarmellose sodium (5%). The formulated fast dissolving tablets of atenolol employing starch glutamate and crosscarmellose sodium exhibited good dissolution efficiency in 5 min which can be used for the fast therapeutic action of atenolol. Overall, Starch glutamate was found to be a superdisintegrant which enhanced the dissolution efficiency when combined with crosscarmellose sodium, with the atenolol and hence it could be used in the formulation of fast dissolving tablets to provide immediate release of the contained drug within 15minutes.

Abbreviations

FTIR - Fourier transform infrared spectra
DSC - Differential scanning calorimetry
ANOVA - Analysis of variance
PD_5 -Percent dissolved in 5 minutes
DE_5% - Dissolution efficiency in 5 minutes

REFERENCES

1. Bradoo R, Shahani S, Poojary S. Fast dissolving drug delivery systems. JAMA.2001; 4: 27-31.
2. Seager H. Drug delivery product and zydis-fast dissolving dosage form. J Pharm Pharmacol. 1998; 50: 375-82.
3. Abdelbary G, Prinderre P, Couani C, Taochim J, Reynier JP, Riccerelle P. The preparation of orally disintegrating tablets using a hydrophilic waxy binder. Int J Pharm. 2004; 278(2): 423-33.
4. Sastry SV, Nyshadham JR, Fix JA. Recent technological advances in oral drug delivery: a review. Pharm Sci Techol Today. 2000; 3(4): 138-45.
5. Lachman L, Libermann HA, Kanig JL. The theory and practice of industrial pharmacy. 3rd edition. 1991; p: 233-5.
6. Biradar S, Bhagavati S, Kuppasad I. Fast dissolving drug delivery system. A brief overview. Internet J Pharmacol. 2005; 4:2. edition; 199;. P: 233-5.
7. Indurwade NH, Rajyaguru TH, Nakhat PD. Novel approach-fast dissolving tablets. Indian Drug. 2002; 38(8): 405-9.
8. The United States Pharmacopoeia 29. National Formulary 24. Asian Edition. Rockville, MD. United States Pharmacopoeia Convention. Inc. 2006; p: 1890.
9. Jacob S, Shirwaikar A, Joseph A, Srinivasan KK. Novel co-processed excipient of mannitol and microcrystalline callous for preparing fast dissolving tablet of Glipizide. Indian J Pharm Sci. 2007; 69(5): 633-9.
10. Hiremath JG, Shastry CS, Srinath MS. Pharmaceutical approaches of taste masking in oral dorage forms.Indian Drugs. 2004; 41: 253-7.
11. Abdelbary A, Elshafeey AH, Zidan G. Comparative effects of different cellulosic-based directly compressed orodispersible tablets on oral bioavailability of famotidine. Carbohydrate Polymers. 2009;77: 799-806.
12. Battu SK, Michael AR, Soumyajit M, Madhusudan Y. Formulation and evaluation of rapidly disintegrating fenoverine tablets: effect of super disintegrants. Drug Dev Ind Pharm. 2007; 33: 1225-32.
13. Goel H, Vora N, Rana V. A novel approach to optimize and formulate fast disintegrating tablets for nausea and vomiting. AAPS PharmSciTech. 2008; 9: 774–8.
14. Puttewar TY, Kshirsagar MD, Chandewar AV, Chikhale RV. Formulation and evaluation of orodispersible tablet of taste masked doxylamine succinate using ion exchange resin. J King Saud University (Sci). 2010; 22: 229–40.

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