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Research Article

Optimization of starch oxalate as a novel superdisintegrant in fast dissolving systems of poorly soluble drugs

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ABSTRACT

Objective: To enhance the solubility of poorly soluble drugs by using 2^3 factorial design in the formulation of fast dissolving tablets by employing starch oxalate as a superdisintegrant.

Methods: Starch oxalate was synthesized by gelatinization process. The physical and micromeritic properties were performed to evaluate the synthesized starch oxalate. By using 2^3 factorial design, atenolol fast dissolving tablet was prepared by employing starch oxalate as a superdisintegrant in different proportions in each case by direct compression method. In the evaluation of fast dissolving tablets the drug content, hardness, friability, disintegration time and other dissolution characteristics were utilized.

Results: The starch oxalate prepared was found to be fine, free-flowing completely amorphous powder. The compatibility between atenolol and starch oxalate were studied and showed no interaction. The drug content, hardness, and friability have been effective with regard to all the formulated fast dissolving tablets employing starch oxalate. The optimized formulation F8 has the least disintegration time i.e., 24 ± 0.06 s. The *In-vitro* wetting time was less (i.e., 28s) in optimized formulation F8. The water absorption ratio of the formulated tablets was found to be more in F8 formulation $94.42 \pm 0.18\%$. The cumulative drug dissolved in the optimized formulation F8 was found to be $98.70 \pm 0.24\%$ in 5 min.

Conclusion: The dissolution efficiency of atenolol was enhanced when starch oxalate was found to be a superdisintegrant when combined with sodium starch glycolate, croscopovidone and, hence to provide immediate release of the formulated fast dissolving tablets contained drug it could be used.

Keywords: Fast dissolving, Superdisintegrant, Starch oxalate, Dissolution efficiency.

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INTRODUCTION

Oral administration is the most popular route as it has major patient compliance issues and also due to its ease of ingestion without pain and versatility. Many patients find it difficult to swallow tablets and do not take their medicines as prescribed. Particular by pediatrics and geriatrics patients this difficulty is experienced, but this problem also covers to the patients who are ill in bed or traveling. With conventional oral dosage forms many problems are faced by groups like mentally ill, developmentally disable and patients who are uncooperative. It is estimated that 50% of the population is affected by this problem, which results in a high incidence of noncompliance and in-effective therapy. In the oral cavity, fast dissolving tablets that can dissolve or disintegrate have attracted a great deal of attention¹. Indeed, the fast dissolving tablets are an important and attractive alternative to the liquid dosage form. Fast dissolving tablets are not only indicated for people having difficulty in

swallowing but also ideal for unfavorable conditions of administration where water is unavailable². Liquid dosage forms are preferred for pediatrics because of their more bioavailability when compared to solid dosage forms. But the limitation of liquid dosage forms has less stability when compared to solid dosage forms³. Fast dissolving tablets are unique in nature having both advantages of solid and liquid dosage forms like having more bioavailability as liquid dosage forms and more stability as solid dosage forms⁴. The aim of the present work was to formulate and characterize a novel superdisintegrant i.e starch oxalate in the formulation of fast dissolving tablets (FDT) of atenolol by utilizing optimization techniques for rapid dissolution of the drug.

The selection of several experimental and manufacturing steps for a given product and to quantitatively select a formulation, optimization techniques are used which provide both a depth of understanding and an ability to explore and determine the ranges for formulation and processing factors.

It is at this aspect that optimization can become a useful tool to quantitate 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 oxalate, sodium starch glycolate, and crospovidone as superdisintegrants. A 2³ factorial design was applied to investigate the main and interaction effects of the three formulation variables i.e., starch oxalate (A), sodium starch glycolate (B), crospovidone (C) in each case to find the formula with less disintegration time and more dissolution efficiency in 5 min and to permit arbitrary selection of tablets with immediate release of drug within 5 min.

MATERIALS AND METHODS

Materials

Potato starch, sodium hydroxide, oxalic acid, mannitol was purchased from Finar chemicals Ltd, Ahmedabad. Atenolol, sodium starch glycolate, crospovidone was obtained from Yarrow chem. Products, Mumbai. Microcrystalline cellulose was imported from Qualigens fine chemicals, Mumbai. Magnesium stearate and talc was obtained from Molychem, Mumbai.

Preparation of starch oxalate (a novel superdisintegrant)

Initially 5 ml Oxalic acid was dissolved in 20 ml distilled water and the pH is adjusted to 3.5 using 1M sodium hydroxide or 1M hydrochloric acid. To this 5 parts potato starch was added and conditioned for 16 h; the product was kept in the oven at 60 °C for 1 h. Then the product was washed with water to remove any unreacted oxalic acid if present. After washing, the resultant starch oxalate was kept in the oven for 60 °C until it gets dried. The product obtained was ground through sieve no.120.

Characterization of starch oxalate

The starch oxalate prepared was evaluated for the following

Solubility

Starch oxalate solubility was tested in various solvents like distilled water, aqueous buffers of pH 1,2,3,4,6 and organic solvents such as alcohol, dichloromethane, chloroform, acetone and petroleum ether⁵.

pH

The pH of 1% w/v slurry was measured with a pH meter⁵.

Melting point

Melting point was determined by using melting point apparatus⁵.

Viscosity

The viscosity of 1% dispersion in water was measured using Ostwald's viscometer⁵.

Swelling index

Starch oxalate (200 mg) was added to two different graduated test tubes containing 10 ml water and light liquid paraffin and mixed. Then the dispersed solution in the tubes was allowed to stand for 12 h. The volumes of the residue in the tubes were noted. The swelling index (*S.I*) of the material was calculated as follows⁶.

$$S.I(\%) = \frac{\text{Volume of residue in water} - \text{Volume of residue in light liquid paraffin}}{\text{Volume of residue in light liquid paraffin}} \times 100$$

Test for gelling property

The evaluation of the gelling property (gelatinization) of the prepared starch oxalate and starch was done by heating a 7% w/v dispersion of each in water at 100 °C for 30 min⁷.

Moisture absorption

The hygroscopic nature of starch oxalate was evaluated by moisture absorption studies in a closed desiccator at 86% relative humidity and at room temperature⁷.

Particle size

Particle size analysis was determined by sieving using standard sieves⁷.

Density

Density (g/cc) was determined by liquid displacement method using distilled water as liquid⁷.

Bulk density

Both loose bulk density (LBD) and tapped bulk density (TBD) were determined by transferring the proper weighed amount of sample in 50 ml measuring cylinder, the granules of without any agglomerates were taken and measured the volume of packing and tapped 50 times on a plane surface and tapped volume of packing recorded LBD and TBD calculated by following formula^[7].

$$LBD = \frac{\text{Mass of powder}}{\text{Volume of packing}}$$

$$TBD = \frac{\text{Mass of powder}}{\text{Tapped volume of packing}}$$

Percentage compressibility index

Percentage compressibility of the powder mix was calculated by Carr's compressibility index by using the following formula⁸.

$$\% \text{ Carr's Index} = \frac{(\text{Final} - \text{Initial})}{\text{Final}} \times 100$$

Where Final= Tapped bulk density; Initial= Loose bulk density.

Angle of repose

The angle of repose was done by the fixed funnel method. The frictional forces in loose powder or granules can be determined by the angle of repose. This is the maximum angle possible between the surface of a mass of powder or granules along with the horizontal plane. The angle of repose is calculated by using the following equation⁸;

$$\tan \theta = \frac{h}{r} \quad \theta = \tan^{-1} \frac{h}{r}$$

Where θ =angle of repose; h=height of the pile; r=radius of the pile.

Fourier transform infrared (FTIR) spectroscopy

FTIR spectra of starch oxalate were recorded on samples prepared in potassium bromide (KBr) disks using a Bruker FT-IR, (Tokyo, Japan). In (KBr) disks the Samples were

prepared by means of a hydrostatic press at 6-8 tons pressure. The scanning range was 500 to 4000cm⁻¹⁸.

X-ray diffraction

The diffraction pattern of starch oxalate was recorded with an X-ray diffractometer (analytical spectra's Pvt. Ltd., Singapore). X-ray diffraction was worked at room temperature (30 °C) with a diffractometer; target, Cu(λ=1.54 Å), filter, Ni, voltage, 45 kV, current 40 mA; time constant 10mm/s; scanning rate 2 °/min; measured from 10-35 ° at full scale 200⁸.

Drug-excipient compatibility studies

The compatibility of starch oxalate with the selected drug (atenolol) was evaluated in DSC and FTIR studies.

Differential scanning calorimetry (DSC)

In Perkin Elmer thermal analyser the samples (2- 5 mg) of atenolol and their mixtures (1: 1) with starch oxalate were sealed into aluminum pans and scanned at a heating rate of 10 °C min⁻¹ over a temperature range 30 – 350 °C and was recorded to get DSC thermograms⁸.

Infrared Spectroscopy

Fourier transform infra red (FTIR) spectra of atenolol, and their mixtures (1: 1) with starch oxalate were recorded on a

Perkin Elmer, IR Spectrophotometer model: Spectrum RXI, using KBr disc as a reference ⁸.

Preparation of atenolol fast dissolving tablets

The tablets were prepared by direct compression method employing 2³ factorial design in which three independent variables {superdisintegrants i.e., starch oxalate (A), sodium starch glycolate (B), crospovidone (C)} and one dependent variable (dissolution efficiency in 5 min) were preferred. The composition of a 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 oxalate (A), sodium starch glycolate (B) and crospovidone (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 to get fine particles before mixing. All the excipients namely starch oxalate, sodium starch glycolate, crospovidone, mannitol, and microcrystalline cellulose were geometrically weighed and mixed by trituration to which atenolol was added. Finally, talc and magnesium stearate were administered in the powder mixture. Finally, the mixed blend was compressed by utilizing eight station rotator press Karnawathi Machineries Pvt, Ltd., Ahmedabad, India).

Table 1: Formulation of atenolol fast dissolving tablets employing starch oxalate prepared by direct compression method.

Ingredients(mg/tablet)	F1	F2	F3	F4	F5	F6	F7	F8
Atenolol	50	50	50	50	50	50	50	50
Starch oxalate	-	11	-	11	-	11	-	11
Sodium starch glycolate	-	-	11	11	-	11	-	11
Crospovidone	-	-	-	-	11	-	11	11
Mannitol	61.2	50.2	50.2	39.2	50.2	39.2	39.2	28.2
Microcrystalline cellulose	100	100	100	100	100	100	100	100
Talc	4.4	4.4	4.4	4.4	4.4	4.4	4.4	4.4
Magnesium stearate	4.4	4.4	4.4	4.4	4.4	4.4	4.4	4.4
Total weight (mg)	220	220	220	220	220	220	220	220

Evaluation of atenolol fast dissolving tablets

Hardness

To break a tablet diametrically the compression force, the force of the tablet hardness is required. The hardness tester used in the study was Monsanto hardness tester, which applies force to the tablet diametrically with the help of an in-built spring and expressed in kg/cm²⁹.

Uniformity of weight

Weight variation test was done with 20 tablets. It is the individual variation of tablet weight from the average weight of 20 tablets⁹.

Average weight of tablet	% Deviation
80 mg or less	±10
More than 80 mg or less than 125mg	±7.5
125 mg or less	±5

Friability

The friability of tablets was determined by using a Roche friabilator. Initially, 20 tablets were weighed and the tablets

were kept in Roche friabilator and it was rotated at 25 rpm for 4 min or up to 100 revolutions. After 4 min or 100 revolutions, the tablets were taken out from the friabilator and then reweighed after removal of fines. Finally, the percentage of weight loss was calculated¹⁰.

$$F = \frac{100 \times W(\text{initial}) - W(\text{final})}{W(\text{initial})}$$

Other W (initial) = Initial weight of tablet.

W (final) = Final weight of tablet.

Drug Content Uniformity

For content uniformity, ten tablets were weighed and powdered a quantity of powder equivalent to 10 mg of atenolol was extracted into 0.1N HCl buffer and filtered. The atenolol content was determined by measuring the absorbance spectrophotometrically at 225 nm after appropriate dilution with 0.1N HCl buffer. The drug content was determined as an average of three determinations ¹⁰.

Wetting Time

The wetting time of tablets was determined by using a very simple procedure. Five circular tissue papers of 10 cm

diameter were kept on a petri dish with a 10 cm diameter. Ten milliliters of distilled water containing a water-soluble dye (amaranth) was added to the petri dish. A tablet was gently placed on the tissue paper. The time required for water to reach the upper surface of the tablet was noted as wetting time ¹⁰.

Water Absorption Ratio

In a small petri dish a piece of tissue paper was folded twice and kept according to its size containing 6 ml of water and to that, The tablet was weighed and kept on the tissue paper and was allowed to wet completely. Then the wetted tablet was weighed. Water absorption ratio R was calculated using the following equation ¹¹.

$$R = \frac{100(W_1 - W_2)}{W_2}$$

Where,

W₁ = weight of tablet after water absorption.

W₂ = weight of tablet before water absorption.

In - vitro Disintegration Time

Disintegration time for FDTs was measured by using USP disintegration apparatus 0.1N HCl buffer. The volume of medium was 900 ml and the temperature was 37±0.2 °C. The time in seconds was measured for complete disintegration of the tablet with no palatable mass remaining in the apparatus¹².

In - vitro Dissolution Rate Studies

The *in - vitro* dissolution rate study of atenolol fast dissolving tablets were performed using 8 stage dissolution test apparatus (Electrolab TDT=08L) fitted with paddles (50 rpm) at 37±0.5 °C, using 0.1N HCl buffer (900 ml) as a

dissolution media. At the predetermined time intervals, 5ml samples were withdrawn, filtered through a 0.45µm membrane filter, diluted and assayed at 225 nm using an ELICO UV/Visible spectrophotometer model - 371. Cumulative percentage release was determined by using standard absorbance from the calibration curve. All the dissolution experiments were administered in triplicate (n=3) ¹³.

RESULTS AND DISCUSSION

The starch oxalate prepared was found to be fine, free-flowing amorphous powder. The physical and micromeritics properties of the starch oxalate are summarized in table 2. It was insoluble in aqueous solvents and insoluble in organic solvents tested (methanol, petroleum ether, dichloromethane, and chloroform) the pH of 1% aqueous dispersion was 5.61.

Starch oxalate exhibited good swelling in water. The swelling index was found to be 66.66 % indicating that it is suitable for superdisintegrant. All micrometric properties had shown good flow properties needed manufacturing of tablets. The density of starch oxalate was found to be 1.1792 g/ml. The angle of repose and compressibility index showed good flow properties of starch oxalate. The FTIR spectrum of potato starch and starch oxalate is shown in fig: 1 and 2. The presence of peak absorption at 1637.30 cm⁻¹ in FTIR characteristic peak of ester concluded that starch oxalate (ester) was formed when starch was allowed to react with oxalic acid. The X-ray diffraction pattern (fig: 3) of starch oxalate showed no characteristic peaks, which indicates that the structure is completely amorphous. As the starch oxalate was completely amorphous powder and it had got all the characteristic of superdisintegrants it was concluded that starch oxalate can be used as novel superdisintegrant in the formulation of fast dissolving tablets.

Table 2: Physical and micromeritics properties of the starch oxalate prepared

Parameters	Observation
Solubility	Insoluble in all aqueous and organic solvents tested.
pH (1% w/v aqueous dispersion)	5.61±0.02
Melting point (in °C)	232±0.001
Viscosity(1%w/v aqueous dispersion)(in cps)	1.0242±0.008
Swelling index (in %)	66.66 ±0.05
Gelling property	No gelling and the swollen particles of starch oxalate separated from water. Whereas in the case of starch, it was gelatinized and formed a gel.
Moisture absorption (in %)	4.8±0.2
Particle size (in µm)	135±0.09
Density (in g/cc)	1.1792 ±0.0004
Bulk density (in g/cc)	0.61 ±0.03
Angle of repose (in °)	26.49±0.07
Compressibility index (in %)	35.59±0.01

*SD Standard Deviation from mean, n=3, mean±SD

Figure 1: Fourier transform infrared spectra of potato starch.

Figure 2: Fourier transform infrared spectra of starch oxalate

Figure 3: X-ray diffraction pattern of starch oxalate

The compatibility of starch oxalate with the selected drug (atenolol) was evaluated by DSC, FTIR studies. The DSC thermograms of atenolol and atenolol – starch oxalate are shown in fig.4 and 5. The DSC thermograms of atenolol and atenolol – starch oxalate exhibited exothermic peaks at 155.66 °C and 152.63 °C respectively. These melting peaks of atenolol and atenolol – starch oxalate are nearer to the melting points of atenolol (158-160 °C). The peaks observed in the DSC thermograms of atenolol and atenolol – starch oxalate mixtures correspond to the melting points of the respective drug indicating no interactions between the selected drug and starch oxalate polymer. Thus, the DSC

study of starch oxalate and selected drug indicated no interaction between them.

The FTIR spectra of atenolol and atenolol - starch oxalate are shown in figs. 6 and 7. The characteristic FTIR bands of atenolol at 1637.41 cm⁻¹ (C=O Stretched, N-H Bending), 1583.60 cm⁻¹ (C-C aromatic ring) 1417.66 cm⁻¹ (O-H Bending) and atenolol - starch oxalate at 1637.47 cm⁻¹ (C=O Stretched, N-H Bending), 1583.74 cm⁻¹ (C-C aromatic ring) 1416.35 cm⁻¹ (O-H Bending) was all observed in the FTIR spectra of both atenolol and atenolol - starch oxalate. These FTIR spectral

observations also indicated no interaction between starch oxalate and the drug selected.

Thus, the results of DSC and FTIR indicated no interaction between the selected drug and starch oxalate, the new

superdisintegrant. Hence, starch oxalate could be used as a superdisintegrant in the design of fast dissolving tablets of the selected drug.

Figure 4: DSC Thermogram of atenolol pure drug

Figure 5: DSC Thermogram of atenolol with starch oxalate

Figure 6: FTIR Spectra of Atenolol Pure Drug

Figure 7: FTIR spectra of atenolol with starch oxalate

Evaluation of tablets

Hardness

The hardness of tablets from all batches was found to be in the range of 3.6 ± 0.03 kg/cm² to 4 ± 0.01 kg/cm². All tablets were found to be hard enough so that they could easily withstand the handling and storage conditions.

Friability

All the tablets shown acceptable friability as none of the tested batches showed percentage friability that exceeded 1%. The percent friability of all batches found in the range of 0.12%-0.17% indicating the good mechanical resistance of tablets. Hence, it was observed that tablets could withstand the pressure, mechanical shocks during handling, transportation, storage, and manufacturing processes.

Drug content

Drug content of all the formulation batches was found to be between 47.65 ± 0.55 to 49.95 ± 0.66 mg/tablet. Hence, it can be concluded that all the formulations are having an accurate amount of drug distributed uniformly in powder mass and are within acceptable limits as per IP¹⁴.

Disintegration studies

In vitro disintegration time was determined by the USP dissolution apparatus. The disintegration rate has a correlation with water absorption capacity of the tablet and the *In vitro* disintegration time was found between 24 ± 06 to 156 ± 04 s. The outcomes were arranged in tabulated form and data was demonstrated in table 3.

Table 3: Physical properties: Hardness, Friability, Drug content of atenolol fast dissolving tablets prepared by the direct compression method

Formulation	Hardness (Kg/Cm ²) n±S.D	Friability (%)n±S.D	Drug content (mg/tab)n±S.D	Disintegration Time(sec)n±S.D	Water absorption ratio(%)n±S.D
F1	3.9 ± 0.02	0.13 ± 0.014	48.24 ± 0.17	156 ± 0.04	56.34 ± 0.13
F2	3.8 ± 0.04	0.12 ± 0.013	47.88 ± 0.43	139 ± 0.03	64.61 ± 0.14
F3	3.7 ± 0.03	0.16 ± 0.012	47.69 ± 0.18	121 ± 0.02	65.22 ± 0.17
F4	3.6 ± 0.06	0.13 ± 0.014	48.82 ± 0.56	49 ± 0.04	79.29 ± 0.28
F5	4.0 ± 0.01	0.12 ± 0.013	47.65 ± 0.55	54 ± 0.07	75.26 ± 0.43
F6	3.8 ± 0.05	0.15 ± 0.012	48.66 ± 0.58	35 ± 0.09	79.29 ± 0.28
F7	3.7 ± 0.03	0.17 ± 0.014	49.02 ± 0.67	40 ± 0.08	88.82 ± 0.29
F8	3.9 ± 0.05	0.15 ± 0.012	49.95 ± 0.66	24 ± 0.06	94.42 ± 0.18

*SD Standard Deviation from mean, n=3, mean±SD

All the formulations showed disintegration time of less than 180s. It was found that the formulation of F8 showed least disintegration time i.e., 24s as compared to other formulations. The order for a disintegration time in atenolol fast dissolving tablets was found to be $F8 < F6 < F7 < F4 < F5 < F3 < F2 < F1$. The order of disintegration time may be due to the interaction and main effects of the super disintegrants used in the formulation of fast dissolving tablets.

Water absorption ratio and wetting time

The Water absorption ratio was found to be in between 56.34 ± 0.13 to 94.42 ± 0.18 . This increased behavior due to the water taking the ability of super disintegrants. The wetting time was found to be in between 28 ± 0.41 to 144 ± 0.21 s. The outcomes were tabulated and data demonstrated in Table 3 and fig. 8 and 8a. It was found that the formulation F8 containing 5% starch oxalate, sodium starch glycolate 5% and crospovidone 5% showed less wetting time i.e. 28 ± 0.41 s as compared to other formulations.

In vitro dissolution studies

Dissolution rate depends on the wetting time of the disintegrant, among all the formulations F8 has less wetting time and has greater dissolution rate and then this is the other conformance test for correct selection of desirable. *In vitro* dissolution studies of all the formulation were done and depicted in fig. 9 (F1 to F4) and fig. 9a (F4 to F8). In all formulations F8 formulation was selected as the promising formulation containing 5% starch oxalate, 5% sodium starch glycolate and 5% croscopovidone with 98.70% release in 5 min which may be due to the interaction effect between the three super disintegrants i.e., starch oxalate, Sodium starch glycolate and croscopovidone at a concentration of 5% each. The dissolution parameters of the formulation from (F1–F8) which were made by direct compression method were shown in the table: 4. In all these cases the PD₅ (percent dissolved in 5 min) was more in F₈ which consists of 5%

starch oxalate, 5% sodium starch glycolate and 5% croscopovidone. The same was in the case of DE₅ % (dissolution efficiency in 5 min). The PD₅ & DE₅ % reveals that starch oxalate was effective at 5% along with, 5% sodium starch glycolate and 5% croscopovidone when the formulations were made by direct compression using these superdisintegrants. The K₁ decreased in all the formulation when compared to the F8 formulation which was given in the table 4. The number of folds increases in DE₅% and the number of folds increases in K₁ (min⁻¹) were given in the table 4. From the results, it was concluded that starch oxalate could be used as a super disintegrant in the formulation of fast dissolving tablets of atenolol. To evaluate the individual and combined effects of the three factors involved, fast dissolving tablets were formulated employing selected combinations of the factors as per 2³-factorial design.

Table 4: Dissolution parameters of atenolol fast dissolving tablets formulated employing starch oxalate and other known super disintegrants prepared by direct compression method.

Paramters	F1	F2	F3	F4	F5	F6	F7	F8
PD ₅	36.23±0.39	41.00±0.41	43.86±0.27	58.17±0.86	51.97±0.14	61.03±0.66	80.58±0.92	98.70±0.11
DE ₅ (%)	17.8±0.54	20.5±0.29	24.1±0.61	27.9±0.45	29.4±0.09	30.8±0.39	50.9±0.87	60.2±0.54
Increase in DE ₅ (%) No of Folds	-	1.151	1.353	1.567	1.651	1.730	2.859	3.382
K (min ⁻¹)	0.070±0.003	0.039±0.007	0.082±0.005	0.135±0.001	0.103±0.007	0.159±0.004	0.308±0.002	0.552±0.009
Increase in K (min ⁻¹) No of Folds	-	0.565	1.174	1.924	1.467	2.260	4.371	7.828

*SD Standard Deviation from mean, n=3, mean±SD, PD₅-Percent dissolved in 5 min., DE₅%-Dissolution efficiency in 5 min.,

K₁ =First order rate constant

Figure 9: Dissolution profiles of atenolol fast dissolving tablets prepared employing starch oxalate (F1-F4) (n=3, mean±SD)

Figure 9a: Dissolution profiles of atenolol fast dissolving tablets prepared employing starch oxalate (F5-F8) (n=3, mean $\pm$ SD)

The fast dissolving tablets parameters like disintegration time and dissolution efficiency in 5 min were analyzed as per ANOVA of 2³-factorial design. ANOVA of fast disintegrating times (Table 5) indicated that the individual effects of starch oxalate (A), sodium starch glycolate (B) and crospovidone (C), as well as the combined effects of AB, AC, BC and ABC factors, were significant (P<0.05) on disintegration time and dissolution efficiency in 5 min of atenolol fast dissolving tablets.

ANOVA of dissolution efficiency in 5 min (Table 6) indicated that the individual effects, as well as combined effects of the three factors (i.e., starch oxalate, sodium starch glycolate, and crospovidone), were all significant (p<0.05). The ANOVA results thus indicated that the three factors have a significant influence on the disintegration time and dissolution efficiency in 5 min of atenolol fast dissolving tablets.

Table 5: ANOVA of disintegrating times of atenolol fast dissolving tablets employing starch oxalate

Source of variation	d.f	S.S	M.S.S	Variance ratio	Result
Replicates	2	200.0833	100.0416	3.9573	P > 0.05
Treatments	7	62268.9583	8895.5654	351.8857	P < 0.05
Starch oxalate(A)	1	6240.375	6240.375	246.8532	P < 0.05
Sodium starch glycolate (B)	1	1208.375	1208.375	47.8002	P < 0.05
Starch oxalate X Sodium starch glycolate (AB)	1	1190.0416	1190.0416	47.0779	P < 0.05
Crospovidone (C)	1	37209.375	37209.375	1471.9073	P < 0.05
Starch oxalate X Crospovidone (AC)	1	1276.0416	1276.0416	50.4769	P < 0.05
Sodium starch glycolate X Crospovidone (BC)	1	4845.0416	4845.0416	191.6574	P < 0.05
Starch oxalate X Sodium starch glycolate X Crospovidone(ABC)	1	1162.0416	1162.0416	45.9673	P < 0.05
Error	14	353.9167	25.2797	-	-
Total	23	-	-	-	-

P < 0.05 indicate significance; p > 0.05 indicate non-significance *S.S= Sum of Squares, *M.S.S= Mean Sum of Square, *d.f= Degrees of Freedom

Table 6: ANOVA of dissolution efficiency in 5 min of fast dissolving tablets formulated employing starch oxalate

Source of variation	d.f	S.S	M.S.S	Variance ratio	Result
Replicates	2	134.2406	67.1203	3.5451	P > 0.05
Treatments	7	4814.9833	687.8547	36.3306	P < 0.05
Starch oxalate(A)	1	255.4537	255.4537	13.4923	P < 0.05
Sodium starch glycolate (B)	1	1480.5104	1480.5104	78.1965	P < 0.05
Starch oxalate X Sodium starch glycolate (AB)	1	180.442	180.442	9.5304	P < 0.05
Crospovidone (C)	1	2703.0037	2703.0037	142.7652	P < 0.05
Starch oxalate X Crospovidone (AC)	1	325.678	325.678	17.1656	P < 0.05
Sodium starch glycolate X crospovidone (BC)	1	372.0937	372.0937	19.6529	P < 0.05
Starch oxalate X Sodium starch glycolate X Crospovidone(ABC)	1	223.678	223.678	11.8140	P < 0.05
Error	14	265.0655	18.9332	-	-
Total	23	-	-	-	-

P < 0.05 indicate significance; p > 0.05 indicate non-significance, *d.f= Degrees of Freedom *S.S= Sum of Squares, *M.S.S= Mean Sum of Squares

Fast dissolving tablets formulated employing starch oxalate (5%), sodium starch glycolate (5%) and crospovidone (5%) as super disintegrants exhibited less disintegration time and more dissolution efficiency in 5 min. Formulation F8 gave release of 98.70% in 5 min fulfilling the official specification, based on disintegration time and dissolution efficiency in 5 min, formulation F8 is considered as a good fast dissolving tablet formulations of atenolol which was found to better than the atenolol fast dissolving tablets formulated by Parthiban S. et al.¹⁵.

CONCLUSION

Starch oxalate is an efficient superdisintegrant for fast dissolving tablets. The less disintegration time and dissolution efficiency in 5min of the fast dissolving tablets of atenolol depended on the concentration of superdisintegrant employed i.e., starch oxalate (5%), sodium starch glycolate (5%), and crospovidone (5%). The formulated fast dissolving tablets of atenolol employing starch oxalate, sodium starch glycolate and crospovidone exhibited good dissolution efficiency in 5 min which can be used for the fast therapeutic action of atenolol.

Overall, Starch oxalate was found to be a super-disintegrant when combined with sodium starch glycolate and crospovidone, the dissolution efficiency of atenolol was enhanced and hence it could be used in the formulation of fast dissolving tablets to provide immediate release of the poorly soluble drugs within 5 min.

Abbreviations:

FTIR - Fourier transform infrared spectra

DSC - Differential scanning calorimetry

ANOVA – Analysis of variance

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