DOI: 10.55522/jmpas.v3i1.0040 **ISSN NO. 2320 – 7418**

International peer reviewed open access journal

Journal of Medical Pharmaceutical and Allied Sciences

Journal homepage: www.jmpas.com CODEN: JMPACO

Research article

Formulation and In- Vitro Evaluation of Alfuzosin HCl Floating Tablet

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Received – 20 January 2014**, Revised -** 25 January 2013, **Accepted** – 23 February 2014 **(DD-MM-YYYY)**

Refer This Article

Hemant Mehta, 2014. Formulation and In- Vitro Evaluation of Alfuzosin HCl Floating Tablet. Journal of medical pharmaceutical and allied sciences, V 3 - I 1, Pages -154 – 158. Doi: https://doi.org/10.55522/jmpas.V3I1.0040.

ABSTRACT

The purpose of this Research work was to prepare and optimized floating tablet of Alfuzosin HCl. Alfuzosin HCl is an alpha-1 adrenergic receptor blocker for the treatment of benign prostatic hyperplasia. Alfuzosin HCl exhibits narrow absorption window. Alfuzosin HCl has a short biological half-life (3-5 hours). The dose may range from 2.5 mg thrice a day to a maximum of 10 mg once a day which results into inconveniency to the patients. By preparing sustained release floating tablet of Alfuzosin HCl that deliver drug for longer time, reduce dosage frequency & better patient compliance. The present Research work describes the influence of the concentration of Xanthan Gum and Sodium bicarbonate on Alfuzosin HCl floating tablet using Central Composite Design. The Xanthan Gum (X1) and Sodium bicarbonate (X2) were selected as independent variables, while time required for 50% drug release (t_{50}), time required for 90% drug release (t_{90}), drug release at 12 hr (Q_{12}), floating lag time, diffusion exponent (n), release rate constant (k) were selected as a dependent variables. Tablets were prepared by direct compression technique & evaluated for pre-compression and post-compression parameters. Dissolution data were fitted to various models to ascertain kinetic of drug release. Regression analysis and analysis of variance were performed for dependent variables. All the batches were evaluated for the pre-compression and post- compression parameters and results were within the limits. All the batches exhibited appropriate floating lag time & showed total floating time of more than 24 hrs. It was observed that concentration of Xanthan Gum and Sodium bicarbonate had significant influence on t_{50}, t_{90}, Q_{12}, floating lag time, n, and k. Optimized formulation (H10) showed 99.52% drug release at the end of 24 hrs and maximum similarity factor (f_2=83.15) and minimum dissimilarity factor (f_1=2.80) with Theoritical release profile of Alfuzosin HCl. Optimized formulation followed by anomalous non Fickian release mechanism and found to be stable after 23 days at accelerated condition.

Keywords: Global Health, Robson's Ten Classification, Cesarean Section, WHO, Photodynamic therapy.

INTRODUCTION

Benign prostatic hyperplasia (BPH) is the most common benign condition affecting men and symptoms can start as early as age 30. Benign prostatic hyperplasia is a progressive condition characterized by prostate enlargement accompanied by lower urinary tract symptoms. Benign prostatic hyperplasia involves hyperplasia of prostatic stromal and epithelial cells resulting in the formation of large, fairly discrete nodules in the periurethral region of the prostate. Benign prostatic hyperplasia can result in the prostatic urethra is compressed which restricts the flow of urine from the bladder, this interference with urine flow may cause uncomfortable symptoms such as frequency, urgency, nocturia, intermittency, decreased stream and hesistancy. Benign prostatic hyperplasia can leads to the risk of urinary tract infection, urinary retention and kidney blockage. Benign prostatic hyperplasia does not lead to the risk of cancer. Intially management for benign prostatic hyperplasia includes lifestyle modification, used alpha blockers and 5-alpha reductase inhibitors. The alpha blockers work to relax the smooth muscle at the prostate and bladder neck by blocking alpha1 receptor. By relaxing the smooth muscle at the prostate neck, the urinary channel is opened which allows a less constricted urinary flow.

Alfuzosin HCl is used for the treatment of benign prostatic hyperplasia. Alfuzosin HCl exhibits narrow absorption window.

Alfuzosin HCl has a short biological half life (3-5 hours). The dose may range from

2.5 mg thrice a day to a maximum of 10 mg once a day, if it is formulated as conventional tablets it will required multiple daily administration (2-3 times daily) which results into inconveniency to the patients. So Alfuzosin HCl is an ideal candidate for controlled release in the proximal upper parts of the gastrointestinal tract. Thus formulation of floating drug delivery satisfied these conditions [1].

MATERIAL

Alfuzosin HCl was obtained as gift sample from Sun Pharmaceutical. Xanthan Gum was kindly gifted from Megh Pharmaceutical, Modasa. Guar Gum was gifted from Alembic Pharmaceutical Ltd, Vadodara. Sodium bicarbonate and Microcrystalline cellulose was obtained as gift sample from Finer Chemicals Ltd, Ahmedabad. Magnesium stearate was gifted from Acme Chemicals, Mumbai and Talc was obtained as gift sample from Lesar Chemicals Ltd, Vadodara.

METHODOLOGY

Preparation of Alfuzosin HCl Floating Tablets

Tablets were prepared by direct compression technique. All the ingredients were accurately weighed and passed through sieve no. 60 before using into formulation. All the ingredients mixed except magnesium stearate and talc geometrically. Required quantity of polymer and sodium bicarbonate as gas generating agent were mixed then Alfuzosin HCl is added and mixed properly then diluent is added to make up the weight. The blend obtained was then lubricated by adding magnesium stearate and talc and manually compressed on 10 station rotary tablet machine using flat-faced die punches of 6.0 mm diameter. The tablets were compressed to obtain hardness in a range of 6-7 Kg/cm^2.

Evaluation of Powder Blend and Tablets

Drug-Excipients Compatibility study

Fourier transform infrared spectroscopy has been used to study the physical and chemical interaction between drug and the excipients used. Fourier transform infrared (FTIR) spectra of Alfuzosin hydrochloride, Xanthan Gum were recorded using KBr mixing method.

Loose Bulk Density

Weigh accurately 5 gm of powder blend, and transferred in 100 ml graduated cylinder. Carefully level the powder blend without compacting, and read the unsettled apparent volume (V0). Calculate the apparent bulk density in gm/ml by the following formula:

Bulk Density = Mass/ apparent volume

Tapped Bulk Density

Weigh accurately 5 gm of powder blend, and transferred in 100 ml graduated cylinder. Then mechanically tap the cylinder containing the sample by raising the cylinder and allowing it to drop under its own weight using mechanically tapped density tester that provides a fixed drop of 14 ± 2 mm at a nominal rate of 300 drops per minute. Tap the cylinder for 500 times initially and measure the tapped volume (V1) to the nearest graduated units, repeat the tapping an additional 750 times and measure the tapped volume (V2) to the nearest graduated units, if the difference between the two volumes is less than 2% then final the volume (V2). Calculate the tapped bulk density in gm/ml by the following formula:

Tapped Density = Mass/ tapped volume

Carr's Index

The Compressibility Index of the powder

In Group 1 (nulliparous, ≥37wks in spontaneous labour) out of total 353 cases, 71 (20.1%) women underwent LSCS.

blend was determined by Carr's compressibility index. The formula for Carr's Index is as below:

Carr's Index = Tapped Density-Bulk Density×100/ Tapped Density

Hausner's Ratio

The Hausner's ratio is a number that is correlated to the flow ability of a powder blend material.

Hausner's Ratio = Tapped Density/Bulk Density

Angle of Repose

The angle of repose of powder blend powder was determined by the funnel method. The powder blend was taken in the funnel. The height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. The powder blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder blend cone was measured and angle of repose was calculated using the following Equ.

Angle of Repose **(□)**. = $\tan^{-1}h/r$

Where, h = Height of the powder blend cone, r = Radius of the powder blend cone

Weight Variation Test

The 20 tablets were selected at random, weighed and the average weight was calculated. Not more than two of the individual weights should deviate from the average weight by more > 10%.

F r i a b i l i t y

For each formulation, pre weighed tablet sample (10 tablets) were placed in the Roche friabilator which is then operated for 100 revolutions. The tablets were deducted and reweighed. Conventional compressed tablets that loose < 0.5 to 1% of their weight are considered acceptable.

Hardness

Hardness of tablet was determined using Monsanto hardness tester.

Content Uniformity

The 20 tablets were crushed and the powder equivalent of 100 mg of drug was transferred to 100 ml of 0.1 N HC1 in volumetric flask. The solution was analyzed at 244 nm using double beam UV-Vis spectrophotometer after suitable dilution.

***In vitro* buoyancy study**

The *In vitro* buoyancy was characterized by floating lag time (FLT) and total floating time (TFT). The test was performed using USP 24 type II paddle apparatus using 900

The statistical analysis of the factorial design batches was performed by multiple regression analysis using Microsoft Excel. Data obtained from all formulations were analyzed using statistica software and used to generate the study design and the response surface plots. Polynomial models were generated for all the response variables using Microsoft Excel. In addition analysis of variance (ANOVA) was used to identify significant effects of factors on response regression coefficients. The F value and p values were also calculated using Microsoft Excel. The relationship between the dependent and independent variables was further elucidated using response surface plots.

Similarity factor (f2)

To evaluate and comparison of dissolution profiles, the dissolution profiles were analyzed using similarity factor f_2 The equation for calculating f_2 is given below.

Substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity, and light, and to establish a re-test for the drug substance or a shelf life for the drug product and recommended storage

Where, n is numbers of dissolution time point, W_t is optional weight factor, R_t is reference dissolution point at time t and T_t is test dissolution point at time t. The f_2 value between 50 and 100 suggests that the dissolution profiles are similar.

Dissimilarity factor (f_1)

The dissimilarity factor (f_1) calculates the percent difference between the two curves at each time point and is a measurement of the relative error between the two curves:

(40^0C ± 2^0C / 75 % ± 5% RH). Stability study was carried out for the optimized formulations. Tablets of optimized formulation were striped packed and kept in humidity chamber on above mention temperature [3].

RESULT AND DISCUSSION

Drug Excipient Compatibility Study

Fourier transform infrared spectroscopy has been used to study the physical and chemical interactions between drug and the Accelerated stability study.

The purpose of stability testing is to provide evidence on how the quality of drug.

Xanthan Gum were recorded using KBr mixing method. FTIR study showed that there was no interaction between drug and polymer that are shown in figure 1. So, the drug and polymer were compatible with each other.

Results of Pre-Compression evaluation parameter of trial batches The powder mixture used for tablet preparation was evaluated for pre-compression parameters results

Results of Pre-Compression parameters of CCD batches

The tablet blend of all the batches was evaluated for Post-Compression parameters.

Results of Post-Compression evaluation parameter of trial batches

All the prepared tablets showed acceptable pharmaceutical properties. All the tablets passed weight variation test as the percent weight variation was within the pharmacopoeial limits. Hardness were shown in the range of 6.2-6.4 kg/cm2 in all the formulations which indicated good mechanical strength with an ability to withstand physical and mechanical stress conditions while handling. In all the formulations, the friability value was less than 1% and meets the official limit. The percentage drug content of all the tablets was found to be between 96.1%-101.0% of Alfuzosin HCl which was within acceptable limit.

Results of Post-Compression parameters of CCD batches

All the prepared tablets showed acceptable pharmaceutical properties. All the tablets passed weight variation test as the percent weight variation was within the pharmacopoeial limits. Hardness were shown in the range of 6.0-7.0 kg/cm2 in all the formulations which indicated good mechanical strength with an ability to withstand physical and mechanical stress conditions while handling. In all the formulations, the friability value was less than 1% and meets the official limit. All the batches exhibited appropriate floating lag time and showed total floating time of more than 24 hrs. The percentage drug content of all the tablet**s was within acceptable limit** [4].

Result of In-Vitro drug release of trial batches

The results of in vitro drug release study are depicted in figure 2. From the dissolution profile it was observed that there was significant outcome of different polymers and polymer load on drug release. All batches exhibit initial burst release of drug due to rapid dissolution of drug from tablet surface. Formulations containing higher viscous polymer and higher amount of polymer have slower drug release rates when compared to formulations with lower viscous polymer and lower amount and low

amount of polymer. Formulation F1 contain 20 mg Xanthan Gum shows release 97.00% in 10 hr. F2 contain 40 mg Xanthan Gum shows release 100.39% in 13 hr. F3 contain

60 mg Xanthan Gum shows release 105.72% in 19 hr. F4 contain 80 mg Xanthan Gum shows release 83.10% in 24 hr. F5 contain 20 mg Guar Gum shows release 94.13% in 3 hr. F6 contain 40 mg Guar Gum shows release 98.14% in 5 hr. F7 contain 60 mg Guar Gum shows release 104.22% in 9 hr. F8 contain 80 mg Guar Gum shows release 103.00 % in 13 hr. Results revealed that the drug release rate was decreased as polymer weight and viscosity increases. All the formulations were floated.F3 formulation shows release up to 19 hr and F4 formulation shows release greater than 24 hr which contain 60 mg and 80 mg Xanthan Gum respectively So finally, it was concluded

that the concentration of Xanthan gum can be required between 1:6 and 1:8 of drug to polymer ratio which can be used as release retarding polymer in the formulation of Alfuzosin HCl floating drug delivery system.

The results of In vitro drug release study are depicted in Figure 3&4. All batches exhibits burst release of drug at the initial stage due to rapid dissolution of drug from tablet surface. The formulation batches H1 & H3 contain 70 mg & 80mg Xanthan gum respectively and 5% sodium bicarbonate. Formulation batches H1 shows 99.59% drug release at the end of 23 hrs and H3 shows 81.33% drug release at the end of 24 hrs due to the higher concentration of polymer. Formulation batches H2 & H4 contain 70 mg & 80mg Xanthan gum respectively and 15% sodium bicarbonate. Formulation batches H2 Shows 97.87% drug release at the end of 12 hrs and H4 shows 98.07% drug release at the end of 13 hrs. Formulation batches H2 and H4 contain higher concentration of Sodium bicarbonate that causes the pore in tablet and ultimately shows faster drug release. Formulation batches H5 & H6 contain 67.93 mg and 82.07 mg Xanthan Gum respectively and both contain 10% Sodium bicarbonate. H5 shows 99.89% drug release at the end of 23 hrs and H6 shows 79.92% drug release at the end of 24 hrs due to the higher amount of Xanthan Gum. Formulation batches H7 to H10 contain 75 mg Xanthan Gum and 2.93%, 17.07%, 10% & 10% Sodium bicarbonate respectively. H7 Shows 91.85% drug release at the end of 24 hrs. H8 shows 99.57% drug release at the end of 11 hrs due to the extremely high amount of Sodium bicarbonate and H9 & H10 shows 99.05% and 99.52% drug release at the end of 24 hrs respectively.

Response surface plot shows that X1 as concentration of drug to polymer ratio increase from level -1.41 to 1.41 the stiff gel is formed due to increase in the gel strength so time required to release 50% of drug increases and X2 concentration of sodium bicarbonate increase from level -1.41 to 1.41 the more acid is penetrated in matrix so time required to release 50% of drug decreases. The calculated value (F= 0.870) is less than the critical value (F= 6.944), It may be concluded that the omitted terms do not contribute significant**y to the prediction of t50 (hr)** [5].

Full and reduced model for t90 (hr)

Full Model Y1= 21.32 + 2.146 (X1) – 5.305 (X2) + 0.586 (X1X1) – 3.438(X2X2) – 1.214 (X1X2)

Reduced Model Y1'=21.99 +2.146(X1) - 5.305(X2) – 3.689 (X2X2)

Response surface plot shows that X1 as concentration of drug to polymer ratio increase from level -1.41 to 1.41 the stiff gel is formed due to increase in the gel strength so time required to release 90% of drug increases and X2 concentration of sodium bicarbonate increase from level -1.41 to 1.41 the more acid is penetrated in matrix so time required to release 90% of drug decreases. The calculated value (F= 0.783) is less than the critical value (F= 6.944), It may be concluded that the omitted terms do not contribute significantly to the prediction of t90 (hr).

Full and reduced model for Q12 (%)

Full Model Y1= 58.73 – 4.53 (X1) + 18.76

(X2) – 0.300 (X1X1) + 14.24 (X2X2) + 0.79 (X1X2)

Reduced Model Y1'= 58.39 - 4.53 (X1) +

18.76 (X2) + 14.37 (X2X2)

Response surface plot shows that X1 as concentration of drug to polymer ratio increase from level -1.41 to 1.41 the stiff gel is formed due to increase in the gel strength so release rate of the drug (% drug release at 12th hr) is decrease and X2 concentration of sodium bicarbonate increase from level -

1.41 to 1.41 the more acid is penetrated in matrix so release rate of the drug (% drug release at 12th hr) is increased. The calculated value (F= 0.0681) is less than the critical value (F= 6.944), It may be concluded that the omitted terms do not contribute significantly to the prediction of Q12 (%).

Full and reduced model for Floating lag time (sec)

Full Model Y1= 197.50 + 6.25 (X1) – 82.38 (X2) -8.37 (X1X1) – 17.37 (X2X2) –+5.33E- 15 (X1X2)

Reduced Model Y1'=176.9 - 82.38 (X2)

Response surface plot shows that X1 as concentration of drug to polymer ratio increase from level -1.41 to 1.41 the stiff gel is formed due to increase in the gel strength so floating lag time is increase and X2 concentration of sodium bicarbonate increase from level -1.41 to 1.41 the more acid is penetrated in matrix so floating lag time is decreased. The calculated value (F= 0.510) is less than the critical value (F= 6.388), It may be concluded that the omitted terms do not contribute significantly to the prediction of floating lag time (sec).

Full and reduced model for Diffusion exponent (n)

Full Model Y1= 0.545 + 0.0169 (X1) – 0.0096 (X2) - 0.0095 (X1X1) -0.0092 (X2X2)

– 0.00153 (X1X2)

Reduced Model Y1'=0.530+ 0.0169 (X1) – 0.0096 (X2)

Response surface plot shows that X1 as concentration of drug to polymer ratio increase from level -1.41 to 1.41 the stiff gel is formed due to increase in the gel strength so diffusion exponent is increase and X2 concentration of sodium bicarbonate increase from level -1.41 to 1.41 the more acid is penetrated in matrix so is diffusion exponent decreased. The calculated value (F= 1.990) is less than the critical value (F= 6.5913), It may be concluded that the omitted terms do not contribute significantly to the prediction of diffusion exponent (n).

Full and reduced model for Release rate constant (k)

Full Model Y1= 0.159- 0.0182 (X1) + 0.0436 (X2) + 0.0023 (X1X1) + 0.0338 (X2X2) + 0.0036 (X1X2)

Reduced Model Y1'=0.161- 0.0182 (X1) + 0.0436 (X2) + 0.0327

(X2X2)

Response surface plot shows that X1 as concentration of drug to polymer ratio increase from level -1.41 to 1.41 the stiff gel is formed due to increase in the gel strength so release rate constant is decrease and X2 concentration of sodium bicarbonate increase from level -1.41 to 1.41 the more acid is penetrated in matrix so is release rate constant increased. The calculated value (F= 0.254) is less than the critical value (F= 6.944), It may be concluded that the omitted terms do not contribute significantly to the prediction of release rate constant (k).

Result of kinetic treatment of dissolution data

The kinetics of the dissolution data were well fitted to zero order, Higuchi model and Korsmeyer-Peppas model as evident from regression coefficients [6, 7].

CONCLUSION

In the present Research work, attempt has been made to develop Alfuzosin HCl floating tablets based on Natural Polymers as matrix forming material utilizing effervescent approach. FTIR spectroscopy revealed that there was no chemical interaction between drug and polymer. The drug content was uniform in all the formulation of the tablets prepared. It was concluded that Xanthan Gum retards the drug release more as compared to Guar Gum. The polymer concentration was found to influence the release of drug from the formulation. As the polymer level was increased, the release rates were found to be decrease. Amount of sodium bicarbonate has influence on floating lag time. It was found that increases in the concentration of sodium bicarbonate decrease the floating lag time and increase the drug release rate. It was found that 10% sodium bicarbonate is required to attain buoyancy. The influence of different concentration of Xanthan Gum and Sodium bicarbonate on kinetics of Alfuzosin HCl was studied and successfully optimized by using Central Composite Design. From the Central Composite Design and different graphical representation, it was finalized that batch H10 was found to be optimized batch having drug release upto 24 hr. More ever, the dissolution profile of optimized batch H10 was found to be similar with theoretical drug release profile having similarity factor more than 50 (*f2*= 83.44) and dissimilarity factor less than 15 (*f1*=2.80) which reflects the feasibility of the optimization procedure in successful development of floating matrix tablet containing Alfuzosin HCl by using Xanthan Gum. The *In vitro* data is fitted in to different kinetic models and the best fit was achieved with zero order model and Higuchi model. The optimized formulation followed by anomalous non Fickian release mechanism and found to be stable after 23 days at accelerated condition.

REFERENCES

1. Briganti A, Capitanio U, Suardi N and Gallina A, 2009. Benign prostatic hyperplasia & its aetiologies. Eur. Urol. Supplements. 8, Pages 865-871. Doi: https://doi.org/10.1016/j.eursup.2009.11.002.
2. Brennan DJ, Robson MS, Murphy M, 2009. Comparative analysis of international caesarean delivery rates using 10-group classification identifies significant variation in spontaneous labor. Am J ObstetGynecol. 201(308), Pages e301- e308.
3. Habib, Khankari, Hontz J, 2000. Fast dissolving drug delivery systems, critical review in therapeutics. Drug Carrier Systems. 17(1), Pages 61-72.
4. Robert A. Freitas, 2005. Current Status of Nanomedicine and Medical Nanorobotics. Journal of Computational and Theoretical Nanoscience. 2, Pages 1–25. Doi: 10.1142/9789812835581_0001
5. Glenn GM, Kenney RT, Ellingsworth LR, 2003. Transcutaneous immunization and immunostimulant strategies: capitalizing on the immunocompetence of the skin. Expert Rev Vaccines. 2, Pages 253–267. Doi: 10.1586/14760584.2.2.253.
6. Harsh Mohan, 2012. Textbook of Pathology; 2006, 4th Edn; Japee Brothers Medical Publishers Ltd, New Delhi.
7. Kapoor A, 2012. Benign prostatic hyperplasia management in the primary care setting. Can. J. Urol. 19(1), Pages 10-17.

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