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ORIGINAL ARTICLE **OPEN ACCESS**

Design and Evaluation of Oral Raft Forming *In Situ* Gelling System of Atomoxetine Hydrochloride For Ease of Pediatric Use

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ABSTRACT

Raft forming chewable tablets of Atomoxetine Hydrochloride were prepared by using direct compression method. Polymers such as Xanthan gum were used as gelling agent, and Compritol 888ATO as drug release retardant. The complex formation of Atomoxetine Hydrochloride and Compritol 888ATO for prolong release of drug by melt granulation method. Taste masking of Atomoxetine Hydrochloride is done by Kyron T 134 using simple slurry method. Other excipients like sodium bicarbonate, calcium carbonate, aspartame, magnesium stearate, and talc were used. 3^2 full factorial design was used. There were various parameters consider for evaluation of raft forming chewable tablets like angle of repose, Carr's index, hausner's ratio, hardness, friability, weight variation test, drug content, raft strength, in vitro drug release study at 8hr and12hr. Formulation batch f7 of full factorial batches prepared with high concentration of xanthan gum (X1) and Compritol 888 ATO (X2) (X1: X2=300:350) was give the excellent result of all the evaluation parameters.

Keywords: *Atomoxetine Hydrochloride, Raft forming chewable tablets, 3^2 full factorial design, raft strength, in vitro drug release*

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INTRODUCTION

Oral drug delivery system has various physiological difficulties such as variation in gastric retention and emptying time. Gastro retentive drug delivery system is facing many challenges which can be overcome by upcoming newly emerging approach i.e. Raft forming system [1]. Gastro-retentive dosage forms (GRDFs) are designed to be retained in the stomach for a prolonged time and release their active ingredients and thereby enable sustained and prolonged input of the drug to the upper part of the gastrointestinal (GI) tract. This technology has generated enormous attention over the last few decades owing to its potential application to improve the oral delivery of some important drugs, for which prolonged retention in the upper GI tract can greatly improve their oral bioavailability and/or their therapeutic outcome [2] The raft forming system is one of the approaches which involve the formulation of effervescent floating liquid with in situ gelling properties, which has been assessed for sustaining drug delivery and targeting [3]. Moreover, the gels formed in situ remained intact for more than 48 h to facilitate sustained release of drugs. The mechanism of the raft forming system involves the formation of continuous layer called a raft [4]. The system involves the formation of a viscous cohesive gel in contact with gastric fluids, wherein each portion of the liquid swells forming a continuous layer called a raft [5].

The layer of the gel floats on the gastric fluid because it has bulk density less than the gastric fluid, as low density is created by the formation of CO2. So the system remains buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. The gel formed from in situ gelling, being lighter than gastric fluid, floats over the stomach contents or adheres to the gastric mucosa due to the presence of a bioadhesive nature of the polymer and prevents the reflux of gastric content into the esophagus by acting as a barrier between the stomach and the esophagus. Thus it produces retention of dosage form and increases gastric residence time resulting in prolonged drug delivery in gastrointestinal tract. When the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of the drug, the residual system is emptied from the stomach. This results in an increased gastro retention time and a better control of the fluctuations in plasma drug concentration [6]. There are various advantages of Raft like Raft-forming system forms a low-density viscous layer on gastric contents and hence provides more effective surface area than other formulation. These lead to more drug release and improve

bioavailability. Floating obtained faster than the other floating dosage form. Improve patient compliance by making a once a day therapy. Improve therapeutic efficacy & easy to administer to a patient. It increases the contact time of drug at the site of maximum absorption (stomach). It provides advantages such as the delivery of drugs with narrow absorption in the small intestinal region; reduction in plasma level fluctuation [7]. Atomoxetine Hydrochloride have narrow absorption window, which is responsible for poor bioavailability. The purpose of present research work is to development of oral raft forming in situ gel of Atomoxetine Hydrochloride for the treatment of attention deficit hyperactivity disorder. Tetrahedron structure of the raft is responsible to increase gastric retention and give prolonged release, improve therapeutic efficiency which may improve bioavailability. It gives rapid onset of action. The aims of developing this formulation are to making more comfortable and ease to administration with pediatric patients [8].

MATERIAL AND METHODS

Atomoxetine Hydrochloride was obtained as kind gift sample from Cadila pharmaceuticals, India. Kyron T 134 was also obtained as gift sample from coral pharmaceuticals, India. Other excipients like Compritol 888 ATO, Sodium bicarbonate, Calcium carbonate, Aspartame, Magnesium stearate, and Talc were purchased from ChemDyes.

Selection of excipients

These excipients were selected by making various formulations batches of different types of gelling agents. Formulation batches are prepared by direct powder mixture and the composition is shown in (Table 1). Weighed each required ingredients were mixed thoroughly. Prepared mass was passed through a 20# sieve. Weighed amount of powder equivalents to the dose and add into the 0.1N HCl. Observe the formation of Raft and total floating time of Raft.

Table 1: Trial batches for selection of excipients

Ingredients (mg)	ATH1	ATH2	ATH3	ATH4	ATH5	ATH6	ATH7	ATH8
Xanthan gum	-	250	-	100	-	-	**300**	-
Chitosan	300	-	-	-	-	-	**-**	-
Pectin	-	-	300	-	-	-	**-**	-
Carbopol 934	-	-	-	-	300	-	**-**	-
Sodium alginate	-	-	-	-		300	**-**	250
Sodium bicarbonate	25	25	25	25	25	25	**25**	25
Calcium carbonate	232	232	232	232	232	232	**232**	232

Compatibility of Drug and Excipients by FTIR

Compatibility study of drug and excipients were performed by using Jasco FT-IR spectrophotometer, in the spectral range of 400-4000cm^{-1}. Samples were analyzed and compared with the standard FT-IR spectrum. The IR spectra of pure Atomoxetine HCl showed peaks at 3195.15, 3395.76,1629.90, 2630.99, 732.97 for C-CH stretch , N-H stretch, N-H stretch(Secondary amine), N-H stretch, C-O stretch.

Taste masking of Atomoxetine Hydrochloride

Kyron T-134 was used in 1:3 Ratio for taste-making of atomoxetine hydrochloride (bitter in taste) using slurry method with water. In this method, KyronT134 was soaked in solvent for 1h followed by addition of the drug. This aqueous mixture was triturated for 30 min and dried at 80–90°C in order to obtain Drug – Kyron complex [9].

Preparation of Chewable Tablets Formulation of hot melt granulation

Weighed quantity of Compritol was melt upto 70°C. Drug–Kyron Complex was added. The melted solution was cooled at room temperature for solidification. The obtained mass was passed through 20# sieve [10].

Preparation of Formulation

Weighed all other ingredients & Passed through 20# sieve. Compressed through rotary tablet compression machine.

Optimization of formulation by 32 full factorial design

- Optimization of formulation (Shown in Table 2) is done using 3^2 full factorial design by design expert software.
- 3 levels and 2 factors are selected for formulation of chewable raft forming in situ gelling tablets. Total 9 factorial batches (Shown in Table 3) were given by design expert software.

Table 2: **Optimization of formulation**

Factors	Levels		
Independent variables	Low (mg)(-1)	Medium(mg) (0)	High(mg)(+1)
A (xanthan gum)	100	200	300
B (compritol 888 ato)	250	300	350
Dependent variable		Response	
Y1		Raft Strength(gm)	
Y2		% Drug Release at 8 hr	
Y3		% Drug Release at 12 hr	

Table 3: 3^2 full factorial design composition

Batch number	ATH9	ATH10	ATH11	ATH12	ATH13	ATH14	ATH15	ATH16	ATH17
X1 [amount of xanthan gum(mg)]	200	300	100	200	200	100	300	300	100
X2 [amount of compritol 888 ato]	350	250	250	300	250	300	350	300	350
Drug + kyron t134 complex	240	240	240	240	240	240	240	240	240
Sodium bicarbonate	75	75	75	75	75	75	75	75	75
Calcium carbonate	175	175	175	175	175	175	175	175	175
Aspartame	25	25	25	25	25	25	25	25	25
Magnesium stearate	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Talc	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5

Formulation of check point batch for evaluation of model

Purpose: To evaluate the dependability of model, performed to verify the effectiveness of the established contour plot and reduced polynomial equation in the development of in situ Raft gel.

Batch formulated: Two check point batch was prepared, one from lower side (X1: X2 = 150:275) and another from higher level (X1: X2 = 250: 325). Each batch was fabricated 3 times and average value was calculated.

Evaluation: By comparing the predicted and observed experimental value of responses obtained.

Formulation of optimized batch based on desirability function

Purpose: To find out the effect of independent variables (X1 and X2) based on the provided results of dependent variables (Y1 and Y2). The main function of desirability was to unite the responses of required attribute and provide the probability of predicting highest level for independent variables.

Batch formulated: Desirable result outcomes when added to the software, final optimized batch formulation (Shown in Table 4) was suggested and the batch was prepared accordingly.

Evaluation: By comparing the predicted value given by the software and observed experimental value of responses obtained.

Evaluation of optimized formulation Pre-Compression parameter

Angle of repose: Commonly used method is to suspend the granules of the material from a funnel on a flat surface. Classical method to calculate the repose angle using the relation $\tan(\Theta)=2h/r$ is subject to caution on account of formation of irregular shaped piles.

Carr's index: The Carr index (also: Carr's index or Carr's Compressibility Index) is an indication of the compressibility of a powder. It is calculated by following equation:

Carr Index=(ρ tapped-ρbulk)/ρtapped*100.

Hausner's ratio: The Hausner ratio is a number that is correlated to the Flowability of a powder or granular material. The ratio of tapped density W/V50 to fluffy density (W/V0 g/ml) is known as the Hausner ratio.

Table 4: Optimized batch formulation

Optimized batch no	ATH18
Amount of xanthan gum	300
Amount of compritol 888ato	323
Drug+ kyront134 complex	240
Sodium bicarbonate	75
Calcium carbonate	175
Aspartame	25
Magnesium stearate	2.5
Talc	2.5
Desirability	0.965

Evaluation of optimized formulation Pre-Compression parameter

Angle of repose: Commonly used method is to suspend the granules of the material from a funnel on a flat surface. Classical method to calculate the repose angle using the relation tan(Θ)=2h/r is subject to caution on account of formation of irregular shaped piles.

Carr's index: The Carr index (also: Carr's index or Carr's Compressibility Index) is an indication of the compressibility of a powder. It is calculated by following equation:

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Post Compression parameter

Hardness: Tablet hardness testing, is a laboratory technique used by the pharmaceutical industry to determine the breaking point and structural integrity of a tablet and find out how it changes "under conditions of storage, transportation, packaging and handling. Friability: Friability is when a tablet has the tendency to chip, crumble or break during transportation. This can happen when the tablet is being handled, packaged or transported and may mean the patient receives an incorrect dose. Tablet friability testing involves weighing the sample of tablets and then placing them into a rotating drum. The drum is then rotated 100 times. The sample is then reweighed to find the % weight loss.Weight variation: Weigh an intact capsule. Open the capsule without losing any part of the shell and remove the contents as completely as possible. Weigh the shell. The weight of the contents is the difference between the weighing. Repeat the procedure with a further 19 capsules selected at random. Determine the average weight. Drug Content: Twenty tablets were weighted and powdered in a mortar. Accurately weighted quantity of the powder equivalent to about 240 mg of Atomoxetine Hydrochloride and Kyron T134 complex was diluted to100 ml with 0.1NHCl in 100ml volumetric flask. It was stirred for 15 minutes and filtered.1ml of the filtrate was diluted with 0.1 N HCl to produce100 mcg/ml solution. The absorbance of the resulting solution was measured at λ_{max} 270 nm and the content of Atomoxetine Hydrochloride was calculated from the absorbance obtained. Raft Strength: A tablet powder equivalent to unit dose was transferred to 150 ml of 0.1 N HCl and maintained at 37°C in a 250 ml glass beaker. Each raft was allowed to form around an L-shaped wire probe (diameter: 1.2 mm) held upright in the beaker throughout the whole period (30min) of raft development. Raft strength was estimated using the modified balance method. Water was added drop wise to the pan and the weight of water required to break the raft was recorded. **Note**: A double-pan dispensing balance was modified for raft strength measurement. One pan of the dispensing balance was replaced with an L-shaped wire probe as shown in Figure 1 [11].

Figure 1: Raft strength by modifying weigh balance

In Vitro Drug Release Study: In vitro drug release study of Atomoxetine Hydrochloride chewable tablets (n = 3) was performed using USP apparatus II fitted with a paddle (50 rpm) at 37 ± 0.5°C using a simulated gastric fluid (pH 1.2; 900 ml) as a dissolution medium. Unit dose was powdered and then added to the dissolution medium. At pre-determined time intervals, 10- ml samples were withdrawn, filtered through a

0.45-µm membrane filter and analyzed at 270 nm using a UV spectrophotometer. Cumulative percentage drug release was calculated using an equation obtained from a calibration curve.

Stability Study

Stability storage criteria were Temperature 40°C ± 2°C, Relative Humidity 75%RH ± 5% RH, Time period 1 month. Parameters were analyzed like Hardness, Friability, Drug content, Moisture content.

RESULTS AND DISCUSSION

Selection of excipients

- After performing the trial batches of various gelling agents it can be concluded that ATH7 which was prepared with xanthan gum was give the best result in comparison of other gelling agents (Shown in Table 5).

Table 5: Result of trial batch of excipients selection

Batch	Total floating time	Raft formation
F1	Not properly formed	Very poor
F2	Less than 8 hr	Poor
F3	Less than 4 hr	Poor
F4	Less than 5 hr	Poor
F5	Less than 4 hr	Poor
F6	5 to 6 hr	Poor
F7	More than12 hr	Excellent
F8	Less than 8 hr	Good

- ATH7 is give the good result and float on the GI fluid more than12 hr.

Compatibility of Drug and Excipients by FTIR

As per (table 6) it can be concluded that there is no major changes in drug and excipient's FTIR study. So there are no interaction between drug and excipients shown in figure 2.

Table 6: Compatibility of Drug and Excipients

Functional group	Drug	Drug + $CaCO_3$	Drug + Sodium bicarbonate	Drug+ Kyron T134	Drug+ xanthangum
C-CH	3195.15	2978.52	2984.3	2949.59	3185.63
N-H	3395.76	2516.65	3654.44	3630.34	3185.83
N-H	1629.98	1600.63	1693.19	1696.09	1602.56
N-H	2630.99	2516.65	2704.67	2359.48	2135.78
C-O	732.97	711.604	754.99	756.923	709.676

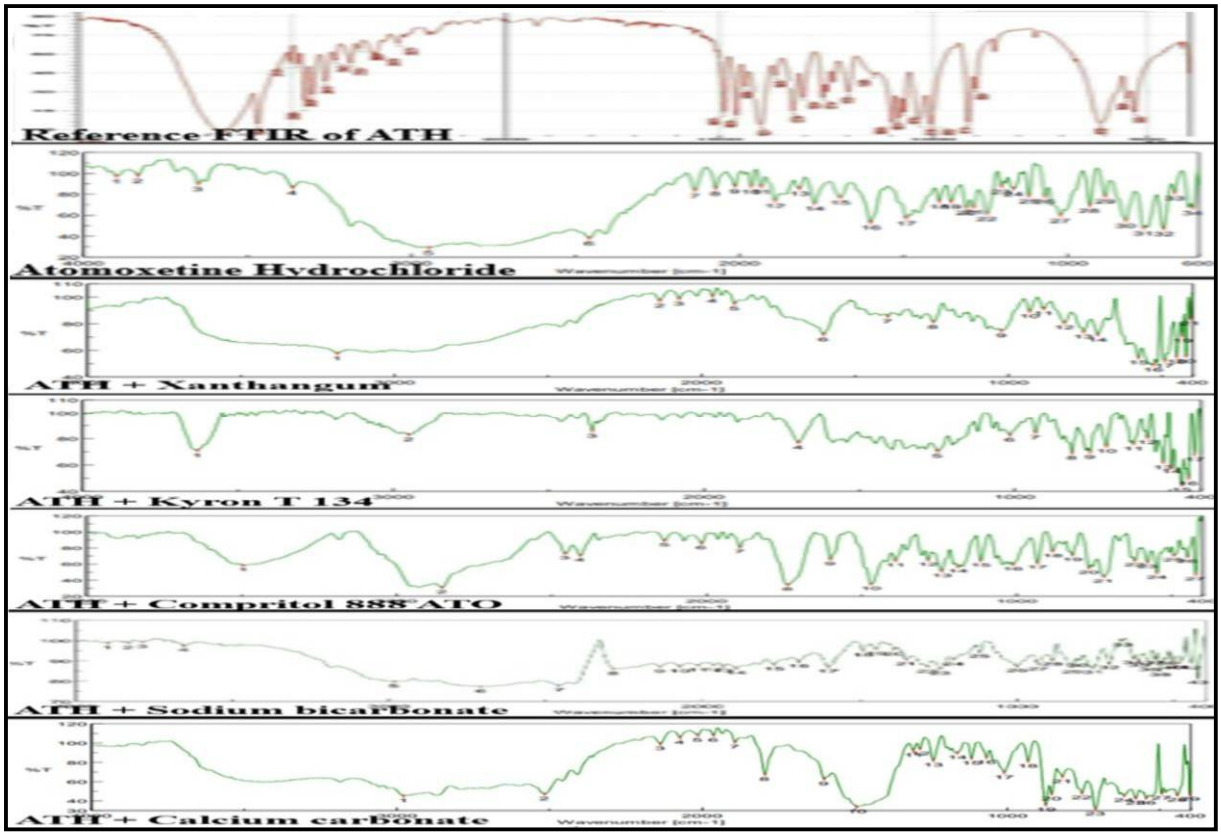

Figure 2: FTIR of Drug and Excipients

Conclusion of DSC

The DSC of Pure drug is shown in figure 3. DSC of ATH and Compritol 888ATO is shown in figure 4. The DSC analysis of KyronT134 and Drug complex confirmed the complex formation. The sharp melting endothermic peak of atomoxetine hydrochloride at 171.69°C completely disappears in the complex (Drug and Kyron T 134) shown in figure 5.

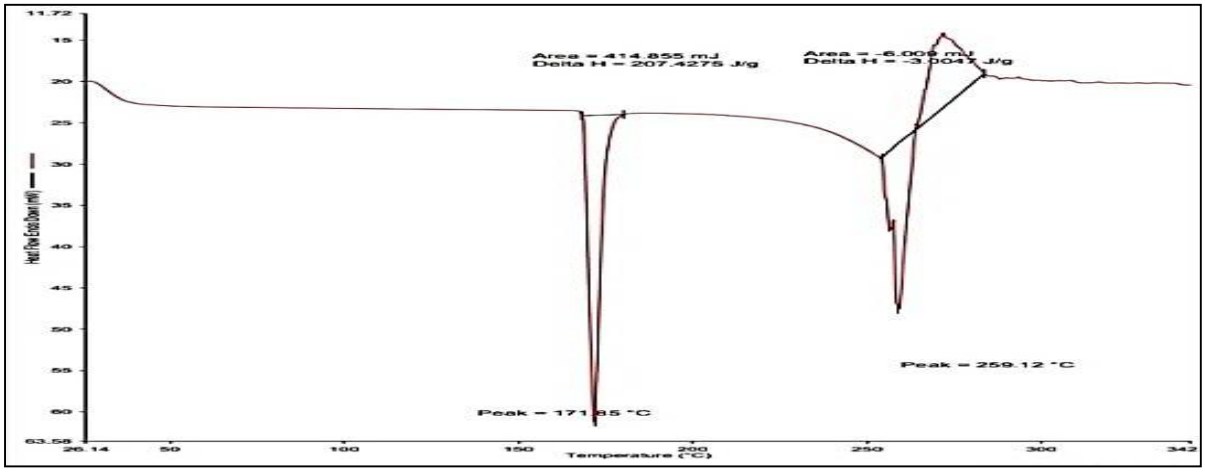

Figure 3: DSC of Atomoxetine hydrochloride

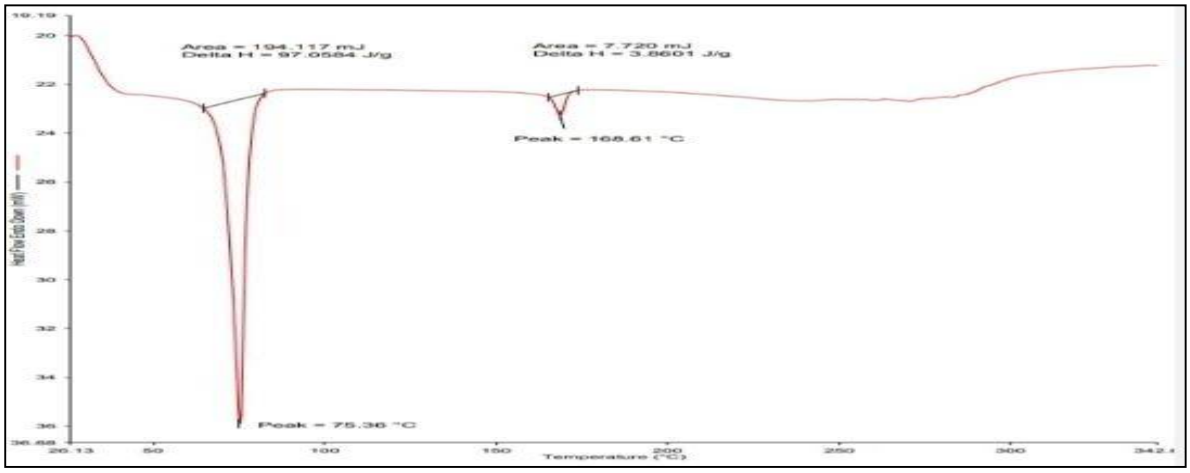

Figure 4: DSC of Compritol 888ATO+Atomoxetine hydrochloride

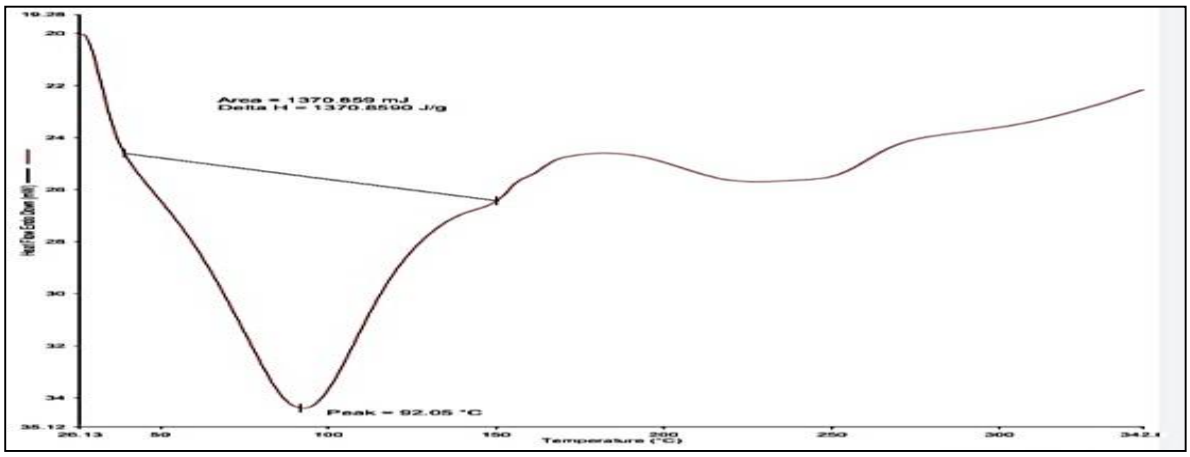

Figure 5: DSC of Kyron T134+Atomoxetine Hydrochloride

Result of full factorial Optimized batches (Shown in Table 7)

Discussion for Raft strength (gm) analysis: The Model F-value of 26.69 implies the model is significant. There is only a 1.08% chance that an F-value this large could occur due to noise. Values of "Probe > F" less than 0.0500 indicate model terms are significant. In this case A, Bare significant model terms. Values greater than 0.1000 indicate the model terms are not significant. If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model.

Raft Strength (Y1) = +2.06+0.881*A+0.338*B+5.0*AB+0.045*A2+0.115*

Influence of Amount of Xanthan gum (X1) and Concentration of Compritol 888 ATO(X2) on Raft strength (Y1) (gm): Raft strength is an important parameter in Raft formulation evaluation. Correlation results between amount of Xanthan gum and Raft strength revealedpositive effect of Xanthan gum on Raft strength of Raft. Increase in the amount of Xanthan gum from 200-300 gm significantly resulted in increase of raft strength from 3-4 gm. This might be due to formation of viscous gel of Raft with increasing Xanthan gum content thus, increasing the raft strength. On the other side Concentration of Compritol 888 ATO showed positive correlation effect on raft strength i.e., increase in the concentration of Compritol 888ATO (250-350 gm) resulted in increased raft strength of formulation (as per figure 6).

Discussion for % drug release at 8 hr: The Model F-value of 16.43 implies the model is significant. There is only a 2.18% chance that a F-value this large could occur due to noise.

Values of "Probe > F" less than 0.0500 indicate model terms are significant. In this case B,A^2 are significant model terms. Values greater than 0.1000 indicate the model terms are not significant. If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model.

% drug release at 8 hr= +79.177-0.815*A-3.111*B-1.265*AB-11.571*A2-4.481*B2

Table 7: Result of full factorial batches

Batch number	X1 [amount of xanthan gum (mg)]	X2 [amount of Compritol 888 ATO (gm)]	Raft strength (gm)	% drug release at 8 hr	% drug release at 12 hr
ATH9	200	350	2.3 ± 0.01	71.80 ± 0.006	94.06 ± 0.004
ATH10	300	250	2.65 ± 0.02	67.75 ± 0.004	98.41 ± 0.120
ATH11	100	250	0.96 ± 0.01	64.72 ± 0.012	98.92 ± 0.001
ATH12	200	300	2.12 ± 0.021	78.96 ± 0.003	97.54 ± 0.009
ATH13	200	250	1.99 ± 0.10	77.81 ± 0.110	99.91 ± 0.015
ATH14	100	300	1.13 ± 0.21	70.66 ± 0.101	97.99 ± 0.110
ATH15	300	350	3.52 ± 0.05	58.89 ± 0.005	92.89 ± 0.002
ATH16	300	300	3.02 ± 0.11	64.77 ± 0.002	96.64 ± 0.031
ATH17	100	350	1.81 ± 0.03	60.92 ± 0.017	95.76 ± 0.001

(Mean± SD)n =3

Influence of Amount of Xanthan gum (X1) and Concentration of Compritol 888 ATO(X2) on % Drug release at 8hr (Y2)(%): Drug release is an also important parameter in Raft formulation evaluation. Correlation results between amount of Xanthan gum and Drug release revealed positive effect of Xanthan gum on Drug release of Raft. Increase in the amount of Xanthan gum from 200-300 gm significantly resulted in increase of drug release from 60-70 %. On the other side Concentration of Compritol 888ATO showed negative correlation effect on drug release i.e., increase in the concentration of Compritol 888ATO (250-350gm) resulted in decreased drug release of formulation; which is good for prolonged release (as per figure 7).

Discussion for % Drug release at 12 hr: The Model F-value of 32.29 implies the model is significant. There is only a 0.06% chance that an F-value this large could occur due to noise. Values of "Probe > F" less than 0.0500 indicate model terms are significant. In this case A, B are significant model terms. Values greater than 0.1000 indicate the model terms are not significant. If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model.

% drug release at 12 hr=+97.66-0.79 *A-2.42*B-0.59*AB-0.40*A2-0.73*B2

Influence of Amount of Xanthan gum (X1) and Concentration of Compritol 888 ATO(X2) on % Drug release at 12 hr (Y3) (%): Drug release is an also important parameter in Raft formulation evaluation. Correlation results between amount of Xanthan gum and Drug release revealed positive effect of Xanthan gum on Drug release of Raft. Increase in the amount of Xanthan gum from 200-300 gm significantly resulted in increase of drug release from 80-90 %. On the other side Concentration of Compritol 888 ATO showed negative correlation effect on drug release i.e., increase in the concentration of Compritol 888 ATO (250-350 gm)resulted in decreased drug release of formulation; which is good for prolonged release (as per figure 8).

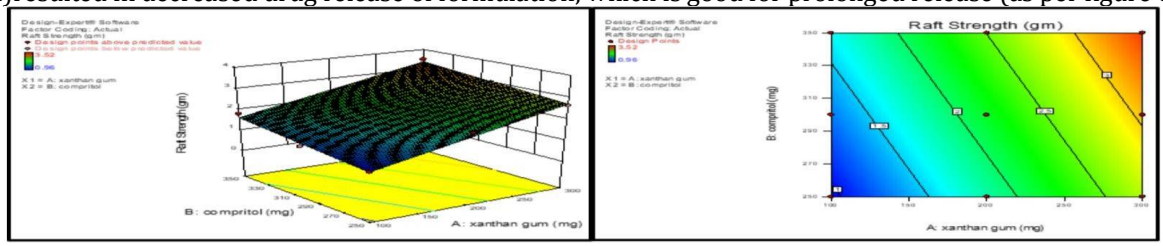

Figure 6: Surface plot and contour plot for Raft Strength

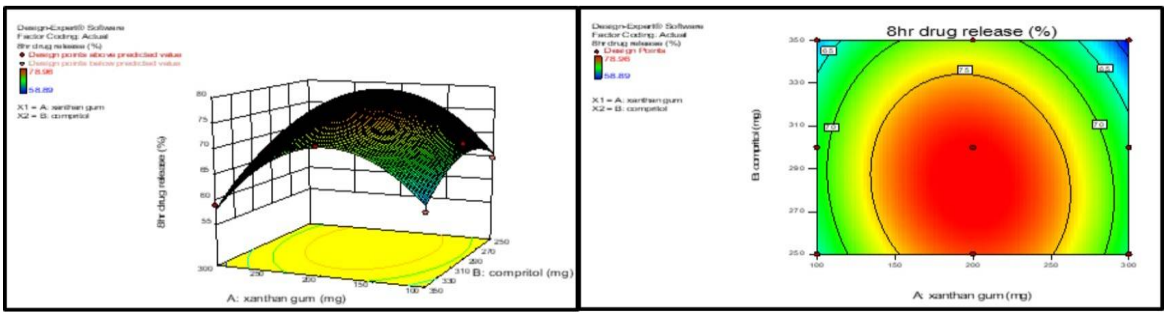

Figure 7: Surface plot and contour plot for% Drug Release at 8 hr

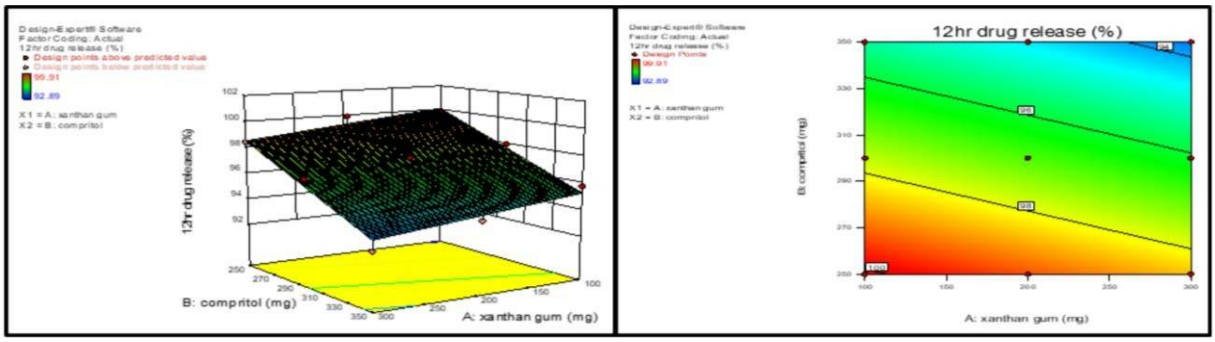

Figure 8: Surface plot and contour plot for% Drug Release at 12hr

Evaluation of checkpoint batch

Two Check points batches prepared and evaluated were compared for both predicted and experimental value, in conclusion no major were observed as showed in Table 8.

Table 8: Check point batch analysis

Check point batch	Predicted value			Experimental value		
	Raft Strength (gm)	% drug release at 8 hr	% drug release at 12 hr	Raft Strength (gm)	% drug Release at 8hr	% drug release at 12hr
ATH19	1.55	76.81	92.18	1.03 ± 0.3	75.22 ± 0.01	90.54 ± 0.09
ATH20	2.77	72.88	97.06	1.97 ± 0.2	70.27 ± 0.06	95.98 ± 0.07

(Mean± SD)n =3

Evaluation of Raft formable optimized batch (Shown in Table 9 & 10).

Comparison of % drug release of optimized formulation with % pure drug release: It can be concluded that the drug release of pure drug is show the completely drug release within 2 hr. where after making the raft forming chewable tablet of drug is show prolong drug release (Shown in figure 9 & 10).

Table 9: Result for optimized batch

Optimized batch no.	Predicted value			Experimental value		
	Raft strength (gm)	% drug release At 8 hr	% drug release at 12 hr	Raft strength (gm)	% drug release at 8 hr	% drug release at 12 hr
ATH18	3.17	63.77	96.99	3.01 ± 0.2	61.59 ± 0.10	94.89 ± 0.002

(Mean± SD) n =3

Table 10: Drug release comparison

Time	% drug release of pure drug	% drug release of raft formulation
0	0	0
30	25.63 ± 0.006	15.96 ± 0.001
60	54.87 ± 0.001	17.22 ± 0.003
90	77.91 ± 0.018	20.38 ± 0.0015
120	99.06 ± 0.012	22.75 ± 0.007
180	99.96 ± 0.004	33.61 ± 0.018
240	-	33.99 ± 0.011
300	-	35.98 ± 0.014
360	-	42.15 ± 0.013
420	-	51.68 ± 0.009
480	-	61.59 ± 0.008
540	-	72.56 ± 0.018
600	-	80.61 ± 0.012
660	-	91.68 ±0.006
720	-	94.89 ± 0.0014

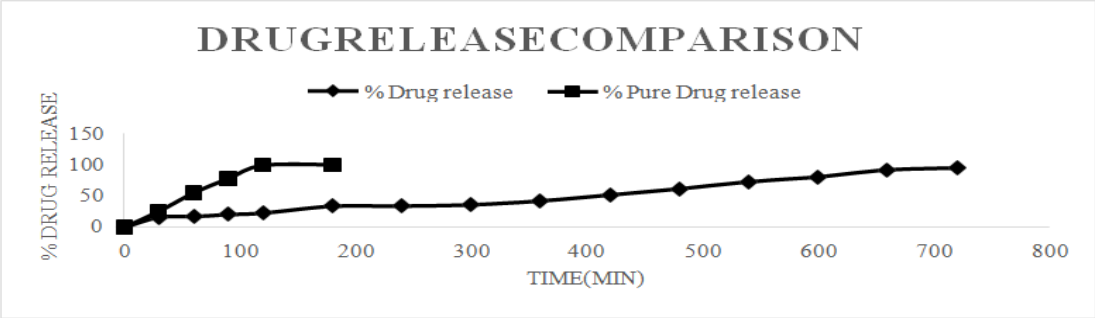

Figure 9: Drug release comparison

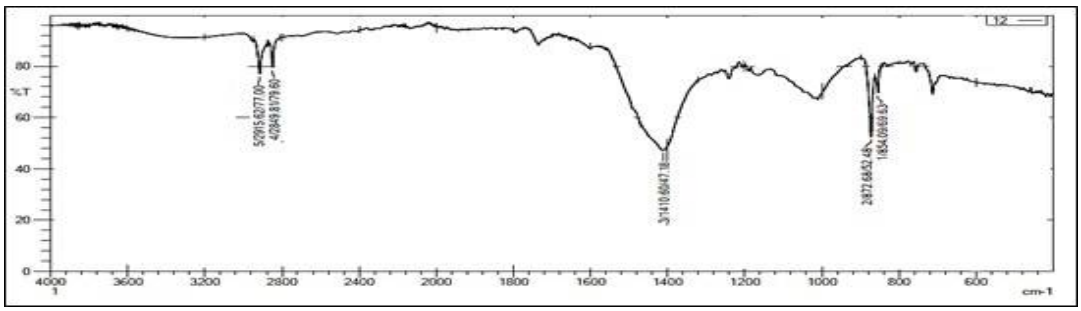

Figure 10: FTIR of optimized batch

Pre-compression data

The prepared granules for raft forming chewable tablets were characterized for angle of repose, bulk density, tapped density, Carr's index and hausner's ratio which are shown in table. Angle of repose of optimized batch was within 25°–30°, Carr's index of optimized batch was within 0 – 10 and hausner's ratio of optimized batch was found within 1.00 – 1.11 which indicate Excellent flow property of granules as per table 11.

Table 11: Pre compression data analysis

Optimized batch no.	Angle of repose(θ)	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's ratio
ATH18	29.94±0.3	0.36±0.5	0.45± 0.06	9± 0.01	1.08± 0.14

(Mean± SD)n =3

Post-compression data

The prepared raft forming chewable tablets were characterized for tablet weight, friability, drug content, hardness which is shown in table. Friability of optimized batch was less than 1%, Drug content of optimized batch was within 85%-115% and Hardness of optimized batch was within 4 – 6 kg/cm^2 which showed Excellent Results as per table 12.

Table 12: Post-compression data analysis

Optimized batch no.	Tablet weight (mg)	Diameter (mm)	Friability (%)	Drug content	Hardness (kg/cm^2)
ATH18	997.0 ±6.5	11.96±0.1	0.52±0.1	97.21±0.14	5.4±0.55

(Mean ± SD) n = 3

Stability Study

There is no different in stability parameters after1month observation shown in table 13.

Table 13: Stability Criteria

Sampling time Intervals	Storage conditions:40°c± 2^{0}c,75%Rh±5%Rh			
	Hardness	Friability	Drug content	Moisture content
Initial	5.4±0.55	0.52±0.1	97.21±0.14	2.5 ± 0.007 %
After 15 days	5.3±0.52	0.51±0.3	97.20±0.11	2.7 ± 0.013 %
After 1 month	5.3±0.50	0.51±0.1	97.20±0.01	2.8 ± 0.038 %

(Mean± SD)n =3

CONCLUSION

Many of the patients are suffering from the ADHD and this can be overcome by using raft forming chewable tablets of Atomoxetine Hydrochloride with more patient compliance. Raft forming chewable

tablets of Atomoxetine Hydrochloride were successfully prepared with hot melt granulation method. Taste masking of Atomoxetine Hydrochloride is done by simple slurry method; which is successfully masking the bitter test of Atomoxetine Hydrochloride. In hot melt granulation method Compritol 888ATO is mainly used for controlling drug release which may give prolonged drug release. Compritol 888 ATO concentration is increased, which decrease the drug release time and give prolong drug release and decrease the dose frequency, which may improve paediatric patient compliance. Whereas increases the concentration of xanthan gum it also increase the raft strength which may improve raft stability in stomach which may lead to prolonged release of Atomoxetine Hydrochloride. It was concluded that prepared raft forming chewable tablets Formulation ATH 15 which containing combination of 300 mg Xanthan gum, 350 mg Compritol 888ATO, sodium bicarbonate and calcium carbonate form raft which gives good prolong drug release about 92% at 12 hr in compare to other formulation, which may improve bioavailability and decrease the dose frequency.

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