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RESEARCH ARTICLE

FORMULATION AND EVALUATION OF ORAL FLOATING BEADS OF TRAMADOL HYDROCHLORIDE

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ABSTRACT:

Aim of present work was to formulate and evaluate oral floating beads of Tramadol hydrochloride. Floating beads were fabricated using modified ionotropic gelation technique using various natural and synthetic polymers in different proportion. In the formulated batches BT1 to BT11 not have ability to extend drug release for 12 hours. In formulated batch BT 12 (Sodium alginate 6%: Carbapol 940 1.2 %) show in vitro release for 12 hours (100.26 ± 0.66%). It also has floating lag time and floating time immediate, and floating duration more than 12 hours. In kinetic model fitting it follows Korsemeyers Peppas equation. Also it was found stable after 6 months in accelerated stability study. From all the formulation of oral floating beads of Tramadol Hydrochloride; it was concluded that, among all different polymer ratio Sodium Alginate 6% and $CaCl_2$ 3% (2:1 ratio) gives best results. Among different polymers Carbapol 940 gives retarded drug release for 12 hours. The optimized batch was found to be stable after 6 Months in accelerated stability studies.

Key Words: Ionotropic gelation, Tramadol Hydrochloride, floating beads, Carbapol 940

1. INTRODUCTION:

Rapid GI transit can prevent complete drug release in the absorption zone and reduce the efficacy of the administered dose since the majority of drugs are absorbed in stomach or the upper part of small intestine. To overcome these limitations, several controlled oral drug delivery systems with prolonged gastric residence times have been reported recently such as: floating drug dosage systems (FDDS). Swelling or expanding systems, mucoadhesive systems, modified-shape systems, high-density systems and other delayed gastric emptying devices. Among these systems, FDDS have been most commonly used. FDDS have lower density than gastric fluids and thus remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating in the gastric content, the drug is released slowly from the system at a desired rate. Materials used for FDDS include carbon dioxide gas-forming agents (carbonate or bicarbonate compounds) highly swellable hydrocolloids and light mineral oils. Multiple unit systems and hollow systems prepared by solvent evaporation methods have also been developed.[1]

Floating drug delivery systems (FDDS) are classified depending on the use of two formulation variables: (i) Effervescent system and (ii) Non effervescent system. Effervescent floating drug delivery systems are again classified into volatile liquid containing systems and gas-generating systems. In volatile liquid containing systems, the gastro retention time of a drug delivery system can be sustained by incorporating an inflatable chamber, which contains a liquid e.g. ether, cyclopentane, that gasifies at body temperature to cause the inflation of the chamber in the stomach. The device may also consist of a bioerodible plug made up of PVA, Polyethylene, etc., that gradually dissolves causing the inflatable chamber to release gas and collapse after a predetermined time to permit the spontaneous ejection of the inflatable systems from the stomach. In gas-generating systems, the buoyant delivery systems utilize effervescent reactions between carbonate / bicarbonate salts and citric / tartaric acid to liberate CO2, which gets entrapped in the jellified hydrocolloid layer of the systems thus decreasing its specific gravity and making it to float over time.

Non-effervescent floating drug delivery systems are again classified into:

(i) ***Colloidal Barrier systems*** **contains**

(ii) ***Micro Porous Compartment Systems***

(iii) Alginate beads

(iv) Hollow microspheres

Alginate beads**:** Beads are small, solid and free flowing particulate carriers containing dispersed drug particles either in solution or crystalline form[2]. Spherical beads of approximately 2.5 mm in diameter

can be prepared by dropping a sodium alginate solution in to aqueous solutions of calcium chloride, causing precipitation of calcium alginate. The beads are then separated snap and frozen in liquid nitrogen, and freeze dried at -40°C for 24 h, leading to the formation of porous system, which can maintain a floating force over 12 h.[3]

In multiple-unit particulate dosage forms (e.g. microspheres, gel beads) have the advantages that they pass uniformly through the GIT to avoid the vagaries of gastric emptying and provide an adjustable release, thereby, reducing the inter subject variability in absorption and risk of local irritation.[4]

The beads are generally fabricated using modified ionotropic gelation technique. In this approach, an aqueous dispersion of negatively charged polymer together with a gas generating agent ($CaCO_3$ or $NaHCO_3$) was added drop-wise into acidic gelation medium consisting of divalent cations such as Ca_2+. As the droplet dips into the acidic gelation medium, gas-generating agent effervesces, releasing CO_2 which then is entrapped in the gel matrix making it lighter than stomach fluids and simultaneously Ca_2+ present in gelation medium interacts with anionic groups on polymer molecule causing immediate formation of strong aggregation of pairs of helices, leading to strong bead shaped gel structures.[5]

In the present study Tramadol Hydrochloride was used, it is a NSAID drug having suitable Pharmacokinetic criteria for formulation of sustains release dosage form. [6-8]

2. MATERIAL AND METHOD:

2.1 Material:

Drug: Tramadol Hydrochloride (Yarrow Chem), **Polymers:** sodium alginate, pectin, ethyl cellulose, HPMC K100M, guar gum, carbapol 940. **Excipients:** Sodium bicarbonate, calcium chloride, glacial acetic acid.

2.2 Method:

Floating beads were fabricated using modified ionotropic gelation technique using various natural and synthetic polymers in different proportion. Firstly to the water sodium alginate was incorporated with constant stirring at 1000 rpm on magnetic stirrer for half hour. Then other polymers like pectin, HPMC K100 M, Carbapol 940 etc were added one by one after interval of 45 minutes. Then to this sodium bicarbonate was added and again it was stirred for 30 minutes or until solution should be clear. Lastly drug was added and solution was stir for 1 hour.

In another beaker 99ml of water was taken to then 3% $CaCl_2$ was added in water and was stirred for 10 minutes on magnetic stirrer at 500 rpm. Then to this solution of water and $CaCl_2$, 1% glacial acetic acid was added it was again stir of 10 minute.

Then the mixture of drug and polymer was filled in 10 ml syringe. The needle used was 20 G number. this solution was then drop by drop added to water $CaCl_2$ and Glacial acetic acid solution with constant stirring at 400-450 rpm. Then beads were formed. These beads were filtered through whattman's filter paper. Then these are air dried overnight to get constant weight.

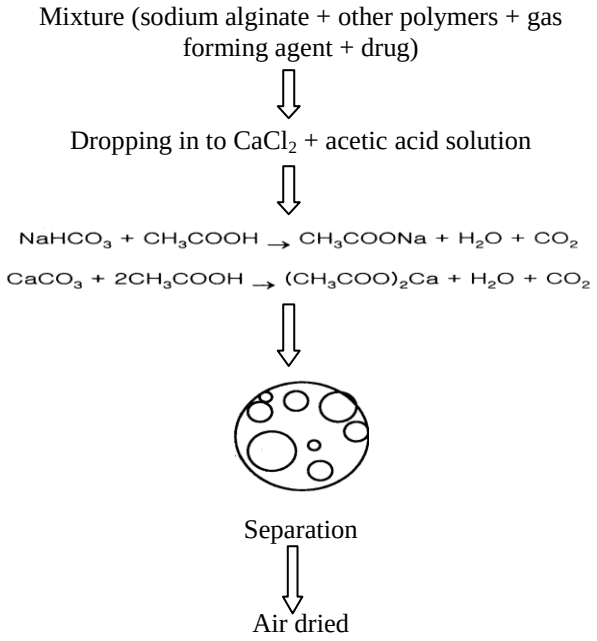

Figure 1: Schemes diagram of formulation of Floating Beads of Tramadol Hydrochloride[9]

3. Evaluation of Oral Floating Beads:[10-13]

3.1 Preformulation Studies:

In the preformulation studies Bulk density, Tapped density, Compressibility index, Hausner's ratio, Angle of repose, FTIR were performed.

3.2 Morphological Study using SEM:

Scanning electron microscopy (SEM): The surface topography of the (optimized) beads formulations were examined under a FEI-Philips XL-30 Analytical Electron microscope (VNIT NAGPUR). The sample was loaded on copper sample holder and sputter coated with platinum.

3.3 Percentage Drug Entrapment Efficacy (%DEE):

The yield of beads were determined by comparing the whole weight of beads formed against the combined weight of the copolymer and drug.

$$\% \text{ Practical yield} = \frac{\text{Mass of beads obtained}}{\text{Total wt of drug \& polymer}} \times 100$$

Table 1: Formulation of oral floating Beads of Tramadol beads (weights in %)

Name of ingredients	Formulation Code											
	BT1	BT2	BT3	BT4	BT5	BT6	BT7	BT8	BT9	BT10	BT11	BT12
Tramadol HCl (mg)	100	100	100	100	100	100	100	100	100	100	100	100
Sodium alginate	6	6	6	6	6	6	6	6	6	6	6	6
Pectin	3	-	-	-	-	2	-	-	-	-	-	-
Ethyl cellethyl	-	3	5	-	-	-	-	-	-	-	-	-
Guar gum	-	-	-	-	-	-	0.7	-	-	-	-	-
HPMC K100 M	-	-	-	1.5	2	3	-	-	-	-	-	-
Carbapol 940	-	-	-	-	-	-	-	0.5	0.7	0.9	1	1.2
Sodium bicarbonate	3	3	3	3	3	3	3	3	3	3	3	3
Calcium chloride	3	3	3	3	3	3	3	3	3	3	3	3
Glacial acetic acid	1	1	1	1	1	1	1	1	1	1	1	1
Distilled water	99	99	99	99	99	99	99	99	99	99	99	99

3.4 Drug Content Uniformity:

Accurately weighed beads equivalent to 100 mg were suspended in 100 ml of 0.1 N Hydrochloric acid, it was shaked for 30 min and kept for 24 hrs. Next day it was stirred for 5min and filtered. After suitable dissolution, the drug content in the filtrate was analyzed spectro photo metrically at using Shimadzu UV spectrophotometer at 271 nm.

The drug content uniformity was calculated by-

Percentage Drug Entrapment Efficiency
= *Actual drug content/ Theoretical drug content* X 100

3.5 Floating lag time In this parameter 100 mg of beads formulation were added into the 900 ml dissolution vessel containing 0.1N HCl at 37^0C. It was the time the formulation took to emerge on surface of dissolution medium is referred as floating lag time.

3.6 Floating duration In this parameter 100 mg of beads formulation was added into the 900 ml dissolution vessel containing 0.1N HCl at 37^0C. The time for which the formulation remains constantly floating on surface of dissolution medium was referred as duration of floating.

3.7 Filled capsules parameter:

a. Capsule appearance: The prepared capsule was evaluated visually.

b. Capsule lock length: The capsules lock length was determined using Vernier caliper. Six capsules from each batch of formulation were used and mean lock length value and stand.

c. Weight variation: To study the weight variation, 20 capsule of each formulation were weighed using an electronic digital balance. The average weight of each capsule was calculated and the percentage deviation in weight was calculated.

3.8 In vitro dissolution study An in vitro release study was carried out using dissolution test apparatus USP Type II (Paddle Method). Dissolution parameters used for the study are as given in table no.2.

Table 2: Parameters used in Invitro dissolution study of oral floating beads:

Dissolution medium	900 ml of Hydrochloric acid buffer solution of pH 1.2
Temperature	37^0C ± 0.2^0C
Speed of rotation(RPM)	50
Wavelength of drug	271 nm

3.9 **Drug Kinetic study:**

The release data obtained from various batches were studied with respect to effect of drug: polymer ratio. To analyze the mechanism of drug release from the formulation, the dissolution profile of optimized batches was fitted to zero-order, first-order, Higuchi, Hixson-Crowell, Korsemeyer and Peppas, models to ascertain the kinetic modeling of drug release.

3.10 Statistical Analysis:

In this study the Bonferroni method was applied to dissolution study to check there was significant difference or not

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3.11 Stability testing:

Stability studies were carried out as per ICH guidelines. During the stability studies, the product is exposed to normal conditions of temperature and humidity. The optimized were subjected for stability studies.

4. RESULT AND DISCUSSION:

4.1 Preformulation Studies:

All the preformulation studies like bulk density , tap density, angle of repose etc, physical characterization of drug sample, Analytical characterization of drug sample were performed.

Table 3: Preformulation testing (g= gram)

Sr. No	Formulation Code	Bulk density (gm/cm3)	Tapped density (g/cm3)	Compressibility Index (%)	Hausner Ratio	Angle of Repose (θ)
1	BT1	0.54 ±0.21	0.62 ±0.29	11.96 ±0.17	1.14 ±0.17	26.57 ±0.33^0
2	BT2	0.62 ± 0.23	0.69 ±0.27	11.11 ±0.33	1.13 ±0.22	27.51 ±20^0
3	BT3	0.57 ±0.098	0.63 ±0.19	9.71 ±0.25	1.11 ±0.16	29.05 ±0.21^0
4	BT4	0.65 ± 0.13	0.71 ±0.17	9.68 ±0.29	1.11 ±0.20	28.52 ±0.26^0
5	BT5	0.54 ± 0.33	0.59 ±0.13	8.60 ±0.12	1.09 ±0.16	29.60 ±0.32^0
6	BT6	0.56 ±0.20	0.77 ±0.19	27.78 ±0.22	1.38 ±0.13	30.76 ±0.22^0
7	BT7	0.58 ±0.22	0.65 ±0.22	10.47 ±0.31	1.12 ±0.21	27.51 ± 0.19^0
8	BT8	0.63 ±0.11	0.70 ±0.15	11.25 ±0.18	1.13 ±0.13	29.38 ±0.28^0
9	BT9	0.63 ±0.15	0.74 ±0.25	15 ±0.19	1.18 ±0.19	29.89 ±0.17^0
10	BT10	0.64 ±0.99	0.72 ±0.27	11.54 ±0.17	1.13 ±0.099	27.22 ±0.13^0
11	BT11	0.58 ±0.19	0.66 ±0.34	11.63 ±0.22	1.13 ± 0.14	26.89 ±0.25^0
12	BT12	0.68 ±0.12	0.77 ±0.17	12.16 ±0.32	1.14 ±0.22	28.52 ±0.15^0

N=3

The results of the bulk density and tapped density were mentioned in an above table. The bulk density and tapped density values were lies in between **0.54 ±0.21** to **0.68 ±0.12 g/cm^3** and **0.62 ±0.29** to **0.77 ±0.19 g/cm^3** i.e. less than 1.2, indicates good packing.

The values of % compressibility, Hausner ratio and angle of repose were lies in between **8.60% ±0.12%** to **27.78% ±0.22%, 1.09 ±0.16** to **1.38 ±0.13 and 26.57 ±0.33^0** to **30.76 ±0.33^0** respectively indicates acceptable flow property and also good packing ability.

4.2 FTIR Spectroscopy:

IR spectra of pure Tramadol Hydrochloride and polymers viz. Sodium Alginate, Carbapol 940 etc were taken separately. Then to know if there is any interaction between drug and polymer, IR spectra of Tramadol Hydrochloride and other polymers were taken in combination.(fig no 2, 3, 4, 5)

Interpretation:

There was no drug interaction in drug and polymers since the peaks of pure drug and polymers retains in combination.

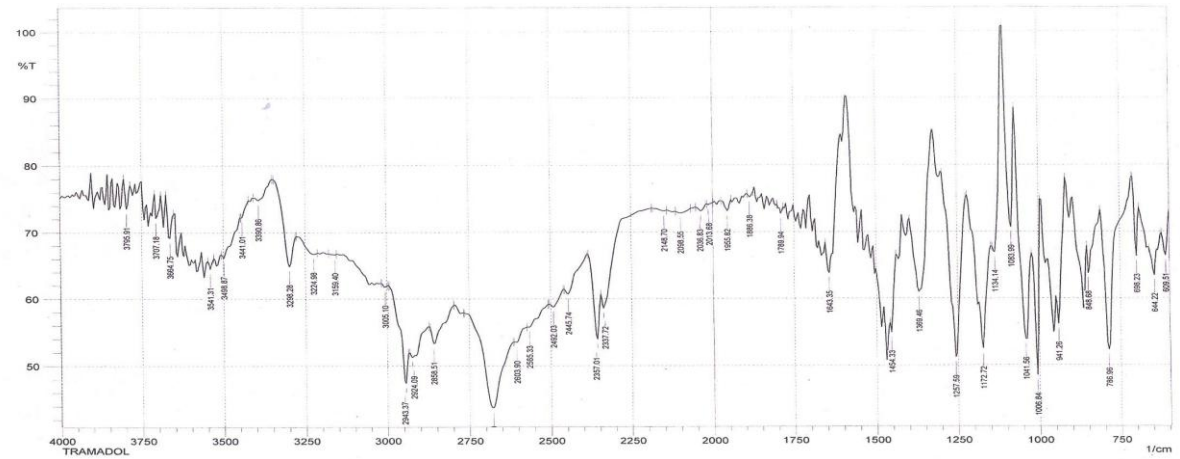

Figure 2: IR of Tramadol HCl

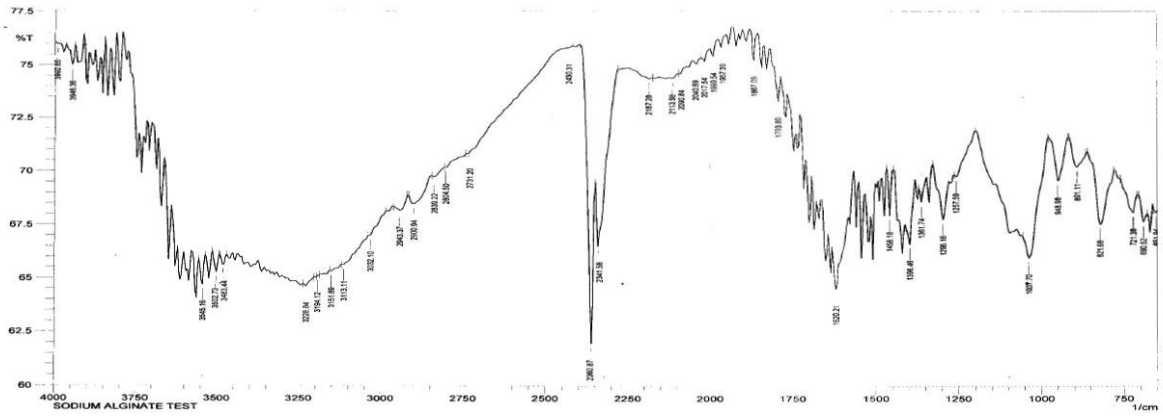

Figure 3: IR of Sodium Alginate

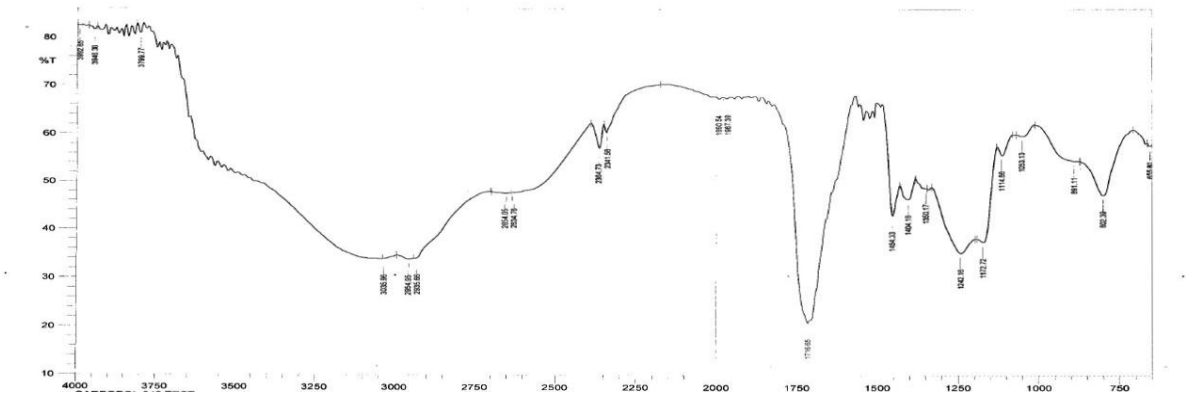

Figure 4: IR of Carbapol 940

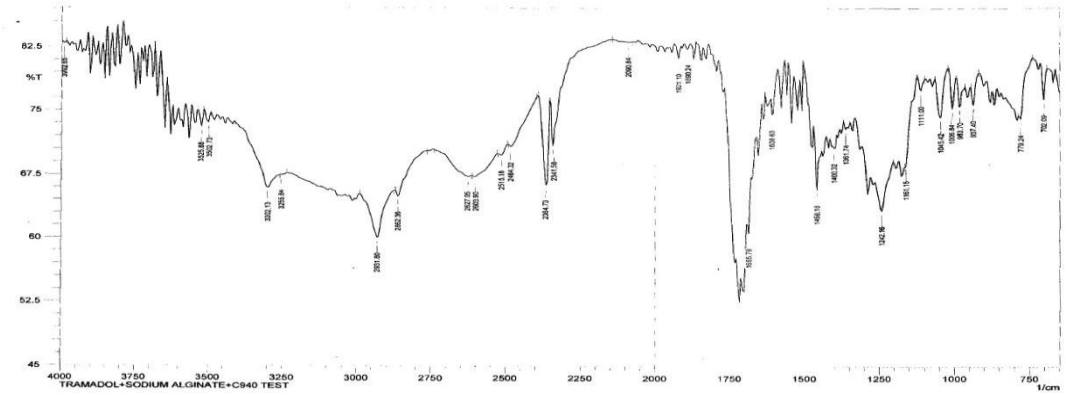

Figure 5: IR of Tramadol HCl + Sodium Alginate + Carbapol 940

Table 4: Principle peaks and chemical groups present in IR spectrum of Tramadol HCl, Sodium Alginate and carbapol 940

Sr no	Functional groups in Tramadol HCl	Peaks values (cm^{-1}) in Tramadol HCl	Peaks values (cm^{-1}) in Sodium Alginate	Peaks values (cm^{-1}) in Carbapol 940	Peaks values (cm^{-1}) in Constitution Combination	Interpretation
1	-OH	3298	-	-	3302.13	No Interaction
2	=C-H	3008	-	-	2931	No Interaction
3	-C-H	2943.37	-	-	2862.36	No Interaction
4	-C-O	-	1620	1716.06	1684	No Interaction
5	-C=C	1789.94	1747.84	-	1700	No Interaction
6	-COOH	-		3700 -3000 Broad peak	3700 -3000 Broad peak	No Interaction

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4.3 Morphological Studies Using SEM:

The morphology of optimized batch of bead was characterized by Scanning Electron Microscope (SEM). The surface topography of the (optimized) beads formulations were examined under a FEI-Philips XL-30 Analytical Electron microscope (VNIT NAGPUR). The sample was loaded on copper sample holder and sputter coated with platinum. (fig no 6,7)

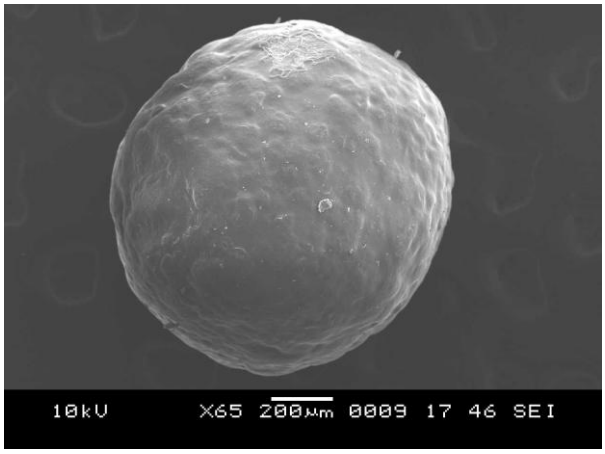

Figure 6: SEM of Oral Floating Beads of Tramadol HCl (A)

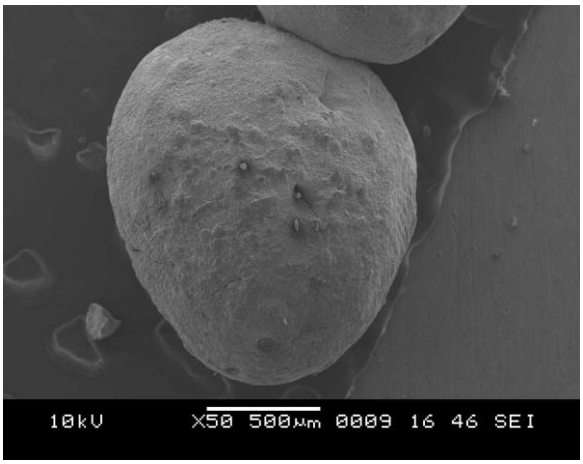

Figure 7: SEM of Oral Floating Beads of Tramadol HCL (B)

4.4 Characterization of oral floating beads of Tramadol Hydrochloride:

For the Characterization of oral floating beads of Tramadol Hydrochloride, Percentage Drug Entrapment Efficacy (%DEE), Drug content uniformity, Floating lag time, Floating duration etc tests were performed and the results were as follows:

Table 5: Various Characterizations of Oral Floating Beads of Tramadol HCl

Formulation code	%DEE	Drug content Uniformity (%)	Floating lag time (Sec)	Floating Time (Hr)
BT1	89	30	23	>12
BT2	90	29	25	>12
BT3	92	25	27	>12
BT4	93	25	12	>12
BT5	88	31	16	>12
BT6	85	35	10	>12
BT7	81	34	10	>12
BT8	86	38	10	>12
BT9	77	32	Immediate	>12
BT10	79	30	Immediate	>12
BT11	84	33	Immediate	>12
BT12	90	35	Immediate	>12

a) **% Drug Entrapment Efficiency (%DEE):** The yield of beads were determined by comparing the whole weight of beads formed against the combined weight of the polymer and drug and excipients. %DEE of formulated beads was found to be 77 to 93%. The optimized batch BT12 shows % DEE as 90% (as given in table 5)

b) Drug Content Uniformity: All the prepared formulations show drug content uniformity in the range of 25-38 %. The optimized batch show drug content uniformity 35%.(as given in table 5)

c) Floating Lag time : Floating lag time of all the prepared formulations was observed by visual examination. All the prepared formulations show Floating lag time from 27 seconds to immediate. And the optimized batch BT 12 show immediate floating after entering in 0.1 N HCl and show floating for more than 12 hrs. (as given in table 5)

d) Floating Duration: All prepared formulation show floating duration more than 12 hours. (as given in table 5)

4.5 Evaluation of Filled Capsule:

- Physical Description
- Colour : Yellow
- Weight of empty capsule :65±3 mg

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Table 6: Other Evaluation parameters of Floating Beads of Tramadol HCl

Parameters	BT1	BT2	BT3	BT4	BT5	BT6	BT7	BT8	BT9	BT 10	BT 11	BT 12
Capsule Lock Length	15.6	15.6	15.6	15.6	15.6	15.6	15.6	15.6	15.6	15.6	15.6	15.6
Weight Variation	Passes	Passes	Passes	Passes	Passes	Passes	Passes	Passes	Passes	Passes	Passes	Passes

Capsules of different formulations were subjected to various evaluation tests, such as capsule lock length, uniformity of weight, drug content. All batches showed uniform capsule lock length. The weight variation test was carried out as per official method and the per cent deviation of formulation was found to be within limit.

4.6 Invito Dissolution Study for Oral Floating Beads of Tramadol HCl

Drug release from beads, depends upon the extent of cross– linking, morphology, size and density of beads, physicochemical properties of the drug as well as the presence of adjuvants. In vitro release also depends upon pH, polarity and presence of enzymes in the dissolution media.

- The formulated batch BT1(Sodium alginate 6%:Pectin 3%) gave in vitro release for 2 hours, batch BT2(Sodium alginate 6%: Ethyl cellulose 3%) gave in vitro release for 2 hours, batch BT4(Sodium alginate 6%:HPMC K100 M 1.5%) gave in vitro release for 1 hours, batch BT5(Sodium alginate 6%:HPMC K 100M 2%) gave in vitro release for 3 hours, batch BT6 (Sodium alginate 6%:HPMC K100 M 3%) gave in vitro release for 4 hours, formulated batch BT7 (Sodium alginate 6%:Guar gum 0.7 %) gave in vitro release for 5 hours, batch BT8 (Sodium alginate 6%:Carbapol 940 0.5%) gave in vitro release for 4 hours, batch BT9(Sodium alginate 6%: Carbapol 940 0.7 %) gave in vitro release for 7 hours, batch BT10 (Sodium alginate 6%: Carbapol 940 0.9 %) gave in vitro release for 9 hours, batch BT11 (Sodium alginate 6%: Carbapol 940 1 %) gave in vitro release for 10 hours. As all these batches did not show drug release for 12 hours they did not give gastro retentive drug release. In all these batch use of polymers like pectin, guar gum, ethyl cellulose, HPMC K100 M were used in different polymeric ratio but cross linking was not enough to retard the drug release.
- In the formulated batch BT12 (Sodium alginate 6%: Carbapol 940 1.2 %) gave in vitro release for 12 hours. As it releases drug for 12 hours (100.26±0.66), and gave floating lag time immediate and floating duration more than 12 hours. It can be because sodium alginate is gel formulating agent and swelling agent and Carbapol 940 is emulsifying and gelling agent so combination of these two polymers gave release retarding beads with 90% drug entrapment efficiency. Also it follows all pre requisitions, on this basis this batch was optimized. Statistically it show significant difference from other batches.

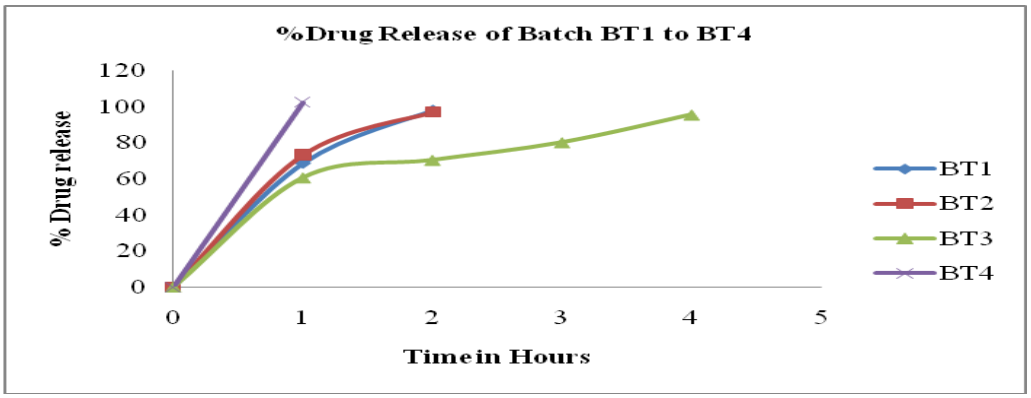

Figure 8: % Invitro drug release of batches BT1 to BT4

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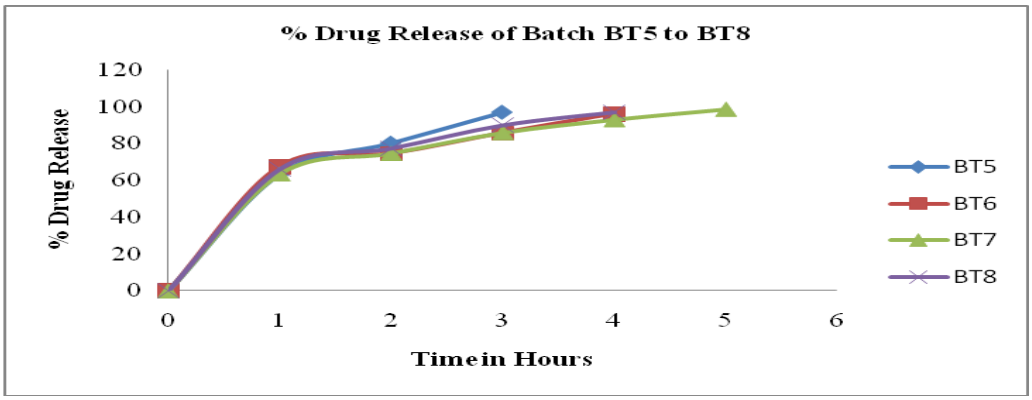

Figure 9: % Invitro drug release of batches BT5 to BT8

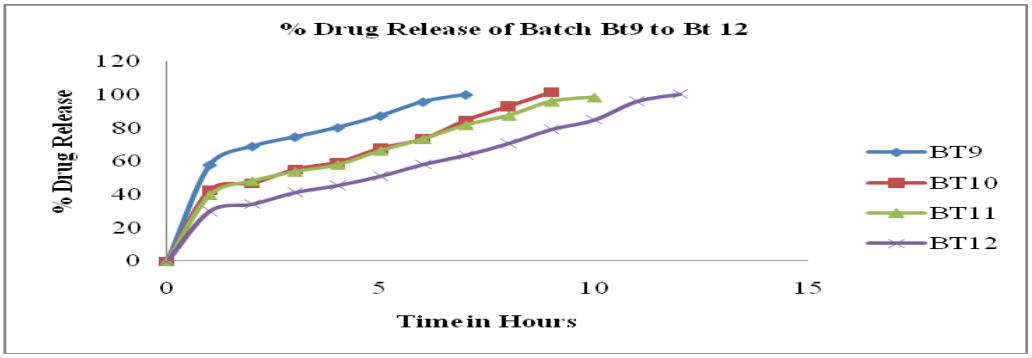

Figure 10: % Invitro Drug release of batches BT9 to BT12

In the present study various natural as well as synthetic polymers were used in the combination and in different ratio. But in the formulated batches BT1 to BT11 did not gave drug release for 12 hours. In formulated batch BT 12 (Sodium alginate 6% : Carbapol 940 1.2 %) show in vitro release for 12 hours (100.26 ± 0.66%). It also gave floating lag time and floating time immediate, and floating duration more than 12 hours. Hence it show gastric retention it can be because sodium alginate is gel formulating agent and swelling agent and Carbapol 940 is emulsifying and gelling agent so combination of these two polymers formulates release retarding beads with 90% drug entrapment efficiency. In kinetic model fitting it follows Korsemeyers Peppas equation. Also it was found stable in 6 months of accelerated stability study. So batch BT 12 was optimized.

4.7 Kinetic Studies:

The release data obtained from various batches was studied with respect to effect of drug: polymer ratio, diluents ratio. Dissolution data of drug from prepared in situ gel at different time periods was plotted as cumulative % drug release v/s time. The dissolution data so obtained was fitted to various kinetic models like Zero Order, First order, Higuchi, Korsmeyer-Peppas models. It was found that the optimized batch IB12 follow Korsmeyr-pappas model.

The drug release kinetics from all the batches were calculated, which was illustrated as follows-

Table 7: Kinetic study of Oral Floating Beads of Tramadol HCl

Batch	Zero order	First order	Matrix	Peppas	Hixon crowell	Best model fit
BT1	0.9685	0.9663	0.998	1	0.9969	Peppas
BT2	0.9508	0.9888	9986	1	0.97	Peppas
BT3	0.8437	0.9591	0.9846	0.9727	0.964	Matrix
BT4	0.652	0.9799	0.9547	0.9939	0.9362	Peppas
BT5	0.9091	0.9729	0.9959	0.996	0.9902	Peppas
BT6	0.7764	0.9764	0.9685	0.9764	0.9368	Peppas
BT7	0.7441	0.9758	0.9707	0.9976	0.967	Peppas
BT8	0.8043	0.9879	0.978	0.9943	0.968	Peppas
BT9	0.6599	0	0.9615	0.9901	0.9303	Peppas
BT10	0.8613	0	0.9863	0.9608	0.8458	Matrix
BT11	0.8529	0	0.9914	0.9776	0.8673	Matrix
BT12	0.9389	0	0.9693	0.9797	0.8606	**Peppas**

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4.8 Stastical Analysis:

In this study the Bonferroni method was applied to dissolution study to check there was significant difference or non significant difference in release of drug in formulated formulations. The optimized batch show significant difference from all other formulated batches. The description is given in table no 8.

Table 8: Statistical Analysis of Dissolution parameters of Floating Beads of Tramadol HCl:

Sr. No	Between batches	t-test	P-value (<0.05)	Significance
1	BT12 vs BT 1	2.840	P < 0.05	S
2	BT12 vs BT 2	2.906	P < 0.05	S
3	BT12 vs BT 3	3.704	P < 0.05	S
4	BT12 vs BT 5	2.781	P < 0.05	S
5	BT12 vs BT 6	3.874	P < 0.05	S
6	BT12 vs BT 7	4.784	P < 0.05	S
7	BT12 vs BT 8	3.839	P < 0.05	S
8	BT12 vs BT 9	6.799	P < 0.05	S
9	BT12 vs BT 10	7.286	P < 0.05	S
10	BT12 vs BT 11	8.789	P < 0.05	S

4.9 Stability Study:

Stability studies were carried out as per ICH guidelines. The optimized formulation BT12 was exposed to accelerated stability conditions as 40°C±2°C 75%RH±5% RH for the period of 6 months. In between the stability studies the formulation was removed at 3 month and 6 month to check all the evaluation tests as floating lag time, floating time, Floating duration, Dissolution studies etc. During the stability studies, the product was exposed to normal conditions of temperature and humidity. The optimized batch was found to be stable for all the evaluation tests in this time period of stability testing.

Table 9: Various characteristics of oral floating Beads of Tramadol HCl during stability study

Stability Duration	%DEE	Drug content Uniformity (%)	Floating lag time (Sec)	Floating Time (Hr)
Zero month	90	35	Immediate	> 12
After 3 Month	90	35	Immediate	> 12
After 6 Month	90	35	Immediate	> 12

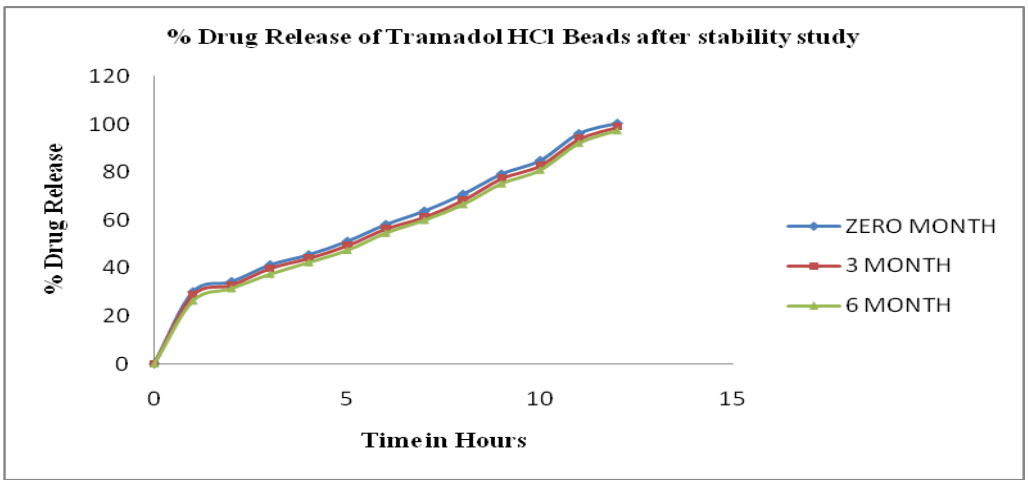

Figure 11: % Drug release of Oral Floating Beads of Tramadol HCl during stability study.

Table 10: Kinetic study of Oral Floating Beads of Tramadol HCl during stability study

Time / Model	Zero order	First order	Matrix	Peppas	Hixon crowell	Best Model fit
ZERO MONTH	0.9389	0	0.9693	0.9797	0.8606	**Peppas**
3 MONTH	0.9456	0.8483	0.9715	0.9780	0.9453	**Peppas**
6 MONTH	0.9518	0.8853	0.9732	0.9766	0.9564	**Peppas**

5. SUMMARY:

In the present study various natural as well as synthetic polymers were used in the combination and in different ratio. Batch BT 12 (Sodium alginate 6% : Carbapol 940 1.2 %) show in vitro release for 12 hours (100.26 ± 0.66%). It also gave floating lag time and floating time immediate and floating duration more than 12 hr with 90% drug entrapment efficiency. In kinetic model fitting it follows Korsemeyers Peppas equation. Also it was found stable in 6 months of accelerated stability study.

6. CONCLUSION:

Sustained release floating beads of Tramadol Hydrochloride were successfully prepared by modified ionotropic gelation technique which is a very simple technique.

From all the formulation and evaluation studies of oral floating beads of Tramadol Hydrochloride it was concluded that:

- ⇨ Among all different polymer ratio Sodium Alginate 6% and $CaCl_2$ 3% (2:1 ratio) gives formulation of beads.
- ⇨ Among different polymers Carbapol 940 gives retarded release for 12 hours .
- ⇨ There was increase in residence time of drug in stomach also there was reduction of dosing frequency also the drug show safety profile.

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