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Formulation and Evaluation of Amitriptyline Hydrochloride Microbeads by Using Synthetic Polymer

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ABSTRACT:

Multiple unit dosage forms such as microbeads have increased acceptance because of added even spreading of the drug in the gastrointestinal tract, unvarying drug absorption, abridged local irritation and removal of undesirable intestinal retaining of polymeric material, when compared to non-disintegrating single unit dosage form. The main aim of the study is to formulate Amitriptyline Hydrochloride loaded microbeads of sodium alginate using HPMCK15M as release modifiers by Ionotropic Gellation Method. The microbeads were prepared by varying the concentration of sodium alginate, HPMCK15M.The drug – polymer compatibility was studied by FTIR studies. No significant drug-polymer interaction were observed in FTIR studies. The microbeads represented good yield, high drug entrapment, low microbeads size and appropriate swelling property. Henceforth, the formulated HPMCK15M coated sodium alginate beads can be utilized as a substitute and cost-effective carrier for the oral controlled delivery of Amitriptyline hydrochloride.

Key words: Amitriptyline hydrochloride, $HPMCK_{15}M$, Sodium alginates, drug release

I. INTRODUCTION:

Oral drug delivery is the furthermost required and ideal way of administering therapeutic candidates for their systemic effects. Sustained release technology has emerged as an important new field in the development of pharmaceutical dosage form. Sustained release systems include any drug delivery system that achieves slow release of drug over an extended period of time. More precisely, sustained drug delivery can be defined as "Sustained drug action at a predetermined rate by maintaining a relatively constant, effective drug level in the body with concomitant minimization of undesirable effects". In sustained release dosage forms, a sufficient amount of drug is initially made available to the body to cause a desired pharmacological response. The remaining fraction is released periodically and is required to maintain the maximum initial pharmacological activity for some desirable period of time in excess of time expected from usual single dose. The onset of its pharmacologic action is the often delayed and the duration of its therapeutic effects is sustained. A sustained release is facilitated through the consistent rejuvenation of drug molecules. The aim of the presented research is to develop sustained release oral product namely microbeads of pseudoephedrine hydrochloride using sodium alginate as the hydrophilic carrier in combination with HPMCK15M as drug release modifier to reduce the dosing frequency and thereby improve the patient compliance. Also, to improve its bioavailability by passing the first pass metabolism because alginate beads shrink and unable to swell at acidic environment and the encapsulated drugs are not released whereas they easily swell in an alkaline environment and release the drug.

MICRO BEADS:

Micro beads are nearly spherical, small with diameter 1000µm.The solid and free flowing particulate carriers containing dispersed drug particles either in either in solution or crystalline form allow a sustained release or multiple release profiles of treatment with various active agents without major side effects. The micro beads are produced from several polymers such as cationic polymers, example sodium alginate, and binding components, example: chondroitin sulfate, avidin in predetermined ratio. Micro encapsulation has become common technique in the production of controlled release dosage forms. The beads are discrete spherical microcapsule that serve as the solid substrate on which the drug is coated or encapsulated in the core of the beads.

II. MATERIALS AND METHODS:

Amitriptyline hydrochloride is obtained as gift sample from Medopharm pharmaceutical pvt. ltd. $HPMCK_{15}M$ polymer is obtained as gift sample from colorcon asia pvt. Ltd. Goa. Sodium alginate is brought from Isochemicals. Calcium chloride is brought from Isochemicals.

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FORMULATION OF AMITRIPTYLINE HCl MICROBEADS:

Amitriptyline HCl microbeads was formulated by using Ionotropic gelation method.

Figure 1: Microbeads Formulation

PREPARATION OF SODIUM ALGINATES BEADS BY USING HPMCK_{15}M POLYMER:

In a blender, add 2 g of sodium alginate for every 100 ml of deionized or distilled water. (2% Sodium Alginate Solution)

Mix the contents using a hand blender for about 15 minutes or until all of the sodium alginate has been dissolved. Avoid blending too long or you will get a foamy solution. If your solution contains many bubbles, you may want to leave this solution overnight in a refrigerator.

Add 0.5g of HPMCK15M polymer and 100mg of amitriptyline HCl in a beaker and dissolve it in 100ml of hot distilled water by using magnetic stirrer. Cool the solution for few minute until it becomes bubble free solution.

Mix the contents of sodium alginate and HPMCK15M polymeric solution in one beaker.

For the 5% calcium chloride solution, add 5 g of calcium chloride for every 100 ml of deionized or distilled water, making sure to mix the solution well to dissolve the calcium chloride completely into the deionized or distilled water.

Procedure:

Pour the 5% calcium chloride solution into a small bowl.

Fill a syringe with mixture of Amitriptyline HCl, HPMCK_{15}M and sodium alginate solution.

Give the syringe to a kid and let them create beads by putting drops from the syringe into the 5% calcium chloride solution. They can also make worms by placing the syringe into the solution and allowing a continuous stream of sodium alginate to flow out of the syringe while moving it.

For those kids that want to take their beads and worms home, fill a sandwich bag with some water and place the beads and worms into the bag. Make sure that the beads and worms have been drained from the calcium chloride solution.

Table 1:FORMULATION CHART

S.no	Parameters	F1(g)	F2(g)	F3(g)
1	Drug	0.1	0.1	0.1
2	Sodium Alginate	2	4	6
3	HPMCK15M	0.5	1	1.5
4	Calcium chloride	5%	5%	5%

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EVALUATION OF AMITRIPTYLINE HCl MICROBEADS:

1.Percentage yield

The yield of the prepared formulations was calculated as the percentage of the weight of the dried product at room temperature compared to the theoretical amount. Production yield is calculated using the following equation:

Percentage yield = [weight of product/(weight of drug + polymer)] × 100

2.Size analysis and determination

In size distribution analysis, the micro beads of different size in a batch was separated by sieving, using standard sieves. The amounts were weighed retained on different sieves.

Mean particle size of the micro beads are calculated by this formula:

Mean particle size = Σ mean particle size of the fraction × weight fraction

Weight fraction

3.Swelling index:

Degree of swelling illustrates the ability of the microbeads to get swelled at the absorbing surface by absorbing fluids available at the site of absorption.

The swelling properties of the drug loaded microbeads were determined in various solution (0.1N HCl, pH 7.5 phosphate buffer) 50 mg of dried beads from each formulation were weighed and placed in a two separate petridish containing 25 ml of solutions(0.1N HCl, pH 7.5 phosphate buffer) and allowed to swell at room temperature. At the end of 1 hour interval, the beads were withdrawn, soaked with tissue paper and weighed. Then for every 1 hour, weights of beads were noted and the process was continued till the end of 8 hours.

The % weight gain by beads was calculated by following formula.

Swelling Index = Wt–W0/W0 ×100

Where, Wt – Mass of swollen beads at time t

W 0 – Mass of dry beads at t=0 8.8)

4.FTIR spectral analysis:

FTIR study was carried out to check identity of drug. Infrared spectrum of Amitriptyline HCl was determined on Fourier transform Infrared Spectrophotometer using KBr dispersion method. The base line correction was done using dried potassium bromide. Then the spectrum of dried mixture of drug and potassium bromide was run followed by drug by using FTIR spectrophotometer. The absorption maximums in spectrum obtained with the substance being examined correspond in position and relative intensity to those in the reference spectrum.

III. RESULTS AND DISCUSSION:

Analytical methods:

Determination of λ max by using 0.1N HCl:

The maximum absorption for Amitriptyline hydrochloride in 0.1N HCl was found to be 239nm and it is shown in the figure

Figure 2: λ max observed for Amitriptyline hydrochloride in 0.1N HCl.

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Preparation of standard curve of Amitriptyline HCl 0.1N HCl:

UV absorption spectrum of Amitriptyline hydrochloride in 0.1N HCl showed λ max at 239nm. Absorbance obtained for various concentration of AMT HCl in 0.1 HCl are given in the table. The graph of absorbance vs. concentration for AMT HCl was found to be linear in the concentration range of 20-100µg/ml. the drug obeys Beer- Lambert's law in the range of 2-10µg/ml.

Table 2 Data of absorbance vs. concentration for AMT HCL

S.no	Concentration(µg/ml)	Absorbance(nm)
1	2	0.092
2	4	0.173
3	6	0.258
4	8	0.345
5	10	0.430

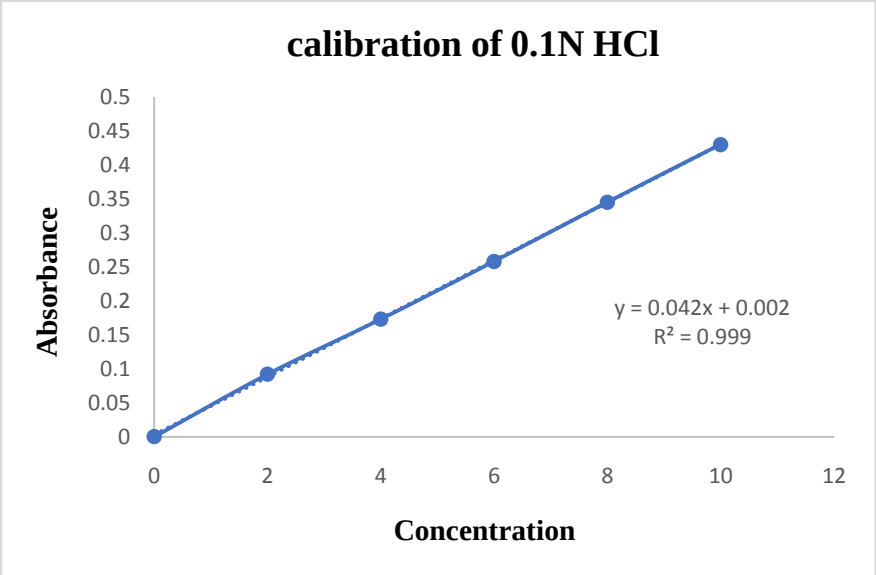

Figure 3: Standard graph of AMT HCl in 0.1N HCl

Percentage yield:

The percentage yield of microbeads of ATM were found to increase as the polymer ratio was also increased. The maximum yield of microbeads were found in F3 formulation – 90.78%. Percentage yield of all the formulations data represented in table 6

Table 3: Percentage yield.

S.NO.	Formulation code	Percentage yield(%)
1	F1	88.077 %
2	F2	84.44 %
3	F3	90.78 %

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Size Analysis and Determination:

Particle size of prepared microbeads was determined by optical microscopy method and the average particle sizes of all batches of microbeads were represented in table10. The particle sizes of the controlled release microbeads were found to be in the range of 734 ± 0.41µm to 804 ± 0.41 µm.

Table 4 Size of Particles Determination.

S. NO	Formulation code	Particle Size (µ m ±S.D)*
1	F1	734±0.41
2	F2	804±0.41
3	F3	764±0.32

Swelling index:

Swelling study of Amitriptyline HCl micro beads were performed in 0.1NHCl up-to 3 hours.

S.No	HOURS	In 0.1N HCl%		
		F1	F2	F3
1	1	6	8	10
2	2	10	12	20
3	3	16	20	32

Table No:5 swelling index

FTIRSpectral Analysis:

IDENTIFICATION OF AMITRIPTYLINE HCL BY FTIR SPECTROSCOPY:

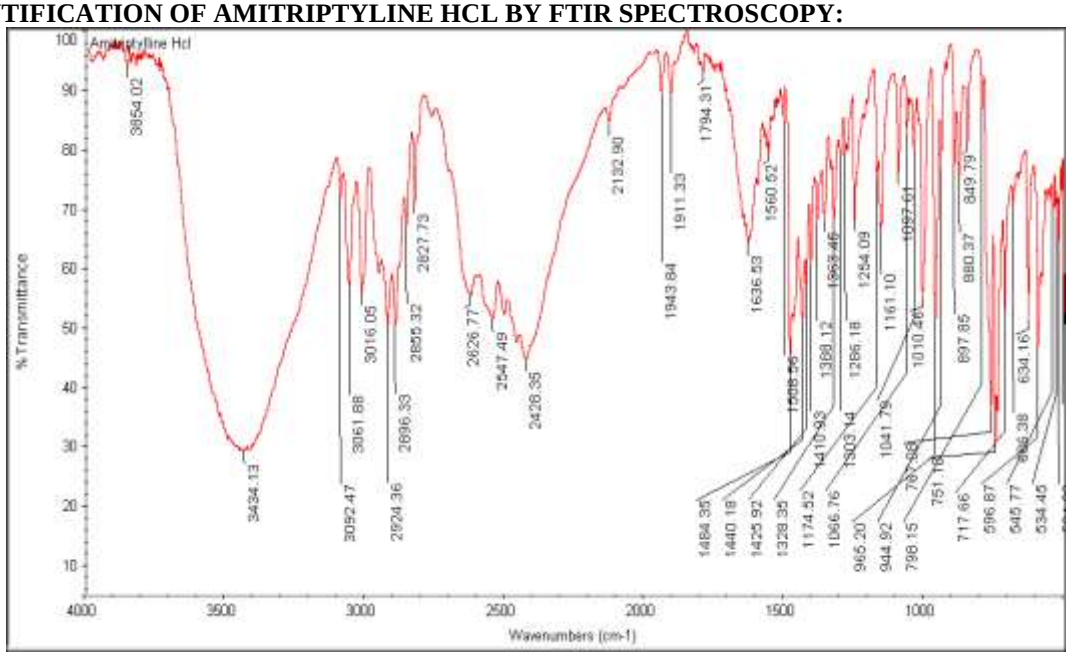

Figure 4 : FT IR spectrum of pure drug Amitriptyline HCl

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Table 6:FTIR Spectral interpretation of AMT HCl

S.No	Frequency cm⁻1	Functional group
1	3061.88	Aromatic C-H stretching
2	2924.36,2855.32	Asymmetric & symmetric CH_3stretching
3	2896.33,2827.73	Asymmetric &symmetric CH_2 strecthing
4	2428.35	Characteristic of HCl salt of tertiary amine
5	1254.9	Nitro compound
6	751.18	C-H bending
7	767.08	C_6 H_6 (N)substitution
8	717.66	C_6 H_6 (O) substitution

DRUG EXCIPIENT COMPACTABILITY STUDIES:

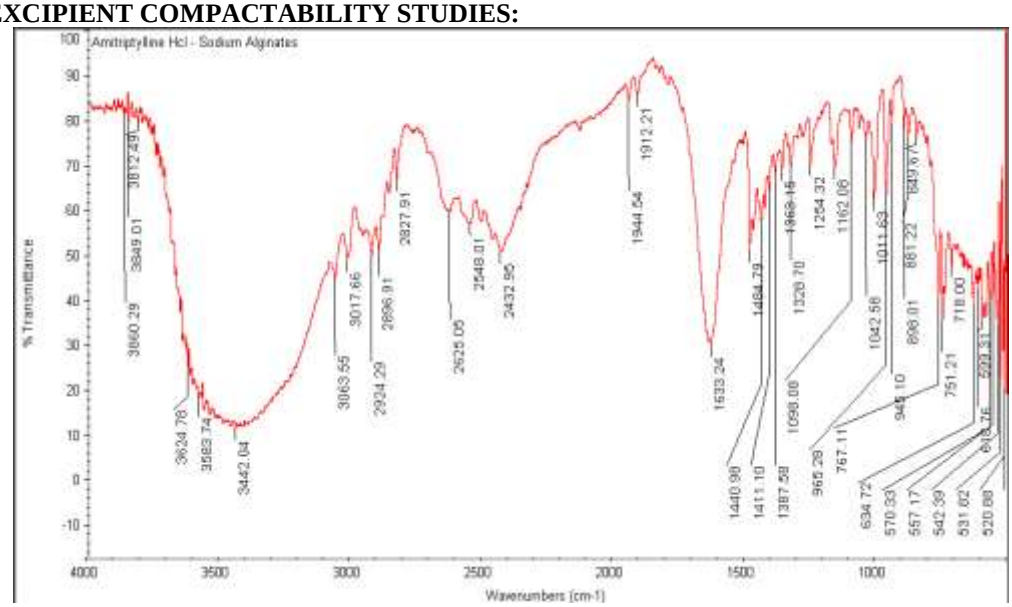

Figure 5: FT IR spectrum of pure drug Amitriptyline HCl and sodium alginates.

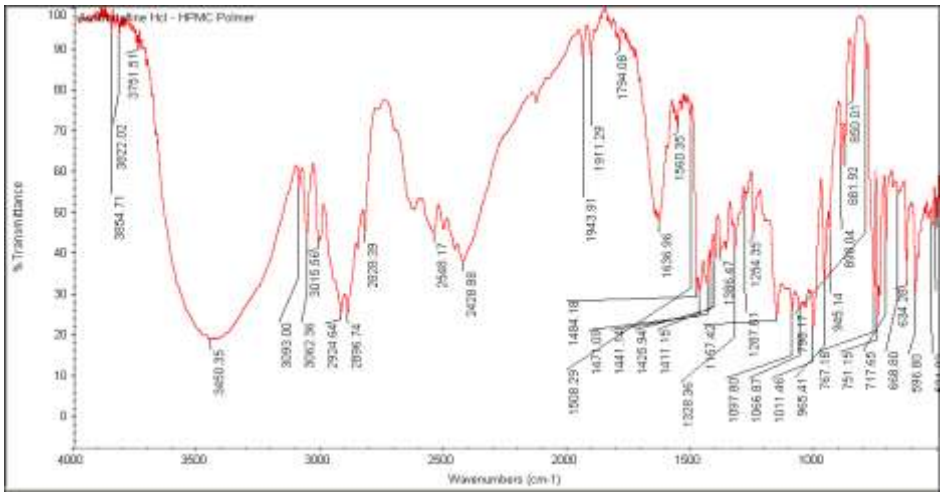

Figure 6 FT IR spectrum of Amitriptyline HCl and HPMCK_{15} polymer.

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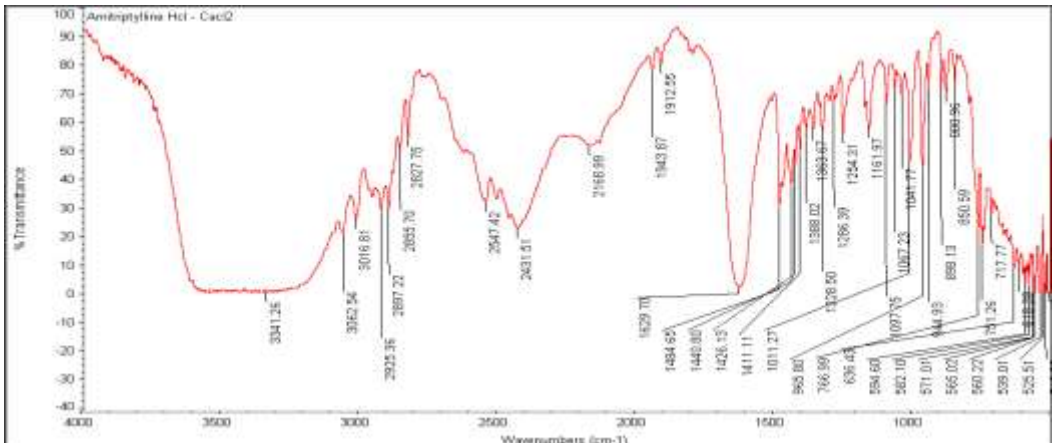

Figure 7: FT IR spectrum of pure drug Amitriptyline HCl and $CaCl_2$

Table7:Major peaks observed in FTIR spectrum of AMT HCl and drug with different polymers used in the formulation.

Functional group	Wave No.(cm^{-1})	Drug	Drug+ sodium alginates	Drug + HPMC K_{15}	Drug+ $CaCl_2$
Aromatic C-H Stretching	3061.88	yes	Yes	Yes	Yes
Asymmetric & symmetric CH_3 stretching	2924.36,2855.32	yes	Yes	Yes	Yes
Asymmetric &symmetric CH_2 stretching	2896.3,2827.73	yes	Yes	Yes	Yes
Characteristic of HCl salt of tertiary amine	2428.35	yes	Yes	Yes	Yes
Nitro compound	1254.9	yes	Yes	Yes	Yes
C-H bending	751.18	yes	Yes	Yes	Yes
C_6H_6(N) substitution	767.08	yes	Yes	Yes	Yes
C_6H_6(O) substitution	717.66	yes	Yes	Yes	Yes

According to Table No: 7 and Figure 5 to 8 the major peaks observed in the drug spectrum were also absorbed in the spectrum of drug with polymer. It could indicate that there was no compatibility between drug and different polymer.

IV. CONCLUSION

Novel drug delivery system has achieved a great interest in recent years. Amitriptyline hydrochloride was chosen as a drug for the treatment of Antidepressant. FTIR scan and UV scan of amitriptyline hydrochloride was performed. From the result of above studies it may be concluded that the drug was pure with no impurities and can be used in preparing microbeads.

Microbeads paly an important role in the drug release and bio availability of the drug also effective. Thus on future microbeads will play an important role in the development of new pharmaceutical techniques and materials.

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