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ISSN: 0975-7538
Review Article

Formulation and evaluation of alginate microbeads of ondansetron by ionotropic gelation technique

Sivakumar G*, Gnana prakash K, Kumar B, Gobinath M

Ratnam institute of Pharmacy, Pidthapolur, SPSR Nellore District – 524 346, Andhra Pradesh, India

ABSTRACT

Ondansetron is an anti emetic agent for the treatment of nasia and vomiting and also used chemotheraphy in cancer. Ondansetron drug is 5ht3 receptor antagonist. it has shorter biological half-life (3 – 4 hrs) necessitates that it to be administered in frequent doses of 4mg. The main objective of this study was to develop suitable micro particulate system of ondansetron for controlled release delivery system by varying the alginate, CaCl2 and HPMC concentrations. In the present work ondansetron microbeads were formulated using sodium alginate by ionotropic gelation technique. Prepared beads were evaluated for granulometric studies, micromeretic, scanning electron microscopy, drug entrapment efficiency and in-vitro dissolution studies etc. The prepared beads were free flowing and white in colour. The drug loaded beads showed 84.6–98.2 % drug entrapment, which was found to increase with increase in sodium alginate concentration. Scanning electron microscopy revealed that the beads were spherical and rough in structure. *In vitro* drug release study of these microbeads indicated controlled release for ondansetron 85.54 – 97.2 % released. Hence the observation of all results of the different batches third and fourth showed controlled release action and improved drug availability. The release of ondansetron was found to be affected by both concentration of polymers such as sodium alginate and HPMC. By the observation of accelerated stability studies second batch formulation was found to be best formulation. From this study, it could be concluded that the spherical and free flowing microbeads of ondansetron could be successfully prepared by ionotropic gelation technique with high entrapment efficiency and prolonged release characteristics.

Keywords: Hydroxy propyl methyl cellulose (HPMC); *In-vitro* drug release; microbeads; ondansetron; sodium alginate.

INTRODUCTION

The role of the ideal drug delivery system is to provide a therapeutic amount of drug to the proper site of the body to achieve the promote response and maintain drug concentration. Oral sustained release dosage forms have been developed for the part three decades due to their considerable therapeutic advantages there are many methods achieved controlled release dosage forms. Gell forming ability of alginate salts is simple way obtaining particulate drug carriers. Alginate salts are known to form a regulated structure when contact with calcium ions and characteristic has been used produce sustained release particulate systems for the variety of drugs. The use of alginate gell beds in the delivery of low solubility or macromolecular drugs has been suggested successful involving cross linking of sodium alginate or gelation alone, using aldehydes, have also been reported. Ondansetron is anti-emetic drug and also used in chemotherapy in cancer disease. it is short biological half-life (3-4 hrs) it is to be administered in frequent dose of 4mg the main objective of in this study was to develop suitable microparticulate system of ondansetron for controlled released delivery system by the sodium alginate ,cacl $_2$,and HPMC concentrations. (Beckett AH et al., 1980)

* Corresponding Author
Email: shivakumarreddy333@gmail.com
Contact: +91-9000242229
Received on: 15-06-2015
Revised on: 04-08-2015
Accepted on: 10-08-2015

MATERIALS AND METHODS

Ondansetron I.P was obtained as a gift sample from the twenty first century pharmaceuticals pvt Ltd, Chennai Hydroxy propyle methyl cellulose, sodium alginate, calcium chloride commercially from Lab India, Hyderabad Andhra Pradesh, India. (Lym.LY et al., 1997)

Preparation of Microbeads

Microbeads of ondansetron where prepared by i onotropic gelation technique. Weighed accurately sodium alginate (4%, 3%, 2%, 1% w/v) and also weighed HPMC (0.5%, 1% ,1.5% ,2%w/v) and also weighed drug 100mg. and also weighed calcium chloride (6%) first take 100ml of distilled water in beaker after then add sodium alginate and also add HPMC and drug string maintaining speed 50rpm to form aqueous mucilage after then take distilled water in 100ml add calcium chloride string after then using 10ml syringe 20g nee

Table 1: Composition of alginate Microbeads of ondansetron

Ingredient	F1	F2	F3	F4	F5	F6	F7	F8
Ondansetron Drug (4mg)	100 mg	100 mg	100 mg	100 mg	100 mg	100 mg	100 mg	100 mg
HPMC K30	0.5%	1%	1.5%	2%	0.5%	1%	1.5%	2%
Sodium alginate	4%	3%	2%	1%	4%	3%	2%	1%
Calcium chloride	6%	6%	6%	6%	6%	6%	6%	6%
Water	100ml	100ml	100ml	100ml	100ml	100ml	100ml	100ml

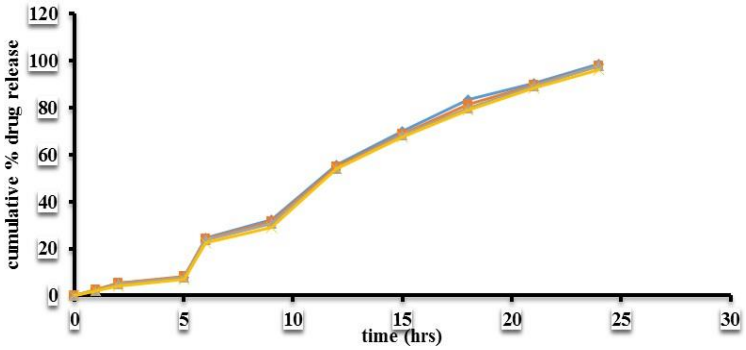

Figure 1: Cumulative drug release F1, F2, F3, F4, formulations

Table 2: In-vitro drug release studies for prepared ondansetron Microbeads F1 formulation

Zero order		First order First order		Higuchi's data Higuchi's data		Peppas data Peppas data	
Time (h)	% CDR	Time (h)	% Log CD Remaining	SQRT of time	% CDR	Log time	% Log CDR
1	3.6	1	1.984	1.0	3.6	0	0.556
2	6.2	2	1.972	1.414	6.2	0.30	0.792
3	9.5	3	1.956	1.732	9.5	0.477	0.977
6	25.7	6	1.870	2.449	25.7	0.778	1.409
9	38.5	9	1.788	3.0	38.5	0.954	1.585
12	59.2	12	1.610	3.464	59.2	1.079	1.772
15	73.5	15	1.423	3.872	73.5	1.176	1.866
18	89.4	18	1.025	4.242	89.4	1.255	1.951
21	96.4	21	0.556	4.582	96.4	1.322	1.984
24		24		4.898		1.380	

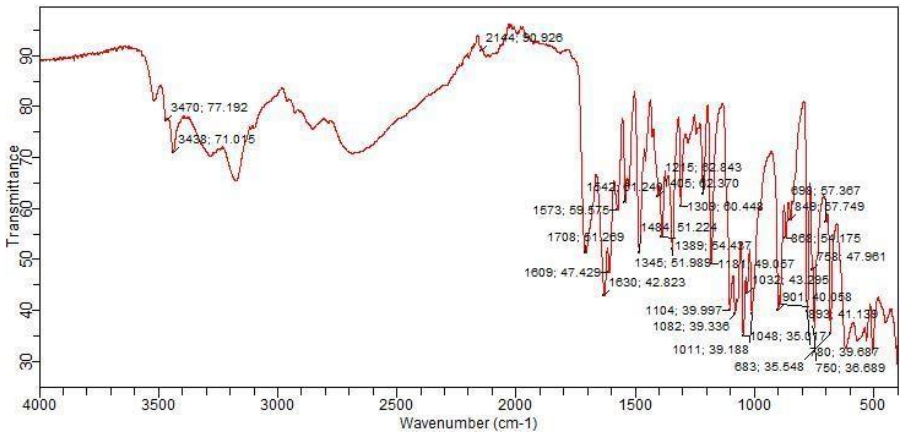

Figure 2: FTIR Spectrum of ondansetron

dle take sodium alginate and drug aqueous mucilage drop by drop add in calcium chloride solution to form the microbeads after then to separate the microbeads wash and kept the tray dryer in 40^0c after then dried beads will be various formulations, where mentioned in Table No:01 (B. vishnu vardhan reddy et al., 2012)

Scanning electron microscopy

Morphological details of the specimens were determined by using scanning electron microscope (SEM), model ISM 35 CF, JEOL, Japan.

Table 3: In-vitro drug release studies for prepared ondansetron Microbeads F2 formulation

Zero order		First order		Higuchi's data		Peppas data	
Time (h)	% CDR	Time (h)	% Log CD Remaining	SQRT of time	% CDR	Log time	% Log CDR
1	1.9	1	1.991	1.0	1.9	0	0.278
2	3.5	2	1.984	1.414	3.5	0.301	0.544
3	7.8	3	1.964	1.732	7.8	0.477	0.892
6	23.8	6	1.881	2.449	23.8	0.778	1.376
9	32.4	9	1.829	3.0	32.4	0.954	1.510
12	48.8	12	1.709	3.464	48.8	1.176	1.688
15	66.2	15	1.528	3.872	66.2	1.176	1.820
18	78.4	18	1.334	4.242	78.4	1.255	1.894
21	88.3	21	1.068	4.582	88.3	1.322	1.945
24	97.2	24	0.447	4.898	97.2	1.380	1.987

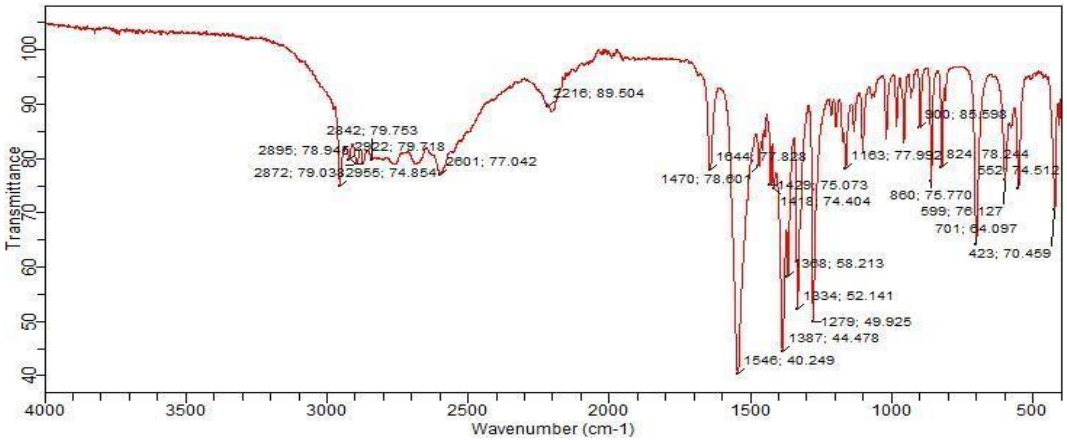

Figure 3: FTIR Spectrum of HPMC

Table 4: In-vitro drug release studies for prepared ondansetron Microbeads F3 formulation

Zero order		First order		Higuchi's data		Peppas data	
Time (h)	% CDR	Time (h)	% Log CD Remaining	SQRT of time	% CDR	Log time	% Log CDR
1	1.2	1	1.994	1	1.2	0	0.079
2	3.4	2	1.984	1.414	3.4	0.301	0.531
3	5.6	3	1.974	1.732	5.6	0.477	0.748
6	19.9	6	1.903	2.449	19.9	0.778	1.298
9	29.4	9	1.848	3	29.4	0.954	1.468
12	46.2	12	1.730	3.464	46.2	1.176	1.664
15	58.6	15	1.617	3.872	58.6	1.176	1.767
18	72.1	18	1.445	4.242	72.1	1.255	1.857
21	80.4	21	1.292	4.582	80.4	1.322	1.905
24	94.2	24	0.763	4.898	94.2	1.380	1.974

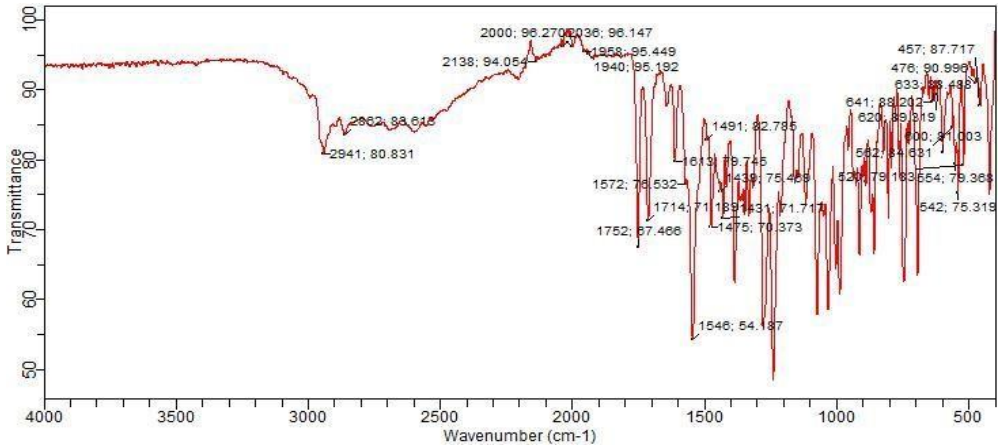

Figure 4: FTIR Spectrum of Sodium alginate

Table 5: In-vitro drug release studies for prepared ondansetron Microbeads F4 formulation

Zero order		First order		Higuchi's data		Peppas data	
Time (h)	% CDR	Time (h)	% Log CD Remaining	SQRT of time	% CDR	Log time	% Log CDR
1	2.5	1	1.989	1	2.5	0	0.397
2	5.4	2	1.975	1.414	5.4	0.301	0.732
3	8.6	3	1.960	1.732	8.6	0.477	0.934
6	24.3	6	1.879	2.449	24.3	0.778	1.385
9	32.1	9	1.831	3	32.1	0.954	1.506
12	55.6	12	1.647	3.464	55.6	1.176	1.745
15	69.8	15	1.480	3.872	69.8	1.176	1.843
18	83.4	18	1.220	4.242	83.4	1.255	1.921
21	90.4	21	0.982	4.582	90.4	1.322	1.956
24	98.4	24	0.204	4.898	98.4	1.380	1.992

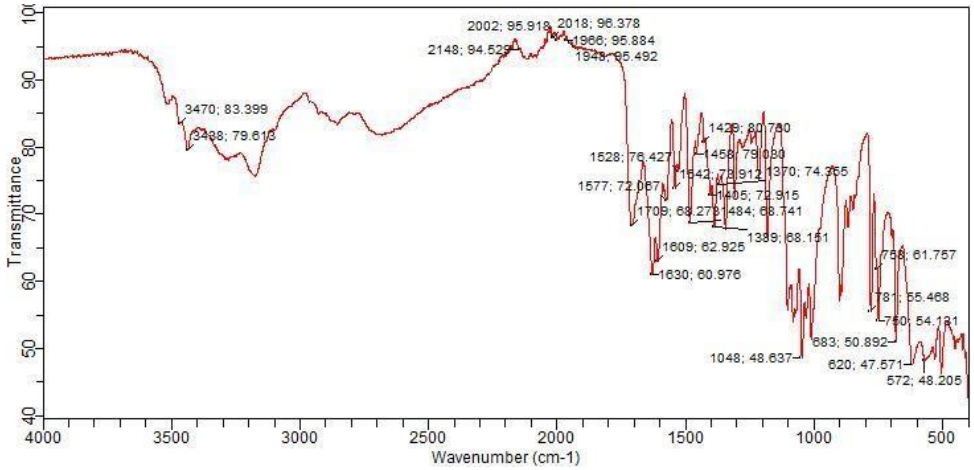

Figure 5: FTIR Spectrum of HPMC + Ondansetron

Table 6: Stability data

Days	F3(37^0)	F3(60^0)	F4(37^0)	F4(60^0)
1	96.46	94.33	97.52	96.66
7	94.50	93.37	97.22	96.33
14	93.50	92.56	96.65	95.44
21	93.23	92.33	96.25	95.51
38	92.78	97.74	95.75	95.43
45	92.55	91.44	95.43	94.22

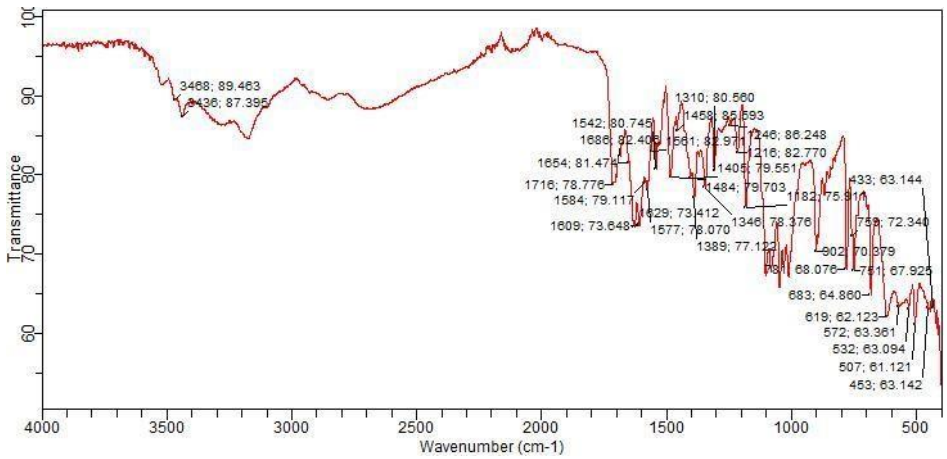

Figure 6: FTIR Spectrum of sodium alginate + Ondansetron

Estimation of ondansetron

About 25mg of microbeads were weighed and added to 50ml of 0.1N HCL the resulting mixture was agitated on mechanical shaker for 24 hrs, then solution was filtered and the drug content was estimated at 248 nm spectrophotometrically after suitable dilution. (patil DA et al., 2009)

In-vitro release studies

In-vitro release studies of prepared microbeads carried out 0.1N HCL buffer using USP-XXII apparatus at 100 rpm maintained at temperature of 37±1^{0}c for a period up to 24 hrs. Each time interval 5ml of sample was withdrawn, at the same time 5ml of fresh dissolution media was added to maintain the sink condition. The samples were suitably diluted and measure the absorbance 248nm spectrophotometrically. Absorbance values the concentration values from the standard calibration curve. Then calculated the cumulative drug release percentage at regular time intervals. The in-vitro release studies were mentioned in table No: 02-05 the formulations stored in oven at 37±10^{o}C and 60±10^{o}C period of 6 weeks. Samples are analyzed for drug content spectrometically at 248 nm the accelerated stability study results in F3, F4 Formulations mentioned in Table No: 06 (Anand rao R et al., 2001)

RESULTS AND DISCUSSION

Microbeads of ondansetron were prepared by i onotropic gelation technique and different evaluation parameters were assessed with a view to obtain oral controlled release of ondansetron in this prepared microbeads formulations drug entrapment efficiency range of 87.25-97.87% the drug entrapment efficiency of all the formulations were in the range 83.6-98.2 drug entrapment efficiency values of different formulations were observed reported as increase the concentration of sodium alginate and HPMC automatically drug entrapment efficiency is also increases. The in-vitro drug release studies of the different formulations cumulative drug release percentage range 87.54-97.2% the in-vitro drug release profile mentioned Table No:03 the formulations F1, F2, F3, F4 containing 0.5, 1, 1.5, 2% sodium alginate respectively showed release of 97.2, 94.2 and also 92.55% after 24 hours. This shows more sustained release is observed with increase in the sodium alginate. The formulation F2, F3, F4 containing 1, 1.5, 2% sodium alginate showing release 97.2, 88.3 and 80.4% after 24 hour. This indicates release rate further retarded due to addition of increasing concentration of HPMC. In the best formulation was observed as F2, the prepared best formulation was observed spherical shape.

Drug and polymer interaction (FTIR) Study

The IR spectrum of ondansetron showed characteristic peas ondansetron and were not affected and prominently observed in IR spectra of ondansetron and polymers interactions as shown in Fig:2 to Fig:6 spectra indicated no interaction between ondansetron and polymers.

CONCLUSION

Ondansetron is lower biological half-life drug was made to increase its kinetics and dynamic activities by adapting the method of preparation of microbeads . The sodium alginate once again proved to best class of anti-emetic agent for controlled release of the drug. Successfully achieved by ionotropic gelation technique using polymers sodium alginate and HPMC. Prepared microbeads shown higher drug entrapment efficiency and prolonged release microbeads was influenced by alginate and HPMC contractions. Different formulations of microbeads F2, F3 where estimated best formulations drug release controlled manner. The comparison of those two formulations best formulation is F2.

ACKNOWLEDGEMENT

The authors are thankful to twenty first century pharmaceuticals Pvt. Ltd, Chennai for providing the gift sample of ondansetron. The authors also thankful lab India, Hyderabad, for providing the polymers and solvent systems and also thankful to management of Ratnam institute of Pharmacy for providing the all facilities for carried out this research work.

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