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FORMULATION AND EVALUATION OF OMEPRAZOLE DOUBLE WALLED MICROSPHERES USING DIFFERENT POLYMERS

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ABSTRACT

Inthepresent work, double walled microspheres of Omeprazole using Sodium alginate,HPMC K100,Guar gum, Ethyl celluloseascopolymers and along with Carbopol wereformulated to deliver Omeprazole through oral route.Details regarding thepreparation and evaluation ofthe formulations have beendiscussedinresults.From the study following conclusions couldbedrawnThe results of this investigation indicate that Ion gelation method canbesuccessfullyemployedtofabricate Omeprazole microspheres. FT-IR spectraof the physical mixture revealed thatthedrug is compatible with the polymers and copolymer used. Microspheres containing sodium alginate along with carbopol and Guar gum in 1:1.5 ratio had a least size range of 613µm.Increase in thepolymerconcentrationledto increase in% Yield,%Drugentrapment efficiency, Particle size. The *invitro* drug releasedecreased with increase in thepolymer and copolymerconcentration.Among all formulations F4 shows Maximum drug release in 10 th hr when compared with other formulations.Analysis ofdrug release mechanism showedthatthedrug release fromthe formulations followed the Non fickian diffusion mechanism and follows zero order kinectics.Based on the results of evaluation tests formulation codedF4 was concluded as best formulation

Key Words: Carbopol , Microspheres , Diffusion , Kinetics , Copolymers.

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INTRODUCTION

For many decades, medication of an acute disease or a chronic illness has been accomplished by delivering drugs to the patients via various pharmaceutical dosage forms like tablets, capsules, pills, creams, ointments, liquids, aerosol 1, injectables and suppositories as carriers. To achieve and then to maintain the concentration of drug administered within the therapeutically effective range needed for medication, it is often necessary to take this type of drug delivery systems several times a day. This results in a fluctuated drug level and consequently undesirable toxicity and poor efficiency. This factor as well as other factors such as repetitive dosing and unpredictable absorption lead to the concept of controlled drug delivery systems [1, 2]. The objectives of controlled release drug delivery includes two important aspects namely spatial placement and temporal delivery of drug.Spatial placement relates to targeting a drug to a specific organ or tissue, while temporal delivery refers to controlling the rate of drug delivery to the target tissue. An approximately designed controlled release drug delivery system can be a major advance towards solving these two problems [3]. It is this reason that the science and

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technology responsible for development of controlled release pharmaceuticals have been and continue to be the focus of a great deal of attention in both industrial and academic laboratories. Controlled release systems includes any drug delivery system that "achieves slow release of the drug over an extended period of time." If the system can provide some control weather this is of a temporal or spatial nature, in other words, if the system issuccessful in maintaining predictable and reproducible kinetics in the target tissue or cell, it is considered as a controlled release system. If the system only extends the duration of release without reproducible kinetics it is considered as a prolong release system. The objectives in designing a controlled release system are to deliver the drug at a rate necessary to achieve and maintain a constant drug blood level. This rate should be analogous to that achieved by continuous intravenous infusion where a drug is provided to the patient at a rate just equal to its rate of elimination. This implies that the rate of delivery must be independent of the amount of drug remaining in the dosage form and constant over time. That is release from the dosage form should follow zero-order kinetics [4].Aim of the study is to formulate Omeprazole double walled microspheres using different polymers.

MATERIALS AND METHODS

Formulation of Double Walled Microspheres

The previously formulated microspheres were dispersed in the organic phase. The second polymer 3%HPMC Phthalate was dissolved in the same organic phase. The resulting organic phase solution was emulsified in liquid paraffin. 1% span 80 solutions were used as emulsifying agent. Above emulsion was stirred for complete evaporation of the organic solution. After complete evaporation of the organic solution the double walled microspheres were collected by vacuum filtration and washed with n-hexane. The resulted double walled microspheres were freeze dried for 24hrs (Table-1) [5, 6].

Table-1 Formulation of Microspheres

Ingredients (%)	F1	F2	F3	F4	F5	F6	F7
Omeprazole (mg)	20	20	20	20	20	20	20
HPMC	1	-	-	1.5	1.5	1.5	1.5
Ethyl cellulose	-	1	-	-	-	-	-
Guar gum	-	-	1	-	-	-	-
Carbopol	0.5	0.5	0.5	0.5	0.5	1	1
Sodium alginate	1	1	1	1	1.5	1.5	1

Stability studies

Stability of a drug has been defined as the ability of a particular formulation, in a specific container, to remain within its physical, chemical, therapeutic and toxicological specifications.The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity, light, and enables recommended storage conditions. Overall observations from different evaluation studies such as drug-polymer interactions, evaluation of prepared formulations and drug release studies were carried out. Based on the obtained results best formulation was subjected for further stability study. The stability study was conducted as per ICH guidelines for the period of six months at various accelerated temperature and humidity conditions of 25°C/60%RH, 40°C/70%RH, 60°C/80%RH.The accelerated stability study of the best formulations was carried out as per the ICH guidelines.The selected formulation was analyzed for the drug entrapment efficiency and in vitro release study at different temperatures [7-9].

RESULTS AND DISCUSSION

The low percentage yield in some formulations may be due to blocking of needle andwastage of the drug-polymer solution, adhesion ofpolymer solution tothe magnetic bead and microspheres lost during the washing process. The percentage yield was found to be in the range of79.6 to 88.5% for microspheres containing sodium alginate along with different ratios of polymers.The percentage yield of the prepared microspheres is recordedin Table-2. Percentage Drug entrapment efficiency of Omeprazole ranged from 75.3 to 88.7% for microspheres containing sodium alginate along with withdifferent ratios of polymers. The drug entrapment

efficiency of the prepared microspheres increased progressively with an increase in proportion of the respective polymers. Increase in the polymer concentration increases the viscosity of the dispersed phase. The particle size increases exponentially with viscosity. The higher viscosity of the polymer solution at the highest polymer concentration would be expected to decrease the diffusion of the drug into the external phase which would result in higher entrapment efficiency. The % drug entrapment efficiency of the prepared microspheres is displayed in Table -2.

Table-2Percentage yield and percentage drug entrapment efficiency of the prepared microspheres

S.No.	Formulation code	% yield	%Drug entrapment efficiency
1	**F1**	82.0	77.5
2	**F2**	85.1	75.1
3	**F3**	86.0	85.4
4	**F4**	88.5	85.3
5	**F5**	79.6	87.1
6	**F6**	85.0	88.7
7	**F7**	84.2	87.2

The mean size increased with increasing polymer concentration which is due to a significant increase in the viscosity, thus leading to an increased droplet size and finally a higher microspheres size. Microspheres containing sodium alginate along with carbopoland HPMChad a least size range of 611µm.The particle size data is displayed in Figure-1.The effect of drug to polymer ratio on particle size is displayed in Figure-1. The particle size as well as % drug entrapment efficiency of the microspheres increased with increase in the polymer concentration.

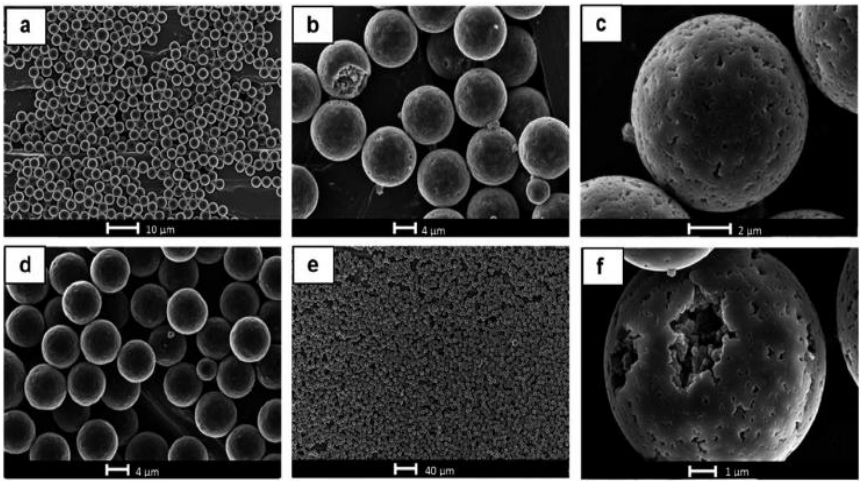

Fig-1 Double walled microspheres of Omeprazole

Dissolution studies of all the formulations were carriedout using dissolutionapparatusUSPtype I. The dissolution studies were conducted by using dissolution media,0.1 N HCl for 2hrs and 6.8 pH phosphate buffer for next hours.The results of the in-vitro dissolution studiesof formulations F1 –F7**,** shown in table no.-- The plots ofCumulativepercentage drug releaseVsTime.Figure -- shows the comparison of %CDR forformulationsF1 –F7.TheformulationsF1,F2showed a maximum release of98.76, 92.35 % at 8 hours, respectively, While F3 and F4 showed a maximum release of 95.61,99.24% at 10hrs respectively.The formulationsF5showed a maximum release of95.53% at 10 hours ,F6 andF7 showed 97.82and 95.46 % at 12 hours respectively.Among all formulations F6 shows Maximum drug release in 12hrs when compared with other formulations (Table-3).

This shows that more sustained release was observed withthe increase in percentage ofpolymers.As the polymer to drug ratio was increased the extent of drug releasedecreased.A significant decrease in the rate and extent of drug release is attributed to the increase in density of polymer matrix that results in increased diffusion pathlength which the drug molecules have to traverse. Additionally, the larger particlesizeathigher polymerconcentration also restricted the total surface area resulting inslower release.

Table -3In-Vitro drug release data of Omeprazolemicrospheres

TIME (hrs)	Cumulative Percent Of Drug Released						
	F1	F2	F3	F4	F5	F6	F7
0	0	0	0	0	0	0	0
1	5.08	2.60	1.82	1.78	4.70	5.61	8.20
2	9.70	8.01	12.62	11.07	15.62	12.07	12.60
3	22.68	24.80	20.96	28.86	22.40	22.46	20.34
4	44.25	40.68	38.84	45.42	36.16	37.01	28.00
5	51.36	47.13	50.80	56.62	43.80	46.90	34.31
6	72.74	53.69	62.26	67.71	50.91	60.22	45.52
7	86.47	76.81	72.18	72.92	65.40	74.07	55.61
8	98.76	92.35	80.11	86.54	71.82	85.09	70.11
10	--	--	95.61	99.24	95.53	94.58	85.98
12	--	--	--	--	--	97.82	95.46

CONCLUSION

Inthepresent work, double walled microspheres of Omeprazole using Sodium alginate,HPMC K100,Guar gum, Ethyl celluloseascopolymers and along with Carbopol wereformulated to deliver Omeprazole via oral route.Details regarding thepreparation and evaluation ofthe formulations have beendiscussedinthe previous chapter. From the study following conclusions couldbedrawn:-The results of this investigation indicate that Ion gelation method canbesuccessfullyemployedtofabricateOmeprazole microspheres. FT-IR spectraof the physical mixture revealed thatthedrug is compatible with the polymers and copolymer used. Microspheres containing sodium alginate along with carbopol and Guar gum in 1:1.5 ratio had a least size range of 611µm.Increase in thepolymerconcentrationledto increase in% Yield,%Drugentrapment efficiency, Particle size. The *invitro* drug releasedecreased with increase in thepolymer and copolymerconcentration.Among all formulations F4shows Maximum drug release in 10 th hr when compared with other formulations.Analysis ofdrug release mechanism showedthatthedrug release fromthe formulations followed the Non fickian diffusion mechanism and follows zero order kinectics.Based on the results of evaluation tests form ulation codedF4 was concluded as best formulation.

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