INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH AND NOVEL SCIENCES

IJPRNS

FORMULATION AND EVALUATION OF POSACONAZOLE FLOATING MICROSPHERES DOUBLE WALLED ANTIFUNGAL USING DIFFERENT POLYMERS

N. Sony Priyanka*, A.Satya Sri, B.Satyavathi, N.Vennela, V.Bhanu Prasad, K.Nageswari, S.Akhil

Department of Pharmaceutics, JITS College of Pharmacy, Kalgampudi, Andhra Pradesh, India.

ABSTRACT

The present study has been a satisfactory attempt to formulate a floating Microspheres double walled antifungal of Posaconazole with a view to control the release of the drug. From the experimental results it can be concluded that, FT-IRstudyshowsnosignificantshiftingofthepeakstherefore itconfirms the short term stability of the drug in the microspheres. Biocompatible polymers like can be HPMC, Ethyl cellulose and Eudragitused to formulate a floating Microspheres .Good percentage drug entrapment and practical yields were obtained with the polymers. Theflowpropertiesofallformulationswerewithintheacceptablerangeand therefore they could be easily filled into capsules. The floating microspheres of drug with HPMC and Ethyl cellulose were buoyant while those with Eudragit S 100 showed greater buoyancy. Cumulativepercentagedrugreleasesignificantlydecreasedwithincreasein polymer concentration. Formulated microspheres were stable and compatible at the room and accelerated temperature and humidity in storage for 90days. Thus, the formulated floating microspheres seem to be a potential candidate as an oral gastroprotective controlled drug delivery system in prolonging the drug retention stomach and increasing the bioavailability of drug. .Formulated microspheres were stable and compatible at the room and accelerated temperature and humidity in storage for 90days. Thus, the formulated floating microspheres seem to be a potential candidate as an oral gastroprotective controlled drug delivery system in prolonging the drug retention stomach and increasing the bioavailability of drug.

Key Words: Posaconazole, floating microspheres

Author for correspondence
N. Sony Priyanka,
Department of Pharmaceutics,
JITS College of Pharmacy, Kalgampudi,
Andhra Pradesh, India.
Email id: leelasiddardha @gmail.com

INTRODUCTION

Oral controlled release drug delivery is a drug delivery system that provides the continuous oral delivery of drugs at predictable and reproducible kinetics for a predetermined period throughout the course of GI transit and also the system that target the delivery of a drug to a specific region within the GI tract for either local or systemic action. All the pharmaceutical products formulated for systemic delivery via the oral route of administration, irrespective of the mode of delivery (immediate, sustained, or controlled release) and the design of dosage form (solid dispersion or liquid), must be developed within the intrinsic characteristics of GI physiology. Therefore, the scientific framework required for the successful development of oral drug delivery systems consists of basic understanding of (i)

Physicochemical, pharmacokinetic and pharmacodynamic characteristics of the drug (ii) the anatomic and physiologic characteristics of the gastrointestinal tract and (iii) physicochemical characteristics and the drug delivery mode of the dosage form to be designed. One of the most feasible approaches for achieving a prolonged and predictabledrug delivery profiles in gastrointestinal tract is to control the gastric residence time (GRT) using gastro retentive dosage forms (GRDFs*)* that offer a new and better option for drug delivery[3].Dosage forms that can be retained in stomach are called **gastro retentive drug delivery systems** (**GRDDS).** GRDDS can improve the controlled delivery of drugs that have an absorption window by continuously releasing the drug for a prolonged period ensuring its optimal bioavailability.During the last decade many studies have been performed concerning the sustained release dosage form of drugs, which have aimed at the prolongation of gastric emptying time (GET). The GET has been reported to be from 2 to 6 hrs in humans in the fed state. Controlled release drug delivery systems that can be retained in stomach for a long time are important for drugs that are degraded in intestine or for drugs like antacids or certain enzymes that should act locally in the stomach. If the drugs are poorly soluble in intestine due to alkaline pH, gastric retention may increase solubility before they are emptied, resulting in improved gastrointestinal absorption of drugs with narrow absorption window as well as for controlling release of drugs having site-specific absorption limitation [1-4].

The aim of the study is to formulate and evaluate Posaconazolefloatingmicrospheres double walled antifungal using different polymers i.e., Xanthan gum and Guar gum in different ratios.

MATERIALS AND METHODS

Drug-Excipients Compatibility study

Posaconazole was mixed with all excipients, used in the formulation in different ratios and subjected to Physical observation/FTIR.

Drug-Excipient Compatibility study (FTIR)

The IR absorption spectra of the pure drug and with different excipients were taken in the range of 4000-400 cm^{-1} using KBr disc method, 1-2 mg of the substance to be examined was triturated with 300-400 mg, specified quantity, of finely powered and dried potassium bromide .These quantities are usually sufficient to give a disc of 10-15mm diameter and pellet of suitable intensity by a hydraulic press [5, 6].

Preparation Of Microspheres double walled antifungal OfPosaconazole

Microsphereswerepreparedbythesolventevaporationmethod. Variousconcentrationofpolymerinsuitable solventsweremixedwellwiththe PosaconazolewithdifferentratiosofpolymerasshowninTableandthispasty,mass was introduced into50mlofaqueoussalinephasecontaining0.04%(20mg)polyvinylalcohol (PVA)and10%(5ml)ethanol.Thesystemisstirredusingpropellerat300rpmat roomtemperaturefor2-3hr.Thedrugloadedfloatingmicrospheresformedwere filtered, washed and dried in a hot air oven at 60˚C[52]

Formulationdesign

Table-1 Formulation of Posaconazole Floating Microspheres

Ingredients(mg/Dose)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Posaconazole	50	50	50	50	50	50	50	50	50
HPMC	50	100	150	-	-	-	-	-	-
Eudragit S100	-	-	-	50	100	150	-	-	-
Ethyl cellulose	-	-	-	-	-	-	50	100	150

$NaHCO_3$	50	100	150	50	100	150	50	100	150
Water (ml)	q.s	q.s	q.s	-	-	-	-	-	-
Dichloromethane:Ethanol (2:1) (ml)	-	-	-	q.s	q.s	q.s	-	-	-
Ethanol (ml)	-	-	-	-	-	-	q.s	q.s	q.s

q.s – Quantity sufficient

Evaluation of Microspheres

Scanning electron microscopy (SEM)

The morphology of the microspheres was studied using scanning electron microscopy (SEM).The samples for SEM were prepared by lightly sprinkling on a double adhesive tape stuck to an aluminum stub. The stubs were then coated with gold film under reduced pressure. The stub containing the coated samples was placed in the scanning electron microscope (Hitachi S3400N) chamber. The samples were then randomly scanned, and photomicrographs were taken at the acceleration voltage of 5 kV. Microphotographs were taken on different magnification and higher magnification was used for surface morphology.

Drug content

20 microspheress of each formulation were weighed and powdered. The quantity of powder equivalent to 100 mg of Posaconazolewas transferred in to a 100 ml volumetric flask and the volume adjusted to 100ml with 0.1N HCl. Further 1ml of the above solution was diluted to 100 ml with 0.1NHCl and the absorbance of the resulting solution was observed at 221 nm [7].

*In-vitro*ReleaseStudy

The drug release study was performed for microsphere containing nquantity equivalent to Posaconazole dose by using USP dissolution apparatus TypeIin 900ml of 0.1NHCl dissolution media(pH-1.2)at100rpmand37^0Ctemperature.10mlof sample was with drawn at predetermined time interval for 12hours and same volume of fresh medium was replaced to maintained sink condition.Withdrawn samples were as sayed spectrophotometrically at 272nm.Drug release was also performed for pure drug.The cumulative % drug release was calculated using standard calibration curve [8].

RESULTS AND DISCUSSION

All the formulations were evaluated for bulk density, tapped density, % compressibility, hausner's ratio and angle of repose. The results of % compressibility, hausner's ratio and angle of repose were found to be <16, <1.25 and <30 respectively. These results show that the formulations have very good flow properties (Table-2).

Table-2 EvaluationandCharacterisation of Microspheres

Mean particle size was determined by optical microscopy and the average particle size was calculated .The results were shown in fig-1.

Formulation code	Bulk density (g/cc)	Tapped density (g/cc)	Carr's Index	Hausner Ratio	Angle of repose(θ)
F1	0.46±0.045	0.53 ± 0.09	15.60±0.2	1.15±0.02	28.06± 0.31
F2	0.44±0.041	0.52 ± 0.11	15.48±0.54	1.18±0.12	28.52± 0.15
F3	0.44±0.044	0.50 ± 0.09	12.58±0.8	1.13±0.08	28.44± 0.13
F4	0.45±0.045	0.52 ± 0.04	15.19±0.1	1.15±0.06	28.36± 0.13
F5	0.45±0.041	0.52± 0.10	15.60±0.21	1.15±0.04	28.06± 0.19
F6	0.45±0.045	0.51 ± 0.04	13.48±0.8	1.13±0.09	29.32± 0.41
F7	0.50±0.045	0.57 ± 0.04	14.48±0.8	1.15±0.09	29.67± 0.19
F8	0.44±0.044	0.52 ± 0.01	15.48±0.6	1.18±0.08	28.52± 0.19
F9	0.45±0.045	0.50± 0.07	12.23±0.6	1.11±0.04	27.57± 0.15

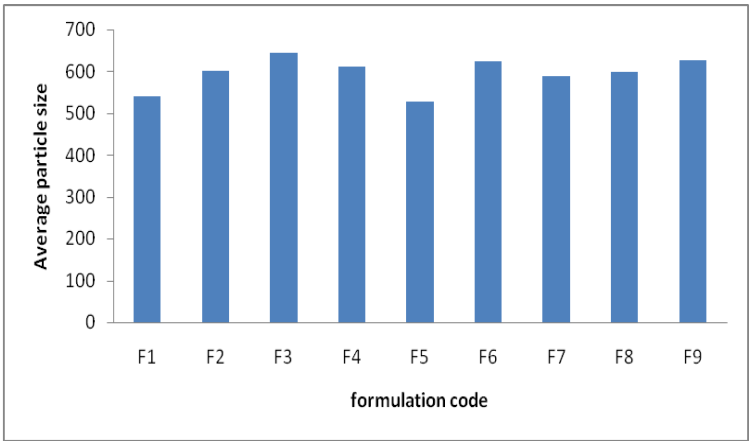

Fig-1 Average particle size of microspheres from formulations F1 to F9

Dissolution studies of all the formulations were carriedout using dissolutionapparatusUSPtype I. The dissolution studies were conducted by using dissolution media, pH 1.2.The results of the in-vitro dissolution studiesof formulations F_1 to F_9 are shown in table no.25The plots ofCumulativepercentage drug releaseVsTime.Figure-2, 3, 4 shows the comparison of %CDR forformulations$F_1$to F_3,figure for formulations F4toF6 and figure forformulations F7toF9.

ISSN: 2395-0536 **Impact Factor- 3.50***

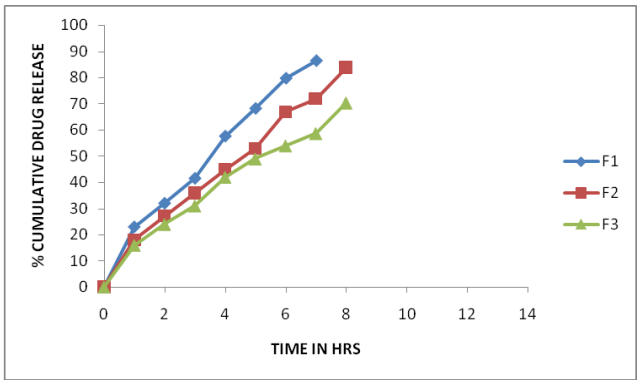

Fig-2Dissolution graph for formulation F1-F3

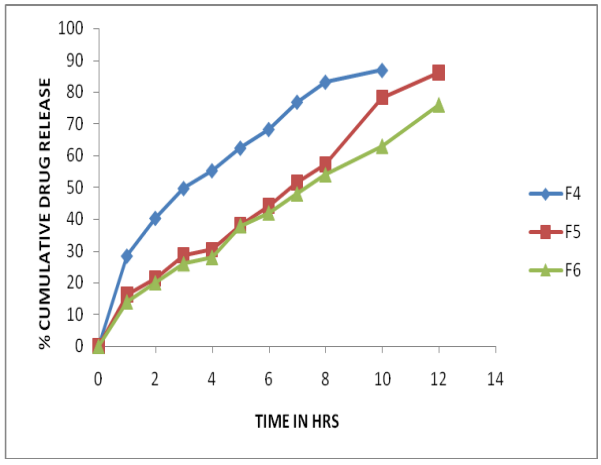

Fig-3Dissolution graph for formulation F4 –F6

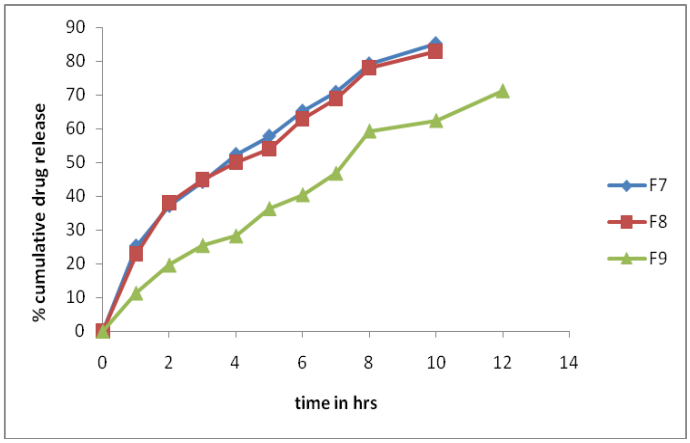

Fig-4Dissolution graph for formulation F7 –F9)

Thegoalofanydrugdeliverysystemistoprovideatherapeuticamountof drugto the proper site in the body and to achieve and maintain the desired plasma concentrationofthedrugforaparticularperiod.However,incompletereleaseofthedrug,shorterresidencetimesofdosagefor msintheupperGITleadstolower oralbioavailability.Suchlimitationsoftheconventionaldosageformshavepaved way to an era of controlled and novel drug delivery systems. Posaconazole Is A Triazole Antifungal Drug That Is Used To Treat Invasive Infections By Candida Species And Aspergillus Species In Severely Immunocompromised Patients AfloatingdrugdeliverysystemwasplannedforAlso for the treatment of oropharyngeal candidiasis Therefore,in the

present study an attempt has been made to formulate Posaconazole floating microspheres which can be expected to prolong the gastric residence time of active compounds and reduce the variability of transit. They can increase the bio availability of drugs that are mainly absorbed in the upper gastro intestinal tract.For that purpose,drugreleasemustbecontrolled.Itwouldbefasterandmoreeconomicaltoalterbeneficiallythe properties of the existing drugs than developing new drug entities. For the formulation,three biocompatible polymers HPMC, Ethyl cellulose and Eudragit were chosen in varying proportions with the drug.Solvent evaporation method was used to prepare microspheres employing different solvent to dissolve the drug and the polymer. The prepared formulations were characterized for their percentage yield, micromeritic properties,morphology,buoyancystudies,drug entrapment, drugreleasestudies. Percentage Drug entrapment efficiency of F1 to F3 ranges from 78.70 to 79.65% for microspheres containing HPMC as polymer, formulations F4 to F6 ranges from 72.25 to 83.5% for microspheres containing Eudragit S 100 as polymer and formulations F7 to F9 ranges from 75 to 83% for microspheres are containing Ethyl cellulose as polymer.Almost all the formulations showed acceptable values for all the parameters evaluated.The average particle size of floating microspheres was in the range of 527 µm- 644 µm and improved drug entrapment efficiency could be depending upon the type and ratio of polymer used. The particle size increased significantly as the amount of polymer increased. The formulations showed good flow properties, suggesting that, in future they could be easily and successfully packed and developed into a capsule dosage form. Among all formulations F5 formulation with drug: polymer (1:2) was found to be satisfactory in terms of excellent micromeritic properties, percent yield(87%), drug entrapment efficiency (82%) , percent buoyancy (76%), and highest invitro drug release of 86.7% in sustained manner over a extended period of time for 12 hrs.Thus, the prepared microspheres proved to be a potential candidate as a micro particulate controlled release drug delivery device in this era of patenting novel and controlled release formulations.

CONCLUSION

The present study has been a satisfactory attempt to formulate a floating Microspheres of Posaconazole with a view to control the release of the drug.From the experimental result sit can be concluded that, FT-IRstudyshowsnosignificantshiftingofthepeakstherefore itconfirms the short-term stability of the drug in the microspheres. Biocompatible polymers like can be HPMC, Ethyl cellulose and Eudragitused to formulate a floating Microspheres .Goodpercentage drug entrapment and practical yields wereobtained with the polymers.

Theflowpropertiesofallformulationswerewithintheacceptablerangeand therefore they could be easily filled into capsules.The floating microspheres ofdrugwith HPMC and Ethyl cellulose werebuoyantwhile those with Eudragit S 100 showed greater buoyancy. Cumulativepercentagedrugreleasesignificantlydecreasedwithincreasein polymer concentration. Formulatedmicrospherewerestableandcompatible at the room and accelerated temperature and humidity in storage for 90days. Thus, the formulated floating microspheres seem to be a potential candidate as an oral gastroprotective controlled drug delivery system in prolonging the drug retention stomach and increasing the bioavailability of drug. .Formulated microspheres were stable and compatible at the room and accelerated temperature and humidity in storage for 90days. Thus, the formulated floating microspheres seem to be a potential candidate as an oral gastroprotective controlled drug delivery system in prolonging the drug retention stomach and increasing the bioavailability of drug.

REFERENCES

1. Trotta M, Gasco MR, Morel S. Release of drugs from oil-water microemulsions. J Control Release 1989;10:237-43.
2. C. Narendra, M. S. Srinath and G. Babu, Optimization of bilayer floating tablet containing metoprolol tartrate as a model drug for gastric retention,AAPSPharmSciTech. 7 (2006) 23-29; DOI: 10.1208/pt070234.
3. H. Ravishankar, P. Patil, A. Samel, H-U. Petereit, R. Lizio and J. Iyer-Chavan, Modulated release metoprolol succinate formulation based on ionic interactions: in-vivo proof of concept, J. Control. Rel. 111 (2006) 65-72.

4. United States Pharmacopoeia 30, National Formulary 25, USP Convention, Rockville 2007, p. 2648. USP 26 / NF 21 2003, Asian edition, 1220-1221.
5. Hamid AM, Harris MS, Jaweria T, and Rabia IY. Oncedaily tablet formulation and in vitro release evaluation of cefpodoxime using hydroxypropyl methylcellulose: a technical note. AAPS PharmSciTech. 2006; 7: Article 78
6. Atsuko F, Ryuta F, Yorinobu Y, and HisakazuS.Analysis of the release process of phenylpropanolamine hydrochloride from ethyl cellulose matrix granules iv.
7. Evaluation of the controlled release properties for in vivo and in vitro release systems. Chem. Pharm. Bull. 2007;55: 1569—1573.
8. Narendra C, Srinath M, Ganesh B, Optimization of bilayer floating tablets containing Metoprolol tartrate as a model drug for gastric retention, AAPS Pharm Sci.Tech 2006; 7;E1-E7.