Journal of Pharmacreations

PharmaCreations

Pharmacreations | Vol.4 | Issue 2 | April- June- 2017

Journal Home page: www.pharmacreations.com

Research article ***Open Access***

Design, development and evaluation of microspheres loaded with Metoprolol Succinate

Kotra CSR, Ch. Mounika, Jameel, Nikhat Fathima, M. Sruthi, T. Shiva Priya.

Vision Institute of Pharmaceutical Science and Education, Boduppal, Hyderabad.

***Corresponding Author**: **Kotra CSR**

Email id: kcsrangaiah@gmail.com

ABSTRACT

The present work was designed to formulate Metoprolol Succinate microspheres by using ethyl cellulose polymer by solvent evaporation method and by using sodium alginate by ion gelation method and comaprision was made and evaluated that solvent evaporation method proves to be best method than ion gelation method. Preformulation studies were done for bulk drugs. The Metoprolol Succinate microspheres were formulated and evaluated. The formulation F3 has the highest entrapment efficiency. The drug loading was found to decrease with increase in the amount of polymer related to drug. The particle size of a microsphere was determined by optical microscopy and all the batches of microspheres show uniform size distribution. The particle size was found to be in the range of 39.72 to 57.26 µm. The prepared microspheres had good spherical geometry with smooth surface as evidenced by the scanning electron microscopy. The invitro dissolution studies that the Metoprolol Succinate microspheres formulation F3 showed better controlled release over a period of 12hrs than the other formulations.It was concluded that as the polymer concentration increases, density of polymer increases that results in increased diffusion path length, which the drug molecules have to traverse so, the drug release of F_3 formulation takes long time than other formulations. For all the formulations dissolution profile graph and percentage of drug release Vs time was plotted. From all the parameters mentioned above were taken, including surface characteristics of the formulation, drug polymer ratio and time F3 Shows the reliable results.

INTRODUCTION

In contrast to drug delivery system, the word novel is searching something out of necessity. The drug has to be delivered for a prolonged period of time and many medicines have to be taken simultaneously in case of chronic patients. Frequent administration of drug is necessary when those have shorter half-life and all these leads to decrease in patient compliance [1]. In order to overcome the above problems, various types of controlled release dosage forms are formulated and altered, so that patient compliance increase through prolonged effect , adverse effect decreases by lowering peak plasma concentration [2].

The controlled release dosage form maintaining relatively constant drug level in the plasma by releasing the drug at a predetermined rate for an extended period of time. One such in Microspheres as carriers of drug become an approach of controlled release dosage form in novel drug delivery system [2].

Microspheres are defined as “Monolithic sphere or therapeutic agent distributed throughout the matrix either as a molecular dispersion of particles” (or) can

be defined as structure made up of continuous phase of one or more miscible polymers in which drug particles are dispersed at the molecular or macroscopic level [4].

It has a particle size of (1-1000nm) [3]. Further, currently available slow release oral dosage forms, such as enteric coated/ double-layer tablets which release the drug for 12-24 hours still result in inefficient systemic delivery of the drug and potential gastrointestinal irritation. Microencapsulation for oral use has been employed to sustain the drug release, and to reduce or eliminate gastrointestinal tract irritation. In addition, multi particulate delivery systems spread out more uniformly in the gastrointestinal tract [9-12]. This results in more reproducible drug absorption and reduces local irritation when compared to single-unit dosage forms such as no disintegrating, polymeric matrix tablets. Unwanted intestinal retention of the polymeric material, which may occur with matrix tablets on chronic dosing, can also be avoided [5-8].

EXPERIMENTAL WORK

Preformulation studies

Organoleptic properties

The Organoleptic character of the drug like color, odor and appearance play an important role in the identification of the sample and hence they should be recorded in a descriptive terminology.

Solubility studies

Very soluble in water, freely soluble in alcohol, chloroform and acetone.

Melting point

Melting point of Metoprolol Succinate was determined by melting point apparatus.

Drug & excipient compatibility study

The Fourier transform infra-red analysis was conducted for the analysis of drug and polymer interactions. FTIR spectra of the drug, ethyl cellulose, polyvinyl alcohol and formulated microspheres were recorded using Shimadzu FTIR spectrophotometer. The samples were prepared as KBr (potassium bromide) disks compressed under a pressure of 10 Ton/nm^2. The wave number selected ranged between 4000 - 400 cm^{-1}.

ANALYTICAL METHODS

Determination of λ_{max} of Metoprolol Succinate in 0.1N Hcl

Metoprolol Succinate was dissolved in water and the λ_{max} was obtained at 275 nm against the blank primary stock solution concentration of Metoprolol Succinate 1000 µg/ml was prepared. All measurements were made at room temperature.

Standard Stock solution

100 mg of Metoprolol Succinate was dissolved in 100 ml water to give a concentration of (1000 µg/ml)

Scanning

From the stock solution 10µg/ml was prepared in water and UV scan was taken between 200 to 400 nm. The absorption maximum was found to be 275 nm and was used for the further analytical studies.

Calibration curve of Metoprolol Succinate in 0.1N Hcl

The standard solutions were prepared by proper dilutions of the primary stock solution with absolute 0.1N Hcl to obtain working standards in the concentration range of 5-25µg/ml of pure sample of Metoprolol Succinate. The concentration of Metoprolol Succinate present in the microspheres was obtained from the calibration curve.

METHOD OF PREPARATION

Ion gelation method is based on the ability of polyelectrolytes to cross link in the presence of counter ions to form hydrogel beads also called as gelispheres. Gelispheres are spherical cross linked hydrophilic polymeric entity capable of extensive gelation and swelling in simulated biological fluids and the release of drug through it controlled by polymer relaxation. The hydrogel beads are produced by dropping a drug-loaded polymeric solution into the aqueous solution of polyvalent cations. The cations diffuses into the drug-loaded polymeric drops, forming a three dimensional lattice of ionically crosslinked moiety. Biomolecules can also be loaded into these gelispheres under mild conditions to retain their three dimensional structure.

Polyelectrolyte solution

Drug + polymer solution (water as solvent)
↓
Added drop wise under magnetic stirring by needle
↓
Counter ion solution
[2%Calcium chloride solution w/v] + [2% acetic acid]
↓
Gelispheres

In Ion gelation technique, there has been a growing interest in the use of natural polymers as drug carriers due to their biocompatibility and biodegradability. The natural or semisynthetic polymers i.e. Alginates, Gellan gum, Chitosan, Pectin and Carboxymethyl cellulose are widely use for the encapsulation of drug by this technique Natural polymers used in ion gelation method. These natural polyelectrolytes contain certain anions/cations on their chemical structure, these anions/cations forms meshwork structure by combining with the counter ions and induce gelation by cross linking. In spite of having a property of coating on the drug core these natural polymers also acts as release rate retardant.

EXPERIMETAL RESULTS

Calibration curve data for Metoprolol Succinate in 0.1N Hcl

S.No	Drug	sodium alginate	Xanthum Gum	HPMC	Water	$Cacl_2$
F1	500	2%	-	-	q.s	2% w/v
F2	500	1%	1%	-	q.s	2% w/v
F3	500	1%	-	1%	q.s	2% w/v
F4	500	1%	1%	1%	q.s	2% w/v

Table1: Calibration curve data for Metoprolol Succinate in 0.1N Hcl

CONCENTRATION (µg /ml)	ABSORBANCE
0	0
5	0.16
10	0.3
15	0.454
20	0.605
25	0.739

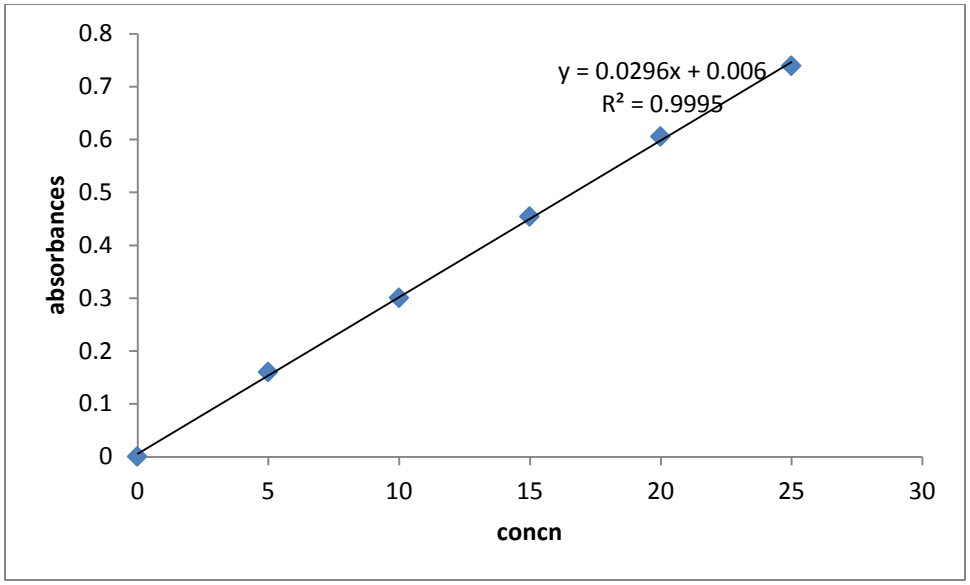

Figure1: Standard graph of Metoprolol Succinate in 0.1N Hcl

Pre formulation studies

Percentage Yield, Entrapment Efficiency, Drug Loading Of Microspheres by Solvent Evaporation Method

Table3: Percentage yield, entrapment efficiency, drug loading of microspheres

Formulations	Percentage yield (%)	Entrapment efficiency(%)±SD
Ion Gelation Method		
F_1	82.1	90.6±0.378
F_2	84.1	91.8±0.208
F_3	85.92	93.2±0.1527
F4	86.25	94.3±0.156

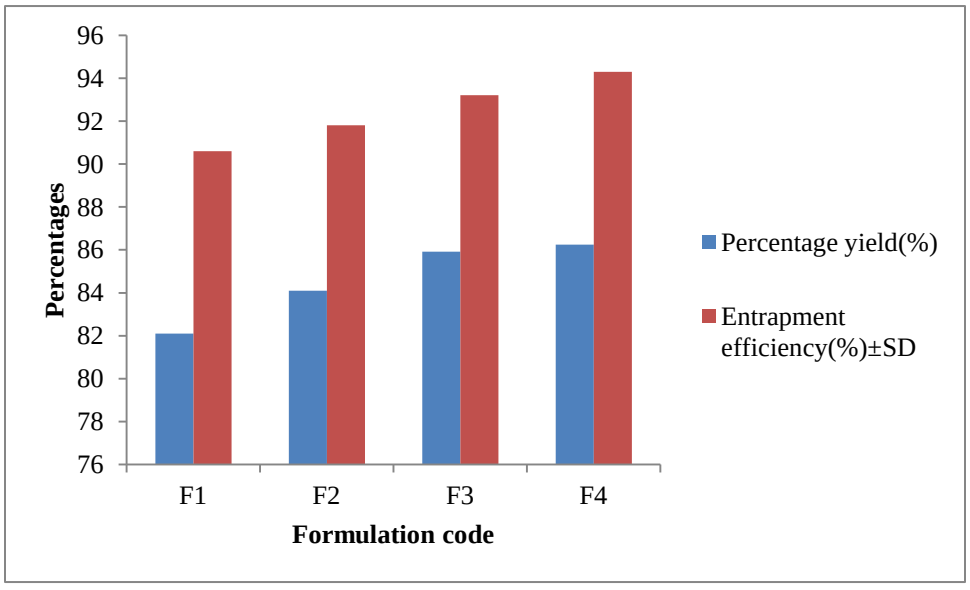

Fig1: percentage yield and percentage entrapment of microspheres (Ion gelation method)

SWELLING INDEX

Table4: Swelling index of Metoprolol Succinate microspheres.

S.No	Swelling index
F1	25
F2	27
F3	33
F4	28

The swelling index for all microspheres formulations were in the order F3>F4>F2>F1.The optimized formulation F3 showed 33 percentage of swelling index.it purely depends on the amount of polymer and nature of polymer whereas polymer concentration increases swelling index increases and percent of drug release decreases.

Mean particle size

Mean particle size was determined by optical microscopy and the average particle size was calculated. The results were shown in table7 and figure7

Table5. Mean particle size of Metoprolol Succinate microspheres

		Solvent Evaporation Method
S.No	**Batches**	**Mean Particle Size(µm)**
1	F_1	39.72
2	F_2	46.69
3	F_3	57.26
4	F4	83

Scanning Electron Microscopy

The microspheres prepared by solvent evaporation method showed a good sphericity, with smooth surface and the particles were distributed uniformly without any lumps.

Invitro release studies

The invitro release profile of Metoprolol Succinate microspheres were conducted in 0.1 N Hcl for 12 hours for ion gelation method.

Dissolution conditions

Medium : 0.1 N Hcl.
Apparatus : basket (USP Apparatus I)
RPM : 50
Temperature : 37.0 ±0.5ºC
Time : 12hrs
Volume : 900ml
Sampling times :
1hr,2hr,3hr,4hr,5hr,6hr,7hr,8hr,9hr,10hr,11hr,12hr.

Table6: Cumulative drug release of Metoprolol Succinate microspheres

Time (hrs)	% Cumulative drug release			
	F_1	**F_2**	**F_3**	**F4**
0	0	0	0	0
1	9.98	8.62	7.32	16.34
2	38.61	33.70	31.0	24.42
3	42.47	39.84	34.5	31.29
4	53.18	45.26	38.7	42.65
5	67.52	58.55	45.93	49.53
6	70.05	67.31	58.84	51.32
7	76.33	73.28	67.18	54.09

8	83.14	80.73	76.80	57.21
9	-	82.62	79.14	59.34
10	-	-	81.05	67.54
11	-	-	83.8	72.65
12	-	-	94.9	76.34

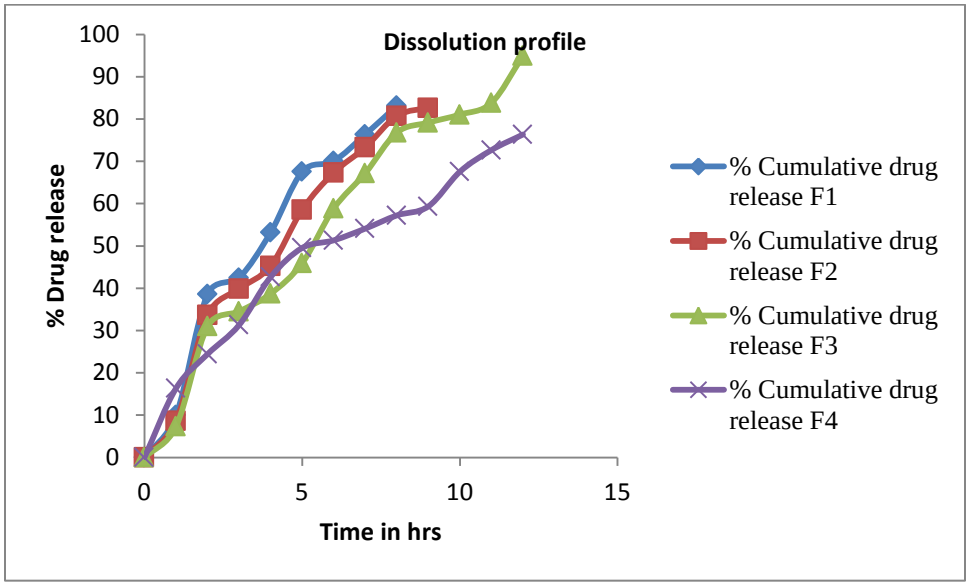

Fig2: Cumulative drug release of Metoprolol Succinate.

REFERENCES

[1]. Yie W. Chien, "Concepts and System Design for Rate-controlled Drug Delivery", Chapter 1 in Novel Drug Delivery System', 2nd Edition, Marcel Dekker, Inc, New York, 1992, l-42.

[2]. Yie W. Chien, 'Rate-controlled Drug Delivery Systems'. Ind. J. Pharm. Sci., 1988, 63-65.

[3]. Thomas Wai-Yip Lee and Joseph R. Robinson, "Controlled / Release Drug-Delivery Systems", Chapter 47 in 'Remington's Pharmaceutical Sciences', Mack Publishing Company, I(20), 2000; 903-929.

[4]. D. M. Brahmankar, Sunil B. Jaiswal., Biopharmaceutics and Pharmacokinetics a Treatise, First edition, Vallabh Prakashan Pitampura, Delhi- 2001, 337-341.

[5]. Herbert A. Lieberman, Leon Lachman, and Joseph B. Schwartz Pharmaceutical dosage forms I(2), 7.

[6]. Edith M. and Mark R.K., "Microencapsulation" in 'Encyclopedia of Controlled Release', John Wiley and Sons, Inc. London, 1998, 493-510.

[7]. Chowdary K.P.R. and Sri Ram Murthy A., "Microencapsulation in Pharmacy". Indian Drugs, 25(10), 1998, 389-402.

[8]. Simon Bonita, "A survey of Microencapsulation process" chapter 1 in 'Microencapsulation, Method and Industrial Application' 2nd Edition, Marcel Dekker, Inc. New York, 198, 2-5.

[9]. Manekar N.C. and Joshi, S.B., “Microencapsulation Technique". The Eastern Pharmacist, 1998, 47-49.

[10]. Patrick B. Deasy, "Microencapsulation and Related Drug Processes", Chapter 1 in 'Drugs and the Pharmaceutical Sciences', 2nd Edition, James Swarbrick, Marcel Dekker Inc, New York, 20, 1984, l-13.

[11]. Vyas and Khar, “Targeted and Controlled Drug Delivery Novel Carrier System” First Edition, C B S Publishers and Distributers, New Delhi, 2002, 419-424.

[12]. Rajesh, K.S., Khanrah, A. and Biswanath Sa, "Release of Ketoprofen from Alginate Microparticles Containing Film Forming Polymer". J. Sci. Ind. Res., 62(10), 2003, 987.