CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://doi.org/10.5281/zenodo.7004318

Available online at: http://www.iajps.com *Research Article*

FLOATING MICROSPHERES ENCAPSULATING CARVEDILOL FOR EFFECTIVE MANAGEMENT OF HYPERTENSION

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Article Received: July 2022 **Accepted:** July 2022 **Published:** August 2022

Abstract:

The objective of the present study was to formulate and evaluate floating microspheres of carvedilol. Carvedilol has a terminal half-life of 7-10 hr, but most of the drug is eliminated with a half-life of about 2hr.Besidesbeingabeneficialdrugcomparedtoother drugs of the same class, it has narrow absorption window in upper part of the gastro intestinal tract, hence a floating drug delivery system is preferred, such that the formulation will be available for a longer duration than usual for absorption. Floating microspheres were prepared by emulsion solvent diffusion method using ethanol and dichloromethane as solvents. Ethyl cellulose and Hydroxy propyl methyl cellulose, HPMC K 4 M, were used to prolong the release of the drug from microspheres. The prepared microspheres were subjected to various evaluatory studies. All the microspheres were found to have a size in the range of 20-40 µ and were nearly spherical in shape. For optimization of Formulation F1 (EudragitRS100), F2 (Acrycoat S 100) and F3 (Cellulose Acetate) was selected. The formulation F1 prepared using EudragitRS100 showed 82.5±2.76 percentage drug release AFTER 24 Hrs. as compare to other formulations.

Key words: *Carvedilol, Floating microspheres, Hypertension*

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Please cite this article in press Mahak Modi et al, ***Floating Microspheres Encapsulating Carvedilol For Effective Management Of Hypertension****., Indo Am. J. P. Sci, 2022; 09(8).*

INTRODUCTION:

The floating drug delivery system was first described by Davis (1968). Several approaches are currently used to prolong gastric retention time. These include floating drug delivery systems. FDDS are known as Hydro dynamically balanced systems or low-density system that has been made developed to increase the gastric transit time of drug [1]. Since the last three decades many drug molecules formulated as Gastroretentive Drug Delivery System (GRDDS) have been patented keeping in view its commercial success. Oral controlled release (CR) dosage forms have been extensively used to improve therapy of many important medications [2]. These microspheres are characteristically free flowing powders consisting of natural or synthetic polymers m.µand ideally having a particle size less than 200µm. Microspheres incorporating a drug dispersed or dissolved throughout particle matrix have the potential for the controlled release of drug [3]. Floating microspheres are one of the multiparticulate drug delivery systems and are prepared to obtain prolonged or controlled drug delivery, to improve bioavailability and to target drug to specific sites. Floating microspheres can also offer advantages like limiting fluctuation within therapeutic range, reducing side effects, decreasing dosing frequency, and improving patient compliance [4]. Carvedilol phosphate displays typical solubility activities in neutral or alkaline media, specifically, the solubility extended at pH 3 in the upper area of the GI tract [5, 6]. Due to its pH-dependent solubility, it is necessary to improve the absorption of the drug in the stomach to improve its absorption on that point, which makes carvedilol phosphate, a commendable candidate for GRDDS. Steady-state plasma concentration of carvedilol vary between 22-160 mg/ml [7]. The present works aims to design gastroretentive drug delivery system for floating microspheres of carvedilol as the carrier system that could give site specific and controlled drug release. The prepared microspheres were evaluated for particle size, entrapment efficiency, % yield, % drug release, % buoyancy, in vitro drug release studies and stability study.

MATERIAL AND METHODS:

Preparation of microballons of carvedilol

Microballons with an internal hollow structure were prepared by emulsion solvent evaporation method with slight modification in the method established by Kawashima et al 1992, using Eudragit RS100 or Acrycoat S100 or Cellulose acetate. Drug and polymerin the ratio of 1:5 were dissolved in 1:1 mixture of solvent system of dichloromethane (DCM) and ethanol for Eudragit RS100 and also for Acrycoat S100. This clear solution was poured slowly in a thin stream into the aqueous solution of 0.75% w/v polyvinyl alcohol (PVA). The emulsion was continuously stirred for 1 hour at speed of 500 rpm using mechanical stirrer (Remi, India), equipped with a blades propeller at 40^0C. Microballons were collected by filtration, washed distilled water and dried at room temperature for 24 hours.

Table 1: Optimized formulation on the basis of formulation and process variables

S. No.	Optimized parameter	Eudragit RS 100	Acrycoat S 100	Cellulose acetate	Final code for optimized preparation
1.	Drug polymer ratio	1:5	1:5	1:4	F1
2.	Emulsifier agent concentration	0.75% w/v	0.75% w/v	0.75% w/v	F2
3.	Stirring speed	500 rpm	500 rpm	500 rpm	F3
4.	Temperature	40°C	40°C	40°C	

Evaluation of microspheres

Drug Entrapment

The various formulations of the Floating microspheres were subjected for drug content. 10 mg of Floating microspheres from all batches were accurately weighed and crushed. The powder of microspheres were dissolved in 10 ml 0.1 N HCl and centrifuge at 1000 rpm. This supernatant solution is than filtered through whatmann filter paper No. 44. After filtration, from this solution 0.1 ml was taken out and diluted up to 10 ml with 0.1 N HCl. The percentage drug entrapment was calculated using calibration curve method.

Floating behavior

Ten milligrams of the floating microspheres were placed in 0.1 N HCl (100 mL). The mixture was stirred at 100 rpm in a magnetic stirrer. After 10 h, the layer of buoyant microsphere was pipetted and separated by filtration. Particles in the sinking

particulate layer were separated by filtration. Particles of both types were dried in desiccators until a constant weight was obtained. Both the fractions of microspheres were weighed and buoyancy was determined by the weight ratio of floating particles to the sum of floating and sinking particles.

$$\text{Percent buoyancy} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} x\ 100$$

Measurement of mean particle size

The mean size of the microspheres was determined by Photo Correlation Spectroscopy (PCS) on a submicron particle size analyzer (Malvern Instruments) at a scattering angle of 90°. A sample (0.5mg) of the microspheres suspended in 5 ml of distilled water was used for the measurement.

***In-vitro* release studies**

The *in vitro* drug release rate from Floating microspheres was carried out using the USP type II (Electro Lab.) dissolution paddle assembly. A weighed amount of floating microspheres equivalent to 100 mg drug were dispersed in 900 ml of 0.1 N HCI (pH=1.2) maintained at 37 ± 0.5°C and stirred at 55rpm. One ml sample was withdrawn at predetermined intervals and filtered and equal volume of dissolution medium was replaced in the vessel after each withdrawal to maintain sink condition. The collected samples analyzed spectrophotometrically at 316nm to determine the concentration of drug present in the dissolution medium [7, 8].

Drug release kinetic data analysis

Several kinetic models have been proposed to describe the release characteristics of a drug from matrix. The following three equations are commonly used, because of their simplicity and applicability. Equation 1, the zero-order model equation (Plotted as cumulative percentage of drug released vs time); Equation 2, Higuchi's square-root equation (Plotted as cumulative percentage of drug released vs square root of time); and Equation 3, the Korsemeyer-Peppas equation (Plotted as Log cumulative percentage of drug released vs Log time) [9-11].

RESULTS AND DISCUSSION:

Table 2: Results of Evaluation of prepared Microspheres formulations

F. Code	Particle size	Percent buoyancy	Drug entrapment efficiency	Total Floting Time
F1	192.02±7.85	91.24±3.24	68.97±1.94	More than 12 Hrs
F2	162.49±6.32	90.82±3.76	78.25±2.18	More than 12 Hrs
F3	145.42±5.36	86.13±2.49	74.17±2.06	More than 12 Hrs

Table 3: In Vitro drug release profile from Carvedilol bearing Eudragit RS 100 Microballoons in SGF (pH 1.2)

S. No.	Time (hrs)	F1	F2	F3
1.	0	0	0	0
2.	1	17.8±0.09	11.2±0.13	9.7±0.06
3.	2	25.7±0.43	17.9±0.48	12.4±0.32
4.	3	32.6±0.56	22.7±0.39	17.5±0.48
5.	4	37.6±0.92	27.5±1.28	21.8±1.31
6.	5	48.3±1.23	33.8±1.33	27.8±1.04
7.	6	59.8±1.67	45.3±1.82	34.7±1.12
8.	7	62.4±1.94	50.3±2.15	40.1±1.71
9.	8	69.8±1.53	53.7±2.03	45.8±2.14
10.	12	78.6±2.05	60.8±1.91	49.4±2.07
11.	24	82.5±2.76	72.7±2.63	55.3±1.46

CONCLUSION:

Carvedilol is rapidly and extensively absorbed following oral Administration; it rapidly absorbed and undergoes extensive first pass metabolism in the liver. Less than 2% off the dose was excreted unchanged in the urine. The most common effect of Carvedililol are dizziness, edema (fluid accumulation), decreased heart rate, diarrhea And postural Hypotension (A rapid decrease in blood pressure when going From the seated to the standing position that cause Lightheadedness and/ or fainting). Taking carvedilol with food minimizes the risk of postural taken while keeping the other parameters kept constant. For optimization of Formulation F1 (EudragitRS100), F2 (Acrycoat S 100) and F3 (Cellulose Acetate) was selected. The formulation F1 prepared using EudragitRS100 showed 82.5±2.76 percentage drug release AFTER 24 Hrs. as compare to other formulations.

REFERENCES:

1. Roy P, Shahiwala A. Multiparticulate formulation approach to pulsatile drug delivery: A current perspectives. Journal of Controlled Release. 2009; 134(2): 74-80.
2. Dehghan Mohamed HG, Khan FN. Gastroretentive Drug Delivery Systems: A Patent Perspective. International Journal of Health Research. March 2009; 2(1): 23-44.
3. Nayak AK, Maji R, Das B. Gastro retentive drug delivery systems: A review. Asian Journal of Pharmaceutical and Clinical Research. 2010; 3(1): 1-10.
4. Emeje MO, Kunle OO. Compaction characteristics of ethyl cellulose in presence of some channeling agent: technical note. AAPS Pharm SciTech. 2006; 7 (3): article58.
5. Avachat AM, Patel KB, Rokade MS, Dash RR. Formulation and characterization of an expandable gastroretentive system of carvedilol phosphate by 32 factorial design. PDA J Pharm Sci Technol 2011;65:12-9.
6. Chakraborty S, Shukla D, Jain A. Assessment of solubilization characteristics of different surfactants for carvedilol phosphate as a function of pH. J Colloid Interface Sci 2009;335:242-9.
7. Agrawal SS, Aggarwal A. Randomised, cross-over, comparative bioavailability trial of the matrix type transdermal drug delivery system of carvedilol and hydrochlorothiazide combination in healthy human volunteers: a pilot study. Contemporary Clin Trials 2010;31:272-8.