AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

FORMULATION AND EVALUATION OF MICROCAPSULES OF FUROSEMIDE

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ABSTRACT

Present research work was focused to enhance bioavailability and reduce the short half life problem of Furosemide by preparation of sustained release microcapsule. Cellulose acetate microcapsules were prepared by co-acervation phase separation technique and phase separation was induced using distilled water. Prepared microcapsules were evaluated for Particle Size Analysis, Flow properties i.e. Angle of Repose Carr's Index and Hauser's Ratio, Scanning Electron Microscopy, Coating Wall Thickness, Drug Content and Microencapsulation efficiency, Dissolution studies. All the studies were performed in triplicate and standard deviation was calculated.

Key Words: Furosemide, Microcapsules, co-acervation phase separation technique.

INTRODUCTION

Furosemide(5-(aminosulfonyl)-4-chloro-2-[(2-furanylmethyl) amino] benzoic acid) is a potent diuretic agent that induces a powerful diuresis, followed by the loss of sodium, potassium and chloride into the urine, by acting on the thick ascending limb of the loop of Henle. Its usual daily dose for adults is 20–80 mg, while for pediatric use ranges from 1 mg/kg up to a maximum of 40 mg daily. It is commonly used in the treatment of cardiac and pulmonary disorders in premature infants and neonates. The half-life of Furosemide is about 2 h and its oral bioavailability has been reported to be about 60–70%[1].

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Received 3 October 2011, Accepted 17 October 2011

Please cite this article in press as: Solanki NS *et al.*, Formulation and evaluation of Microcapsules of Furosemide . American Journal of PharmTech Research 2011.

Microcapsules are small particles that contain an active agent or core material surrounded by a coating or shell. Commercial microcapsules typically have a diameter between 3 and 800 µm and contain 10-90 wt. percent core. A wide range of core materials has been encapsulated, including adhesives, agrochemicals, live cells, active enzymes, flavors, fragrances, pharmaceuticals, and inks. Most capsule shell materials are organic polymers, but fats and waxes are also used[2].

MATERIALS AND METHOD

Furosemide was obtained as gift sample from Intas labs, Mumbai; Cellulose acetate was purchased from Intas Lab Pvt Ltd., Mumbai. All other chemicals and solvents used were of analytical grade and double distilled water was used during whole study.

Cellulose acetate microcapsules were prepared by co-acervation phase separation technique and phase separation was induced using distilled water[3].Table1 shows different formulation codes with Drug: Polymer ratios for the prepared microcapsules.

Table 1: Formulation Code

Formulation Code	Polymer(s)	Drug :Polymer
F_1	Cellulose acetate	1:2
F_2	Cellulose acetate	1:3
F_3	Cellulose acetate	1:4

Prepared microcapsules were evaluated for Particle Size Analysis[4], Flow properties[5] i.e. Angle of Repose Carr's Index and Hauser's Ratio, Coating Wall Thickness[6], Drug Content and Microencapsulation efficiency[7], Dissolution studies[8]. All the studies were performed in triplicate and standard deviation was calculated. For Dissolution Studies release of Furosemide from the microcapsules was studied in phosphate buffer pH 7.4(900ml) using an USP XXll six station Dissolution Rate Test Apparatus with a rotation paddle stirrer at 50 rpm and 37 ±1^{o}c. A Sample of microcapsule equivalent to 100mg of Furosemide was used in each test. Dissolution fluid was withdrawn at different time intervals, filtered and assayed Samples of at 237nm for Furosemide using a U.V. spectrophotometer.

RESULT AND DISCUSSION

The physical characterizations of prepared microcapsules are represented in Table 2. The amount of Furosemide released was determined at predetermined time intervals and the data were expressed graphically as: Cumulative % drug release Vs Time (Zero order release kinetics plot).

In-vitro release data were fitted to zero order kinetics (Figure 1), the kinetic parameters were calculated and fits for Zero order kinetics are presented in Table 3. The maximum drug release at the end of 12 hours was found to be 55.77 for cellulose acetate microcapsules (F1) and release

follows the order F1, > F2 >F3. It is evident from the data that as the polymer concentration increased the rate of release decreased significantly. Change in the proportion of the polymer also affected the release profile and can alter the release characteristics.

Table 2: Characterization of prepared Microcapsules

Code	Yield (% w/w)	D mean (μm)	Angle of Repose (θ)	Carr's Index (%)	Hauser's Ratio	Coating Wall Thickness (μm)	Drug Content (mg/250mg)	Encapsulation Efficiency (%)
F1	4.132±0.01	67.48±.01	19.79^0±0.02	14.02±0.01	3.08±0.01	16.13±0.03	190.22	76.09
F2	4.798±0.02	69.87±0.00	17.17^0±0.03	6.07±0.02	1.14±0.01	18.66±0.01	183.23	73.29
F3	5.926±0.12	74.89±0.01	17.92^0±0.03	7.14±0.01	1.42±0.05	20.01±0.00	199.48	79.79

Table 3: Fit to Zero order kinetics

Code	Zero order		
	Intercept	R^2	K(mg.hr^{-1})
FI	0.1696	0.9975	5.612
F2	0.4627	0.9978	5.4092
F3	0.5643	0.9980	5.3007

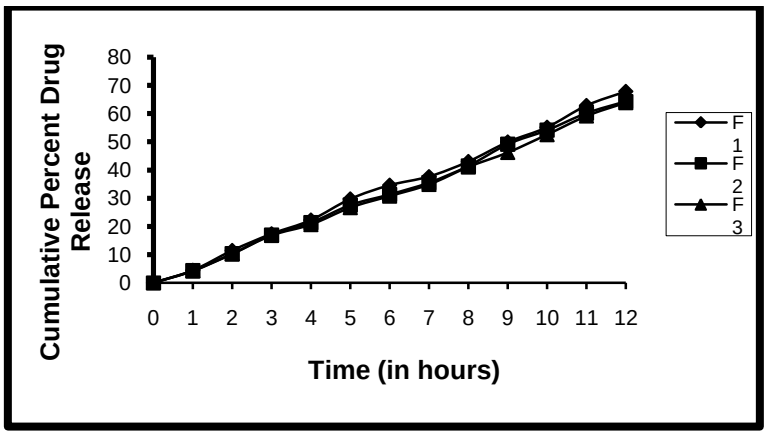

Figure 1: In-vitro Drug release plot of Microcapsules of Furosemide for formulation code F1 to F3 (Zero order kinetics)

CONCLUSION

From the above study, it can be concluded that the nature, proportion of polymer and the manufacturing process influenced the release characteristics of Furosemide from the microcapsules. Furosemide microcapsules were successfully prepared by co-acervation phase separation techniques. From this study it is possible to formulate microcapsules of Furosemide for disorders like acute pulmonary edema, chronic heart failure, cirrhosis of liver, nephritic syndrome and renal failure with more effectiveness and better patient compliance. The prepared

microcapsules exhibited satisfactory physio-chemical properties and were found to be dependent on the nature of the polymer. Prepared microcapsules exhibited zero order kinetics and the permeation profile was matrix diffusion type. Further in-vivo investigations are required to correlate in-vitro data.

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