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FORMULATION AND EVALUATION OF MICROSPHERES OF CFFDINIR

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ABSTRACT

Microspheres are sub-micron size polymeric drug carrier systems in which the therapeutic agents are loaded micrometer. These particles consist of core material, which is the drug, and a coating material. Microspheres are considered as a very promising controlled and targeted drug delivery system. The formulation and clinical application of microspheres is based on the physicochemical pharmacokinetic and pharmacological properties of drugs. Cefdinir is a beta-lactam antibiotic and is mainly bactericidal. Cefdinir inhibits the third and final stage of bacterial cell wall synthesis by preferentially binding to specific penicillin binding proteins; those are located inside the bacterial cell wall. Cefdinir is the third generation anti-biotic used for the treatment of community -acquired pneumonia, acute bacterial otitis media and uncompleted skin and skin structure infections in adult and pediatric patient. Incorporation of Cefdinir in polymeric microspheres can successfully increase the biological half-life and reduce the therapeutic dose of their drug, thereby minimizing the adverse drug reaction. Cefdinir microspheres were formulated by emulsion solvent evaporation method using ethyl cellulose polymer. All the above studies reveal that the microsphere can serve as an ideal drug delivery system for Cefdinir. Further studies can be done on the stability of cefdinir-loaded microspheres and the improvement in therapeutic efficacy due to the targeting effect on to the specific receptor sites.

Key words: Microspheres, Cefdinir, Antibiotic, Ethyl Cellulose and chloroform.

INTRODUCTION

Microspheres are submicron size polymeric drug carrier systems in which the therapeutic agents are loaded inside the polymeric matrix or encapsulated or physically absorbed or chemically coupled on to the surface. The size range of these colloidal particles is from 1-1000 micro meter .These particles consist of core material ,which is the drug and a coating material [1].The coat material can be of various types ranging from natural polymers such as albumin, gelatin [2], chitosan [3] and synthetic such as poly(vinyl alcohol) [4], poly(lactate-co-glycolide) [5] and combination of two polymers such chitosan sodium CMC [6] and alginate –chitosan [7] etc. The microspheres are characteristically free flowing powders consist of proteins or synthetic polymers that are biodegradable in nature [8], and ideally having a particle size less than 200 micro meter .Solid biodegradable microspheres incorporating a drug dispersed or dissolved throughout particle matrix have the potential for the controlled release of drug [9]. These carriers received much attention not only for prolonged release but also for the targeting of the anti-cancer to the tumor. Microspheres are effective for delivery of both the entrapped and absorbed antigen [10]. Microspheres are applied for diseased cell sorting, diagnostics genes and genetic materials [11,12].

MATERIALS AND METHODS

Drug-Cefdinir
Polymer-CMC & Methyl Cellulose [13,14]
Solvent-Chloroform

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Asian J. Pharm. Res. Vol 3, Issue 2, 75-79, 2013.

Methods

Preparation of Reagents

Phosphate Buffer P ^{H} 7.4

Dissolve 2.38gm of disodium hydrogen phosphate, 0.19 gm of Potassium dihydrogen phosphate and 8gm of NACL in sufficient water to produce 1000 ml. Adjust the P H if necessary

Preparation of Standard Curve

Accurately 50 mg of drug was dissolved in 50 ml of phosphate buffer. A stock solution was prepared by withdrawing 10 ml of the above solution and made up to 100 ml. From the stock solution 2 ml, 4 ml, 6 ml, up to 20 ml were taken and made up to the volume in a 100 ml volumetric flask to get a concentration of 2 µgm, 4 µgm, 6µgm up to 20µgm respectively. Then the absorption was measured at 220nm using phosphate buffer pH 7.4 as blank. The absorbance of the drug at various concentrations is enlisted in table 1 and the standard plot is shown in Fig: 1.

Preparation of Microspheres

Microspheres are prepared by emulsion solvent evaporation method employing chloroform as a solvent for the polymer [11]. Ethyl cellulose polymer is dissolved in chloroform to form a homogenous solution. Core material is added to the polymer solution and mixed thoroughly. The resulting mixture is then added in a thin stream to 200 ml of an aqueous mucilage of sodium carbaoxy methyl cellulose (0.5%)contained in a beaker with constant stirring at 1000rpm to emulsify the added dispersion as fine droplets. The solvent chloroform was then removed by continuous stirring at room temperature for 3 hrs to produce spherical microspheres. The microspheres are collected by vacuum filtration and washed repeatedly with water. The produc t is then air - dried to obtain discrete microspheres [12-14].

RESULTS AND DISCUSSION

Cefdinir is the third generation anti-biotic used for the treatment of community –acquired pneumonia, acute bacterial exacerbations of chronic bronchitis, acute maxillary sinusitis, pharyngitis, tonsillitis, acute bacterial otitis media and uncompleted skin and skin structure infections in adults and pediatric patient. Incorporation of Cefdinir in polymeric microspheres can successfully increase the biological half –life and reduce the dose of their drug, their by minimizing the adverse drug reaction. Cefdinir in ethyl cellulose microspheres were prepared and its physico chemical parameters were evaluated**.**

Morphological Structure

The external appearance of the cefdinir microspheres were smooth and pure white in colour .Cefdinir were spherical, discrete in shape and covered with coating material.

Particle Size Analysis

The size distributions of the various batches of microspheres were determined by optical microscope. The average particle size of the various batches of Cefdinir micro spheres are shown in table 3. The mean size of the microspheres was increased as the proportion of coat material in the microspheres was increased.

Drug Loading Analysis

The drug content was increased with the ratio of polymer. The drug content was maximum with CEFMS-3, which indicates that the increased in the particle size also favours the drug loading capacity. The drug contents are given in table 3.

Table 1. Standard Curve of Cefdinir

Concentration micro gram/ml	Absorbance
2	**0.064**
4	**0.135**
6	**0.205**
8	**0.276**
10	**0.346**
12	**0.418**
14	**0.475**
16	**0.525**
18	**0.583**
20	**0.632**

Table 2. Formula for the Preparation of Microspheres

S No	Batch Code	Concentration Of Drug	Concentration Of Polymer	Drug Polymer ratio	Concentration of NaCMC
1	MS	-	100mg	-	0.5%
2	CEFMS1	50 mg	50 mg	1:1	0.5%
3	CEFMS2	50 mg	100mg	1:2	0.5%
4	CEFMS3	50 mg	150mg	1:3	0.5%

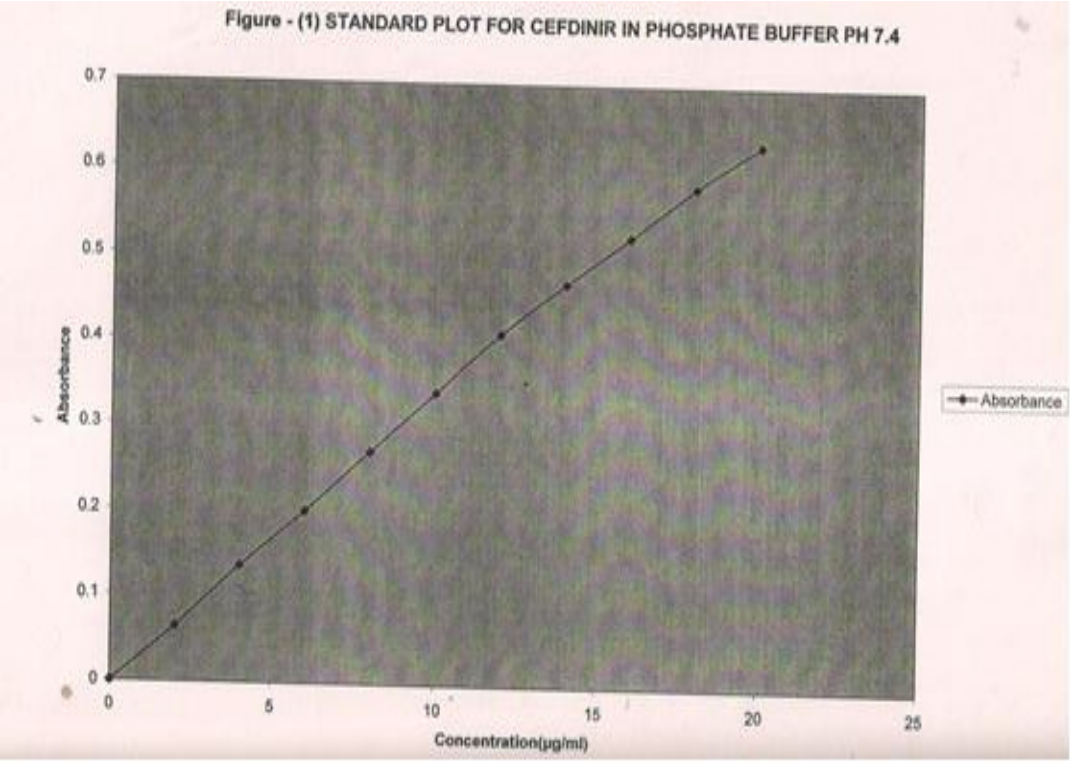
Asian J. Pharm. Res. Vol 3, Issue 2, 75-79, 2013.

Table 3. Characterization of Cefdinir Microspheres

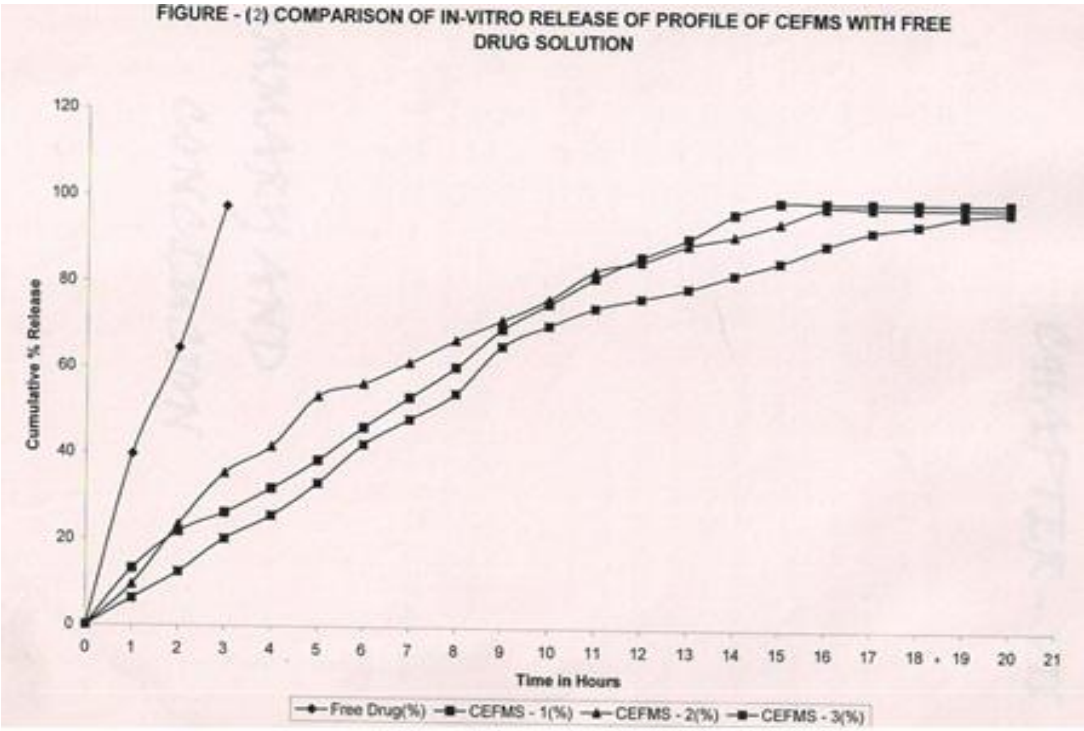
S No	Batch Code	Drug Polymer Ratio	Particle Size (µm±s.d)	Drug Content(%)
1	CEF	-	90±3.58	-
2	CEFMS1	1:1	175±3.39	45.2
3	CEFMS2	1:2	180±4.25	53.1
4	CEFMS3	1:3	395±6.2	62.8

Table 4. Invitro Release Profile of Cefdinir Microspheres

Time in hrs	Free drug (%)	CEFMS-1 (%)	CEFMS-2 (%)	CEFMS-3 (%)
1	39.6	13.2	9.5	6.3
2	64.5	21.8	23.4	12.5
3	97.5	26.2	35.4	20.2
4	-	31.9	41.4	25.6
5	-	38.5	53.4	33.2
6	-	46.2	56.4	42.2
7	-	53.2	61.4	54.5
8	-	60.4	66.8	58.5
9	-	69.4	71.5	65.4
10	-	75.5	76.5	70.3
11	-	81.5	83.2	74.5
12	-	86.4	85.4	76.8
13	-	90.7	89.2	78.2
14	-	96.5	91.4	82.6
15	-	99.3	94.5	85.4
16	-	99.3	98.2	89.4
17	-	99.3	98.2	92.7
18	-	99.3	98.2	94.3
19	-	99.3	98.2	96.5
20	-	99.3	98.2	97.3



Asian J. Pharm. Res. Vol 3, Issue 2, 75-79, 2013.



Invitro Release Studies

The *invitro* release of the Cefdinir from microspheres are enlisted in table 4 and graphically represented in figure 2.All the three batches of Cefdinir exhibited sustained release for about period of 12 hrs (CEFMS-1)to 20 hrs. All the three batches exhibited a biphasic release pattern in which about 60%(approval) of the drug was released within 5 hrs (CEFMS-1) to 10 hrs (CEFMS-3). This burst release will be quiet effective in achieving the minimum effective concentration (MEC)whereas the remaining 40% was released slowly and this may help to maintain the plasma drug concentration with in the therapeutic range .This biphasic release of the drug from the microspheres may be due to the quick release of the drug molecule adsorbed on the surface of the microspheres. The constant release of the remaining drug from inner polymeric matrix may be by the mechanism leaching.

CONCLUSION

Microspheres are one of the most promising controlled and targeted drug delivery systems. Cefdinir is a broad spectrum antibiotic having low plasma half-life. Hence, it was formulated in microspheres to improve the therapeutic efficacy thereby reducing the development of drug resistance. Cefdinir Microspheres were formulated by emulsion solvent evaporation method using ethyl cellulose polymer. All the above studies reveal that the microsphere can serve as an ideal drug delivery system for cefdinir. Further studies can be done on the stability on cefdinir loaded microspheres and the improvement in therapeutic efficacy due to the targeting effort on to the specific receptor sites.

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Asian J. Pharm. Res. Vol 3, Issue 2, 75-79, 2013.

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