Pharmacokinetic Studies on Sepia Nanoparticles Containing Ciprofloxacin for Oral Delivery

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***Abstract*—**The major objectives of the investigation are to design nanoparticles of ciprofloxacin hydrochloride by using the naturally available polymer sepia obtained from sepia officinalis. To evaluate the biopharmaceutical parameters such as Cmax, Tmax, AUC, $t_{1/2}$ etc. The sepia nanoparticles were prepared by controlled gellification process. The drug and polymer ratio were 1:1.0, 1:1.5, 1:2.0, 1:2.5, 1:30, 1:3.5,1:40. The biopharmaceutical evaluation were done by administering the nanoparticle formulations. to the healthy rabbits and withdrawing the blood samples at different intervals of time. The t1/2 was 10.43hrs, Ka was 0.0069, Ke was 0.634, T_{max} was 39.25hrs, Vd was 3.76litres, C_{max} was 8.6µ/ml and AUC was 130.5 µ-hr/ml.

***Keywords*—** Sepia Nanoparticles Containing Ciprofloxacin For Oral Delivery.

I. Introduction

A NANOPARTICLE is a particle having a size range of 1-1000 nm. The main objective of the present research work is to prepare the nanoparticles for the sustained delivery of Ciprofloxacin5.It possess less biological half–life which helps in frequent administrations when given in the form of conventional dosage forms such as tablets, capsules, etc.

Studies have been carried out on the preparation of nanoparticles with the ink of cuttlefish(sepia) 4 belonging to the marine mollusc, Sepia officinalis with an objective of designing and developing nanoparticles for oral administration for sustained release of Ciprofloxacin. For the present research work, the ink of cuttle fish, Sepia officinalis 3 was selected as a carrier material with the preparation of the said nanoparticles. The latter were prepared by controlled gellation method1. The selected nanoparticle formulation is subjected to in-vivo pharmacokinetic parameters viz. elimination rate constant, absorbtion rate constant, AUC, Cmax, Tmax and biological halflife. The halflife is about 4hrs.

II. Materials And Methods

Ciprofloxacin is procured from the Dr.Reddy's Labs, Hyderabad.Chitosan is a gift sample from the Fisheries College and Research Institute, Thoothukudi, TamilNadu, India. Sepia officinalis (cuttlefish) ink is procured from fish vendors in Thoothukudi and authenticated by Dr.R.Santhanam, Professor, Fisheries College and Research Institute, Thoothukudi, India and all the chemicals used were of the analytical grade

The In-vivo evaluation of selected formulations was carried out with a view to assess the pharmacokinetics of absorption and elimination bioavailability. Formulation batch CN3 in which, the drug Ciprofloxacin and polymer ratio was 1:2. The experimental protocol was approved by the Institution's Ethical Committee. Adult healthy rabbits (n = 4) were used for the experimental study2. All animals were kept in fasting for a period of 18hrs (over night fasting) before experimentation. The selected nanoparticle formulation of was poured in a small empty capsule and administrated orally. The dose of the nanoparticle was 10mg/kg with 100ml of water for all the 4 rabbits. Before the administration of the doses, blood samples were collected from the above experimental animals and the same served as blank. During experimentation, 1 ml of blood samples were collected from animals at the following intervals.

TABLE I
SERUM CONCENTRATION (µG/ML) OF CIPROFLOXACIN

TIME	ANIMAL 1	ANIMAL 2	ANIMAL 3	ANIMAL 4	MEAN X ± SEM
15 Min	1.90	1.7	0.9	1.6	1.5 ± 0.217
30 Min	2.25	2.12	1.5	2.0	1.9675±0.164
1 Hr	2.40	2.38	2.0	2.35	2.285±0.094
2 Hr	2.65	2.50	2.25	2.55	2.4875±0.008
4 Hr	2.77	2.65	2.30	2.70	2.6±0.104
8 Hr	3.05	2.90	2.45	2.85	2.812±0.1281
12 Hr	3.33	3.10	2.70	3.0	3.035±0.131
24 Hr	3.41	3.20	2.90	3.25	3.19±0.106
36 Hr	2.90	2.75	2.65	2.70	2.75±0.054
48 Hr	1.95	1.60	1.50	1.85	1.725±0.1051
72 Hr	0.90	0.85	0.70	0.65	0.775±0.059

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TABLE II
BIOPHARMACEUTICAL PARAMETERS OF CIPROFLOXACIN LOADED SEPIA NANOPARTICLES

S.NO	Parameters	Value
1.	Absorption Constant (Ka)	0.0069
2.	Elimination Constant (Ke)	0.634
3.	Half – Life (t ½)	10.43 hours
4.	Tmax	39.25hrs
5.	Apparent volume of distribution (Vd)	3.76 liters
6.	C Max	8.6µ/ml
7.	AUC	130.5 µ-hr/ml.

III. RESULTS AND DISCUSSION

The above research work relates to the preparation of nanoparticles and the evaluation. The Ciprofloxacin and the polymer used was sepia (cuttlefish ink) and chitosan. The above said drug possess a less biological half-life which demands for the frequent administration leading to dose dumping finally. So in this work, an oral controlled release formulation was made through the preparation of nanoparticles. The nanoparticles which are smaller in size have also been known to be a very good carrier of the drug molecules.

The carrier used in the above formulation was obtained from a marine source. The drug and polymer ratios formulated were 1:1, 1:15, 1:2, 1:2.5, 1:3, 1:3.5 and 1:4.

In the Ciprofloaxacin nanoparticles, the formulation CN3 was found to be the best as at the 24th hour, the drug release was 85%. The drug release profiles of CN3 formulation showed that it was 39.25% in 15min and 50% in 4hrs. The formulations which showed good release profiles were subjected to size analysis using Scanning Electron Microscope (SEM). The size of the nanoparticles of Ciprofloxacin was found to be 500nm. For the formulation CN3, the mean concentration of drug in blood plasma after 15min of administration was 1.5µg/ml and the peak plasma concentration obtained at 24th hr was 3.19µg/ml. After that, the elimination was found to start. A plasma drug concentration of 0.775µg/ml at the 72nd hr showed that the drug release from the nanoparticle was in a sustained manner. The t1/2 was 10.43hrs, Ka was 0.0069, Ke was 0.634, Tmax was 39.25hrs, Vd was 3.76litres, Cmax was 8.6µ/ml and AUC was 130.5 µ-hr/ml.

IV. CONCLUSION

The CN3 formulation in which the size of the particle was 500nm showed a maximum release of drug (85%) at the 24th hr. Hence, it was also considered to be a stable formulation.Regarding the In-vivo characteristics, the formulation CN3 showed good release characteristics. However, the maximum release was at 24th hr and beyond that, the drugs were found to be slowly eliminated.

The formulation CN3 is therefore considered as good oral-controlled release formulations of Ciprofloxacin.

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