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Original Artile

IN VIVO EVALUATION OF SUSTAINED RELEASE GASTRORETENTIVE CINNARIZINE LOADED SUNFLOWER OIL ENTRAPPED FLOATING BEADS

SURVE, R.[1] AND GADAD, A. P.[2]

[1]Department of Pharmaceutics, Rani Chennamma College of Pharmacy, Belgaum- 590010, Karnataka, India;
[2]Department of Pharmaceutics, KLEU's College of Pharmacy, JNMC Campus, Nehru nagar, Belgaum-590010, Karnataka, India. E-mail: rashmisurve08@gmail.com, Cell: 081478 64963

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Abstract: Motion sickness is a very common disturbance of the inner ear. It is caused by repeated motion from movements that disturb the inner ear. An immediate and sustained relief is required to overcome this condition. Hence cinnarizine beads were formulated by emulsion gelation method by using low methoxy pectin (LMP) and sodium alginate. In this study, the best formulation was subjected to in vivo pharmacokinetic study and compared with the marketed formulation. The results revealed that cinnarizine beads exhibited better area under plasma drug concentration time curve (AUC) than marketed formulation. Thus it was concluded that the sustained release formulation containing Cinnarizine was found to be efficacious and satisfactory.

Key words: Cinnarizine, Floating drug delivery system

INTRODUCTION

In order to overcome the drawbacks of conventional drug delivery systems, several technical advancements have led to the development of controlled & sustained drug delivery system that could revolutionize the method of medication and supply variety of therapeutic benefits. Sustained oral drug delivery system with prolonged gastric residence time, such as floating dosage system has been proved to be more advantageous particularly in the treatment of conditions like motion sickness, where immediate and sustained effect is required. Motion sickness or kinetosis or travel sickness is a condition in which a disagreement exists between visually perceived movement and the vestibular system's sense of movement. Cinnarizine, an antihistaminic drug is H1 antagonist having added properties as anticholinergic, anti-5-HT, sedative and vasodilator is made use in the treatment of this condition [1-6].

Mrs. Rashmi Surve, Asst. Professor, Dept of Pharmaceutics, Rani Chennamma College of Pharmacy. She is working on areas of Gastroretentive drug delivery system, and bioavailabilty enhancement of poorly soluble drugs.

Dr. Anand Panchakshari Gadad, Professor, Department of Pharmaceutics. He is working on areas of targeted drug delivery system viz., Gastror-etentive drug delivery system, Polymeric nanoparticles, enhancing solubility of poorlysoluble drugs, etc. He has published his research works in many well known journals.

Fig. 1: Plot of plasma drug concentration against time of Formulation and Marketed

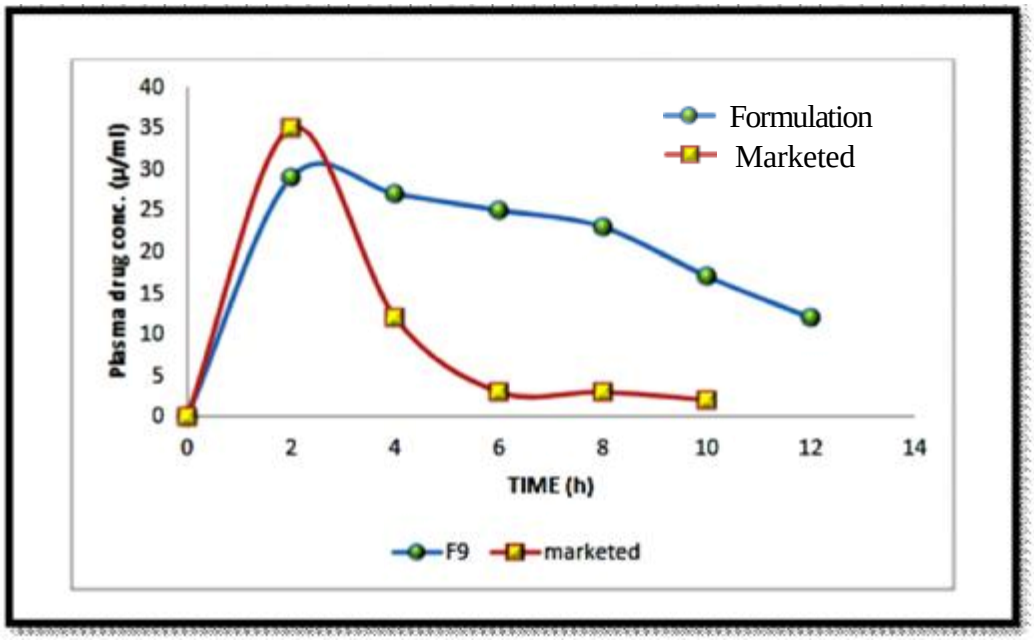

Table 1: HPLC specifications

Sl. No	Parameters	Specifications
1.	System	Perkin Elmer, Europe
2.	Pump.	Series 200
3.	Detector	UV-Visible
4.	Software	Total Chrom Workstation 6.2.1. Chromatography system Software (Perkin Elmer)
5.	Stationary phase	BDS Hypersil C18 column (150×4.6 mm, id 3µm)
6.	Mobile phase	0.01 M Ammonium dihydrogen phosphate buffer, ph 4.2, which contained 0.038 % triethylamine and acetonitrile(25:75, v/v)
7.	Flow rate	1 ml/min
8.	Injection volume	20µl
9.	Wavelength	253

Table 2: Pharmacokinetic parameters

Pharmacokinetics parametre	Bead Formulation	Marketed product
Cmax	29 µg/ml	35 µg/ml
Tmax	2h	2h
AUC	254 µg/ml/h	216 µg/ml/h

MATERIALS AND METHODS

***In vivo* pharmacokinetic study [7-9]:** Approval for *in vivo* study in rabbits was obtained prior to commencing the pharmacokinetic study by Institutional animal ethical committee, KLEU's college of pharmacy, Belagavi. Male albino rabbits (n=2) weighing 2.835 and 2.851 kg each were used for the study. The rabbits were categorized as formulation and marketed. One albino rabbit was administered with formulated Cinnarizine beads whereas the other received marketed Cinnarizine tablet (Stugeron manufactured by Johnson & Johnson Ltd.); in an equivalent dose of 0.600 mg/kg. Both the formulations were administered using a 10 ml syringe by inserting it directly to the stomach via esophagus and then immediately administering it with 20 ml water. Xylene was applied to the depilated surface of the ear to facilitate dilation of blood vessels. Aliquotes of blood samples were collected using 27 gauge needle from the marginal ear vein into heparinized tubes at time intervals of 0, 2, 4, 6, 8, 10 and 12 h. The removed blood sample was immediately centrifuged at 6000 rpm for 10 minutes to separate the plasma and stored at -20^0C until further analysis. The HPLC specifications are as mentioned in Table 1.

RESULTS AND DISCUSSION

***In vivo* pharmacokinetic study:** The *in vivo* evaluation of floating beads of Cinnarizine was conducted in 2 male rabbits. Fig 1 depicts the plot of plasma drug concentration of cinnarizine bead formulation and marketed formulation against time. The AUC was calculated by trapezoidal method. The peak plasma concentration (C_{max}) and the time to attain peak plasma concentration (T_{max}) for marketed formulation was 35µg/ml and 2 h respectively, whereas that of the bead formulation C_{max} was found to be 29 µg/ml and T_{max} as 2 h. Assessment of the AUC showed that the bioavailability of bead formulation was better than that of the marketed formulation. Thus it can be concluded that the bioavailability of Cinnarizine was found to be significantly increased by formulating it into oil entrapped gel beads. The various pharmacokinetic parameters are depicted in Table 2. Plot of plasma drug concentration against time of bead formulation and marketed formulation is depicted in Fig 1.

CONCLUSION

In the present study the formulated floating beads of Cinnarizine was compared with marketed formulation for *in vivo* drug release. Due to the retention of the formulation for longer time in stomach an enhancement in the bioavailability of the drug was observed in contrast to the marketed formulation. By this method we can thus reduce the dosing frequency and improve patient compliance.

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