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Research Article

Masking Bitter Taste of Ciprofloxacin by Microbeads Using Hydrophilic Polymer

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ABSTRACT

Taste is a valuable parameter in administering drugs orally. The problems encountered in formulation with many drugs like ciprofloxacin are the undesirable or bitter taste. The physiology and sensitivity of the taste mainly depend up on taste bud of tongue. While, formulating the oral dosage, taste is considered as an important parameter. The challenging problem for health care providers was undesirable taste. Different techniques are used in masking the taste, but in modern days the most improved and easy technique is to formulate tasteless micro beads of ciprofloxacin with varied concentrations of methyl cellulose polymer by using Ionic Orifice Gelation technique. Various techniques used not only serve as to mask the taste of drug but also to enhance the bioavailability of dosage form. The evaluation of masked ciprofloxacin microbeads was done and the results were found to be satisfactory.

Keywords: Bitter taste masking, Ciprofloxacin, Micro beads, Ionic Gelation

1. INTRODUCTION

The flavor of a substance is attributed to its taste, sight, odor and qualities such as mouth feel. Taste refers to a perception arising from the stimulation of taste buds present on the surface of the tongue. Humans can distinguish among five components of taste: sourness, saltiness, sweetness, bitterness, and umami (savory) [1, 2]. The sweet and the sour-taste receptors are concentrated on the tip and both edges of the tongue respectively; bitter taste is perceived by the receptors at the back of the tongue and umami taste receptors are located all over the tongue. Taste is an important parameter in administering drugs orally. Undesirable taste is one of the important formulation problems that are encountered with many drugs. Administration of bitter drugs orally with acceptable level of palatability is a key issue for health care providers.

Taste masked bitter drugs have been proved to be accepted for pediatric and geriatric patients. The bitterness of pharmaceutical medicines plays critical role in patient compliance, as the oral administration of bitter drugs is often hampered by their unpleasant taste which leads to non-compliance and further worseness of diseased condition [1].

The various methods for the reduction of bitterness and inhibition have improved palatability of oral pharmaceuticals [2]. By the process of micro encapsulation, very tiny droplets for particles of liquid or solid materials are surrounded or coated with a continuous film of polymeric material [3]. Ciprofloxacin is a highly bitter taste drug. So for better patient compliance and to remove other side effects related to the ciprofloxacin the taste is masked by using the ionic gelation technique.

2. MATERIAL AND METHODS

Ciprofloxacin was procured as a gift sample from scientific company, Sodium alginate, Methyl cellulose, Calcium chloride from central drug house, New Delhi and all other chemicals used were of analytical grade.

2.1. Method of Preparation

2.1.1. Preparation of Micro Beads by Orifice-Ionic Gelation Method

The alginate beads were prepared by employing the sodium alginate with hydrophilic polymer methyl cellulose which is suitable for taste masking. In this method sodium alginate and methyl cellulose in 3%, 4%, 5% and 6% solutions were prepared by dissolving the calculated quantity of the polymer in 45 ml of purified water (Table 1). The viscous solutions is also prepared separately by dissolving 250 mg of Ciprofloxacin, in 5 ml of purified water and add few drops of glacial acetic acid for preparation of clear drug solution. The prepared drug solution was added to the above polymer solution and mixed well. The resulting dispersion of drug polymer solution was added drop wise into 8 %w/v calcium chloride solution through a syringe with a needle of size 26. The added droplets were retained in the calcium chloride solution for 30 minutes to complete the curing reaction and

after completion of rigidity, the micro beads were obtained. These beads were separated and washed with n-hexane repeatedly and then dried at 40 °C for 12 hours.

Table: 1 Composition of the Micro Beads formulations

Micro bead Formulation code	% of Polymer used	Polymer blend Composition	
		Sodium Alginate (mg)	Methyl Cellulose (mg)
B1	3	750	450
B2	4	1000	600
B3	5	1250	750
B4	6	1500	900

2.2. Particle Size Analysis

The size of microbeads was measured by optical microscopy. The eye piece micrometer and stage micrometer were calibrated and the micro beads of different formulation were evaluated. The determination was done for at least 300 Microbeads.

2.3. Drug Incorporation Efficiency [5]

The drug incorporation efficiency in the beads was evaluated. The micro beads were dissolved in phosphate buffer of pH 6.8 and kept in it for 24 hours and sonicated for 1 hour. The drug extraction was done and solution was centrifuged at 1000 rpm for 10 minutes. The supernatant liquid was analyzed for ciprofloxacin content at wavelength max of 277 nm. The percentage incorporation efficiency was calculated as follows.

Percentage incorporation efficiency = Actual drug content / Theoretical drug content ×100

2.4. Scanning Electron Microscopy

SEM photograph were obtained to examine shape of surface morphology of microbeads. The microbeads were dusted onto double sided tape on a copper stub, which were coated with gold by a sputter coated and the sample was imaged.

2.5. Characteristics of Microbeads [6]

All other parameters like mean particle size, and % yield were calculated and discussed in Table-2.

2.6. Stability Studies [7]

Stability of a drug has been defined as the ability of a particular formulation in a specific container, to remain within physical, chemical, therapeutic and toxicological specifications. The purpose of stability testing is to provide evidence on how the quality of drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light, and enables recommended storage conditions and shelf lives to be established. ICH specify the length of study and storage conditions: Long term study as 25 °± 2 °C/ 60 % RH ± 5 % for 12 months, accelerated testing 40° C ± 2 ° C/ 75 % RH ± 5 % for 6 months

3. RESULTS AND DISCUSSION

The present study deals with the production of microbeads by orifice gelation technique by cross linking with calcium chloride solution. Microbeads of ciprofloxacin with a coat consisting of sodium alginate and hydrophilic polymer, methyl cellulose in different concentrations were prepared. The microbeads were found to be discrete, spherical, free flowing and monolithic type, when it was analyzed by the SEM. The microbeads of all formulations were uniform in size with mean size ranging from 300-600µm. Microbeads were prepared by taking 3%, 4%, 5%, and 6% (w/v) polymer solution for masking of the taste of the drug. The characteristics of the microbeads greatly depend upon the concentration of the sodium alginate. The formulation of good spherical beads of sodium alginate ranges from 3% to 6% in concentration with methyl cellulose. When the concentration of sodium alginate is too low or too high the microbeads formed were not properly of spherical shape.

The size of microbeads is improved depending upon the concentration of the polymer. The incorporation efficiencies of the microbeads were affected by the ratio of drug and polymer.

3.1. Evaluation of Taste Masking

Ciprofloxacin is extremely bitter quinoline antibiotic. It may be that different polymers have the different articles to mask the unpleasant taste of drugs.

The microbeads formed were used for taste masking of ciprofloxacin by using the alginate in combination with methyl cellulose in different concentration. The taste masked microbeads prepared were evaluated by ranking method i.e.by scoring at scale [8, 9]. The taste panel consisting of 5 volunteers were given very little amount of pure drug sample for the response of bitterness and asked to compare the taste of the formulated microbeads. The response of the volunteers was noted on the scale of 0-5 as described below [10].

0- Feel no bitter taste
1- Very little bitter taste
2- Slightly bitter taste
3- Bitter taste
4- Bearable bitter taste
5- Unbearable bitter taste.

Table: 2 Results of the incorporation efficiency and particle size of the formulated Bead

Formulation code	Polymer conentration (%w/v)	% incorporation efficiency	Mean particle size	Cross linking agent(%w/v)	Time of cross linking	% yield
B_1	3%	58±1.6	300±4.5	8%	30mins	98.11±1.4
B_2	4%	59±2.1	427±1.2	8%	30mins	94.69±1.4
B_3	5%	59±2.5	505±4.5	8%	30mins	90.03±2.1
B_4	6%	62±2.9	600±2.5	8%	30mins	91.23±1.4

The sodium alginate in combination with methyl cellulose were used for the microbeads and reducing the bitter taste of drug in various concentration of polymers. The effect of the taste masking gradually improved as the ratio of polymer increased. The 3% w/v polymer concentration solution was not sufficiently masked but when the concentration was increased up to 6% the taste masking efficiency was also enhanced upto the maximum.

3.2. Scanning Electron Microscopy Studies

The shape and surface characteristics of the microbeads formulation were characterized by SEM analysis (Figure 1). Drug loaded alginate microbeads were spherical in shape and the microbeads containing higher amount of polymer concentration (6%) exhibited smoother surface than those prepared by taking the lower amount of polymer concentration.

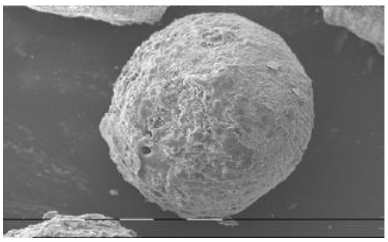

Fig : 1 SEM image of micro bead B_4

3.3. Stability Studies

The accelerated stability is defined as the validated method by which the product stability may be predicted by storage of the product under conditionsthat accelerate the change in defined and predictable manner. The stabiliity studies were carried out at 40 o c and at room temperature and the different parameters were noted. The results showed that there was no significant change in physical , and chemical parameter of the tablet. Hence the formulation was found to be stable.

4. CONCLUSION

The formulation of the microbeads is the best technique for masking the bitter taste of the drug and also for the sustained release of the drug. The taste masking was done by orifice ionic gelation technique using different polymer blend concentration. The drug ciprofloxacin was entrapped into the polymer and was stable without undergoing any chemical changes during the bead preparation. The microbeads were spherical, but their morphologies were changed due to the amount of the various concentrations used in the formulation. The evaluation studies indicated that, masking of bitter taste of ciprofloxacin can be done by the microbead formulation.

In addition it can be concluded that the taste masked drug delivery research is gaining importance and commercial success for the bitter quality of treatment, especially to children. A number of technological developments were also made to mask the taste which is widely accepted in the development of more palatable and acceptable dosage forms, which not only lead to better patient compliance but with an ultimate clinical output.

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