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Namita S Naikkhanvte *
Visveswarapura Institute of Pharmaceutical Sciences, BSK II stage Bangalore - 560070.
Email: namsp79@gmail.com

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Cefpodoxime Proxetil: Consumer Friendly Palatable Formulations

Namita S Naikkhanvte, Nilay Kapuriya, Rajarajeshwari N
Visveswarapura Institute of Pharmaceutical Sciences, BSK II stage Bangalore - 560070.

Abstract

Cefpodoxime proxetil, a third generation antibiotic used to treat upper and lower respiratory tract infections is bitter in taste thereby hampering the development of a palatable oral dosage form. In this study, Cefpodoxime proxetil was taste masked by microencapsulation technique (solvent evaporation method) with methacrylic acid copolymer (Ecopol™) in various ratios of drug and polymer. The taste masked microspheres were incorporated into dispersible tablets and dry syrup for reconstitution. Tablets were prepared by direct compression technique. Dry syrup was prepared using sweeteners, flavors and diluents. The formulations were evaluated for quality control parameters. Results indicated successful formulation of mouth dissolving tablets and dry syrup for reconstitution with optimum physicochemical properties.

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INTRODUCTION

Cefpodoxime proxetil, is a third generation cephalosporin antibiotic useful in the treatment of infections of respiratory tract, urinary tract, skin and STDs caused by susceptible strains of specific microorganisms. But, Cefpodoxime proxetil is bitter in taste and thus hampers oral delivery in pediatrics and geriatrics. Several methods can be employed to mask the bitter taste, like microencapsulation, ion exchange resin, coating etc.[1,2,3] Microencapsulation involves coating of drug particles using a natural or synthetic polymer or wax. The objective of present work is to taste mask Cefpodoxime proxetil using microencapsulation technique with Ecopol™ L 100 (methacrylic acid copolymer) and check the feasibility of incorporating the microcapsules into mouth dissolving tablets and dry syrup for reconstitution.[5,6] Mouth dissolving tablets disintegrate rapidly in the saliva with the need of water, thereby providing a good opportunity for drug delivery in paediatrics and geriatrics.[7,8,9]

METHODS

Materials:

Cefpodoxime proxetil was obtained as a gift sample from Endoc Pharma, Gujarat. Ecopol ™ L 100 and Instacoat strawberry flavour was obtained as a gift sample from Ideal Cures, Mumbai. Indion 414 was gifted by Ion Exchange (India) Ltd, Mumbai. Polyplasdone INF 10 and PVP S630 were gifted by Anshul Agencies. Avicel CL 611, Pearlitol and Avicel PH 102 were gifted by Signet Chemical Corporation. All solvents and reagents used were of analytical grade.

Taste masking of Cefpodoxime proxetil:

Taste masking of Cefpodoxime proxetil was attempted by preparing microcapsules using Solvent evaporation method.[1] Weighed amount of Ecopol was dissolved in varying amount of acetone and mixed. Cefpodoxime proxetil was added to the polymer solution. Subsequently, magnesium stearate was added to the solution of polymer and drug in acetone. This organic phase was poured in liquid paraffin and n hexane with vigorous stirring over a Remi mixer with an approximate speed of 2000 rpm for 3hours. It was filtered and microcapsules were washed with n-Hexane to remove any adhering liquid paraffin from the surface. Finally, washings with distilled water were given to remove any unentrapped drug from the surface of the microcapsules. This was followed by drying of microcapsules in hot air oven at 40^0C for 12 hours.

Characterization of microspheres:

Scanning electron microscopy

The surface morphology and particle size of microspheres was examined by scanning electron microscope. The samples were fixed on a brass stub using double-sided tape and then gold coated in a vacuum by sputter coater. The pictures were taken at excitation voltage of 20KV. JSM-840A scanning Microscope; Jeol-Japan with JFC-1100E ion sputtering device and are depicted in Fig1.

Drug entrapment efficiency

Microspheres equivalent to 100 mg of drug were accurately weighed and transferred to 100 ml volumetric flask. 15 ml of methanol was added to dissolve the microspheres and the volume was made upto the mark with phosphate buffer pH 6.8. Further dilutions were made and drug content was analysed by UV spectrophotometer at 232 nm.

Development of mouth dissolving tablets

The tablets were prepared using direct compression method.[10] Accurately weighed microcapsules, equivalent to 100 mg Cefpodoxime, Avicel PH 102, Indion-414, Polyplasdone INF-10, Pearlitol were geometrically mixed along with sweetener, flavors, anti-adherents. Then it was compressed into tablets using 12mm punches on a rotary tablet machine. Tablet weight was approximately fixed to 550mg.

Development of dry syrup for reconstitution

Dry syrup was prepared by simple mixture. For simple mixture, all the excipients were passed through sieve no. 44 and then mixed geometrically to get a uniform mixture. The final weight was adjusted to 18 gm with sucrose. The product was transferred to a container.

Evaluation of formulations

The tablets were evaluated for various quality control parameters like appearance, hardness, weight variation, *in-vitro* dispersion time, drug content and *in-vitro* drug release. Hardness of the tablet was determined with a Monsanto hardness tester. To test friability pre-weighed tablets were placed in a Roche Friability tester which was rotated for 4 min at 25 rpm. Then the tablets were weighed and the loss in weight (%) was calculated. *In-vitro* dispersion time was measured by placing one tablet in a beaker containing 6ml of water. The time required for uniform dispersion of tablet was noted. The reconstitution dry syrup was evaluated for various quality control parameters like appearance, sedimentation rate and the pH. The pH was recorded on a Systronics pH meter. I*n vitro* dissolution studies were carried out using USP XXIII Dissolution apparatus II (paddle type) for six tablets. Each of the six rapidly disintegrating tablets containing microspheres were placed separately in dissolution flasks containing dissolution medium (900 ml) which was rotated at a speed of 50 rpm by means of a paddle. A temperature of 37±0.5°C was maintained throughout the study.

Ingredients	F1 mg/tab	F2 mg/tab	F3 mg/tab	F4 mg/tab	F5 mg/tab	F6 mg/tab	F7 mg/tab	F8 mg/tab
Taste masked Microcapsules	s	390	390	390	390	390	390	390
Indion-414	-	22	26	28	25	33	-	17
Polyplasdone INF-10	-	-	-	6	8	-	33	16
PVP -S- 630	20	17	-	-	-	-	-	-
Avicel PH 102	45	-	53	55	55	55	55	55
Aspartame	-	4	4	4	4	4	4	4
Pearlitol	-	90	29	44	43	44	44	44
Talc	10	6	6	5	6	5	5	4
Aerosil	10	5.5	6	5	6	5	5	6
Instacoat strawberry flavor	10	11	13	13	14	14	14	14

Table 1 Formulation development of mouth dissolving tablet

Ingredients	DF1(mg)	DF2(mg)
Taste masked Microcapsules	1950	1950
Sodium benzoate	18	18
Citric acid	90	75
Avicel CL611	450	375
Aspartame	105	90
Instacoat strawberry flavour	40	30
Sucrose	15347	15462

Table 2 Formulation development of dry syrup for reconstitution

Volunteers / Parameters	Mouth dissolving tablets						Dry syrup for reconstitution					
	1	2	3	4	5	6	1	2	3	4	5	6
Bitterness	0	0	0	0	0	0	0	0	0	0	0	0
Sweetness	0.5	0	0.5	1	0	0	0	0	0	0	0	0
Flavor	0	0.5	0.5	0.5	0	1	0	0.5	0	0.5	0	1
Mouth feel	0.5	1	0.5	0.5	0.5	1	1	1	1	0.5	1	1
After taste	0	0	0	0	0	0	0	0	0	0	0	0

Table 3 Taste evaluation of developed formulation in healthy human volunteers

Bitterness and Aftertaste: - Non- Bitter (0-1), less bitter (1-2), bitter (2-2.5), very bitter (2.5-3). Sweetness: - Less sweet (2-3), sweet (1-2), very sweet (0-1). Flavor and mouth feel: - Bad (3), Moderate (2), good (1-0).

The release profile was studied both in phosphate buffer at pH 6.8 and hydrochloric acid buffer pH 1.2. Samples were analysed spectrophotometrically at λ_{max} 232 nm using buffer as the blank. Taste evaluation for both the formulation was done on 6 healthy human volunteers. They were asked to grade the formulations on various parameters as mentioned in Table 3. The protocol was approved by the institutional human ethical committee and an informed consent was also obtained from the volunteers.

RESULTS AND DISCUSSION

Cefpodoxime proxetil was successfully taste masked using Ecopol ™. Drug and polymer ratio of 1:1 was found to be optimum. SEM indicated a particle size of 150-350 µm and the microcapsules were found to be spherical as shown in figure 1. The entrapment efficiency was found to be 94.21±1.2%. The taste masked complex was successfully incorporated into mouth dissolving tablets. Indion 414 alone as a superdisintegrant, gave a high *in vitro* dispersion time of 3 minutes, hence combination was used with Polyplasdone INF10. The tablets were pink in color with a smooth texture. The hardness of the formulation was found to be 3-4kg/cm^2. Also, developed microcapsules when incorporated into dry syrup, gave a uniform pink dispersion with an acceptable taste. DF2 was found to be the best formula.The drug content of the tablet formulation and dry syrup was found to be 99 ± 1.75% and 100 ±1.1 % respectively. Both the formulations were found to be non bitter with acceptable taste and released more than 80% of the drug within 30 minutes. pH of the reconstituted dry syrup was found to be 5-6.

Thus the process of taste masking was optimized with respect to polymer concentration which could be easily incorporated into prototype syrup for reconstitution and mouth dissolving tablet.

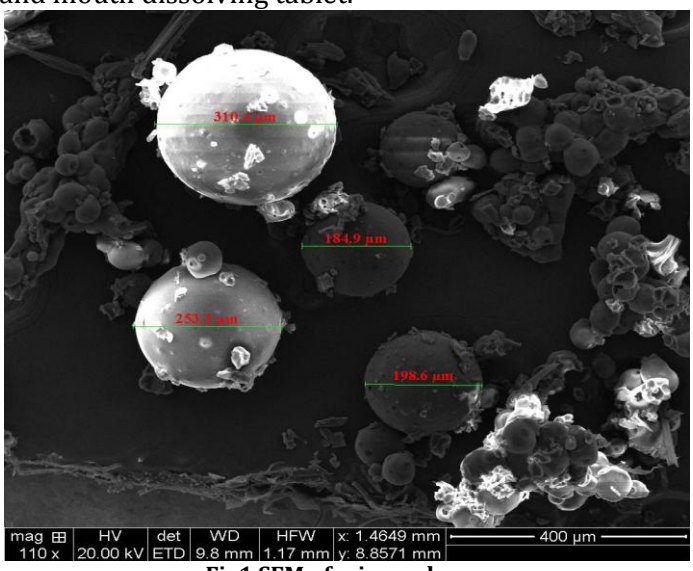

Fig1 SEM of microspheres

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