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FORMULATION AND EVALUATION OF TASTE MASKED ORAL DISPERSIBLE TABLET OF CIPROFLOXACIN WITH ION EXCHANGE RESIN

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ABSTRACT

Bitter taste is one of the important formulation problems that are encountered with many drugs, like Ciprofloxacin. In modern times, the most improved & easy technique is to formulate tasteless complexes of ciprofloxacin with ion exchange resin (Indion 234). After acid activation and swelling in water, resin & ciprofloxacin (proper ratio) was stirred for definite time & unbound drug in filtrate was estimated spectrophotometrically and drug-loading efficiency was calculated. The molecular properties of drug complexes by FT-IR study confirm the complexation of ciprofloxacin with Indion 234. The influence of superdisintegrants, crospovidone and sodium starch glycolate on disintegration time, wetting time and water absorption ratio was studied.

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INTRODUCTION:

Taste is the ability to detect the flavour of substances like food, drugs etc. Taste is now considered an important factor governing the patient compliance[1].The purpose of the research was to formulate tasteless complexes of ciprofloxacin with Indion 234 and to evaluate molecular properties of drug complexes[2]. Ciprofloxacin is a broad spectrum fluoroquinolone antibiotic. It has a narrow absorption window and is mainly absorbed in the proximal areas of GIT. The present study is an attempt to select best possible combination of drug and disintegrating agent to formulate rapidly disintegrating tablet of ciprofloxacin which disintegrates faster thereby reducing the time of onset of action[3].

MATERIALS AND METHODS:

Materials

Ciprofloxacin, Croscarmellose Sodium, Crosspovidone, MCC, Mannitol, SLS, Saccharin Sodium, Orange Flavor, Talc, Magnesium Stearate. Drug-excipent interactions were studied by IR spectroscopy at Modern Laboratories, Pvt. Ltd., Indore. All other chemicals used were of analytical reagent grade. Double distilled water was used in entire study.

Preparation of Oral Dispersible Tablet Drug-Resin Complex

Formation of drug-resin complex

The batch process was used for complexation. Drug-resin complex was prepared by placing 10 g of activated resin in a beaker containing 300 ml deionized water and allowed to swell for 30 minutes. Accurately weighed drug (as per 1:1, 1:1.2, and 1:1.3, drug-resin ratio) was added and stirred for 30 minutes. On filtration, the residue was washed with 700 ml of deionised water. Unbound drug in filtrate was estimated at 278 nm and drug-loading efficiency was calculated.

Method of Complexation

Selection of resins

Resins were selected on the basis of the nature of drug and requirement of formulation. Depending on the basis of acidic and basic nature of the drug, cation and anion exchange resins can be used. In the present work, weak cation exchange resin Indion 234 was selected based on their Ion exchange capacity and used for the taste masking of model drug

Table 1: Different Compositions of Oral Disintegrating Tablets

S.N.	Ingredients	Quantity of Ingredients (mg)							
		F1	F2	F3	F4	F5	F6	F7	F8
1	**DRC Eq. to 100 mg of drug**	235.1	235.1	235.1	235.1	235.1	235.1	235.1	235.1
2	**Croscarmellose Sodium**	10.0	16.5	23.0	29.5	-	-	-	-
3	**Crosspovidone**	-	-	-	-	10.0	16.5	23.0	29.5
4	**MCC**	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0
5	**Mannitol**	40.85	34.35	27.85	21.35	40.85	34.35	27.85	21.35
6	**SLS**	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
7	**Saccharin Sodium**	10.0	10.0	10.0	10.0	10.0	10.0	10.0	10.0
8	**Orange Flavour**	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0
9	**Talc**	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
10	**Magnesium Stearate**	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
Total weight of tablet		330	330	330	330	330	330	330	330

Batch process

Indion 234 resin in three different drug- resin ratios (1:1, 1:1.2, and 1:1.3) was studied. Activated resins (Indion 234) (10 g) were taken in a 1000 ml beaker; 300 ml of deionized water was added. The resins were allowed to swell in water for 30 min. Model drug (Ciprofloxacin) (10 gm) was added. The contents of beaker were stirred on a magnetic stirrer for 30 min. The complex was filtered using a whatman's filter paper. The residue was further washed with 700 ml of deionized water to remove any unbound drug. The filtrate was then analyzed at 278 nm. By subtracting the quantity of unbound drug from the concentration of the drug solution added, the amount of bound drug was calculated.

RESULTS AND DISCUSSION:

Determination of threshold bitterness concentration of model drug (Ciprofloxacin)

It was found that all the volunteers felt bitterness, after 30 sec of time, for the concentration of 150µg/ml and above.

Table 2: Determination of threshold bitterness concentration

No. of Volunteer	Concentration of Drug (µg/ml)					Interpretation
	50	75	100	150	200	
01	1	1	1	2	3	0= Good 1=Tasteless 2=Slightly Bitter 3=Bitter
02	1	1	1	2	3	
03	1	1	1	2	3	
04	1	1	1	2	3	
05	1	1	2	2	3	
06	1	1	1	2	3	

Process optimization

The process to prepare drug-resin complex was optimized. Model drug (Ciprofloxacin) was loaded on ion exchange resin by batch process to optimize the drug-resin complex.

***In Vitro* Taste Masking Evaluation:** Results of *In Vitro*taste masking evaluation of drug-resin complex are tabulated, it was revealed that the drug released in phosphate buffer pH 6.8 from drug-resin complex at the end of 120 sec was less than the threshold bitterness concentration of model drug (Ciprofloxacin) i.e.150 µg/ml.

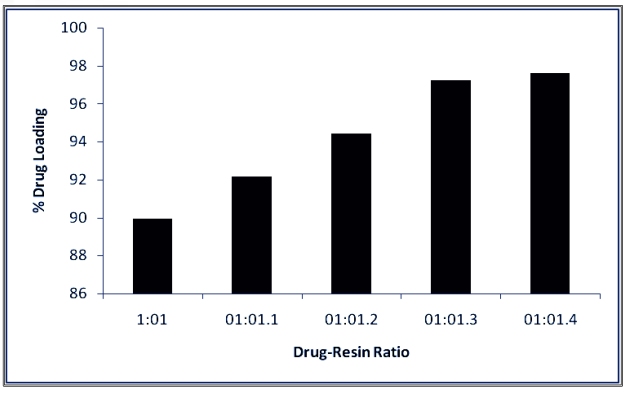

Figure 1: Optimization of drug-resin ratio

Table 3: *In Vitro* Taste Masking Evaluation of Indion 234

DRCs With Indion 234	Time (in sec)	Concentration (µg/ml)			
		1	2	3	Average Concentration
	60	99.36	100.17	100.04	99.85 ± 0.435
	120	114.77	114.98	114.26	114.67 0.370

a. Sensory Evaluation of Taste Masked drug-resin complex: When the drug-resin complexes were subjected to sensory evaluation by human volunteers, the volunteers did not feel any bitter taste after keeping the drug resin complex in mouth for 30 sec, which confirmed that bitter taste of model drug (Ciprofloxacin) was masked successfully.

b. Determination of drug content

Table 4: Determination of drug content from drug-resin complex

S. N.	Drug-resin complex	% Drug content (in 30 min)
1	Drug-Indion 234 complex (1:1.3)	97.84 0.48

c. Drug releases from drug-resin complex: The release of model drug (Ciprofloxacin) from the drug-resin complex was observed in deionizer water , salivary pH of 6.8 and at gastric pH of 1.2 . The results are given in the following Tables and figure. The results indicated that insignificant amount of drug (less than 0.3%) was released in demonized water in 30 min, indicating the stability of complexes. In vitro drug release in salivary pH 6.8 was less than 5% within 60 sec. The drug-resin complex is stable in salivary pH for a period of administration. The amount released is insufficient to impart bitter taste while the formulation passes through the mouth to further parts of gastrointestinal (GI) tract. At gastric pH of 1.2, model drug (Ciprofloxacin) was completely released in 30 min.

Table 5: Drug release from drug-resin complex in deionised water

S. N.	Time (min)	Percent drug release
1	5	0.010±0.48
2	10	0.058±0.74
3	20	0.077±0.18
4	30	0.091±0.18

Table 6: Drug release from drug resin complex at salivary pH 6.8

S. N.	Time (sec)	Percent drug release
1	15	2.14±0.72
2	30	3.79±0.49
3	60	4.46 ±0.86
4	120	4.77±0.37

d. Evaluation of oral disintegrating tablet

Table 7: Post compression parameters of oral disintegrating tablets

Formulation code	Hardness (kg/cm^2)	Friability (%)	Wetting Time (sec)	*In vitro* Disintegration Time (sec)
F_1	2.97±0.45	0.512	88 ±1.21	65 ±1.26
F_2	2.99±0.41	0.447	72±1.41	53 ±1.34
F_3	2.94±0.38	0.411	62 ±1.35	39 ±1.67
F_4	3.01±0.37	0.276	46±1.02	32 ±1.01
F_5	2.55±0.49	0.534	76 ±1.61	59 ±1.23
F_6	2.67±0.61	0.476	60 ±0.98	40 ±1.64
F_7	2.79±0.17	0.379	40 ±1.11	28 ±1.89
F_8	2.68±0.45	0.345	34 ±1.94	22±1.91

e. Dissolution test of ODT F7 in Phosphate Buffer pH 6.8 (at salivary pH):

Dissolution testing of ODT F7 at salivary pH showed that at the end of 120 sec, less than 5% of drug was released which indicated adequate taste masking.

Table 8: *In Vitro*Drug Release of Batch F7 in Phosphate Buffer pH 6.8

S.N.	Time (sec)	% Drug Release	Standard deviation
1	0	0	± 0.00
2	5	0.66	± 0.21
3	10	1.33	± 0.21
4	20	1.83	± 0.15
5	30	2.64	± 0.14
6	60	3.76	± 0.24
7	120	4.37	± 0.26

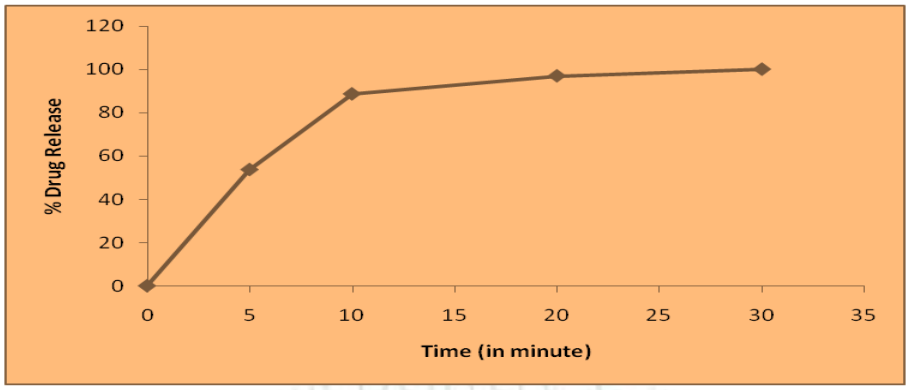

Figure 2: Drug release from drug resin complex at pH 1.2

CONCLUSION:

Drug release from drug resin complex was less than 5% at salivary pH 6.8. Bitterness evaluation results made by the consensus of trained persons confirmed that the bitter taste of Model drug (Ciprofloxacin) was masked by complexation with Resin. Micromeritics properties of drug-resin complex were evaluated. Amongst the various batches studied, Drug:Resin complex was successfully formulated into oral disintegrating tablet by direct compression method. Amongst the different superdisintegrants, combination of two superdisintegrants indicated improved disintegration time. Various drug formulations were compared with respect to *In Vitro* disintegration time and *in vitro* drug release profile. Formulation F7 was found to be palatable with *In Vitro*disintegration time of 28 sec. Dissolution studies showed complete release of F7 within 30 minutes. *In Vivo*taste masking evaluation revealed that the oral disintegrating tablet was adequately taste masked and had a pleasant mouth feel.In conclusion, an effective and pleasant tasting oral disintegrating tablet, of model drug (Ciprofloxacin) exhibiting satisfactory disintegration time and dissolution profile, was formulated using Indion 234 as a taste masking agent and crospovidone as a superdisintegrant by direct compression method.

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