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FORMULATION AND CHARACTERIZATION OF TASTE MASKED ORO-DISPERSIBLE TABLETS OF METFORMIN HYDROCHLORIDE

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ABSTRACT

Metformin hydrochloride is an oral antidiabetic biguinide agent, used in the management of non-insulin dependant (type-2) diabetes mellitus. The purpose of present work was to mask the taste of metformin hydrochloride and to formulate its patient friendly dosage form. Complexation technique using Indion 234 (Polycyclic potassium with carboxylic functionality), an ion-exchange resin was used to mask the bitter taste and then the taste masked drug was formulated into an orodispersible tablet (ODT). The drug loading onto ion-exchange resin was optimized for mixing time, activation, effect of pH, mode of mixing, ratio of drug: resin and temperature. The resinate was evaluated for taste masking and characterized by X-Ray diffraction study and IR. Using drug-resin complex ODTs were formulated. The developed tablets were evaluated for hardness, friability, drug content, weight variation, content uniformity, friability, water absorption ratio, *in vitro* and *in vivo* disintegration time and *in vitro* drug release. The tablets disintegrated *in vitro* and *in vivo* within 20 sec and 25 sec respectively. Drug release from tablet was completed within 3 minutes. The obtained results revealed that metformin HCl has been successfully taste masked and formulated into an ODT as a suitable alternative to the conventional tablets.

Key words: Metformin hydrochloride, Indion 234, Taste masking, Sodium starch glycolate, Orodispersible tablet.

INTRODUCTION

Convenience of administration and patient compliance are gaining significant importance in the design of dosage forms. Recently more stress is laid down on the development of organoleptically elegant and patient friendly drug delivery system for pediatric and geriatric patients.[1-2] More than 50 percent of pharmaceutical products are orally administered for several reasons and undesirable taste is one of the important formulation problem encountered with such oral products.[3] Taste of a pharmaceutical product is an important parameter for governing compliance. Thus, taste masking of oral pharmaceuticals has become an important tool to improve patient compliance and the quality of treatment especially in pediatrics. Therefore, formulation of taste masked products is a challenge to the pharmacists.[4-5]

Metformin hydrochloride is an orally administered antihyperglycemic agent, used in the management of type 2 diabetes (NIDDM), type 1 diabetes (IDDM).It is a very bitter drug and highly soluble in water.[6-7] The main objective of the present work is to formulate taste masked dispersible or oro-dispersible tablets of metformin hydrochloride. Such taste-masked formulations have been found to improve the quality of treatment in pediatric patients. The orodispersible tablets can be swallowed without water in the form of dispersion. They increase the patient compliance as well as provide quicker onset of action.

Thus in the present study an attempt has been made to mask the taste of metformin HCl and to formulate ODTs with good mouth feel so as to prepare a “patient-friendly dosage form.”
Orally disintegrating tablets disintegrate or dissolve in saliva and are swallowed without water. The main purpose of this work is only to improve patient compliance without compromising the therapeutic efficacy. [8-10]

Ion exchange resins have been increasingly used as taste masking agents.[11] They are also known to be useful as disintegrating agents superior to other conventional agents. [12-13] Thus, the study undertaken was aimed at using ion exchange resins for both the purposes, thus formulating taste-masked oro-dispersible tablets of ondansetron HCl.
The complex of cationic drug and weak ion exchange resin does not break at the pH of saliva i.e. 6-7 with cation concentration of 40 meq/l. But at high cationic concentration in stomach

and pH 1.2, free drug is immediately released. This implies that while passing through mouth, the drug remains in the complex form, thereby imparting no bitter taste in the mouth. This property was exploited to formulate the "consumer friendly dosage form" i.e. mouth dissolving tablets. [14-15]

MATERIALS AND METHODS

Materials

Metformin hydrochloride–IP was a Gift sample from Zim Laboratories (Nagpur, India).Indion 234 was obtained from Ion Exchange India Ltd. (Mumbai, India). Starlac and MCC were provided by Signet Chemicals Ltd., Mumbai, India.

Preparation of Resinate

Resinate were prepared using batch method. [16, 17]An accurately weighed amount of resin (100mg) was placed in a beaker containing 50 ml of demonized water. Accurately weighed 100 mg of metformin hydrochloride was added to the resin solution and stirred for 180 min. The mixture was filtered through whatman filter paper and residue was washed with 50 ml of deionised water to remove any uncomplexed drug. Unbound drug in filtrate was estimated at 233.5 nm and drug-loading efficiency was calculated.

Optimization of Metformin hydrochloride–Indion resin complexation

The drug loading on to resin was optimized for various parameters such as mixing time, activation, effect of pH, mode of mixing, ratio of drug: resin and effect of temperature. These parameters were studied and optimized for the maximum amount of drug loading.

Optimization for stirring time on drug loading

Separate batches of indion 234 (100 mg) were soaked in 50 ml of distilled water in a beaker and about 100 mg of drug was added and stirred for 3 hours. Amount of bound drug at the end was estimated at 233.5 nm by UV spectroscopy and the time required for maximum adsorption of drug was optimized.

Effect of activation of resin on drug loading

Resins were washed with distilled water and subsequently with 1N HCl. The resins were rewashed with water until neutral pH was reached. Drug: resin complexes were prepared by

placing 100 mg of acid-activated resins, in a beaker containing 50 ml distilled water and about 100 mg of drug and stirred for 3 hours & drug content was determined. Similarly, alkali activation of indion 234 was performed, replacing 1 N HCl with 1 N NaOH.

Effect of pH, mode of mixing, ratio of drug: resin and temperature on drug loading

For optimization of pH [16,], weighed, 100 mg of drug was added to 100 mg of activated resins in 50 ml of distilled water. The pH of solutions were adjusted at 3.0, 3.5, 4.0, 4.5, 5.0, 5.5, 6.0 and 6.5 and stirred for 3 hours and the drug content was determined. For optimization of mode of mixing, Rotary shaker & Magnetic stirrer were used. All activated resins (100 mg) in 50 ml of distilled water and about 100 mg of drug. The pH was adjusted at 3.5 & drug content was determined. For optimization of ratio of drug: resin [17], three batches were prepared containing drug-resin in the ratio of 1:1, 1:2, 1:3. The pH was maintained at 3.5.The solution was stirred for 3 hours. To study the effect of temperature, separate batches were prepared containing drug-resin in the ratio of 1:3 was taken. The pH was maintained at 3.5 and was stirred at 30^0C, 35^0C, 40^0C, 50^0C, 60^0C and the drug content was determined.

CHARACTERIZATION OF RESINATE

Infra Red (IR) Study

FT-IR spectrum of the drug, resin and resinate were recorded over the wave no 4000 to 400 cm^{-1} to check the interaction in the resinate on Jasco Dispersive type FT-IR spectrophotometer using the KBr disc technique .Then the spectra were comparatively analyzed for drug interaction.

X-ray diffraction study

The drug, resins and resinate was subjected to X-ray diffraction study for the confirmation of complex formation. X-ray diffraction studies were carried out on Phillips analytical X-ray BV (pw1710) using cu anode 40 KV voltage and 30 mA current.

Determination of Drug content

Resinate equivalent to 200 mg of drug was stirred with 100 ml of 0.1N HCl for 3 hours, till the entire drug leached out, then the solution was filtered through Whatman filter paper.

Further dilutions were made with 0.1 N HCl and the drug content was determined spectrophotometrically at 233.5 nm using 0.1 N HCl as blank.

Taste evaluation of solid drug: resin complex

Drug resin complex (1:3) was subjected to sensory evaluation by a panel of nine members using time intensity method. The pure drug without complexation with ion exchange resin was used as control in this study. Sample equivalent to 200 mg (dose of drug) was held in mouth for 10 sec. Bitterness was recorded instantly and then after 20,30,40,50 and 60 minutes. The evaluation was performed by classifying bitter taste into five classes. Level 0: No bitter taste is sensed, 1: Acceptable bitterness, 2: Slightly bitterness, 3: Moderately bitterness Level 4: Strongly bitterness. Descriptive statistics mean and standard deviation were calculated for all variables. Paired t test was applied using INSTAT software. Value $p < 0.05$ has been considered as statistical significant level.

***In-vitro* dissolution**

Complexes of metformin hydrochloride with indion 234 were subjected to in vitro dissolution studies using USP 24 method. Weigh quantity of complexes equivalent to normal dose was suspended in 0.1 N HCL using USP II dissolution apparatus and the quantity of drug released was determined periodically.

Formulation development

Resinates of drug (dose of drug 200 mg) were formulated into tablet by direct compression technique. using sodium starch glycolate, microcrystalline cellulose (PH-101), spray dried mixture of starch and lactose (Starlac).Each formulation was composed of drug and Excipients in various proportions as shown in Table 1. All ingredients were passed through mesh no.60. Required quantity of each was taken for particular formulation and the blend was mixed using mixer. Powder blend was evaluated for micromeritic properties like Shape, Angle of Repose, Bulk Density, Tapped Density, and Housner ratio. [18-20] Mixed blend of drug and excipients was compressed on 8-station rotary punch tablet machine (Karnavati, India). Tablets, each weighing 500 mg, were prepared.

Table 1: Formulation Design.

Ingradients	Formulations							
	B-1	B-2	B-3	B-4	B-5	B-6	B-7	B-8
Indion 234 Resinate	208*	208	208	208	208	208	208	208
Sodium starch glycolate	----	----	15	20	25	15	20	25
Starlac	230	----	215	210	205	----	----	----
Avicel(ph 101)	----	230	----	----	----	215	210	205
Mannitol	50	50	50	50	50	50	50	50
Aspartame	2	2	2	2	2	2	2	2
Mg. Stearate	5	5	5	5	5	5	5	5
Aerosil	5	5	5	5	5	5	5	5
Orange flavor	QS	QS	QS	QS	QS	QS	QS	QS
Total	500	500	500	500	500	500	500	500

- Containing 200 mg of drug

Evaluation of Tablets

The prepared tablets were evaluated for various official and nonofficial specifications. Tablets were evaluated for hardness and friability testing using Monsanto hardness tester and Roche friabilator respectively.

Weight Variation, Hardness, Friability and Content Uniformity Test

Twenty tablets were selected at a random and average weight was calculated. Then individual tablets were weighed and the individual weight was compared with an average weight. Tablets were evaluated for hardness [21] and friability testing [22] using Monsanto hardness tester and Roche Friabilator respectively. For drug content uniformity [23], 20 tablets were weight and crushed. Weight accurately to get 8 mg drug equivalent resinate powder and transferred it to 100 ml of 0.1 N HCl and shake for 15 min and centrifuged. Further dilutions were made with 0.1 N HCl and the drug content was determined spectrophotometrically at 233.5 nm using 0.1 N HCl as blank.

Water Absorption Ratio

A piece of tissue paper folded twice was placed in a small petri dish containing 6 ml of water. A tablet was put on the tissue paper and allowed to wet completely. The wetted tablet was then weighed. Water absorption ratio [22,23], R, was determined using following equation:

$$R = 100 \times W_a - W_b / W_b$$

Where, W_b = Weight of tablet before water absorption

W_a = Weight of tablet after water absorption.

***In-vitro* Dispersion Time**

Tablet was put into 100 ml distilled water at 37 ± 2 ^{0}C.Time required for complete dispersion of a tablet was measured with the help of digital tablet disintegration test apparatus.

***In-Vivo* Dispersion Time**

In-Vivo dispersion time of a tablet was checked in healthy human volunteers by putting a tablet on tongue and time required for complete dispersion of a tablet was checked.

Dissolution Study

Tablets formulated with resinates were subjected to in-vitro dissolution studies using USP type II apparatus (paddle type) at 100 rpm with temperature of 37^{0}c ± 0.5^0 C. Dissolution was carried in 0.1 N HCl as dissolution medium. After specific time interval, 5 ml dissolution medium was withdrawn by pipette and replaced with fresh medium for maintaining sink condition. Sample was filtered and absorbance of filtered solution was determined by UV spectroscopy at 233.5 nm. Dissolution rate was studied for all designed formulations and conventional marketed tablet.

RESULTS AND DISCUSSION

Metformin hydrochloride was loaded on Indion 234 by batch process. Complexation is essentially a process of diffusion of ions between the resin and surrounding drug solution. As reaction is equilibrium phenomenon, maximum efficacy is best achieved in batch process. Complexation between drug and resin increase up to optimum time and then remain almost constant. It was found to be optimum after 3 hour of mixing in the resin investigated. Highest drug binding on resin was achieved when activated with 1N HCl. The percentage drug

loading with inactivated resin, treated with acid and alkali was found to be 48.22 ±0.34, 58.42±0.7 and 52.47 ± 0.7 respectively. After activation with acid treatment, the exchangeable ion on the resin is H^+. Relative selectivity of H^+ is least than other ionic form and therefore it increases percent complexation. The mode of complexation between drug and resin can be affected by pH of the media. Maximum drug loading on the resin occurs at pH 3.5; a maximum of 75.34 ±1.52 for indion 234. As pH increases above 3.5, percentage of drug loading decreases. pH of the solution affects both solubility and degree of ionization of drug and resin. Results can be attributed to the fact that a cationic drug is ionized at lower pH value and hence demonstrate high binding capacity while at higher pH protonated fraction of cationic drug decreases and hence interaction with resin also decreases. [21] Hence metformin hydrochloride as a cationic drug will have maximum solubility and complete ionization in this range. Decreased complexation at lower pH i.e. below 2 is due to excess H^+ ions in solution which have more binding affinity to the –COO- group of resin and compete with drug for binding. Complexation was found to be optimum in case of stirring, a maximum of 75.34 ±1.52, for indion 234 and in case of shaking 68.56±0.23. This finding may indicate the significant involvement of vander waal's forces taking place along with drug exchange during complexation. [22] The drug loading in various drug: resin concentration was found to be 75.34 ±1.52, 81.34 ± 0.28, 85.53 ±0.19 for 1:1, 1:2, and 1:3 ratio respectively. It is due to the fact that, increase in the amount of resin increases the amount of drug adsorbed from the solution. The % drug loading (w/w) with temperature of 30^0C,35^0C 40^0C, 50^0C and 60^0C was found to be 77.67 ±0.83, 85.53 ±0.19, 91.25 ± 0.23 , 96.13±0.62 and 96.78 ± 1.16 respectively. These figures reveal that as temperature increases percentage of drug loading also increases rapidly upto 50^0C. Increase in temperature above 50^0C did not further increase the percentage drug loading. Increased temperature during complexation increases ionization of drug and resin. Higher temperatures tend to increase the diffusion rate of ions by decreasing the thickness of exhaustive exchange zone.[23] Also at increased temperature swelling of resin takes place. Due to swelling ionic sites are open for exchange of counter ions.

The drug content in the resinate was found to be 99.12 %.The dissolution profile of drug showed complete drug release within 98 sec. Results of evaluation of taste indicated complete masking of bitter taste as no bitterness was felt in the drug-resin complex (Table 2).

Table 2: Volunteers opinion test for Metformin HCL before and after taste masking

Time (s)	Before taste masking Mean±SD	After taste masking Mean±SD
10	4.0±0.00**	0.32±0.28**
20	3.3 ±0.50**	0.11±0.83**
30	2.55±0.52**	0
40	2.0±0.50**	0
50	1.77±0.44**	0
60	1.22 ±0.44**	0

P<0.0001** n=9

The infrared spectra of drug, indion 234 resin and resinate are depicted in Figure 1. FT-IR spectra of drug shows peak at 1028 cm $^{-1}$ corresponding to the NH stretching in a secondary amine. Indion 234 shows characteristic peaks at 1674 cm^{-1} and 1722 cm^{-1} corresponding to – C = O stretching of aryl acids and due to aromatic C = C stretching. The absence of peak at 1028 cm^{-1} in DRC confirms the complexation of the secondary amine group in the drug with resin.

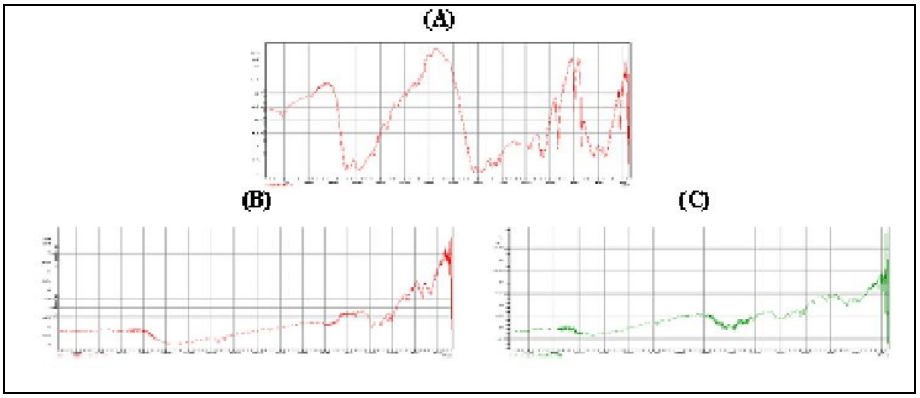

Figure 1: FT-IR spectra of A. Metformin hydrochloride, B. Indion 234 Resin, C. Indion-234 resinate.

The X-Ray Diffraction study of metformin hydrochloride shows highly crystalline nature. Resins indion 234 showed amorphous nature and the resinates showed noncrystalline characteristics. This might be because of entrapment of drug molecule in the polymer matrix of the resins. From all the evidences it can be concluded that the drug resinate was a chemical complex (Figure 2). Studies have shown that the molecules of the entrapped drug changes from crystalline to amorphous state. [24]

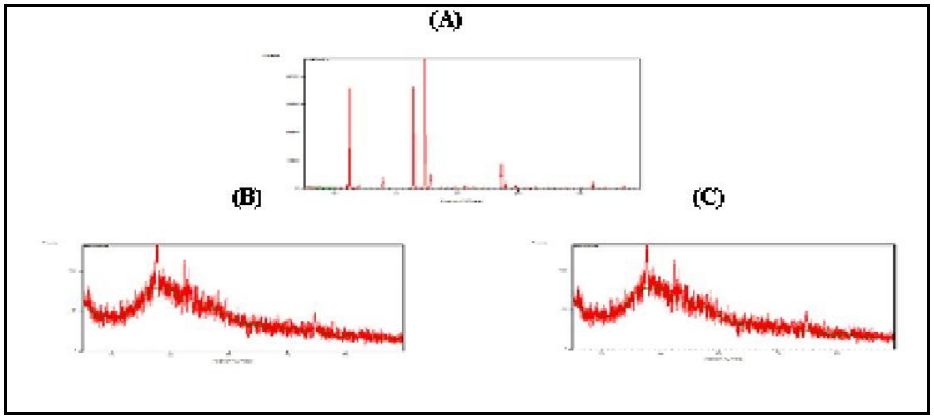

Figure 2: X-Ray diffraction pattern of A. Metformin hydrochloride, B. Indion 234 resin, C. Indion-234 resinate.

The batches of controlled formulations and formulations containing superdisintegrant were designed, using higher and lower concentrations of Sodium starch glycolate and employing different filler, binders, MCC PH-101 and Starlac and other excipients and compressed on tableting machine. For each designed formulation, blend of drug and excipients was prepared and evaluated for micromeritic properties as depicted in Table 3.

Table 3: Micromeritic properties of powder blend*

	Evaluation parameters						
Formulations	**Shape**	**Angle of repose**	**Bulk density (g/cm^3)**	**Tap density (g/cm^3)**	**Carr's Index (%CC)**	**Housner ratio**	**Flowability**
B-1	Irregular	31.9±0.3	0.782±0.6	0.845±0.8	7.466±0.8	1.0806	Excellent
B-2	Irregular	32.8±0.7	0.714±0.8	0.765±0.8	6.664±0.9	1.0566	Excellent
B-3	Irregular	31.5±0.9	0.815±0.9	0.876±0.0	6.949±0.4	1.0616	Excellent
B-4	Irregular	32.8±0.5	0.763±1.7	0.806±0.4	5.357±0.3	1.0566	Excellent
B-5	Irregular	31.4±0.3	0.767±0.5	0.812±1.8	5.478±0.7	1.0579	Excellent
B-6	Irregular	30.8±0.2	0.702±0.0	0.768±0.4	8.565±0.3	1.1257	Excellent
B-7	Irregular	29.4±0.5	0.713±0.4	0.763±0.8	6.588±0.9	1.0705	Excellent
B-8	Irregular	31.2±0.7	0.744±0.4	0.793±0.3	6.212±0.9	1.0662	Excellent

***** Average of three determinations

Then, the formulated orodispersible tablets were evaluated for weight variation, hardness, friability and uniformity of content, Water absorption ratio and *in-vivo* and *in-vitro* dispersion time as shown in Table 4.After evaluation Batch B-5 with 5% sodium starch glycolate and starlac and Batch B-8 with 5% sodium starch glycolate and avicel PH 101 was found to be optimum batch as it shows lowest disintegration time with desired friability values.

Table 4: Evaluation of physical characteristics of tablets (Batch B-1-B-8)

Evaluation parameters		Formulations							
		B-1	**B-2**	**B-3**	**B-4**	**B-5**	**B-6**	**B-7**	**B-8**
Hardness (kg/cm^2)		2.7±0.2	2.8±0.5	2.9±0.2	3.1±0.3	3.2±0.6	2.6±0.8	2.9±0.1	2.7±0.5
Friability (%w/w)		0.66±0.3	0.77±0.2	0.78±0.2	0.68±0.5	0.69±0.5	0.61±0.5	0.72±0.8	0.53±0.1
Drug Content(%w/w)		97.2±0.2	97.7± 0.9	98.6±0.3	98.4±0.2	99.3±0.2	97.7±0.6	101.3±0.6	99.6±0.4
% Weight variation		2.02±0.3	3.55 ±0.1	3.35 ±0.4	2.35±0.2	3.67±0.9	3.36 ±0.6	2.92±0.3	3.38±0.8
Water absorption Ratio		74.0±0.8	65.8 ±0.7	82.3±0.6	95.6±0.9	106.4±0.3	95.9±0.8	98.5±0.9	108.4±0.5
	In-vitro	64±1.3	55±0.5	32 ±0.9	29± 1.2	20 ±0.6	33 ±0.9	25±1.5	23± 0.3
Disintegration time (sec)	In-vivo	74±0.9	66±0.2	55±0.7	38±0.3	25±0.7	48±0.3	39±0.8	32±1.6

Dissolution rate was studied for batch B-5 and B-8 and conventional marketed tablet. For batch B-5 and B-8 formulations, the tablets show about 97 % drug release within 6 minutes, while conventional marketed tablet required 9 minutes for complete release of drug (Figures 3, 4 and 5). The formulations B-5 consisting Starlac as filler binder and sodium starch glycolate showed complete drug release drug within 3 minutes (Figure 3) and formulation B-8 consisting MCC as filler binder and sodium starch glycolate showed complete drug release within 4 minutes (Figure 4).

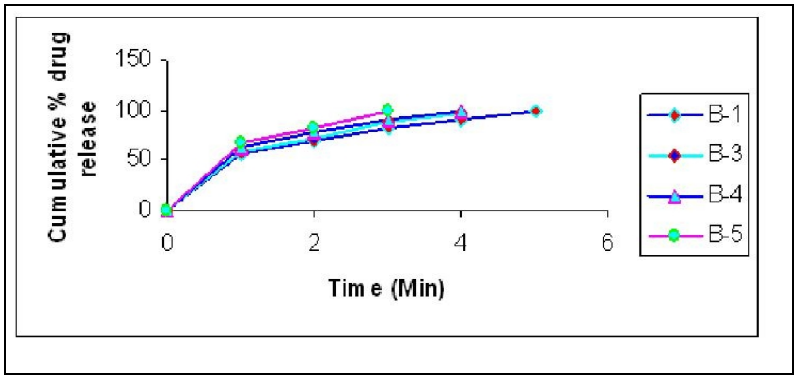

Figure 3: Dissolution profile of control tablet and tablets consisting Sodium starch glycolate containing Starlac as filler binder.

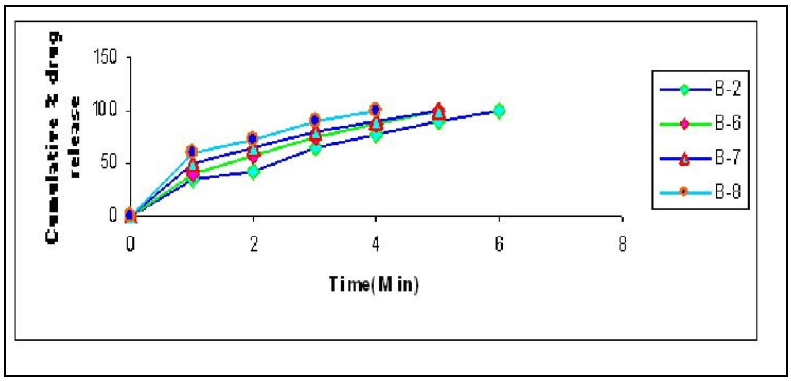

Figure 4: Dissolution profile of control tablet and tablets consisting Sodium starch glycolate containing MCC as filler binder.

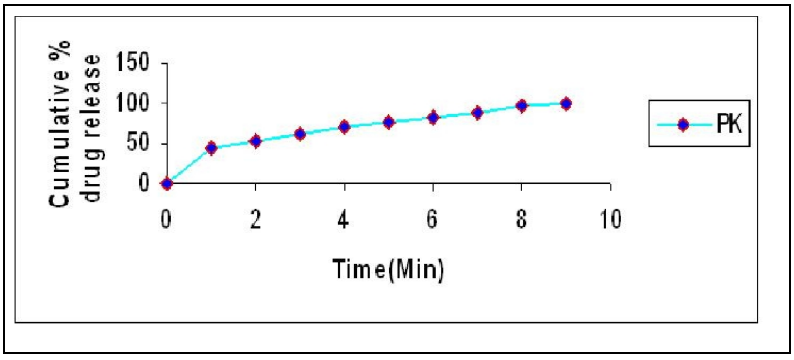

Figure 5: Dissolution profile of conventional marketed tablet

The drug release from all formulations was too fast as compared to the conventional marketed tablet. Formulated tablets masked the bitter taste of drug completely, whereas marketed tablets failed

CONCLUSION

Use of cation exchange resin offers good method for preparing taste masked substrates of Metformin hydrochloride. Results obtained in this work show that drug resin complexes effectively masked bitter taste of Metformin hydrochloride. Formulated orodispersible tablets showed good release profile as that of marketed orodispersible tablet and having additional advantage of complet taste masking. Thus, complexation of metformin hydrochloride with indion 234 increses acceptability and palatability of formulated orodispersible tablets.

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REFERENCES

1. Bhusan SY, Sambhaji SP, Anant RP, Kakasaheb RM. New drug delivery system for elderly. Ind Drugs, 2000; 3(7):308-12.
2. Wadhwani AR, Prabhu NB, Nandkarni MA, Amin PD. Consumer friendly mucolytic formulations. Ind J Pharm Sci, 2004; 7: 506-07.
3. Lachman L, Lieberman HA, Kanig JL. The Theory and Practice of Industrial Pharmacy. 3rd ed., Mumbai; Varghese Publishing House: 1991.
4. Bi Y, Sunada H, Yonezawa Y, Danjo K, Otsuka A, Iida K. Preparation and evaluation of a compressed tablet rapidly disintegrating in the oral cavity. Chem Pharm Bull, 1996; 44: 212-17.
5. Nanda AR, Garg S. An update on Taste masking technologies for oral pharmaceuticals. Ind J Pharm Sci, 2002; 64:10-17.
6. Hermann LS, Melender A. Biguanides: Basic aspects and Clinical use. 5th ed., New York; Wiley Publishing House: 1992.
7. Tucker GT, Casey C, Phillips PJ. Metformin kinetics in health subjects and in patients with diabetes mellitus. Br J Cli Pharmacology, 1981; 12:235-46.
8. Kaushik D, Dureja H, Saini TR. Mouth dissolving tablets: A review. Indian Drugs, 2004; 41: 503-08.
9. Ansel HC, Popovich NG, Allen LV. Pharmaceutical Dosage Forms and Drug Delivery System. 2nd ed., New Delhi; Waverly pvt. Ltd: 1995.

10. Rajyaguru TH, Indurwade NH, Nakhat PD. Novel approach-Fast dissolving tablets. Ind Drugs, 2002; 3(9): 405-09.
11. Michael P, Hein RD. US Patent, US 6001392, 1997.
12. Venkatesh DP, Geetha Rao CG. Formulation of taste masked oro-dispersible tablets of ambroxol hydrochloride. Asian J of Pharma, 2008; 32: 261-4.
13. Chaudhari PD, Chaudhari SP, Lanke SD, Patel N. Formulation and *in vitro* evaluation of taste masked orodispersible dosage form of Levocetirizine dihydrochloride. Ind J Pharm Educ, 2007; 41: 221-8.
14. Joshi AA, Duriez X. Added functionality excipients: An anwser to challenging Formulations. 3rd ed., New York; While publishing house: 2004.
15. Borodkin S, Sundberg DP. Carboxylic acid ion –exchange resin adsorbates for taste coverage in chewable tablets. J Pharm Sci, 1971; 60: 1523-7.
16. Avari JG, Bhalekar M. Cation exchange resins for taste masking and rapid dissolution of sparfloxacin. Ind Drugs, 2004; 4(5): 19-23.
17. Pisal S, Nalawade P, Mahadik K, Kadam S. Molecular properties of ciprofloxacin-indion 234 complexes. AAPS Pharm Sci Tech, 2004; 62:1-8.
18. Banker GS, Anderson NR. Theory and Practice of Industrial Pharmacy. 5th ed., London; Philadelphia: 2000.
19. Mahajan HS, et al. Mouth dissolving tablets of Sumatriptan succinate. Ind Drugs, 2004; 41: 592-8.
20. Cooper J, Gunn C. Powder flow and compaction. 6th ed., New Delhi; Haven press: 1986.
21. Indian Pharmacopoeia, Government of India, ministry of health and family welfare. Controller of Publication of India. 4th ed., New Delhi;1996.
22. Kuchekar BS, Badhan AC, Mahajan HS. Mouth dissolving tablets of salbutamol sulphate : A novel drug delivery system. Ind Drugs, 2004; 41: 592-8.
23. Aly A, Semreen M, Qato M. Rapidly disintegrating Tenoxim tablets via camphor sublimation. Pharm Tech, 2005; 45:68-78.
24. Akkaramonkolporn P. Molecular properties of propranolol hydrochloride prepared as drug-resin complexes. Drug Devlop Ind Pharm, 2001; 27:359-64.