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Research Article

FORMULATION AND EVALUATION OF TASTE MASKED ORALLY DISINTEGRATING TABLET OF TINIDAZOLE

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ABSTRACT

Tinidazole is a broad spectrum antiprotozoal agent having bitter taste. The present study concerns to mask the bitter taste of tinidazole as an orally disintegrating tablet (ODT) using Indion 294 and Indion 204 (ion exchange resin) as a taste masking agent. In first method, 1:1, 1:2 and1:3 ratios of drug and resin were stirred for six hour. Percent drug losses were found to be on higher side in this method. In second method, drug-resin complexes were prepared by wet granulation method with different concentration ratios of drug with Indion 294 as well as with Indion 204(1:0.5, 1:1,1:1.5) using lactose as diluent and polyvinylpyrrolidone k-30 as binder. On the basis of disintegration time, optimum concentration of superdisintegrants i.e. crosscarmollose sodium and crosspovidone were found to be 8% w/w. The tablets were prepared by direct compression method using orange flavour and evaluated for taste, weight variation, hardness, friability, disintegration test, content uniformity, dissolution study & FTIR study. The best formulations were found to be containing (1:1.5) drug: Indion 204 & (1:1.5) drug: Indion 294.

Keywords: Tinidazole, Indion 294, Indion 204, Resin, Complexes.

INTRODUCTION[1,2,3,4]

Tinidazole is a broad spectrum antiprotozoal agent. It is extremely bitter. Therefore, in the present study, an attempt has been made to mask its bitter taste and to formulate it into more accessible and patient-compliant mouth-disintegrating tablets. Taste masking was achieved by using ion exchange resin Indion 294 (Polacrilin potassium) and Indion 204. Indion 294 is a high purity pharmaceutical grade weak acid cation exchange resin, supplied in potassium form as a free flowing powder . It is suitable for use in the pharmaceutical applications such as taste masking and tablet disintegration. Indion 294 is derived from cross linked polymethacrylic acid. Indion 204 is a high purity pharmaceutical grade weak acid cation exchange resin, supplied in hydrogen form as a free flowing powder . It is suitable for pharmaceutical applications such as taste masking of bitter drugs. It is based on a cross linked polyacrylic matrix.

MATERIALS AND METHODS

Tinidazole was obtained as a gift sample from Nicholas Piramal private limited. Indion 294 & Indion 204 were obtained as gift samples from Ion Exchange India Ltd.

Preparation of drug-resin complex[5,6,7,8,9]

For preparation of drug-resin complex, required quantity of resin was placed in drug solution (drug: resin ratio 1:1,1:2 &1:3) and was stirred for six hour .Then the solution was filtered. The drug content in residue and in filtrate was found out. Percent drug losses were found to be on higher side in this method. Therefore, further research work is required to optimize this technique. So second method is used in which required amount of drug was mixed with different amount of powdered ion-exchange resin i.e. they were mixed at 1:0.5, 1:1, 1:1.5 ratio. The taste masked resinates (equivalent to 150mg of tinidazole) were granulated along with lactose as diluents using PVP K 30 as a binder.

Evaluation of granules[10,11]

Angle of repose

Angle of repose is a relatively simple technique for estimation of the flow property of a powder. Powders with low angle of repose are free flowing and those with a high angle of repose are poorly flowing powders.10 gm of granules were passed through funnel and the pile was formed. The height and weight of the pile was measured and the angle of repose was calculated by using the formula:-

Angle of repose (θ) = $\tan^{-1}$ (height /radius)

Carr`s compressibility index

The Carr's compressibility index was calculated by calculating the tapped and bulk density using the 100 ml measuring cylinder. Compressibility is calculated by the formula,

$$C = 100 \times (1 - \frac{\rho_B}{\rho_T})$$

Where ρ_B is the freely settled bulk density of the powder, and ρ_T is the tapped bulk density of the powder.A carr`s index greater than 25 is considered to be an indication of poor flowability, and below 15, of good flowability.

Hausner's Ratio

The Hausner's ratio is a number that is correlated to the flowability of a powder or granular material. It is calculated by the formula

$$H = \frac{\rho_T}{\rho_B}$$

Where ρ_B is the freely settled bulk density of the powder, and ρ_T is the tapped bulk density of the powder. Hausner's ratio greater than 1.25 is considered to be an indication of poor flowability.

Optimization of superdisintegrant concentration

This was done by using different concentration ratio of superdisintegrants between 2-10% and optimum concentration was found out.

Formulation of taste masked ODT tablet of tinidazole

Orally disintegrating tablets of tinidazole: Indion 294 and tinidazole:Indion 204 granules were prepared using direct compression method after incorporating different superdisintegrants crosscarmellose sodium and crosspovidone. Six formulations of each of tinidazole: Indion 294 and tinidazole:Indion 204 granules were prepared. Orange flavour is used as flavouring agent. Magnesium stearate was added as lubricant.

Evaluation of tablet

Taste evaluation

The tastes of prepared tablet were evaluated by group of six volunteers and categorized into any one of the category: extremely bitter, bitter, slightly bitter, acceptable, and pleasant.

Diameter and Thickness

It was measured by using vernier calliper scale.

Weight variation

The USP weight variation test is run by weighing 20 tablets individually, and comparing individual weight to the average. Thetablets meet the USP test if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.

Hardness

The Pfizer tester was used.

Disintegration time

This test was carried out using USP disintegration apparatus.

Content uniformity

Content uniformity was found out by caliberation method using uv instrument (Varian).

Procedure

Preparation of standard solutions: Dissolve 10mg of drug in a solution containing 10 ml methanol & dilute with methanol to get concentrations of 5 ppm, 10 ppm, 15 ppm, 20 ppm &25 ppm. Carry out uv sphectrophotometric determination at 310 nm.

Preparation of sample solution

Triturate the tablet. Powder equivalent to 10mg of drug was dissolved in methanol. Filter solution using whatman filter paper. With further dilution, spectrophotometric determination was carried out at 310nm.

Dissolution test[12]

Dissolution test was carried out in phosphate buffer pH 6.8 by using USP dissolution apparatus 2.A tablet was placed in 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.

FTIR study

This study was carried out to check incompatibility between drug and excipients by using IR spectrophotometer (Varian).

RESULTS AND DISCUSSION

The first method cannot be used as drug losses were found to be on higher side in external media i.e. 98.93%, 97.25% & 96.53% for drug: resin ratio 1:1, 1:2, 1:3 respectively. So wet granulation method was used for preparation of drug-resin complex using superdisintegrants crosscarmellose sodium and crosspovidone. Optimum concentration of superdisintegrant was found out which was found to be 8% for both superdisintegrants as shown in fig. (1). The granules were free flowing with angle of repose below 15^0, Hausner's ratio below 1.15 and Carr's index below 8 as shown in table (2).The tablets meet test for weight variation, hardness, thickness and diameter. Relatively acceptable taste was achieved in tablets containing drug: resin ratio 1: 1.5.Rapid disintegration time (21 sec.) was achieved in tablets containing crosspovidone as super disintegrating agent with Indion 204. Hardness was found to be between 3.2-4.2 kg for all the batches. Friability was found to be within USP limits. Content uniformity was found to be between 97-102 %w/w. From dissolution study, it is concluded that complete drug release was obtained within 15 minutes as shown in fig. (2) in all batches. FTIR study shows compatibility between drug and excipients. FTIR study showed decrease in intensity of major peaks of drug in the formulation which is a good sign for complexation indicating taste masking of drug.

Table 1: Formulation chart of taste masked ODT of tinidazole containing Indion 294

Ingredients (mg/tablet)	Formulation code					
	F_1	F_2	F_3	F_4	F_5	F_6
Tinidazole	150	150	150	150	150	150
Indion 294	225	150	75	225	150	75
PVP	8	8	8	8	8	8
Lactose	25	100	175	25	100	175
Crosscarmellose Sodium	40	40	40	-	-	-
Crosspovidone	-	-	-	40	40	40
Orange flavour	15	15	15	15	15	15
Magnesium stearate	7	7	7	7	7	7
Total	470	470	470	470	470	470

Table 2: Formulation chart of taste masked ODT of tinidazole containing Indion 204

Ingredients (mg/tablet)	Formulation code					
	F_7	F_8	F_9	F_{10}	F_{11}	F_{12}
Tinidazole	150	150	150	150	150	150
Indion 204	225	150	75	225	150	75
PVP	8	8	8	8	8	8
Lactose	25	100	175	25	100	175
Crosscarmellose Sodium	40	40	40	-	-	-
Crosspovidone	-	-	-	40	40	40
Orange flavour	15	15	15	15	15	15
Magnesium stearate	7	7	7	7	7	7
Total	470	470	470	470	470	470

Table 3: Evaluation of granules of ODT of tinidazole containing Indion 294

Parameter	Formulation code					
	F_1	F_2	F_3	F_4	F_5	F_6
Angle of Repose	$13^0$11'	$12^0$13'	$13^0$24'	$11^0$22'	$12^0$41'	$14^0$47'
Hausner`s Ratio	1.08	1.12	1.06	1.13	1.04	1.15
Carr`s Compressibility Index	6.3	7.4	6.8	5.2	4.5	7.8

Table 4: Evaluation of granules of ODT of tinidazole containing Indion 204

Parameter	Formulation code					
	F_7	F_8	F_9	F_{10}	F_{11}	F_{12}
Angle of Repose	12⁰42’	12⁰29’	14⁰18’	13⁰25’	11⁰35’	13⁰42’
Hausner`s Ratio	1.06	1.03	1.057	1.13	1.08	1.10
Carr`s Compressibility Index	6.3	5.7	5.9	6.8	6.5	6.7

Table 5: Evaluation of ODT of tinidazole containing Indion 294

Parameter	Formulation code					
	F_1	F_2	F_3	F_4	F_5	F_6
Taste	Pleasant	Acceptable	Slightly bitter	Pleasant	Acceptable	Slightly bitter
Diameter (cm)	0.9±0.05	0 9±0.05	0 9±0.05	0 9±0.05	0 .9± .05	0 .9± .05
Thickness(cm)	0.5±0.02	0.5±0.02	0.5±0.02	0.5±0.02	0.5±0.02	0.5±0.02
%Weight variation	1.3145 ±0.7985	1.3275 ±0.2575	1.3255 ±0.2515	1.3195 ±0.7305	1.3385 ± 0.3525	1.3205 ±0.4315
Hardness (kg)	3.2	4.2	3.4	3.4	4	3.6
Disintegration time (sec.)	28	30	33	24	27	29
% Drug content	99.43	97.21	100.78	98.23	101.35	97.65

Table 6: Evaluation of ODT of tinidazole containing Indion 204

Parameter	Formulation code					
	F_7	F_8	F_9	F_{10}	F_{11}	F_{12}
Taste	Pleasant	Acceptable	Slightly bitter	Pleasant	Acceptable	Slightly bitter
Diameter (cm)	0.9±0.05	0 9±0.05	0 9±0.05	0 9±0.05	0 .9± .05	0 .9± .05
Thickness(cm)	0.5±0.02	0.5±0.02	0.5±0.02	0.5±0.02	0.5±0.02	0.5±0.02
%Weight variation	1.3075 ±0.2365	1.3415 ±0.2535	1.3245 ±0.2945	1.4275 ±0.2275	1.3875 ± 0.3325	1.3935 ±0.3565
Hardness (kg)	3.6	4	3.2	3..8	4.2	3.6
Disintegration time (sec.)	24	27	32	21	23	27
% Drug content	98.53	96.33	101.43	99.57	101.89	98.93

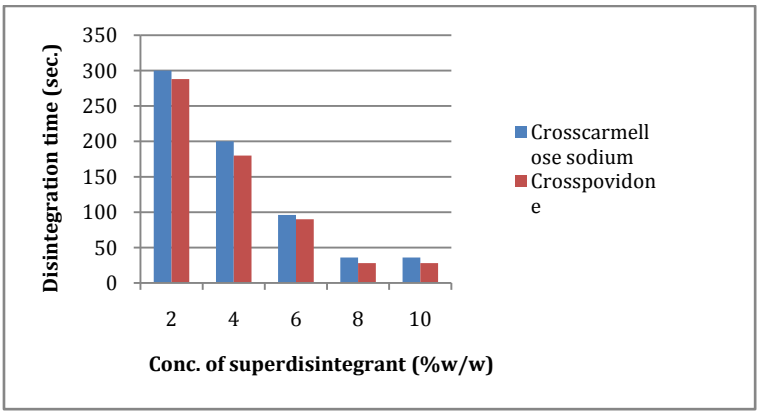

Fig. 1: Optimisation of superdisintegrant concentration

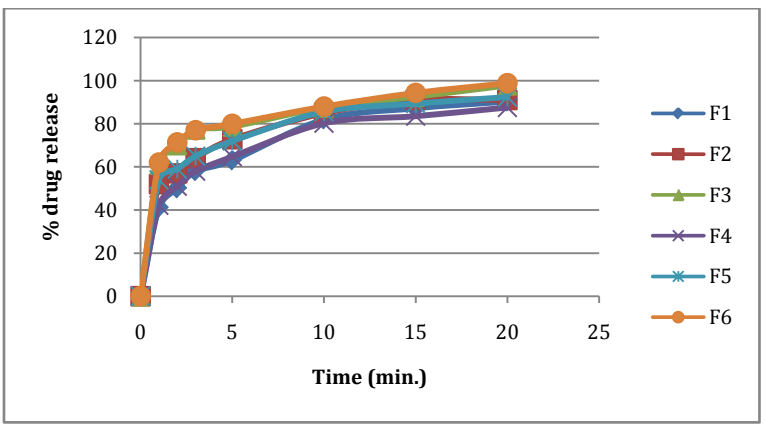

Fig. 2: Dissolution study of ODT of tinidazole containing Indion 294

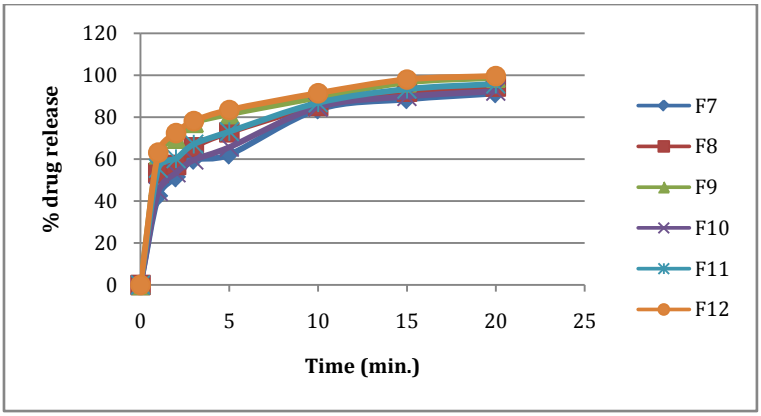

Fig. 3: Dissolution study of ODT of tinidazole containing Indion 204

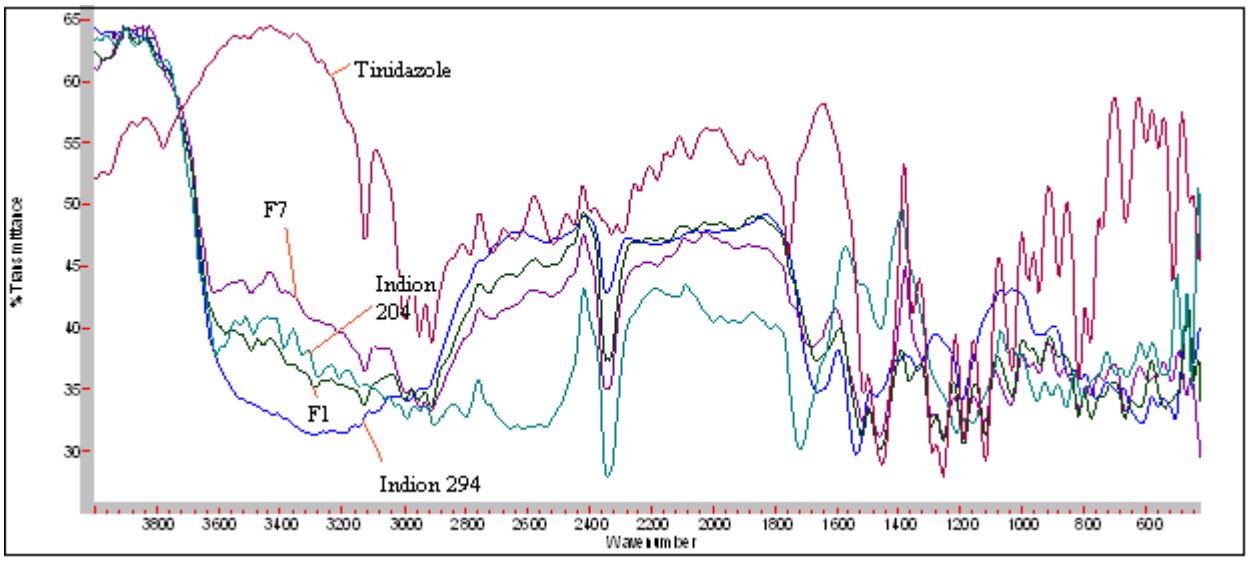

Fig. 4: FTIR overlay of Tinidazole, Indion 204, Indion 204, F_1 and F_7

CONCLUSION

The orally disintegrating tablet of tinidazole using Indion 294 and Indion 204 as taste masking agent in the ratio 1:1.5 containing crosspovidone (8 %w/w) as superdisintegrant have acceptable taste with sufficient hardness, disintegration time and dissolution rate. So this can be used in patients having swallowing problem and geriatric and paediatric patients.

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