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Research Article

FORMULATION DESIGN AND OPTIMIZATION OF AN ENTERIC COATED SUSTAINED RELEASE MUCOADHESIVE TABLET OF METRONIDAZOLE

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ABSTRACT

The purpose of my study was to formulate and evaluate the mucoadhesive tablet of metronidazole for the treatment and management of Amoebaisis. Metronidazoleis a nitro-imidazole antibiotic medication used particularly for anaerobicbacteria and protozoa. Metronidazole is an anti-bacterial against anaerobic organisms, amoebicide and anti-protozoa. It is the drug of choice for first episodes of mild-to-moderate *Clostridium difficile* infection.

Mucoadhesion is a field of current interest in the design of drug delivery systems. Mucoadhesive drug delivery system prolong the residence time of the dosage form at the site of application or absorption and facilitate an intimate contact of the dosage form with the underline absorption surface and thus contribute to improved and or better therapeutic performance of the drug. In recent years many such mucoadhesive drug delivery systems have been developed for oral, buccal, nasal, rectal and vaginal routes for both systemic and local effects. The mucoadhesive tablet was prepared by wet granulation. The mucoadhesive tablets were coated with Eudragit S-100 by dip coating method. The prepared mucoadhesive tablets were evaluated by hardness, friability, weight variation, wash off test, in -*vitro* drug release.

Keywords: Mucoadhesive drug delivery system, wet granulation method, enteric coating.

INTRODUCTION

Mucoadhesion is defined as the adhesion between two materials, at least one of which is a mucosal surface. Mucoadhesion is a current interest in the designing of drug delivery systems. Mucoadhesive drug delivery system may be designed to enable prolonged residence time of the dosage form at the site of application or absorption. Facilitate an intimate contact of the dosage form. The idea behind designing mucoadhesive tablet is to build a sustained release formulation anddanger of modification in drug release profile. Extending the residence time of a dosage form at a particular site and controlling the release of drug from the dosage form are useful especially for achieving controlled plasma level of the drug as well as improving bioavailability.

Metronidazole is used for the management of amoebaisis. The site of absorption of metronidazole is in the whole GI tract and has a long half life of 8 h. The aim of the study was to develop a sustained releasemucoadhesivedosage form of metronidazole using Chitosansodium alginate, and Eudragit S-100 as coating material in the treatment of amoebaisis[1,2].

Significance

Aprolonged residence time at the site of drug action or absorption. A localization of drug action of the delivery system at a given target site. An increase in the drug concentration gradient due to the intense contact of particle with the mucosal. A direct contact with intestinal cells that is the first step before particle absorption. Ease of administration. Offers an excellent route, for the systemic delivery of drugs with high first pass metabolism, there by offering a greater bioavailability. A significant reduction in dose can be achieved there by reducing dose related side effects.

MATERIALS AND METHODS

Metronidazole as a gift sample from (La Pharma,Ludhiana),Chitosan, Sodium alginate and Eudragit S-100 was purchased from the Balaji Pharmaceutical pvt.ltd.

Preparation of mucoadhesive tablet

I. Metronidazole ,Chitosan and Sodium alginate were weighed and passed through sieve number 60.
II. Now add 10% of starch paste until wet mass is formed pass wet mass through sieve number 12.
III. Wet granules were dried at 60^{0}C for half an hour ,after then dried granules were passed through sieve number 12 to form a uniform sized granules.
IV. Granules were lubricated with talc and magnesium stearate.
V. Granules were compressed in tablet form by using tablet punching machine(DhimanUdyog India).

Coating of Mucoadhesive tablet

Metronidazole tablet was coated with Eudragit S-100 by dip coating method. Tablet was dipped in Eudragitcoating solution prepared by dissolution of 500mg of Eudragit S-100 in 10 ml of Ethanol: Acetone (2:1). Then dried at 45^{0}C temperature[3].

Evaluation of Mucoadhesive tablet

Evaluation of granules

1) Bulk density = *U =M/Vb*

(M = Mass of microspheres (g), Vb= volume of microspheres, after three tapping)

2) Tapped density = *b = m/vt*

(m = mass of microspheres (g), Vt= volume of microspheres ,final tapped volume)

3) **Carr's Index** = $\frac{\text{tappeddensity} - \text{bulkdensity}}{\text{tappeddensity}} \times 100$

4) **Hausner'sratio** = = $\frac{\text{tappeddensity}}{\text{bukdensity}}$

5) **Angle of repose**= $\theta = \text{Tan-1}(h/r)$

(θ = Angle of Repose, h= height of the heap, r= radius of the heap formed)

Evaluation of tablets

1. Weight Variation
2. Friability
3. Wash off test
4. In –vitro drug release

CONCLUSION

The successful sustained release can be achieved by protecting the drug from absorption in the environment of the upper GIT. The results demonstrated that Eudragit S-100 coated mucoadhesive tablet have the potential carrier to be used as drug delivery system.

RESULTS AND DISCUSSION

Table 1: Composition of Mucoadhesive Tablet

S. No	Formulation Code	Drug(mg)	Chitosan (Polymer) (mg)	Sodium Alginate(Polymer) (mg)
1.	F1	200	0	**180**
2.	F2	200	30	**150**
3.	F3	200	80	**100**
4.	F4	200	90	**90**
5.	F5	200	100	**80**
6.	F6	200	150	**30**
7.	F7	200	180	**0**

Table 2: Solubility of the drug

S. No.	Properties	Volume used in ml	Observation
1.	Water	110	Slightly Soluble
2.	Ethanol	102	Slightly Soluble
3.	Acetone	112	Slightly Soluble

- **UV Spectroscopy (λmax Determination)**

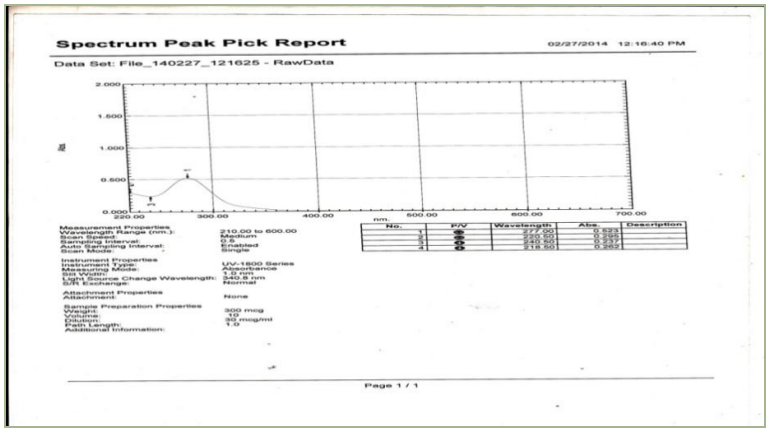


Fig. 1: UV Spectrum of Metronidazole in Methanol

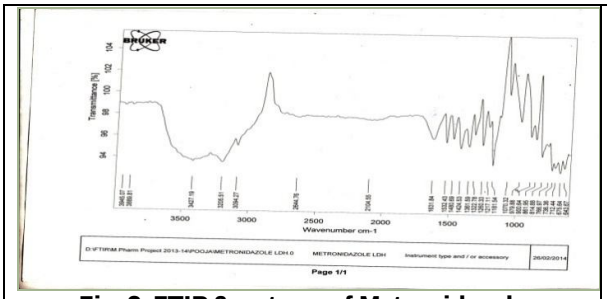


Fig. 2: FTIR Spectrum of Metronidazole

S. No.	Groups	Wavenumber Observed (cm^{-1})
1.	N-H	3453.77
2.	$-NO_2$	1633.53
3.	-OH	1264.87
4.	C=O	643.22

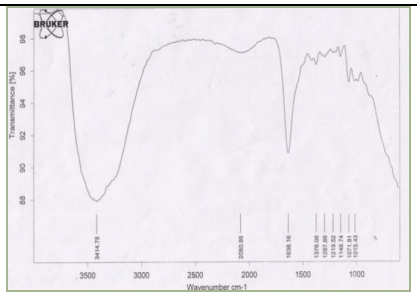


Fig. 3: FTIR Spectrum of Chitosan

S. No.	Groups	Wavenumber Observed (cm^{-1})
1.	-OH Free	3414
2.	CH_2OH	1015
3.	CH-OH	1071
4.	C-O-C	1219

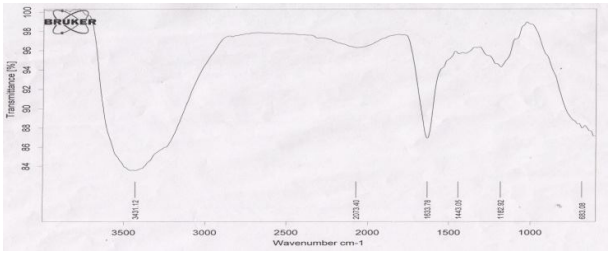
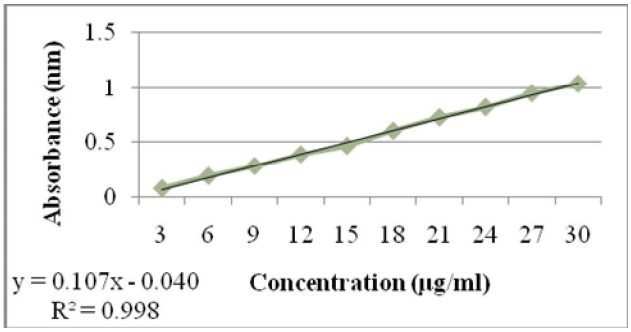


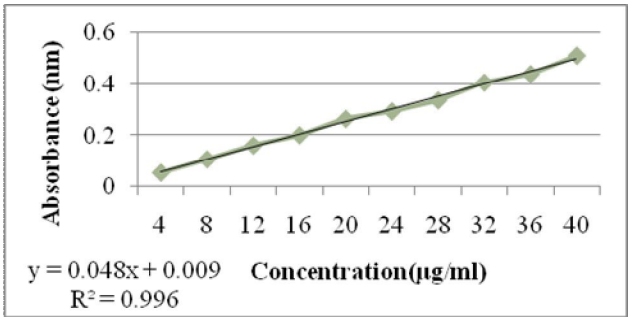
Fig. 4: FTIR Spectrum of Eudragit S-100

S. No.	Groups	Wavenumber Observed (cm^{-1})
1.	C-O	1182
2.	C=O	1633
3.	C-H-CH_2	1443
4.	-OH Strech	2073

- **Standard Curve of Metronidazole**



A



B

Fig. 6: Standard Curve of Metronidazolein
A) 0.1N HClpH 1.2
B) Phosphate buffer

Table 3: Evaluation of granules

S.No.	Formulation	Bulk Density (g/cm^2)	Tapped density (g/cm^3)	Carr's Index (%)	Hausner's Ratio	Angle of repose
1	F1	0.50	0.58	13.79	1.16	35.37
2	F2	0.45	0.52	13.46	1.16	34.99
3	F3	0.41	0.48	13.58	1.17	34.60
4	F4	0.46	0.52	11.5	1.13	33.61
5	F5	0.44	0.50	12.00	1.12	33.82
6	F6	0.52	0.58	11.23	1.13	32.61
7	F7	0.47	0.53	11.32	1.12	31.38

Table 4: Thickness, Width, Weight Variation

S.No.	Formulation Code	Thickness(mm)	Width(mm)	Weight Variation(mg)
1	F1	4.07	12.17	400
2	F2	4.06	12.16	399
3	F3	4.08	12.18	395
4	F4	4.09	12.17	397
5	F5	4.10	12.13	392
6	F6	4.12	12.18	391
7	F7	4.16	12.17	396

Table 5: Hardness and Friability

S.No.	Formulation Code	Hardness(kg/cm^2)	Friability(%)
1	F1	3.16	0.81
2	F2	3.22	0.86
3	F3	3.20	0.55
4	F4	3.32	0.70
5	F5	3.41	0.75
6	F6	3.17	0.91
7	F7	3.25	0.76

Table 6: Detachment Time exhibited by the formulated tablets

Formulation Code	No. of tablets	Detachment time (mm)
F1	1	473
F2	1	404
F3	1	361
F4	1	433
F5	1	370
F6	1	418
F7	1	370

Table 7: In vitro dissolution studies (For Uncoated Tablets)

Time (hrs)	F1(%)±S.D.* S:180 C:00	F2(%)±S.D.* S:150 C:30	F3(%)+S.D.* S:100 C:80	F4(%)+S.D.* S:90 C:90	F5(%)+S.D.* S:80 C:100	F6(%)+S.D.* S:30 C:150	F7(%)+S.D.* S:00 C:180
2	11.14±0.05	11.25±0.54	11.27±0.51	11.31±0.63	11.30±0.19	11.14±0.45	11.04±0.65
5	31.12±1.40	31.11±1.15	32.24±2.19	38.10±1.28	35.21±1.25	36.17±1.25	35.20±1.69
7	54.46±1.74	60.41±1.65	63.30±1.55	69.09±2.09	66.24±2.03	68.18±2.35	65.37±1.36
9	74.99±1.81	79.87±2.08	81.82±2.04	90.51±1.65	89.76±1.43	85.19±1.96	82.83±2.06
12	82.81±2.15	85.74±1.32	86.72±1.93	94.46±1.95	90.66±1.65	91.66±2.46	93.75±1.98

*values are mean ±SD. Number of determination =3 , S =Sodium alginate, C = Chitosan

EVALUATION OF PARAMETERS OF COATED MUCOADHESIVE TABLETS

In vitro dissolution studies of mucoadhesive tablets of metronidazole of batch F1coated with 1%, 2% eudragit solution.

S. No.	Time(hrs)	Batch F1 (% Release±S.D.*)	
		Coated with 1%	Coated with 2%
1	2	9.65±0.36	7.15±0.05
2	5	29.86±1.86	11.05±1.40
3	7	49.77±1.57	25.54±1.77
4	9	65.32±1.38	32.36±1.81
5	12	75.12±1.95	65.66±1.62

*values are mean ±SD. Number of determination =3

In vitro dissolution studies of mucoadhesive tables of metronidazole containing 200 mg dose coated with 2 % eudragit solution.

Table : Percent Release comparison of mucoadhesive tablets of metronidazole containing 200 mg coated with eudragit 2% solution

Time (hrs)	F1(%)±S.D.*	F2(%)±S.D.*	F3(%)±S.D.*	F4(%)±S.D.*	F5(%)±S.D.*	F6(%)±S.D.*	F7(%)±S.D.*
2	6.15±0.85	6.34±1.15	6.96±2.09	6.82±1.08	6.72±1.36	6.80±1.23	6.74±1.63
5	11.05±1.40	11.12±1.52	11.79±1.47	12.2±2.00	12.02±1.08	12.15±1.74	12.11±1.03
7	24.56±1.77	25.52±1.97	30.36±1.68	41.90±1.32	33.28±1.79	38.11±1.46	35.22±2.11
9	33.35±1.81	34.31±1.38	38.21±1.35	53.70±1.59	42.09±1.48	49.82±1.57	45.22±1.51
12	50.78±2.68	52.72±1.20	57.57±1.47	69.23±1.68	62.421.27	64.39±1.29	60.54±60.51

*values are mean ±SD. Number of determination =3

The F4 formulation gives the best result as compared to the other formulations.

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