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RESEARCH ARTICLE

FORMULATION AND EVALUATION OF TINIDAZOLE ENTERIC COATED TABLETS FOR COLON TARGETING DRUG DELIVERY SYSTEM

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Abstract

Aim and Objective: Colon-specific delivery systems have garnered significant attention for their capacity to localize therapy within the large intestine, thereby enhancing treatment efficacy for colonic disorders and reducing systemic toxicity.
Methods: Core tablets containing tinidazole were prepared using a variety of polymers in distinct ratios, followed by application of an enteric coating. Pre-compression evaluation included assessment of powder flow characteristics and compatibility checks between the drug and excipients via FT-IR spectroscopy, with all batches demonstrating no evidence of interaction. Post-compression, tablets were tested for weight uniformity, mechanical strength, friability, and content uniformity, alongside in vitro dissolution studies under conditions simulating gastrointestinal transit.
Results: All formulations exhibited acceptable chemical and physical properties, with assay values ranging from 98.44 % to 99.89 %, indicating consistent drug loading across batches F1 through F5. The F5 batch emerged as the optimal candidate, sustaining tinidazole release for six hours and achieving a cumulative release of 98.32 %. Stability testing of F5 at 45°C and 75 % relative humidity over three months revealed no significant changes in performance or integrity. Consequently, formulation F5 is proposed as a robust platform for targeted colonic delivery of tinidazole.
Conclusion: The investigation achieved the formulation of enteric-coated tinidazole tablets optimized for oral delivery and targeted release in the distal gastrointestinal tract.
Keywords: Compatibility testing, colon-targeted drug, enteric coated tablets, gastro intestinal tract, tinidazole.

INTRODUCTION

Colon-targeted drug delivery has attracted growing interest because it can concentrate therapy within the large intestine and limit systemic exposure. Examples of colonic disorders include: crohn's disease, ulcerative colitis, irritable bowel syndrome. Delivering medication directly to the colon bypasses release and absorption in the upper gastrointestinal tract, allowing higher local drug levels with minimal systemic uptake[1]. The extended residence time in the colon often up to five days combined with the absorptive capacity of the colonic mucosa makes this site particularly advantageous for controlled release formulations. Drugs destined for the colon may be administered orally or rectally, but oral systems remain the preferred choice due to patient convenience, flexible manufacturing options, and improved compliance[2].

The performance of a colon-specific formulation depends on the drug's physicochemical profile, the design of the delivery system, gastrointestinal transit dynamics, and interactions with the intestinal environment. Strategies typically focus on preventing premature release until the formulation reaches the distal gut.

Tinidazole, an imidazole derivative, is widely prescribed for protozoal infections such as trichomoniasis, giardiasis, and amoebiasis. Its primary targets include Trichomonas vaginalis, Trichomonas foetus, and Entamoeba histolytica[3]. Although conventional oral tablets of tinidazole achieve rapid and complete absorption, this profile limits local drug availability in the colon and can elicit systemic side effects. Therefore, there is a clear need for a delivery system that ensures controlled release of tinidazole at the colonic site of infection[4].

The present work aims to develop and assess enteric-coated tinidazole tablets engineered for colon targeting. It also evaluates how varying concentrations of hydroxyllpropyl methylcellulose affect tablet hardness, friability, and drug release kinetics.

MATERIALS AND METHODS

Tinidazole, Azal Industries, Khartoum, Sudan. Maize starch, Riddhi siddhi gluco boils limited, India. Talc, Golcha associated exports, India. Magnesium stearate, united pharma industries, China. Microcrystalline cellulose, Gujarat microwax private limited, India. Hydroxyl propyl methyl cellulose (606), Shin-etsu chemical co. LTD, Japan. Hydroxyl propyl methyl cellulose (E5), Shaudeng head co. LTD, China.

Compatibility study of tinidazole and excipients

Infrared spectra of pure tinidazole and each excipient were collected over the 400-4000 cm^{-1} range using a Fourier transform infrared spectrometer to identify any interactions. Samples were prepared by the potassium bromide disk method, and the resulting spectra were examined for shifts or alterations in characteristic absorption bands[5].

Method of Preparation of Tinidazole Core Tablets

Accurate weights of Tinidazole (1 kg) and micro-crystalline cellulose (0.166 kg) were mixed (in high speed mixer) for five minutes. A paste of maize starch was prepared by mixing maize starch (0.103 kg) with cold water (20 ml) in a conical flask and then distilled water was added in paste kettle and allowed to boil. After that the solution of maize starch was added, and stirred well till a paste was formed. An accurate weight of hydroxyl propyl methyl cellulose was dissolved in water for 30 minutes, and added it with the maize starch paste to the mixed material placed in high speed mixer granulator (Tinidazole and micro-crystalline cellulose), then mixed till obtain good granules. The wet granules were placed in fluid bed dryer for 30 minutes (with additional 15 minutes in some formulations) until complete drying, then milling the dry granules (in multi mill) using mesh number 2, finally talc (0.011 kg) and magnesium stearate (3.6 kg) were added to the meshed granules and mixed properly for 10 minutes. The powder was compressed (rotary tablet press) to tablets using punches and disc (size 18×8.5 mm). The different formulations prepared in this study which designated as K1, K2, F1- F5 are shown in the Table 1[6].

Table 1: Composition of Tinidazole core tablets.

Ingredients	Formulation Code						
	K1	K2	F1	F2	F3	F4	F5
Tinidazole	400	400	400	400	400	400	400
HPMC 606	-	200	-	25	75	-	-
HPMC E5	150	-	-	-	-	25	75
Maize starch	30	30	51.9	51.9	51.9	51.9	51.9
Microcrystalline cellulose	140	115	83.35	83.35	83.35	83.35	83.35
Sodium carboxy methyl cellulose	30	30	-	-	-	-	-
Talc	2	2	5.6	5.6	5.6	5.6	5.6
Magnesium stearate	2	2	1.8	1.8	1.8	1.8	1.8
Tablet Total	724	749	542.65	567.65	617.65	567.65	617.65

Method of preparation of enteric coating of tinidazole tablets

Distilled water (900 ml) was placed in magnetic stirrer and mixed till vortex was formed. The coating material (Titanium dioxide) was added as fast as possible into the vertex without allowing the powder to float on the surface and was allowed to stir for 30 minutes and then propylene glycol was added and continued stirring for 10 minutes. The suspension was stirred gently while coating the tablets[7].

Evaluation of tinidazole granules:

The prepared granules were assessed for bulk density, tapped density, Carr's index, Hausner ratio, and angle of repose.

Evaluation of enteric coated tinidazole tablets

Weight variation test

Twenty tablets were randomly selected to establish the mean tablet mass. Each unit was then weighed individually, and its mass was compared against the calculated average to determine any deviations[8]. Compliance with USP (2016) was established if, among the twenty units tested, no more than two tablets deviated by more than ±5% from the mean mass and no single tablet exceeded a ±10% deviation. Tablets meeting these conditions were deemed acceptable[9].

Hardness test

Tablet crushing strength, essential for withstanding stresses during storage, transportation, and handling, was evaluated using a Monsanto hardness tester. Hardness readings were expressed in kg/cm^2, and all measurements followed the procedures outlined in USP (2016)[9].

Friability test

Friability, an indicator of robustness of a tablet, was measured using an Erweka Friabilator. Twenty tablets were accurately weighed and subjected to rotation at 25 revolutions per minute, causing them to fall approximately six inches with each turn. After four minutes of tumbling, the tablets were reweighed and the percentage weight loss was calculated. Tablets losing less than 0.5–1.0% of their mass are considered acceptable. All procedures followed USP (2016) guidelines[10].

Thickness test

Tablet thickness was assessed using a vernier caliper. Ten units from each formulation were measured, and the mean thickness was computed, in accordance with USP (2016) guidelines.

***In–vitro* drug release study**

The release profile was evaluated using USP Type I (basket) apparatus at 50 rpm, with the dissolution vessel maintained at 37±0.5 °C. For the first two hours, 500 mL of 0.1 N HCl (pH 1.2) was employed to simulate gastric conditions, corresponding to average stomach transit time. After two hours, the acid medium was replaced with 500 mL of phosphate buffer (pH 6.8) to replicate intestinal fluid, and testing continued for six more hours to cover typical small-intestinal passage. At the five-hour point, the medium was again exchanged this time with 500 mL of phosphate buffer at pH 7.4 to mimic colonic conditions, and sampling was extended for an additional 19 hours. Ten-milliliter aliquots were withdrawn at predetermined intervals and immediately replaced with fresh medium. Tinidazole concentration in each sample was quantified by UV spectrophotometry at 319 nm[9].

Absolute Drug Content

An accurately weighed sample equivalent to one tablet was obtained by crushing five pre-weighed units. The powdered material was transferred into a 500 mL volumetric flask, brought up to volume with 0.1 M NaOH, and filtered. The absorbance of the filtrate was then measured at 319 nm using a UV–visible spectrophotometer.

Stability Study

The optimal tablet formulation was subjected to an accelerated stability protocol as per ICH Q1A(R2) guidelines. Present stability data in tabular form, showing means and standard deviations for each property at every time point. Plotting assay and key physical parameters against time will help visualize any trends toward degradation or physical change.

Statistical Analysis

The results are presented as mean ± standard deviation, calculated using Microsoft Excel 2010. Statistical analyses were performed with SPSS for Windows, version 20.0 (SPSS Inc., September 2011).

RESULTS AND DISCUSSION

Compatibility Studies

Compatibility between the active ingredient and excipients was evaluated using a Fourier transform infrared spectrophotometer (FT-IR), with IR spectra recorded for pure tinidazole and for the drug–excipient mixtures (different hydroxy propyl methyl cellulose) are determined (Table 2).

IR spectra of individual Tinidazole and the combination of drug with polymers (different hydroxy propyl methyl cellulose) indicate that there was no interactions between the drug and both hydroxy propyl methyl cellulose.

Evaluation of tinidazole granules

The angle of repose values obtained for the formulations ranged from 24.33 to 30.40 which indicate that the powder has excellent flow property. The bulk density values ranged from 0.43 to 0.59. The tapped density values ranged from 0.49 to 0.68 (Table 2). The compressibility index values for the formulations (F2, F5 and K2) ranged from 12.24 to 15.68 which indicate good compression properties whereas the formulations (F1 and K1) show fair compression properties because compressibility index exceed 21. The Hauser's ratio values for the formulations (K2, F2, F5) ranged from 1.14 to 1.16 which indicate good flow properties as they are below 1.18[10], whereas the F1 and K1 showed possible flow properties.

Table 2: FT-IR Interpretation.

S. N.	Interpretation	FT-IR absorption bands		
		Pure drug	Drug + PHMC E5	Drug +HPMC 606
1	NO_2 stretching mode	1537.16	1537.16	1537.16
2	C-N stretching mode	1188.07	1186.14	1151.42
3	C=C stretching mode	1934.47	1639.38	1641.31
4	C-H Stretching mode	2948.96	2941.24	2929.67

Evaluation of enteric coated tinidazole tablets

Core tinidazole tablets were prepared using various polymers at different ratios and then coated with an enteric polymer. Table 4 represents the weight variation, hardness, friability, and thickness test results for all colon-targeted matrix tablet formulations. The results show that weight variation across all formulations remained within the USP limit of 5%, and tablet thickness was consistent and reproducible. The measured hardness of formulations (K1 and K2) was below the recommended range 5.8 therefore it failed to pass. The formulations (F1- F5) were ranging from 5.8 – 6.5 kg/cm^2 which show a good hardness[10].

Table 3: Results of evaluation of Tinidazole granules.

Code	Bulk density (gm/cc)	Tapped density (gm/cc)	Compressibility index (%)	Hauser's ratio	Angle of repose
K1	0.43	0.55	27.9	1.27	24.33
K2	0.51	0.59	15.68	1.15	28.81
F1	0.46	0.56	21.39	1.19	25.42
F2	0.59	0.68	13.04	1.15	29.19
F3	0.49	0.57	14.04	1.16	30.40
F4	0.43	0.49	12.24	1.14	26.72
F5	0.55	0.64	14.06	1.16	26.21

Table 4: Results of evaluation of enteric coated Tinidazole tablets.

Formulation code	Hardness (kg/cm^2)	Weight variation (%)	Friability (%)	Content uniformity (%)
K1	5.2±0.23	-	-	-
K2	5.4±0.32	-	-	-
F1	5.8±0.21	642.65± 0.32	0.98	98.64
F2	5.9±0.1	667.65± 0.36	0.43	99.16
F3	6.0±13	717.65± 0.24	0.24	98.44
F4	6.2±0.12	667.65± 0.21	0.21	99.89
F5	6.5±13	717.65± 0.28	0.16	99.35

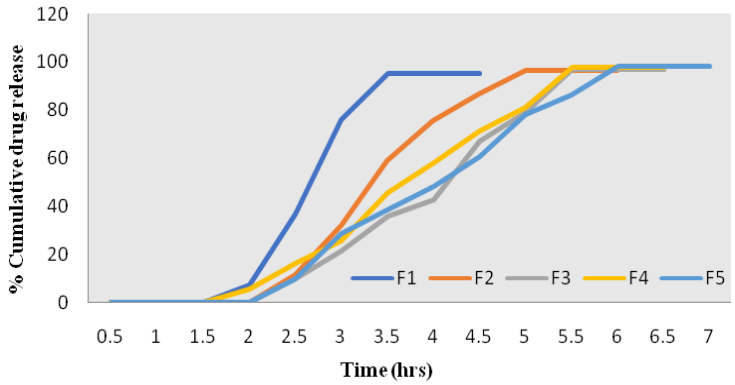

Figure 1: Dissolution profile for the formulations.

The hardness of the tablets determined that as the amount of hydroxyl propyl methyl cellulose increased. The friability values were found to be less than 1% in the formulated tablets (F1- F5) which are considered to be acceptable[10].

***In–vitro* drug release study**

The release profile of Tinidazole from the enteric coated tablets of different formulations were investigated. Upon using 0.1 N HCl as dissolution medium, for 2 hours. No drug release was recorded during this time from F2, F5 but there was drug release recorded in F1. Then the same formulations were subjected to *in vitro* dissolution test with of Phosphate buffer for next 8 hrs. It was found that the release of drug in F5 which contain hydroxyl propyl methyl cellulose E5 gave the best release. The sustainability of the drug in F5 was found to show better targeted site controlled drug delivery, as it showed 98.32% drug release for 6 hours (Figure 1).

Content uniformity

Drug content was determined (Table 4) and described which was in the range of 98.44 to 99.89 % which indicating good content uniformity in the all formulations[7].

Table 5: The accelerated stability study test for the formula (F5).

Test time	Average weight (mg)	Hardness (kg/cm^2)	Friability (%)	Content %
Zero Time	717.65± 20	6.5±0.3	0.16	99.35
1 month	717.65± 20	6.6±0.2	0.16	99.35
2 months	712.65± 40	6.5±0.5	0.16	99.10
3 months	713.65± 30	6.9±0.2	0.15	98.80

Stability study

Accelerated stability testing of the optimal formulation (F5) demonstrated that after three months of storage under ICH conditions, the matrix tablets maintained their organoleptic and physicochemical properties as well as their drug content (Table 5). Consequently, F5 satisfies the stability requirements set forth by the ICH guidelines.

Limitations of the study

Kinetic analysis of the release data of Tinidazole from developed formulations must be established and calculated and further preclinical and clinical studies are required. Further research work can proceed to combine various polymers to get the best formulation, and in vivo performance of these formulations should also be investigated.

CONCLUSIONS

The study had successfully formulated enteric coated tablets of Tinidazole for oral administration, with a view of targeting the drug to lower part of gastro intestinal tract. The identification and compatibility studies showed that active ingredient used was Tinidazole and determined that there were no interactions between the active ingredient and the excipients. The pre-compression study indicates that the granules of the formulations (F1-F5) have excellent flow properties and compression properties. The weight variation of the tablets was within the limits of 5%. The measured hardness of the formulations (F1-F5) was ranged from 5.8-6.5 kg/cm^2 which are acceptable. When the amount of hydroxy propyl

methyl cellulose increased the hardness of the tablets increased. Friability values were found to be less than 1% formulations (F1-F5) and considered to be successfully. Therefore, the friability decreased as the amount of hydroxy propyl methyl cellulose increased.

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AUTHOR'S CONTRIBUTION

Magbool FF: conceived the research idea, designed the work, carried out the experiment. **Elnima EI:** wrote the first draft of the manuscript, supervised the study. **Shayoub ME:** critical review, formal analysis. All authors read and approved the final version of the manuscript for publication.

DATA AVAILABILITY

Data will be made available on request.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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