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FORMULATION AND EVALUATION OF SECNIDAZOLE CONVENTIONAL TABLETS BY DIRECT COMPRESSION METHOD

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ABSTRACT

Among the different routes of administration, the oral route of administration continues to be the most preferred route due to various advantages including ease of ingestion, avoidance of pain, versatility and most importantly patient compliance. The different dosage forms include tablets and capsules. Recently immediate release tablets have started gaining popularity and acceptance as a drug delivery system, mainly because they are easy to administer and lead to better patient compliance. The present work involves the formulation development, optimization and in-vitro evaluation of immediate release secnidazole tablets. To minimize critical process parameters and since secnidazole is hygroscopic in nature, direct compression method was selected for the formulation of immediate release secnidazole tablets. The objective of present study was to formulate and evaluate immediate release secnidazole tablets: comparative study of different diluents (Dicalcium phosphate, starch, lactose) with various concentrations by direct compression method which are simple and cost effective. Nine formulations were conducted F1 to F9 for selection optimum concentration of diluent. Immediate release secnidazole tablets were evaluated for various pre and post compression parameters. The optimum formulation was chosen and their optimum results were found to be in close agreement with experimental finding.

KEYWORDS

Secnidazole, Immediate release tablets, diluents, direct compression

INTRODUCTION

An immediate release dosage form allows a manufacturer to extend market exclusivity, while offering patients a convenient dosage form or dosage regimen. Immediate Release Tablets are those tablets which are designed to disintegrate and release their medication with no special rate controlling features, such as special coatings and other techniques[1]. Immediate release and fast dispersing drug delivery system may offer a solution to these problems. Recently immediate release tablets have started gaining popularity and acceptance as a drug delivery system, mainly because they are easy to administer, has quick onset of action is economical and lead to better patient compliance[2]. They are also a tool for expanding markets, extending product life cycles and generating opportunities.

Protozoal infections are more common among people in the under developed tropical countries and subtropical countries where sanitary conditions, hygienic practises and control of the vectors of transmission are inadequate[3]. Amoebiasis is caused by Entamoeba Histolytica, named for its lytic action on tissues. The disease can be acute or chronic with patients showing varying degrees of illness, from no symptoms to fulminating dysentery[7]. Secnidazole is the drug proposed for the present

study. It is used in the treatment of amoebiasis, giardiasis, and trichomoniasis. Chemically Secnidazole is 5-Nitroimidazole derivative, it is 1-[2-Hdroxy]-2-methyl-5Nitroimidazol[4]. It works by forming reactive oxygen intermediate which cause damage to the DNA.

MATERIALS AND METHODS

Materials:

Secnidazole is obtained from Qualitek Pharma. All other chemicals were of analytical grade.

Preparation of Immediate Release Tablets:

All the ingredients were accurately weighed as per formula F1 to F9 which is shown in **Table 1** and were dispensed in clean polythene covers. Secnidazole and diluents were accurately weighed, geometrically mixed and passed through #80 mesh and then, micro crystalline cellulose, common diluents and pvpk-30(binder) were accurately weighed and passed through #20 mesh. Both mixtures are transfer into the V-cone blender for 10 minutes. Then, magnesium stearate was passed through #40 meshes; added to the mixture in the V-cone blender and the blend for 5 minutes. Then the powder was compressed into tablets using 16 stations rotary compressed machine with punch size 9.0 mm.

Table No: 1
Formulation of Immediate Release Tablets Of Secnidazole

Ingredients (mg Per Tablets)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Secnidazole	200	200	200	200	200	200	200	200	200
Microcrystalline Cellulose	160	110	60	160	110	60	160	110	60
Di Calcium Phosphate	100	150	200						
Starch				100	150	200			
Lactose							100	150	200
Pvpk-30	25	25	25	25	25	25	25	25	25
Magnesium Stearate	15	15	15	15	15	15	15	15	15
Total tablet weight (mg)	500	500	500	500	500	500	500	500	500

EVALUATION OF IMMEDIATE RELEASE TABLETS

Pre compression parameters

Angle of repose

Angle of repose (θ), the blend was poured through the walls of a funnel, which was fixed at a position such that its lower tip was at a height of exactly 2.0 cm above hard surface. The blends were poured till the time when upper tip of the pile surface touched the lower tipoff the funnel. The **tan^{-1}** of the (height of the pile/radius of its base) gave the angle of repose[5].
(**Table no: 2**)

$$tan\theta = h/r$$

Where, h is height of powder cone, r is radius of powder cone.

Bulk density and tapped density

Blends were poured gently through a glass funnel into a graduated cylinder cut exactly to 10 ml mark. Excess blend was removed using a spatula and the weight of the cylinder with pellets required for filling the cylinder volume was calculated. The cylinder was then tapped from a height of 2.0cm until the time when there was no more decrease in the volume. Bulk density (BD) and tapped density (TD) were calculated[5]. (**Table no: 2**)

Bulk density= weight of the blend/ untapped volume

Tapped density= weight of the blend/tapped volume

Hausner's ratio and compressibility index

Hausner's ratio (H_R) and Carr's compressibility index (I_C) were calculated according to the two equations given below: (**Table no: 2**)

H_R = TD/BD

I_C = (TD- BD)/TD * 100

Table no: 2
Precompression Parameters

Property	F1	F2	F3	F4	F5	F6	F7	F8	F9
Angle of Repose	30.34	28.58	27.24	25.56	26.32	25.01	35.32	27.12	31.53
Bulk Density gm/cm^3	0.475	0.432	0.421	0.452	0.488	0.456	0.469	0.441	0.522
Tapped Density gm/cm^3	0.586	0.502	0.515	0.567	0.539	0.553	0.585	0.572	0.663
Compressability Index (%)	18.94	16	16	15.17	16.18	14.19	19.82	22.80	21.26
Hausner's Ratio	1.236	1.903	1.190	1.192	1.204	1.173	1.24	1.30	1.27

Post compression parameters

Uniformity of weight

Twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight[6]. (**Table no: 3**)

Table no: 3
Post Compression Parameters

Property	F1	F2	F3	F4	F5	F6	F7	F8	F9
Uniformity of Weight (mg)	502	501	504	501	504	496	501	501	500
Hardness (N)	4.5	4.8	4.9	5.1	4.2	4.6	5.2	5.1	5.0
Friability (%)	0.412	0.510	0.436	0.430	0.654	0.550	0.477	0.410	0.385
Disintegration Time (minutes)	12	15	14	12	11	18	10	16	11
Drug Content Uniformity (mg/tab)	496	495	501	499	498	496	501	498	498

Hardness

Hardness was determined by taking six tablets from each formulation, using a Monsanto Hardness Tester. (**Table no: 3**)

Friability

The friability of sample of six tablets was measured using a Roche Fribilator. Six pre-weighed tablets were rotated at 25 rpm for 4 minutes. The tablets werethen reweighed after removal of fine's using 60 mesh screens and the percentage of weight loss was calculated. (**Table no: 3**)

Friability = [(Initial weight-Final weight) / Initialweight)] x100 [%]

Disintegration time

Disintegration time was measured in 900 ml 0.1N HCl according to the USP 24 method without disc at 37 ± 0.5oC temperature. The disintegration time of 6 individual tablets were recorded and the average was reported. (**Table no: 3**)

Drug content uniformity

From each batch three randomly selected tablets were weighed accurately and powdered in a glass motor with pestle. Powder equivalent to 500 mg of drug was transferred into 100ml volumetric flask containing little amount of methanol, the remaining volume is made up to 100 ml of methanolic acid shake it for 24 hours and filter the solution, make up desired dilutions and analyzed for drug content spectrophotometrically at 320.5nm against a blank tablet prepared in same manner. (**Table no: 3**)

In-Vitro Drug Release Study:

In-vitro drug release studies were carried out using 900 ml of 0.01N Hydrochloric acid as dissolution medium using USP Apparatus-II (Electro lab) at 100 rpm and the temperature

was maintained at 37±0.5°C. The dissolution was continued for 45minutes while samples of 10ml were withdrawn at regular interval and replaced with equal volume of fresh dissolution medium to maintain the volume constant. The samples were filtered, diluted and analyzed for drug content. The amount of drug released was determined by UV at 320.5 nm. (**Table no: 4**) and (**Figure no: 1-3**)

Table no: 4
Dissolution Profile

Formulation	Time in minutes				
	0min	10min	20min	30min	45min
F1	0	63	71.8	80.5	87.8
F2	0	63.8	72	83	89.2
F3	0	64.6	75.5	83.5	93.5
F4	0	66.6	75.5	86.3	92.4
F5	0	66	76.3	85.5	95.2
F6	0	67.3	76.2	86.5	97.3
F7	0	77.6	90.2	99.5	100.1
F8	0	66.8	76.8	87.8	97.3
F9	0	64.2	73.5	85.5	93.5

Figures No: 1 Dissolution profile of Dicalcium Phosphate (DCP)

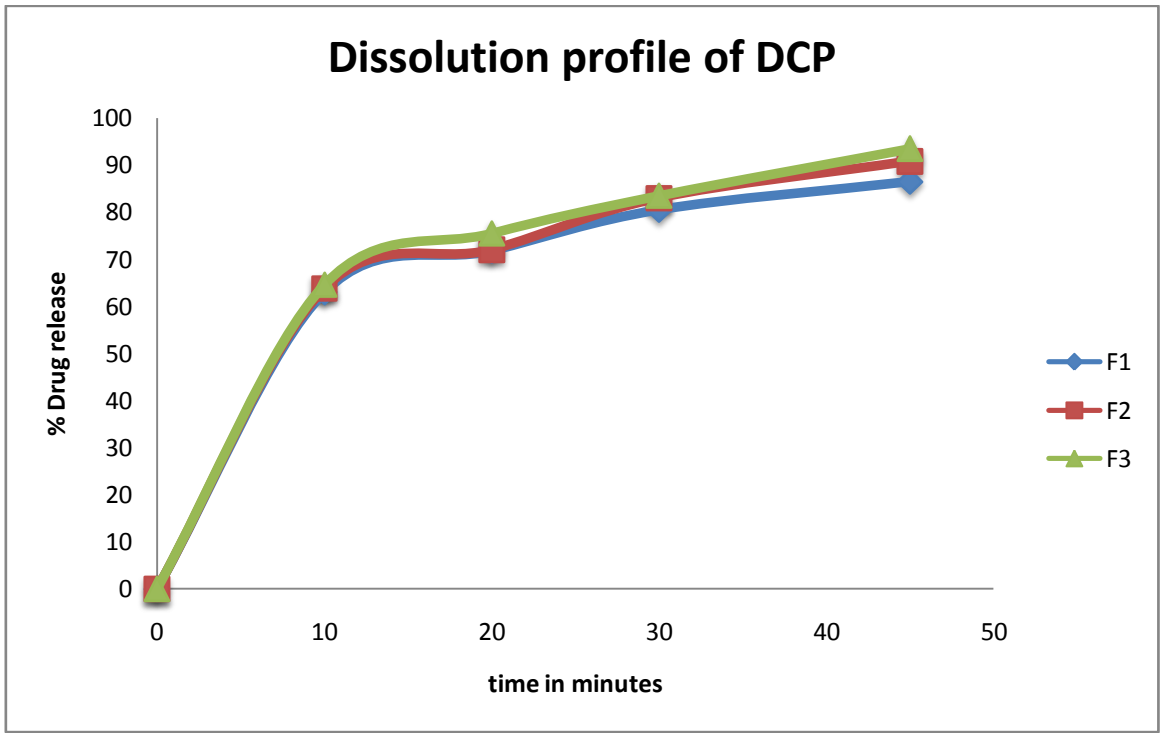


Figure No: 2 Dissolution Profile of Starch

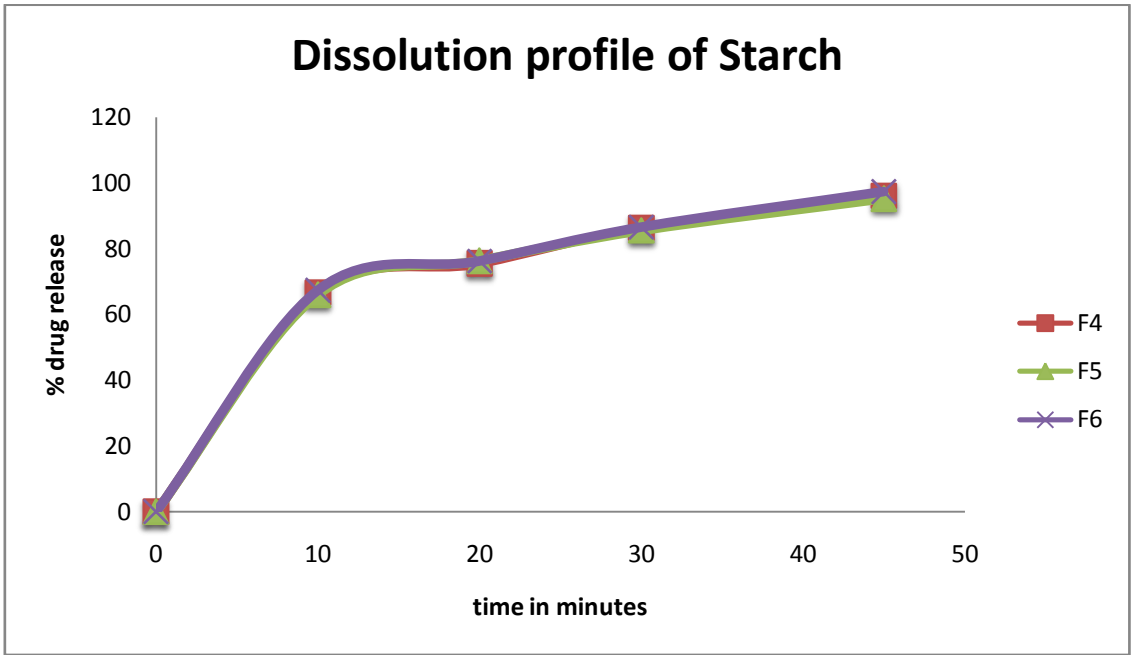
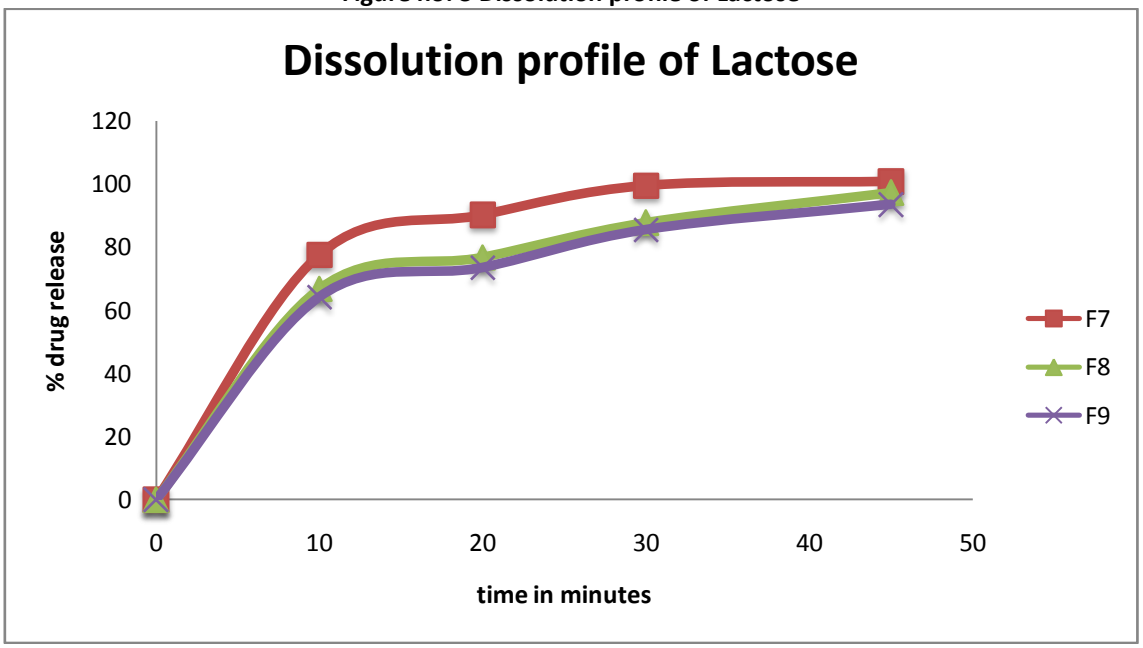


Figure no: 3 Dissolution profile of Lactose



FT-IR Spectroscopic Studies:

The IR spectra of the samples were recorded on an FTIR spectrophotometer (Shimadzu Affinity-1) using KBr pellet (12 mm disc), compressed in a hydraulic press at 10 tons for 30 seconds.

RESULTS AND DISCUSSION

In the present study, an attempt has been made to formulate and evaluate rapid disintegration tablets of Secnidazole (200mg) tablets by direct compression method; employing diluents like

Dicalcium Phosphate (DCP), Starch, and Lactose along with other excipients nine formulations are prepared. The formulation is subjected to both pre and post formulation studies.

Hardness and friability: The hardness of the tablet formulations was found to be in the range of 4.2 to 5.2 kg/cm^2 (**Tables-3**). The friability values were found to be in the range of 0.385 to 0.654 %.(**Tables-3**).

Disintegration time: The disintegration time of formulation seven was 10minutes which is the best result obtained than the rest of the formulation.

Uniformity of weight: All the prepared tablets of Secnidazole were evaluated for weight variation. The weight of all the tablets was found to be uniform with low values of standard deviation and within the prescribed IP limits of ±5%.

Drug Content Uniformity: The low values of standard deviation indicates uniform drug content within the tablets The percent drug content of all the tablets was found to be in the range of 495 to 501 mg/tab (which was within the acceptable limits of ±5%. **Table-3**)

***In vitro* dissolution study:** *In vitro* dissolution studies were performed in 0.1N HCL on the above promising formulation, namely, formulation 7 .The results are shown in **Table-4**.

FT-IR Spectroscopic Studies:

There no interaction found in the Formulation 7 and the functional groups of secnidazole were observed.

Figure No: 4 FT-IR graph of Pure Drug

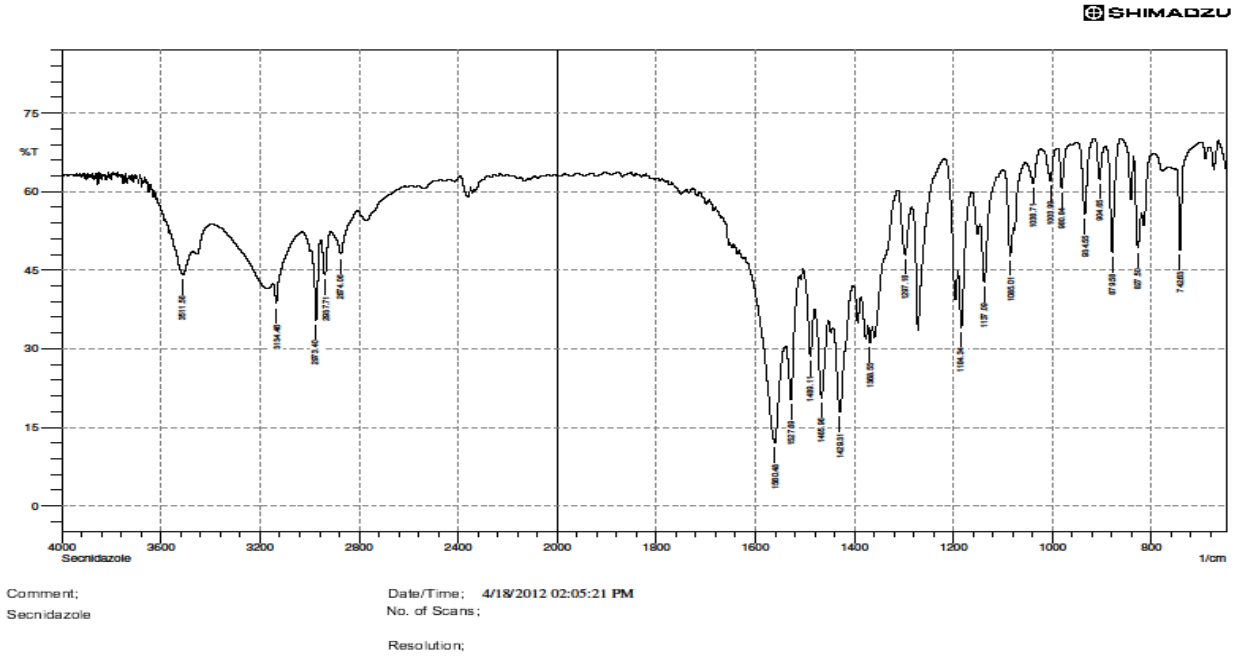
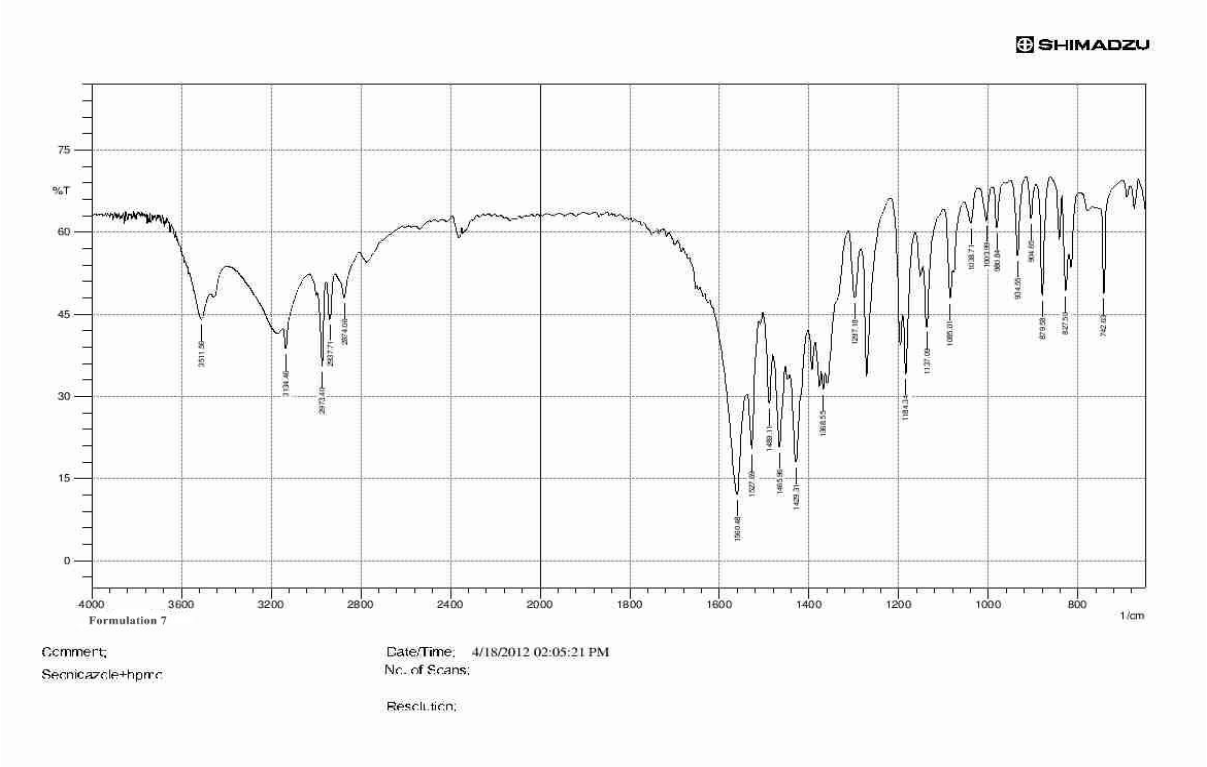


Figure No: 6 FT-IR graph of best formulation



CONCLUSION

In the present study, the formulation and evaluation of secnidazole tablets have been developed. Secnidazole immediate release tablets were successfully prepared (Formulation, F7) with Lactose and Microcrystalline cellulose excipients by direct compression method, which produced immediate release with good physical characteristics, predictable and reproducible drug release profile. Results of the present study confirmed that the Lactose in combination with microcrystalline cellulose showed better drug release profile as compare with starch and Dicalcium phosphate.

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