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# Formulation and *In-Vitro* Characterization of Nimorazole Mouth Dissolving Tablets

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## ABSTRACT

Nimorazole is an antimicrobial with activity against anaerobic bacteria and protozoa. Its actions and properties are similar to Nimorazole.easily absorbed from the GI tract. Peak plasma levels within 2 hr. As precision of dosing and patient compliance become important prerequisite for quick relief from motion sickness, there is a need to develop a formulation for this drug which overcomes problems such as difficulty in swallowing, inconvenience in administration while traveling and better compliance. Hence in the present research work mouth dissolving tablets of Nimorazole were developed with Superdisintegrants like Crospovidone, Indion 414, L . HPC and Pregelatinised starch in various concentrations like 8 % and 10 % w/w by wet granulation method. All formulations were evaluated for physical characteristics of compressed tablets such as weight variation, hardness, friability, drug content, disintegration time and in vitro dissolution study. Among all, the formulation F4 (containing 10% w/w concentration of Crospovidone) was considered to be the best formulation, having disintegration time of 27 sec, hardness 2.56 kg/cm2 and in vitro drug release of 92.23% in 15 min. All the formulation follows Higuchi order release kinetics.

**Keywords:** Mouth dissolving tablet, Nimorazole, Indion 414, Crospovidone, L-HPC, Pregelatinised starch.

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## INTRODUCTION

Orally administered dosages form e.g. tablets; capsules are convenient dosage form for many drugs. Polymer coating enables the formulation of mouth dissolving and taste masking of bitter taste drugs-thereby giving better patient compliance [1].Tablets that are fast disintegrate or dissolve rapidly in the patients mouth, are convenient for young children, aged and patients with swallowing difficulties [2]. For these formulations, the small volume of saliva is usually sufficient to result in tablet disintegration in the oral cavity [3]. The medication then be absorbed partially or entirely into the systemic circulation from blood vessels in the sublingual mucosa, or it can be swallowed as a solution to be absorbed from the gastrointestinal tract (GIT)[4] .The amount of drug that is subject to first pass metabolism is reduced as compared to mouth dissolving tablets[5]. Orally disintegrating tablets contain wide variety of pharmaceutical active ingredients covering many therapeutic categories. The time for disintegration of orally disintegrating tablets are generally considered less than one minute. Orally disintegrating tablets are characterized by high porosity, low density and low hardness. When administered, an in-situ suspension is created in the oral cavity as the tablet disintegrates and is subsequently swallowed [6]. Chemically, Nimorazole1-(2-N-Morpholinylethyl)-5-nitroimidazole, 1-(beta.-Morpholinoethyl)-5-nitroimidazole,1-(beta-Morpholinoethyl)-5-nitroimidazole, 1-imorazole(N-p-Ethylmorpholine)-5-nitroimidazole, an oral synthetic antipro-tozoal and antibacterial agent which inhibits nucleic acid synthesis. It had especially high activity in vitro and in vivo against the anaerobic protozoa against T. vaginalis and E. histolytica [7]. The poor water solubility of the drug gives rise to difficulties in the formulation of dosage form leading to variable dissolution rate .Hence it was selected as a model drug. In the present work an attempt has been made to prepare MDTs of Nimorazole using superdisintegrants like Crospovidone, Indion 414, L .HPC and Pregelatinised starch in different concentrations.

## MATERIALS AND METHODS

### Materials

Nimorazole was obtained as a gift sample fromWockhardt Pharmaceutical, Aurangabad, Maharashtra, India, Indion 414 purchased from Ana lab chemical,Mumbai, Crospovidone obtained as gift sample form kopran pharmaceuticals khopoli, maharashtra and Pregelatinised starch were purchdased from Research Lab fine chem ,Mumbai, HPC was obtained as a gift sample from Wockhardt Pharmaceutical,Aurangabad,Maharashtra, India. All other reagents and chemicals used were of analytical grade.

### Preparation of Tablets

Tablets were prepared by wet granulation process using different superdisintegrants and passed through sieve no. 60 prior to mixing. The drug and the excipients were mixed by using a glass mortar and pestle. Solution of Starch paste (10% w/v) was added drop wise to the mixture to get dough mass. The wet masses passed through sieve no.10 and dried at 60°C for 2 hours and again passed through sieve no.16. The dried granules were mixed with lubricant as

magnesium stearate, glidant as talc and compressed into tablets using a 12-punch tablet machine (Cadmach, Ahmedabad, India) with 9 mm punch. The compositions of the different formulations are presented in Table 1. The tablets were then subjected to the following evaluation parameters like weight variation, hardness, drug content, friability, disintegration time and in vitro dissolution study.

**Evaluation of Tablet**

For assessing weight variation, twenty tablets were selected at random and assessed individually using an Analytical balance (Shimadzu balance). The individual weights were compared with the average weight for determination of weight variation [8]. The crushing strength of the tablets was measured using a Monsanto hardness tester (MVTEX, Mumbai, India). The friability of a sample for 20 tablets was measured using a Roche friabilator (Rolex, Mumbai, India) [9].

**Table 1: Formulation of Nimorazole mouth dissolving tablets Quantity per tablet (mg)**

| Ingredients | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 |
|---|---|---|---|---|---|---|---|---|
| **Nimorazole** | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 |
| **Indion 414** | 24 | 30 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Crospovidone** | 0 | 0 | 24 | 30 | 0 | 0 | 0 | 0 |
| **L-HPC** | 0 | 0 | 0 | 0 | 24 | 30 | 0 | 0 |
| **Pregelatinised Starch** | 0 | 0 | 0 | 0 | 0 | 0 | 24 | 30 |
| **Mannitol** | 22.5 | 22.5 | 22.5 | 22.5 | 22.5 | 22.5 | 22.5 | 22.5 |
| **Starch** | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 |
| **Lactose** | 27.5 | 21.5 | 27.5 | 21.5 | 27.5 | 21.5 | 27.5 | 21.5 |
| **Magnesium stearate** | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| **Talc** | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| **Total Weight** | 310 mg | 310 mg | 310 mg | 310 mg | 310 mg | 310 mg | 310 mg | 310 mg |

Twenty preweighed tablets were rotated at 25 rpm for 4 minutes. The tablets were then reweighed after removal of fines and the percentage of weight loss were calculated. The in vitro disintegration test[10]. was carried out on six tablets using USP disintegration test apparatus with distilled water at 37°± 0.5°C and the time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured. Drug content was determined by dissolving powder equivalent to dose in 100 ml of 0.1N HCl. An aliquot of 0.5 ml sample was withdrawn and diluted to 100 ml and analyzed by UV spectrophotometer at 246 nm against blank [11]. The results of all evaluations are shown in Table 2. The In vitro dissolution study of the formulations was carried out using USP apparatus type II (VEEGO, Mumbai, India) at 100 rpm with 900 ml of 0.1N HCl as dissolution medium at 37°± 0.5°C. Aliquots of dissolution medium (0.9 ml) were withdrawn at specific intervals of time and replaced with fresh dissolution medium at 2, 4, 6, 8, 10, 12 and 15 min. The samples were filtered through a 0.45 µ membrane filter. Absorbance of these solutions was measured at 246 nm using Shimadzu 1800 UV/Vis spectrophotometer. The percentage of drug release was

calculated using an equation obtained from a standard curve and results are presented in Figure1.

**Table 2 Evaluation of tablets Formulation**

| Formulation | Weight variation (mg) | Drug content (%) | Hardness (kg/cm$^2$) | Friability (%) | Disintegration Time (sec) | %Drug released at 15 min |
|---|---|---|---|---|---|---|
| **F1** | 309±2.20 | 96.46±1.32 | 2.51 ± 0.11 | 0.436±0.02 | 57 ± 0.68 | 92.40±0.5 |
| **F2** | 308 ±2.24 | 97.74±1.01 | 2.52 ±0.13 | 0.426±0.02 | 54 ±0.65 | 92.37±0.31 |
| **F3** | 310 ±2.30 | 99.57±1.96 | 2.70 ±0.14 | 0.266±0.0 | 46 ±0.86 | 90.30±0.26 |
| **F4** | 310±2.98 | 99.75±2.06 | 2.49.63±2 | 0.285±0.0 | 29 ±0.89 | 92.89±0.39 |
| **F5** | 310 ±2.16 | 96.18±1.4 | 3. 43 ±0.16 | 0.363±0.0 | 128 ±0.01 | 84.01±0.36 |
| **F6** | 308 ±2.19 | 97.96±1.5 | 3.18 ±0.04 | 0.323±0.0 | 120 ±0.16 | 86.78±0.64 |
| **F7** | 308 ±2.39 | 99.40±1.33 | 3.48±0.0 | 0.182±0.0 | 80 ± 0.01 | 86.93±0.4 |
| **F8** | 310 ±2.246 | 97.59 ±1.40 | 3.1 ±0.04 | 0.279±0.0 | 69 ± 0.18 | 87.49±0.8 |

## RESULTS AND DISCUSSION

This present investigation was performed to fabricate and evaluate mouth dissolving tablets of Nimorazole by the wet granulation method. Super disintegrates at different concentration levels (8 and 10 % w/w) were used to assist disintegration. All the formulations exhibited white color, odorless, convex in shape with smooth surface. Weight variation was found within the specification of the IP limits. Average weight of all formulations was found in the range of 308-310 mg. Hardness and friability of all formulations was within acceptable limits. The friability of all formulations was found to be less than 1.0% and hence the tablets with lower friability may not break during handling on machines and or shipping. In vitro disintegration time is very important for mouth dissolving tablets which is desired to be less than 180 sec. The rapid disintegration may be due to the rapid uptake of water from the medium, swelling, burst effect and thus promoting bioavailability. The in vitro disintegration time was rapid with crosspovidone i.e. 29 s and delayed with L-HPC i.e. 120 s and the order was Crospovidone< Indion 414< Pregelatinesed Starch< LHPC. As the concentration of superdisintegrants in the formulations increased the disintegration time was found to decrease. The content uniformity of all the formulations was found in the range of 96.46 to 99.75 %. Hardness of tablets prepared by wet granulation method was found to be 2.49 to 3.48 kg/cm$^2$

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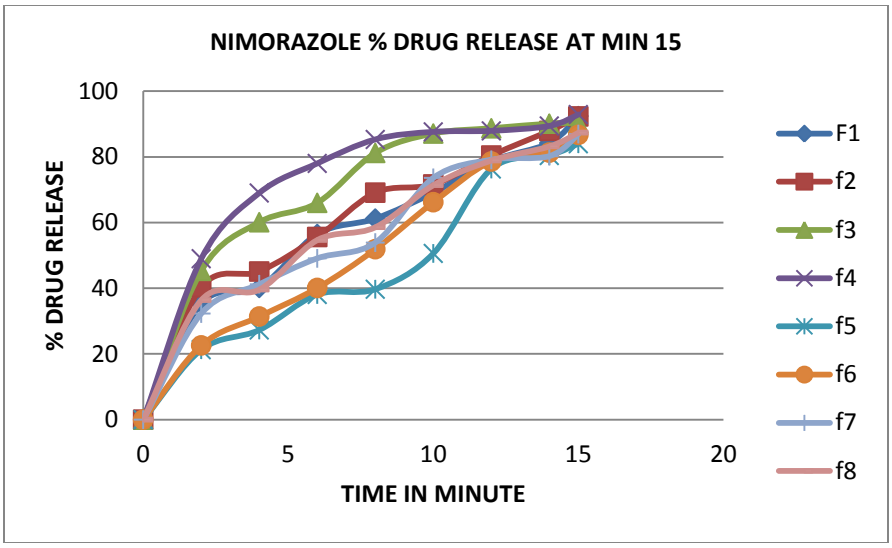


**Figure 1. Comparative Dissolution Profile of Various formulations**

In vitro dissolution studies of various formulations at different time intervals were given in Figure 1. The formulations containing various superdisintegrants like Crospovidone, Indion 414, Pregelatinesed Starch, L-HPC showed 92.89%, 92.37%, 87.49% and 86.78% drug release in 15 min, respectively. This shows that the effectivenessof superdisintegrants was in the order of Crospovidone > Indion 414 > Pregelatinesed Starch > L-HPC. From the overall observations, formulation F4 containing 10% w/w Crospovidone was considered to be the best formulation, comparison to all other formulation used in the management of motion sickness and antiprotozoal.

## CONCLUSION

It was concluded that mouth dissolving tablets of Nimorazole can be successfully prepared by wet granulation techniques using selected superdisintegrants for the better patient compliance and effective therapy. The relative efficiency of these superdisintegrants to improve the disintegration and dissolution rate of tablets was in the order, crospovidone > Indion 414 > pregelatinated starch > L-HPC. From the above all evaluation parameters, formulation F4 containing 10% w/w crospovidone was considered to be the best formulation, compared to all other formulation.

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