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Formulation and evaluation of immediate release folic acid tablets

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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. They are also a tool for expanding markets, extending product life cycles and generating opportunities. An overage is fixed amount of drug added to the formulation in excess of label claim. The present work involves the formulation development, optimization and in-vitro evaluation of immediate release Folic Acid tablets. To minimize critical process parameters and since folic acid is moisture and heat sensitive, direct compression method was selected for the formulation of immediate release Folic Acid tablets. Tablets were prepared containing 40% overages using cross carmellose sodium, crosspovidone, pre gelatinized starch and sodium starch glycolate as disintegrants since tablets containing 10% overages failed to meet the desired specifications. During the course of study it was found that the formula G_8 containing pregelatinized starch as disintegrant exhibited acceptable disintegration time, percentage drug content per tablet and in vitro drug release. So at last it was concluded that immediate release folic acid tablets containing 40% overages can be prepared using direct compression which met the required specifications.

Keywords: Immediate release tablets; Folic Acid; cross carmellose sodium; crosspovidone; pre gelatinized starch ; sodium starch glycolate.

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.[1,2] 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. They are also a tool for expanding markets, extending product life cycles and generating opportunities.[3,4]

Folic acid (also known as vitamin B_9 or folacin) are forms of the water-soluble vitamins. Folic acid is itself not biologically active, but its biological importance is due to tetrahydrofolate and other derivatives after its conversion to dihydrofolic acid in the liver. Absorption of folic acid by the body is facilitated by enzymes associated with the mucosal cell membrane. More specifically, absorption primarily occurs in the mucosa of the upper intestine, known as the jejunum and duodenum. Insufficient folic acid in the diet and the inability to absorb folic acid can cause anemia or birth defects, namely, anecephaly and spina bifida, the latter resulting in brain development abnormalities.

MATERIALS AND METHODS

Materials

Folic acidwas obtained from SAS pharma, Vadodara while crosspovidone, pre gelatinized starch and sodium starch glycolate were obtained from Global Ltd,Kannur. All other chemicals were of analytical grade.

Preparation of immediate release folic acid tablets [5,6,7]

All the ingredients were accurately weighed as per formula F_1 to F_6 which is shown in Table 1 and were dispensed in clean polythene covers. Folic acid and disintegrants were sifted through sieve no-30. Mannitol and Lactose were passed through sieve no-20 while Magnesium stearate and Talc were passed through sieve no-40. All the ingredients were mixed thoroughly for 45 min. All the materials were directly compressible so this uniformly mixed blend was compressed into tablets using concave face round tooling on a Rimek- rotary tablet machine.

Evaluation of immediate releasefolic acidtablets

1. Uniformity of weight [8]

The weights were determined to within ±1mg by using Sartorious balance (Model CP- 224 S). Weight control is based on a sample of 20 tablets. Determinations were made in triplicate.

2. Tablet hardness [9]

The hardness of the tablets was determined by diametral compression using a dial type hardness tester (Model no 1101, Shivani Scientific Ind). A tablet hardness of about 4-5 kg is considered adequate for mechanical stability. Determinations were made in triplicate.

3. Tablet friability [10,11]
The friability of the tablets was measured in a Roche friabilator (Camp-bell Electronics, Mumbai). Tablets of a known weight (W0) or a sample of 20 tablets are dedusted in a drum for a fixed time (100 revolutions) and weighed (W) again. Percentage friability was calculated from the loss in weight as given in equation as below. The weight loss should not be more than 1 %. Determination was made in triplicate.

$$F = \frac{(W_{initial}) - (W_{final})}{(W_{initial})} \times 100$$

Where $W_{initial}$ = Initial weight of tablets .
W_{final} = Final weight of tablets.

4. In-vitro disintegration test [12, 13, 14]
The test was carried out on 6 tablets using Tablet disintegration tester ED-20 (Electrolab, Mumbai, India) distilled water at 37ºC ± 2ºC was used as a disintegration media and the time in second taken for complete disintegration of the tablet with non palable mass remaining in the apparatus was measured in seconds.

5. **In-vitro dissolution study [**15, 16, 17,18]
The release rate of diphenhydramine from immediate releasetablets was determined using United State Pharmacopoeia (USP) XXIV dissolution testing apparatus II (paddle method). The dissolution test was performed using 500 ml of distilled water, at 37± 0.5^0C and 50 rpm. A sample (10 ml) of the solution was withdrawn from the dissolution apparatus 5, 10, 5,20,25, 30,35,40 and 45 minutes. The samples were replaced with fresh dissolution medium of same quantity. The samples were filtered through a 0.45 µ membrane filter. Absorbance of these solutions was measured at 283 nm using a Shimadzu UV-1601 UV/Vis double beam spectrophotometer. Cumulative percentage of drug release was calculated using an equation obtained from a standard curve.

Limit – Not less than 75% of labeled amount of folic acid was dissolved in 45 min.

RESULTS AND DISCUSSION

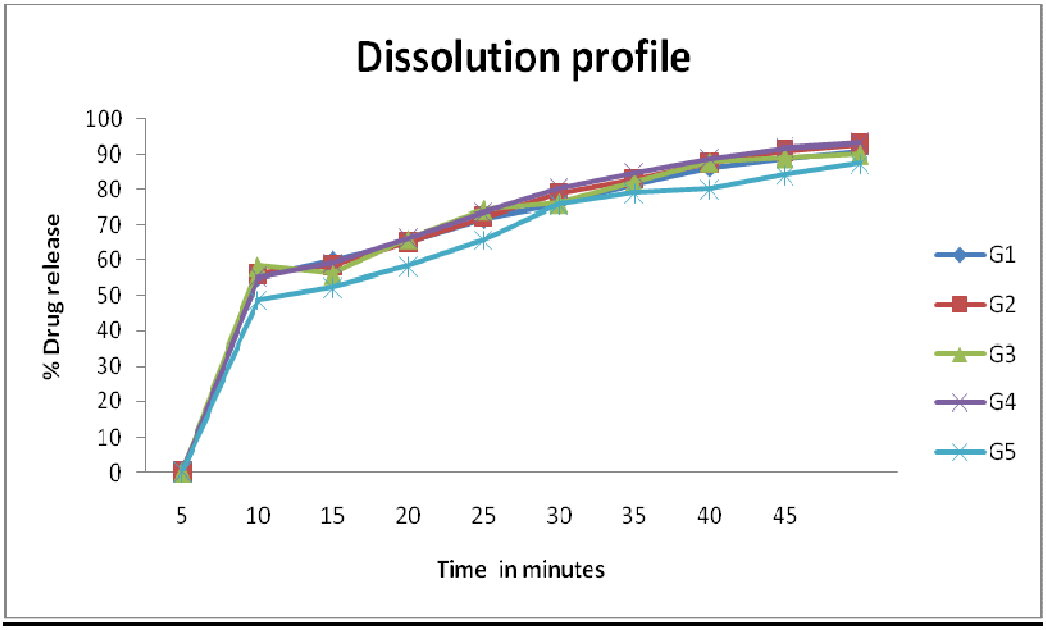
In the present study, various formulations of immediate release folic acidtablets were prepared by direct compression. The use of super disintegrants for preparation of immediate releasetablets is highly effective and commercially feasible. These super disintegrants accelerate disintegration of tablets by virtue of their ability to absorb a large amount of water when exposed to an aqueous environment. The absorption of water results in breaking of tablets and therefore faster disintegration. This disintegration is reported to have an effect on dissolution characteristics as well. Flow properties of the powder, resistance to particle movement can be judged from the angle of repose. Based on angle of repose it was observed that G_4 showed excellent flow properties than the rest of formulations. Carr's index of the prepared blends falls in the range of 10.54 to 18.08 % and Hausner factor values were in the range of 1.11 to 1.22. Based on the results obtained we can conclude that G_4 showed excellent flow.

Disintegration time is very important for immediate release tablets as it assists swallowing and also plays a role in increasing drug absorption, thus promoting bioavailability. Disintegration time of prepared tablets was within the range (Table 2). Invitro drug release study on the prepared tablets were done using phosphate buffer pH-6.8, at 37± 0.5^0C from the results it was observed that G_4 showed maximum drug release of 93.20% which was higher than other formulations (Table 3).

Table 1: Formulae for Preparation of Immediate Release Folic acid Tablets with 40% Overages

SL.NO	INGREDIENTS	G_1	G_2	G_3	G_4	G_5
1.	FolicAcid(40%overages)	7mg	7mg	7mg	7mg	7mg
2.	MicrocrystallineCellulosepH-102	91mg	91mg	91mg	91mg	92mg
3.	Lactose	20mg	20mg	20mg	20mg	22.3mg
4.	Di calcium phosphate	24.3mg	24.3mg	24.3mg	24.3mg	25mg
5.	Magnesium stearate	1.5mg	1.5mg	1.5mg	1.5mg	1.7mg
6.	Colloidalsilicon dioxide	1.2mg	1.2mg	1.2mg	1.2mg	2mg
7.	Croscarmellose sodium	5mg	--	--	--	--
8.	Crosspovidone	--	5mg	--	--	--
9.	Sodium-starch glycolate.	--	--	5mg	--	--
10.	Pre gelatinized Starch	--	--	--	5mg	--
Total Tablet Weight		150mg	150mg	150mg	150mg	150mg

Figure 1: Dissolution Profile of Formulations



CONCLUSION

Considering some important parameters like disintegration time (2.53 min), percentage drug content per tablet (112.85%) ,in vitro drug release (93.20%) and cost factor **G_4** containing pre gelatinized starch as disintegrant was selected as the best formulation .It was also observed that direct compression was the best suitable method used for producing immediate releasefolic

acidtablets since it is cost effective and less time consuming. Based on all the above considerations these formulas can be subjected for bio availability studies and if it complies to all the requirement of those studies the same formula can be commercialized.

Table 2-Evaluation of post -compression Parameters

Formulation Code	Evaluation of post -compression Parameters						
	Hardness of tablets* (kg/cm^2)	Friability of tablets*(%)	Weight variation (mg)	Percentage drug content per tablet* (%)	Drug content per tablet* (mg)	Thickness of tablets* (mm)	Disintegration time (min)*
G_1	4.3	0.789	1.89	111.92	5.600	2.53	3.53
G_2	4.4	0.854	1.76	109.95	5.490	2.54	3.53
G_3	4.7	0.590	1.10	111.02	5.501	2.56	4.18
G_4	4.5	0.545	1.05	112.85	5.642	2.55	2.53
G_5	4.9	1.276	2.19	107.69	5.385	2.54	5.48

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