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FORMULATION DEVELOPMENT AND EVALUATION OF FAST DISSOLVING TABLETS OF AN ANTI-DEPRESSION DRUG

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ABSTRACT

The concept of formulating fast dissolving tablets containing Imipramine offers a suitable and practical approach in serving desired objective of faster disintegration and dissolution characteristics with increased bioavailability. Fast dissolving tablets of Imipramine were prepared by direct compression methods and blend was evaluated for the pre-compression parameters such as bulk density, compressibility, angle of repose etc. The tablets were prepared by using croscarmellose sodium, crospovidone and sodium starch glycolate, as superdisintegrants in different concentration along with microcrystalline cellulose. Total six formulations were prepared and evaluated for hardness, friability, weight variation, content uniformity, wetting time, water absorption ratio, disintegration time and invitro drug release. In-vitro dissolution studies are performed by using phosphate buffer pH 6.8 at 75 rpm by paddle method. The *in vitro* dissolution studies showed that Imipramine tablets formulation F6 showed maximum 95.85% over a period of 10 min. Overall the results of the dissolution rate studies indicated greater dissolution rate of Imipramine from fast dissolving tablets.

KEYWORDS: Imipramine, Fast Dissolving tablets, croscarmellose sodium, crospovidone and sodium starch glycolate, Formulation, Development.

INTRODUCTION

Formulation of drugs into a presentable form is the basic requirement and need of today. The dosage form is a mean of drug delivery system, used for the application of the drug to a living body. Various type of dosage forms are available such as tablets, syrups, suspensions, suppositories, injections, transdermal and patches having a different type of drug delivery mechanisms. These classical/ modern dosage forms have some advantages and

disadvantages. Therefore, the development of an ideal drug delivery system is a big challenge to the pharmacist in the presence scenario. In order to get the desired effect, the drug should be delivered to its site of action at such rate and concentration to achieve the maximum therapeutic effect and minimum adverse effect. For the development of a suitable dosage form a thorough study about the physicochemical principles that governs a specific formulation of a drug should be subjected.[1]

Oral routes of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, self-medication, pain avoidance and most importantly the patient compliance. The most popular solid dosage forms are being tablets and capsules; one important drawback of this dosage forms for some patients is the difficulty to swallow. Drinking water plays an important role in the swallowing of oral dosage forms. Often times people experience inconvenience in swallowing conventional dosage forms such as tablet when water is not available, in the case of the motion sickness (kinetosis) and sudden episodes of coughing during the common cold, allergic condition and bronchitis. For these reason, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention.[2]

The problem of swallowing is a common phenomenon in a geriatric patient due to fear of choking, hand tremors, dysphasia and in young individuals due to underdeveloped muscular and nervous systems and in schizophrenic patients which leads to poor patient compliance. Approximately one-third of the population (mainly paediatric and geriatric) has swallowing difficulties, resulting in poor compliance with oral tablet drug therapy which leads to reduced overall therapy effectiveness. For these reason, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention.[3-4]

Fast dissolving drug delivery systems were first developed in the late 1970s as an alternative to conventional dosage forms for the pediatric and geriatric patient. These tablets are designed to dissolve or disintegrate rapidly in the saliva generally less than 60 seconds.[5]

To fulfill these medical needs, pharmaceutical technologists have developed a novel oral dosage forms known as orally disintegrating (dispersible) tablets (ODTs) or Fast disintegrating (dissolving) tablets (FDTs) or mouth melting tablets (MMTs) or mouth dissolving tablets(MDTs), immediate release tablets which disintegrate rapidly in saliva, usually in a matter of seconds, without the need to take water.

Imipramine is a tricyclic antidepressant (TCAs) which is widely used in the treatment of unipolar depression characterized by extreme sadness; despair and anhedonia. The most popular solid dosage forms are being tablets and capsules. One important drawback of these forms for some patients population prefers FDTs to other dosage forms and most consumers would ask their doctors for FDTs (70%), purchase FDTs (70%) or prepare FDTs to regular tablets. Some drugs are absorbed from mouth, pharynx and oesophagus as the saliva passes down in to stomach and in such cases bioavailability of drug is increased, pre-gastric absorption can result in improved bioavailability and as result of reduced dosage form, improved clinical performance through a reduction of unwanted effects. So our aim of the study was formulated fast dissolving tablets of Imipramine for effective treatment of depression.

MATERIAL AND METHODS

Material

Imipramine was purchased from Sun Pharmaceutical Industries Limited, Mumbai, India. Crospovidone, croscarmellose sodium and sodium starch glycolate was obtained from Hi-Media Laboratories Pvt. Ltd., Mumbai, India. Micro crystalline cellulose, mannitol, talc and magnesium stearate was procured from Central Drug House (P) Ltd. New Delhi. All other solvents and chemicals used were of analytical grade.

Methods

Preparation of tablets of imipramine

Fast dissolving tablets of Imipramine (25mg) were prepared by direct compression method after incorporating different superdisintegrants such as, croscarmellose sodium (Ac-Di-Sol) 10 and 20mg, crospovidone in different concentrations 10 and 20mg and crospovidone 10 and 20mg for optimization of best formulation. The ingredients given below were weighed and mixed in geometric progression in a dry and clean mortar. Then the ingredients were passed through mesh 60.

Magnesium stearate (6mg) as lubricant and talc (5 mg) as glidant and Microcrystalline cellulose as bulking agent (94, 84 and 74mg) were added in a final step and mixed, this blend was subjected to analysis of pre-compression parameters which included Angle of repose, Bulk density, Tap density, Carr's index and Hausner's ratio.

The Blend was compressed on 8 mm (diameter) fat punches on a 'Rimek mini press 16 station rotary compression machine. Six formulations of Imipramine granules were prepared and each formulation contained one of the three disintegrant in different concentration.[6] Each tablet weighing 150 mg was obtained. Composition of tablets is mentioned in Table 1.

Table 1: Composition of imipramine fast dissolving tablets.

Ingredients (mg)	Formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Imipramine	25	25	25	25	25	25	25	25	25
Sodium Starch glycolate	10	20	30	-	-	-	-	-	-
Croscarmellose sodium	-	-	-	10	20	30	-	-	-
CP	-	-	-	-	-	-	10	20	30
Mannitol	10	10	10	10	10	10	10	10	10
Microcrystalline cellulose	94	84	74	94	84	74	94	84	74
Talc	5	5	5	5	5	5	5	5	5
Magnesium stearate	6	6	6	6	6	6	6	6	6
Total weight	150	150	150	150	150	150	150	150	150

Evaluation of post compression parameter

Shape and Colour of tablets

Uncoated tablets were examined under a lens for the shape of the tablet and colour was observed by keeping the tablets in light.

Thickness test

Three tablets were picked from each formulation randomly and thickness was measured individually. It is expressed in mm and standard deviation was also calculated. The tablet thickness was measured using dial-caliper (Mitutoyo, Japan).[7]

Weight variation test

Twenty tablets were selected randomly from each formulation and average weight was determined. The tablets were weighed individually and compared with average weight. The U.S Pharmacopoeia allows a little variation in the weight of a tablet.

Hardness test

The hardness of tablet was measured by Pfizer hardness tester and results were expressed in Kg/cm^2.

Friability test

For this, 20 tablets were taken from each formulation and the friability was determined using Roche friabilator. The equipment was run for 4min at 25 revolutions per minute.[8] The tablets were taken out, dedusted and reweighted and % friability was calculated. The friability was determined as the mass loss in percent according to Equation:-

$$\%\text{Friability} = (\text{Loss in weight}/\text{Initial weight}) \times 100$$

The test complies if tablets not loss more than 1% of their weight.

Uniformity of drug content

The test is mandatory for tablets with 10 mg or less weight of active ingredient. Ten randomly selected tablets from each formulation (F1 to F6) were finely powdered and Drug equivalent to 10 mg of drug dissolved in 10 ml phosphate buffer pH 6.8) sonicate it for 20 minutes, till the entire drug leached out from complex, then the solution was filtered through whatman filter paper No. 41. From this Solution take 1 ml and Diluted up to 100 ml with Phosphate buffer pH 6.8 and the drug content was determined spectrophotometrically at 248.0 nm.[9]

***In-vitro* dissolution rate studies**

The prepared tablets were evaluated for *in vitro* drug release. The drug release studies were carried out using USP XXII paddle type Dissolution test apparatus.[10] The dissolution study was carried out in 900 ml dissolution medium which was stirred at 75 rpm maintained at 37±0.2°C. The scheme of using the simulated fluids at different timing was as follows:

A tablet placed in dissolution media (900 ml) at 37±0.2°C. Samples were withdrawn at different time interval and compensated with same amount of fresh dissolution medium. Volume of sample withdrawn was made up to 10ml Phosphate buffer pH 6.8. The samples withdrawn were assayed spectrophotometrically at 248.0 nm using UV visible spectrophotometer. The release of drug was calculated with the help of standard curve of Imipramine.

RESULTS AND DISCUSSION

Fast dissolving tablets containing Imipramine were prepared using direct compression method. Total nine formulations were prepared using varying amount of Sodium Starch

glycolate, Croscarmellose sodium and Crospovidone. The prepared Tablets were further evaluated for Hardness, Friability, disintegration time, and uniformity of drug content, and *In-vitro* Release Studies. Percentage assay of different formulation was determined by U.V. vis Spectroscopy. The percentage assay of different formulation was in range of 97.78±0.25 to 99.12±0.14%. The maximum percentage assay (99.12±0.14%) and less disintegration time (25 Sec.) were found to be formulation F6 in Fast dissolving tablets. The optimized formulation of batch F6 subjected to further *In vitro* drug release.

The *in vitro* drug release studies of the enhanced detailing was subjected to integrity of fit test by linear regression analysis as indicated by zero order, first order kinetic Higuchi and peppas release equation, in order to decide the mechanism of drug release. When the regression coefficient values of were compared, it was observed that 'r^2' values of First order was maximum i.e. 0.989 hence indicating drug release from formulations was found to follow first order kinetics.

Table 1: Results of Post-Compression parameters of all formulations.

F. Code	Hardness test (kg/cm^2)*	Friability (%)*	Weight variation (%)*	Thickness (mm)*	Drug content (%)*	Disintegration Time (sec.)* Mean ± SD
F1	3.2±0.1	0.854±0.045	152±5	2.3±0.2	98.85±0.23	48
F2	3.3±0.2	0.658±0.065	148±4	2.4±0.1	99.12±0.41	46
F3	3.3±0.3	0.745±0.032	150±3	2.3±0.2	98.45±0.25	49
F4	3.4±0.2	0.745±0.052	149±2	2.4±0.3	98.65±0.36	45
F5	3.5±0.1	0.882±0.047	155±5	2.5±0.2	97.74±0.32	42
F6	3.3±0.2	0.742±0.036	148±2	2.6±0.1	99.12±0.14	40
F7	3.4±0.2	0.658±0.045	147±3	2.4±0.4	98.45±0.42	25
F8	3.3±0.2	0.698±0.074	153±2	2.3±0.5	98.65±0.36	36
F9	3.4±0.3	0.745±0.036	151±1	2.4±0.4	97.78±0.25	30

***Average of three determinations (n=3)**

Table 2: *In-vitro* drug release data for optimized formulation F6.

Time (min)	Square Root of Time(h)$^{1/2}$	Log Time	Cumulative* % Drug Release	Log Cumulative % Drug Release	Cumulative % Drug Remaining	Log Cumulative % Drug Remaining
1	1.000	0.000	25.65	1.409	74.35	1.871
2	1.414	0.301	45.85	1.661	54.15	1.734
5	2.236	0.699	65.85	1.819	34.15	1.533
10	3.162	1.000	95.85	1.982	4.15	0.618

Table 3: Regression analysis data.

Batch	Zero Order	First Order	Higuchi	Korsmeyer-Peppas
	R^2	R^2	R^2	R^2
F6	0.962	0.989	0.981	0.976

CONCLUSION

Fast dissolving tablets of Imipramine were conveniently formulated by direct compression method. The *in vitro* dissolution studies showed that Imipramine tablets formulation F6 showed maximum 95.85% over a period of 10 min. Overall the results of the dissolution rate studies indicated greater dissolution rate of Imipramine from fast dissolving tablets.

REFERENCES

1. Hannan PA, Khan JA, Khan A, Safiullah S. Oral dispersible system: a new approach in drug delivery syste. Indian J Pharm Sci, 2016; 78: 2-7.
2. Bhowmik D, Chiranjib B, Krishnakanth, Pankaj, Chandira RM. Fast dissolving tablet: an overview. J Chem Pharm Res, 2009; 1: 163-77.
3. Siddiqui N, Garg G, Sharma PK. Fast dissolving tablets: preparation, characterization and evaluation: an overview. Int J Pharm Sci Rev Res, 2010; 2: 87-96.
4. Gupta DK, Bajpai M, Chatterjee DP. Fast mouth is dissolving disintegrating tablet and patient counselling points for FDDTS: A review. Int J Res Dev Pharm L Sci, 2014; 3: 949-58.
5. Nautiyal U, Singh S, Singh R, Gopal, Kakar S. Fast dissolving tablets as a novel boon: A review. J Pharm Chem Biol Sci, 2014; 2: 5-26.
6. Liberman HA, Lachman L. Pharmaceutical Dosage Form: Tablets. 2nd Edition Inc. New York Marcel Dekker, 2005; 332–5.
7. Gohel M, Patel M, Amin A, Agrawal R, Dave R, Bariya N. Formulation design and optimization of mouth dissolve tablets of nimesulide using vaccum drying technique. AAPS PharmSciTech, 2004; 5: 212–8.
8. Shoukri R.A., Ahmed I.S., Shamma R.N. In vitro and in vivo evaluation of nimesulide lyophilized orally disintegrating tablets. Eur. J. Pharm. Sci, 2009; 73(1): 162–71.
9. United States Pharmacopoeia, National Formulary, 30th Edition. Rockville, United State Pharmacopeial Convection, 2007; 2149–52.

10. Newa M, Bhandari KH, Kim JO et al. Enhancement of solubility, dissolution and bioavailability of ibuprofen in solid dispersion systems. Chem Pharm Bull, 2008; 56(4): 569–74.