Drug Release Profile of Aripiprazole Mouth Dissolving Polymeric Formulation

Parida P[1], Tripathy S P[2], Mishra S C[3], Behera A[4]

[1] University Department of Pharmaceutical Sciences,
Utkal University, Bhubaneswar-751 004, Odisha, India,
[2]School of Pharmaceutical Education & Research,
Berhampur university, Berhampur-760007, odisha
[3, 4] Department of Metallurgical & Materials Engineering
National Institute of Technology, Rourkela-769008, Odisha, India

*Corresponding author: patitapabana.pharma@gmail.com

ABSTRACTS

In the case of pediatrics & geriatric patients it was the opportunity which impacts highest component of compliance that the administration of mouth dissolving tablet (MDT) which were orally disintegrate & differentiated among the delivery systems. The alternative way to formulate conventional tablets design was to dissolve in the part of tongue. Dysphasia, motion sickness, repeated emesis and mental disorders like patients were not able to take medication easily through swallowing. In the recent decade much research were going on to investigate about mouth dissolving preparation which leads significance roles for patient dose satisfaction. MDT simply vanishes when placed in the mouth, so cannot be hidden in mouth by psychotic patients. Aripiprazole used as anti-psychotic drug therapy in the form of mouth dissolving tablet. This paper represents the biopolymers like Mannitol and Microcrystalline cellulose which were used as suitable excipient for taste masking. The investigation of drug release profile in the formulation of mouth dissolving tablet with manufacturing includes the use of direct compression & wet granulation processes. In this paper the Characteristic study of drug release through bio-polymers from MDT by taking different buffer preparations. It was obtained that Biopolymers like Mannitol and Microcrystalline Cellulose were used to improve dissolution property. There was no more significant impact on drug concentration release profile from the formulation by interchanging Mannitol or MCC.

Keywords: MDT, Aripiprazole, Biopolymer, Direct compression, Wet granulation.

INTRODUCTION

Aripiprazole is an atypical antipsychotic and antidepressant used in the treatment of schizophrenia, bipolar disorder, and clinical depression. It was approved by the US Food and Drug Administration (FDA) for schizophrenia [1]. Aripiprazole is also a partial agonist at the 5-HT_{1A} receptor and like the other atypical antipsychotics displays an antagonist profile at the 5-HT_{2A} receptor [2]. Fast dissolving tablets (FDTs) have received ever-increasing demand during the last decade and the field has become a rapidly growing area in the pharmaceutical industry. Upon administration, these tablets dissolve or disintegrate in the mouth in the absence of additional water generally within less than 60 seconds [3]. The purpose of the study was to improve the physicochemical properties of aripiprazole, a poorly water soluble drug by forming dispersion with mannitol as water soluble carrier [4].To make rapidly disintegrating tablets with sufficient mechanical integrity as well as a pleasant taste, microcrystalline cellulose (MCC) [5]. Super disintegrant, microcrystalline cellulose along with shows the uniform drug release pattern with mannitol [6].

EXPERIMENTAL PROCEDURE

Chemicals

Aripiprazole (IP), Mannitol (BP), Microcrystalline Cellulose (Sancel P^H-102) (BP).

Formulation

Aripiprazole working standard powder was used without further purification. Tablets containing 15 mg aripiprazole as per label claim at market. Advancements in the technology Electrolab was used for manufacturing. Systems include the use of direct compression & the classical wet granulation processes. The average mass complied with the limits specified in the individual specification/monograph. Not more than two of the individual mass deviates from the average mass by more than percentage shown in table1 & none deviates by more than twice that percentage.

Table 1. Weigh acceptance

Average mass of tablets	Percentage deviation
15 mg or less	± 10.0
More than 15 mg but less than 30 mg	± 7.5
30 mg or more	± 5.0

Instrumentation

UV-Spectrophotometer-Shimadzu-1700 (Pharmaspec), PH Meter-Model-744 Methom, Dissolution Apparatus USP-II –Electrolab.

In-vitro dissolution study

Medium; 0.1 N HCl, Apparatus USP(II): 75 rpm, Time: 45 min, Temp: 37.5 ^{0}C +/- 0.5 ^{0}C, Volume: 800 ml, Wavelength: 255 nm.

Media Preparation: - Taking 8.5ml of con.HCL and make up the vol. 1000ml with DM Water.

Standard Preparation

Weights accurately 30 mg of Aripiprazole in to 100 ml standard volumetric flask add 50 ml of 0.1N HCL. Sonicate for 10 mins. Cool it to room temperature and make volume up to 100 ml with 0.1N HCL. Take 2.0 ml of the above solution in a 50 ml volumetric flask & make up the volume with 0.1N HCL. So final solution concentration should be 12.0 mcg/ ml. Measure the absorbance at 255 nm.

Procedure

Fill up bowl with 800 ml medium allows it to warm up to 37 ± 0.5°C. Add one tablet in each bowl. Rotate the paddle at 75 RPM, After 45 mins. Withdraw 20 ml solution and filter it through 0.45µ filter paper. So final concentration of Test solution obtained 12.5 mcg/ml, consider with comparison to blank dissolution medium.

RESULTS AND DISCUSSION

Impact of Mannitol and Microcrystalline Cellulose (MCC)

In this study two trials were taken, one with 50% mannitol and 25% MCC and other with interchanging the concentration, keeping the concentration of API and other excipients constant. Tablets were compressed with same compression parameters. The comparative results of both trials are tabulated in Table 2 and the graphical representation of the comparative dissolution profiles with the helpof 0.1 N HCl & appropriate buffer, 4.5 Acetate buffer, 6.8 Phosphate buffer were shown in (Fig 1-3). In the Evaluations of Trial Batch data, Drug Released profile of MDT formulated through Direct compression (DC), Wet granulation (WG) shown in Table 2.

1. Evaluations of Trial Batch data

Table 2. % Drug Released profile of Direct compression (DC), Wet granulation (WG)

% Drug Released	0.1 N HCl		4.5 Acetate buffer		6.8 Phosphate buffer	
Time Points	**D.C**	**W.G**	**D.C**	**W.G**	**D.C**	**W.G**
5	68.92	95.32	65.15	87.07	23.65	83.93
10	93.47	98.94	90.72	90.11	34.97	87.53
15	100.64	100.82	94.91	99.20	60.58	90.86
30	101.8	102.74	96.23	99.93	85.06	95.54

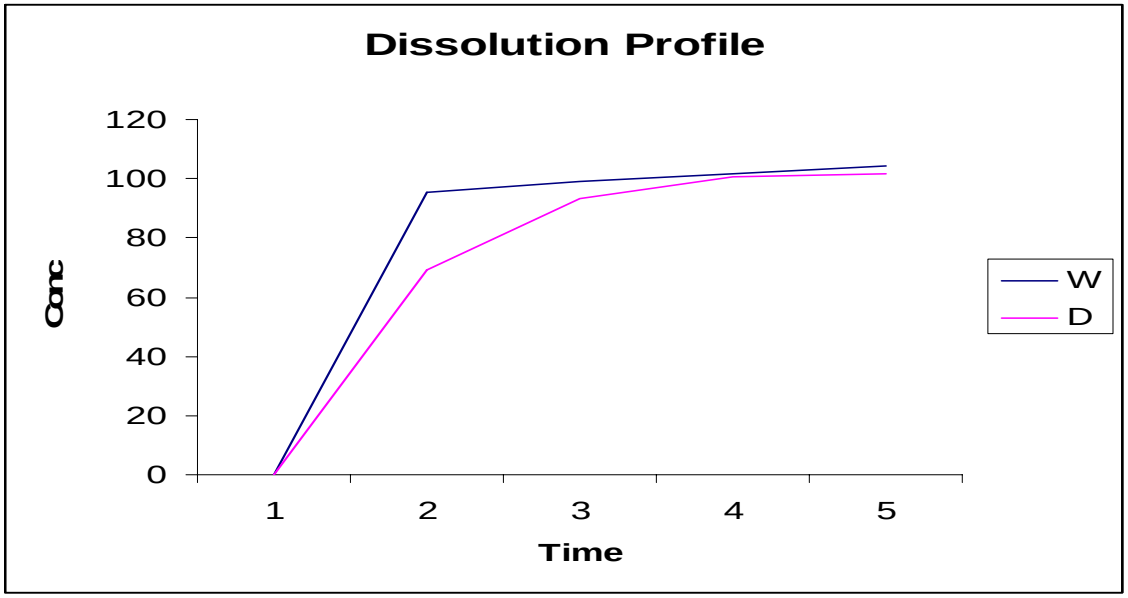

Fig 1. Comparison of dissolution in 0.1 N HCL

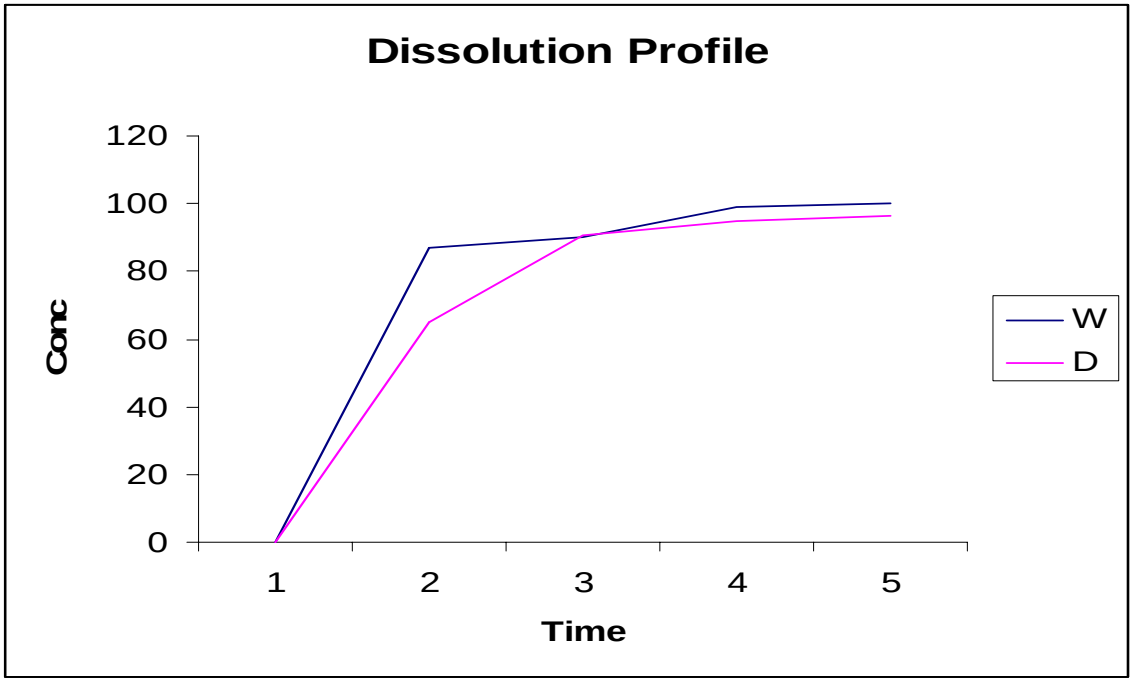

Fig 2. Comparison of dissolution in pH 4.5 Acetate buffer

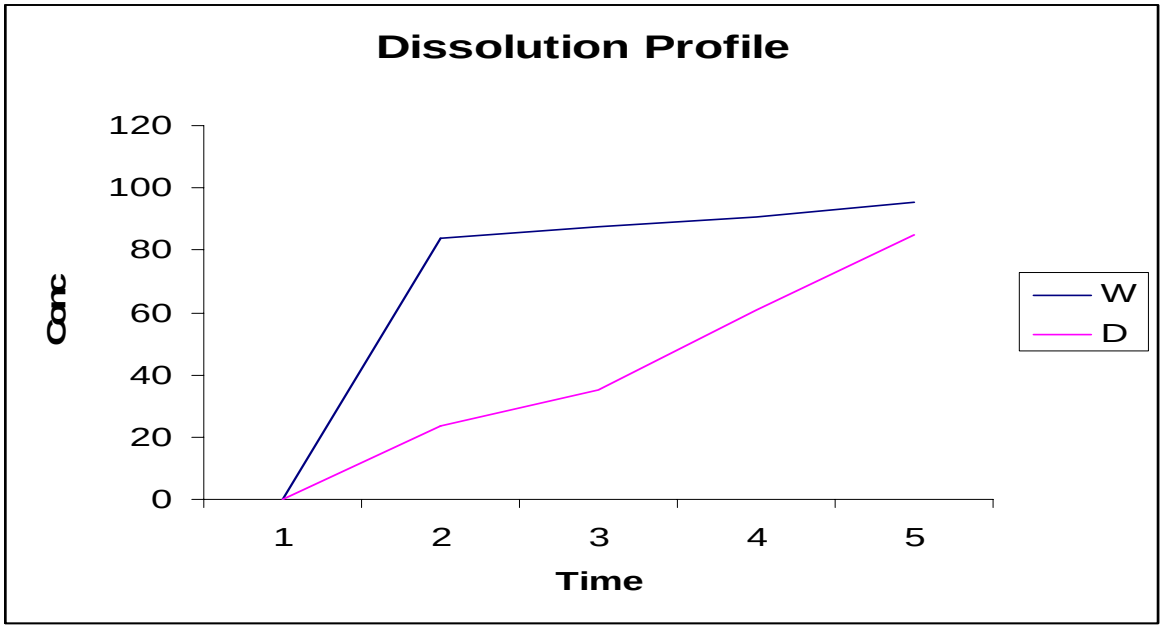

Fig 3. Comparison of dissolution in pH 6.8 Phosphate buffer.

2. Evaluations of final product

In this study, Mouth dissolving Tablets were prepared by direct compression and Wet Granulation method. In both methods same concentration of ingredients were used and tablets were compressed with same compression parameters. The comparative results of both trials are tabulated in (Table 3) and the graphical representation of the comparative dissolution profiles is shown in (Fig 4) with 0.1 N HCL**.**

Table 3. Impact of Wet granulation and direct compression of final product

Evaluation Tests		**Direct Compression (DC)**	**Wet Granulation (WG)**
Drug content (% Assay)		103.10	103.8
Dissolution profile	Time points (minutes)	% Drug Released	% Drug Released
	2	95.32	95.32
	5	98.94	98.94
	10	101.82	100.82
	30	101.54	102.74

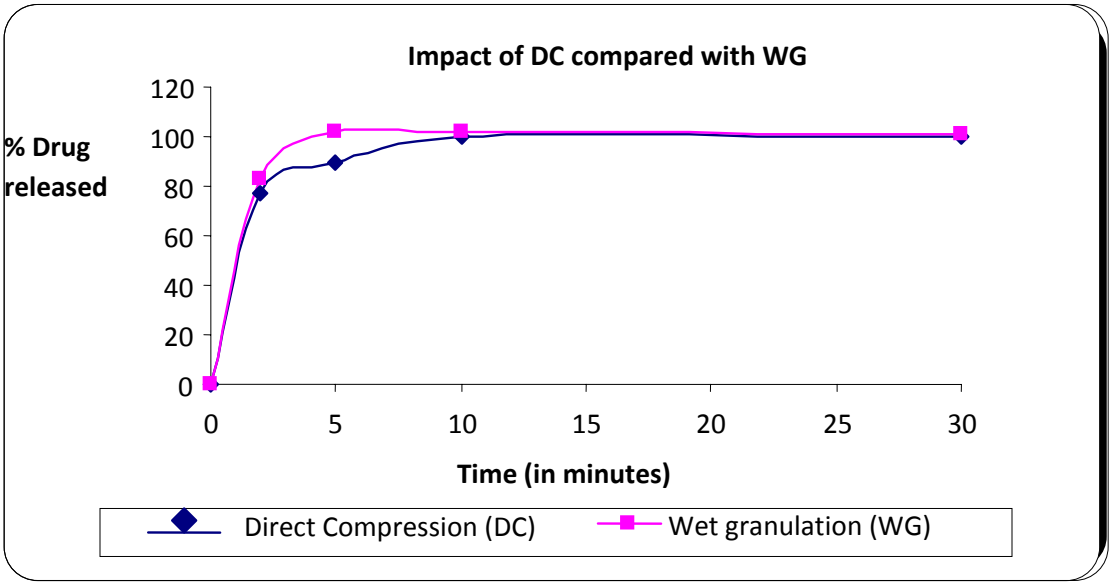

Fig 4. Comparison of dissolution profile of DC and WG processes

Between the two methods, wet granulation process was proved to be the better method than direct compression. Mouth dissolving tablet prepared by wet granulation method disintegrates in less time and has good dissolution profile than the tablets prepared by direct compression. In the wet granulation method Formulation has the good flow property compared to direct compression blend. Also it has the bursting effect at the time of dispersion.

CONCLUSIONS

By observation of the results of Trial Batch, it is concluded that, the composition of the product and method of wet granulation for manufacturing is Satisfactory and reproducible and is decided to continue with the same formulation & procedure to ensure reproducibility and quality.

REFERENCES

1. Hitti, Miranda. "FDA OKs Abilify for Depression", WebMD, Retrieved 8 December 2008.

2. Jordan, S et al. "The antipsychotic aripiprazole is a potent, partial agonist at the human 5-HT1A receptor"(2002), Eur J Pharmacol 441 (3): 137–140.

3. Hitesh Jagani, Fast Dissolving Tablets, JAPHR 2011, Vol 2, Issue1p-57-70.

4. Punitha S (et.al), Enhancement of celecoxib solubility by solid dispersion using mannitol, ISSN- 0975-1491, Vol 2, Issue 4, 2010.

5. S Jacob **(et** al), Novel co-processed excipients of mannitol and microcrystalline cellulose, ijps, 2007, Volume: 69, Issue: 5, Page: 633-639.

6. P.S. Kawtikwar et al. Formulation, Evaluation and Optimization of Fast dissolving tablet containing Tizanidine Hydrochloride, Int.J. PharmTech Res.2009, 1(1).