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Formulation and evaluation of aripiprazole tablets for oral suspension

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ABSTRACT

The present study is to develop and evaluate Aripiprazole (10 mg) tablet for oral suspension. Based on Literature survey and Compatibility Tests excipients like Microcrystalline Cellulose (pH 101), mannitol, crosscarmellose sodium, cross povidone, sodium starch glycolate, Magnesium Stearate were used. In this present study, the tablets were prepared by using direct compression technique. In order to optimize the product, different formulations were developed. All the formulations were evaluated for physical characteristics, Disintegration, Dissolution studies. Based on the results of the above mentioned tests **F–06** was selected as the best formulation as it showed total drug release with in 12 min than all other formulations.

Key words: Aripiprazole**,** mannitol, crosscarmellose sodium and cross povidone

INTRODUCTION

Oral solid dosage forms

A solid dosage form is drug delivery system that includes tablets, capsules, sachets and pills as well as a bulk or unit-dose powders and granules[1]. Among the various dosage forms an oral solid dosage form has greater importance and occupies a prime role in the pharmaceutical market. Oral route of drug administration is widely acceptable and drugs administered orally as solid dosage form represents the preferred class of products[8]. Over 90% of drugs formulated to produce systemic effects are produced as solid dosage forms. Because of these reason whenever New chemical entity (NCE) has discovered, which shows a sufficient pharmacological action, first the pharmaceutical company asks whether the drug is successfully administered by oral route or not[4]. The oral route of administration still continues to be the most preferred route due to its manifold advantages including:

- Tablets and capsules represent unit dosage forms in which the accurate dose of drug to show sufficient pharmacological action can be administered. In case of liquid oral dosage forms such as Syrups, Suspensions, Emulsions, Solutions and Elixirs the patient is asked to administer the medication of 5-30 ml. Such dosage measurements are typically error by factor ranging from 20-50 %, when the drug is self administered by patient.
- Solid dosage forms are less expensive to shipping and less prone for the degradation when compared to liquid dosage forms.

Tablets

"In 1843, the first patent for a hand operated device used to form a tablet was granted." Tablets are defined as solid preparations each containing a single

dose of one or more active ingredients and obtained by compressing uniform volumes of particles. They are intended for oral administration, some are swallowed whole, some after being chewed. Some are dissolved or dispersed in water before being administered and some are retained in the mouth, where the active ingredient "liberated". Tablets are used mainly for systemic drug delivery but also for local drug action[4]. For systemic use drug must be released from tablet that is dissolved in the fluids of mouth, stomach and intestine and then absorbed into systemic circulation by which it reaches its site of action. Tablets remain popular as a dosage form because of the advantages, afforded both to the manufacturer [e.g. simplicity and economy of preparation, stability and convenience in packing, shipping and dispensing] and the patient[6] [e.g. accuracy of dosage, compactness, portability, blandness of taste and ease of administration].

They may differ greatly in size and weight depending on the amount of drug substance present and the intended method of administration. They may have lines or break-marks and may bear a symbol or other markings. Tablets may be coated.

Types of tablets

The main reasons behind formulation of different types of tablets are to create a delivery system that is relatively simple and inexpensive to manufacture, provide the dosage form that is convenient from patient's perspective and utilize an approach that is unlikely to add complexity during regulatory approval process[7,8]. To understand each dosage form, tablets here are classified by their route of administration and by the type of drug delivery system they represent within that route.

Tablets ingested orally

1. Compressed tablet, e.g. Paracetamol tablet
2. Multiple compressed tablet
3. Repeat action tablet
4. Delayed release tablet, e.g. Enteric coated Bisacodyl tablet
5. Sugar coated tablet, e.g. Multivitamin tablet
6. Film coated tablet, e.g. Metronidazole tablet
7. Chewable tablet, e.g. Antacid tablet

Tablets used in oral cavity

1. Buccal tablet, e.g. Vitamin-c tablet
2. Sublingual tablet, e.g. Vicks Menthol tablet
3. Troches or lozenges
4. Dental cone

Tablets administered by other route

1. Implantation tablet
2. Vaginal tablet, e.g. Clotrimazole tablet

Tablets used to prepare solution

1. Effervescent tablet, e.g. Dispirin tablet (Aspirin)
2. Dispensing tablet, e.g. Enzyme tablet (Digiplex)
3. Hypodermic tablet
4. Tablet triturates e.g. Enzyme tablet (Digiplex)

AIM & OBJECTIVE

Aim of the study

The aim of present work is to develop a solid oral dosage form of Aripiprazole feasible for oral suspension.

Objectives

The main objective is to make a tablet for oral suspension which is a unit dosage for an oral suspension and this does not need any preservatives for long term conditions of suspensions[10].

The formulation is made with super disintegrents to break and form a suspension as it comes in contact with water.

Primary Objective

1. To formulate and evaluate Aripiprazole 10mg.

Secondary Objectives

1. To perform preformulation studies.
2. To develop various formulations with different excipients.
3. To study the effect of excipient concentrations on the tablet characteristics.
4. To achieve fast dissolving drug release profile for the developed formulation

Formulation of aripiprazole 10 mg tablets for oral suspension

Formulation Planning

The immediate release tablets for containing 10mg of ARIPIPRAZOLE were prepared with a total tablet weight of 150mg.

Manufacturing Procedure

- Micro crystalline cellulose, mannitol and respective super disintegrants were weighed and sifted through 40mesh.
- To the above blend aripiprazole was added and sifted through 18 mesh.
- The sifted material was placed in polyethene bag and mixed for 10 min.
- Magnesium Stearate was weighed and sifted through 40mesh.
- To the mixture of Micro crystalline cellulose, mannitol, disintegrants and aripiprazole lubricated blend was added and placed in polyethene bag and mixed for 3 min.
- The lubricated blend was compressed using 12 mm round punches.

Formulation trials

Table No 1: Formulation Trials - Formula

Ingredients	**F1(mg)**	**F 2 (mg)**	**F 3 (mg)**	**F4 (mg)**	**F5 (mg)**	**F6 (mg)**	**F7 (mg)**	**F8 (mg)**	**F9 (mg)**
ARIPIPRAZOLE	10	10	10	10	10	10	10	10	10
MCC -101	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs
CCS	-	-	-	12.5	25	37.5	-	-	-
SSG	12.5	25	37.5	-	-	-	-	-	-
Mannitol	25	25	25	25	25	25	25	25	25
CP	-	-	-	-	-	-	12.5	25	37.5
Magnesium Stearate	10	10	10	10	10	10	10	10	10
Total (mg)	500	500	500	500	500	500	500	500	500

- **Place the tablet in a small amount of water (about 2 teaspoons/10 mL). Do NOT use any other liquid. Swirl or stir until the tablet is completely mixed in the water. Drink right after mixing. Be sure to drink the entire mixture. Rinse the container with an additional small amount of water and drink to be sure all the medicine is taken**.

RESULTS

Drug-excipients compatibility studies

Fourier transform infrared spectroscopy (FTIR)

FTIR spectra of the drug and the optimized formulation were recorded in range of 4000-400 cm^{-1}. Aripiprazole showed some prominent and characteristic peaks. In the optimized formulation, the presence of all the characteristic peaks of the Aripiprazole indicates that no interaction was occurred between the drug and the excipients.

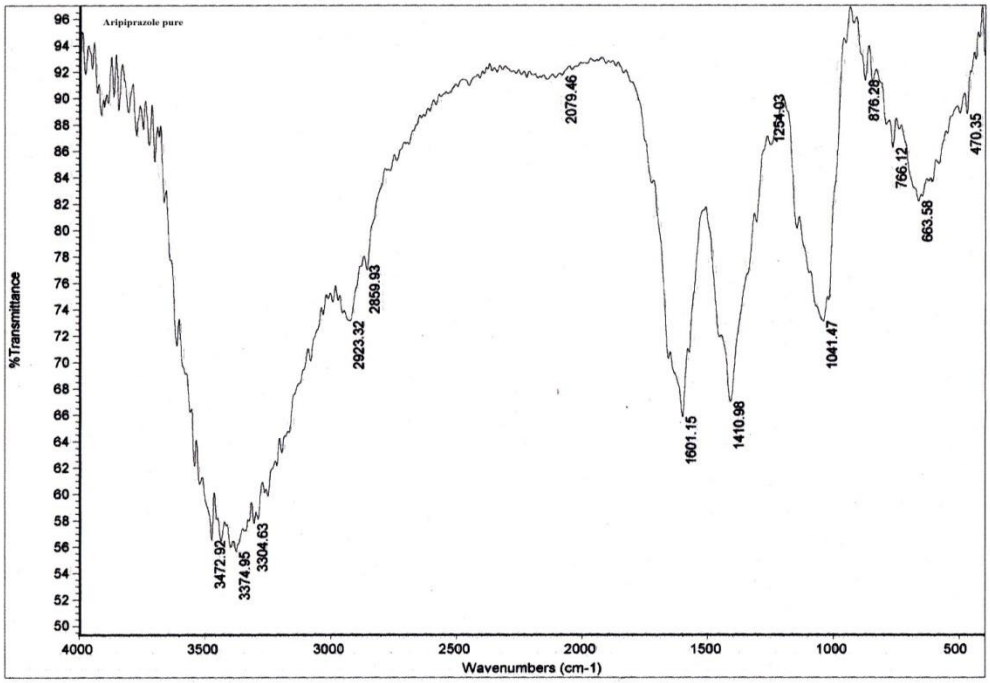

Fig No 1: FT-IR spectra of Aripiprazole pure drug

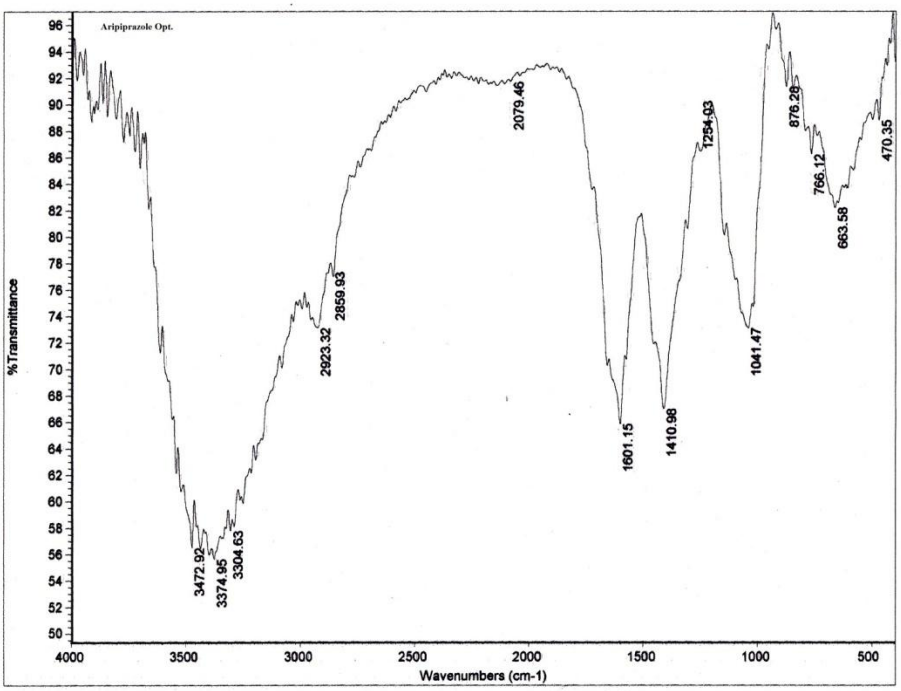

Fig No 2: FT-IR spectra of Aripiprazole optimized formulation

Results of flow properties of lubricated blend

The evaluation results for flow properties of lubricated blend are described in the following table

Table No 2: Evaluations of blends

S.No	Formulations	Bulk Density (g/ml)	Tapped Density (g/ml)	Compressibility Index (%)	Hausner's Ratio	Angle of repose
1	F-1	0.33	0.4	16.66	1.2	21.23^0
2	F-2	0.43	0.51	14.72	1.17	22.43^0
3	F-3	0.33	0.4	16.66	1.2	22.37^0
4	F-4	0.4	0.47	15	1.17	23.45^0
5	F-5	0.4	0.46	13.4	1.15	24.56^0
6	F-6	0.29	0.32	8.67	1.09	21.43^0
7	F-7	0.4	0.5	20	1.25	22.47^0
8	F-8	0.43	0.52	17.67	1.21	24.36^0
9	F-9	0.35	0.429	16.78	1.20	22.23^0

Inference

A. All formulations showed "Good" flow properties

RESULTS OF EVALUATION OF TABLETS

The evaluation results of in process properties of tablets are described in the following table

Table No 3: Evaluation of Tablets

S.No	Formulations	Thickness (mm)	Hardness (kg/cm^2)	Disintegration	Friability (%)	Assay (%)
1	F-1	4.63	5.9	1 min 10 secs	0.22	102.8
2	F-2	4.62	6.1	44 secs	0.26	100.3
3	F-3	4.86	6.2	35 secs	0.19	98.1
4	F-4	5.44	6.4	57 secs	0.25	103.9
5	F-5	5.82	6.0	38 secs	0.28	99.4
6	F-6	5.50	6.2	18 secs	0.25	102.8
7	F-7	4.61	6.0	39 secs	0.21	99.2
8	F-8	4.59	6.3	32 secs	0.23	103.8
9	F-9	4.86	5.9	22 secs	0.29	102.5

In-vitro dissolution release

Table No 4: % of Drug Release of formulations

S.No	Time (mins)	F-1	F-2	F-3	F-4	F-5	F-6	F-7	F-8	F-9

1	0	0	0	0	0	0	0	0	0	0
2	2	17.5	20.2	23.2	19.8	21.9	39.0	12.1	15.1	24.4
3	4	28.0	34.6	39.1	33.6	39.4	54.5	25.6	39.2	41.6
4	6	37.1	47.4	55.4	45.4	56.6	70.3	38.8	48.1	52.2
5	8	56.0	62.4	66.5	58.9	65.4	84.7	52.8	51.4	68.4
6	10	61.4	75.6	78.0	70.4	84.2	96.4	64.9	76.9	77.2
7	12	83.6	88.4	91.6	85.7	93.0	99.9	78.4	84.8	96.8
8	14	90.0	96.2	98.7	96.2	99.9	-	90.1	99.1	98.8
9	16	98.5	99.4	-	99.7	-	-	98.9	-	-

We selected **F - 6** as the best formulation as it showed total drug release with in 12 min than all other formulations.

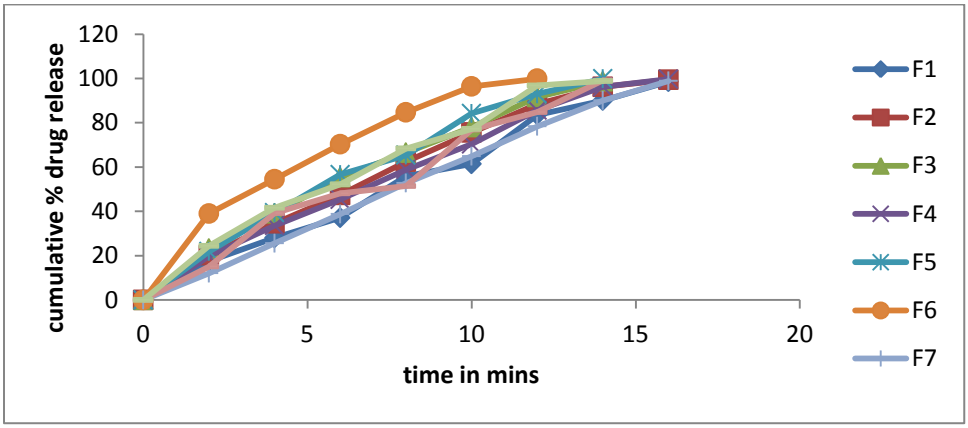

Fig No 3: Comparative In-vitro Drug release of formulations F1-F9

Stability data for optimized formulation

Table No 5: Stability studies of aripiprazole at room temperature

Time	Colour	Percent drug content at Room Temperature	Cumulative % drug release After 12mins
First day	White	102.8	99.9
30 days	White	100.5	98.6
60 days	White	98.25	98.0
90 days	White	96.89	97.6

Results from stability studies indicate that the formulated tablets are stable for a period of 3 months under room temperature i.e., 30˚C temp and 65±5% RH. There were no remarkable changes were observed during the period of storage.

DISCUSSION

All the formulations were evaluated for physical characteristics, Disintegration, Dissolution studies. Based on the results of the above mentioned tests **F–06** was selected as the best formulation as it showed total drug release 99.9% within 12 min than all other formulations.

CONCLUSION

Aim of the present study is to develop and evaluate Aripiprazole (10 mg) tablet for oral suspension. Based on Literature survey and Compatibility Tests excipients like Microcrystalline Cellulose (pH 101), mannitol, crosscarmellose sodium, cross povidone, sodium starch glycolate, Magnesium Stearate were used. In this present study, the tablets were prepared by using direct compression technique. In order to optimize the product, different formulations were developed. All the formulations were evaluated for physical characteristics, Disintegration, Dissolution studies. Based on the results of the above mentioned tests **F–06** was selected as the best formulation as it showed total drug release with in 12 min than all other formulations.

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