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Formulation and evaluation of oral dispersible tablets of aripiprazole

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ABSTRACT

An **orally disintegrating tablet** or **orally dissolving tablet** (**ODT**) is a drug dosage form available for a limited range of over-the-counter (OTC) and prescription medications. ODTs differ from traditional tablets in that they are designed to be dissolved on the tongue rather than swallowed whole. The ODT serves as an alternative dosage form for patients who experience dysphagia (difficulty in swallowing) or for where compliance is a known issue and therefore an easier dosage form to take ensures that medication is taken. Common among all age groups, dysphagia is observed in about 35% of the general population, as well as up to 60% of the elderly institutionalized population and 18-22% of all patients in long-term care facilities ODTs also have a faster onset of effects than tablets or capsules, and have the convenience of a tablet that can be taken without water. During the last decade, ODTs have become available in a variety of therapeutic markets, both OTC and by prescription. Oro-dispersible tablet refers to tablet which easily. Our objective is to formulate and evaluate the oro-dispersible tablets an anti-psychotic drug. The formulation is optimized by incorporating varying composition of polymers such as Manitol, Micro crystalline cellulose and Povidone. All the excipients are tested for compatibility with model drug. The pre-formulation parameters such as Tapped density, Bulk density, Compressibility index, Hausner's ratio and Angle of repose were analyzed. The Thickness, Hardness, Friability, Disintegration time, Weight variation and Content uniformity was evaluated for core tablets. The In-vitro drug release was performed by using dissolution apparatus-II (USP paddle type) by maintaining temperature of $37^{o}C \pm 5^{o}C$. Based on the dissolution result $\mathbf{B_6}$ formulation (containing cross povidone) was selected as best formulation. The drug release of $\mathbf{B_6}$ follows zero-order. The total amount of drug released from the $\mathbf{B_6}$ is the maximum and it reached to about **85.39%**

Keywords: Bipolar disorder, OTC, Oro-dispersible tablets, Crospovidone, Cross carmellose, Sodium starch glycilate.

BIPOLAR DISORDER

Bipolar disorder is an illness of the brain that causes severe cycles in a person's frame of mind (mood), energy level, thinking and activities. The disorder was first described by French scientist Jules Baillarger in 1854 as "dual-form mental illness." Later in the 19th century, German psychiatrist Emil Kraepelin coined the term "manic-depressive psychosis." By the 1980s, the term bipolar disorder replaced manic-depressive illness as the name psychiatrists use to describe this condition [1]. Patients with bipolar I disorder have experience at least one episode of mania; they may have experienced mixed, hypo manic (calm), and depressive episodes as well. Patients with bipolar II disorder have experienced hypo manic and depressive episodes [2-6].

Bipolar disorder is a brain disorder that causes severe shifts in mood, energy level, thinking, and behaviour. For example, people with bipolar disorder often experience episodes of overly high "highs", extreme irritability, and depression. While everyone has good and bad moods and can feel irritable, the unprovoked and intense highs and lows of people with bipolar disorder can be unpredictable, extreme, and debilitating. For those with bipolar disorder, these mood swings or "episodes" take four forms: mania, depression, mixed episodes (when mania and depression occur together), and hypomania (primarily irritable [7].

PREFORMULATION STUDIES

Bulk density

It is determined by measuring the volume of a known mass of powder sample that may have been passed through a sieve then into graduated cylinder.
Bulk density = Bulk mass / bulk volume

Tapped density

It is the ratio of total mass of powder to the tapped volume of powder; It is obtained by mechanically tapping a graduated measuring cylinder or vessel containing the powder sample, Tapped density values were noted down by substituting the tapped density values in this equation.
Tapped density = mass of powder/tapped volume of powder

Compressibility

Used to indicate powder flow properties. It was measured by tapped density of powder to bulk density of powder.
% Compressibility: tapped density –bulk density/ tapped density ×100

Hausners ratio

This is simple index for measurement of powder flow
Hausners ratio = tapped density/ bulk density
Angle of repose: It is an indicative of the flow properties of powder
Tan Ɵ =h/r

The powder mixer was allowed to flow through the funnel fixed to a stand at definite height. Angle of repose was calculated by measuring the height n radius of the heap of powder formula.

DIRECT COMPRESSION

Formulation	Bulk density	Tapped density	% Compressbility	Hausners Ratio
B1	0.35	0.46	23.91	1.31
B2	0.39	0.46	15.2	1.18
B3	0.59	0.67	13.9	1.13
B4	0.59	0.68	13.2	1.15
B5	0.37	0.44	15.9	1.19
B6	0.55	0.63	12.7	1.11
B7	0.36	0.52	30.76	1.44
B8	0.42	0.48	12.5	1.42
B9	0.39	0.49	20.40	1.25

Direct compression method

Accurate amount of drug was weighed and excipients are mixed together. Later they are compressed directly in tablet punching machine using suitable hardness for punching of tablets. Later tablets were prepared by direct compression method.

Table.1 Formulation of Tablets

Ingredients	B1	B2	B3	B4	B5	B6	B7	B8	B9
Aripiprazole(mg)	10	10	10	10	10	10	10	10	10
Mannitol(mg)	102.2	99.4	96.6	102.2	99.4	96.6	102.2	99.4	96.6
MCC(mg)	18	18	18	18	18	18	18	18	18
Povidone (PVPK30)(mg)	4	4	4	4	4	4	4	4	4
SSG(mg)	2.8	5.6	8.6	-	-	-	-	-	-
Cross povidone(mg)	-	-	-	2.8	5.6	8.6	-	-	-
Cross carmellose sodium(mg)	-	-	-	-	-	-	2.8	5.6	8.6
Aspartame(mg)	1	1	1	1	1	1	1	1	1
Lemon flavour(mg)	1	1	1	1	1	1	1	1	1
Mg stearate(mg)	1	1	1	1	1	1	1	1	1

RESULTS AND DISCUSSIONS

Organoleptic properties

A small quantity of aripiprazole was taken in a butter paper and viewed in well illuminated place. It is a colorless powder.

ODOUR : Odourless.

INVITRO DISSOLUTION STUDIES

Preparation of 0.1n HCL

8.5ml of HCl was measured and makeup to 1000ml with distilled water.

Procedure

The prepared 0.1N Hcl was poured in a dissolution basket, the drug was added to the dissolution basket and the paddle was made to rotate at 50 rpm and temperature was maintained at 37.8°c. The samples were collected at different time intervals. 5ml of sample was collected from dissolution basket. The samples were filtered and filtrate was obtained, 1ml of filtrate was collected to that add 4ml of ferric nitrate. The absorbence was measured at257nm by using UV visible spectrophotometer.

Table.2 Formulation B1

Sl. no	Time(min)	cumulative% drug dissolved
1	0	0
2	5	8.8
3	10	17.77
4	20	30.4
5	30	54.3
6	45	70.79
7	60	87.59

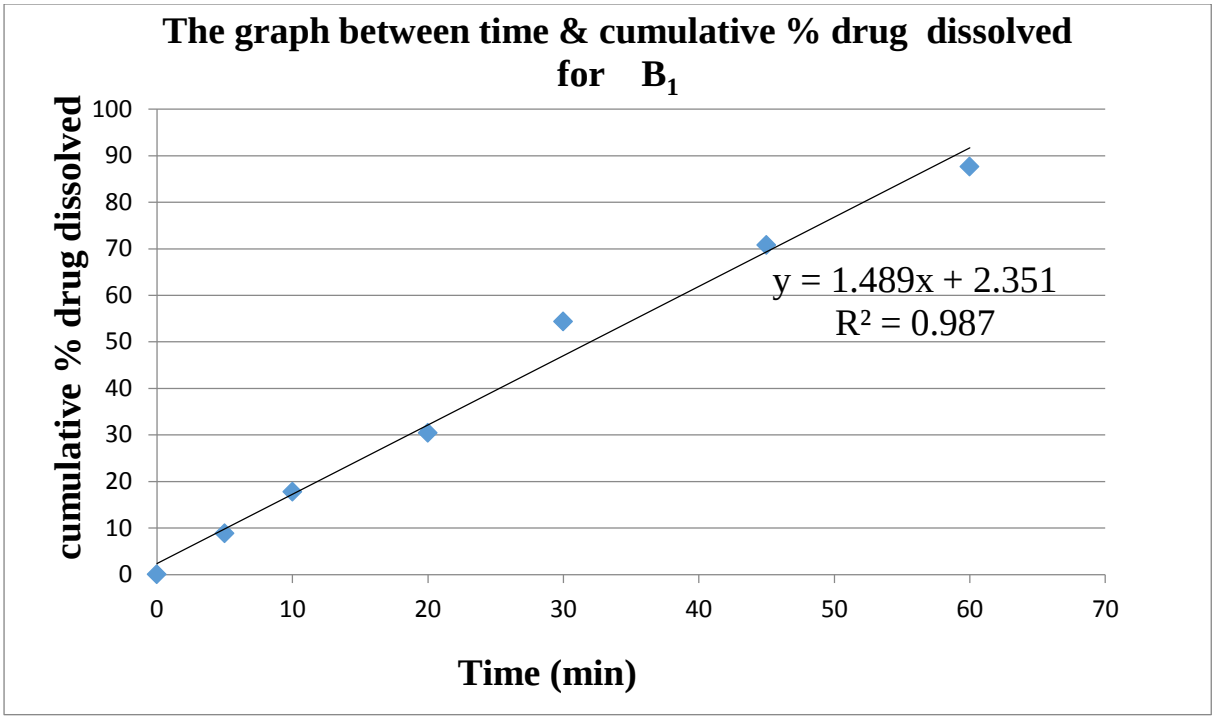

Fig: The zero order of B_1

Table.3 Formulation B2

Sl no.	Time(min)	cumulative % drug dissolved
1	0	0
2	5	7.9
3	10	21.46
4	20	34.87
5	30	44.67
6	45	57.2
7	60	81.43

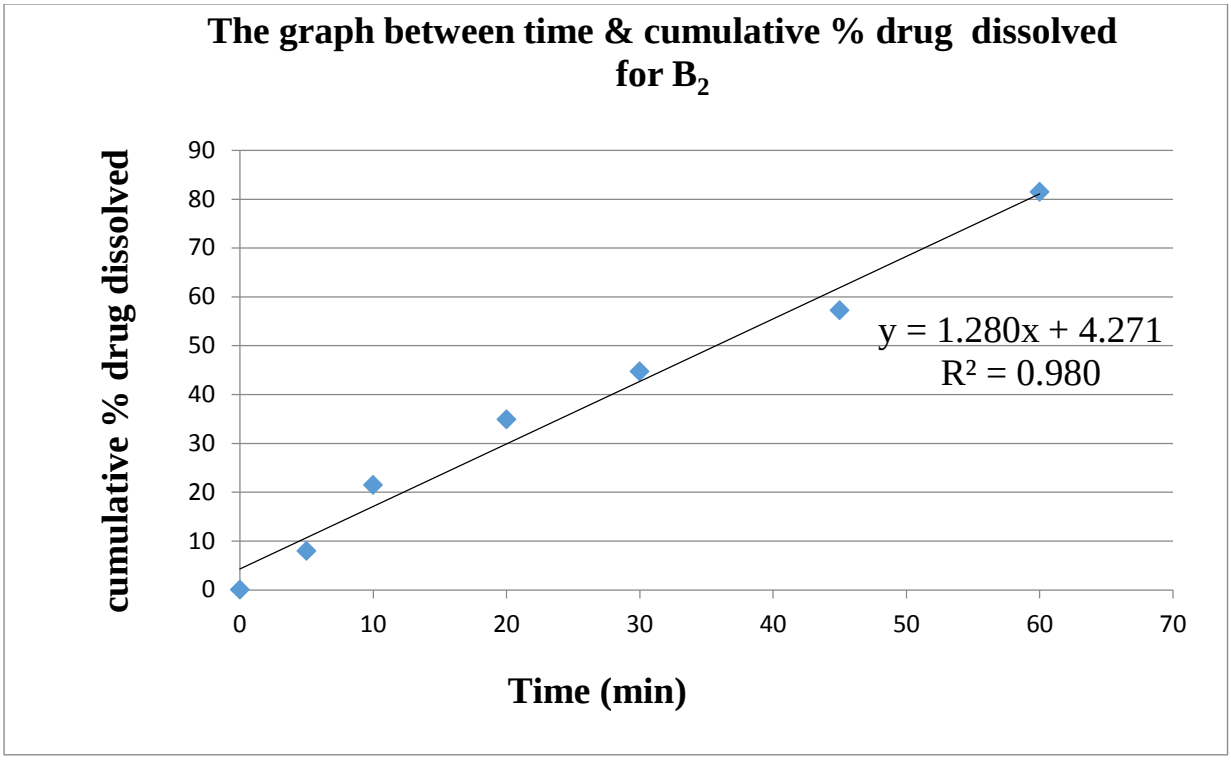

Fig: The zero order of B_2

Table.4 Formulation B3

Sl no.	Time(min)	cumulative % drug dissolved
1	0	0
2	5	10.39
3	10	19.99
4	20	24.19
5	30	32.2
6	45	43.66
7	60	67.24

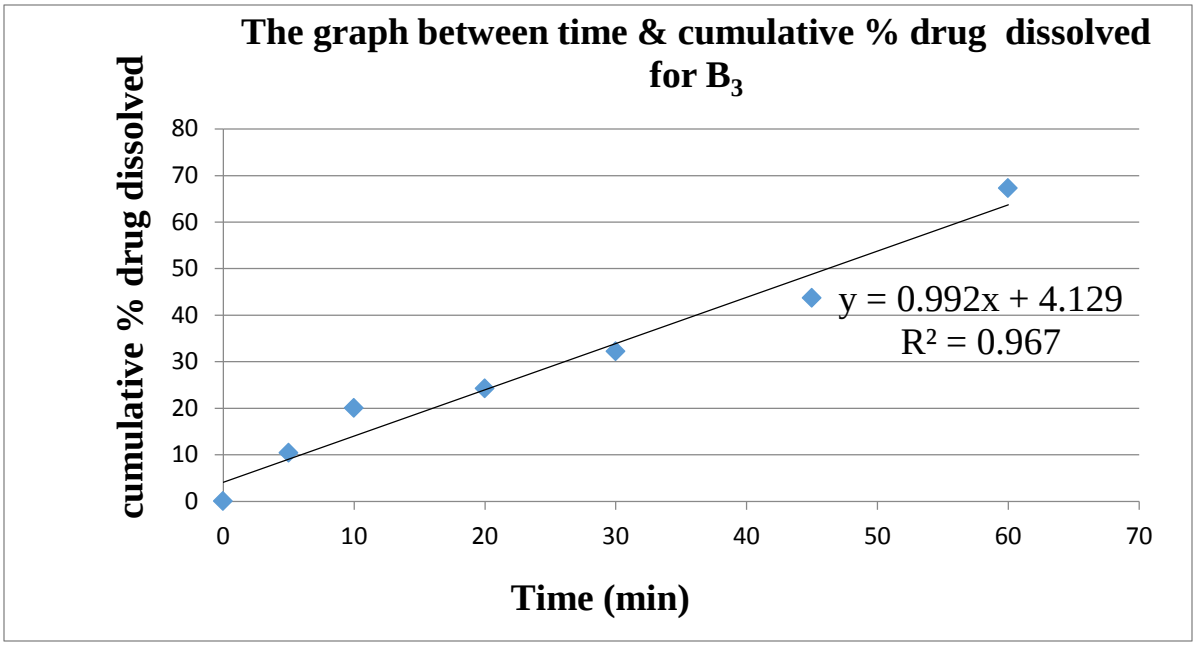

Fig: The zero order of B_3

Table.5 Formulation B4

Sl no.	Time(min)	cumulative % drug dissolved
1	0	0
2	5	10.67
3	10	27.67
4	20	35.67
5	30	47.78
6	45	58.6
7	60	80.56

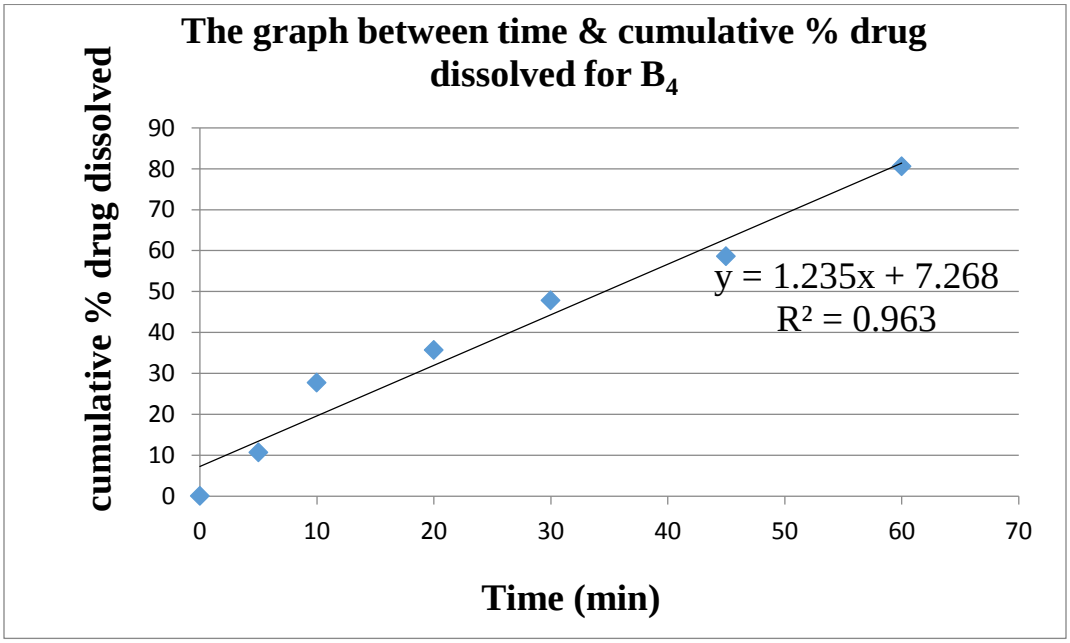

Fig: The zero order of B_4

Table.6 Formulation B5

Sl no.	Time(min)	cumulative % drug dissolved
1	0	0
2	5	8.28
3	10	18.76
4	20	28.56
5	30	47.67
6	45	60.31
7	60	79.69

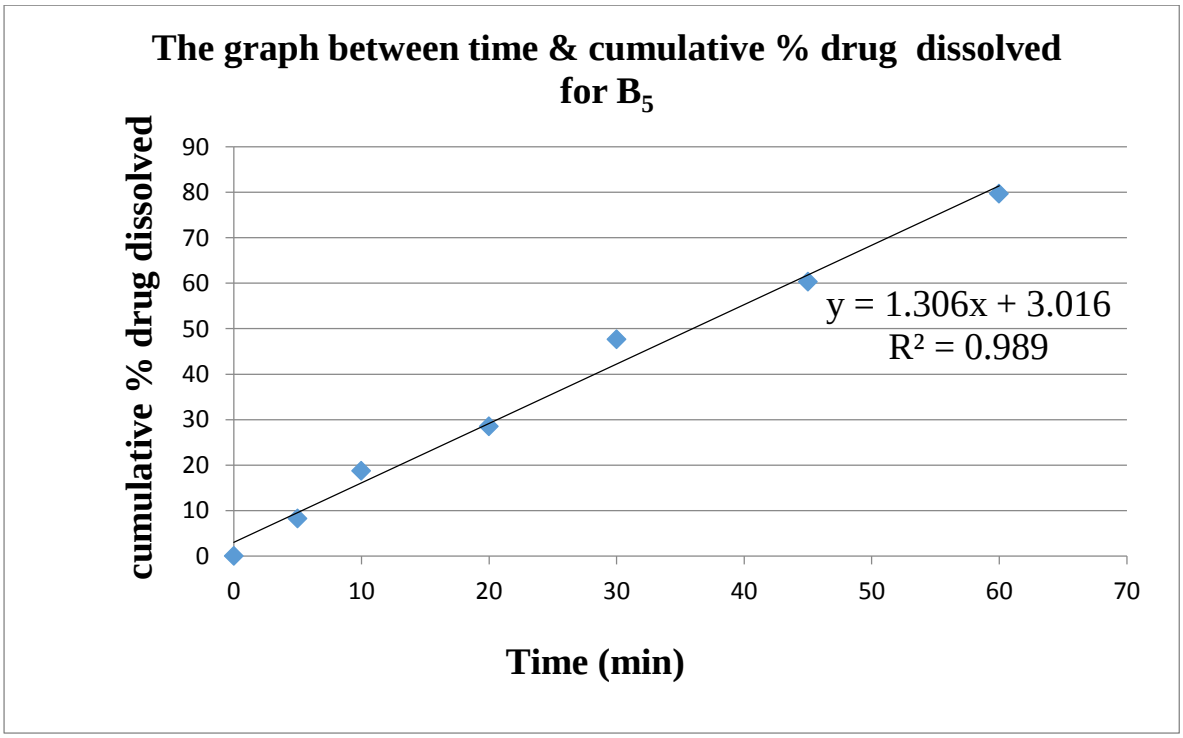

Fig: The zero order of B_5

Table.7 Formulation B6

Sl no.	Time(min)	cumulative % drug dissolved
1	0	0
2	5	9.5
3	10	18.46
4	20	31.56
5	30	45
6	45	59.09
7	60	85.36

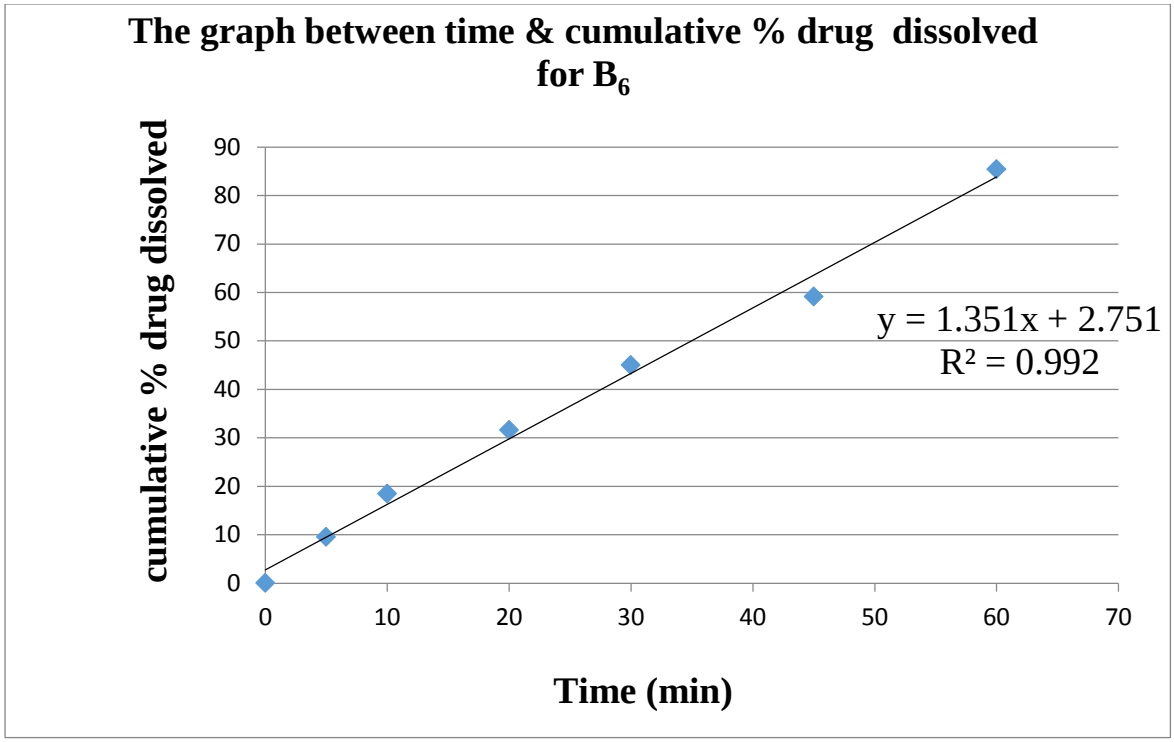

Fig: The zero order of B_6

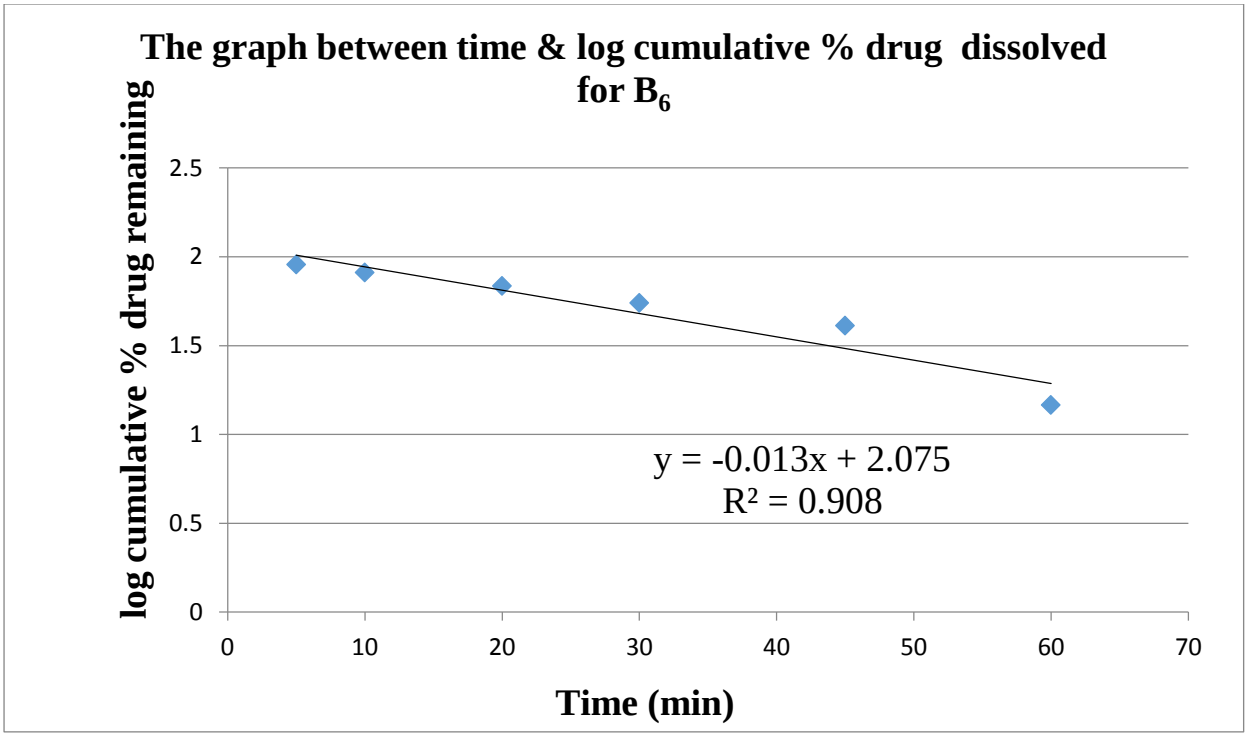

Fig: The first order of B_6

CONCLUSION

- *In vitro* drug release studies recommended the product for further *in vivo* studies and stability studies and which may improve patient compliance.
- From the literature it was known that Aripiprazole is used as oral dispersible dosage

form in the treatment of bipolar disorder. Oral dispersible tablets will improve the patient compliance.

- From the result B_6 has been selected as best formulation among all the other formulation. B_6 provide better in vitro release from the dosage form.
- The data obtained from in vitro release study was fitted to various mathematical models like Zero order & First order kinetics.
- The result of mathematical fitting of data obtained indicated that, the best fit model in all the cases was found to be diffusion for optimize formulation B_6.
- Thus the release of the drug from the dosage form was found to be Zero order kinetics.

SUMMARY

- This work involves the formulation development, optimization and invitro evaluation of oral dispersible tablet containing Aripiprazole using sodium starch glycolate , Crosspovidone and Crosscarmellose sodium as super disintegrating agents and polymers such as Mannitol, MCC and Povidone in different.
- Oral dispersible tablets show immediate release of the drug from the dosage form which is useful for the treatment of Bipolar disorder.
- To minimize the critical process parameter, direct compression method was selected for the formulation of Aripiprazole.
- Under the pre-formulation studies API characterization and drug–excipient compatibility studies were carried out. The polymer and other excipients are selected based on the satisfactory results produced during drug- excipient compatibility studies to develop new formulation.
- The invitro study showed that the formulation $B_6$was ideally suitable for oral dispersible tablets.
- The final suitable formulation was achieved fruit fully by direct compression technique.
- B6 formulation containing SSG, Crosspovidone and Crosscarmellose in the ratio of 0:8:4:0 has produced desired release profile for Aripiprazole ODT's.

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