IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

DESIGN AND DEVELOPMENT OF RAPIMELT TABLET

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Abstract: Rapimelt Tablet tablets are those that dissolve or disintegrate quickly in the oral cavity, resulting in solution or suspension. Almotriptan significantly reduced the number of Migraine Pain, their intensity score and their duration compared to the placebo both in MD and PPV. In the present study Rapimelt Tablet tablet for the treatment of Migraine was prepared by direct compression method using crosspovidone, Crosscarmellose and Indion 414, as superdisintegrants in a ratio of 6%, 9% and 12% respectively. FT-IR study shows that there is no significant interactions occur between drug and excipient. The tablets prepared were evaluated for various parameters like various density parameters, thickness, hardness, friability, disintegration time, wetting time and In-vitro dissolution time. All the parameters were found to be within limits. The developed formulation of Almotriptan batch F8 (9% Indion 414) showed good palatability and dispersed within 30 seconds as compared to other superdisintigrants..

Index Terms - Rapimelt Tablet**,** Almotriptan**,** superdisintegrants**,** Indion 414 and In-vitro dissolution time

I. INTRODUCTION

Drug Delivery Systems (DDS) are a strategic tool for expanding markets/indications, extending product life cycles and generating opportunities. DDS make a significant contribution to global pharmaceutical sales through market segmentation, and are moving rapidly. Drug delivery systems are becoming increasingly sophisticated as pharmaceutical scientists acquire a better understanding of the physicochemical and biochemical parameters pertinent to their performance1.

Despite of tremendous advancements in drug delivery, the oral route remains the perfect route for the administration of therapeutic agents because of low cost of therapy, ease of administration, accurate dosage, self‐medication, pain avoidance, versatility, leading to high levels of patient compliance. Tablets and capsules are the most popular dosage forms. But one important drawback of such dosage forms is ‘Dysphagia’ or difficulty in swallowing. This is seen to afflict nearly 35% of the general population. This disorder is also associated with a number of conditions like:

1. Parkinsonism
2. Motion sickness
3. Unconsciousness
4. Elderly patients
5. Children
6. Mentally disabled persons
7. Unavailability of water

Improved patient compliance has achieved enormous demand. Consequently demand for their technologies is also increasing many folds. To develop a chemical entity, a lot of money, hard work and time are required. So focus is rather being laid on the development of new drug delivery systems for already existing drugs, with enhanced efficacy and bioavailability, thus reducing the dose and dosing frequency to minimize the side effects. It is always the aim of a scientist or a dosage form designer to enhance the safety of a drug molecule while maintaining its therapeutic efficacy. Recent advances in Novel Drug Delivery Systems (NDDS) aim for the same by formulating a dosage form, convenient to be administered so as to achieve better patient compliance. Pharmaceutical technologists have put in their best efforts to develop a Fast Dissolving Drug Delivery System, i.e DispersibleTablet1.

1.2 Orally Disintegrated Tablet (RAPIMELT TABLET)

It is a tablet that disintegrates and dissolves rapidly in the saliva, within a few seconds without the need of drinking water or chewing. A Dispersible tablet usually dissolves in the oral cavity within 15 s to 3 min. Most of the RAPIMELT TABLETs include certain super disintegrants and taste masking agents.

1.3 Ideal properties of RAPIMELT TABLET

1. A Orally Disintigrated Tablet should
    a. Not require water or other liquid to swallow.
    b. Easily dissolve or disintegrate in saliva within a few seconds.
    c. Have a pleasing taste.
    d. Leave negligible or no residue in the mouth when administered.
2. Be portable and easy to transport.
3. Be able to be manufactured in a simple conventional manner within low cost.
4. Be less sensitive to environmental conditions like temperature, humidity etc1.

1.4 Advantages of RAPIMELT TABLET

1. No need of water to swallow the tablet.
2. Can be easily administered to pediatric, elderly and mentally disabled patients.
3. Accurate dosing as compared to liquids.
4. Dissolution and absorption of drug is fast, offering rapid onset of action.
5. Bioavailability of drugs is increased as some drugs are absorbed from mouth, pharynx and esophagus through saliva passing
   down into the stomach.
6. Advantageous over liquid medication in terms of administration as well as transportation.
7. First pass metabolism is reduced, thus offering improved bioavailability and thus reduced dose and side effects.
8. Free of risk of suffocation due to physical obstruction when swallowed, thus offering improved safety.
9. Suitable for sustained/controlled release actives1.

1.5 Desired Criteria for Rapimelt Tablets2

Rapimelt Tablet should-

- Not require water to swallow, but it should dissolve or disintegrate in the mouth within matter of seconds.
- Be compatible with taste masking
- Be portable without fragility concern.
- Have a pleasing mouth feel.
- Leave minimal or no residue in the mouth after oral administration.
- Exhibit low sensivity to environmental condition as humidity and temperature.
- Be manufactured using conventional processing and packaging equipment at low cost.
- Salient features of mouth fast dissolving tablets
- Ease of administration to patients who refuse to swallow a tablet, such as pediatric and geriatric patients and psychiatric patients.
- Convenience of administration and accurate dosing as compared to liquids.
- No need of water to swallow the dosage from, which is highly convenient feature for patients who are traveling and do not have immediate access to water.

- Good mouth feel property of MDDS helps to change the basic view of medication as "bitter pill", particularly for pediatric patients.
- Rapid dissolution and absorption of drug, which may produce rapid onset of action.
- Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach, and in such cases bioavailability of drugs in increased.
- Ability to provide advantages of liquid medication in the form of solid preparation.
- Pre gastric absorption can result in improved bioavailability and as a result of reduced dosage, improved clinical performance through a reduction of unwanted effects.

1.6 Mechanism of action of disintegrants

The tablet breaks to primary particles by one or more of the mechanisms listed below: -

a. By capillary action
b. By swelling
c. Because of heat of wetting
d. Due to release of gases
e. By enzymatic action
f. Due to disintegrating particle/particle repulsive forces
g. Due to deformation

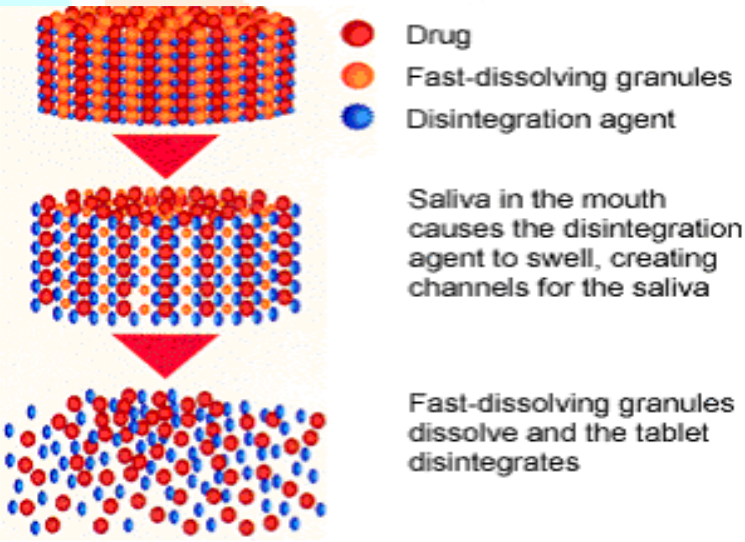

Fig. 1: Mechanism of Action of Superdisintegrants

2. Formulation Development

Rapimelt tablet were prepared by superdisintegrant addition method. The tablets were formulated employing direct compression method using 8 mm biconcave punches. It is the process by which tablets are compressed directly from mixtures of the drug and excipients without preliminary treatment such as granulation.

Almotriptan (12.5 mg), super disintegrants in different ratios and excipients were blended using mortar and pestle. The drug and the disintegrants were sieved through mesh # 120 before blending. The mixture was evaluated for angle of repose, bulk density and compressibility. The mixture was mixed with 1% magnesium stearate as lubricant and mint as flavoring agent. The powder blends were then compressed by using Fluidpack multistation rotary tablet machine using 8 mm punch. The hardness was adjusted to 2-5 kg/cm^2.

Table 1. Formulation of Rapimelt tablets

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Almotriptan	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5
MCC (PH-102)	28.5	28.5	28.5	28.5	28.5	28.5	28.5	28.5	28.5
Crosscarmellose sodium	9 (6%)	13.5 (9%)	18 (12%)	-	-	-	-	-	-
Crosspovidone	-	-	-	9 (6%)	13.5 (9%)	18 (12%)	-	-	-
Indion 414	-	-	-	-	-	-	9 (6%)	13.5 (9%)	18 (12%)
Povidone	1	1	1	1	1	1	1	**1**	1
Pearlitol SD200	96	91.5	87	96	91.5	87	96	**91.5**	87
Aspartame	q.s	q.s	q.s	q.s	q.s	q.s	q.s	**q.s**	q.s
Talcum powder	1%	1%	1%	1%	1%	1%	1%	**1%**	1%
Mg. Stearate	1%	1%	1%	1%	1%	1%	1%	**1%**	1%

3. IDENTIFICATION OF PURE DRUG (Almotriptan):-

Pure drug has been identified by using technique like IR.

3.1 INFRA-RED SPECTROPHOTOMETRY

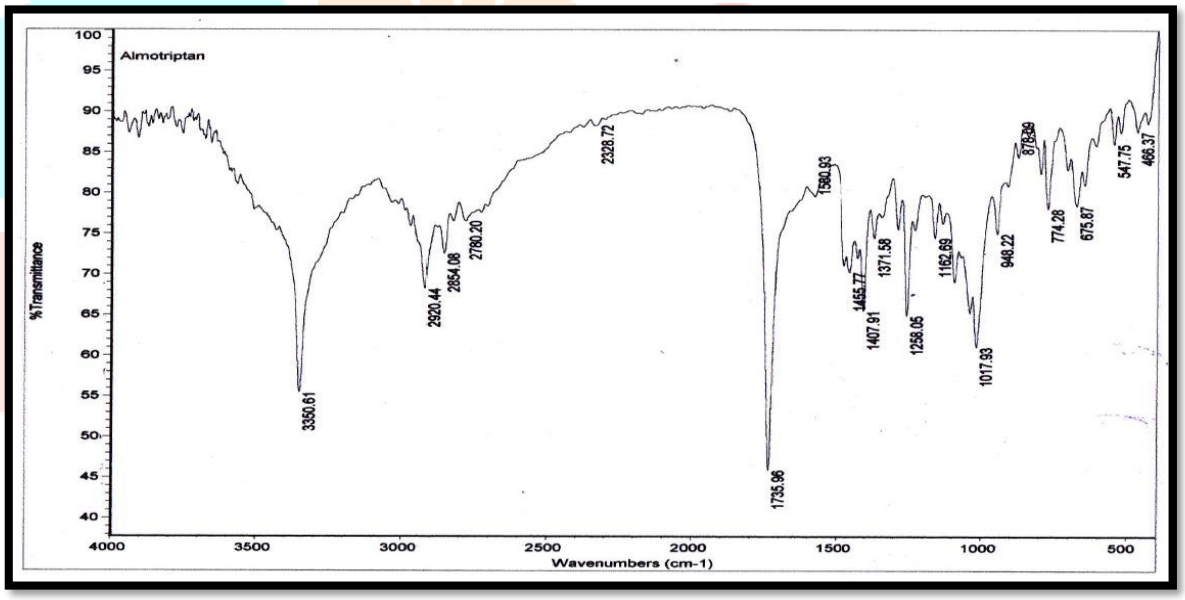

Fig. 2: FT-IR Spectra of pure drug Almotriptan

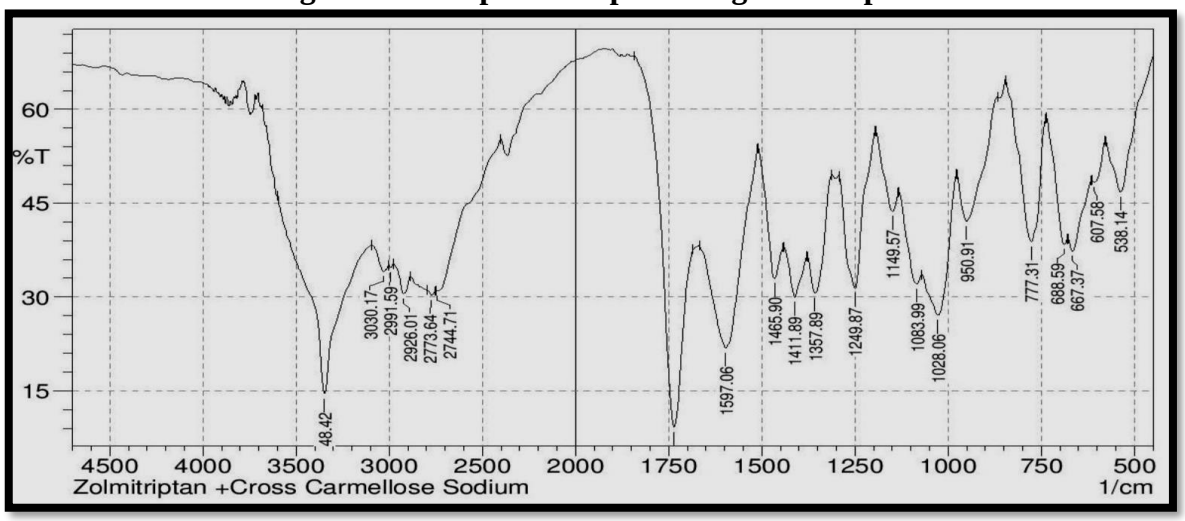

Fig. 3: FT-IR Spectra of physical mixture of drug and Croscarmellose sodium

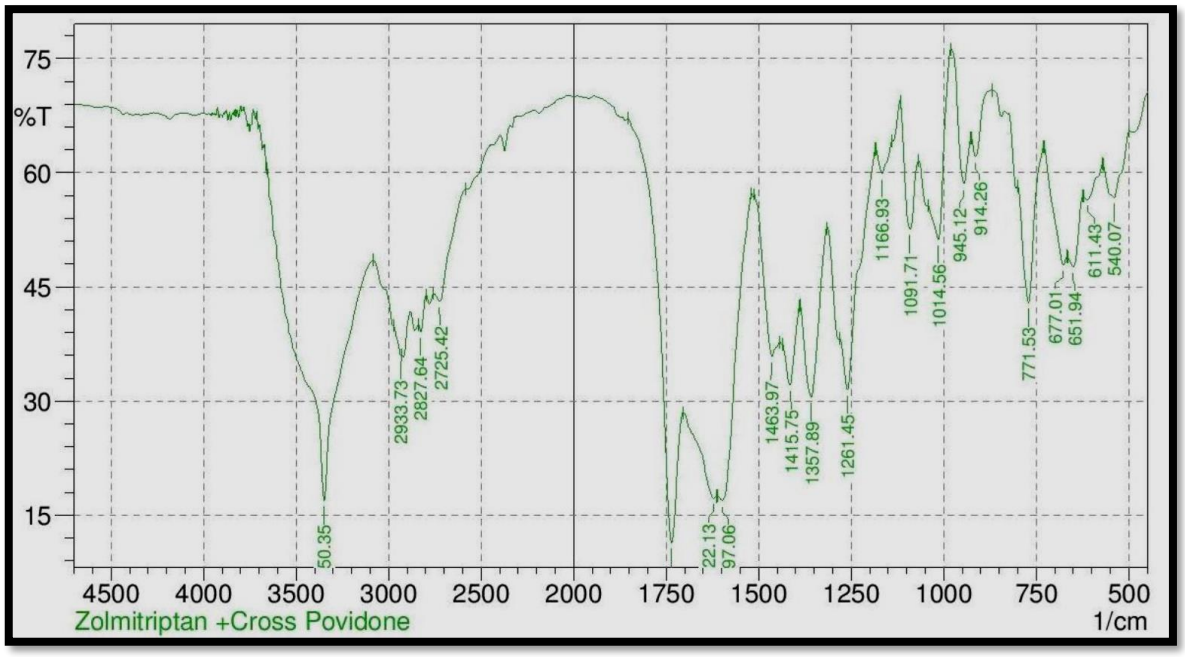

Fig. 4: FT-IR Spectra of physical mixture of drug and Crospovidone

4. Evaluation of powder parameters (Pre-Compression):-

Table No. 2: Preformulation studies of various batches

Batch	Angle of Repose (θ)/ ± SD	Bulk Density (g/cc)/ ±SD	Tapped Density (g/cc)/ ±SD	(%) Compressibility /±SD	Hausner's Ratio/ ±SD
F1	33.13^0 ± 0.003	0.47 ± 0.007	0.54± 0.003	14.23± 1.601	1.16 ± 0.802
F2	32.55^0 ± 0.201	0.44 ± 0.017	0.50± 0.017	12.62± 1.032	1.14 ± 0.010
F3	33.25^0 ± 0.045	0.56 ± 0.024	0.66± 0.038	15.15± 1.926	1.16 ± 0.802
F4	31.21^0 ± 0.675	0.48 ± 0.003	0.54 ± 0.003	12.40± 0.954	1.14 ± 0.010
F5	38.36^0 ± 1.852	0.45 ± 0.014	0.48 ± 0.024	5.20± 1.590	1.06 ± 0.017
F6	33.74^0 ± 0.219	0.47 ± 0.007	0.50 ± 0.017	5.25± 1.573	1.06 ± 0.017
F7	32.05^0 ± 0.378	0.48 ± 0.003	0.56 ± 0.003	6.36± 1.180	1.14 ± 0.010
F8	31.03^0 ± 0.738	0.51 ± 0.007	0.54 ± 0.003	4.42± 1.866	1.04 ± 0.024
F9	32.82^0 ± 0.106	0.53 ± 0.014	0.60 ± 0.017	11.66± 0.692	1.13 ± 0.007

5. Evaluation of Tablet (Post-Compression):-

Table No.3: Physical evaluation of formulated tablet batches

Parameter	F1	F2	F3	F4	F5	F6	F7	F8	F9
Thickness (mm)/± SD	2.61 ±0.00	2.64 ±0.01	2.63 ±0.01	2.62 ±0.01	2.64 ±0.01	2.61 ±0.00	2.51 ±0.02	2.52 ±0.02	2.54 ±0.01
Hardness (kg/cm^2)/± SD	3.6 ±0.17	3.2 ±0.19	2.9 ±0.07	3.4 ±0.10	3.1 ±0.00	3.4 ±0.10	3.2 ±0.19	2.9 ±0.07	2.5 ±0.21
Friability (% w/w)/ ± SD	0.21 ±0.11	0.73 ±0.06	1.16 ±0.21	0.53 ±0.00	0.41 ±0.04	1.07 ±0.18	0.12 ±0.14	0.32 ±0.07	0.33 ±0.07
Wetting time (sec)/ ± SD	19 ±0.51	14 ±1.21	16 ±0.50	15 ±0.86	18 ±0.19	19 ±0.55	16 ±0.50	12 ±1.92	28 ±3.73
Disintgration time (sec)/± SD	25 ±0.86	21 ±0.54	22 ±0.19	27 ±1.57	24 ±0.51	25 ±0.86	23 ±0.15	17 ±1.96	19 ±1.25
Drug content (% w/v)/± SD	87.53 ±0.20	87.80 ±0.10	88.16 ±0.01	87.48 ±0.22	87.80 ±0.10	78.40 ±3.43	87.96 ±0.05	95.11 ±0.93	92.76 ±1.64
Dissolution (%w/v)/± SD	67.71 ±5.83	81.32±1.02	69.0 ±5.38	89.43±1.84	85.53±0.46	87.93±1.31	89.98±2.03	95.48±3.98	91.68± 2.63

6. In-Vitro Dissolution Study (In vitro drug release)

Table no. 4 In vitro drug release from blended formulation

Time	F1	F2	F3	F4	F5	F6	F7	F8	F9
30 sec	9.44	14.73	11.08	13.72	14.96	13.5	14.58	14.73	14.17
60 sec	20.41	29.76	21.87	27.75	29.95	27.47	29.55	29.33	28.68
90 sec	31.71	48.40	33.40	41.55	45.7	41.73	45.0	45.08	43.13
120 sec	43.18	61.49	44.98	57.26	61.71	36.96	61.61	61.28	59.17
150 sec	53.33	77.80	56.80	73.12	78.1	72.6	77.36	78.16	75.15
180 sec	67.71	81.32	69.0	89.43	85.3	87.93	89.98	95.48	91.68

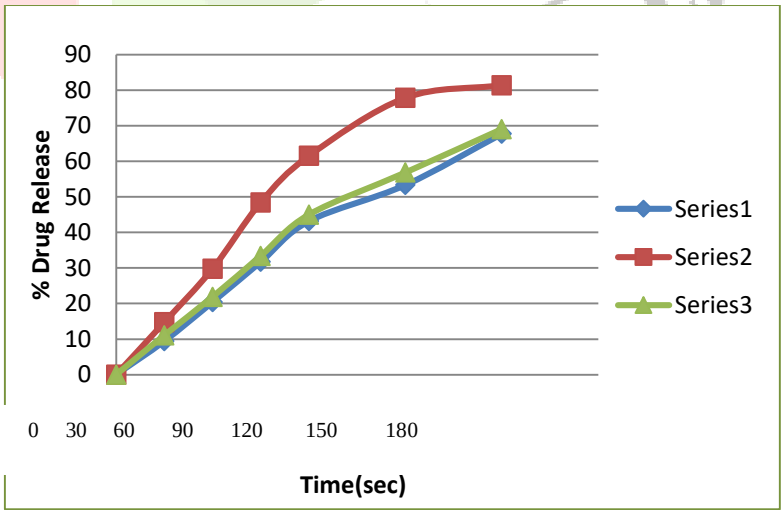

Figure 5: Comparative study of % Drug release (Batch F1, F2 and F3)

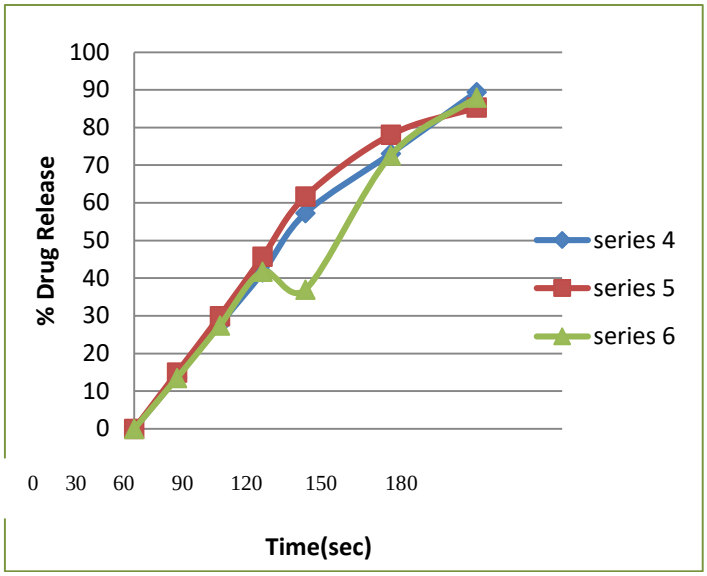

Fig No. 6: Comparative study of % Drug release (Batch F4, F5 and F6)

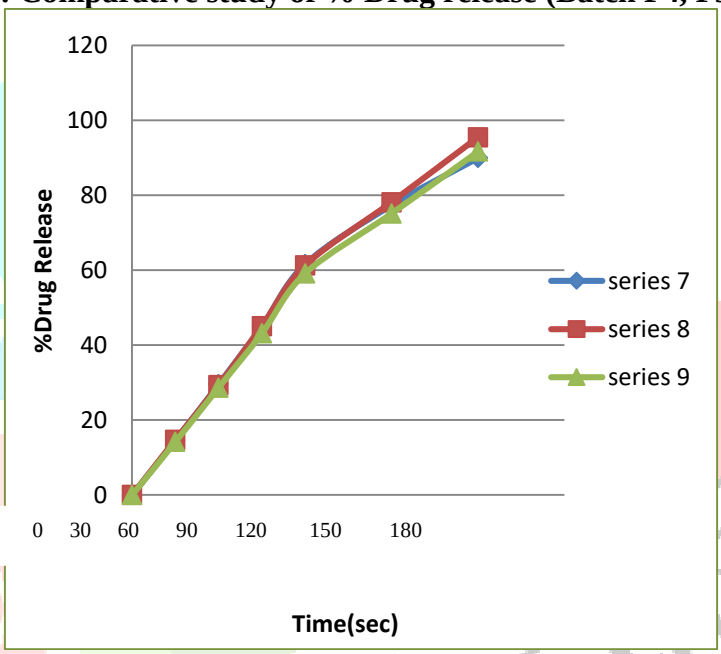

Fig No. 7: Comparative study of % Drug release (Batch F7, F8 and F9)

7 Mechanism of Release from Matrix tablets:

From the data obtained after applying all suitable mathematical models we can conclude that the optimized formulations selected are proposed to explain the mechanism of release of drug from formulation

Table.no.5: Drug release kinetic study of optimized batch

MODELS		F_8 (Almotriptan)
Korsmeyer- peppas	n	0.987
Zero order	R	0.976
First order	R	0.846
Higuchi model	R	0.996
Best fit model		Higuchi

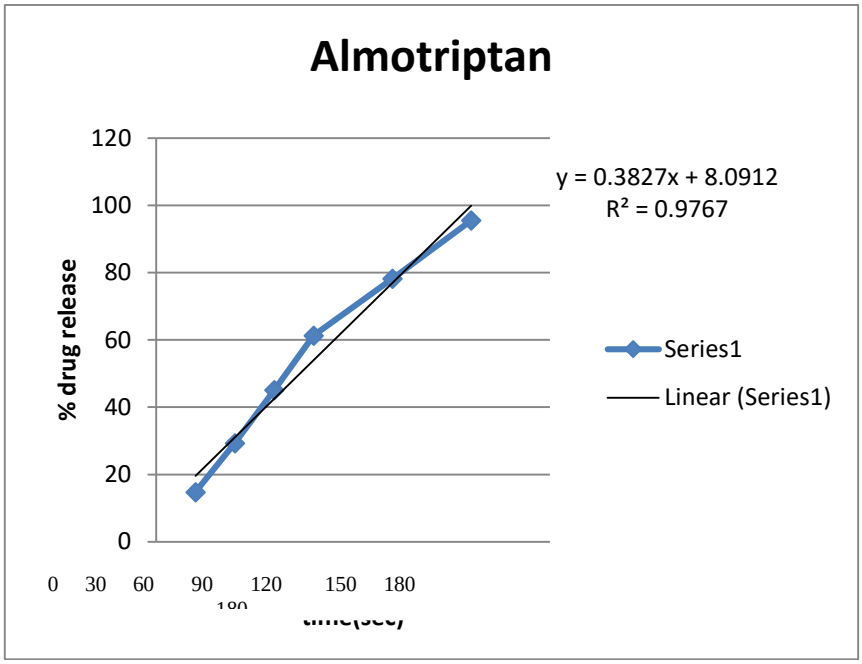

Fig No. 8: Curve fitting data of the release rate profile of zero order.

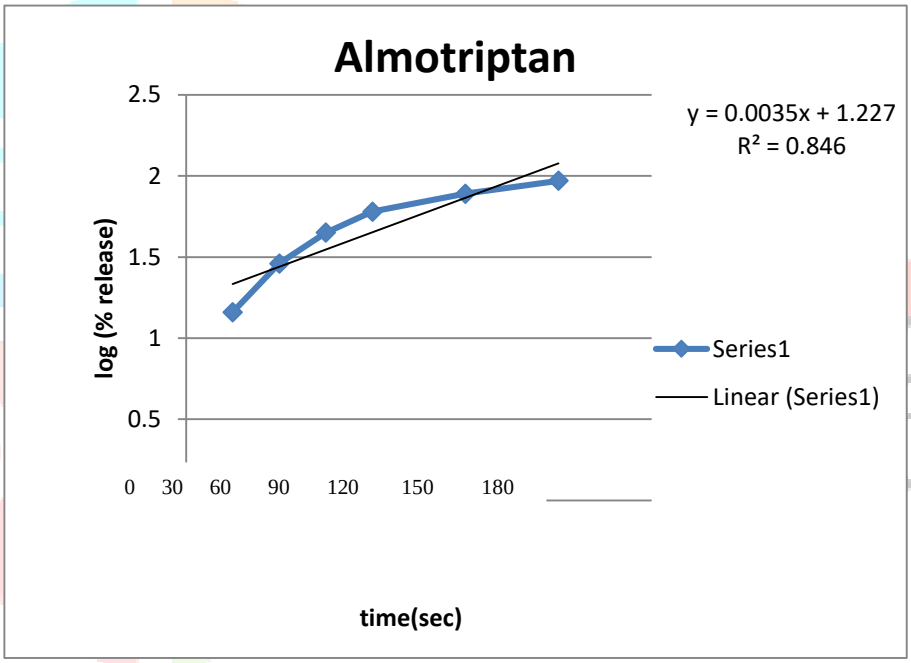

Fig No.9: Curve fitting data of the release rate profile of first order.

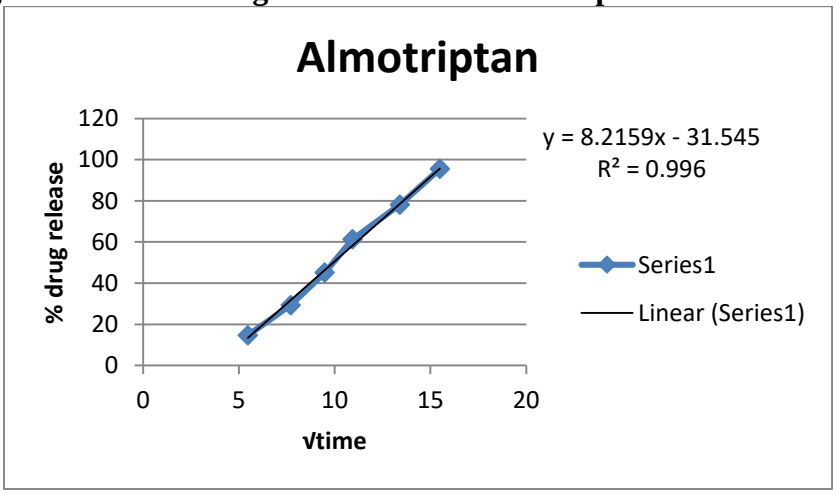

Fig No.10: Curve fitting data of the release rate profile of Higuchi model

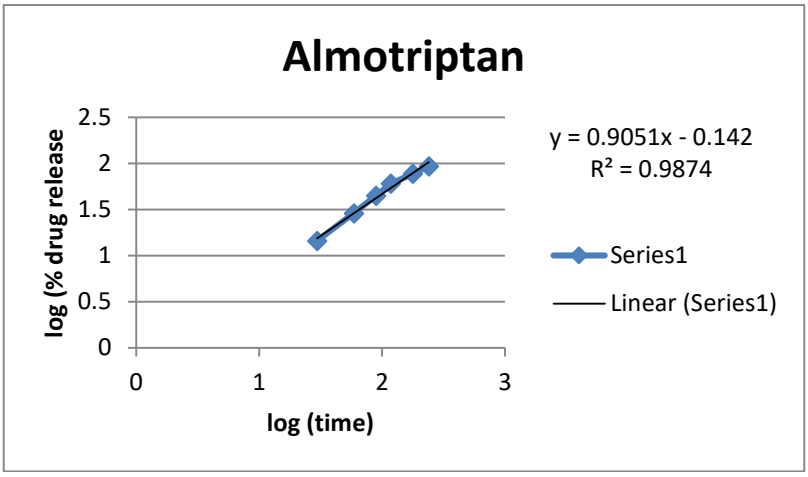

Fig No.11: Curve fitting data of the release rate profile of Korsmeyer-peppas.

8. Conclusion

In present study Almotriptan Rapimelt tablet prepared using different types and concentrations of superdisintegrant in a different ratio of 6%, 9% and 12% respectively by direct compression method which was confirmed by various characterization and evaluation studies. Indion 414 (9%) as superdisintegrant gives better result as compared to crosscarmellose sodium and crosspovidone. Tablets disintegrate within 30 sec in mouth having better mouth feel.

9. References

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