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FORMULATION AND ITS CHARACTERIZATION OF ASTEMIZOLE DISPERSIBLE TABLET

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Abstract:

Mouth dissolving tablet or dispersible table is a widely acceptable dosage forms which dissolves rapidly in the saliva, without water. It enhanced efficacy and bioavailability, thus reducing the dose and dosing frequency to minimize the side effects. In the present work Astemizole dispersible tablet of was prepared by direct compression method using polymers like crosspovidone, Crosscarmellose and Indion 414, as superdisintegrants. 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 Astemizole batch F8 (9 % Indion 414) showed good palatability and dispersed within 30 seconds as compared to crosscarmellose.

Keywords: Dispersible tablet, Astemizole, Compression method, Crosscarmellose, Indion 414.

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 performance. [1] 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. [2] 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. [3]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. [4] 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 DispersibleTablet.

Dispersible tablet (DT)

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 Dispersibletablet usually dissolves in the oral cavity within 15 s to 3 min. Most of the DTs include certain super disintegrants and taste masking agents. [5]

Ideal properties of DT

It does not require water or other liquid to swallow. [6]

Easily dissolve or disintegrate in saliva within a few seconds.

It can be easily administered to pediatric, elderly and mentally disabled patients.

Dose accuracy maintain, rapid and onset of action is fast. [7]

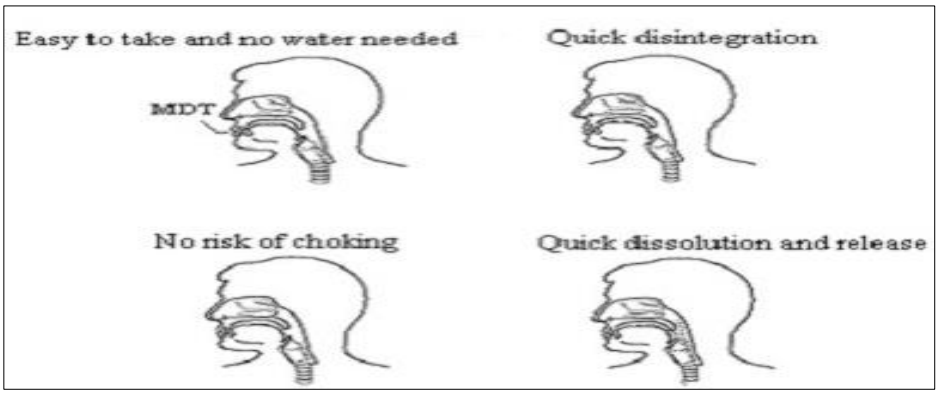
Advantages of DT

Bioavailability of drugs is increased

Advantageous over liquid medication.

First pass metabolism is reduced, thus offering improved bioavailability and thus reduced dose and side effects. [8]

Fig. 1: Advantages of DT



MATERIAL AND METHOD

The drug Astemizole was a gift sample from Anazeal Analyticals & Research Private Limited, Mumbai, and the MCC (PH-102), Crosscarmellose sodium, Crosspovidone, Indion 414, Povidone, Pearlitol SD200, Aspartame, Talcum powder, Mg. Stearate, were purchased from sudarshan chemicals Raipur C.G Other solvents and materials used in this study were of analytical grade.

Preparation of Mouth-dissolving tablets by direct compression method

Dispersible tablet prepared by superdisintegrant addition method. [9] 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. Drug (10 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. [10] 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/cm2.

Table No. 1: Formulation of Mouth-disssolving tablets

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Astemizole	10	10	10	10	10	10	10	10	10
MCC (PH-102)	39	39	39	39	39	39	39	39	39
Crosscarmellose sodium	9	13.5	18	-	-	-	-	-	-
Crosspovidone	-	-	-	9	13.5	18	-	-	-
Indion 414	-	-	-	-	-	-	9	13.5	18

Povidone	1	1	1	1	1	1	1	1	1
Pearlitol SD200	89	84.5	80	89	84.5	80	89	84.5	80
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%

EVALUATION PARAMETERS OF "ASTEMIZOLE" DISPERSIBLE TABLET

The tablets were compressed using 8 mm diameter, round, biconcave punches on a Fluidpack multistation rotary tablet machine. The tablet weight was kept 150 mg and hardness between 2 – 5 kg/cm2. [11]

Taste and Colour

The tablets of prepared formulations were observed for taste and colour. Taste was observed by taste panels. Colour comparisons require that a sample be compared against some colour standard

Thickness and Shape

Shape and thickness was measured using sliding Caliper scale. Five or Ten tablets from each formulation were selected and their crown thickness was measured with a sliding Caliper scale. Shapes of the tablets were observed.

Hardness

Tablets require a certain amount of strength or hardness to withstand mechanical shocks of handling in manufacturing, packing and shipping. The Monsanto hardness tester consists of a barrel containing a compressible spring held between two plungers. The lower plunger is placed in contact with the tablet and zero reading is taken. [12] The upper plunger is then forced against a spring by turning threaded bolt until the tablets break. As the spring is compressed, a pointer rides along a gauge in the barrel to indicate the force. The force of break is recorded and zero force reading is deducted from it.

Friability

Tablets were tested for friability using Roche Friabilator. This is important to know the mechanical strength of the tablet while handling. Twenty tablets were weighed initially and transferred to the Friabilator. The instrument was set to 25 rpm for 100 rotations. The resulting tablets were reweighed and percentage loss was calculated using the formula.

Friability= (Initial weight – Final Weight) / Initial Weight ×100

Conventional compressed tablet that lose less than 0.5 to 1.0% was acceptable.

Weight Variation

Weight variation was measured to ensure that tablet contain proper amount of drug. Weighed 20 tablets individually, calculated the average weight, and compared the individual tablet weights to the average. The tablets meet the test if not more than two tablets are outside the percentage limit and none of the tablet differs by more than two times the percentage limit. The weight variation tolerance for uncoated tablets differs depending on average weight of the tablets.

Wetting time

This is carried out to measure the time, which is required for the complete wetting of tablet formulations five circular tissue papers of 10 cm diameter are placed in a petridish with a 10 cm diameter. Ten millimeters of water-containing Eosin, a water-soluble dye, is added to petridish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time.

IN-VITRO DISINTEGRATION TEST

Wire Basket Type Disintegration Apparatus:

The disintegration taster consists of 6 glass tubes that was 3 inch long and 10-mesh screen at the bottom, one tablet was placed in each tube and basket was placed in 1 litre beaker of simulated gastric fluid at 370C ± 20C. The basket assembly containing the tablet up and down through distance of 5 to 6 cm at a frequency of 28 to 32 cycles per minute.

IN-VITRO DISSOLUTION STUDY:

The development of dissolution methods for Dispersible tablet is comparable to the approach taken for conventional tablets, and is practically identical. Dissolution conditions for drugs listed in a pharmacopoeia monograph, is a good place to start with scouting runs for a bioequivalent Dispersible tablet. Other media such as 0.1N HCl and buffers (pH - 4.5 and 6.8) should be evaluated for Dispersible tablet much in the same way as their ordinary tablet counter parts. The USP 2 Paddle apparatus is used for this purpose which is the most suitable and common choice for orally-disintegrating tablets, with a paddle speed of 50 rpm commonly used. Typically the dissolution of Dispersible tablet is very fast when using USP monograph conditions; hence slower paddle speeds may be utilized to obtain a profile. The USP 1 Basket apparatus may have certain applications but sometimes tablet fragments or disintegrated tablet masses may become trapped on the inside top of the basket at the spindle where little or no effective stirring occurs, yielding irreproducible dissolution profiles.

RESULTS

CHARACTERIZATION OF PURE DRUG (ASTEMIZOLE)

Sr.No	Characterization	Specification	Result
1.	Description	Almost white ,crystalline powders, odorless	Almost white powder
2.	Solubility	Soluble in DMSO (25mg/ml), ethanol (25 mg/ml), chloroform, methanol, and water (partly miscible)	Complies
3.	FT-IR	To match with workingstandard	Matches
4.	Melting range	172.9^{0}C	Complies
5.	Sulphated ash	Not more than 0.1%	Complies
6.	Loss on drying	Not more than 0.5%	Complies
7.	Heavy Metals	20 ppm max	Complies
8.	Assay	98.0-100.5%	Complies

IDENTIFICATION OF PURE DRUG (ASTEMIZOLE):-

Pure drug has been identified by usingtechnique like IR and Solubility Test.

INFRA-RED SPECTROPHOTOMETRY

Apparatus

An infra-red spectrophotometer for recording the spectra in the infra-red region consists of an optical system capable of providing the monochromatic light in the region of 4000 to 625 cm-1 (about 2.5 to 16mm) and the means of measuring the quotient of the intensity of the transmitted light and the incident light.

Preparation of sample: A sample of the Astemizole is being examined may be prepared by the following ways.

Discs – Triturate about 1 mg of the Astemizole with approximately 300 mg of dry, finely powdered potassium bromide IR. These quantities are usually suitable for a disc 13 mm in diameter.

Grind the mixture thoroughly, spread it uniformly in a suitable die and compress under vacuum at a pressure of about 800 Mpa. Mount the resultant disc in a suitable holder in the spectrophotometer. Several factors, such as inadequate or excessive grinding, moisture or other impurities in the halide carrier, may give rise to unsatisfactory discs.

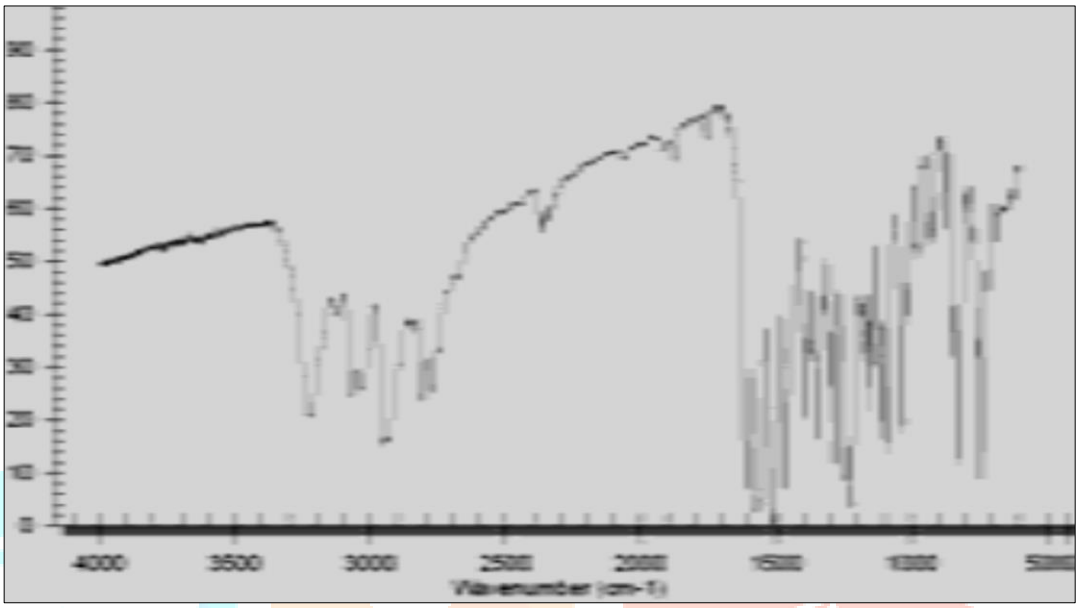


Fig 9 IR Spectra of Astemizole Powder

8.3.2 SOLUBILITY TEST:-

Solubility Test is performed as per mention in the I.P. and followingresults were obtained –

Table 19: Solubility Test of pure drug.

Sr. No.	Solvents	Solubility
1.	Ethanol	Freely Soluble
2.	Chloroform	Freely Soluble
3.	Methanol	Freely Soluble
4.	DMSO	Freely Soluble
5.	Water	Partly soluble

Evaluation of powder parameters (Pre-Formulation):-

Table No. 24: 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± 003	12.40±0.954	1.14± 0.010
F5	38.36^0± 1.852	0.45± 0.014	0.48± .024	5.20±1.590	1.06± 0.017
F6	33.74^0± 0.219	0.47± 0.007	0.50±0.01	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	0.53	0.60	11.66±	1.13

Evaluation of Tablet (Post-Formulation):-

Table No.25: 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

Table No. 26: Standard Calibration curve

Conc. (mcg/ml)	**Absorbance**	**± S.D.**
0	0.0000	0.00
15	0.225	± 0.036
30	0.285	± 0.012
45	0.341	± 0.01
60	0.401	± 0.034
75	0.438	± 0.049
90	0.523	± 0.084

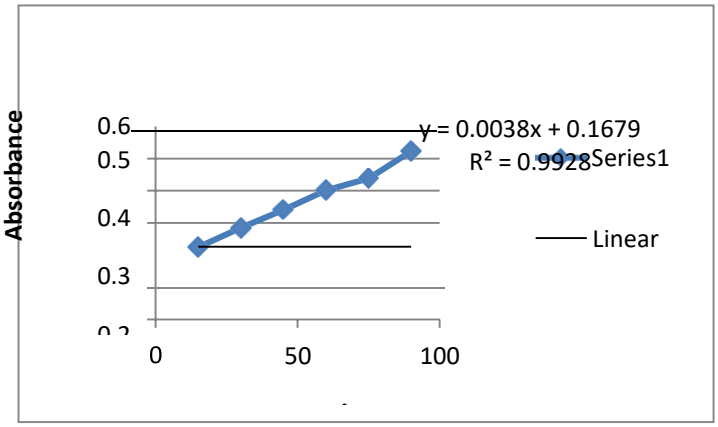


Fig. No. 10: Standard calibration curve of Astemizole

Table No. 27: Comparative study of % Drug release from Dispersibletablet of Batch F1, F2 and F3

Timein Min	% drug release		
	F1	F2	F3
30 sec	9.44	14.73	11.08
60 sec	20.41	29.76	21.87
90 sec	31.71	48.40	33.40

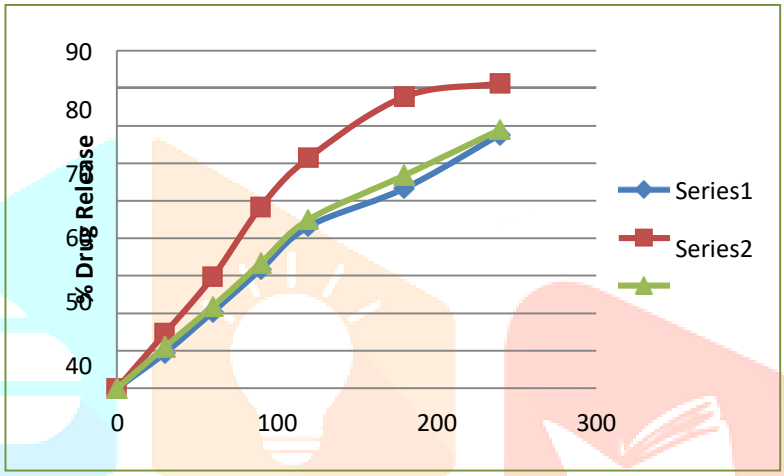


Fig. No. 11: Comparative study of % Drug release (Batch F1, F2 andF3)

Table No. 28: Comparative study of % Drug release from Dispersibletablet of Batch F4, F5 and F6

Timein Min	% drug release		
	F4	F5	F6
30 sec	13.72	14.96	13.5
60 sec	27.75	29.95	27.47
90 sec	41.55	45.7	41.73
2	57.26	61.71	36.96
3	73.12	78.1	72.6
4	89.43	85.3	87.93

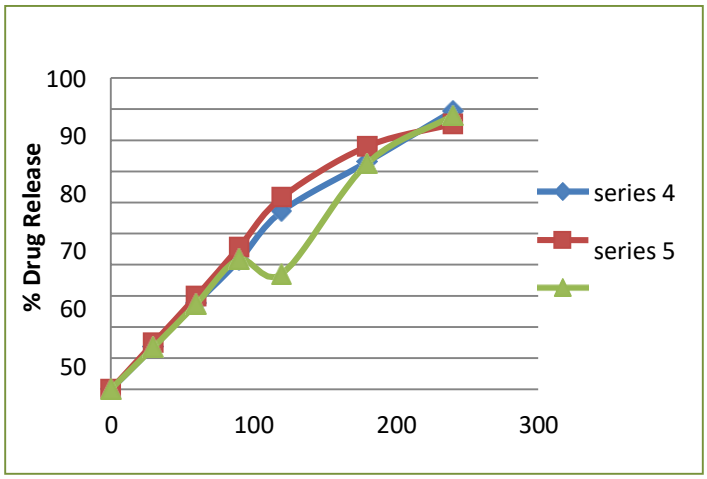


Fig No. 12: Comparative study of % Drug release (Batch F4, F5 andF6)

Table No. 29: Comparative study of % Drug release from Dispersibletablet of Batch F7, F8 and F9

Timein Min	% drug release		
	F7	F8	F9
30 sec	14.58	14.73	14.17
60 sec	29.55	29.33	28.68
90 sec	45.0	45.08	43.13
2	61.61	61.28	59.17
3	77.36	78.16	75.15
4	89.98	95.48	91.68

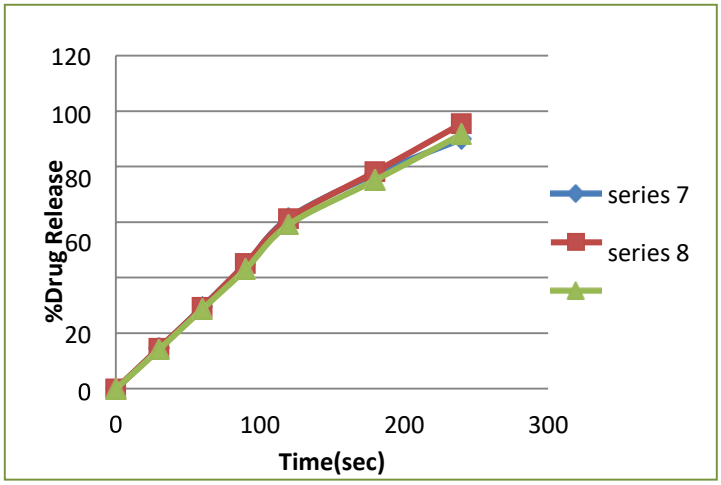


Fig No. 13: Comparative study of % Drug release (Batch F7, F8 andF9)

Mechanism of Release from Matrix tablets:

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

Table no. 30: Drug release kinetic study of optimized batch

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

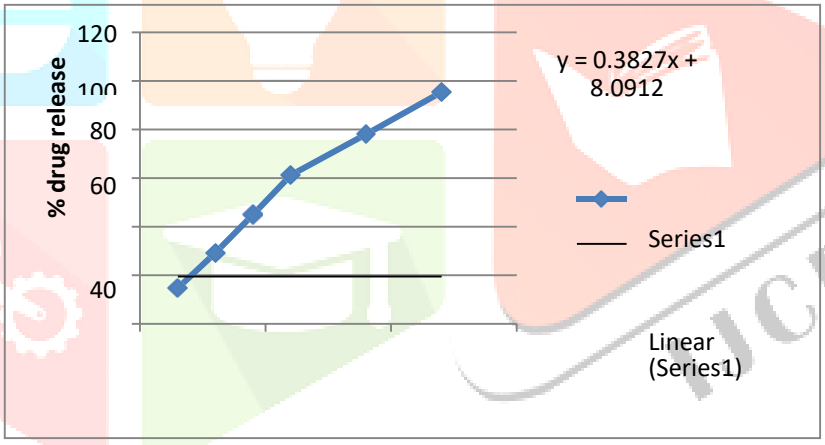


Fig No. 14: Curve fitting data of the release rate profile of zero order.

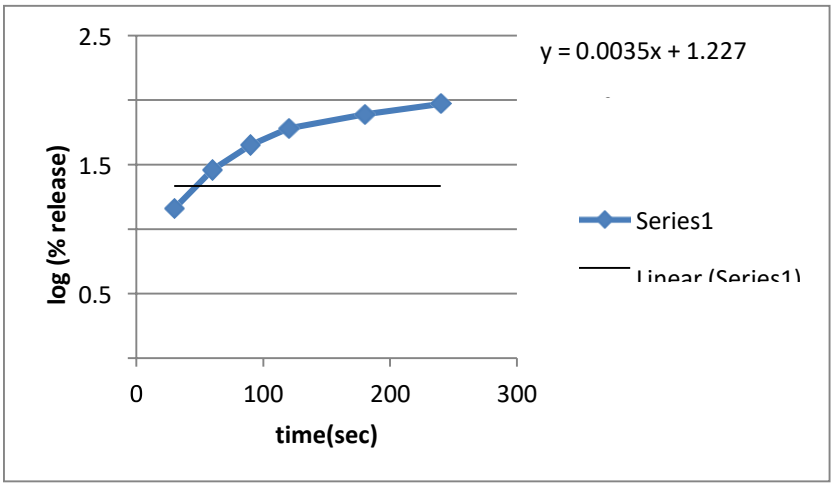


Fig No.15: Curve fitting data of the release rate profile of first order.

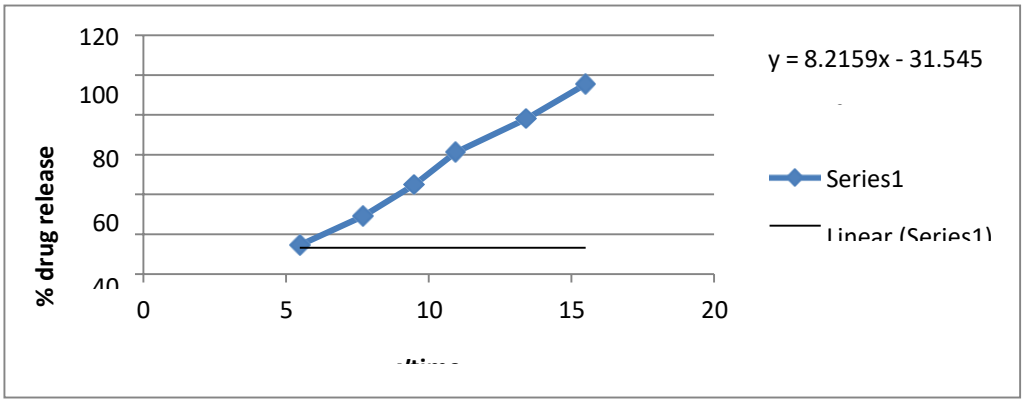


Fig No.16: Curve fitting data of the release rate profile of Higuchimodel

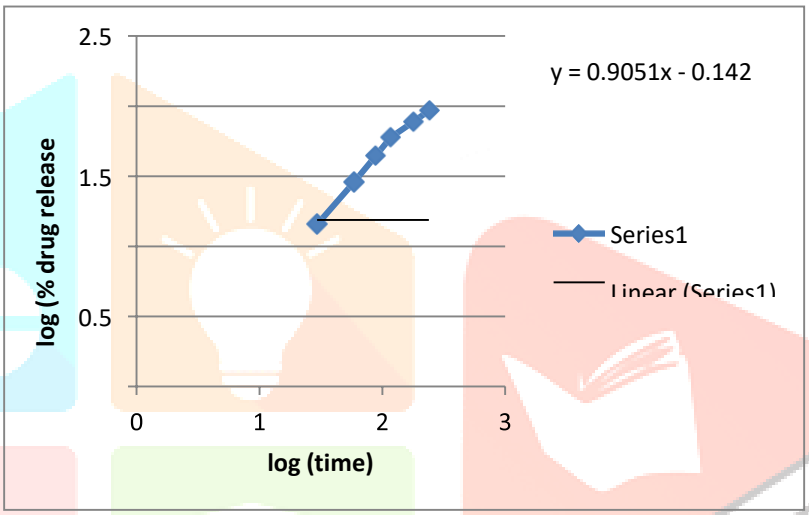


Fig No.17: Curve fitting data of the release rate profile of Korsmeyer-peppas

CONCLUSION

In present study Astemizole Dispersible tablet prepared using different types and concentrations of superdisintegrant by direct compression method which was confirmed by various characterization and evaluation studies.

Indion 414 as superdisintegrant gives better result as compared to crosscarmellose sodium and crosspovidone.

Tablets disintegrate within 30 sec in mouth having better mouth feel.

SUMMARY

Dispersible tablets are those that dissolve or disintegrate quickly in the oral cavity, resulting in solution or suspension. In the present study Dispersible tablet of Astemizole was prepared by direct compression method using crosspovidone, Crosscarmellose and Indion 414, as superdisintegrants. Release profile of the dispersible table follows the first pass metabolism and best fitted in the higuchimodel in that around 99% of the drug release with in the 30 sec in the mouth cavity which gives the effective bioavailability and better therapeutics responses.

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