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Formulation and evaluation of almotriptan chewable tablets

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ABSTRACT

In the present work, Almotriptan chewable tablets were prepared. All the tablets were subjected to weight variation, drug content uniformity, lock length, dissolution, drug excipients interaction and short-term stability studies. There was no difference in the position of the absorption bands, hence providing evidence for the absence of any chemical incompatibility between pure drugs with the excipients. The bulk density and tapped density for all formulation (F1 – F9) varied from 0.423 - 0.485 gm/cm^3 and 0.501 - 0.593 gm/cm^3 respectively. The results of carr's consolidate index or % compressibility index and hausner's ratio for the entire formulation (F1 – F9) blend range from 15.5- 19.1 and 1.10-1.28 respectively, shows fair flow properties. All the tablets show similar color, odour, taste and physical appearance. There is no impact of different in their organoleptic properties. By using the different excipient, the hardness values ranged from 3.0-3.5 kg/cm^2 for formulations (F1-F9) .The entire tablet passes weight variation test, as the average % weight variation was within the Pharmacopeial limit - 7.5%. It was found to be 149mg - 152 mg. The weight of all the tablets was found to be uniform with less deviation. The concentration of the drug in all the formulations with different polymers was found to be 97.35 – 99.58%. It was within the IP limits.

Keywords: Almotriptan, Direct compression.

INTRODUCTION

Chewable release tablets [5, 6]

The need for new oral drug delivery system continues, due to poor patient acceptance for invasive methods, need for exploration of new market for drugs and coupled with high cost of disease management. Developing new drug delivery techniques and utilizing them in product development is critical for pharmaceutical companies to survive this century [5].

The oral route of drug administration is the most important method of administering drugs for systemic effects. Tablets are single-dose preparations intended for oral administration. Some are intended to be swallowed whole, some after being chewed and some after being crushed, some are intended to be dissolved or dispersed in water

before being taken and some are intended to be retained in the mouth where the active ingredient(s) is/are liberated. Administration of drugs through oral route is the most common and the easiest way to administer a drug. But it is a challenge in children who have not yet learned to swallow tablets. Hence chewable tablets are formulated to improve the compliance in children [1].

Chewable tablets are the tablets which are required to be broken and chewed in between the teeth before ingestion. Chewable tablets are usually uncoated .These are intended to be chewed in the mouth prior to swallowing and are not intended to be swallowed intact. Chewable tablets are designed for use by the children and such persons who may have difficulty in swallowing the tablets [2].

Additionally, chewable tablets facilitate more rapid release and hence more rapid absorption of active ingredients and provide quick onset of action [4]. A non-dissolving polymer matrix modified release dosage form containing the drug and other excipients that must be chewed but not swallowed to promote release of the drug from the dosage form in the oral cavity.

In the manufacture of chewable tablets, measures are taken to: ensure that the tablets are easily crushed by chewing; ensure that the tablets are palatable [3].

Chewable tablets disintegrate slowly when chewed or allowed to dissolve in the mouth for local action .Chewable tablets are especially useful in the tablet formulations for children and are commonly employed in the preparation of multiple vitamin tablets .Wherever feasible and practical, the first step in the formulation of a chewable tablet is to obtain a complete profile of the active drug. This usually leads to the most efficient formulation of a stable and quality product as the drug usually dictates the choice of fillers, carriers, sweeteners, flavor compounds, and other product modifiers. Many of the excipients commonly used in tablet formulation are especially applicable for use in chewable tablets due to their ability to provide the necessary properties of sweetness and chew ability. In general, these fall into the sugar category [6], although a combination of bland excipients with artificial sweeteners may provide a satisfactory alternative .Important aspects of chewable tablet manufacture are the proper incorporation of the coloring agent, assurance of necessary particle size distribution) maintenance of correct moisture content, and achievement of proper tablet hardness. All of these are the routine responsibility of the manufacturing department once the parameters have been established during development [7]. Two common approaches are the use of low concentrations of light colors and the use of high-intensity mixing of reduced particle size materials in order to assure thorough blending. Mannitol is widely used as excipients in chewable tablets for its non-hygroscopic nature of moisture sensitive drugs [8]. Chewable tablet formulation, particularly those containing pharmaceutically active agents, present issue of the organoleptic characteristics of odor, taste, appearance and mouth feel. The formula ingredients and manufacturing process both play a role in obtaining the desired organoleptic properties [9].

AIM AND OBJECTIVE

Aim

- To formulate and evaluate tablets Almotriptan chewable tablets using different excipients and selecting best of them.

Objective

- To design the formula for chewable Release tablet.
- To carry out compatibility studies of drug and disintegrants
- To incorporate selected model drug candidates in the formula and prepare tablets.
- To evaluate the formulated tablets.
- By physical parameters and
- By *in-vitro* dissolution profile of prepared tablets.

METHODOLOGY

Formulation of different batches

The main aim of the present study was to formulate different batches using three various superdisintegrants and other ingredients in varying concentrations [10]. So, different batches of formulations were planned accordingly. According to that F1, F2, F3 (with Crospovidone-3%, 5%, 7.5%), F4, F5, F6 (with Crosscaramellose-3%, 5%, 7.5%), F7, F8, F9 (with Sodium starch glycollate-3%, 5%, 7.5%).

Table: 1 Formulation of Different Batches (F1-F9)

Formulations Code									
Ingredients (mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Almotriptan	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25
Crospovidone	4.5	7.5	11.25	------	------	-------	------	------	-----
Croscarmellose sod.	------	------	------	4.5	7.5	11.25	------	------	-----
SSG	------	-----	----	-------	------	-----	4.5	7.5	11.25
Mannitol	135.5	132.5	128.75	135.5	132.5	128.75	135.5	132.5	128.75
Magnesium stearate	2.25	2.25	2.25	2.25	2.25	2.25	2.25	2.25	2.25
Aerosil	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5

Total tablet weight 150mg

RESULTS AND DISCUSSIONS

Results

Preformulation Study

Organoleptic Properties (Color, odor, taste and appearance)

Table2. Results of identification tests of drug

Characteristics	Results
Colour	White amorphous powder
Odour	Characteristic odour
Taste	Slightly bitter

Melting point determination: Drug: Almotriptan

Table 3: Results of Melting point determination test of drug

Reported Melting Point	Observed Melting Point
170 - 174	**173**

Determination of solubility

Soluble in methanol water sparingly soluble in ethanol, propylene glycol, and very slightly soluble in chloroform.

DRUG AND EXCIPIENTNCOMPATABILITY STUDIES

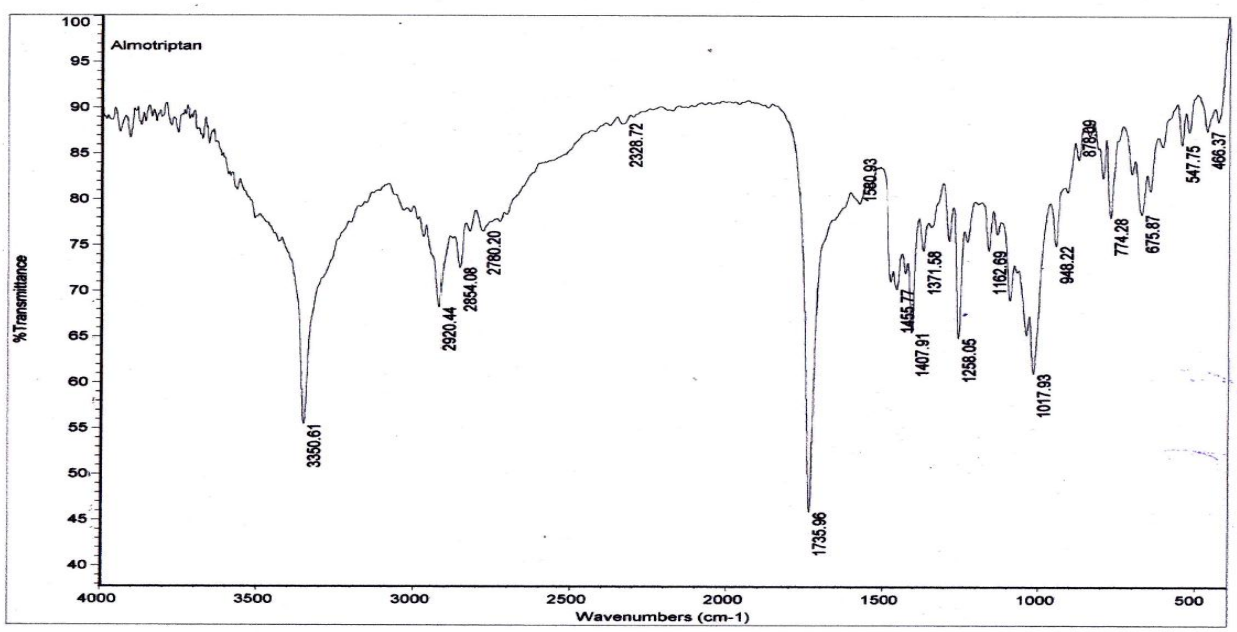


Fig no: 1 FTIR spectrum of Almotriptan pure drug

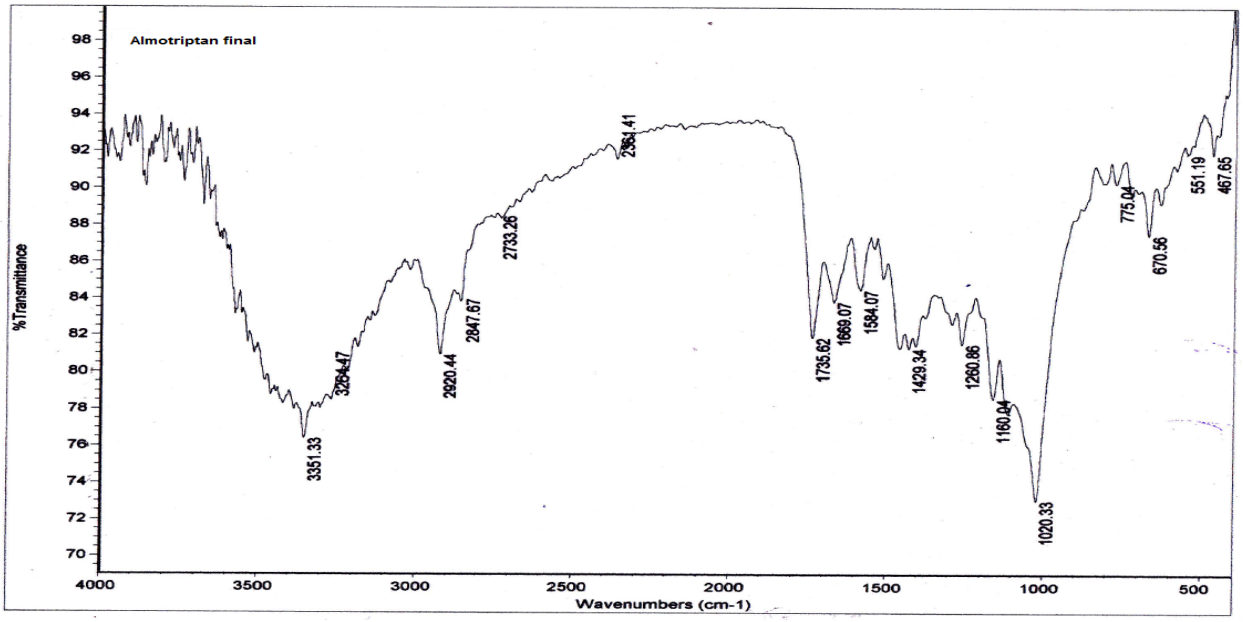
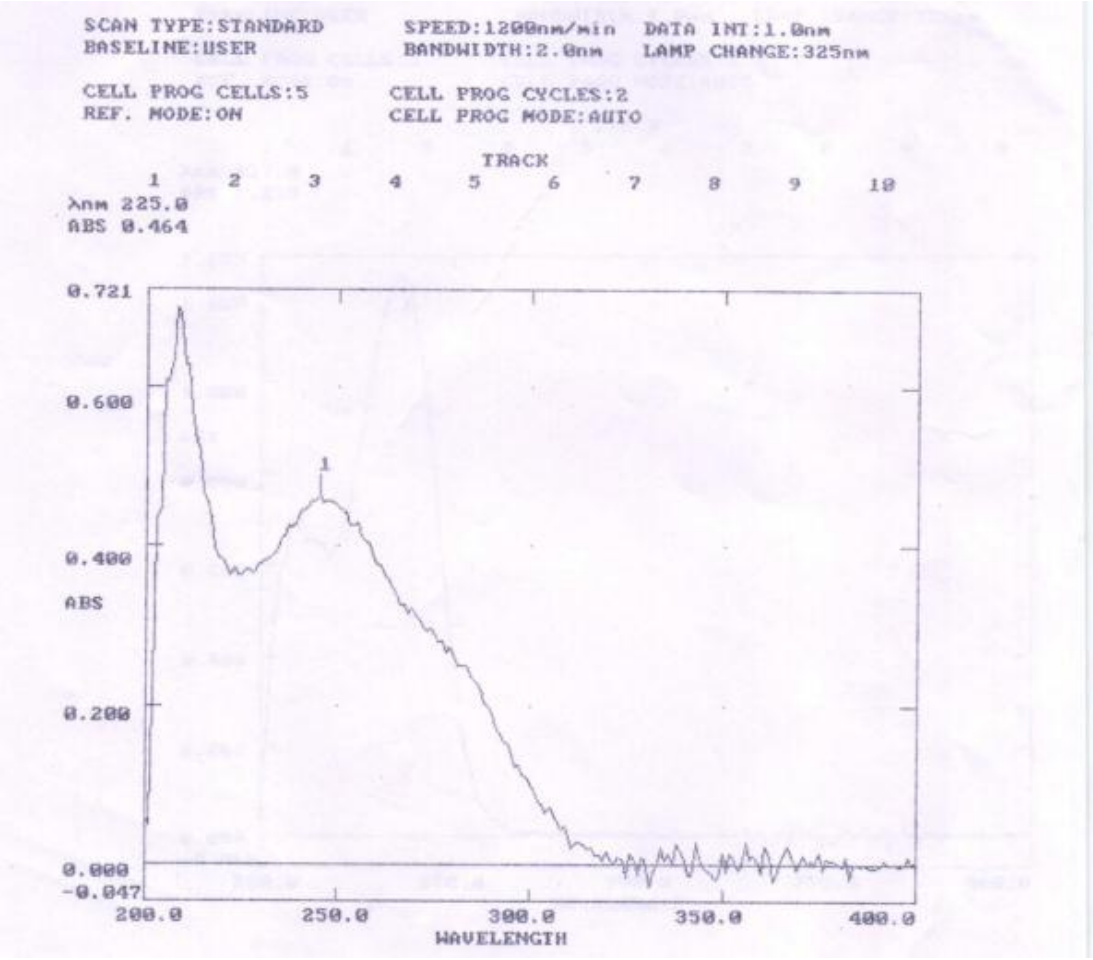


Fig no: 2 FTIR spectrum of Almotriptan optimized formulation

UV-SPECTROSCOPY- ANALYSIS OF DRUG

Ultraviolet Visible (UV-visible) spectroscopy



Drug sample showed wavelength of maximum absorption (λ-max) 232nm.

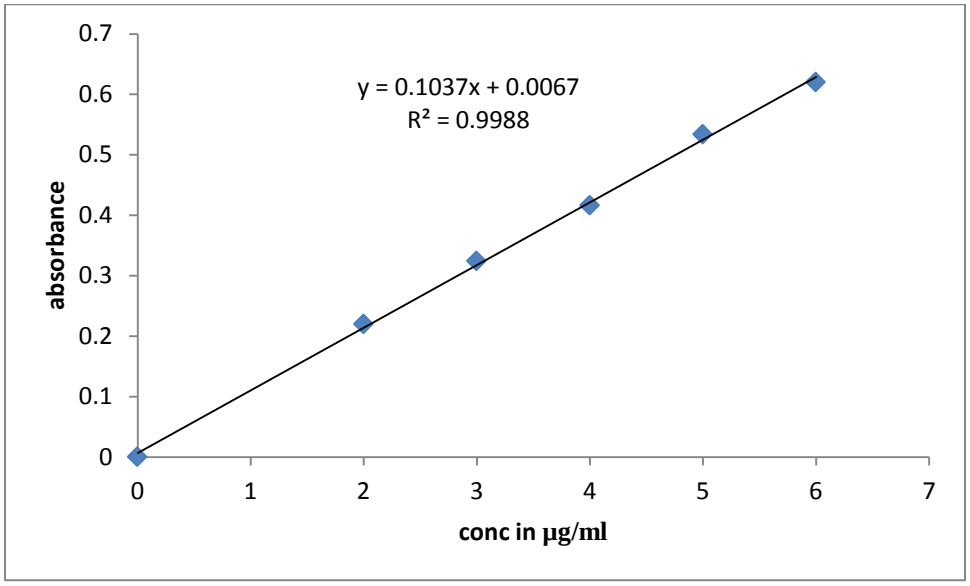
Calibration curve of Almotriptan in 0.1N HCl

Wavelength of maximum absorption: 232 nm.

Table no 4: standard curve of Almotriptan pH 0.1N HCl at λmax 232nm

Table: 4 Calibration Curve of Almotriptan with 0.1NHcl

S. No.	Conc.(µg/ml)	Absorbance
1	2	0.220
2	3	0.324
3	4	0.416
4	5	0.534
5	6	0.620



Graph: 3 Calibration Curve of Almotriptan with 0.1NHcl

PRE FORMULATION STUDIES

Table: 5 Evaluation of tablet blend for formulations (F1 – F9)

Formulation	Bulk Density* (g/cc) ±SD	Tapped Density* (g/cc)±SD	Hausner ratio* ±SD	Compressibility index* (%)±SD	Angle of repose(ɵ) ±SD
F1	0.464±0.063	0.574±0.057	1.23±0.155	19.1±0.556	29.47±0.688
F2	0.423±0.043	0.501±0.040	1.16±0.253	15.5±0.305	27.63±0.287
F3	0.456±0.066	0.542±0.049	1.22±0.212	15.8±0.208	25.54±0.168
F4	0.467±0.068	0.559±0.061	1.25±0.221	16.4±0.401	26.23±0.425
F5	0.485±0.064	0.593±0.053	1.10±0.389	18.2±0.251	27.21±0.458
F6	0.460±0.068	0.556±0.059	1.21±0.120	17.2±0.386	29.38±0.446
F7	0.478±0.050	0.575±0.049	1.24±0.293	16.8±0.256	28.46±0.541
F8	0.450±0.087	0.554±0.067	1.28±0.250	18.7±0.258	25.71±0.181
F9	0.442±0.068	0.537±0.055	1.27±0.096	17.6±0.287	29.82±0.510

POST FORMULATION STUDIES

Table: 6 Evaluation of Chewable Release Tablets for formulations (F1 – F9)

Formulation	Hardness (kg/cm^2)±SD	Friability (%)±SD	Weight (mg)±SD	Thickness (mm)±SD	Disintegration time(sec)±SD	Drug content(%)±SD
F1	3.2±0.286	0.32±0.030	150±0.95	2.20±0.098	17±0.10	97.80±0.981

F2	3.0±0.280	0.35±0.040	149±0.78	2.21±0.017	14±0.14	99.25±0.844
F3	3.4±0.248	0.39±0.062	152±0.47	2.16±0.050	10±0.05	98.13±0.745
F4	3.6±0.246	0.32±0.025	150±0.89	2.11±0.090	25±0.65	99.09±0.947
F5	3.2±0.486	0.36±0.061	151±0.35	2.19±0.030	20±0.32	99.58±0.743
F6	3.5±0.173	0.42±0.045	149±0.74	2.13±0.050	15±0.41	98.26±0.823
F7	3.0±0.115	0.38±0.026	150±0.53	2.20±0.070	32±0.63	97.35±0.935
F8	3.3±0.218	0.33±0.047	151±0.87	2.18±0.068	24±0.69	98.16±0.896
F9	3.5±0.162	0.40±0.052	149±0.98	2.14±0.101	20±0.12	99.05±0.974

Table 7: Evaluation of Chewable Release Tablets for formulations (F1 – F9)

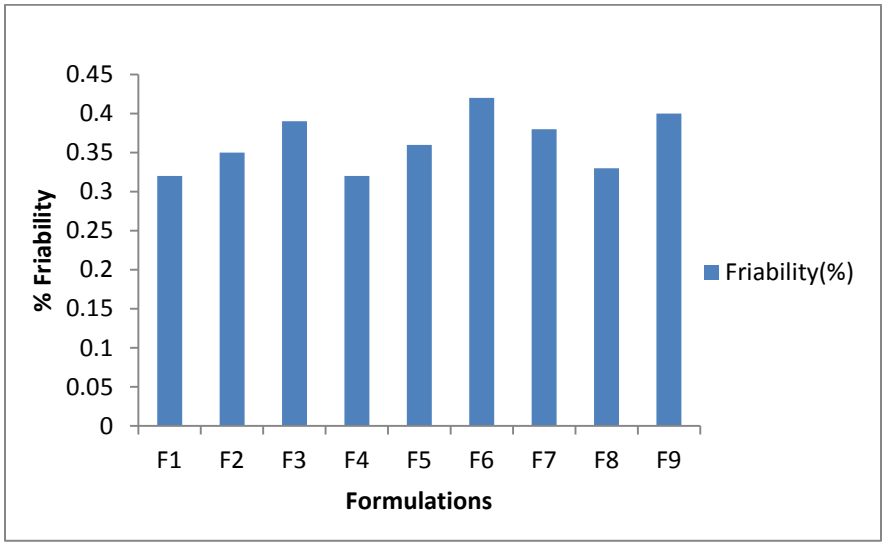


Figure 4: Bar graph comparison friability for formulations (F1- F9)

IN VITRO % DRUG RELEASE

Table: 8 Cumulative % drug releases for formulations (F1 – F9)

	Percentage Drug Release ± SD								
Time in min	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0	0	0	0	0	0	**0**	0	0	0
5	22.41± 0.785	23.74± 0.466	15.86± 0.501	20.41± 0.374	35.68± 0.462	**42.85± 0.563**	26.89± 0.680	30.65± 0.506	29.48± 0.338
10	35.24± 0.521	36.98± 0.331	24.79± 0.695	43.57± 0.335	56.24± 0.474	**58.73± 0.482**	39.99± 0.555	44.85± 0.623	47.54± 0.355
15	42.21± 0.531	48.74± 0.234	52.63± 0.266	55.36± 0.392	64.56± 0.602	**74.89± 0.517**	63.98± 0.238	69.28± 0.488	62.87± 0.497
30	53.35±	55.87±	75.68±	62.95±	73.86±	**98.16±**	75.25±	82.69±	79.98±

	0.436	0.626	0.385	0.452	0.301	**0.872**	0.360	0.551	0.355
45	69.58±	73.65±	98.08±	77.87±	95.28±	**98.86±**	85.68±	90.36±	85.69±
	0.500	0.706	0.342	0.582	0.518	**0.710**	0.576	0.626	0.350
60	83.74±	96.14±	98.49±	87.63±	98.03±	**99.25±**	90.59±	97.68±	98.09±
	0.475	0.715	0.540	0.435	0.180	**0.313**	0.243	0.5406	0.746

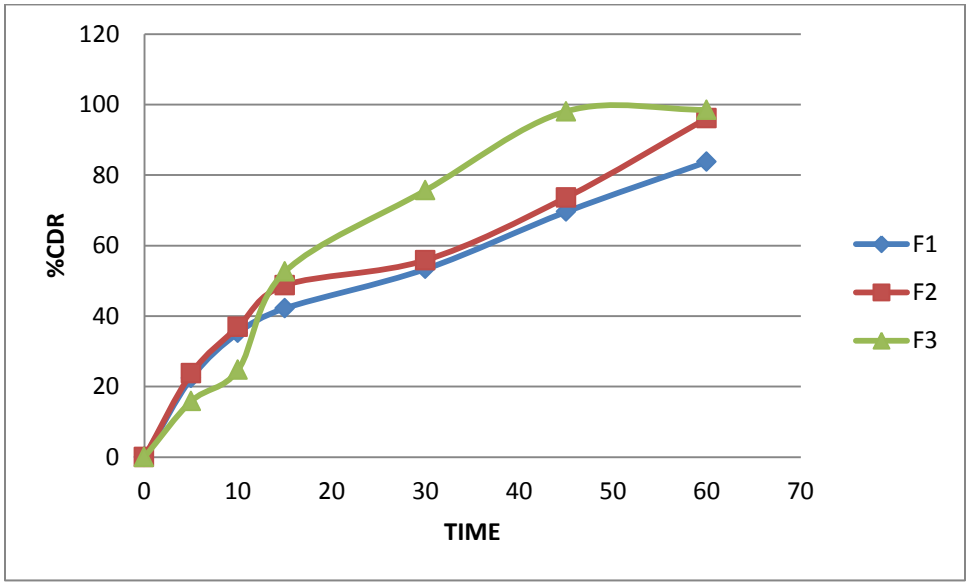


Fig 8.6: Linear graph comparison between cumulative % drug release for formulations (F1- F3)

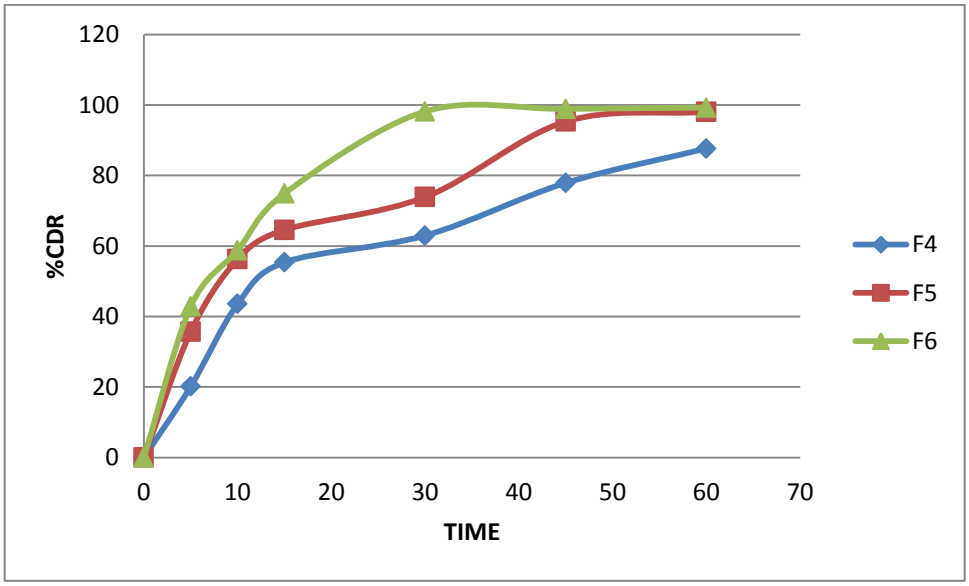


Fig 8.7: Linear graph comparison between cumulative % drug release for formulations (F4 - F6)

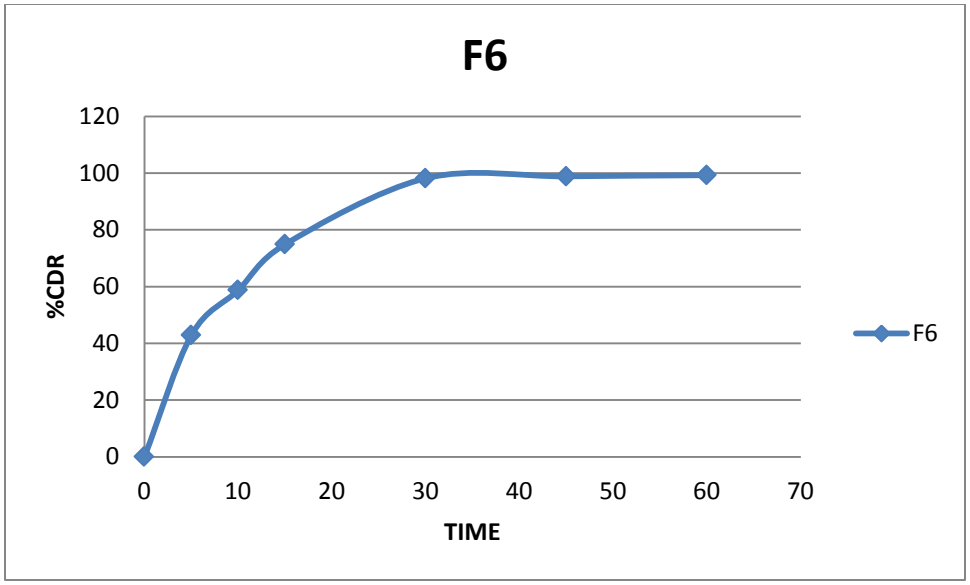


Fig 8.8: Linear graph cumulative % drug release for formulations (F6)

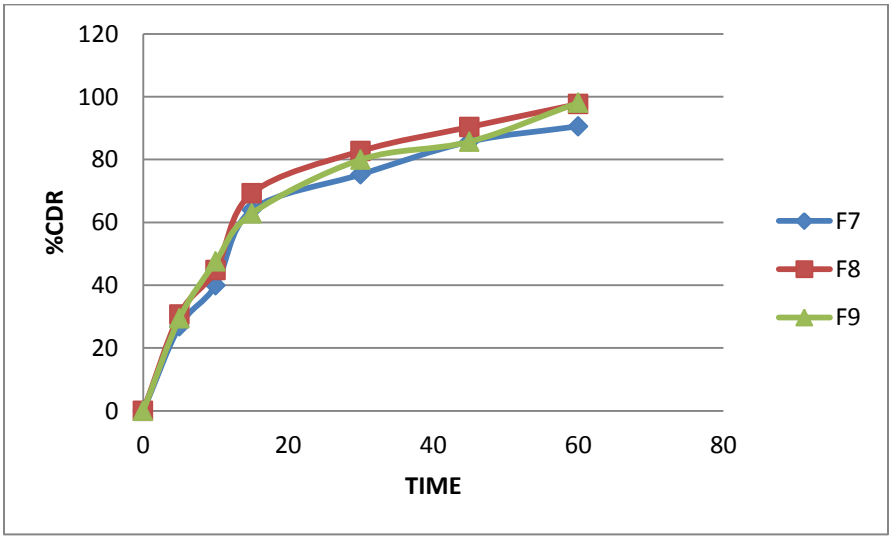


Fig 8.9: Linear graph comparison between cumulative % drug releases for formulations (F7- F9)

In-vitro drug release kinetics

For understanding the mechanism of drug release and release rate kinetics of the drug from dosage form, the in-vitro drug dissolution data obtained was fitted to various mathematical models such as zero order, First order, Higuchi matrix, and Krosmeyer-Peppas model. The values are compiled in Table. The coefficient of determination (R2) was used as an indicator of the best fitting for each of the models considered.

8.9 Drug release kinetics of Almotirptan

8.9.1 Zero order release kinetics

Table: 8.8 Zero order release kinetics of almotriptan

Table No 9- R^2 values for release kinetics

	% Cumulative drug release								
Time in min	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0	0	0	0	0	0	**0**	0	0	0
5	22.41	23.74	15.86	20.41	35.68	**42.85**	26.89	30.65	29.48
10	35.24	36.98	24.79	43.57	56.24	**58.73**	39.99	44.85	47.54
15	42.21	48.74	52.63	55.36	64.56	**74.89**	63.98	69.28	62.87
30	53.35	55.87	75.68	62.95	73.86	**98.16**	75.25	82.69	79.98
45	69.58	73.65	98.08	77.87	95.28	**98.86**	85.68	90.36	85.69
60	83.74	96.14	98.49	87.63	98.03	**99.25**	90.59	97.68	98.09

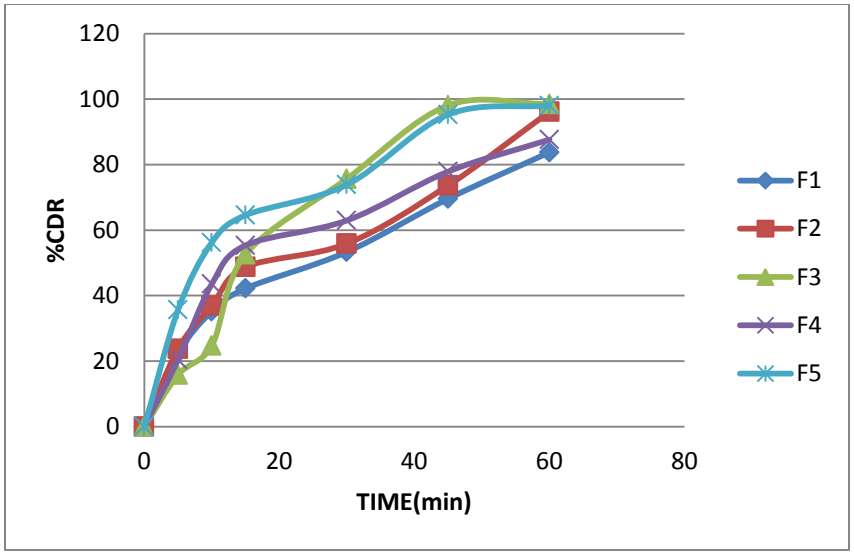


Fig 8.10: Zero order plot of Almotriptan chewable tablets (F1,F2,F3,F4, F5)

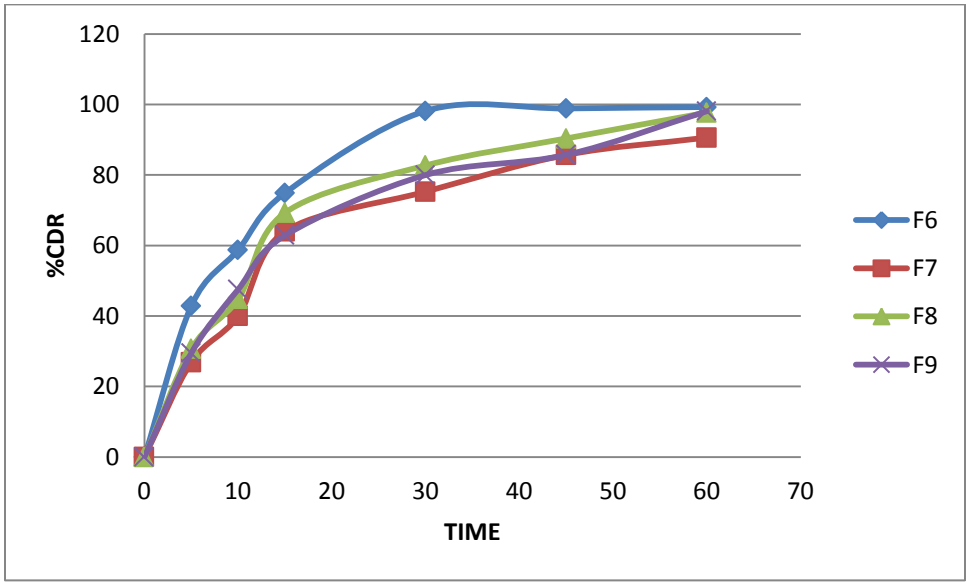


Fig 8.11: Zero order plot of Almotriptan chewable tablets (F6,F7,F8, F9)

8.9.2 First order release kinetics

Table: 8.9 First order release kinetics of Almotriptan

Log% drug remained

Time(min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	2	2	2	2	2	2	2	2	2
5	1.8898	1.8822	1.9250	1.9008	1.8083	1.7570	1.8639	1.8410	1.8483
10	1.8113	1.7994	1.8762	1.7515	1.6410	1.6156	1.7782	1.7415	1.7198
15	1.7618	1.7097	1.6755	1.649	1.5449	1.3998	1.5565	1.4874	1.5697
30	1.6688	1.6447	1.3859	1.5687	1.4173	0.2648	1.3935	1.2382	1.3014
45	1.4831	1.4207	0.2833	1.3449	0.6739	0.0569	1.1559	0.9840	1.1556
60	1.2111	0.5865	0.1789	1.0923	0.2944	-	0.9735	0.3654	02810

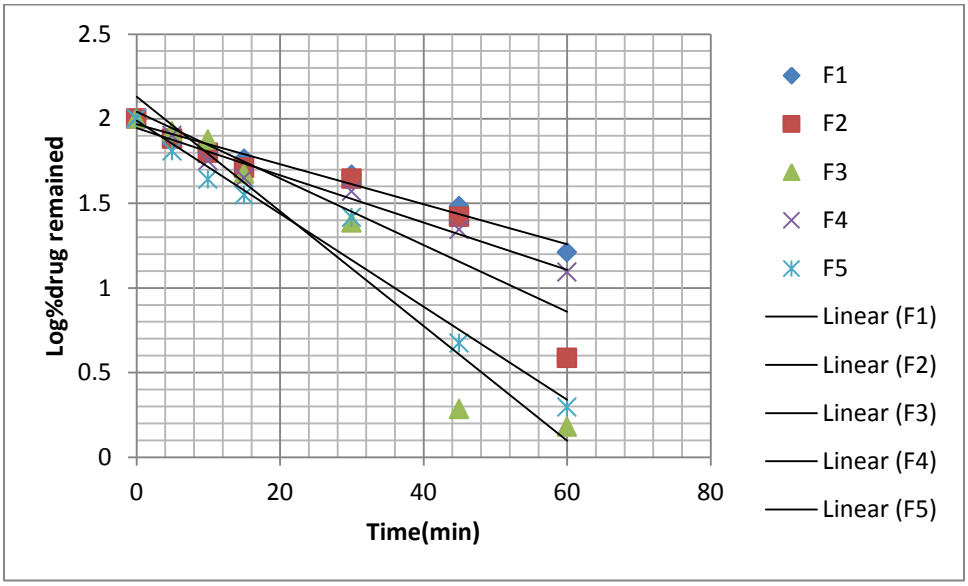


Fig.8.12 First order plot of Alomtriptan chewable tablets

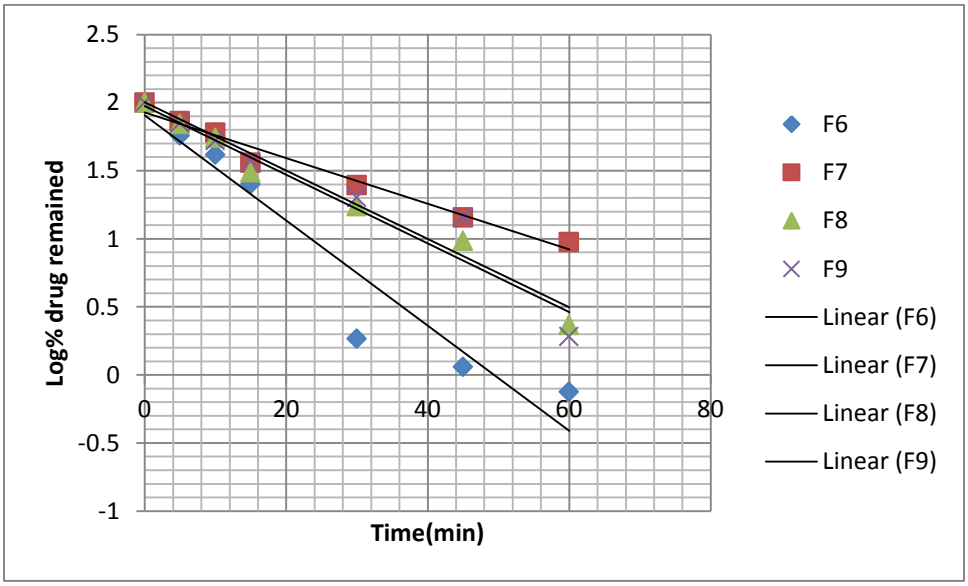


Fig.8.13 First order plot of Alomtriptan chewable tablets

Table: 8.10 data of drug release kinetic models of almotriptan

FORMULATION CODE	ZERO ORDER	FIRST ORDER
F1	0.918	0.973
F2	0.920	0.858
F3	0.905	0.941
F4	0.842	0.971
F5	0.799	0.965
F6	0.794	0.926
F7	0.807	0.971
F8	0.794	0.977
F9	0.821	0.933

CONCLUSION

The above results suggest that the formulated immediate release tablets of Almotriptan exhibited good physical parameters. The overall results indicated that formulation F6 with croscaramellose (7.5%) had a higher edge compared to other formulations containing super disintegrants and palatability is good. They satisfy all the criteria for chewable release tablets. This direct compression process is simple, reproducible and robust to prepare chewable release tablets of almotriptan and other anti-migraine drugs.

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