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FORMULATION AND EVALUATION OF FAST DISSOLVING TABLETS OF CEFUROXIME AXETIL BY USING SUPER DISINTEGRANTS AS DIFFERENT FORMULATIONS

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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]

Oral drug delivery has been known for decades as the most widely utilized route of administered among all the routes that have been employed for the systemic delivery of drug via various pharmaceutical products of different dosage forms. The reasons that the oral route achieved such popularity may be in part attributed to its ease of administration1. It has been reported that Dysphagia (difficulty in swallowing) is common among all age groups and more specific with pediatric, geriatric population along with institutionalized patients and patients with nausea, vomiting, and motion sickness complications. ODTs with good taste and flavor increase the acceptability of bitter drugs by various groups of population. Orally disintegrating tablets are also called as fast dissolving tablets, quick dissolving tablets, mouth dissolving tablets, fast dissolving tablets, fast

dissolving tablets, rapid dissolving tablets, porous tablets, and rapimelts. However, of all the above terms, United States pharmacopoeia (USP) approved these dosage forms as ODTs. Recently, European Pharmacopoeia has used the term fast dissolving tablet for tablets that disperses readily and within 3 min in mouth before swallowing. Despite of tremendous advancements in drug delivery, the oral route remains the perfect route for the administration of therapeutic agents because the low cost of therapy, ease of administration lead to high levels of patient compliance.

Methodology:

Method of manufacturing Cefuroxime axetil tablets[26, 27]

Preparation of C-TXG (Modified xanthan gum):

Modified polysaccharide was prepared by suspending 5gms of xanthan gum in 250ml beaker having 100ml of distilled water. The suspension was stirred at 500 rps using magnetic stirrer for 24hours.The obtained swollen mass was spread on enabled tray and dried at room temperature for 72hours.The dried product was scrapped out using spatula and crushed in a glass mortar with pistle to obtain treated xanthan gum (TxG).TXG was co-grounded with mannitol (1:1) in a glass mortar for 20mints and passed through sieve no:22(#) to get modified C-txg. Stored in a dessicator for further use.

Direct Compression Method

The tablet cefuroxime axetil dispersible tablets were prepared by direct compression method by using 7.5mm oval punches & with a break line on one side.

Formulation of Cefuroxime axetil Fast dissolving tablets

By varying the proportion of KOLLIDON XL and C-TXG of formulation different ratios design into 6 batches which is summarized in table

Table 1: Formulation of Cefuroxime axetil tablets

S.No	EXCIPIENTS (mg)	Formulations					
		F1	F2	F3	F4	F5	F6
1	Drug	150	150	150	150	150	150
2	Mannitol	10	10	10	10	10	10
3	MCC	60	59	60	59	58	58
4	Magnesium stearate	9	9	9	9	9	9
5	C-TXG	1	2	-	-	1	2
6	KOLLIDON XL	-	-	1	2	2	1

RESULTS & DISCUSSION

Standard plot for API in 0.1N HCL

Table 2: Standard plot for API in 0.1N HCl

Concentration(µg/ml)	Absorbance at 281nm
2	0.073
4	0.177
6	0.288
8	0.395
10	0.504

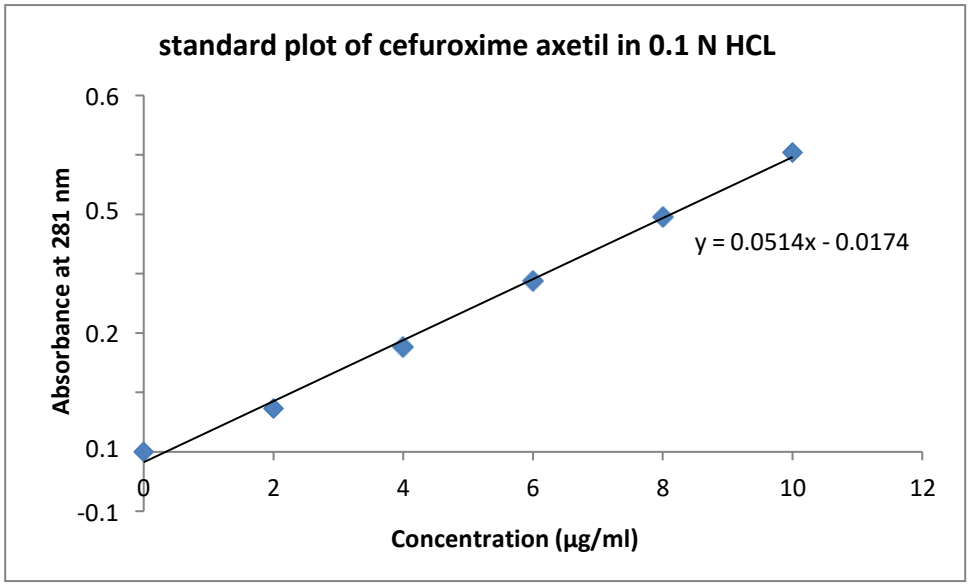
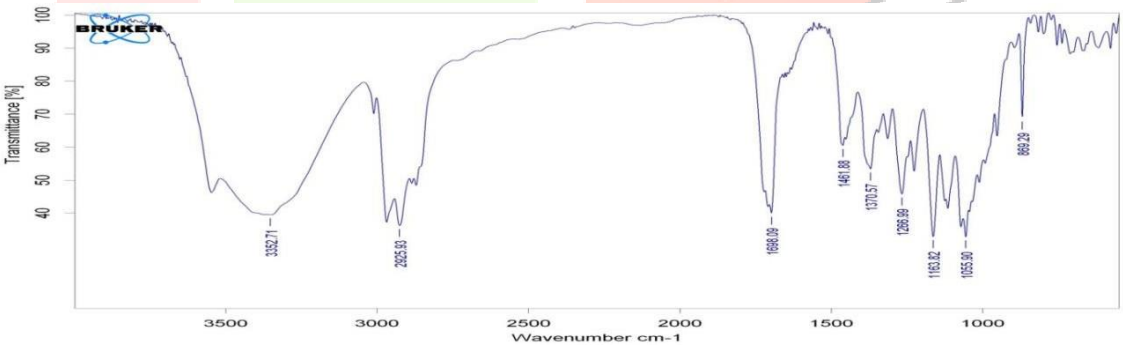
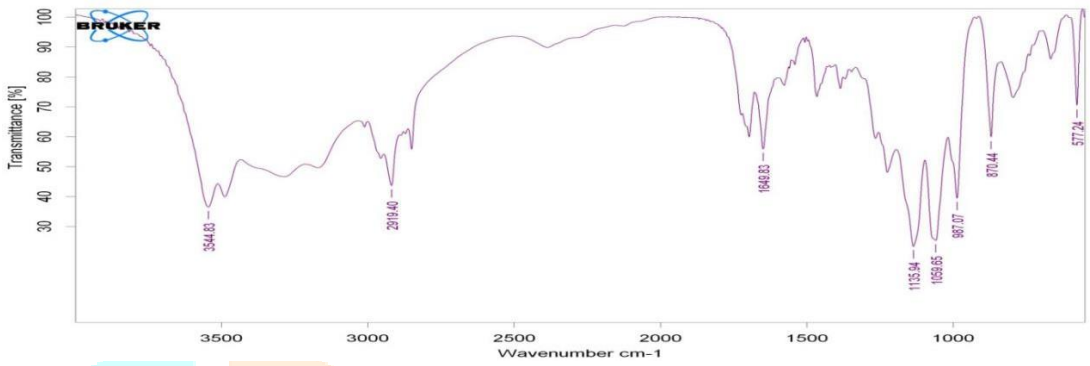


Fig 5:Standard plot in cefuroxime axetil 0.1N HCL

FTIR Graph for Cefuroxime axetil pure drug :



FTIR Graph for Optimized formulation :



Preformulation studies of Cefuroxime Axetil fast dissolving Tablets

Table 10: Preformulation studies of cefuroxime Axetil

Formulation	Angle of repose(°)	Bulk density(gm/cm^2)	Tapped density(gm/cm^3)	Hausner's ratio	Compressibility index (%)
F1	24.55±1.052	0.633±0.007	0.721±0.009	1.136±0.22	12.23±1.033
F2	24.58±0.921	0.626±0.010	0.731±0.006	1.30±0.014	14.44±1.031
F3	23.92±1.435	0.635±0.007	0.727±0.011	1.14±0.021	14.29±1.123
F4	24.38±0.722	0.633±0.002	0.733±0.005	1.15±0.021	13.58±1.632
F5	22.96±1.495	0.633±0.006	0.728±0.012	1.14±0.014	12.98±1.102
F6	24.55±0.868	0.629±0.002	0.724±0.008	1.14±0.025	13.18±1.851

All values were expressed as mean ± S.D; Number of trails (n) = 3

Post compression parameters

Table 11: Evaluation of Cefuroxime Axetil Tablets

Formulation code	weight variation(mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)
MRKT	240 ± 0.51	4.8 ± 0.32	3.4 ± 0.32	0.50 ± 0.11
F1	228.3 ± 0.15	4.0 ± 0.05	3.1 ± 0.85	0.25 ± 0.21
F2	226.6 ± 0.15	4.9 ± 0.10	3.3 ± 1.04	0.30 ± 0.25
F3	232 ± 0.23	4.1 ± 0.10	3.1 ± 0.86	0.27 ± 0.02
F4	230 ± 0.52	4.1 ± 0.10	3.0 ± 0.85	0.28 ± 0.01
F5	228.3 ± 0.52	4.2 ± 0.05	3.2 ± 0.74	0.29 ± 0.16
F6	226.3 ± 0.20	4.9 ± 0.05	3.4 ± 0.90	0.29 ± 0.13

All values were expressed as mean ± S.D; Number of trails (n) = 3

Evaluation of Cefuroxime Axetil tablets

Table 11: Evaluation of Cefuroxime Axetil

Formulation code	Wetting time (sec)	Disintegration time(sec)	Content uniformity(%)
MRKT	35 ± 0.5	38 ± 0.5	101.10 ± 0.1
F1	37 ± 0.4	39 ± 0.4	100.08 ± 0.01
F2	31 ± 0.5	32 ± 0.5	99.38 ± 0.23
F3	39 ± 0.5	41 ± 0.3	99.32 ± 0.15
F4	34 ± 0.3	36 ± 0.2	100.82 ± 0.4
F5	30 ± 0.6	30 ± 0.4	99.48 ± 0.2
F6	28 ± 0.5	29 ± 0.4	99.5 ± 0.6

All values were expressed as mean ± S.D; Number of trails (n) = 3

Invitro Dissolution studies

Table 12:Invitro drug release for all formulations

Time	MRKT	% Drug released					
		F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0	**0**
5	48±0.2	49±0.43	44±0.23	44±0.22	50±0.31	56±0.61	62±0.12
10	62±0.3	68±0.34	58±0.16	69±0.41	69±0.43	74±0.59	80±0.23
15	74±0.3	79±0.36	71±0.21	79±0.35	76±0.55	89±0.26	89±0.24
20	86±0.2	85±0.27	88±0.43	86±0.47	89±0.29	95±0.29	99.6±0.41
25	92+0.4	96±0.50	94±0.63	97±0.28	98±0.27	100.4±0.31	100.6±0.25
30	100±0.5	101±0.19	100.8±0.23	100.1±0.29	101.2±0.41	101.3±0.29	101.2±0.48

All values were expressed as mean ± S.D; Number of trails (n) = 3

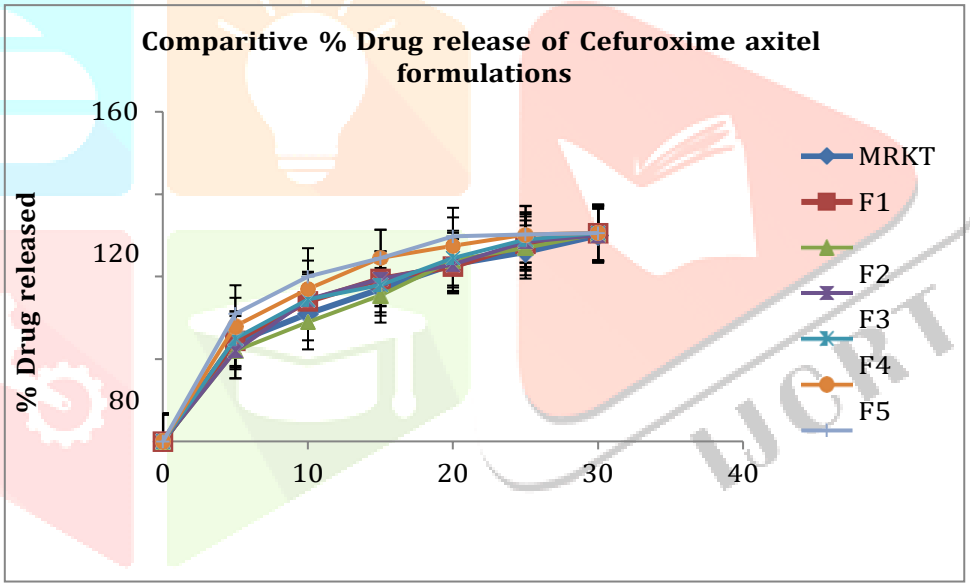


Fig 4.4: Plot for *in vitro* drug release for all formulation

Invitro drug release for marketed & F6 Formulation

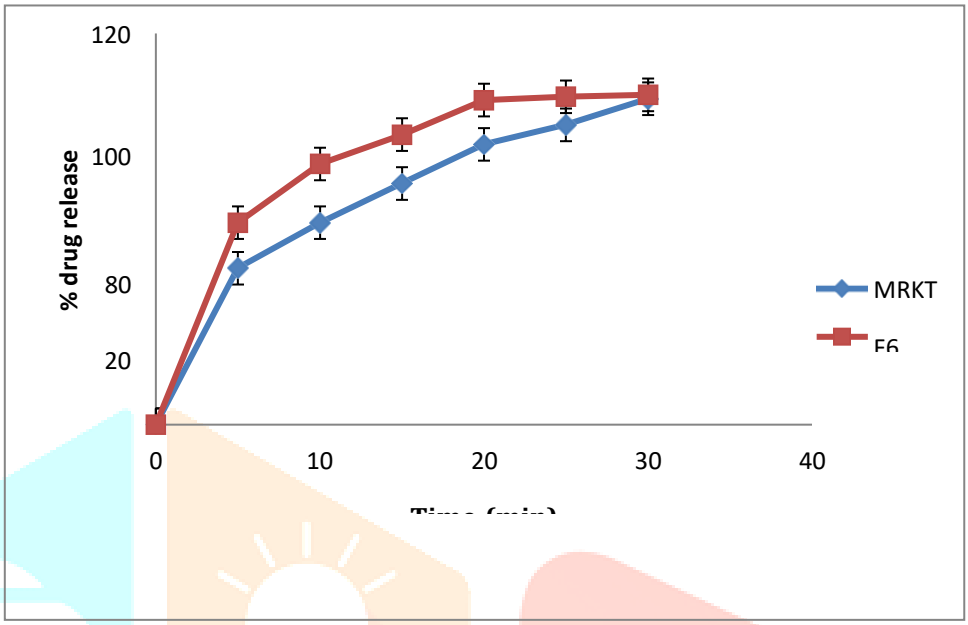


Fig 7: Plot for *in vitro* drug release for marketed and F6 Formulation

Stability studies

Physical and chemical parameters of optimized formulation F6 after 1st, 2nd and 3rd monthat 40±2°C/ 75±5°CRH for 3 months

Table 13: stability studies of optimized formulation F6

Parameter	Initial	After 1st month	After 2nd month	After 3rd month
Description	White coloured flat circular shaped uncoated tablet	No change	No change	No change
Avg. Wt	226.3 mg	226.4 mg	226.3 mg	226.1 mg
Hardness	5.1 kg/cm^2	5.1 kg/cm^2	5.1 kg/cm^2	5.1 kg/cm^2
Thickness	3.4 mm	3.3 mm	3.3 mm	3.3 mm
Friability	0.30 %	0.32 %	0.33 %	0.33 %

DISCUSSION:

Preformulation studies

Bulk characteristics of cefuroxime granules

- Angle of repose of granules are in the range of 22.96 ± 1.49 to 24.58 ± 0.92
- Bulk density was in the range of 0.626±0.01 to 0.633±0.007gm/cm^3.
- Tapped density was in the range of 0.721±0.009 to 0.733±0.005gm/cm^3.
- Percentage compressibility was in the range of 12.23±1.633 to 14.44±1.031%.
- Hausner's ratio was in the range of 1.136±0.021 to 1.30±0.014.

From the above results it was observed that F6 formulation having better bulk characteristics than compared to remaining formulations.

Evaluation of fast dissolving Tablets of Cefuroxime Axetil

Cefuroxime axetil fast dissolving tablets were compressed with 3.5 mm round shaped standard punch.

Weight variation was found to be in the range of 226.3– 228.3 mg. Thickness was found to be 3.0 – 3.4, hardness was found to be in the range 4.0 – 4 kg/cm^2 indicating good mechanical strength, friability was within the USP limits, drug content was found to be within 95- 105% which is acceptable limits, *in vitro* disintegration time of the tablet were evaluated and found to be between 29- 41 sec.

Discussion of results

- Weight variation and hardness of cefuroxime axetil Tablets were within range. Length and breadth of tablet was as per the punch dimension.
- Percentage friability of tablet was evaluated in 100 rpm and tablet passed the friability test.
- Tablets from each batch showed uniformity of weight as per IP limits. Each sample was analyzed in triplicate (n = 3).
- Content uniformity was done as per IP and the values were satisfactory.
- Wetting time was in the range of 28 to 39 sec. As wetting time increases disintegration time of tablet decreases. Wetting time of combination of superdisintegrants shows lower values hence higher disintegration time. Formulations containing of C-TXG showed somewhat lower wetting time than combination batches hence showed satisfactory disintegration time. Formulations containing of KOLLIDON XL showed very low wetting time compared to other formulations hence showed very less disintegration time than other formulations.
- Disintegration Time of tablets was evaluated and was found to be in the range of 29±1 to 41±1.52.

5.4.1 *In vitro* dissolution studies:

Both of superdisintegrants are chosen in the present work were natural superdisintegrants hence all the formulations showed better and satisfactory drug release profile.

The Dissolution study of various batches from F1- F6 shows that cefuroxmine axetil release from tablets containing combination of both KOLLIDON XL and C-TXG at higher concentrations showed higher drug release. The dissolution results show that there was an hike in the dissolution velocity of the tablets.

The maximum drug release was observed at 20 min which is acceptable and more than the marketed sample. Formulation F6 having higher concentration of C-TXG showed more drug release

SUMMARY

The Study was undertaken with an aim to formulate fast dissolving tablets of cefuroxime axetil by using natural superdisintegrants like C-TXG and KOLLIDON XL.
Different formulations were prepared varying the superdisintegrant concentration. Preformulation study of the tablet blend was carried out, the tablet blends showed good flowing properties directing for the further course of formulation.
The tablets were prepared by direct compression method by 3.5 mm, round shaped, B tooling punch.
Tablet blend was evaluated for postformulation studies like hardness, weight variation, friability, wetting time, *in vitro* disintegration time and *in vitro* dissolution, stability studies.
The hardness was found to be in the range of 4.0 -5.1 kg/cm^2.Weight variation was found to be in the range of 226 – 228 mg. Friability was NMT 0.5% meeting the USP limits. Wetting time was found to be within 30 sec.
The formulations were stable at both the temperatures maintained for stability studies and were found to be maintaining the same dissolution velocity.
As concentration of xanthan gum decreased it showed lower drug release in combination batch. The formulation F2 which contain only 2mg of xanthan gum showed 94% of drug release. The formulation F4 containing 2mg of Kollidon XL showed 98% of drug release which is acceptable.

CONCLUSION

It was concluded that the formulations containing C-TXG and KOLLIDON XL as superdisintegrants can be proved to be ideal formulation considering all the evaluation parameters mainly wetting time, *in vitro* disintegration time and *in vitro* dissolution studies.

- Formulations containing of xanthan gum in higher quality showed good disintegration time. Formulations containing of alginic acid showed lesser disintegration time compared with other formulations.
- Superdisintegrants has a dominant role in disintegration as well as drug release form orodispersible tablets.

- Due to the swelling and wicking action of both the superdisintegrants the tablets showed better disintegration time which in turn showed good drugrelease from tablet formulations.
- Further we can say that as concentration of superdisintegrants increases it causes higher % of drug release.
- It is also concluded that modified xanthan gum obtained was biodegradable, direct compressible and exhibited desirable swelling dynamics to be used as hydrophilic excipients for rapidly disintegratingtablets.

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