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Research Article

**PREPATION AND EVALUATION OF MOUTH DISSOLVING
TABLETS OF FOSINOPRIL BY DIRECT COMPRESSION
METHOD****Mourya Rajender*¹, Ch. Sunitha²**Department Of Pharamaceutics, Princeton College Of Pharmacy, Pocharam, Hyderabad,
Telangana 500088.**Abstract:**

The present research was aimed at the preparation and evaluation of mouth dissolving tablets of Fosinopril by the direct compression method to enhance patient compliance and ensure rapid onset of action. Various formulations were developed using different concentrations of suitable super disintegrants and directly compressible excipients. The pre-compression parameters such as angle of repose, bulk density, tapped density, and compressibility index were evaluated and found to be within the acceptable limits of I.P., indicating good flow properties of the powder blend. The prepared tablets were further assessed for post-compression parameters including hardness, friability, weight variation, thickness, drug content uniformity, disintegration time, wetting time, and in vitro drug release. All formulations complied with I.P. specifications, demonstrating good mechanical strength and acceptable physicochemical properties. Among the developed batches, Formulation F6 was identified as the optimized formulation, as it exhibited rapid disintegration, acceptable friability, uniform drug content, and maximum drug release in a short time.

The study concludes that mouth dissolving tablets of Fosinopril prepared by direct compression provide a promising dosage form with improved patient convenience, especially for paediatric, geriatric, and dysphagic patients, while ensuring effective therapeutic performance.

Keywords: Fosinopril , Mouth Dissolving Tablets**Corresponding author:****Mourya Rajender,**Department of Pharmaceutics, Princeton college of Pharmacy,
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QR CODE



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INTRODUCTION:**1. INTRODUCTION**

The oral route of administration is considered as the most widely accepted route because of its convenience of self-administration, compactness and easy manufacturing. But the most evident drawback of the commonly used oral dosage forms like tablets and capsules is difficulty in swallowing, leading to patient's in compliance particularly in case of pediatric and geriatric patients, but it also applies to people who are ill in bed and to those active working patients who are busy or travelling, especially those who have no access to water.

For these reasons, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention. Mouth disintegrating tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people.¹

An Mouth disintegrating tablet (MDT) is a solid dosage form that contains medicinal substances and disintegrates rapidly (within seconds) without water when placed on the tongue. The drug is released, dissolved, or dispersed in the saliva, and then swallowed and absorbed across the GIT.²

US FDA defined MDT tablets as "A solid dosage form containing medicinal substances which disintegrates rapidly usually within a matter of seconds, when placed upon the tongue".

Recently European Pharmacopoeia used the term 'Oro dispersible tablet' as a tablet that is to be placed in the mouth where it disperses rapidly before swallowing.

Mouth disintegrating tablets are also called as mouth-dissolving tablets, fast disintegrating tablets, fast dissolving tablets, orodispersible tablets, rapimelts, porous tablets, quick dissolving tablet.

The US Food and Drug Administration responded to this challenge with the 2008 publication of Guidance for Industry: Mouth Disintegrating Tablets (Rosie et al., 2009). Three main points stand out in the final guidance:

- MDTs should have an *in vitro* disintegration time of approximately 30sec or less.
- Generally, the MDT tablet weight should not exceed 500 mg, although the combined influence of tablet weight, size, and component solubility all factor into the acceptability of an MDT for both patients and regulators.
- The guidance serves to define the upper limits of the MDT category, but it does not supersede or replace the original regulatory definition mentioned. In other words, disintegration within a matter of seconds remains the target for an MDT.

1.1. NEED TO DEVELOP MDT:³⁻⁷

The need for one of the non-invasive delivery system i.e., Mouth disintegrating tablets persists due to patients' poor acceptance of, and compliance with, existing delivery regimes, limited market size for drug companies and drug uses, coupled with high cost of disease management.

PATIENT FACTORS:

Mouth disintegrating dosage forms are particularly suitable for patients, who for one reason or the other; find it inconvenient to swallow tablets and capsules with an 8-oz glass of water. These include the following:

- Paediatric and geriatric patients who have difficulty in swallowing or chewing solid dosage forms.
- Patients who are unwilling to take solid preparation due to fear of choking.
- Very elderly patients who may not be able to swallow a daily dose of antidepressant.
- An eight-year old with allergies who desires a more convenient dosage form than antihistamine syrup
- A middle-aged woman undergoing radiation therapy for breast cancer may be too nauseous to swallow her H₂- blocker.
- A schizophrenic patient in an institutional setting who may try to hide a conventional tablet under his or her tongue to avoid their daily dose of an atypical antipsychotic.
- A patient with persistent nausea, who may be journey, or has little or no access to water

EFFECTIVENESS FACTORS:

- Increased bioavailability and faster onset of action are a major claim of these formulations.
- Dispersion in saliva in oral cavity causes pregastric absorption from some formulations in those cases where drug dissolves quickly.
- Buccal, pharyngeal and gastric regions are all areas of absorption for many drugs.
- Any pregastric absorption avoids first pass metabolism and can be a great advantage in drugs that undergo a great deal of hepatic metabolism.
- Furthermore, safety profiles may be improved for drugs that produce significant amounts of toxic metabolites mediated by first-pass liver metabolism and gastric metabolism, and for drugs that have a substantial fraction of absorption in the oral cavity and pregastric segments of GIT.

MANUFACTURING AND MARKETING FACTORS:

- Developing new drug delivery technologies and utilizing them in product development is

critical for pharmaceutical industries to survive, regardless of their size.

- As a drug nears the end of its patent life, it is common for pharmaceutical manufacturers to develop a given drug entity in a new and improved dosage form.
- A new dosage form allows a manufacturer to extend market exclusivity, unique product

differentiation, value-added product line extension, and extend patent protection, while offering its patient population a more convenient dosage form.

- This leads to increased revenue, while also targeting underserved and under-treated patient populations.

1.2. MECHANISM OF ACTION OF MDT IN ORAL MUCOSA:⁸⁻¹⁰

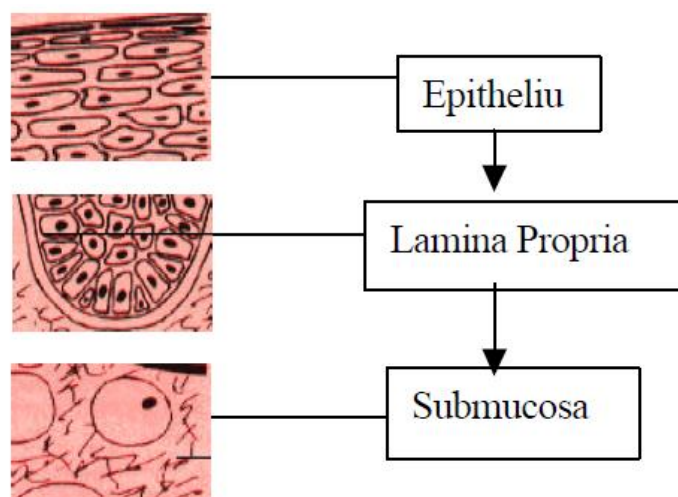


Fig: 1.1 Different layers of oral mucosa (Nehal Siddiqui *et al* .,2011)

MECHANISM OF ACTION: The MDT is placed upon patient's tongue or any oromucosal tissue. It instantly get wet by saliva due to presence of hydrophilic polymer and other excipients, then the tablet rapidly hydrates and dissolves to release the medication for oromucosal absorption.

1.3 ADVANTAGES OF MDTs:

Advantages of MDTs include:

- Ease of administration to geriatric, paediatric, mentally disabled, and bed-ridden patients, who have difficulty in swallowing the tablet.
- The MDTs do not need water for swallowing unlike conventional dosage forms. This is very convenient for patients who are travelling or do not have immediate access to water, and thus, provide improved patient compliance.
- Being unit solid dosage forms, provide luxury of accurate dosing, easy portability and manufacturing, good physical and chemical stability and an ideal alternative for paediatric and geriatric patients.
- Bioavailability of drugs is enhanced due to absorption from mouth, pharynx, and oesophagus.
- Pregastric absorption can result in improved bioavailability and because of reduced dosage, improved clinical

performance through a reduction of unwanted effects.

- Rapid onset of therapeutic action as tablet is disintegrated rapidly along with quick dissolution and absorption in oral cavity.
- Good mouth feels, especially for paediatric patients as taste-masking technique is used to avoid the bitter taste of drugs.
- Minimum risk of suffocation in airways due to physical obstruction, when MDTs are swallowed, thus they provide improved safety and compliance with their administrations.
- Rapid drug therapy intervention is possible.
- Conventional processing and packaging equipments pleat disintegration in the mouth.³

1.4 LIMITATIONS TO MOUTH DISSOLVING TABLETS :

- Drugs with relatively larger doses are difficult to formulate into MDTs e.g. antibiotics like ciprofloxacin with adult dose tablet containing about 500 mg of the drug.
- Patients who concurrently take anti cholinergic medications may not be the best candidates for MDTs.

1.5 DESIRED CHARACTERISTICS AND CHALLENGES TO DEVELOP MOUTH DISSOLVING TABLETS.¹¹⁻¹⁵

RAPID DISINTEGRATION: Rapid disintegration is a desired characteristic of MDT where it rapidly disintegrates in mouth in matter of seconds. Selection of super disintegrants which tends the drug to release fast is a challenging part of formulation scientist.

PALATABILITY: As most of the drugs are bitter in taste or tasteless, effective taste masking technology should be adopted to develop orodispersible tablet as they disintegrate or dissolve in patient's oral cavity. Hence taste masking of orodispersible tablets becomes challenging as well as a desired characteristic for better mouth feel and patient's compliance.

MECHANICAL STRENGTH: The orodispersible tablet should be formulated in such a way that it disintegrates rapidly in fraction of seconds in oral cavity which is a desired characteristic for patients who have swallowing problem and should hold the mechanical integrity of tablet to avoid friability and special packing which is challenging to formulators.

HYGROSCOPICITY: Several Mouth disintegrating dosage forms are hygroscopic and

cannot maintain physical integrity under normal conditions of temperature and humidity. Hence, the formulators should develop a system to maintain low sensitivity to environment conditions which is a challenging as well as desired character to attain.

AMOUNT OF DRUG: The amount of drug incorporated as an orodispersible tablet should give sufficient response as well as it must be lower than 400mg for insoluble drugs and less than 60 mg for soluble drugs.

SIZE OF THE TABLET: The degree of ease when taking a tablet depends on its size. The size of the tablet should be such that it should be easy to swallow and to handle and for good packing.

Non -patented	Patented
Freeze drying Spray drying Molding Phase transition process Melt granulation Sublimation Mass extrusion Cotton candy process Direct compression Nanonization Effervescent method	Zydus technology Orosolv technology Durosolv technology Wowtab technology Fashtab technology Oraquick technology Lyoc technology Quick –Dis technology Nanocrystal technology Frosta technology Pharmaburst technology Flash Dose technology Ziplet/Advatab technology QuickSolv technology

1.5 VARIOUS TECHNOLOGIES USED IN FORMULATION OF MDT:¹⁶⁻²⁰

- The technologies that have been used by various researchers to prepare Mouth disintegrating dosage forms include: Patented and Non patented technologies.

Table.1.1 Patented and Non- patented technologies

1.6 PATENTED TECHNOLOGIES:**ZYDIS TECHNOLOGY:**

- Scherer has patented the Zydis technology. Zydis, the best known of the fast dissolving/disintegrating tablet preparations, was the first marketed new technology tablet. The tablet dissolves in the mouth within seconds after placement on the tongue.
- A Zydis tablet is produced by lyophilizing or freeze-drying the drug in a matrix usually consisting of gelatin. The product is very lightweight and fragile, and must be dispensed in a special blister pack.

WOWTAB TECHNOLOGY:

- The Wowtab fast-dissolving/disintegrating tablet formulation has been on the Japanese market for a number of years. Wowtab technology is patented by Yamanouchi Pharmaceutical Co. The WOW in Wowtab signifies the tablet is to be given "With out. Water". It has just recently been introduced into the U.S.
- This technology utilizes sugar and sugar-like (e.g., mannitol) excipients. This process uses a combination of low mouldability saccharides (rapid dissolution) and high mouldability saccharide(good binding property).
- The two different types of saccharides are combined to obtain a tablet formulation with adequate hardness and fast dissolution rate. Due to its significant hardness, the Wowtab formulation is a bit more stable to the environment than the Zydis or OraSolv.

FROSTA TECHNOLOGY:

- Akina patents this technology. It utilizes the concept of formulating plastic granules and compressing them at low pressure to produce strong tablets with high porosity. Plastic granules composed of porous and plastic material, water penetration enhancer, and binder.
- The tablets obtained have excellent hardness and rapid disintegration time ranging from 15 to 30 sec depending on size of tablet.

ORASOLV TECHNOLOGY:

- OraSolv was Cima's first fast-dissolving/disintegrating dosage form. The OraSolv technology, unlike Zydis, disperses in the saliva with the aid of almost imperceptible effervescence.
- The OraSolv technology is best described as a fast-disintegrating tablet; the tablet matrix dissolves in less than one minute, leaving coated drug powder. The taste

- Patients should be advised not to push the tablets through the foil film, but instead peel the film back to release the tablet. The Zydis product is made to dissolve on the tongue in 2 to 3 seconds.
- In addition, it utilizes microencapsulation with specialized polymers or complexation with ion exchange resins to mask the bitter tasting drug. The combination of lyophilisation and taste masking creates a product that is both pleasing to the eye and also to the senses of taste and touch.

masking associated with the OraSolv formulation is two-fold. The unpleasant flavor of a drug is not merely counteracted by sweeteners or flavors; both coating the drug powder and effervescence are means of taste masking in OraSolv.

- This technology is frequently used to develop over-the-counter formulations. The major disadvantage of this formulation is its mechanical strength because the Orasolv tablets are only lightly compressed. An advantage that goes along with the low degree of compaction of OraSolv is that the particle coating used for taste masking is not compromised by fracture during processing.

DURASOLV TECHNOLOGY:

- DuraSolv is Cima's second-generation fast-dissolving/disintegrating tablet formulation, produced in a fashion similar to OraSolv and has much higher mechanical strength than its predecessor due to the use of higher compaction pressures during tableting. It is so durable that it can be packaged in either traditional blister packaging or vials.
- The tablets are prepared by using conventional tableting equipment and have good rigidity (friability less than that 2%). The product is thus produced in a faster and more cost-effective manner.
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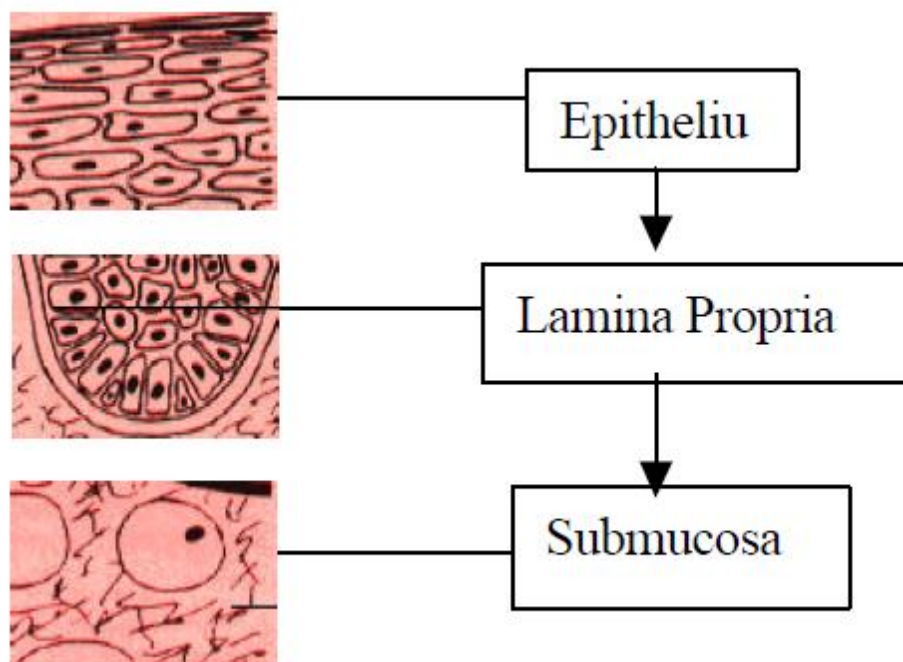


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- This technology is frequently used to develop over-the-counter formulations. The major disadvantage of this formulation is its mechanical strength because the Orasolv tablets are only lightly compressed. An advantage that goes along with the low degree of compaction of OraSolv is that the particle coating used for taste masking is not compromised by fracture during processing.

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- The tablets are prepared by using conventional tableting equipment and have good rigidity (friability less than that 2%). The product is thus produced in a faster and more cost-effective manner.
- One disadvantage of this technology is that it is not compatible with larger doses of active ingredients, because the formulation is subjected to such high pressures on compaction.

METHODOLOGY:

100mg of Deflazacort pure drug was dissolved in 100ml of Methanol (stock solution)10ml of above solution was taken and make up with100ml by using 0.1 N HCL (100µg/ml).From this 10ml was taken and make up with 100 ml of 0.1 N HCL (10µg/ml). The above solution was subsequently diluted with 0.1N HCL to obtain series of dilutions Containing 10, 20, 30, 40 and 50 µg/ml of Deflazacort per ml of solution. The absorbance of

the above dilutions was measured at 244 nm by using UV-Spectrophotometer taking 0.1N HCL as blank. Then a graph was plotted by taking Concentration on X-Axis and Absorbance on Y-Axis which gives a straight line Linearity of standard curve was assessed from the square of correlation coefficient (R^2) which determined by least-square linear regression analysis. The above procedure was repeated by using pH 6.8 phosphate buffer solutions.

9.2. Preformulation parameters

The quality of tablet, once formulated by rule, is generally dictated by the quality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characteristics of blends produced. The various characteristics of blends tested as per Pharmacopoeia.

Angle of repose:

The frictional force in a loose powder can

be measured by the angle of repose. It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles producing a surface angle, is in equilibrium with the gravitational force. The fixed funnel method was employed to measure the angle of repose. A funnel was secured with its tip at a given height (h), above a graph paper that is placed on a flat horizontal surface. The blend was carefully poured through the funnel until the apex of the conical pile just touches the tip of the funnel. The radius (r) of the base of the conical pile was measured. The angle of repose was calculated using the following formula:

$$\tan \theta = h / r \quad \tan \theta = \text{Angle of repose}$$

h = Height of the cone ,

r = Radius of the cone base

Formulation composition for tablets

INGREDIENTS (mg)	FORMULATION CHART								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Deflazacort	6	6	6	6	6	6	6	6	6
Ethyl Cellulose	5	10	15	-	-	-	-	-	-
Eudragit S 100	-	-	-	5	10	15	-	-	-
Hydroxypropyl Cellulose	-	-	-	-	-	-	5	10	15
Lactose	71	66	61	71	66	61	71	66	61
PVP K30	10	10	10	10	10	10	10	10	10
Magnesium stearate	4	4	4	4	4	4	4	4	4
Talc	4	4	4	4	4	4	4	4	4
Total Tablet Weight	100	100	100	100	100	100	100	100	100

All the quantities were in mg

RESULTS AND DISCUSSION:

The present study was aimed to developing Controlled release tablets of Deflazacort using various polymers. All the formulations were evaluated for physicochemical properties and *in*

vitro drug release studies.

10.1. Analytical Method

Graphs of Deflazacort were taken in Simulated Gastric fluid (pH 1.2) and in pH 6.8 phosphate buffer at 244 nm respectively.

Table 10.1: Observations for graph of Deflazacort in 0.1N HCl

Concentration [µg/mL]	Absorbance
0	0
10	0.149
20	0.258
30	0.357
40	0.472
50	0.589

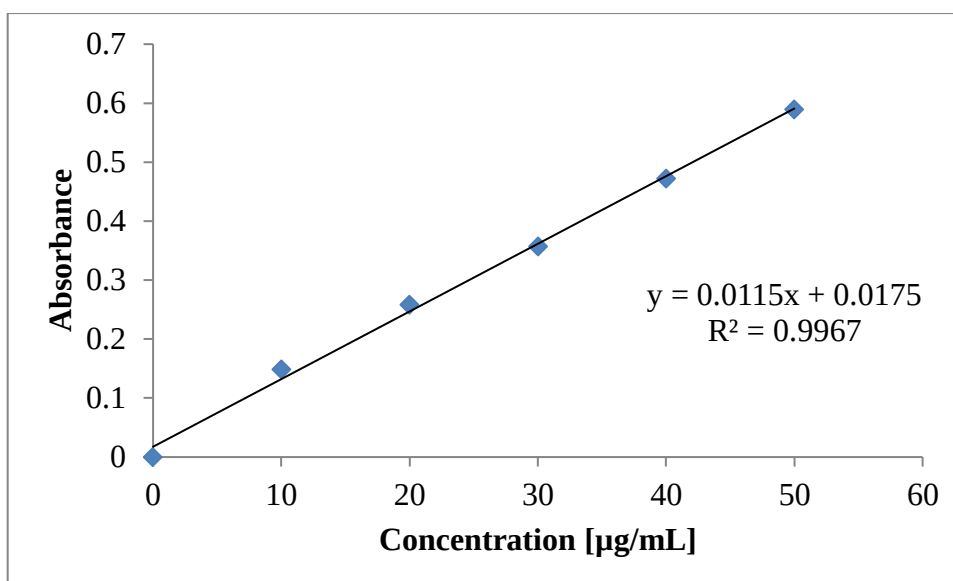


Figure : Standard graph of Deflazacort in 0.1N HCl

Table : Observations for graph of Deflazacort in p H 6.8 phosphate buffer

Conc [µg/ml]	Abs
0	0
10	0.161
20	0.295
30	0.445
40	0.571
50	0.698

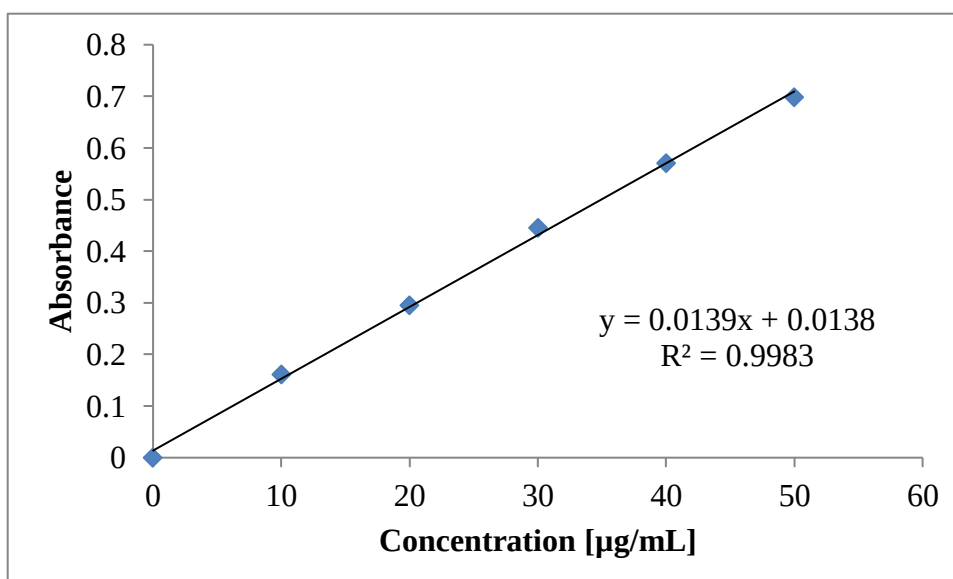


Figure: Standard graph of Deflazacort pH 6.8 phosphate buffer (244 nm)

Preformulation parameters of powder blend

Table : Pre-formulation parameters of Core blend

Table : Pre-compression parameters					
Formulations	Bulk Density(gm/cm ³)	Tap Density (gm/cm ³)	Carr's Index (%)	Hausner ratio	Angle Of Repose(Θ)
F1	0.47±0.001	0.53±0.005	14.11±0.10	1.13±0.011	28.76±0.14
F2	0.44±0.003	0.66±0.003	30.45±0.07	1.55±0.007	5.64±0.20
F3	0.41±0.004	0.59±0.004	18.75±0.09	1.22±0.011	7.01±0.13
F4	0.58±0.004	0.52±0.005	8.27±0.28	1.01±0.010	4.28±0.13
F5	0.55±0.003	0.65±0.002	9.52±0.09	1.14±0.009	31.58±0.24
F6	0.42±0.002	0.58±0.002	19.89±0.11	1.26±0.011	4.22±0.22
F7	0.49±0.004	0.51±0.003	19.33±0.050	1.23±0.010	0.19±0.23
F8	0.56±0.006	0.64±0.005	13.63±0.08	1.14±0.010	2.26±0.07
F9	0.43±0.003	0.57±0.002	18.95±0.12	1.05±0.007	7.03±0.16

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.41±0.004 to 0.58±0.004 (gm/cm³) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.51±0.003 to 0.66±0.003 showing the powder has good flow properties. The compressibility index of all the formulations was found to be ranging

between 8.27±0.28 to 30.45±0.07 which shows that the powder has good flow properties. All the formulations has shown the hausner ratio ranging between 1.01±0.010 to 1.55±0.007 indicating the powder has good flow properties.

Quality control parameters for tablets:

Tablet quality control tests such as weight variation, hardness, and friability, thickness, and drug release studies in different media were performed on the compression coated tablet.

Table: 10.4. *In vitro* quality control parameters for tablets

Formulation codes	Average Weight (mg)	Hardness(kg/cm ²)	Friability (% lose)	Thickness (mm)	Drug content (%)
F1	98.32	5.7	0.79	2.03	99.73
F2	97.54	5.4	0.48	2.16	97.42
F3	97.22	5.1	0.12	2.79	99.10
F4	99.15	5.8	0.85	2.32	97.89
F5	98.10	5.5	0.55	2.55	98.55
F6	95.48	5.2	0.28	2.78	97.23
F7	98.39	5.9	0.94	2.11	99.91
F8	97.56	5.6	0.68	2.24	99.62
F9	100.02	5.3	0.33	2.47	98.34

Weight variation and thickness: All the formulations were evaluated for uniformity of weight using electronic weighing balance and the results are shown in table 10.4. The average tablet weight of all the formulations was found to be between 95.48 to 100.02. The maximum allowed percentage weight variation for tablets weighing >100 mg is 5% and no formulations are not exceeding this limit. Thus all the formulations were found to comply with the standards given in I.P. And thickness of all the formulations was also complying with the standards that were found to be between 2.03 to 2.79.

Hardness and friability: All the formulations were evaluated for their hardness, using Monsanto hardness tester and the results are shown in table 10.4. The average hardness for all the formulations was found to be between (5.1 to 5.9) Kg/cm² which was found to be acceptable.

Friability was determined to estimate the ability of the tablets to withstand the abrasion during packing, handling and transporting. All the formulations were evaluated for their percentage friability using Roche friabilator and the results were shown in table 10.4. The average percentage friability for all the formulations was between 0.12 to 0.94 which was found to be within the limit.

Drug content: All the formulations were evaluated for drug content according to the procedure described in methodology section and the results were shown in table 10.4. The drug content values for all the formulations were found to be in the range of (97.23 to 99.91 %). According to IP standards the tablets must contain not less than 95% and not more than 105% of the stated amount of the drug. Thus, all the FDT formulations comply with the standards given in IP.

All the parameters such as weight variation, friability, hardness, thickness and drug content were found to be within limits.

In Vitro Drug Release Studies

Table : Dissolution Data of Deflazacort Tablets

TIME (hr)	% Cumulative Drug Release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
In dissolution media 0.1 N HCL									
0	0	0	0	0	0	0	0	0	0
1	27.72	19.85	14.62	23.8	27.69	24.72	17.3	16.75	19.35
2	33.39	20.22	18.21	36.4	30.75	37.54	24.4	23.89	25.92
In dissolution media 6.8 Phosphate Buffer									
3	43.75	26.80	23.85	47.3	43.82	49.35	32.6	24.73	33.55
4	56.49	38.35	28.76	53.4	54.46	53.41	38.8	33.27	37.28
5	59.75	43.24	33.93	64.6	65.21	61.46	46.2	38.10	42.10
6	63.12	44.87	34.24	76.5	73.96	68.38	54.4	44.61	48.83
7	74.69	56.42	45.75	83.14	78.43	77.57	57.95	55.46	53.79
8	85.24	59.96	56.36	94.59	82.22	83.26	61.44	63.75	57.97
9	94.14	64.29	67.24		98.43	94.38	65.82	77.51	65.41
10	93.86	76.34	78.10			99.19	74.49	80.28	71.11
11		83.89	80.96				78.20	88.31	72.52
12		88.21	84.75				86.15	96.94	78.63

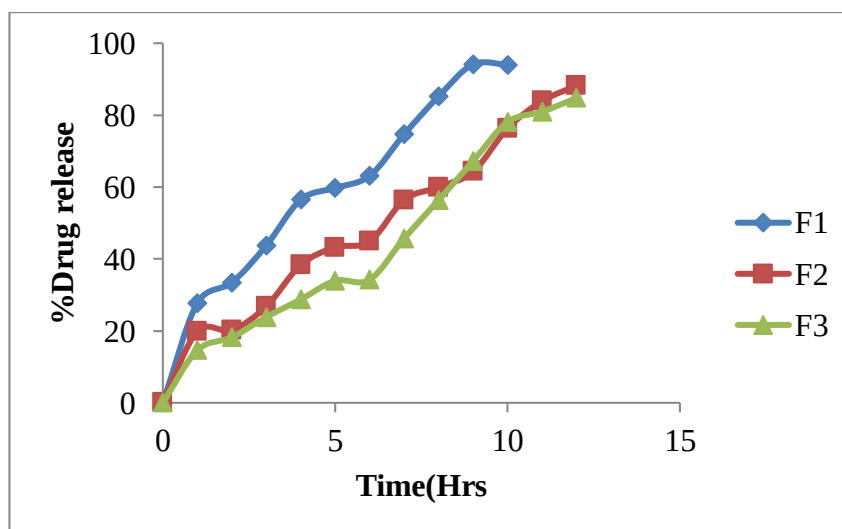


Fig : Dissolution profile of Deflazacort (F1, F2, F3 formulations).

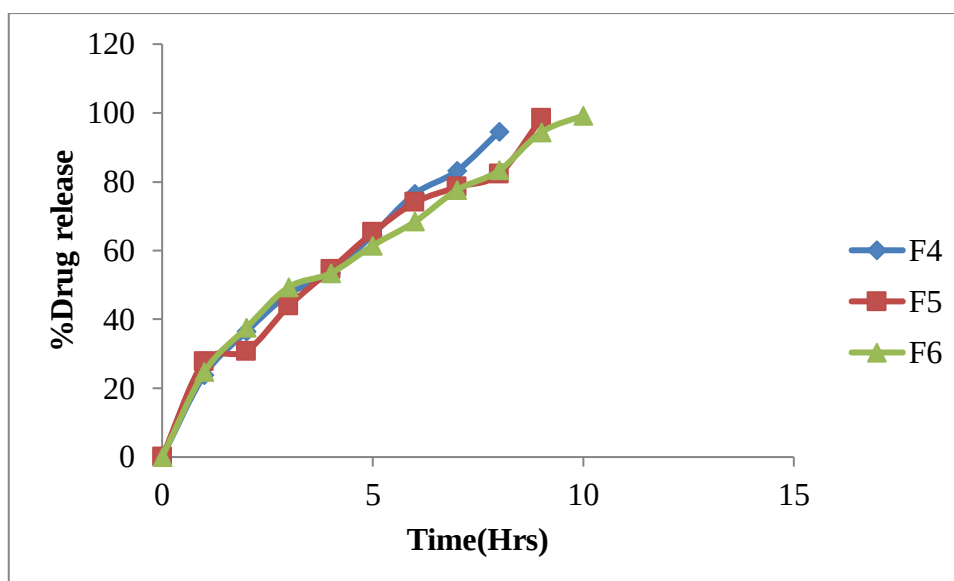


Fig : Dissolution profile of Deflazacort (F4, F5, F6 formulations)

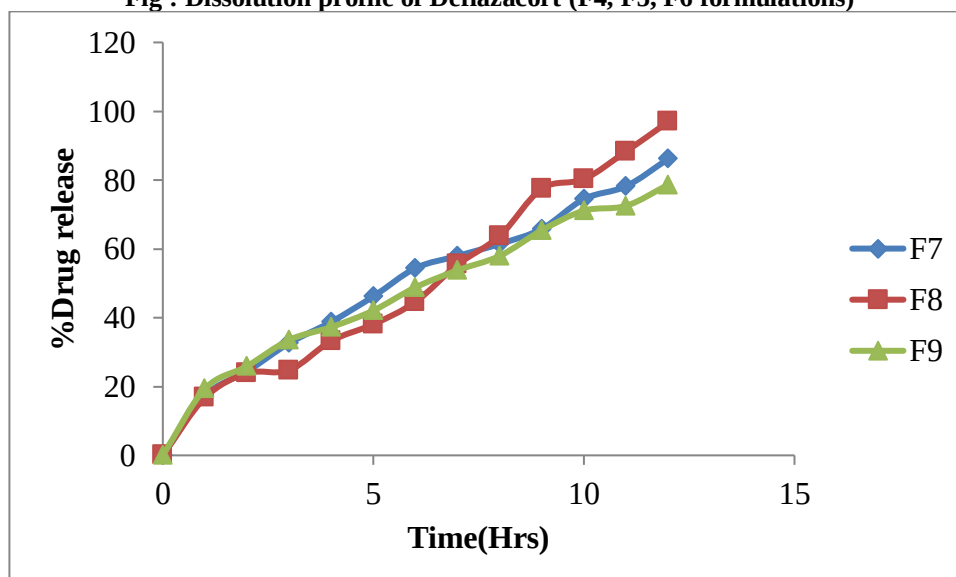


Fig : Dissolution profile of Deflazacort (F7, F8, F9 formulations)

From the dissolution data it was evident that the formulations prepared with Ethyl Cellulose polymer (high concentrations) were able to retard the drug release up to desired time period i.e., 12 hours. The formulations prepared with Eudragit S100 were unable to retard the drug release. Hence they were not considered.

Whereas the formulations prepared with Hydroxypropyl Cellulose were retarded the drug release in the concentration of 10 mg (F8 Formulation) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 96.94 % in 12 hours with

good retardation.

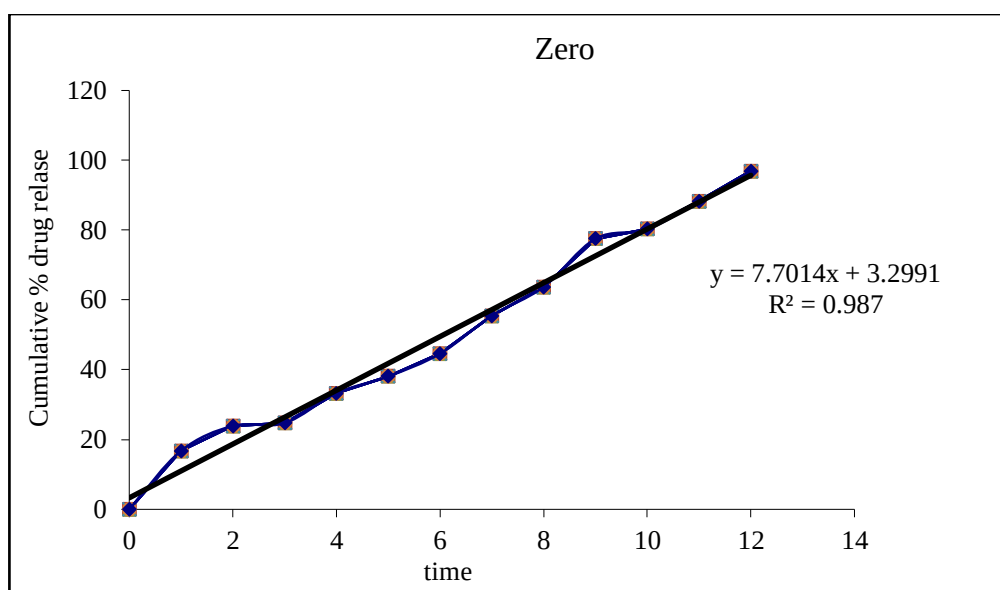
From the above results it was evident that the formulation F8 is best formulation with desired drug release pattern extended up to 12 hours.

Application of Release Rate Kinetics to Dissolution Data:

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

Table 10.6: Release kinetics data for optimised formulation

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG(%) RELEASE	LOG (T)	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE / t)	1/CUM% RELEASE	PEPPAS log Q/100	% Drug Remaining	Q01/3	Qt1/3	Q01/3- Qt1/3
0	0	0			2.000				100	4.642	4.642	0.000
16.75	1	1.000	1.224	0.000	1.920	16.750	0.0597	-0.776	83.25	4.642	4.366	0.275
23.89	2	1.414	1.378	0.301	1.881	11.945	0.0419	-0.622	76.11	4.642	4.238	0.404
24.73	3	1.732	1.393	0.477	1.877	8.243	0.0404	-0.607	75.27	4.642	4.222	0.419
33.27	4	2.000	1.522	0.602	1.824	8.318	0.0301	-0.478	66.73	4.642	4.056	0.586
38.1	5	2.236	1.581	0.699	1.792	7.620	0.0262	-0.419	61.9	4.642	3.956	0.686
44.61	6	2.449	1.649	0.778	1.743	7.435	0.0224	-0.351	55.39	4.642	3.812	0.830
55.46	7	2.646	1.744	0.845	1.649	7.923	0.0180	-0.256	44.54	4.642	3.545	1.097
63.75	8	2.828	1.804	0.903	1.559	7.969	0.0157	-0.196	36.25	4.642	3.310	1.332
77.51	9	3.000	1.889	0.954	1.352	8.612	0.0129	-0.111	22.49	4.642	2.823	1.819
80.28	10	3.162	1.905	1.000	1.295	8.028	0.0125	-0.095	19.72	4.642	2.702	1.940
88.31	11	3.317	1.946	1.041	1.068	8.028	0.0113	-0.054	11.69	4.642	2.270	2.372
96.94	12	3.464	1.987	1.079	0.486	8.078	0.0103	-0.013	3.06	4.642	1.452	3.190

**Fig 10.6 : Zero order release kinetics graph**

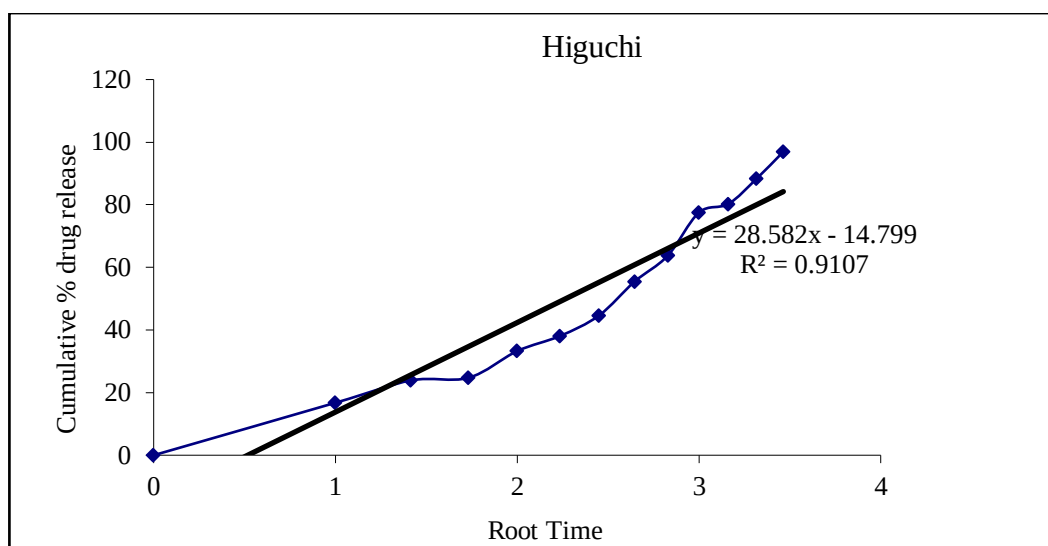


Fig 10.7 : Higuchi release kinetics graph

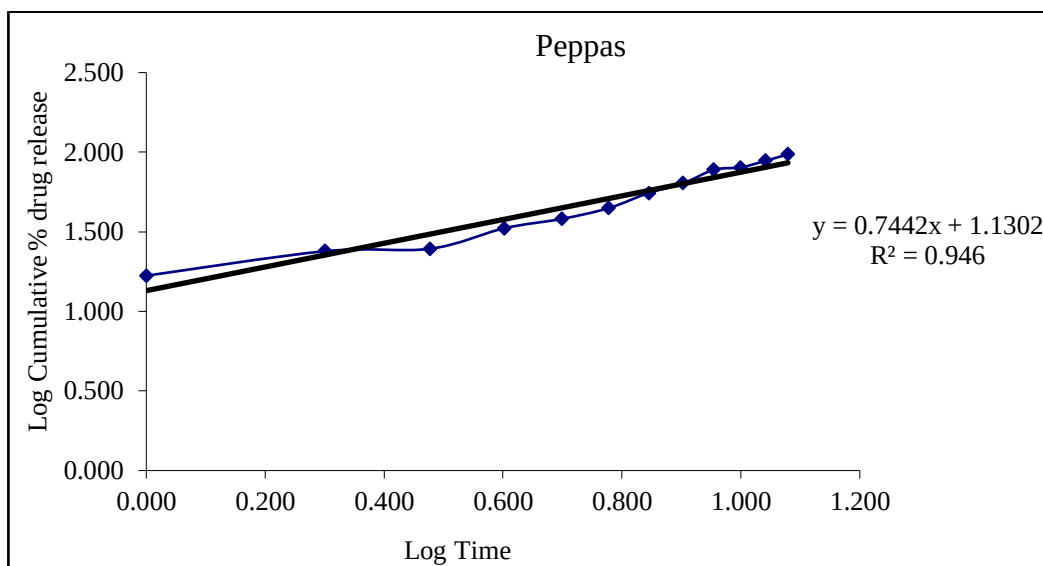


Fig 10.8: Kars mayer peppas graph

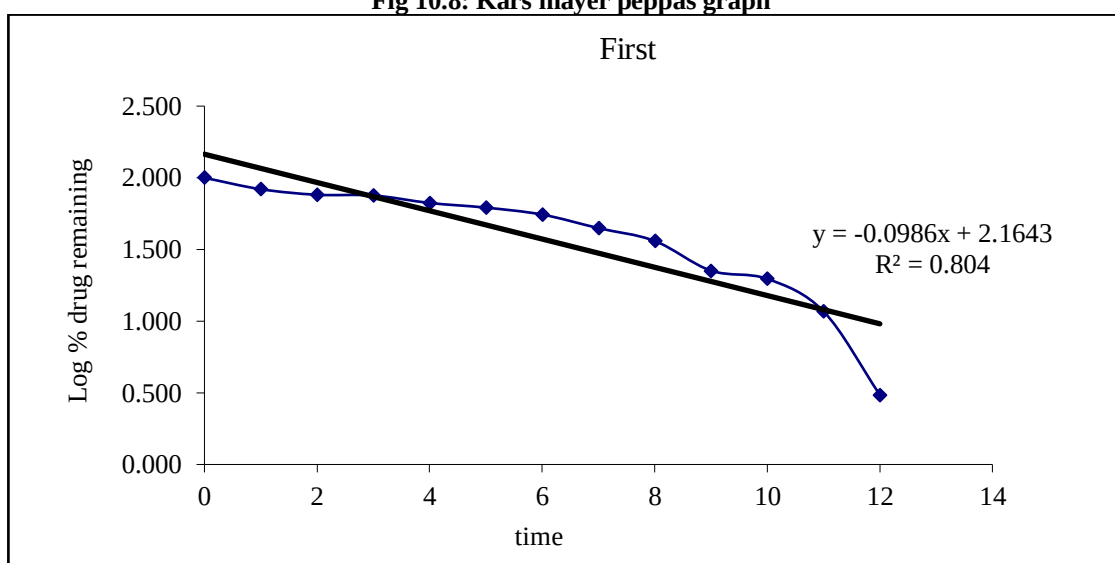


Fig 10.9: First order release kinetics graph

To study the release rate kinetics and the release mechanism of the drug from the tablet formulations, the Optimised *in vitro* drug release data were treated with the mathematical equation such as first order kinetics equation, zero-order kinetics equation

Drug and excipient compatibility studies

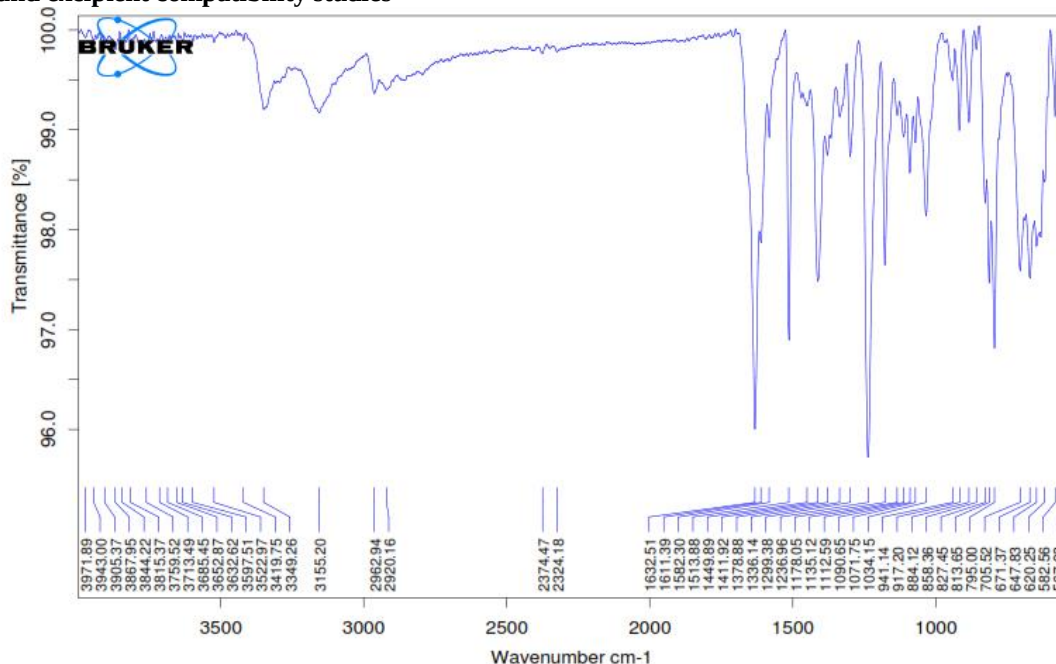


Figure 10.10: FT-IR Spectrum of Deflazacort pure drug

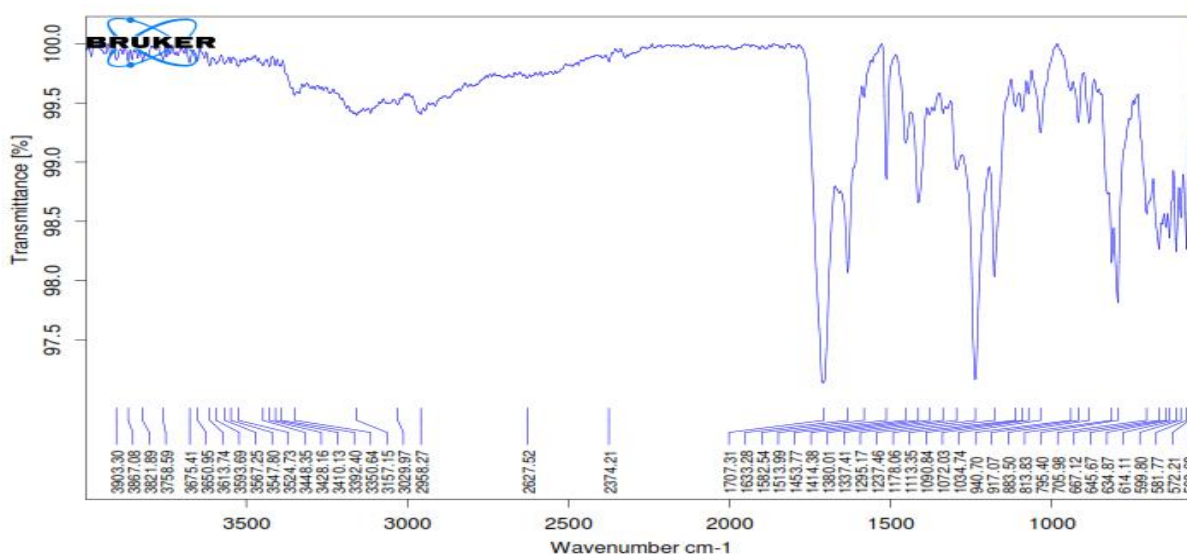


Figure 10.11: FT-IR Spectrum of Optimised Formulation

FTIR spectra of the drug and the optimized formulation were recorded. The FTIR spectra.

CONCLUSION:

The aim of the present study was to develop controlled release formulation of Deflazacort to maintain constant therapeutic levels of the drug for over 12 hrs. Eudragit S 100, Ethyl Cellulose and Hydroxypropyl Cellulose were employed as polymers. Total weight of the tablet was considered as 300 mg. Polymers were used in the concentration of 5, 10 and 15mg concentration. Compatibility study revealed that there was no

interaction between the drug and the excipients in the formulation. The pre-compression and the post compression parameters are found to be within the limits. All the formulations were passed various physicochemical evaluation parameters and they were found to be within limits. Whereas from the dissolution studies it was evident that the formulation (F8) showed better and desired drug release pattern i.e., 96.94 % in 12 hours. It contains the polymer Hydroxypropyl cellulose as

sustained release material. It followed Zero order release kinetics mechanism.

FUTURE SCOPE:

Deflazacort from test tablets showed prolonged release and may be able to sustain the therapeutic effect. This can be further proved by pharmacodynamic study and *In vivo* pharmacokinetic study.

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