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FORMULATION AND EVALUATION OF FOSINOPRIL FAST DISSOLVING TABLETS

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Abstract:
The concept of formulating fast dissolving tablets using super disintegrants offers a suitable and practical approach of faster disintegration and dissolution characteristics. The formulations F1 to F9 Were prepared. Among the various method of preparation fast dissolving tablets were prepared by using super disintegrants like CCS, CP and SSG by direct compression. The formulations F1 to F3 are prepared with 10% concentration of CCS, CP and SSG. The formulations F4 to F6 are prepared with 15% concentration of CCS, CP and SSG. The formulations F7 to F9 are prepared with 20% concentration of CCS, CP and SSG. The prepared tablets of fosinopril were evaluated for precompression parameters like angle of repose, bulk density, tapped density, Carr's index and postcompression parameters like the hardness, friability and weight variation, drug content, disintegration time, and IN VITRO dissolution studies. Among the various fast dissolving tablets of fosinopril F7 formulation shows maximum drug release in 1 min.

Keywords: *fosinopril, super disintegrants, bulk density, Carr's index.*

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INTRODUCTION:

Oral routes of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, selfmedication, pain avoidance and most importantly the patient compliance. The most popular solid dosage forms are being tablets and capsules; one important drawback of this dosage forms for some patients, is the difficulty to swallow.Fast dissolving Tablets are disintegrating and/or dissolve rapidly in the saliva without the need for water. Some tablets are designed to dissolve in saliva remarkably fast, within a few seconds, and are true fast-dissolving tablets. Others contain agents to enhance the rate of tablet disintegration in the oral cavity, and are more appropriately termed fast-disintegrating tablets, as they may take up to a minute to completely disintegrate

Salient Feature of Fast Dissolving:

1. Ease of Administration to the patient who can not swallow, such as the elderly, stroke victims, bedridden patients, patient affected by renal failure and patient who refuse to swallow such as pediatric, geriatric & psychiatric patients.
2. No need of water to swallow the dosage form, which is highly convenient feature for patients who are traveling and do not have immediate access to water.
3. Rapid dissolution and absorption of the drug, which will produce quick onset of action.
4. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases bioavailability of drug is increased.

Techniques for preparing Fast disolving Tablets :

Many techniques have been reported for the formulation of Fast dissolving tablets or Orodispersible tablets.

1. Freeze drying / lyophilization
2. Tablet Moulding
3. Spray drying
4. Sublimation
5. Direct compression
6. Mass extrusion

AIM OF THE STUDY:

The aim of present work is to develop a Orol dispersible tablet/ fast dissolving solid oral dosage form of fosinopril.

1. To perform preformulation studies.
2. To develop various formulations with different excipients.
3. To study the effect of excipient concentrations on the tablet characteristics.
4. To establish the invitro release compliance with the established criteria.
5. To achieve fast release profile for the developed formulation.

LITERATURE REVIEW:

Kunte S[1]., Prepared Fast dissolving films containing Verapamil by solvent casting technique with the help of HPMC E6 and maltodextrin. The strips were evaluated for drug content uniformity, film thickness, folding endurance, *in vitro* disintegration time, *in vitro* dissolution studies, surface pH study, and palatability study. Disintegration time showed by the formulations were found to be in range of 20.4 – 28.6 sec. It was concluded that the fast dissolving strips of verapamil can be made by solvent casting technique with enhanced dissolution rate, taste masking, and hence better patient compliance and effective therapy.

Semalty et al[2], Formulated and evaluated mucoadhesive drug delivery system of enalapril maleate. Prepared films were evaluated for their weight, thickness, surface pH, swelling index, drug content uniformity, *in-vitro* residence time, folding endurance *in vitro* release and permeation studies. It was concluded that the drug can be selected for the development of buccal film for effective therapeutic uses.

Dinge A et al[3], Formulated the fast dissolving films with the easily available components such as HPMC and xanthan gum.Triclosan , a poorly water soluble and bitter drug could be successfully incorporated in the fast dissolving film with the help of solublizers such as poloxamer 407.

Chaudhary D.R et al[4], concluded that the combination of methocel E15 and PEG 400 exhibited excellent mechanism properties (tensile strength 6.32 N/mm2), drug content(98.35%) and dissolution characteristic (DT 47 sec). The research work suggested that the levocetirizine can be formulated as fast dissolving film.

Koland M et al [5] , Prepared fast dissolving films of Ondansetron Hydrochloride by using polyvinyl alcohol, polyvinyl pyrrolidone, carbopol 934P in different ratio by solvent casting method and using mannitol and sodium saccharin as a sweetners and results of study showed that mannitol not only enhance the taste of Ondansetron hydrochloride

containing films but also increase the drug release and permeation.

Murata Y et al [6], developed fast dissolving film using natural polysaccharides such as pullulan and films was loaded with pilocarpine, lidocaine and dexamethasone as a model drugs and concluded that the thickness and the surface shapes were affected by using different concentration of film forming materials.

PLAN OF WORK:

The present proposed research work was planned as per the following experimental protocol

- **Preformulation:**

a. Physical observation
b. Bulk density
c. Tapped density
d. Hausner's Ratio
e. Carr's index
f. Solubility
g. Compatibility studies of drug with various excipients.

- **Formulation:**

Tablets will be prepared by compression method using various grades of excipients in different ratios.

- **Evaluation of tablets:**

a. Thickness
b. Hardness
c. Disintegration test
d. % Friability
e. Weight variation
f. Assay
g. Invitro dissolution testing

METHODOLOGY:

Preformulation Studies:

The overall objective of performing preformation testing is to generate information that will be helpful in developing a stable and bioavailable dosage form when combined with excipients.

A.Organoleptic properties:

The color, odor and taste of the drug were recorded using descriptive terminology.

B.Solubility:

The solubility of the drug sample was carried out in different solvents (aqueous and organic) according to the United States Pharmacopoeia. The results are then compared with those given in the official books and United States Pharmacopoeia.

Drug-excepients compatibility studies by i.r:

Excipients are integral components of almost all pharmaceutical dosage forms. The successful formulation of a stable and effective solid dosage form depends on the careful selection of the excipients, which are added to facilitate administration, promote the consistent release and bioavailability of the drug and protect it from degradation.

Analytical methods for the estimation of Fosinopril

Determination of λ max for Fosinopril:

On the basis of preliminary identification test, it was concluded that the drug complied the preliminary identification. From the scanning of drug, it was concluded that the drug had λ max of 208 nm.

Preparation of standard calibration curve of Fosinopril :

The standard calibration curve for Fosinopril was prepared using 6.8pHPhosphate buffer.

Standard solution:

25 mg of Fosinopril was dissolved in 25 ml of 6.8pHPhosphate buffer solution to give a concentration of 1 mg/ ml (1000 µg/ml).

Stock solution:

From standard solution take 10 ml of solution in 100 ml of 6.8pHPhosphate buffer solution to produce the 100 µg/ml concentration and take from the 100 µg/ml of the solution aliquots of 0.1, 0.2, 0.3, 0.4, and 0.5 ml of stock solution was pipette out in 10 ml volumetric flask. The volume was made up to mark with 6.8pHPhosphate buffer solution to produce concentration as 1, 2, 3, 4, and 5 µg/ml of Fosinopril respectively.

The absorbance of prepared solution of Fosinopril was measured at 208 nm in Shimadzu UV/visible 1700 spectrophotometer against 6.8pHPhosphate buffer solution as blank. The absorbance data for standard calibration curve are given in Table and plotted graphically as shown in the Figure . The standard calibration curve yields a straight line, which shows that drug obeys Beer's law in the concentration range of 1 to 5 mcg/ml.

RESULTS:

Preformulation Study:

A . Organoleptic Properties (Color, odor, taste and appearance)

Results of identification tests of drug

S.NO	Parameter	Drug
1	Color	White to off White color
2	Odor	Odorless
3	Taste	Tasteless
4	Appearance	Crystalline powder

B. Melting point determination: Drug: Fosinopril

Results of Melting point determination test of drug

Reported Melting Point	Observed Melting Point
149-153ºc	**153 ºc**

C. Determination of solubility:

Soluble in water, methanol, ethanol, slightly soluble in hexane.

E. UV-Spectroscopy - Analysis of drug

Ultraviolet Visible (UV-visible) spectroscopy:

Drug sample showed wavelength of maximum absorption (λ-max) 208 nm.

calibration curve plot

S.No	Concentration in µg/ml	Absorbance
1	0	0
2	1	0.165
3	2	0.325
4	3	0.471
5	4	0.627
6	5	0.789

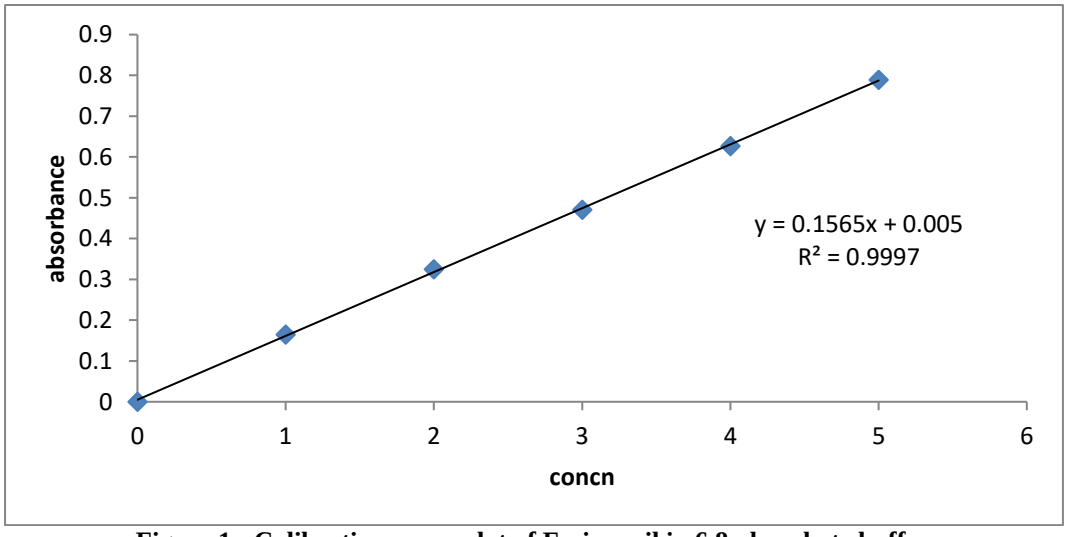

Figure 1 - Calibration curve plot of Fosinopril in 6.8 phosphate buffer

Drug polymer compatibility studies

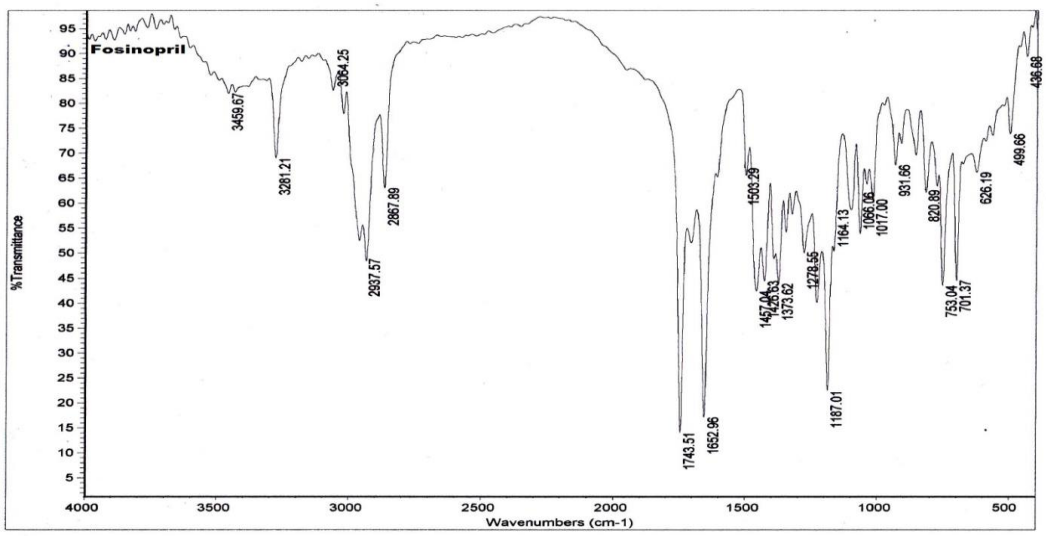

FIG 2: FTIR Spectra of pure drug

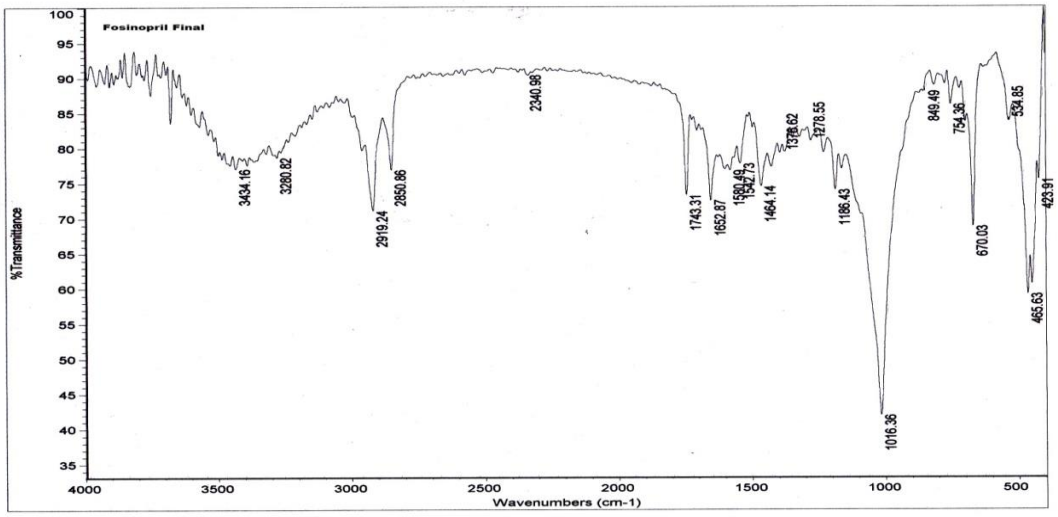

FIG 3: FTIR Spectra of optimized formulation

Table 1: FT-IR Spectra data of FOSINOPRIL fast dissolving tablets

Sno	Functional group	Characteristic peak cm^{-1}	Observed peak for drug cm^{-1}	Peaks for optimized formulation
1	P=O	1300 -1250	1278	1278.55
2	C-N=O	1600 - 1500	1503	1580
3	-CH3	2960 - 2850	2867	2850

Evaluation of Blend:

Table. Bulk density, Tapped density, % Compressibility index, Hausner ratio and Angle of repose. (Precompression studies)

Table 2: Micromeritic properties

FORMULATION CODE	BULK DENSITY gm/ml	TAPPED DENSITY gm/ml	CARR'S INDEX %	Hausner ratio	Angel of repose
F1	0.453	0.689	34.252	1.520	25
F2	0.489	0.710	31.126	1.451	22
F3	0.710	0.873	19.714	1.251	26
F4	0.721	0.870	17.126	1.206	27
F5	0.718	0.871	18.513	1.223	28
F6	0.410	0.483	15.113	1.178	24
F7	0.420	0.482	15.010	1.131	25
F8	0.541	0.691	21.62	1.276	25
F9	0.484	0.615	21.30	1.270	27

Evaluation of Tablets: Were given below in Table

Table 3: Post compression studies

Formulation code	Weight variation	Hardness (kg/cm^2)	Friability (%)	Thickness (mm)	Content uniformity	Disintegration Time (min)
F1	198	6.5	0.65	3.41mm	99.28	4 min 24 sec
F2	198	6.3	0.67	3.43mm	99.16	5 min
F3	199	6.0	0.68	3.45mm	101.1	5 min
F4	200	6.4	0.64	3.42mm	98.68	2min
F5	200	6.1	0.64	3.44mm	99.41	4 min
F6	201	6.0	0.65	3.42mm	102.6	3 min
F7	198	6.2	2.3	3.4mm	99.28	1 min
F8	198	6.5	1.8	3.4mm	99.5	1min 45 sec
F9	200	6.3	0.68	3.43mm	99.6	1min 50 sec

In -vitro drug release study

Paddle method Dissolution data of fast dissolving formulations of Fosinopril by Paddle method (USP II) are reported in Table.

Table 4; Dissolution Values

Time in min	F1	F2	F3	F4	F5	F6	F7	F8	F9
5	**15**	**11**	**14**	**17**	**18**	**20**	**21**	**20**	**22**
10	**24**	**20**	**26**	**28**	**29**	**34**	**55**	**49**	**34**
15	**38**	**31**	**34**	**42**	**36**	**48**	**63**	**58**	**45**
20	**46**	**43**	**47**	**54**	**45**	**59**	**88**	**72**	**67**
30	**68**	**60**	**52**	**72**	**66**	**66**	**98.7**	**89**	**80**
45	**75**	**70**	**68**	**97**	**79**	**83**	**-**	**90**	**95.6**
60	**87**	**81**	**85**	**-**	**86**	**94**	**-**	**-**	

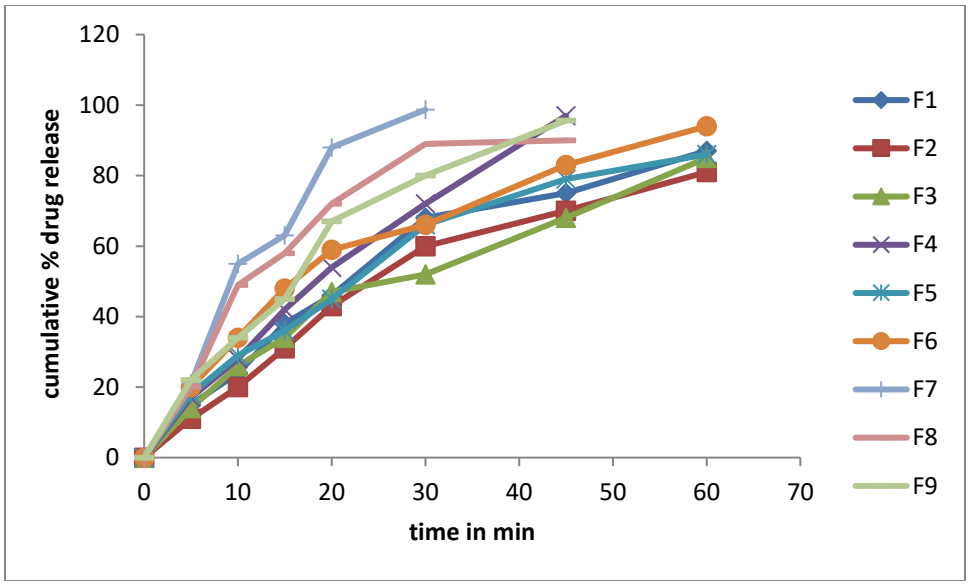

Figure 4: Cumulative % drug release for formulations F1-F9

STABILITY STUDIES:

Fosinopril tablets of F7 formulation were packed in HDPE (High density polyethylene) container with child resistant caps (CRC) and induction sealed. These bottles were charged for stability study at 40^0C &75% RH.

After one month:

Table 5: Physical evaluation of Tablets for stability studies of Optimized formulation:

Parameter	Initial	40^0C / 75%RH
Colour	white	White
Surface	Smooth	Smooth
Disintegration(min)	1min	1min 20 sec
Assay	99.28	99.0

Observation: The Fosinopril tablets were subjected to stability studies at 40ºC and 75% RH for 1 month and from the above results, it was found that there is no significant effect on the tablets

After Three months:

Table 6: Physical evaluation of Tablets for stability studies of optimized formulation:

Parameter	Initial	40^0C / 75%RH
Colour	White	White
Surface	Smooth	Smooth
Disintegration (min)	1min	1min 22 sec
Assay	99.28	98.7

CONCLUSION:

The concept of formulating fast dissolving tablets using super disintegrants offers a suitable and practical approach of faster disintegration and dissolution characteristics. Among the various method of preparation fast dissolving tablets were prepared by using super disintegrants like CCS, CP and SSG by direct compression.The prepared tablets of fosinopril were evaluated for precompression parameters like angle of repose, bulk density, tapped density, Carr's index and postcompression parameters like the hardness, friability and weight variation, drug content, disintegration time, and *IN VITRO* dissolution studies. Among the various fast dissolving tablets of fosinopril F7 formulation shows maximum drug release in 30min.

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