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FORMULATION AND EVALUATION OF FAST DISSOLVING TABLETS OF AN ANTI-ANGINAL DRUG

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Abstract:
The aim of this work is to prepare fast dissolving tablets of Diltiazem Hydrochloride to improve patient compliance. Tablets containing Diltiazem hydrochloride were formulated using various superdisintegrants like crospovidone (CRP), Croscarmellose sodium(CCS) and sodium starch glycolate(SSG) in concentrations ranging from 2-6%. The tablets were prepared bydirect compression method. The flow properties of the granules (F1-F11) were evaluated by determining theCarr's index, Hausner ratio and angle of repose. Poured density values of different batches were found to range between 0.518 and 0.585gm/ml^3, whereas tapped density values were found to vary from 0.641 to 0.668gm/ml^3. Carr's index, Hausner ratio and angle of repose were range between 18.24 to 20.30, 1.22 to 1.25, and 21°40' to 29°66' respectively, which indicates that granules prepared exhibit good flow properties. Tablets (F1-F11) were evaluated for tablet properties like thickness, hardness, friability, disintegration time, weight variation, wetting time and drug content uniformity. Disintegration time of formulations (F10 and F11) prepared by sublimation technique was found to be in the range 25.32±0.258 sec to 26.12±0.215 sec. In vitro dissolution study of formulation of F10 (which gave least disintegration time of 25.32±0.258 sec) showed a cumulative release of 78.115 ± 0.162 after 10 min

Keywords: *Formulation, Evaluation, Fast Dissolving Tablets, Anti-Anginal Drug*

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INTRODUCTION:

The oral passage of medicament administration for illness is measured as the most conventional route. Tablet is a commonly prescribed dosage form as of its accessibility in terms of self-administration, solidity and simplicity in development. Patients particularly pediatric and geriatric, often experience trouble in swallowing conventional tablets and this problem may prove worst during the traveling conditions due to the non-availability or restricted availability of water. These problems of conventional dosage forms can be encountered by the development of mouth dissolving tablets [1, 2, 3] These tablets disintegrate in the mouth within a very short span i.e. 20-30 sec and comes in contact with saliva resulting in the therapeutic action of active agent [4, 5] . Mouth dissolving tablets show better patient compliance and acceptance with improved bioavailability, efficacy and biopharmaceutical properties, in contrast to conventional tablets [6].

Diltiazem hydrochloride is a calcium ion cellular influx inhibitor (slow channel blocker) used to treat angina and hypertension. It acts by inhibiting the cellular influx of calcium ions during membrane depolarization of cardiac and vascular smooth muscle. The aim of this work is to prepare fast dissolving tablets of Diltiazem Hydrochloride to improve patient compliance. Specific objective of the research is as follows, Formulation of fast dissolving tablets of Diltiazem Hydrochloride-drug using various Superdisintegrants by various methods, Evaluation of the prepared FDTs for dissolution, disintegration, wetting time, hardness, etc.

MATERIAL AND METHODS:

Materials: Diltiazem Hydrochloride procured from Anglo-French Drugs and Industries Ltd., Bangalore, India. Crospovidone from International Speciality Product, Hong kong Ltd. Sodium starch glycolate, Mannitol, Magnesium stearate, Ammonium bicarbonate are from S.D. Fine Chemicals Limited, Mumbai. Microcrystalline Cellulose, Croscarmellose Sodium from The Anglo-French Drug Co. Limited, Bangalore. The materials used in the present investigation were either AR/ LR grade or the best possible pharma grade.

UV SPECTROPHOTOMETERIC METHOD FOR DILTIAZEM HCL:

UV SCANNING:

Procedure:

100mg of Diltiazem Hydrochloride was accurately weighed and dissolved in 100ml of phosphate buffer pH 6.8 to get a stock solution of 1mg/ml. Further, an aliquot was pipetted out and diluted suitably to get the concentration in the Beer's range and was scanned in the wavelength region of 200-350nm to record the wavelength of maximum absorption (λ_{max}). Diltiazem hydrochloride was reported to exhibit λ_{max} at 237nm.

Calibration curve for Diltiazem Hydrochloride:

Preparation of standard stock solution:

An accurately weighed quantity of Diltiazem Hydrochloride (100mg) was dissolved in small quantity of phosphate buffer pH 6.8. The volume was made up to 100 ml with phosphate buffer pH 6.8 to generate a primary stock solution of 1mg/ml. 1ml of the primary stock solution was further diluted to 50ml to produce a secondary stock solution having concentration of 20µ/ml.

Preparation of working standard solution:

Working standard solutions having concentrations 2 to 12 µg/ml were prepared by appropriately diluting the stock solution. The absorbance of the working standard solution was recorded and a graph of concentration of the solution was plotted against absorbance using Microsoft Excel software

DRUG EXCIPIENTS INTERACTION STUDY

Fourier Transform Infra-Red (FT-IR) Spectroscopy:

The infrared spectra of Diltiazem Hydrochloride and physical mixture of Diltiazem Hydrochloride and other excipients were recorded using a FT-IR spectrophotometer. The IR spectra's of physical mixture were compared with that of Diltiazem Hydrochloride to check for any possible drug-excipients interaction.

Differential Scanning Calorimetry:

The samples were hermetically sealed in flat-bottomed aluminum pans and heated over a temperature range of 40-240˚C at a rate of 10˚C/min using alumina as areference standard. Thermograms of drugs of optimized batches were recorded using a differential scanning calorimeter and were compared.

FORMULATION OF FAST DISSOLVING TABLETS

By Direct Compression Technique:

Tablets containing Diltiazem hydrochloride were formulated using various superdisintegrants like crospovidone (CRP), Croscarmellose sodium(CCS) and sodium starch glycolate(SSG) in concentrations ranging from 2-6%. The tablets were prepared by direct compression method.

Procedure: The tablets were prepared by direct compression method. All the ingredients were passed

through a sieve number 20 prior to mixing. Diltiazem hydrochloride, Mannitol, MCC, aerosil and the superdisintegrants wereproperly mixed for 30min in a suitable container to obtain a uniform blend. The blendwas further lubricated with magnesium stearate for 5min.The blend was compressed into tablets with an average weight of 200mg using an 8mm flat punch in a rotary tablet press.

TABLE 1 : COMPOSITION OF FAST DISSOLVING TABLETS OFDILTIAZEM HYDROCHLORIDE

Ingredients (mgs)	Formulation code								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Diltiazem Hydrochloride	60	60	60	60	60	60	60	60	60
Croscarmellose sodium	4	8	12	--	--	--	--	--	--
Crospovidone	--	--	--	4	8	12	--	--	--
Sodium starch glycolate	--	--	--	--	--	--	4	8	12
Microcrystalline cellulose	74	70	66	74	70	66	74	70	66
Mannitol	58	58	58	58	58	58	58	58	58
Magnesium stearate	2	2	2	2	2	2	2	2	2
Aerosil	2	2	2	2	2	2	2	2	2

TABLE 2: COMPOSITION OF FAST DISSOLVING TABLETS OFDILTIAZEM HYDROCHLORIDE.

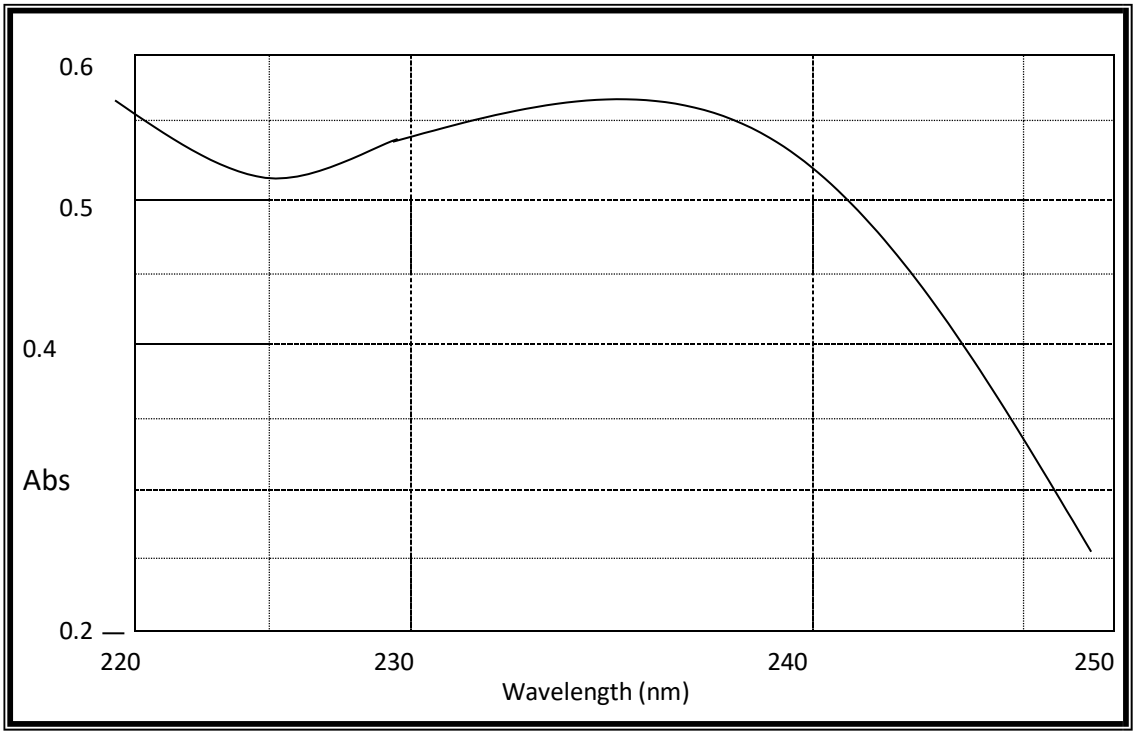
Ingredients (mgs)	Formulation code	
	F10	**F11**
Diltiazem Hydrochloride	60	60
Camphor	10	--
Ammonium bicarbonate	--	10
Sodium starch glycolate	12	12
Microcrystalline cellulose	56	56
Mannitol	58	58
Magnesium stearate	2	2
Aerosil	2	2

RESULTS:

UV SPECTROPHOTOMETRIC METHOD FOR DILTIAZEM HYDROCHLORIDE:

UV scanning: When Diltiazem Hydrochloride was scanned in the wavelengthregion of 200- 350nm, peak was observed at 237nm.

Fig.1. UV Spectrum of Diltiazem Hydrochloride in phosphate buffer pH 6.8.



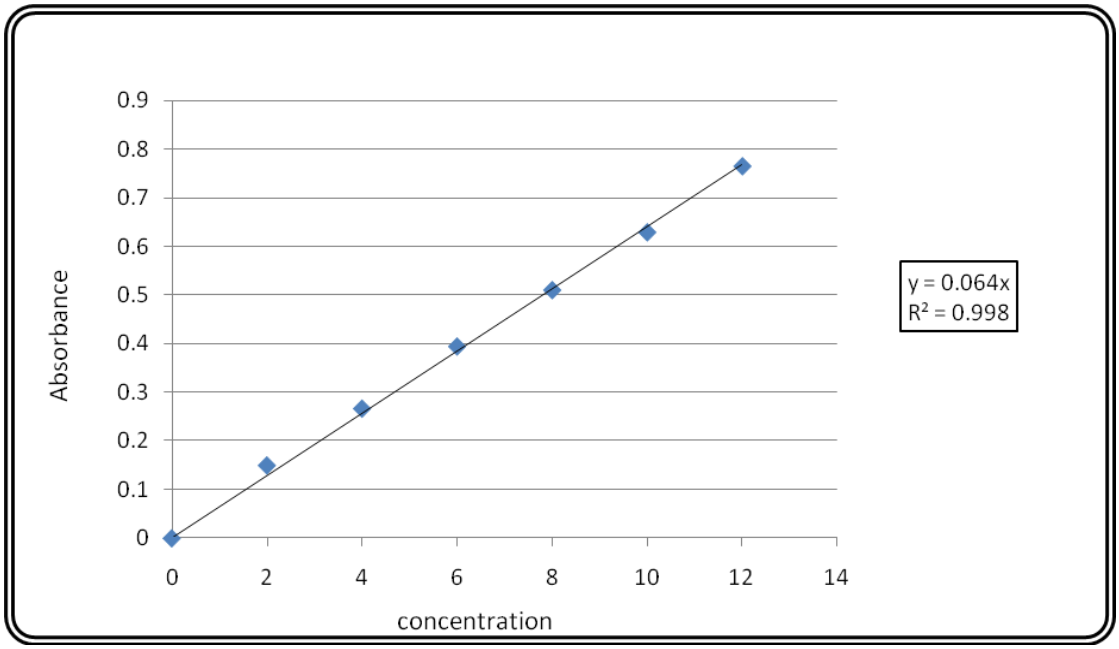
1.b. Calibration curve of Diltiazem Hydrochloride:
The calibration curve for Diltiazem Hydrochloride in phosphate buffer pH 6.8 was foundto be linear with R^2 value 0.998.

Table 3. Data for calibration curve of Diltiazem Hydrochloride in phosphate bufferpH 6.8.

Concentration in g/ml	Absorbance at 237nm*	Standard deviation
0	0	0
2	0.15	0.005
4	0.267	0.007
6	0.395	0.005
8	0.511	0.008
10	0.630	0.005
12	0.766	0.006

*Average of three reading

Fig.2. Calibration curve of Diltiazem Hydrochloride.



DRUG EXCIPIENTS INTERACTION STUDY:

FT-IR Spectroscopy:

The infrared spectra of Diltiazem Hydrochloride and other excipients were recorded using a FT-IR spectrophotometer to check for possible drug-excipients interaction. Distinct peak in the region 2960-2850cm^{-1} for C-H aliphatic, C-H aromatic stretching between 3058-3004cm^{-1}, 1650-1000cm^{-1} for C-N amine and C=O stretching between 1650-1900cm^{-1} of the physical mixture was identical to that of pure drug which confirm the compatibility of the drug and excipients. The spectra are shown in figure 3(a)and 3(b).

Fig.3. IR Spectra of Diltiazem Hydrochloride.

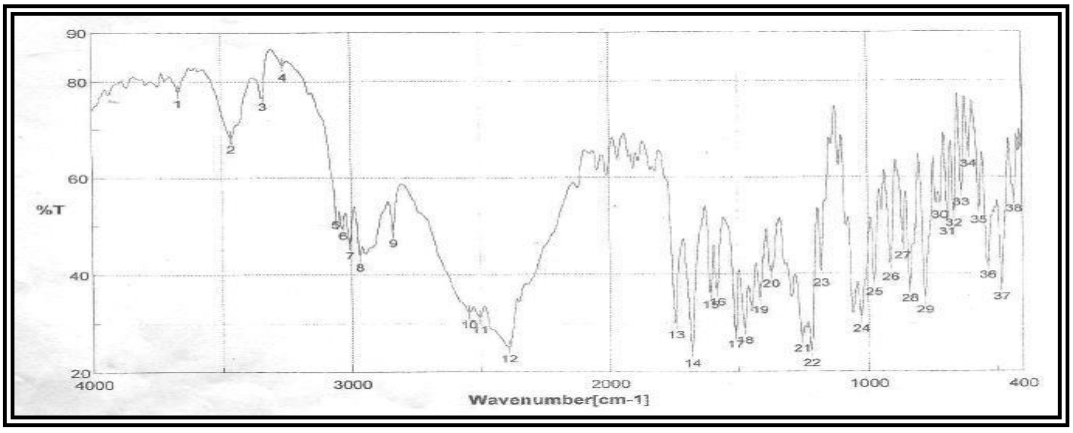
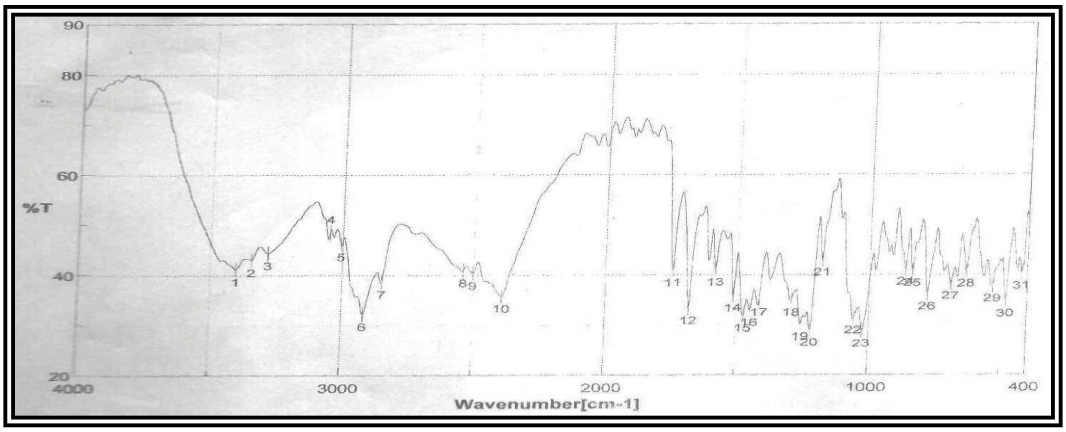


Fig.4. IR Spectra of Diltiazem Hydrochloride with tablet excipients.



Differential Scanning Calorimetery (DSC):

Fig.5. DSC of Diltiazem Hydrochloride.

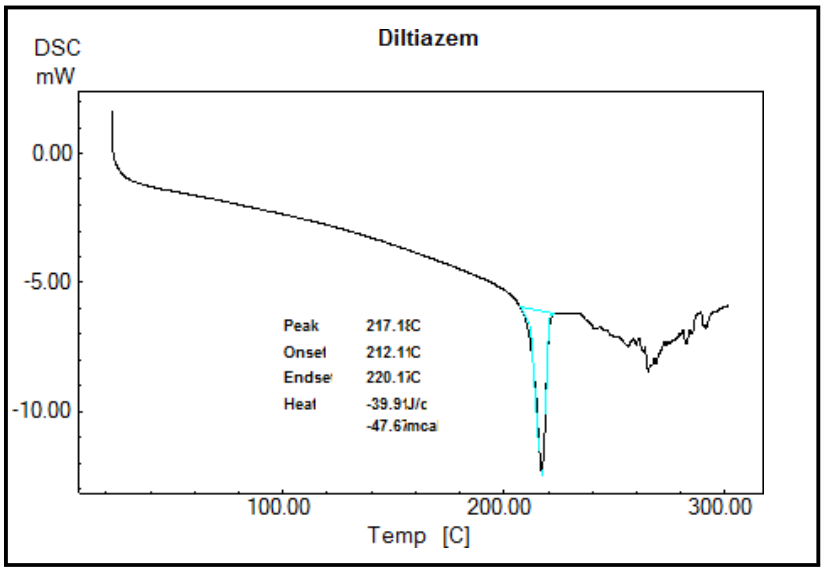
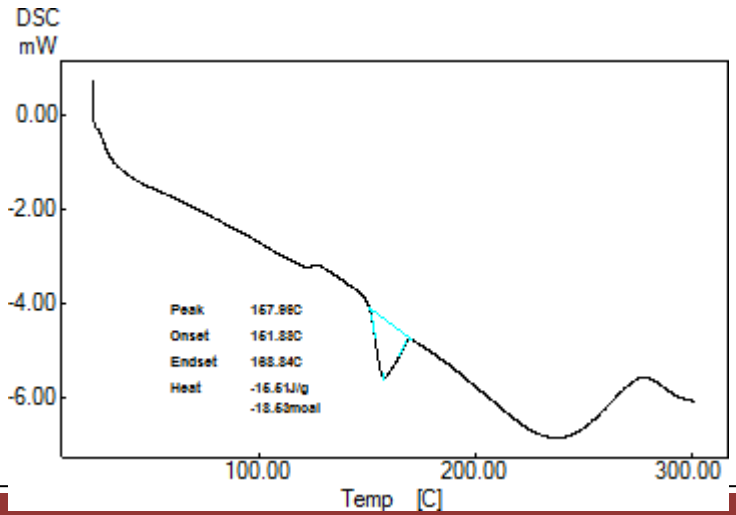


Fig.6. DSC of optimized formulation F10.



EVALUATION OF TABLETS:

DIRECT COMPRESSION TECHNIQUE

3.1.(a) Pre-compression Parameters:

The blend was evaluated for poured density, tapped density, Carr's index, Hausner ratio and angle of repose of formulation F1 to F9 are shown in Table 8(a) and Table 8(b).

Table 4. Results of pre-compression properties of formulations (F1-F9).

Formulation	Poured Density* (gm/ml^3)	Tapped density* (gm/ml^3)	Carr's index (%)	Hausner ratio (%)
F1	0.539	0.668	19.3	1.24
F2	0.585	0.675	13.33	1.22
F3	0.537	0.662	18.88	1.23
F4	0.541	0.668	19.01	1.24
F5	0.539	0.663	18.70	1.23
F6	0.521	0.645	19.22	1.24
F7	0.537	0.660	18.63	1.23
F8	0.518	0.645	19.69	1.24
F9	0.535	0.660	18.94	1.23

* The values represents mean, n = 3

Table 5. Results of pre-compression properties of formulations (F1-F9).

Sl. NO.	Formulation	Angle of repose* (degree)
1.	F1	25° 16'
2.	F2	23° 54'
3.	F3	24° 70'
4.	F4	26° 59'
5.	F5	24° 89'
6.	F6	22° 65'
7.	F7	23° 73'
8.	F8	28° 20'
9.	F9	28°39'

*The values represents mean, n=3

Tablet properties :

The values of thickness, hardness, friability, disintegration time, weight variation and drug content uniformity of formulations F1 to F9 are shown in Table 9(a) and Table 9(b).

Table 6. Results of tablet properties of formulations (F1-F9).

Formulation	Thickness* (mm)	Hardness* (Kg/cm^2)	Friability(%)	Disintegration time*(sec)
F1	3.13±0.01	3.17±0.30	0.44	120.40±0.469
F2	3.18±0.03	3.12±0.34	0.63	85.27±0.782
F3	3.17±0.01	3.53±0.25	0.75	50.40±0.369
F4	2.98±0.01	3.14±0.20	0.32	110.52±0.469
F5	3.13±0.01	3.23±0.15	0.42	75.85±0.813
F6	3.15±0.03	3.36±0.12	0.54	40.91±0.671
F7	2.88±0.03	3.23±0.27	0.73	70.66±0.125
F8	3.02±0.07	3.26±0.19	0.66	40.96±0.0145
F9	2.97±0.02	3.45±0.22	0.51	28.67±0.160

*Average of 3 readings □ SD

Table 7. Results of tablet properties of formulations (F1-F9).

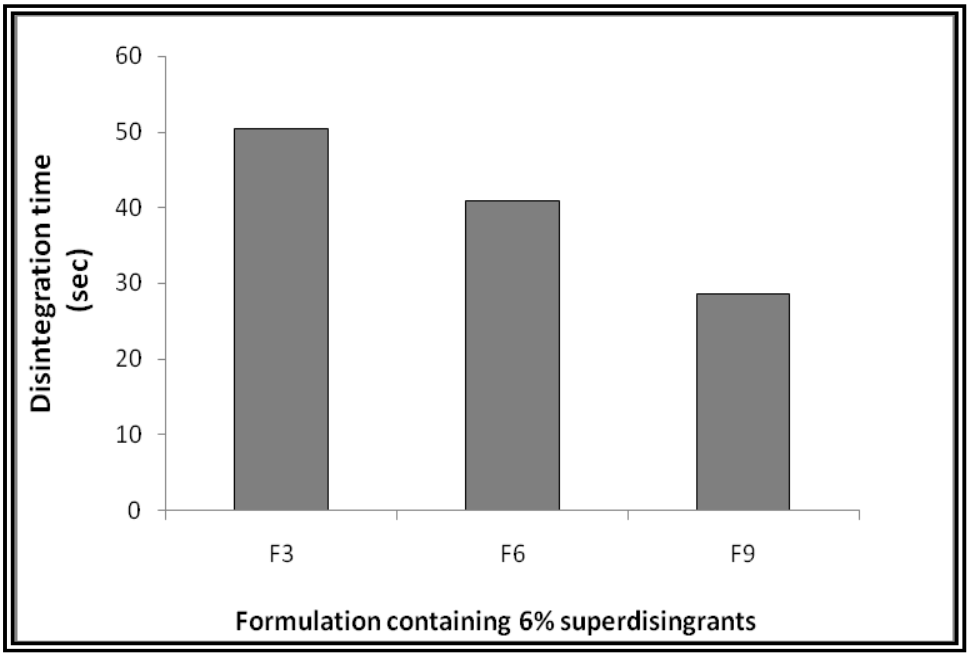
Formulation	Wt. variation	Wetting time*(sec)	Drug content uniformity*
F1	PASS	68.88±2.045	84.50±0.008
F2	PASS	66.55±1.002	84.38±0.015
F3	PASS	60.79±1.712	84.60±0.007
F4	PASS	70.69±0.560	85.00±0.041
F5	PASS	68.17±0.850	84.80±0.006
F6	PASS	65.66±0.995	84.93±0.020
F7	PASS	62.42±1.100	84.63±0.014
F8	PASS	58.28±1.564	85.05±0.005
F9	PASS	55.87±1.014	85.20±0.011

* The values represent mean ± SD, n = 3

Table 8. Effects of 6% Superdisintegrants on Disintegration time of tabletsprepared by direct compression (F3, F6 and F9).

Formulation	Superdisintegrants & its concentration	Disintegration time*(sec)
F3	6% CRP	50.40±0.369
F6	6% CCS	40.91±0.671
F9	6% SSG	28.67±0.160

Fig.7. Comparative graph showing Effects of 6% Superdisintegrants on Disintegration time of tablets prepared by direct compression (F3, F6 and F9).



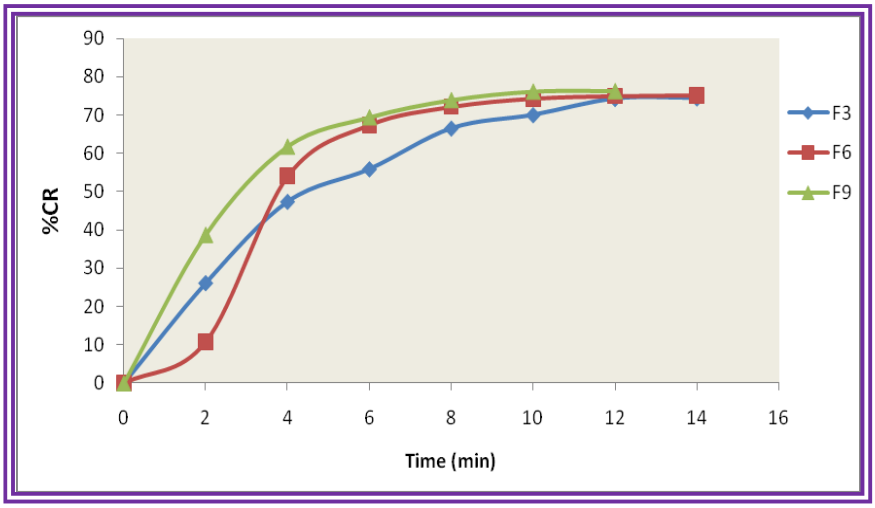
***In-vitro* Dissolution Study.**

Table 9. *In-vitro* dissolution data of F3, F6 and F9.

Time (min)	% CDR*		
	F3	F6	F9
0	0.00±0.00	0.00±0.00	0.00±0.00
2	26.16±1.50	10.86±0.48	38.70±0.48
4	47.39±0.55	54.06±1.9	61.68±0.45
6	55.89±0.70	67.37±1.3	69.29±1.27
8	66.51±1.01	72.10±0.20	73.78±0.31
10	70.01±1.75	74.25±0.05	76.00±0.13
12	74.25±1.04	74.89±1.01	76.14±0.22

* The values represents mean±SD, n = 2

Fig.8. *In-vitro* dissolution profile of F3, F6 and F9.



SUBLIMATION TECHNIQUE

(a) Pre-compression Parameters:

The blend was evaluated for poured density, tapped density, Carr's index, Hausner ratio and angle of repose of formulation F10 and F11 are shown in Table

Table 10. Results of pre-compression properties of formulations (F10-F11).

Formulation	Poured Density* (gm/ml^3)	Tapped density* (gm/ml^3)	Carr's index(%)	Hausner ratio (%)
F10	0.532	0.663	19.76	1.25
F11	0.530	0.653	18.84	1.23

Table 11. Results of pre-compression properties of formulations (F10-F11).

Sl. NO.	Formulation	Angle of repose* (degree)
1.	F10	27°31'
2.	F11	26°28'

*The values represent mean, n=3

Tablet properties:

The values of thickness, hardness, friability, disintegration time, weight variation and drug content uniformity of formulations F10 and F11 are shown in Table.

Table 12. Results of tablet properties of formulations (F10-F11).

Formulation	Thickness*(mm)	Hardness*(Kg/cm^2)	Friability (%)	Disintegrationtime* (sec)
F10	3.16±0.02	3.13±0.29	0.83	25.32±0.258
F11	3.18±0.01	3.10±0.23	0.48	26.12±0.215

*Average of 3 readings □ SD

Table 13. Results of tablet properties of formulations (F10-F11).

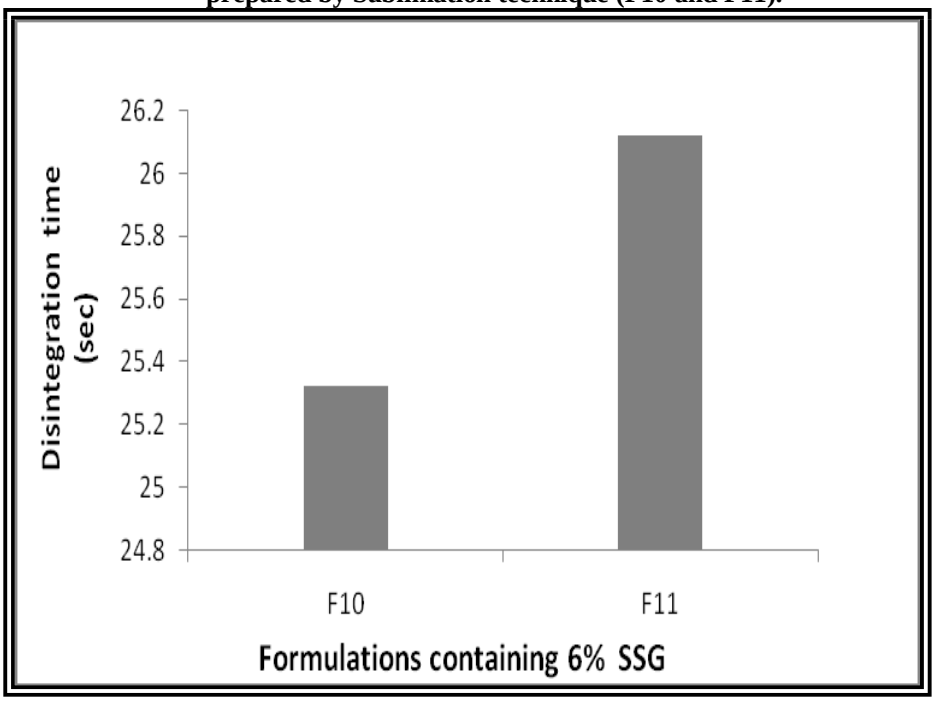
Formulation	Wt. variation	Wetting time* (sec)	Drug content uniformity*
F10	PASS	40.74±1.001	86.00±0.008
F11	PASS	50.88±2.045	84.59±0.009

* The values represent means, n = 3

Table 14. Effects of 6% Superdisintegrants on Disintegration time of tabletsprepared by sublimation technique (F10 and F11).

Formulation	Superdisintegrants & its concentration	Disintegration time*(sec)
F10	6% SSG	25.32±0.258
F11	6% SSG	26.12±0.215

Fig.9. Comparative graph showing Effects of 6% Superdisintegrants on Disintegration time of tablets prepared by Sublimation technique (F10 and F11).



***In-vitro* Dissolution Study:**

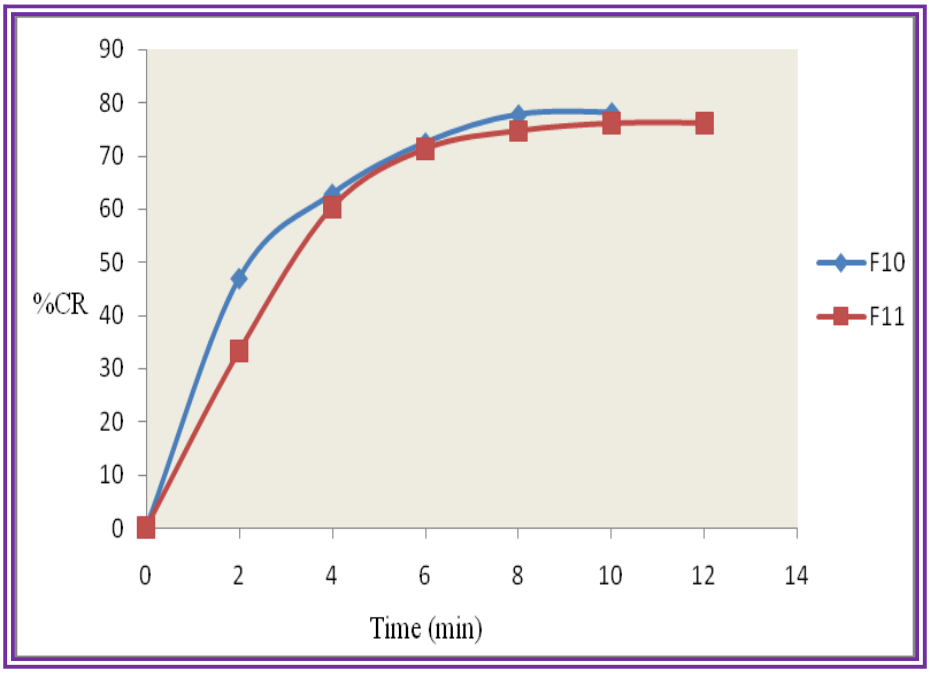
In-vitro dissolution data of the tablet formulations (F10 and F11) are shown inTable. *In-vitro* dissolution profiles are represented in fig.

Table 15. *In-vitro* dissolution data of F10 and F11.

Time (min)	%CDR	
	F10	F11
0	0.00±0.00	0.00±0.00
2	46.95±0.98	33.25±2.77
4	62.81±0.63	59.17±1.62
6	72.45±1.54	71.08±0.28
8	77.74±0.07	74.46±0.28
10	78.11±0.16	75.05±0.21

* The values represents mean±SD, n = 2

Fig.10. *In-vitro* dissolution profile of F10 and F11.



COMPARISON OF THE VARIOUS TECHNIQUES:

COMPARISON OF TABLET PROPERTY OF FORMULATION F9 AND F10.

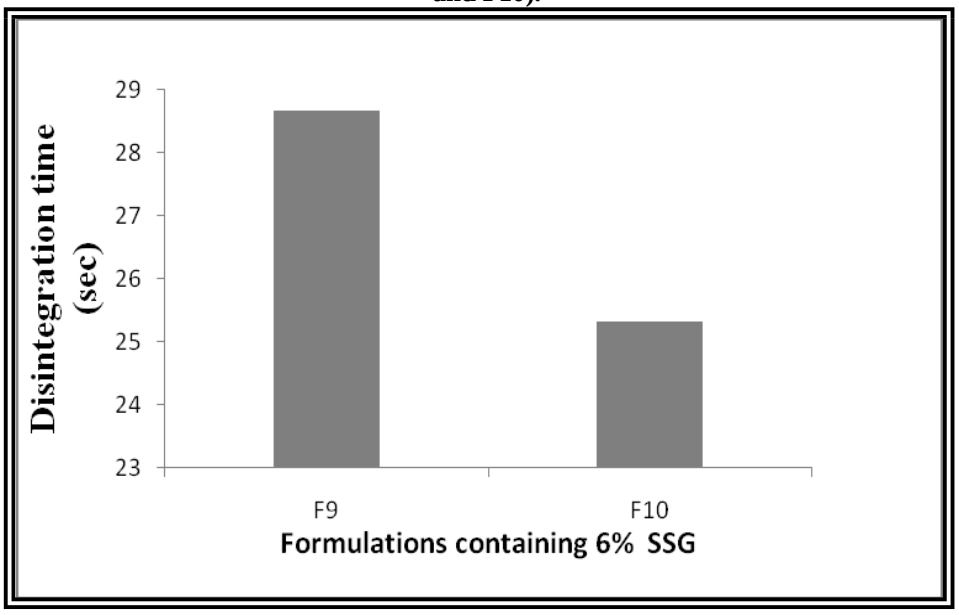
The value of disintegration time, wetting time, hardness, friability of formulationsF9 and F10 are shown in Table.

Table 16. Results of tablets properties of formulations (F9 and F10).

Formulation	Disintegration time* (sec)	Wetting time*(sec)	Hardness* (kg/cm^2)	Friability (%)
F9	28.67±0.160	21.87±1.014	3.45±0.22	0.51
F10	25.32±0.258	27.74±1.001	3.13±0.29	0.83

*Average of 3 readings ± SD

Fig.11. Comparative graph showing Effects of 6% Superdisintegrants onDisintegration time of tablets (F9 and F10).



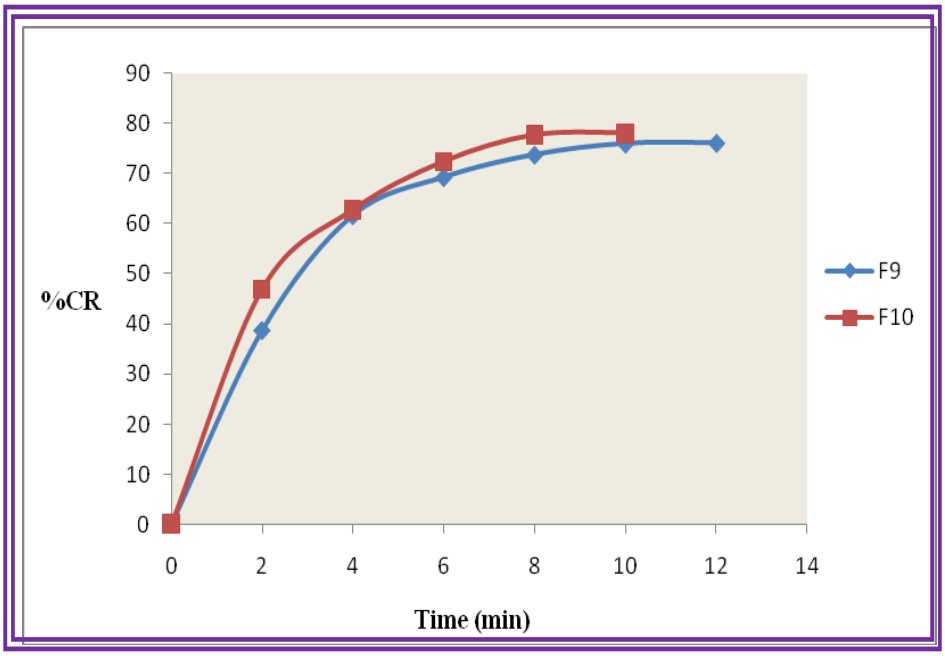
COMPARISON OF *IN-VIRO* DISSOLUTION STUDY OF FORMULATIONS(F9 AND F10).

In-vitro dissolution data of the tablet formulations (F9 and F10) are shown intable. In-vitro dissolution profiles are represented in Fig.

Table 17. *In-vitro* dissolution profile of F9 and F10.

Time (min)	%CDR	
	F9	F10
0	0.00±0.00	0.00±0.00
2	38.70±0.48	46.95±0.98
4	61.68±0.42	62.81±0.63
6	69.29±1.27	72.45±1.54
8	73.78±0.31	77.74±0.07
10	76.00±0.13	78.11±0.16

Fig.12. *In-vitro* dissolution profile of F9 and F10.



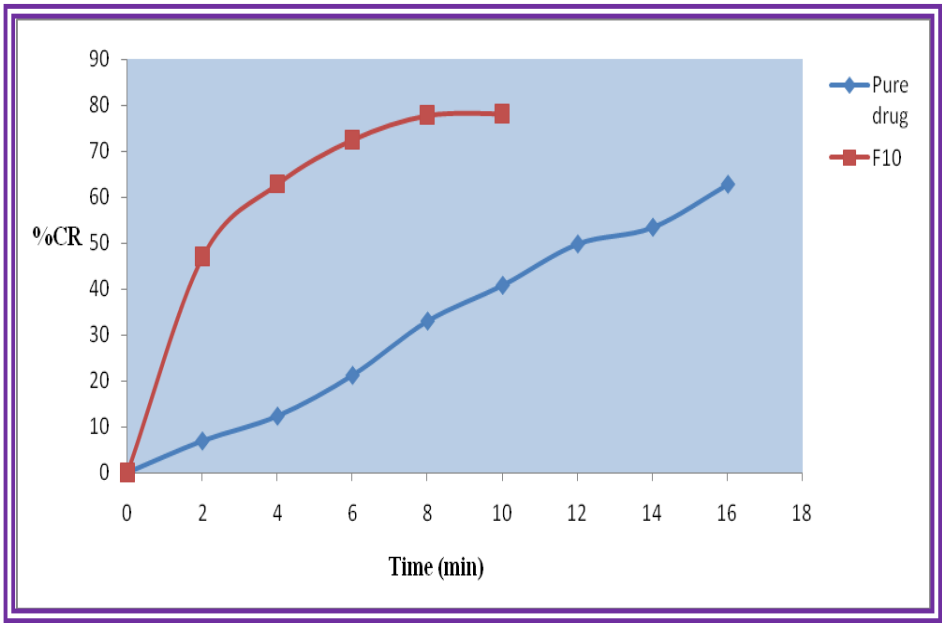
COMPARISION OF *IN-VITRO* DISSOLUTION STUDY OF PURE DRUG WITH OPTIMIZED FORMULATION (F10) PREPARED BY SUBLIMATION TECHNIQUE.

In-vitro dissolution data of pure drug and F10 are shown in Table-18. *In-vitro* dissolution profiles are represented in Fig.

Table 18. *In-vitro* dissolution profile of pure drug and F10.

Time (min)	%CDR	
	Pure Drug	F10
0	0.00±0.00	0.00±0.00
2	6.92±0.75	46.95±0.98
4	12.35±0.34	62.81±0.63
6	21.24±0.54	72.45±1.54
8	33.06±1.21	77.74±0.07
10	40.86±0.16	78.11±0.16

Fig.13. *In-vitro* dissolution profile of pure drug and F10.



RELEASE KINETICS:

The *in –vitro* release data was fitted into various kinetic models. The zero order plot, first order plot, Higuchi plot & Korsmeyer & Peppas plot were shown in Figure. The regression values & slope values of various models were given in Table.

Fig.14. Zero order plot of optimized formulation.

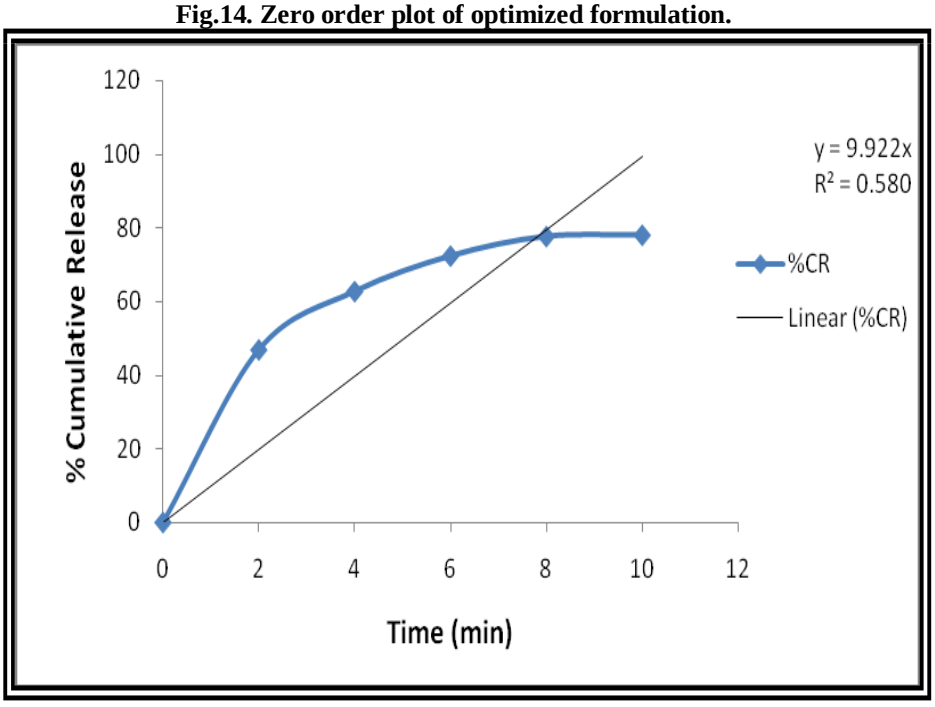


Fig.15. First order plot of optimized formulation.

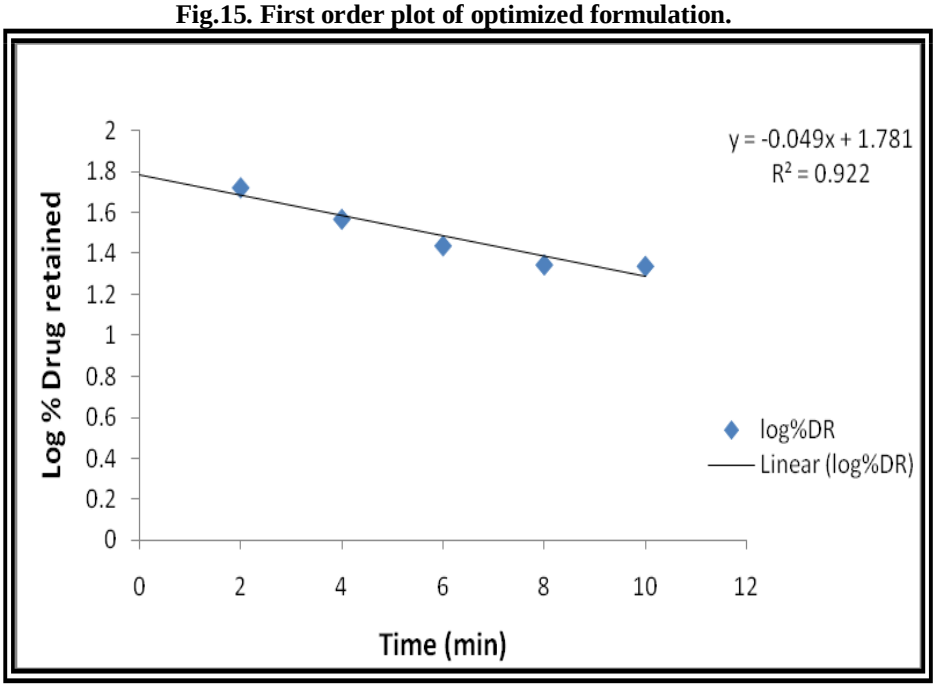


Fig.16. Higuchi plot of optimized formulation.

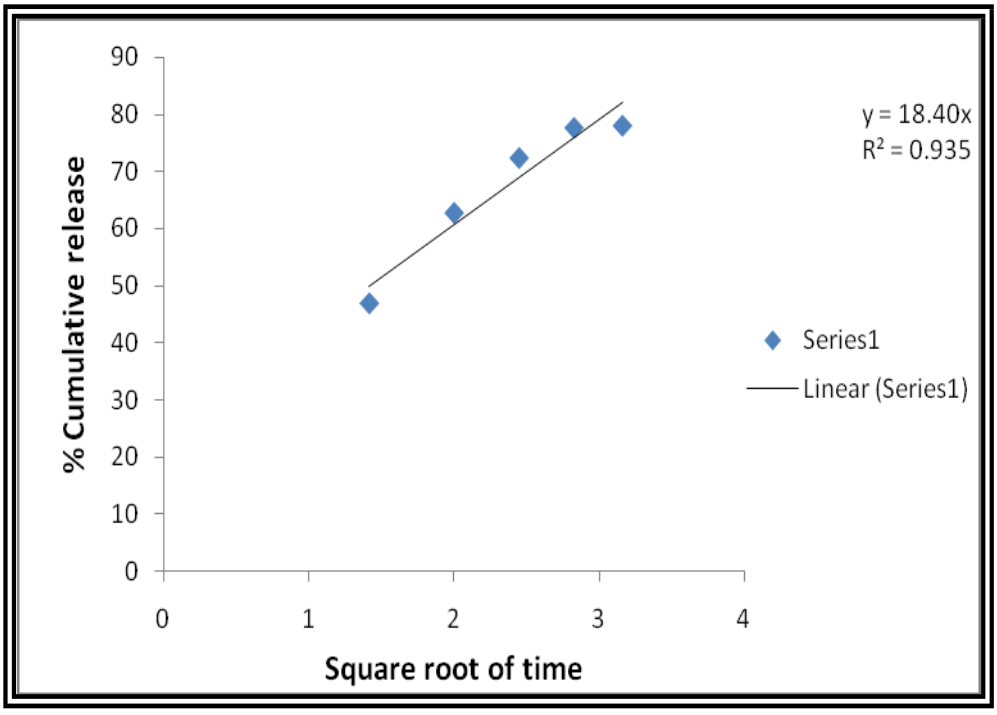


Fig.17. Korsemeyer-Peppas Plot of optimized formulation.

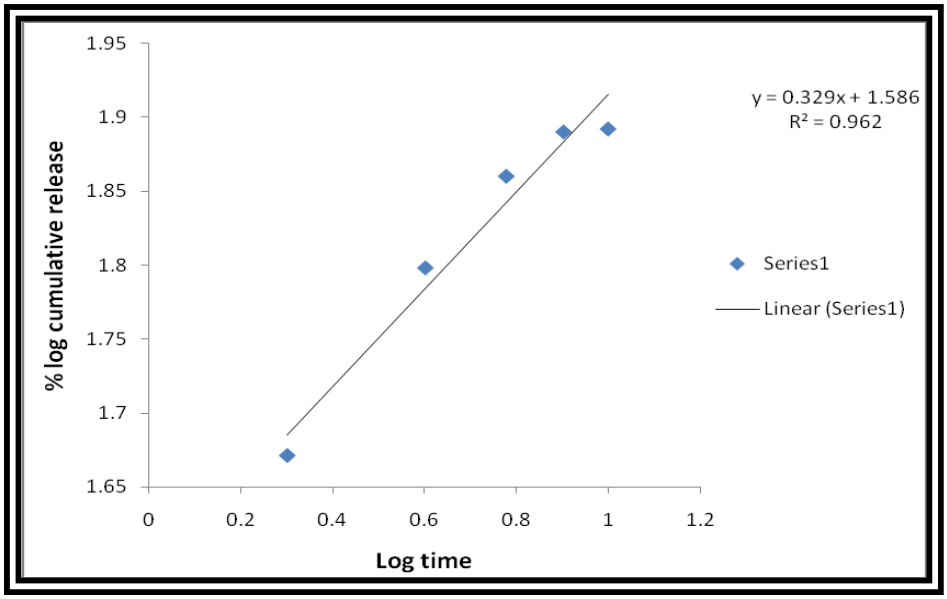


Table 18. Regression Coefficient and Slope values for various kinematic models.

	Zero Order	First Order	Higuchi	Korsmeyer-Peppas
R^2	0.580	0.922	0.935	0.962
Slope	9.922	-0.049	18.40	0.329

DISCUSSION:

UV SPECTROMETRIC METHOD FOR DILTIAZEM HYDROCHLORIDE:

Diltiazem Hydrochloride was scanned in the UV wavelength region of 250- 350nm for maximum absorption (λ_{max}) and the λ_{max} was found to be at 237nm that was same as reported value. Standard curve of the drug prepared in phosphate buffer pH 6.8 showed a linear relationship between the concentration and absorbance values in therange of 2 – 12 g/ml. R^2 value was found to be 0.998.

DRUG EXCIPIENT INTERACTION STUDY:

The infrared spectrum of Diltiazem Hydrochloride and Diltiazem Hydrochloride with other excipients indicated that there was no chemical interaction found between Diltiazem Hydrochloride and other excipients.

CHARACTERIZATION OF DILTIAZEM HYDROCHLORIDE:

The infrared spectra of Diltiazem Hydrochloride and Diltiazem hydrochloride with excipients were recorded using a FT-IR spectrophotometer to check for possible drug-excipients interaction were shown in Fig.respectively. Distinct peak inthe region 2960-2850cm^{-1} for C-H aliphatic, C-H aromatic stretching between 3058- 3004cm^{-1}, 1650-1000cm^{-1} for C-N amine and C=O stretching between 1650-1900cm^{-1} of the physical mixture was identical to that of pure drug which confirm the compatibility ofthe drug and excipients.The DSC thermogram of Diltiazem hydrochloride displayed the characteristics peak at 217˚C compared to its melting point 212˚C. The DSC of formulation F10 showed the thermogram at 157˚C which reveals that drug is complexed with excipients. There was a shift in melting point because of the moisture content and excipients used in the formulation(F10) prepared by sublimation technique.

FORMULATION OF FAST DISSOLVING TABLETS:

The present work was to formulate Fast disintegration tablets of Diltiazem Hydrochloride using various techniques.

The preliminary trials were conducted using 2-6% superdisintegrants (CRP, CCS and SSG). Nine batches (F1 to F9) were prepared using various super disintegrants to formulate the fast dissolving tablets by direct compression method which is reported to be simple and cost effective.

In the next approach the tablets were formulated by sublimation technique using 5% camphor and ammonium bicarbonate as subliming agent. On the basis of result obtained in the preliminary screening studies, the batch containing 6% SSG (F9) prepared from direct compression method showed fastest disintegration. Hence, it was selected for further studies. Sublimation technique is reported to yield porous tablets with low disintegration time and hence this technique was also used in present study.

EVALUATION OF PRE-COMPRESSION PROPERTIES:

The flow properties of the granules (F1-F11) were evaluated by determining theCarr's index, Hausner ratio and angle of repose. Poured density values of different batches were found to range between 0.518 and 0.585gm/ml^3, whereas tapped density values were found to vary from 0.641 to 0.668gm/ml^3. Carr's index, Hausner ratio and angle of repose were range between 18.24 to 20.30, 1.22 to 1.25, and 21°40' to 29°66' respectively, which indicates that granules prepared exhibit good flow properties.

EVALUATION OF TABLET PROPERTIES:

Tablets (F1-F11) were evaluated for tablet properties like thickness, hardness, friability, disintegration time, weight variation, wetting time and drug content uniformity.Tablet thickness was found to range from 2.88±0.03 to 3.18±0.03 mm. Tablets of all the batches were found out to exhibit sufficient hardness, which ranged from 3.10±0.23 to 4.00±0.13 Kg/cm^2. Wetting time of the tablet was found to be in the range of 40.74±1.001 sec to 70.69±0.560 sec. Friability, weight variation test and percentage drug content uniformity met the specification given in the literature. Disintegration time of formulations (F1 to F9) prepared by direct compression method was found to be in the range 28.67±0.160 sec to 135.40±0.469 sec. Increase inthe concentration of superdisintegrants from 2% to 6%, decreases the disintegration time of the tablets. Among the three superdisintegrants used, rapid disintegration was seen in formulation containing SSG. Increase in the concentration of was found to be beneficial in reducing the disintegration time. *In vitro* dissolution study of formulation of F9, (which gave least disintegration time of 28.67±0.160 sec) showed a cumulative release of 76.005±0.134 after 10min. Least disintegration time of 28.67±0.160 sec was obtained with 6% SSG in tablets prepared by direct compression method. This method was found to give a low disintegration time and a good release after 10min.

Disintegration time of formulations (F10 and F11) prepared by sublimation technique was found to be in the range 25.32±0.258 sec to 26.12±0.215 sec. *In vitro* dissolution study of formulation of F10 (which gave least disintegration time of 25.32±0.258 sec) showed a cumulative release of 78.115 ± 0.162 after 10 min. Least disintegration time of 25.32±0.258 sec was obtained with 5% camphor as a subliming agent using 6%SSG in tablets prepared by sublimation technique. The sublimation technique was thus found to give a low disintegration time and a good release after 10min. The various techniques used for fast dissolving tablets of Diltiazem Hydrochloride were compared. It was found that sublimation technique were beneficial in obtaining the low disintegration time (25.32 sec) and increased cumulative released after 10min as compared to direct compression method as shown in Tabler. In sublimation the use of camphor was found to be better than using ammonium bicarbonate as the formulation F10 shown DT of 25.32±0.258 sec compared to DT of F11 which gave DT of 26.12±0.215 sec. Direct compression method was not found to be helpful in getting the product with reduced disintegration time. The techniquethus has to be optimized to get more porous product. The sublimation technique though beneficial, involves an additional step of adding a volatile subliming agent and at a subliming it constant temperature. This could be considered as one of the drawbacks of the technique compared to direct compression technique. The porous structure is responsible for faster water uptake, so it facilitates the action of SSG in bringing about faster disintegration. Formulation F10 prepared by sublimation technique were compared with pure drug. It was found that the formulated fast disintegration tablets showed an increase in % CR of 78.115±0.162 after 10min compared to the pure drug which was found to be 40.86±1 respectively.

To know the order of release, the release rates were subjected to kinetic studies. The co-relation coefficient values obtained for all four models are

tabulated in Table. The R^2 value of Korsmeyer Peppas release as well as R^2 value of formulation F10 was near to one. Formulation F10 followed Higuchi and Fickian Diffusion as 'n' value was found to be 0.935 and 0.962 respectively.

CONCLUSION:

From the present work, it can be concluded that among the various techniques used, sublimation technique is best suitable in the preparation of Fast disintegration tablets of low dose drug like Diltiazem hydrochloride. Use of 5%w/w camphor as a subliming agent was further found to be beneficial in obtaining a product with reduced disintegration time and increased % cumulative release. It can thus be concluded that FDTs with less disintegration time can be prepared by sublimation technique using SSG in concentration of 6%. Formulations needs to be further evaluated for physical and chemical stability under accelerated conditions and on storage at room temperature. However, stability studies could not be performed in the present work due to time constraints.

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