

**Original Article**

**FORMULATION AND *IN VITRO* EVALUATION OF FAST DISSOLVING TABLET OF VERAPAMIL HYDROCHLORIDE**

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**ABSTRACT**

**Objective:** The main objective of this research work was to formulate and evaluate fast dissolving tablet of verapamil hydrochloride for the treatment of hypertension.

**Methods:** In this study, fast dissolving tablet were prepared by wet granulation method by using croscarmellose sodium and sodium starch glycolate as superdisintegrants in the concentration of 2%, 4%, and 6%. Polyvinyl pyrrolidone K30 is used as a binder. The designed tablets were subjected to various assessment parameters like friability test, hardness test, disintegration test, wetting time, *in vitro* drug release and drug content.

**Results:** All the prepared formulations were subjected to various assessment parameters, and the findings obtain within the prescribed limit. The calibration curve of pure drug using various solvents like distilled water, phosphate buffer pH 6.8 was plotted. F1-F9 containing croscarmellose sodium and sodium starch glycolate in various concentration demonstrate the minimum disintegration time. Among all these formulations F8 shows disintegration time upto  $19 \pm 0.06$  seconds due to the high concentration of superdisintegrants. *In vitro* drug release was tested in phosphate buffer pH 6.8 at a time interval of 0, 1, 3, 6, 9, 12, 15 min. The F8 shows drug release  $98.5 \pm 0.567\%$ . Accelerated stability study of optimized formulation (F8) up to 2 mo showed there was no change in disintegration time and percentage drug release.

**Conclusion:** The results obtained in the research work clearly showed a promising potential of fast dissolving tablets containing a specific ratio of croscarmellose sodium and sodium starch glycolate as superdisintegrants for the effective treatment of hypertension.

**Keywords:** Fast dissolving tablet, Verapamil hydrochloride, Superdisintegrants, Bioavailability, Calcium channel blocker

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**INTRODUCTION**

Oral drug delivery remains the preferred route for administration of various drugs. Solid dosage forms are popular because of ease of administration, accurate dosage, self-medication, pain evasion and most importantly the patient compliance. Tablets and capsules are the most popular dosage forms. But one important drawback of such dosage forms is dysphagia or difficulty in swallowing. To solve the above-mentioned problem, pharmaceutical technologists have put in their best efforts to develop a fast dissolving drug delivery, i.e. mouth dissolving tablet that disintegrates and dissolves rapidly in the saliva, within a few seconds without the need of drinking water or chewing. Such formulations provide an opportunity for product line extension in the many elderly persons will have difficulties in taking conventional oral dosage forms (viz., solutions, suspensions, tablets, and capsules) because of hand tremors and dysphagia. Other groups that may experience problems using conventional oral dosage forms include the mentally ill, the developmentally disabled and patients who are uncooperative, on reduced liquid-intake plans, or are nauseated. The technologies utilized for fabrication of fast dissolving tablet include lyophilization, molding, direct compression, cotton candy process, spray drying, sublimation, mass extrusion, nanonization, and quick dissolve film formation.

In case of geriatric and pediatric patients, there is a problem of dysphasia i.e. difficulty in swallowing. The oral bioavailability of verapamil hydrochloride is 35% due to first pass metabolism; therefore the bioavailability of the drug is increased by formulating fast-dissolving drug delivery system. Bioavailability is increased due to absorption from mouth to pharynx and pharynx to the esophagus. Thus, in the present investigation, it was planned to formulate and evaluate fast dissolving tablet of verapamil hydrochloride [1-11].

**MATERIALS AND METHODS**

**Materials**

Verapamil hydrochloride procured from Swapnroop drug agency, Aurangabad. All the other reagents used were of analytical grade.

**Methods**

**Determination of  $\lambda$  max of verapamil hydrochloride**

The UV spectrum of verapamil hydrochloride was obtained by using a UV-visible spectrometer (UV 3000). Accurately weigh 10 mg of the drug was added to 100 ml of volumetric flask. Volume was made up to 100 ml with water (100  $\mu$ g/ml). This solution was used as a stock solution. From the stock solution, 1 ml of aliquots was withdrawn, and the volume was made up to 10 ml using water to obtain the concentration of 10  $\mu$ g/ml. The resultant solution was scanned from 400 to 200 nm, and the spectrum was recorded to obtain the value of the maximum wavelength in respective solvents [12].

**Drug excipients compatibility study**

**Infrared spectrum**

The infrared (IR) spectrum of verapamil hydrochloride was recorded with potassium bromide (KBr) discover the wave number of 4000 to 400  $\text{cm}^{-1}$  by using fourier transform infrared spectrophotometer (FTIR) [13].

**Formulation of fast dissolving tablets**

Weighed a required quantity of all powdered material and mixed properly. Then granules were prepared by the addition of binder solution in the powdered material until dump mass is get formed. These dump mass is screened properly to obtain pellets or granules. After drying milling of the dried mass and then mixed with other ingredients like lubricant or gliadant.

**Formulation optimization**

A  $3^2$  factorial design was applied to a formulation that shows the satisfactory results to see the effect of varying concentration of independent variables croscarmellose sodium ( $X_1$ ), sodium starch glycolate ( $X_2$ ) on dependent variables like disintegration time and cumulative drug release [14].

Table 1: Independent variables

Independent variables	Levels		
	Lower (-1)	Middle (0)	Upper (+1)
crosscarmellose sodium	3	6	9
sodium starch glycolate	3	6	9

Table 2: Composition of fast dissolving tablet of verapamil hydrochloride

S. No.	Excipients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	verapamil hydrochloride	20	20	20	20	20	20	20	20	20
2	crosscarmellose sodium	3	3	3	6	6	6	9	9	9
3	sodium starch glycolate	3	6	9	3	6	9	3	6	9
4	polyvinyl pyrrolidone K30	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
5	magnesium stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
6	talc	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
7	mannitol	118.5	115.5	112.5	115.5	112.5	109.5	112.5	109.5	106.5
8	total weight	150	150	150	150	150	150	150	150	150

## Evaluation

### Precompression parameters

#### Angle of repose ( $\theta$ )

Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and horizontal plane. The frictional force in loose powder or granules can be measured by the angle of repose [1, 15].

$$\tan \theta = \frac{h}{r}$$

$$\theta = \tan^{-1} (h/r)$$

Where  $\theta$  is the angle of repose

h is the height of pile

r is the radius of the base of the pile

#### Bulk density

A quantity of accurately weighed drug excipient powder blend from each formula, previously shaken to break any agglomerates formed was introduced into a 25 ml measuring cylinder, and the initial volume was noted and bulk density calculated by following formula [15]:

$$\text{Bulk density} = \frac{\text{weight of powder}}{\text{volume of packing}}$$

#### Tapped density

After the initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2 Sec intervals. The taping was continued until no further change in volume was noted [15].

$$\text{Tapped density} = \frac{\text{Weight of powder}}{\text{Tapped volume of packing}}$$

#### Hausner's ratio:

Hausner's ratio is an indirect index of ease of powder flow [15].

$$\text{Hausner's ratio} = \frac{\rho_t}{\rho_d}$$

Where  $\rho_t$  is tapped density and  $\rho_d$  is bulk density.

#### Carr's compressibility index

The compressibility index of the granules was determined by the Carr's compressibility index. (%) Carr's Index can be calculated by using the following formula [15].

$$\text{carr's index} = \frac{\text{tapped density} - \text{bulk density}}{\text{tapped density}} * 100$$

### Post compressional parameters of all tablet formulations

#### Hardness test

Tablets require a certain amount of strength, or hardness and resistance to friability, to withstand mechanical shocks of handling during manufacture, packaging, and shipping. The hardness of the tablets was determined using digital hardness tester. It is expressed in Kg/cm<sup>2</sup>. Three tablets were randomly picked from each formulation, and the mean and standard deviation values were calculated. Average of triplicate is taken [15, 16].

#### Friability test

It is the phenomenon whereby tablet surfaces are damaged and/or show evidence of lamination or breakage when subjected to mechanical shock or attrition.

The friability of tablets was determined by using electro lab, USP EF 2 friabilator. It is expressed in percentage (%). Ten tablets were initially weighed ( $W_{\text{initial}}$ ) and transferred into friabilator. The friabilator was operated at 25 RPM for 4 min. The tablets were weighed again ( $W_{\text{final}}$ ). The percentage friability was then calculated by,

$$F = \frac{W_{\text{initial}} - W_{\text{final}}}{W_{\text{initial}}} \times 100$$

% Friability of tablets less than 1% is considered acceptable. Average of triplicate is taken [16, 17].

#### Weight variation test

The 20 tablets were selected randomly from each formulation and weighed individually to check for weight variation. The Indian pharmacopoeia allows a little variation in the weight of a tablet. Average weight was calculated, and the standard deviation was computed. Average of 20 readings is taken [15, 16].

#### Uniformity of thickness

The thickness of individual tablet may be measured with a digital vernier calliper, which permits accurate measurements and provides information on the variation between tablets. Averages of triplicate readings were taken [15].

#### Disintegration test

The process of breakdown of a tablet into smaller particles is called as disintegration. The disintegration test was carried out on 6 tablets of each formulation by using USP disintegration apparatus in distilled water at 37±2 °C and the time in second is taken for complete disintegration of the tablet with no palatable mass remained in the apparatus was noted. Averages of six readings were taken [1].

#### Wetting time

A piece of tissue paper folded twice was placed in a petri dish containing pH 6.8 phosphate buffer. A tablet was placed on paper

and time taken for complete wetting is noted. Averages of triplicate readings were taken [18].

#### Drug content uniformity

Randomly ten tablets from each batch were weighed accurately and powdered; the equivalent weight of 100 mg of verapamil hydrochloride was taken and made the volume up to 100 ml with phosphate buffer pH 6.8 in 100 ml volumetric flask and kept aside with constant shaking for 24 h to extract the total drug present in the tablet. Then the solution was filtered, and the volume was made with phosphate buffer pH 6.8 and analyzed for drug content at  $\lambda_{\text{max}}$  of 278 nm. Averages of triplicate were taken [19].

#### In vitro drug release

Release of the drug *in vitro*, was determined by estimating the dissolution profile, USP 2 paddle apparatus was used and the paddle

was allowed to rotate at 50 rpm, phosphate buffer (pH 6.8) (900 ml) was used as a dissolution medium. At specific time intervals of 0, 1,3,9,12,15 min 5 ml of samples were withdrawn and measured the absorbance at 278 nm after suitable dilution with pH 6.8 phosphate buffer. Average of three readings was taken [20-23].

#### Stability study

Stability study was conducted as per ICH guidelines  $40^{\circ}\text{C}\pm 2^{\circ}\text{C}$ ,  $75\%\pm 2\%$  RH to test the chemical and physical stability of fast dissolving tablets for the period of 2 mo [24].

### RESULTS AND DISCUSSION

#### Determination of $\lambda_{\text{max}}$ of verapamil hydrochloride

$\lambda_{\text{max}}$  of verapamil hydrochloride was determined in water. The calibration curve of verapamil hydrochloride shown linearity as per Beers Lambert's law at 278 nm represented in fig. 1.

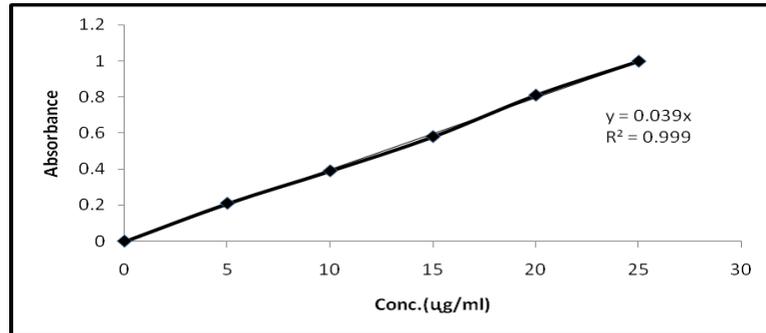


Fig. 1: Calibration curve of verapamil hydrochloride in water

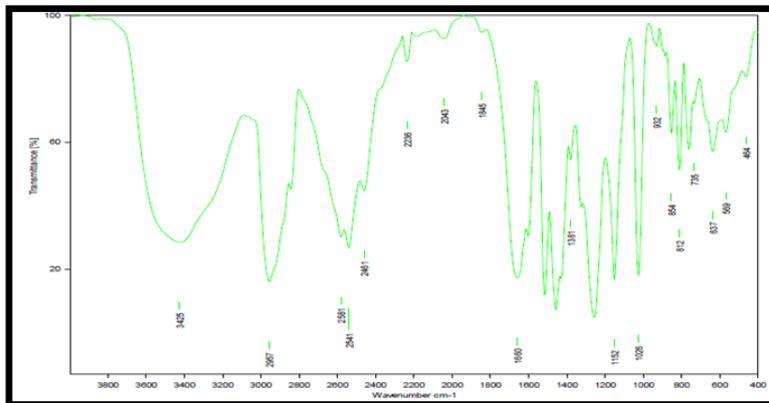


Fig. 2: Drug+crosscarmellose sodium

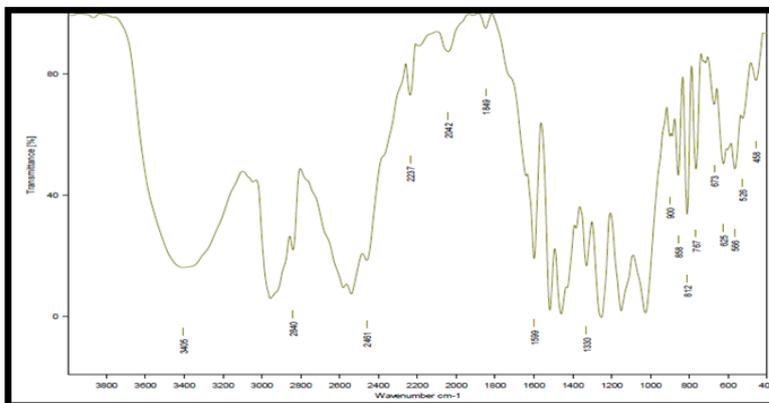


Fig. 3: Drug+sodium starch glycolate

**Drug excipients compatibility study****IR spectrometer study**

The IR spectra of verapamil hydrochloride, polymers, and physical mixture are shown in figures. The IR absorption bands observed in the IR spectrum of drug and polymers resembles with that of found in physical mixture proves compatibility of the drug with polymers. In fig. 2 absorption spectrum of drug and crosscarmellose sodium and in fig. 3 absorption spectrum of drug and sodium starch glycolate.

**Precompression evaluation parameters of powder****Angle of repose**

The angle of repose is an inactive parameter of powder flow ability from the hopper to die cavity. An angle of repose between 25° to 30° indicates excellent flowability of the powder bed. In this work, the

angle of repose was found to be varying between 22.56°-31.68° when glidants were incorporated. These studies indicated that the powder beds of all formulations are easily flow able. All the precompressional parameters were found to be within the acceptable limit.

**Bulk density**

Bulk density was found in the range of 0.26±0.17 to 0.52±0.135 g/ml.

**Tapped density**

Tapped density was found to be in the range of 0.28±0.1858 to 0.59±0.207 g/ml.

**Percentage compressibility index**

Compressibility index was found to be in the range of 11.56 % to 14.73 %. All formulations showed good flow properties which are given in table 3.

**Table 3: Precompression parameters for fast dissolving tablets of F1 to F9**

Formulation code	*Angle of repose (°)	*Bulk density (g/ml)	*Tapped density (g/ml)	Carr's index (%)	Hausner's ratio
F1	31.44±0.14	0.35±0.07	0.39±0.109	10.25	1.11
F2	24.72±0.02	0.39±0.110	0.42±0.098	7.14	1.07
F3	27.58±0.09	0.36±0.096	0.41±0.069	12.19	1.13
F4	25.52±0.43	0.29±0.108	0.32±0.023	9.375	1.10
F5	28.73±0.24	0.52±0.135	0.59±0.207	11.86	1.13
F6	23.85±0.16	0.5±0.160	0.53±0.230	5.6	1.06
F7	30.24±0.04	0.45±0.195	0.48±0.108	8.16	1.08
F8	22.56±0.42	0.26±0.17	0.28±0.1858	7.14	1.07
F9	31.68±0.05	0.33±0.145	0.37±0.138	10.81	1.12

\*All values are mean±SD of three determinations. SD: Standard deviation

**Post-compression evaluation of fast dissolving tablets of verapamil hydrochloride****Hardness**

Hardness of the tablets varied between 2.8±0.11Kg/cm<sup>2</sup> to 3.1±0.25 Kg/cm<sup>2</sup> indicating good binding and satisfactory strength of tablets to withstand stresses during transportation and also may offer good dissolution property.

**% friability**

The % friability was found in the range of 0.50±0.12% to 0.82±0.01%. The weight variation ranges from 149.7±0.44 to 151±1.06 mg which passes the standard.

**Thickness**

The thickness of the tablets was found to be uniform, between 2.68±0.19 mm to 2.84±0.02 mm for (F1 to F9).

**Drug content**

Drug content found in the fast dissolving tablets resembling that of literature value. Range of drug content is 90.8%-99.1%. Therefore

uniformity of content was maintained in all formulations. Drug content of all formulations is listed in table 4.

**Weight variation**

The weight of the formulated tablets of verapamil hydrochloride (F1 to F9) was found to be uniform with low standard deviation values from 149.2±1.25 to 151.3±0.69 mg. The prepared formulations comply with the weight variation test as per IP. The results are given in table 4.

**Wetting time**

It is the time required for complete wetting of tablet. The wetting time was found in the range of 16±0.55 to 25±0.57 sec.

**Disintegration time**

It is the time required for complete disintegration of the tablet. The disintegration time was found in the range of 19±0.06 to 27±0.57 sec.

**% cumulative drug release**

% cumulative drug release was found in the range of 87.12±0.599 to 98.5±0.567 %.

**Table 4: Post compression parameters for fast dissolving tablets of F1 to F9**

Formulation code	Hardness (Kg/cm <sup>2</sup> )* (mean±SD)	Thickness mm (mean±SD)	Friability %* (mean±SD)	Weight variation Mg (mean±SD)	Wetting time* Sec (mean±SD)	Disintegration time (mean±SD) Sec (mean±SD)	Drug content % (mean±SD)
F1	3.3±0.20	2.84±0.02	0.67±0.02	150.9±0.17	25±0.57	27±0.57	90.8±0.92
F2	3.2±0.05	2.8±0.04	0.50±0.12	151±1.06	20±0.23	23±0.53	93.2±0.81
F3	2.9±0.05	2.83±0.08	0.63±0.05	150.1±0.63	22±0.57	26±1.15	95.8±0.50
F4	3.1±0.23	2.82±0.15	0.72±1.35	149.2±1.25	18±1	20±0.28	94.7±0.62
F5	2.9±0.11	2.70±0.07	0.59±0.13	151±0.86	20±0.17	23±0.79	97.2±0.88
F6	3.2±0.15	2.68±0.19	0.82±0.01	149.7±0.44	24±0.28	27±0.55	98.5±0.71
F7	3.1±0.25	2.74±0.21	0.68±0.16	151.3±0.69	18±0.32	21±0.27	97.7±0.87
F8	2.8±0.11	2.77±0.06	0.59±0.10	150±0.73	16±0.55	19±0.06	99.1±0.94
F9	3.3±0.45	2.80±0.26	0.67±0.17	150.1±0.68	19±0.29	23±0.36	98.9±0.79

\*All values are mean±SD of three determinations. [SD: Standard deviation]

% cumulative drug release of the different formulations is shown in Fig.4. In this formulations as the level of croscarmellose sodium and sodium starch glycolate is increased the drug release will also increases. Release of the drug *in vitro*, was

determined by estimating the dissolution profile, USP 2 paddle apparatus was used and the paddle was allowed to rotate at 50 rpm, phosphate buffer (pH 6.8) (900 ml) was used as a dissolution medium.

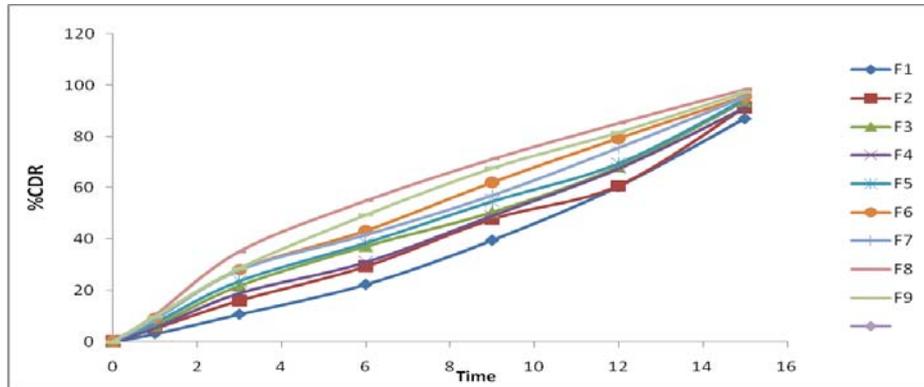


Fig. 4: Cumulative drug release of different formulation

Table 5: Stability study of the optimized formulation

S. No.	Observations	Before stability *(mean±SD)	Stability testing interval days	
			1 mo *(mean±SD)	2 mo *(mean±SD)
1	Visual Appearance	White	White	White
2	disintegration time(sec)	19±0.06	19±0.30	21±0.11
3	drug content	99.1±0.94	99.02±0.499	98.16±0.55

\*All values are mean±SD of three determinations. SD: Standard deviation

**Stability study**

Results of the stability studies showed that there is no change in the physical parameters of the formulation. Drug content of the formulation was also found to be same as that before stability testing. Stability data is shown in table 5.

**Optimization**

The purpose of 3<sup>2</sup> factorial design was to conduct the comprehensive study of the effect of process parameters like croscarmellose sodium (X1) and sodium starch glycolate (X2) and their interactions using a suitable statistical tool (Design expert software version 9.0.2.0) by applying one way ANOVA at 0.05 levels. Mathematical modeling was carried out; the polynomial equation was obtained depending on significant influence among two factors on their experimental design.

The influence of the main effect on responses was further elucidated by response surface methodology. It is a widely used the tool in the development and design of the dosage form. The three-dimensional response surface plot and the corresponding two-dimensional contour plot were generated by software as shown in Fig. 5,6,7 and 8. The response surface plot is very useful for the determination of the main and interaction effects of the independent variables whereas the two-dimensional plot gives a visual representation of values of responses.

In case of *in vitro* drug release, the three-dimensional surface response plot depicted the increase in the drug release and disintegration time as increasing the concentration of superdisintegrants. The two-dimensional contour plot relating X<sub>1</sub>X<sub>2</sub> (interaction between croscarmellose sodium and sodium starch glycolate) was nonlinear indicating interaction between two variables.

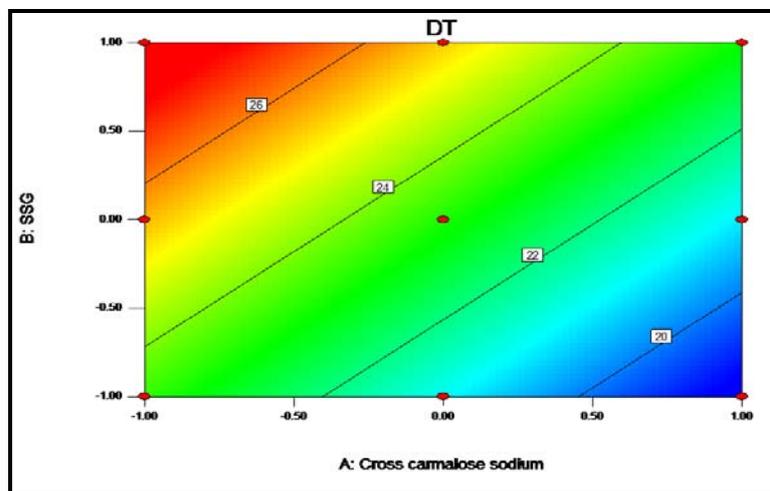


Fig. 5: The counterplot showing the effect of croscarmellose sodium and sodium starch glycolate on disintegration time

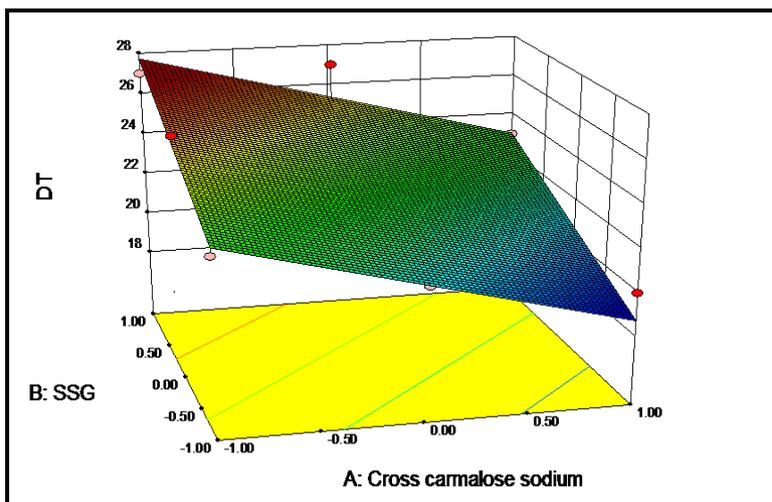


Fig. 6: Surface response plot showing the effect of croscarmellose sodium and sodium starch glycolate on disintegration time

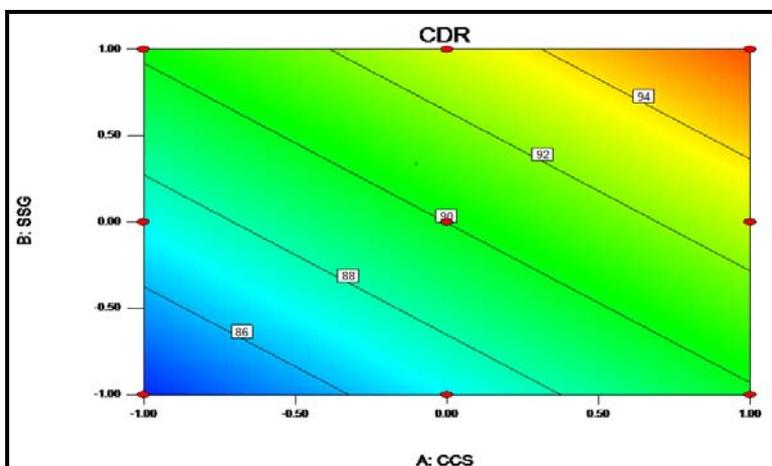


Fig. 7: The counterplot showing the effect of croscarmellose sodium and sodium starch glycolate on % cumulative drug release

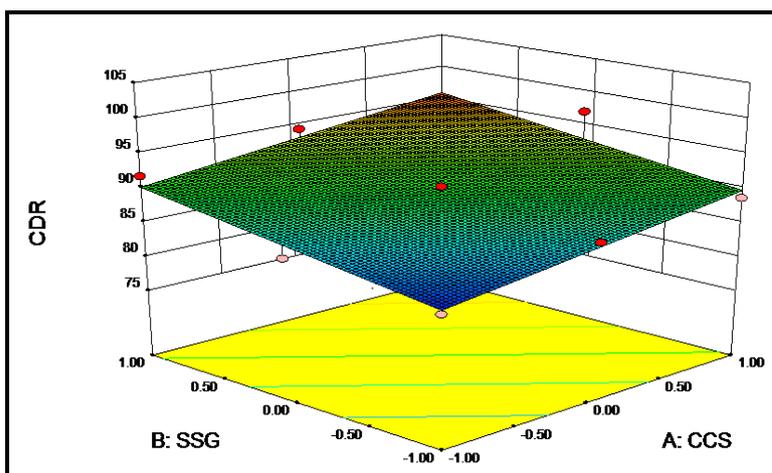


Fig. 8: Surface response plot showing the effect of croscarmellose sodium and sodium starch glycolate on % cumulative drug release

**DISCUSSION**

Prepared formulations were subjected to various assessment parameters and the findings obtained were within the limits which are depicted in table 4. The hardness of all the tablets indicating

good binding and satisfactory strength of tablets to withstand stresses during transportation and may offer good dissolution property. The thickness of the tablets was found to be uniform, and drug content of all formulations shows uniformity in the content of drug in each tablet. All the prepared formulations complies

disintegration and weight variation test as per IP. The F8 formulation containing croscarmellose sodium and sodium starch glycolate in the ratio of (9:6) was selected as optimized formulation on the basis of the result of *in vitro* dissolution test. It is seen that *in vitro* drug release and disintegration increases as an enhancement of the concentration of superdisintegrants like croscarmellose sodium and sodium starch glycolate.

#### CONCLUSION

The current studies are aimed at successful development and optimization of the fast dissolving tablet of verapamil hydrochloride and to enhance the bioavailability of the drug by avoiding first pass effect. Among the prepared batches of tablets based on performance with respect to friability, hardness, uniformity of drug content, disintegration and *in vitro* drug release studies, F8 delivers the best results as compared to other formulations.

Thus, drug release from the fast dissolving tablet was increased by using the increased concentration of superdisintegrants, assisting in faster disintegration in the oral cavity. As the drug having fast disintegration may leads to more drug availability for dissolution, resulting in faster absorption and possibly bioavailability leads to the quick onset of action in the systemic circulation.

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#### AUTHORS CONTRIBUTIONS

Experimental design, guidance, supervision for the research was done by Mr. D. M. Shinkar, Mr. P. D. Kothawade. Support and guidance for the work by Dr. A. D. Maru. Literature review, experimental work, development, optimization of the formulations and interpretation of results was done by Miss. Pooja S. Aher and writing of this manuscript by Mr. D. M. Shinkar. All authors read and approve the final manuscript.

#### CONFLICT OF INTERESTS

All authors have none to declare

#### REFERENCES

- Gandhi A. Mouth dissolving tablet: a new venture in modern formulation tech. *Pharma Innovation* 2012;1:16-21.
- Sastry SV, Nyshadham JR, Fix JA. Recent technological advances in oral drug delivery. A review. *Pharm Sci Technol Today* 2000;3:138-45.
- Habib W, Khankari RK, Hontz J. Fast-dissolve drug delivery systems. *Crit Rev Ther Drug Carrier Sys* 2000;2:61-72.
- Lindgren S, Janzon L. Dysphagia: prevalence of swallowing complaints and clinical finding. *Med Clin North Am* 1993;3-5.
- Sehgal P, Gupta RG, Singh UK, Chaturvedi A, Gulati A, Sharma M. Fast dissolving tablets: a new venture in drug delivery. *Am J Pharm Tech Res* 2012;2:253-79.
- Pahwa R, Gupta N. Orodispersible tablets: superdisintegrants used in an orally disintegrating tablet: a review. *Int J Pharma Sci Res* 2011;2:2767-80.
- Bandari S, Mittapalli R, Gannu R, Rao Y. Orodispersible tablets: an overview. *Asian J Pharm* 2008;2:2-11.
- Hanawa T. New oral dosage form for elderly patients: preparation and characterization of silk fibroin gel. *Chem Pharm Bull* 1995;43:284-28.
- Siddiqui M, Garg G, Sharma P. Fast dissolving tablets: preparation, characterization, and evaluation: an overview. *Int J Pharm Sci Rev Res* 2010;2:87-96.
- Hirani JJ, Rathod DA, Vadhania RK. Orally disintegrating tablets: a review. *Tr J Pharm Res* 2009;8:161-72.
- Sharma N, Sharma J, Jat R, Rathore A. Fast dissolving tablet as a novel dosage form: a review article. In *J of Res and Dev In Pharm and Life Sci* 2012;12:190-4.
- Sharma YR. *Elementary Organic Spectroscopy, Principles, and Chemical Applications*, S. Chand Publication; Reprint; 2016. p. 11-73.
- Chatwal GR, Anand SK. *Instrumental methods of instrumental methods of chemical analysis*. 5<sup>th</sup> Edition. Himalaya Publishing House; 2009. p. 2.49-2.51.
- Banker GS, Rhodes CT. Optimization techniques in pharmaceutical formulation and processing. In: 4<sup>th</sup> Ed. Vol. 121. *Modern Pharmaceutics*. New York; Basal: Marcel Dekkar; 2008. p. 609-10.
- Bele MH. *Pharmaceutics formulation and processing of conventional dosage form*. First Edition. Carrer Publication; 2012. p. 48-55, 128-131.
- Kalia A, Khurana S, Bedi N. Formulation and evaluation of mouth dissolving tablet of oxcabazepine. *Int J Pharm Pharm Sci* 2009;1:12-3.
- Jain C, Naruka P. Formulation and evaluation of fast dissolving tablet of valsartan. *Int J Pharm Pharm Sci* 2009;1:219-26.
- Roy A. Orodispersible tablet: a review. *Asian J Pharm Chem Res* 2016;2:19-26.
- Indian Pharmacopoeia. Government of India Ministry of Health and Family Welfare, Published by The Indian Pharmacopoeal Commission, Ghaziabad; 2014. p. 2964, 1469, 2143, 2151.
- Arunachalam A, Lavakumar V, Shankar M. Formulation and *in vitro* evaluation of levofloxacin oral dispersible tablets. *Asian J Res Chem Pharm Sci* 2013;1:31-9.
- Dobetti L. Fast melting tablet: development and technologies. *Pharm Tech* 2001;2:44-8.
- Lorenzp Lamosa ML, Cuna M, Vila Jato JL, Torres D. Fast dissolving drug delivery system. *J Microencapsul* 1997;14:607.
- Virley P, Zydis YR. A novel fast dissolving dosage form. *Manuf Chem* 1990;2:36-7.
- Caretensen JT. *Guidelines for drug stability: principles and practices*. Third Edition. Marcel Dekkar; 2005. p. 252-5.