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Preparation and characterization of oral fast dissolving tablet containing glibenclamide

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ABSTRACT

The purpose of the study was to achieve rapid onset of action. Glibenclamide is an oral anti-diabetic agent used in the treatment of type-2 diabetes mellitus. The formulation (F1-F16) were developed by using design expert 11 version. Glibenclamide prepared b using direct compression method. 16 batches of fast dissolving tablet of glibenclamide were prepared by using cross carmellose sodium and xanthan gum in different concentration. All the formulation were evaluated for weight variation, hardness friability, thickness, in-vitro disintegration time, in-vitro dissolution time etc., and F3 showed the values within limits. Formulation F3 with cross carmellose sodium showed the less disintegration time (8 sec). In-vitro dissolution studies showed 98.34 %drug release at the end of 30 minutes.

Keywords: Glibenclamide, Cross carmellose sodium and Xanthan gum

INTRODUCTION

Solid dosage forms are popular because of low cost, ease of administration, accurate dosage self-medication, pain avoidance, and the most importantly the patient compliance. The most popular solid dosage forms are being tablets and capsules [1, 2]. One important drawback of such dosage forms is Dysphagia, or difficulty in swallowing is common among all age groups. Common complaints about the difficulty in swallowing tablets are size, surface, and taste of tablets. Geriatric and paediatric patients and travelling patients, who may not have ready access to water, are most in need of easy swallowing dosage forms [3].

To fulfill these medical needs, pharmaceutical technologists have developed a novel oral dosage form known as ODTs which disintegrate rapidly in saliva, usually within a matter of seconds, without the need to take it water. Drug dissolution and absorption, as well as onset of clinical effect and drug bioavailability, may be significantly greater than those as compared with conventional dosage forms [4-6].

ODTs releases the medicament in the mouth for absorption through local oromucosal tissue and through pre-gastric (oral cavity, pharynx, and esophagus), gastric (stomach), and post-gastric astric (oral cavity, pharynx, and esophagus), gastric (stomach), and post-gastric (small and large intestine) segments of gastrointestinal tract (GIT) [7].

Orodispersible tablet [8]

ODTs are also called as orodispersible tablets, quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets, and rapidmelts. However, of all the above terms, United States pharmacopoeia (USP) approved these dosage forms as ODTs. The European Pharmacopoeia has used the term orodispersible tablet for tablets that disperses readily within 3 minutes in the mouth before swallowing.

United States Food and Drug Administration defined ODT as "A solid dosage form containing a medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue." The disintegration time for ODTs generally ranges from several seconds to about a minute.

MATERIALS AND METHODS

Glibenclamide was purchased from Yarrow chemicals and Cross Carmellose Sodium, Xanthan Gum, Talc, Magnesium Stearate, Aspartame, Polyvinyl pyrrolidine K30 and Micro Crystalline cellulose were purchased from SD fine chemicals.

PREFORMULATION STUDIES

Identification Tests

IR Spectroscopy

The FT-IR spectrum of the obtained sample of drug was compared with the standard FT-IR spectra of the pure drug

Melting Point determination

Melting point determination of the obtained drug sample was done because it is a good first indication of purity of the sample since the presence of relatively small amount of impurity can be detected by a lowering as well as widening in the melting point range

COMPATIBILITY STUDIES

IR Spectroscopy

FT-IR spectroscopy was carried out to check the compatibility between drug and polymers. The FT-IR spectra of drug with polymers were compared with the standard FT-IR spectrum of the pure drug.

Preparation of phosphate buffer

Preparation of 0.2M Potassium Dihydrogen Ortho Phosphate

Dissolve 27.218gof KH2PO4 in distilled water and made up the volume to 1000 ml with distilled water Preparation of 0.2M Sodium Hydroxide: Dissolved NaOH in water to produce a 40 to60 % w/v solution and allowed to stand. Taking precautions to avoid absorption of carbon dioxide siphoned off the clear supernatant liquid dioxide free water a suitable volume of the liquid to contain 8 g of NaOH in 1000 ml.

Preparation of pH 6.8 buffer

Placed 50 ml of 0.2M KH2PO, in a 200 ml volumetric flask and 22.4ml of 0.2M NaOH was added the and made up the volume with distilled water.

λ max determination of drug in buffer solution:

10 ug/ml of drug solution was prepared and scanned against pH6.8 buffer as reference solution under wave length range of 200-400nm by using UV spectrophotometer. A graph was plotted by taking absorbance on Y-axis and wavelength on X-axis. mg/ml.

Construction of calibration graph in pH 6.8 buffer

1 to 8 concentrations of drug solutions were scanned against phosphate buffer as reference solution at 204 nm under UV spectrophotometer. A graph was plotted by taking absorbance on Y-axis and concentration (mgml) on X-axis. This graph yields standard calibration graph of drug solutions.

Table 1: Formulations of Glibenclamide containing different superdisintegrants.

	Formulations															
Ingredients(mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**	**F13**	**F14**	**F15**	**F16**
Glibenclamide	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Croscarmellose Sodium	7.5	12.75	13.8	13.95	17.1	19.2	20.25	22.5	-	-	-	-	-	-	-	-
Xanthum Gum	-	-	-	-	-	-	-	-	7.5	12.75	13.8	13.95	17.1	19.2	20.25	22.5
Talc	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Magnesium Stearate	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Aspartame	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Polyvinyl Pyrrolidine K30	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
Micro crystalline Cellulose	114.5	109.25	108.2	108.05	104.9	102.8	101.75	99.5	114.5	109.25	108.2	108.05	104.9	102.8	101.75	99.5
Total	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**

RESULTS AND DISCUSSION

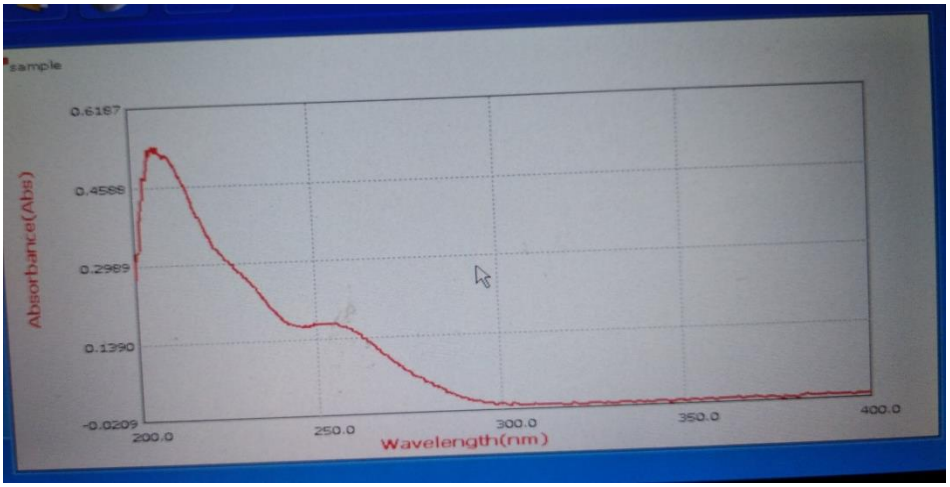

Figure no: 1λmax determination of drug in buffer solution at 204nm

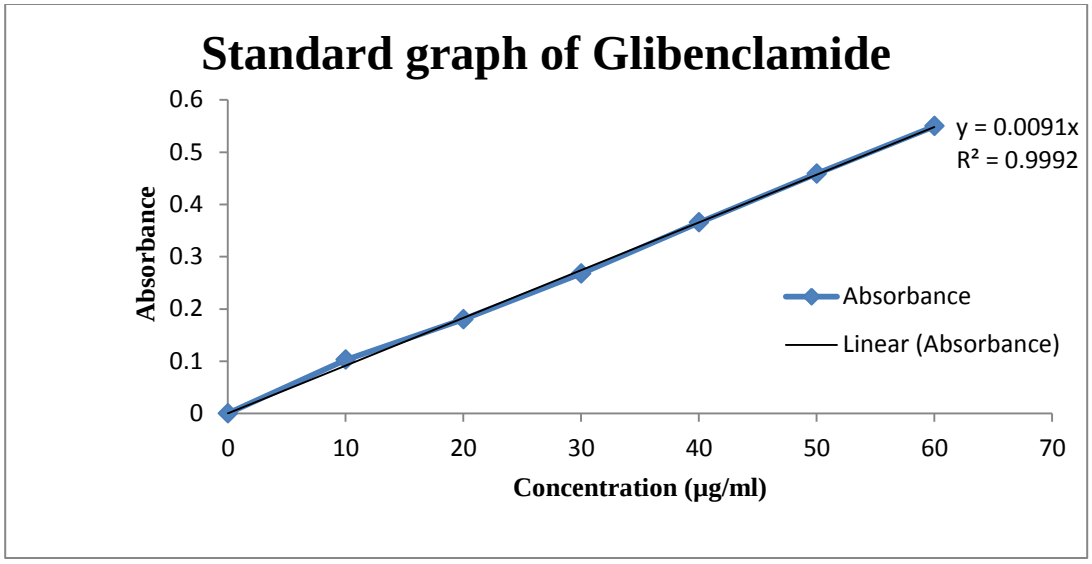

Figure no: 2 Calibration graph of Glibenclamide

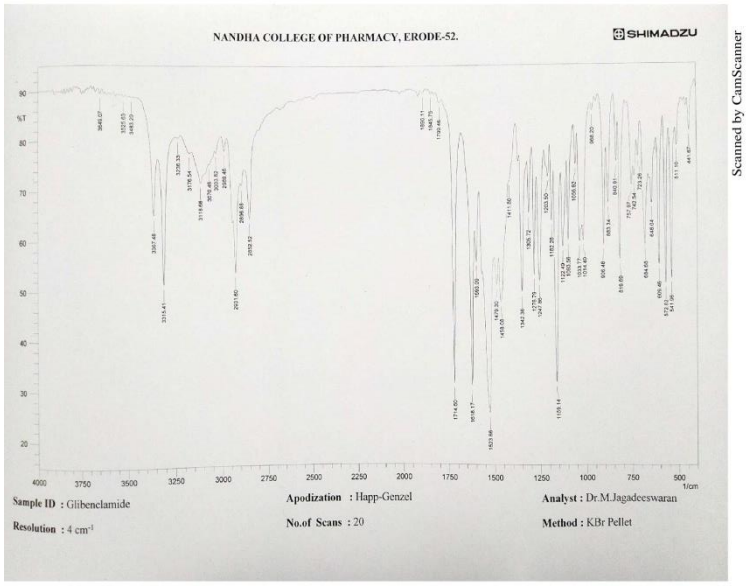

Fig No 3 : FTIR spectrum of Glibenclamide

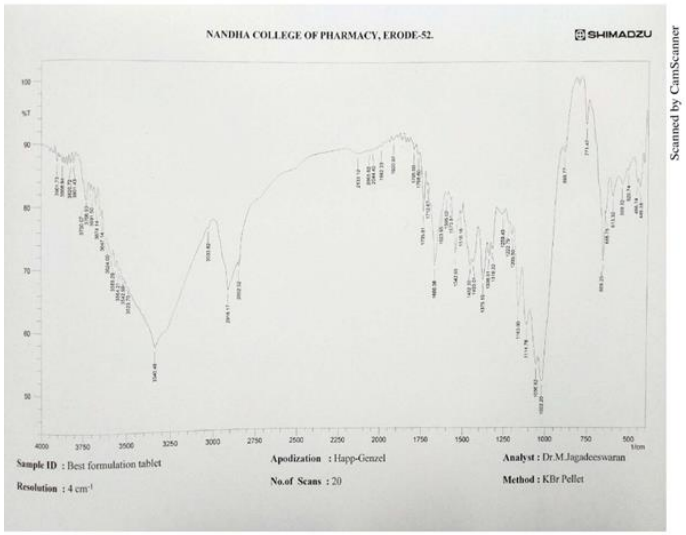

Fig No 4: FTIR spectrum of Optimized Formulation

Table No 2: FTIR interpretation of Glibenclamide pure drug

Characteristic bands	Reference peak(cm^{-1})	Observed peak(cm^{-1})
CH3-O stretch	2830-2810	2852.52
C=O	1725-1705	1714.60
N-H(secondary amine) Deformation	1650-1550	1616.17
S=O stretch	1358-1336	1342.36
C-Cl stretch	730-580	723.28

Melting point determination

The melting point of the obtained drug sample was found to be 169˚C which is the reported range of 168-174˚C. It complies with USP standards thus indicating the purity of the drug sample.

Table No 2: Preformulation Studies of blend of all formulations

Formulation code	Angle of repose (Ɵ)	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Compressibility index (%)	Hausner's ratio
F1	22.4±0.02	0.49±0.03	0.57±0.05	16.1±0.02	1.12±0.03
F2	21.2±0.04	0.51±0.04	0.56±0.03	15.9±0.04	1.11±0.01
F3	19.7±0.06	0.51±0.05	0.57±0.04	17.6±0.01	1.19±0.04
F4	18.8±0.03	0.54±0.06	0.60±0.06	13.2±0.06	1.15±0.05
F5	17.2±0.04	0.52±0.03	0.56±0.04	14.8±0.06	1.18±0.04
F6	19.2±0.05	0.53±0.05	0.58±0.05	15.4±0.09	1.21±0.07
F7	19.8±0.6	0.51±0.06	0.55±0.02	14.4±0.09	1.16±0.04
F8	17.6±0.04	0.50±0.08	0.54±0.06	16.4±0.08	1.19±0.06
F9	17.2±0.06	0.49±0.07	0.50±0.03	17.9±0.09	1.21±0.08
F10	20.4±0.04	0.52±0.03	0.56±0.04	16.3±0.07	1.20±0.04
F11	18.6±0.03	0.50±0.07	0.54±0.05	14.8±0.05	1.15±0.06
F12	17.5±0.04	0.53±0.04	0.60±0.06	15.6±0.04	1.16±0.04
F13	21.3±0.02	0.51±0.05	0.58±0.02	17.8±0.01	1.19±0.07
F14	18.4±0.03	0.52±0.04	0.55±0.04	14.6±0.02	1.15±0.05
F15	17.5±0.05	0.54±0.06	0.56±0.03	15.8±0.08	1.22±0.01
F16	18.8±0.02	0.53±0.03	0.54±0.06	17.9±0.07	1.16±0.08

All the values are expressed as Mean ±SD, n=3

Table No 3: Evaluation of Tablets

Formulation code	‡ Weight variation	*Thickness (mm)	*Hardness (kg/cm^2)	*Friability (%)	*Drug content	*Disintegration time (sec)	*% Cumulative Drug release
F1	150.2±0.5	3.4±0.03	3.14±0.02	0.39±0.03	98.23±1.26	30±0.31	83.48±0.41
F2	151.3±0.3	3.3±0.02	3.16±0.12	0.37±0.07	97.89±1.18	10±0.46	85.38±0.37
F3	150.3±0.2	3.4±0.06	3.27±0.31	0.33±0.06	98.75±0.98	8±0.76	98.34±0.38
F4	149.8±0.3	3.3±0.04	3.15±0.25	0.35±0.05	98.34±1.31	15±0.53	94.36±0.42
F5	150.3±0.7	3.2±0.02	3.17±0.22	0.36±0.06	97.89±1.38	40±0.54	91.48±0.36
F6	150.5±0.5	3.3±0.03	3.19±0.25	0.35±0.03	99.24±1.68	31±0.65	93.54±0.34
F7	150.2±0.6	3.2±0.04	3.24±0.13	0.36±0.04	99.26±1.14	45±0.72	91.97±0.45
F8	149.9±0.7	3.3±0.03	3.21±0.23	0.35±0.02	98.26±1.28	60±0.51	89.79±0.31
F9	149.8±0.3	3.4±0.08	3.20±0.37	0.33±0.06	98.65±1.27	48±0.43	90.59±0.64
F10	150.4±0.4	3.2±0.07	3.19±0.22	0.34±0.08	98.85±1.15	59±0.27	86.18±0.54
F11	150.2±0.2	3.3±0.05	3.25±0.34	0.35±0.07	98.54±1.14	80±0.34	87.41±0.41
F12	151.2±0.7	3.4±0.04	3.22±0.35	0.36±0.02	98.15±1.24	69±0.35	92.89±0.45
F13	151.1±0.5	3.2±0.05	3.19±0.27	0.48±0.06	98.12±1.23	57±0.34	87.98±0.42
F14	150.6±0.5	3.4±0.02	3.20±0.25	0.45±0.05	98.82±1.18	65±0.28	88.06±0.55
F15	150.2±0.6	3.2±0.06	3.18±0.23	0.43±0.06	96.54±1.17	67±0.56	89.61±0.46
F16	150.3±0.3	3.3±0.05	3.19±0.24	0.40±0.04	97.96±1.15	56±0.57	88.88±0.68

*****All the values represented as mean ± Standard Deviation (SD), n=3**.**

In-Vitro Drug dissolution study

The Dissolution study on formulation number: F1-F16 were carried out using 500ml of 6.8pH phosphate buffer as dissolution medium at 50rpm using USP apparatus 2. The formulation F3 shown 36.23- 98.34 in 30 mins. The rapid *In-vitro* dissolution was shown in the formulation F3 containing cross carmellose sodium.

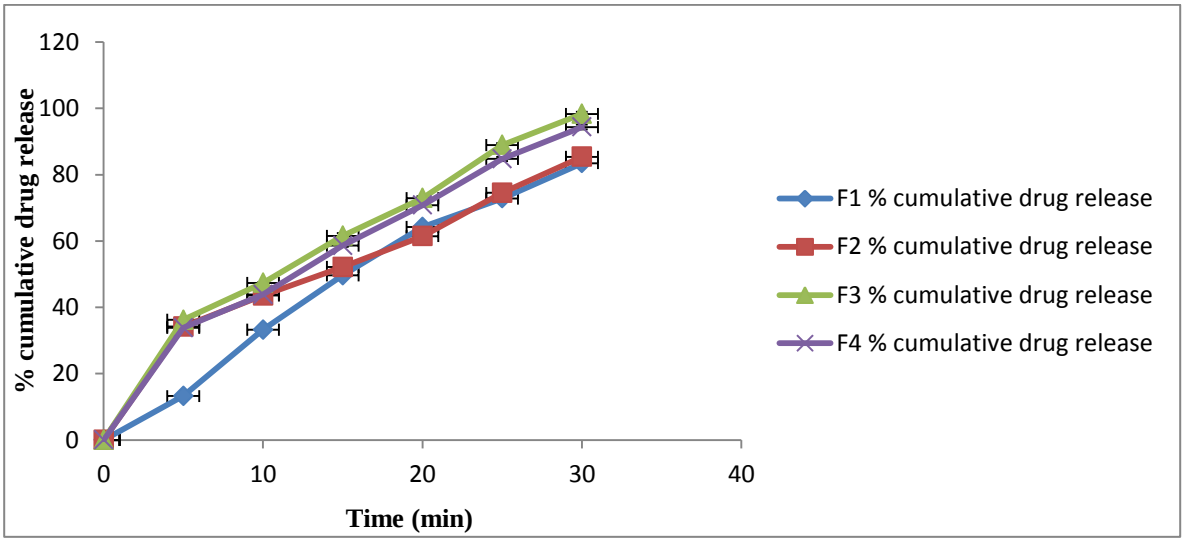

Fig No: 5. Comparison *In-vitro* dissolution profile of F1, F2, F3 and F4 formulations

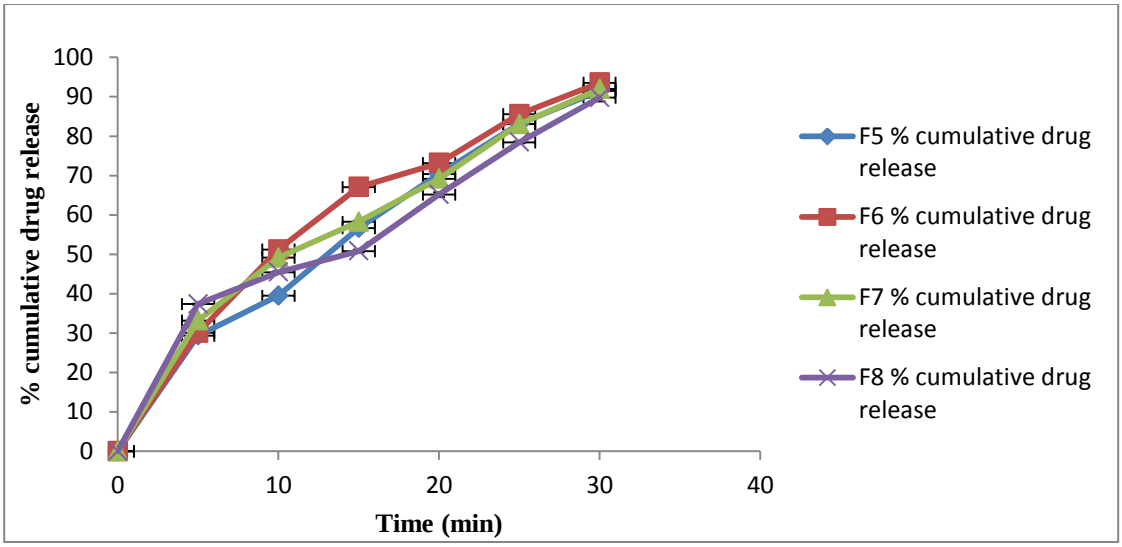

Fig No: 6. Comparison *In-vitro* dissolution profile of F5, F6, F7 and F8 formulations

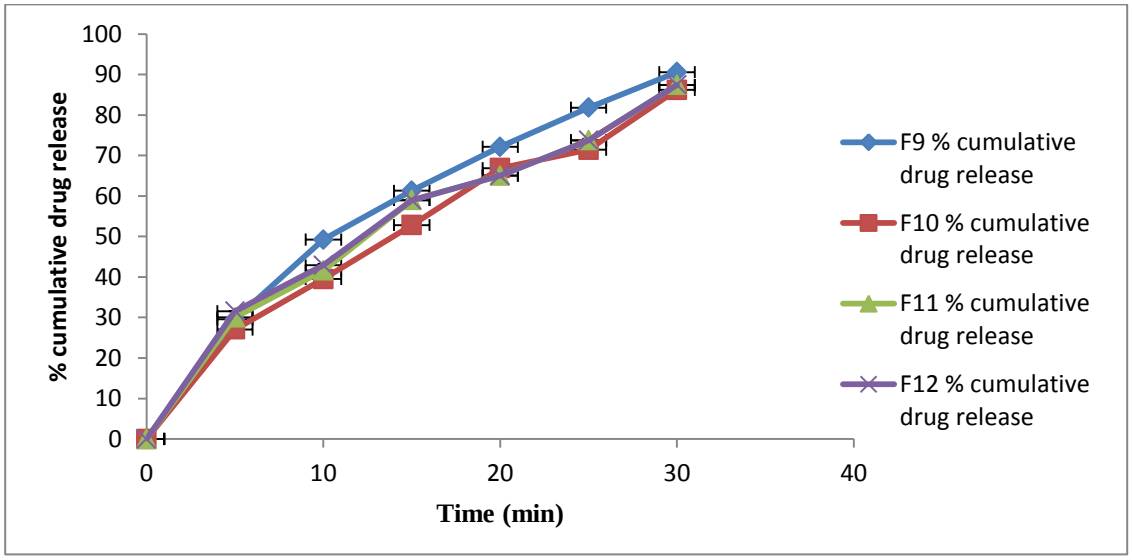

Fig No: 7. Comparison *In-vitro* dissolution profile of F9, F10, F11 and F12 formulations

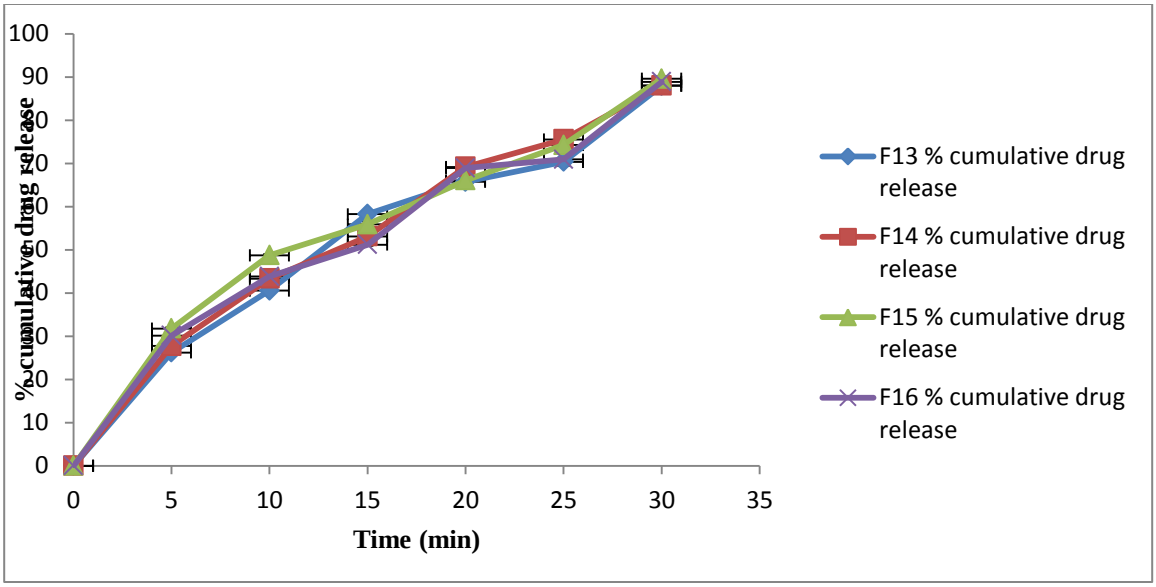

Fig No: 8. Comparison *In-vitro* dissolution profile of F13, F14, F1 and F16 formulations

Percentage of drug release 3D graph by using Factorial design software 11.0 version

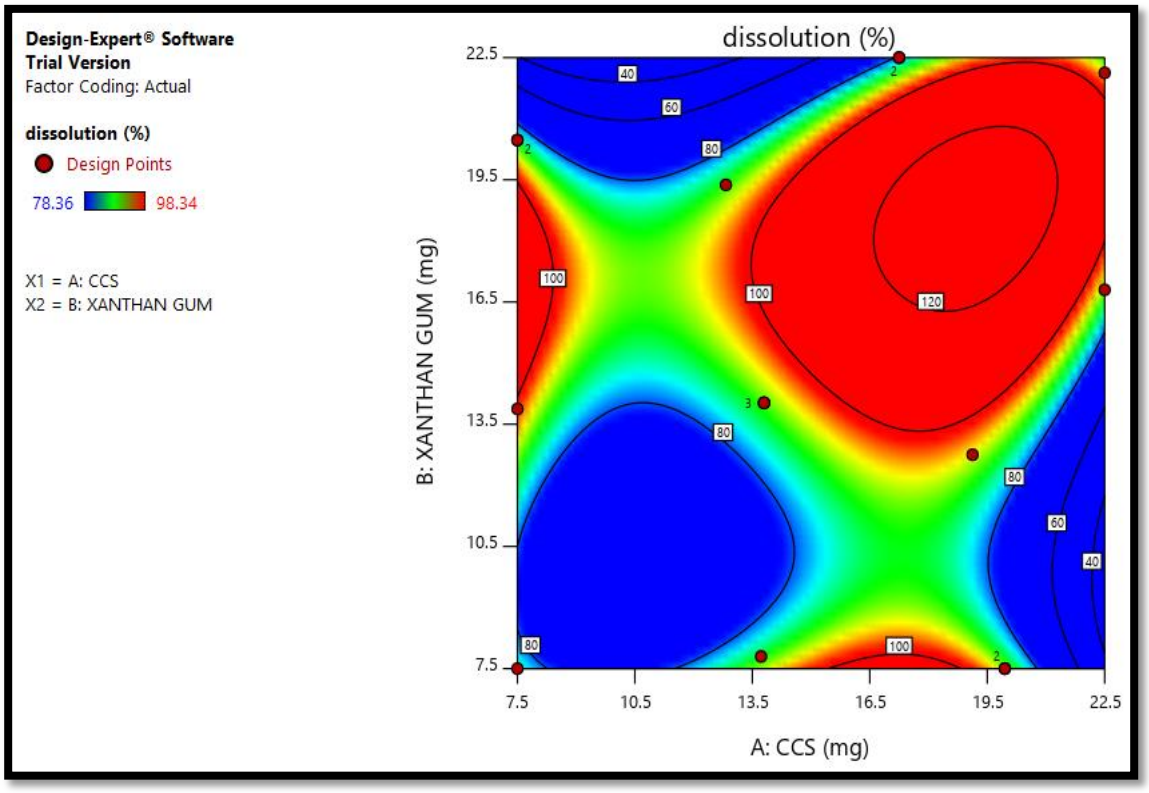

Figure No 9: Drug release (%)

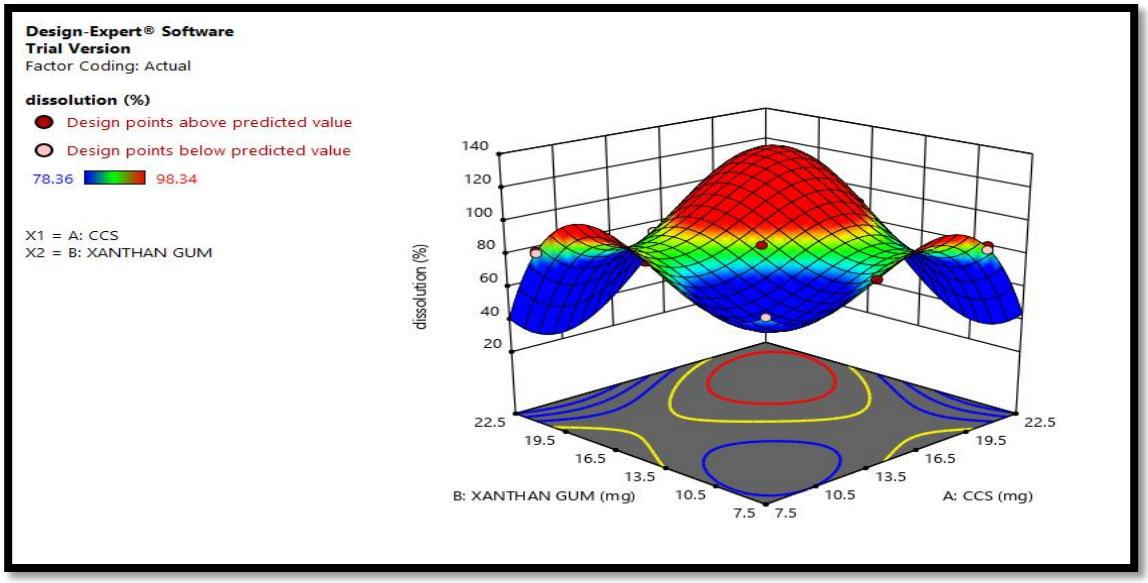

Figure No 10: Drug release (%)

Disintegration of 3D graph by using Factorial design software 11.0 version

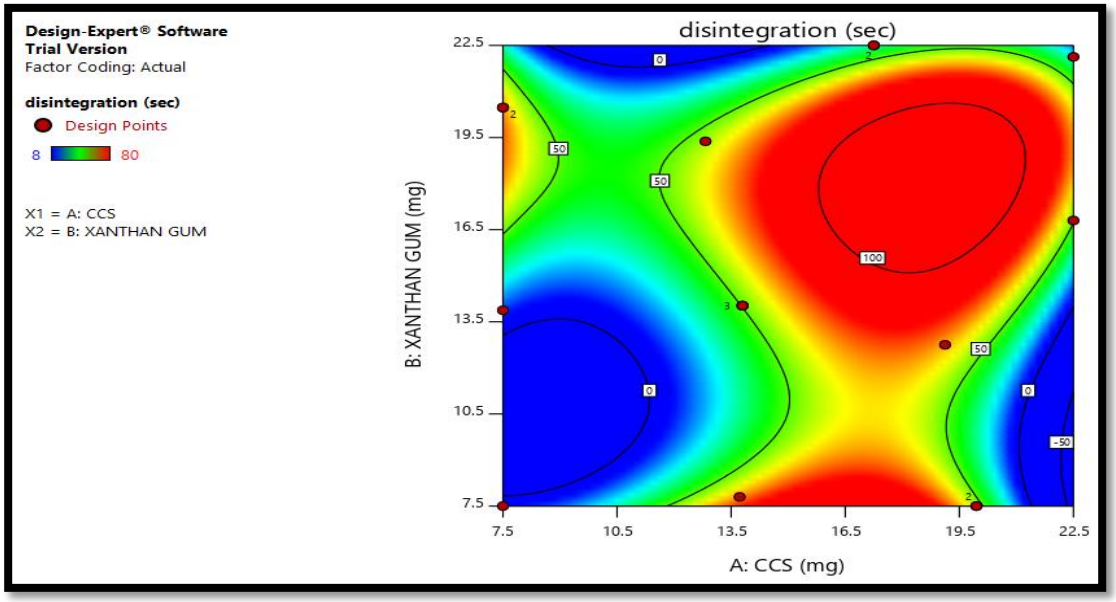

Figure No 11: Disintegration time (sec)

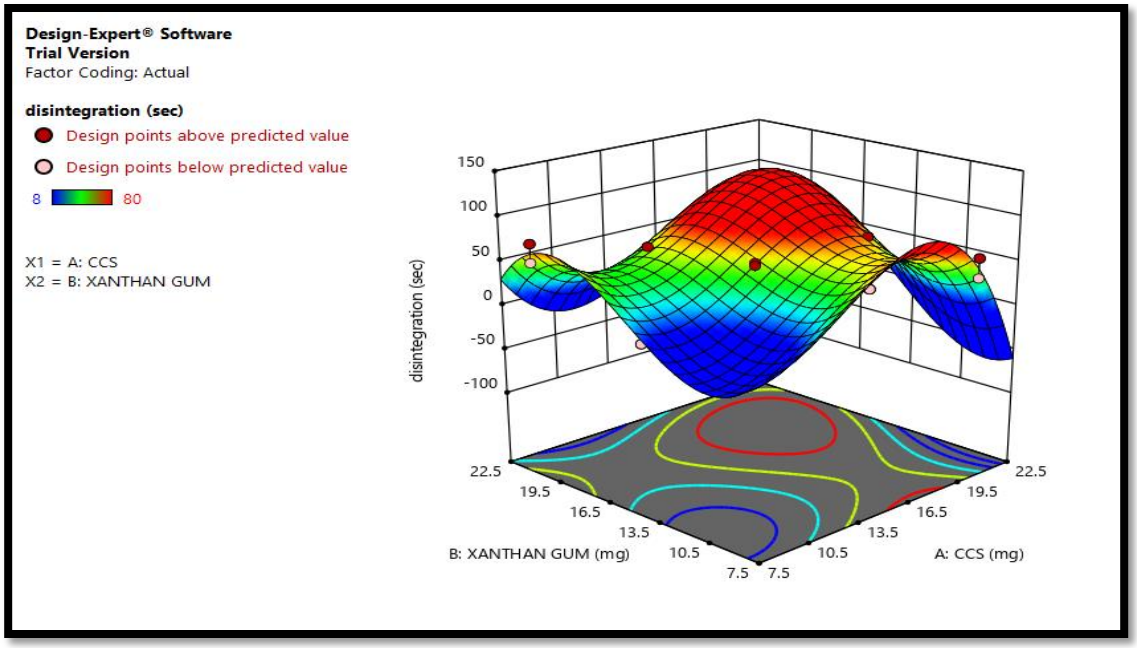

Figure No 12: Disintegration time (sec)

3D response surface plot showing the relationship between various levels of two factors on % cumulative drug release.

Accelerated stability studies

The optimized formulation was subjected to stability studies at 40^0C ± 75% RH for period of 3 months. Each tablet was individually wrapped in aluminium foil and packed in ambered coloured bottle and put at above specified condition in a heating

CONCLUSION

Fast dissolving tablets of Glibenclamide were prepares by using different super disintegrants like cross carmellose sodium and xanthan gum by direct compression method. Pre compression parameters were conducted for all formulations blend and were found to be satisfactory.

The prepared tablets were evaluated for various parameters like weight variation, content uniformity, hardness, thickness, *in-vitro* disintegration time, *in-vitro* dissolution. The results indicated that the tablets complied with the official specifications.

The disintegration studies shown F3 formulation disintegration time of 8 seconds and *in-vitro* drug release of 98.34%.

An accelerated stability study on optimized formulation was performed. The formulation was found to be stable; there was no change in the hardness, friability, disintegration time, and *in-vitro* drug release pattern.

In conclusion, it can be stated that the objective of the study has been achieved. From the above study the formula used for F3 formulation was concluded as an optimized formulation due to its less disintegration time and good % drug release when compared with other formulation.

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