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ISOLATION, CHARACTERIZATION AND INVESTIGATION OF STARCH MALEATE AS NOVEL SUPERDISINTEGRANT IN DEVELOPING OF TELMISARTAN FAST DISSOLVING TABLETS

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Abstract:

Telmisartan, an angiotension II receptor antagonist widely used in the treatment of hypertension, characterized by low aqueous solubility. The present study focus on the formulation and evaluation of Telmisartan fast dissolving a tablet which offers a solution for those patients having difficulty in swallowing. In the formulation of fast dissolving tablets of Telmisartan, superdisintegrants like Starch Maleate (Novel Superdisintegrant), crosscarmellose sodium and crospovidone are employed. The synthesized Starch Maleate was characterized by FTIR, X-ray etc. The Telmisartan - Starch Maleate compatibility studies like DSC, FTIR and TLC were done. From the results, it was observed that no chemical interaction between the drug and Starch Maleate confirmed. 2^3 factorial design was used in formulation of tablets to obtain the ideal concentration of Starch Maleate that is to be used in the formulation of fast dissolving tablets with less experimentation and in short period of time. Telmisartan fast dissolving tablets were subjected to various physical tests and in-vitro dissolution studies. The studies revealed that concentration of 4% w/w of Starch Maleate can be used as superdisintegrant in the formulation of fast dissolving of fast dissolving tablets.

Keywords: *Telmisartan, Starch Maleate, Fast Dissolving Tablets, 2^3 factorial design, Superdisintegrant.*

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INTRODUCTION:

The centre of Drug Evaluation and Research (CDER), US FDA defined fast dissolving/ disintegrating tablets (FDDTs) are "A solid dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue." Fast disintegrating tablets (FDT) are also known as " fast dissolving", " mouth dissolving", " rapid dissolve", " quick disintegrating", "orally disintegrating", " rapimelt", " fast melts ", " orodispersable", " melt in mouth", " quick dissolving" , "porous tablets", " EFVDAS " or "Effervescent Drug Absorption System " . The basic approach in development of FDT is the use of superdisintegrants like cross linked or carboxyl methyl cellulose (crosscarmellose), sodium starch glycolate (primogel, explotab) cross linked polyvinyl pyrrolidone (cross povidone) etc., which provide instantaneous disintegration of tablet after putting on tongue, their by release the drug in saliva.

MATERIALS AND METHODS:

Materials: Maleic anhydride, Dimethyl sulphoxide (DMSO), Acetone, Isopropanol, Hydrochloric acid, Methanol,(Finar chemicals Ltd, Ahmedabad), Ethanol (ChangshuYangyun Chemicals, China), Telmisartan (Dr Reddy's Laboratories), Crospovidone, Crosscarmellose, (Yarrow Chemicals, Mumbai), Microcrystalline cellulose (Qualigens fine chemicals, Mumbai), Magnesium Stearate, Talc (Molychem, Mumbai).

PREPARATION OF STARCH MALEATE (A NOVEL SUPERDISINTEGRANT):

Initially Maleic anhydride was dissolved in methyl sulphoxide (DMSO) and the pH was adjusted to 3.5 using 10M NaOH and finally made upto 50ml. To this potato starch was added and conditioned for 16 h; the product was kept in oven at 60^{o}C for 1h. Then the product was mixed with acetone for 15min and then washed with isopropanol to remove any untreated maleic anhydride if present. After washing, the resultant starch maleate was kept in oven at 60^{o}C until it gets dried. The product obtained was ground and sized.

CHARACTERIZATION OF STARCH MALEATE:

The Starch Maleate prepared was evaluated for the following:

Solubility: Solubility of Starch Maleate was tested in water, aqueous buffers of p^{H}1.2, 4.5 and 7.4, and organic solvents such as alcohol, dichloromethane, chloroform, acetone and petroleum ether.

pH: The p^{H} of 1% w/v slurry was measured.

Melting Point: Melting point was determined by using melting point apparatus

Viscosity: Viscosity of 1% dispersion in water was measured using Ostwald Viscometer.

Swelling Index: Starch Maleate (200 mg) was added to 10ml of water and light liquid paraffin taken in two different graduated test tubes and mixed. The dispersion in the tubes was allowed to stand for 12h. The volumes of the sediment in the tubes were recorded and calculated as per the standard formula for swelling index.

Test for gelling property: The gelling property (gelatinization) of the starch and Starch Maleate prepared was evaluated by heating a 7% w/v dispersion of each in water at 100^{o}C for 30 min.

Moisture absorption: The hygroscopic nature of Starch Maleate was evaluated by moisture absorption studies in a closed dessicator at 84% relative humidity and room temperature.

Particle sizes: Particle size analysis was done by sieving using standard sieves.

Density: Density (g/cc) was determined by liquid displacement method using benzene as liquid.

Bulk density: Bulk density (g/cc) was determined by three tap method in a graduated cylinder.

Angle of Repose:Angle of repose was measured by fixed funnel method.

Compressibility Index: Compressibility index (CI) was determined by measuring the initial volume (V_o)and final volume (V) after hundred tapings of a sample of Starch Maleate in a measuring cylinder. CI was calculated as per standard formula.

Fourier Transform Infrared (FTIR) Spectroscopy: FTIR spectra of Starch Maleate were recorded on samples prepared in potassium bromide (KBr) disks using a BRUKER FT-IR, (Tokyo, Japan). Samples were prepared in (KBr) disks by means of a hydrostatic press at 6-8 tons pressure. The scanning range was 500 to 4000 cm^{-1}.

X-ray diffraction: Diffraction pattern of Starch Maleate was recorded with an X-ray diffractometer (PanalyticalspectrisPvt.Ltd., Singapore). X-ray diffraction was performed at room temperature (30^{o}C) with a diffractometer; target, Cu(λ = 1.54Å), filter, Ni; Voltage, 45kV; Current 40mA; time constant 10mm/s; scanning rate 2^{o}/min; measured from 10-35^{o} at full scale 200.

Ester Test: To 1mg of Starch Maleate, 2ml of ethanol and 1ml of 0.1M NaOH was added. To this, Phenolphthalein indicator was added.

Drug – Excipient Compatibility Studies: The compatibility of Starch Maleate with the selected drug (Telmisartan) was evaluated by DSC, FTIR and TLC studies.

Differential Scanning Calorimetry (DSC):DSC thermo grams of Telmisartan and their mixtures (1:1)

with Starch Maleate were recorded on Perkin Elmer Thermal Analyser. Samples (2-5) were scaled into aluminum pans and scanned at a healing rate of 10°C min^{-1} over a temperature range 30 – 350°C.

Infrared Spectroscopy: FTIR spectra of Telmisartan and their mixtures (1:1) with Starch Maleate were recorded on a Perkin Elmer, IR Spectrophotometer model: Spectrum RXI, using KBr disc as reference.

TLC Study: TLC was carried out on Telmisartan, and their mixtures (1:1) with Starch Maleate follows:

Stationary Phase: Silica gel G (per coated TLC plates)

Mobile Phase: Methanol: Chloroform (1:6)

Procedure: Mobile phase was prepared and taken in a TLC chamber. The chamber was allowed to saturate with solvent vapor for 24h. Standard (pure drug) ant test (Drug- Starch Maleate mixtures) sample were spotted on activated silica plates using narrow capillary tubes. The spotted plates were kept in the TLC chamber and allowed to run the mobile phase. The plates were dried and kept in iodine chamber to develop the spots. The R_f values of standard and test samples were determined by the following formula.

R_f = Distance travelledby sample/ distance travelled by solvent front.

Optimization Technique:

Optimization technique provide both a depth of understanding and an ability to explore and define ranges for formulation and processing factors with a rational approach to the selection of several experimental and manufacturing step for a given product, to quantitatively select a formulation. It is at this point that optimization can become a useful tool to quantitate a formulation that has been qualitatively determined.

The present investigation deals with an attempt of systemic formulation approach for optimization of Telmisartan fast dissolving tablets employing starch maleate, crosscarmellose sodium and crospovidone as superdisintegrants. A 2^3 factorial design was applied to investigate the main and interaction effects of the three formulation variables i.e., starch maleate (A), crosscarmellose sodium (B), crospovidone (C), in each case to find the formula with less disintegration time and more percent released in 10 min and more dissolution efficiency in 5 min and to permit arbitrary selection of tablets with immediate release of drug with in 20 min.

Formulation of Telmisartan Fast Dissolving Tablets as per 2^3 Factorial Design:

The tablets were prepared by direct compression method. The composition of different formulations of Telmisartan fast dissolving tablets is shown in **Table 1**. For uniformity in particle size each ingredient was passed through # 100 mesh sized screen before mixing. Starch Maleate, Crosscarmellose, Crospovidone and Mannitol, Microcrystalline Cellulose were accurately weighed and mixed using mortar and pestle, and then added to Telmisartan. Finally talc and magnesium Stearate were added to the powder. Finally mixed blend was compressed by using eight station rotatory presses (Shakthi Machineries Pvt, Ltd., Ahmedabad, India.)

Table 1: Formula of Telmisartan Fast Dissolving Tablets Employing Starch Maleate

Ingredients (Mg/tablet)	F1	F2	F3	F4	F5	F6	F7	F8
Telmisartan	40	40	40	40	40	40	40	40
Starch Maleate	-----	10	-----	10	-----	10	-----	10
Croscarmellose Sodium	-----	-----	10	10	-----	-----	10	10
Crospovidone	-----	-----	-----	----	10	10	10	10
Mannitol	30	30	30	30	30	30	30	30
Microcrystalline Cellulose	122	112	112	102	112	102	102	92
Talc	4	4	4	4	4	4	4	4
Magnesium Stearate	4	4	4	4	4	4	4	4
Total Weight(mg)	200	200	200	200	200	200	200	200

Evaluation of Telmisartan Fast Dissolving Tablets:

Hardness: The hardness of prepared formulation was measured by using Monsanto hardness tester.

Friability: The friability of tablets was measured using a Roche Friabilator.

Drug Content Uniformity: For content uniformity test, twenty tablets were weighed and powdered a quantity of powder equivalent to 10mg of Telmisartan was extracted into 0.1 N HCL and filtered. The Telmisartan content was determined by measuring the absorbance spectrophotometrically at 216 nm after appropriate dilution with 0.1 N HCL. The drug content was calculated using the standard calibration curve. The mean percent drug content was calculated as an average of three determinations.

Wetting Time: The wetting time of the Telmisartan fast dissolving tablets was measured using a very simple process. Five circular tissue papers of 10 cm diameter were placed in a Petri dish with a 10 cm diameter. Ten milliliters of water containing a water soluble dye (Amaranth) was added to the Petri dish. A tablet was carefully placed on the surface of tissue paper. The time required for water to reach the upper surface of the tablet was noted as the wetting time.

Water absorption ratio: A piece of tissue paper folded twice was placed in a small Petri dish containing 6ml of water. A tablet was put on the tissue paper and allowed to completely wet. The wetted tablet was then weighed. Water absorption ratio, R was determined using following equation.

$$R = 100 (W_a - W_b)/W_a$$

Where, W_a = Weight of tablet after water absorption, W_b = Weight of tablet before water absorption.

***In-vitro* Disintegration Time**: Disintegration time for FDTs was determined using USP disintegration apparatus with 0.1 N HCL. The volume of medium was 900 ml and temperature was 37 ± 0.2°C. The time in seconds taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured.

***In-vitro* Dissolution Rate Studies**: The *In-Vitro* dissolution rate study of Telmisartan fast dissolving tablets was performed using 8-station dissolution test apparatus (Electrolab TDT-08L) fitted with paddles (50 rpm) at 37 ± 0.5°C, using 0.1N HCL (900 ml) as a dissolution media. At the predetermined time intervals, 5 ml samples were withdrawn, filtered through 0.45 µ membrane filter, diluted and assayed at 216 nm using a UV/Visible Double beam spectrophotometer (Analytical technology T360). Cumulative percentage drug release was calculated using standard absorbance from the calibration curve. All the dissolution experiments were conducted in triplicate (n=3).

Stability Studies: The stability study of the optimized fast dissolving tablets of Telmisartan (F8) was carried out according to ICH guidelines at 40°C ± 2°C and 75% ± 5% RH for 6 months by storing the samples in stability chamber (Kemi, Ernakulam).

RESULTS AND DISCUSSION:

The Starch Maleate prepared was found to be fine, smooth and free flowing amorphous powder. The physical and micrometric properties of the Starch Maleateare summarized in **Table 2**. It was insoluble in aqueous solvents and in organic solvents tested (methanol, petroleum ether, dichloromethane, and chloroform) the pH of 0.1% aqueous dispersion was 3.723.

Table 2: Physical and Micromeritic Properties of The Starch Maleate Prepared.

Parameters	Observation
Solubility	Insoluble in all aqueous and organic solvents tested
pH(1% w/v aqueous dispersion)	3.72
Melting Point	Charred at 300^{0}C
Viscosity (1% w/v aqueous dispersion)	1.04cps
Swelling Index	66.6%
Gelling Property	No gelling and the swollen particles of starch maleate separated from water. Where as in the case of starch, it was gelatinized and formed gel.
Moisture Absorption	4.1%
Particle Size	152µm(80/120)
Density	0.514g/cc
Bulk Density	0.562g/cc
Angle of Repose	13.03^{0}C
Compressibility Index	15.53%

Starch Maleate exhibited good swelling in water. The swelling index was 66.6% all micrometric properties indicated good flow and compressibility needed for solid dosage from manufacturing. The density of starch Maleate was found to be 0.514 g/cc.

The FTIR spectrum of Starch Maleate is shown in **Fig:1**. The presence of peaks of absorption at 1722.43 cm^{-1} is a characteristic peak of esters. So from FTIR studies it was concluded that Starch Maleate (ester) was formed when starch was allowed to react with Maleic anhydride. The characteristic FTIR bands of Telmisartan at 2958.80 cm^{-1} (-COOH) were all observed in the FTIR spectra of both TS and TS-SM. These FTIR spectral observations also indicated no interaction between Starch Maleate and the drug selected.

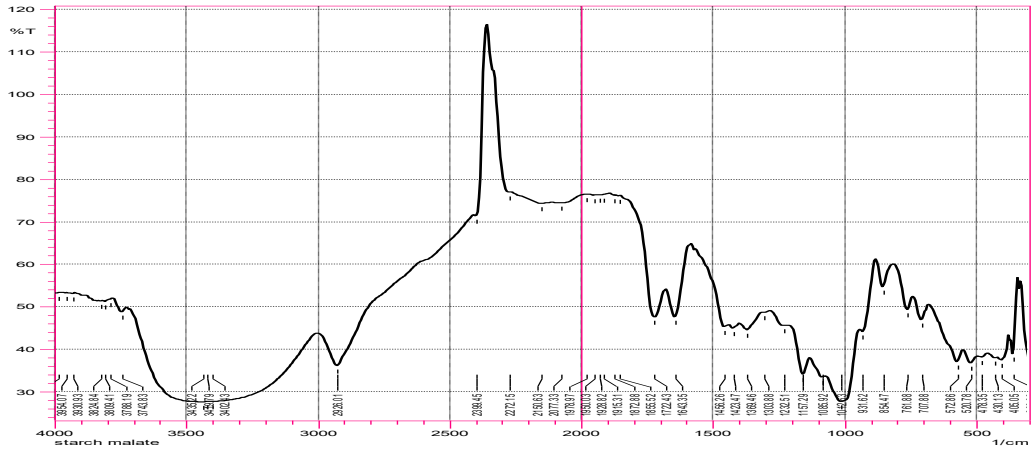


Fig. 1: FTIR Spectra of Starch Maleate

As the Starch Maleate was amorphous, smooth and free flowing powder and it had got all the characteristics of Superdisintegrant. It was concluded that Starch Maleate can be used as novel superdisintegrant in the formulation of fast dissolving tablets.

The compatibility of Starch Maleate with the selected drug (Telmisartan) was evaluated by DSC, FTIR and TLC studies. The DSC thermograms of Telmisartan (TS) and Telmisartan- Starch Maleate (TS-SM) are shown in Fig:2. The DSC thermograms of TS and TS-SM exhibited endothermic peaks at 268.73°C and 266.79°C respectively. The melting peaks of TS and TS-SM correspond to the melting point of Telmisartan (265°C – 270°C). These melting peaks observed in the DSC thermograms of Telmisartan and Telmisartan – Starch Maleate mixtures correspond to the melting points of the respective drug indicating no interactions between the selected drug and Starch Maleate polymer. The DSC study, thus, indicated no interaction between Starch Maleate and selected drug.

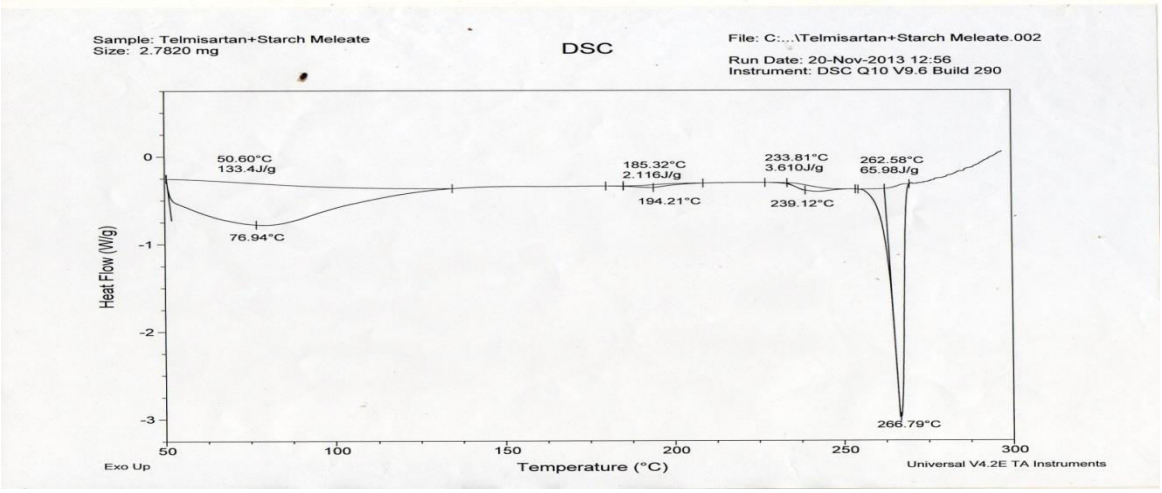


Fig. 2: DSC Thermogram of Telmisartan with Starch maleate

In the TLC study, single spots were observed in the case of pure drugs as well as their mixtures with Starch Maleate shown in **Fig:3**. The close agreement of the R_f values of the drugs and their mixtures with Starch Maleate (**Table:3**)

indicated no interaction between the drug and Starch Maleate

Table 3: R_f Values of Selected Drugs and Their Mixtures (1:1) With Starch Maleate

S.No	Product	R_fValue
1	Telmisartan	0.74
2	Telmisartan- Starch Maleate	0.71

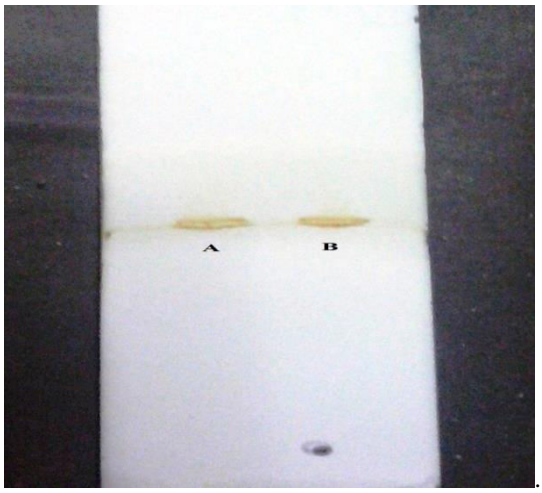


Fig. 3: TLC Plate Showing (A) Telmisartan pure drug (B) Telmisartan and Starch Maleate

Thus, the results of DSC, FTIR and TLC indicated no interaction between the selected Drug and Starch Maleate, the new Superdisintegrant. Hence, Starch Maleate could be used as a superdisintegrant in the design of fast dissolving tablets of the selected drug.

Fast dissolving tablets each containing 40 mg of Telmisartan (TS) could be prepared by employing Starch Maleate and other known superdisintegrantscroscarmellose sodium and crospovidone by direct compression method. Hardness of the tablets was in range of 3-4 kg/sq.cm, indicating good strength with a capability to resist physical and pre-functionary stress conditions during handling. Weight loss on the friability test was less than 0.17% in all cases. All the fast dissolving tablets prepared contained Telmisartan with in 100±5% of the labelled claim. As such the prepared tablets were of good quality with regard to drug content, hardness and friability. The disintegration time of all formulated tablets was found to be in the range of 1±0.5 to 4±0.3 seconds as indicated in the **Table: 4**.

Table 4: Physical Properties: Hardness, Friability, Drug Content, Disintegration Time, Wetting Time, Water Absorption Ratio of Telmisartan Fast Dissolving Tablets Employing Starch Maleate and Other Superdisintegrants.

Formulation	Hardness (Kg/Cm^2) ± S.D	Friability (%) ± S.D	Drug Content (mg/tab) ± S.D	Disintegration time(s) ± S.D	Wetting time (s) ± S.D	Water absorption ratio (%) ± S.D
F1	3.9 ± 0.01	0.12±0.011	38.21±0.11	4 ± 05	250 ± 0.11	128.5±0.01
F2	4.0 ± 0.01	0.13±0.012	39.32±0.57	1 ± 05	115 ± 1.34	95 ± 0.04
F3	3.8 ± 0.04	0.14±0.015	39.81±0.17	1 ± 03	87 ± 0.18	55 ± 0.06
F4	3.6 ± 0.01	0.11±0.014	37.72±0.54	1 ± 04	72 ± 0.56	95 ± 0.31
F5	3.9 ± 0.01	0.12±0.013	39.52±0.55	1 ± 09	51 ±1.11	131.8 ± 0.33
F6	3.7 ± 0.03	0.14±0.012	38.42±0.64	1 ± 05	90 ± 0.37	147 ± 0.52
F7	3.8 ± 0.02	0.15±0.014	37.92±0.78	1 ± 08	32 ± 1.23	123.8 ± 0.44
F8	3.9 ± 0.01	0.12±0.011	38.21±0.11	1 ± 06	77 ± 0.53	160 ± 0.21

The results of *In- Vitro* wetting time and water absorption ratio were found to be within the prescribed limits and satisfy the criteria of fast dissolving tablets (**Fig:4**). The *In- Vitro* wetting time was **less in F8**, which consist of

combination of **5%** Starch Maleate, **5%** Croscarmellose sodium and **5%** Crospovidone.

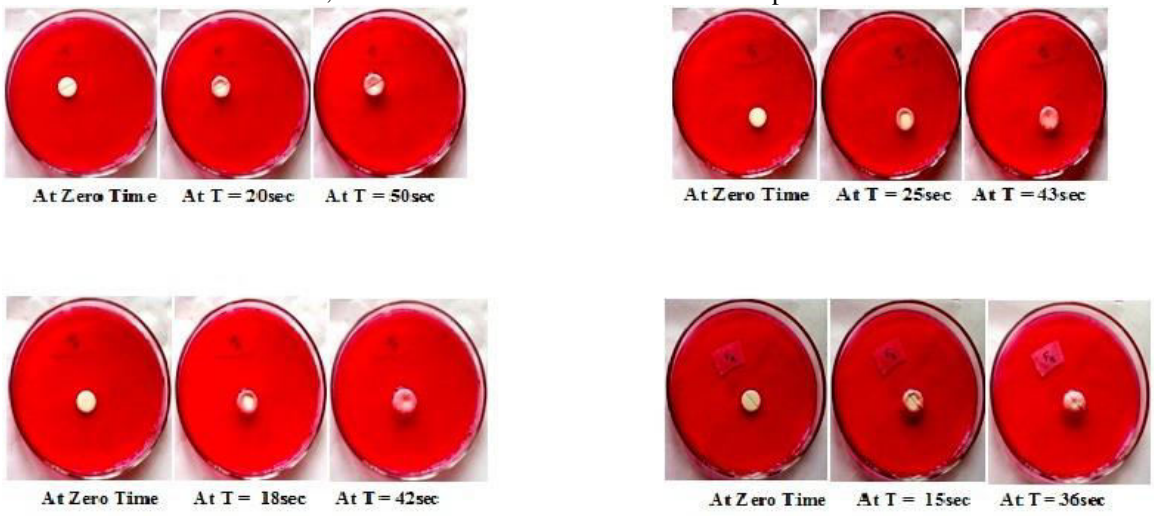
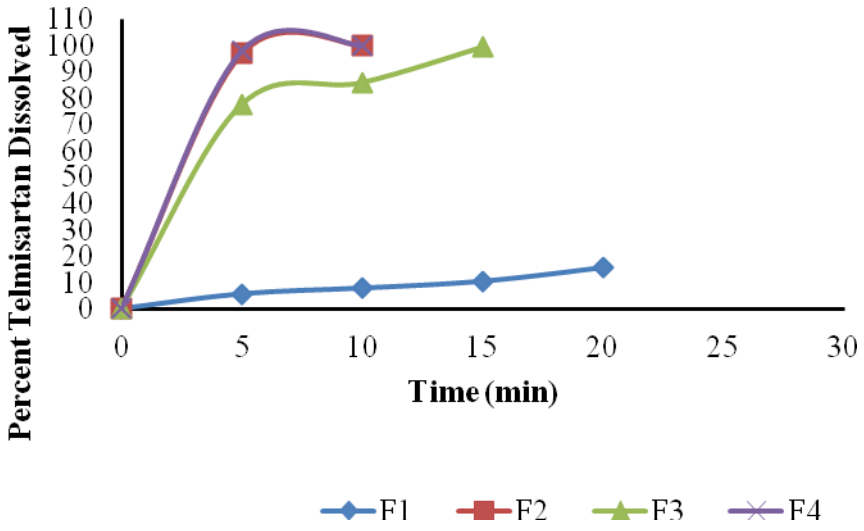


Fig:4 Wetting Time of Telmisartan Fast Dissolving Tablets Prepared Employing Starch Maleate

The drug dissolved from the Telmisartan fast dissolving tablets employing Starch Maleate and other known superdisintegrants were shown in the **Table: 5** and **Fig: 5.**

Table 5: Drug Dissolution Profiles of TelmisartanWith Starch Maleate and Other Superdisintegrants.

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8
5	5.67±0.04	96.87±0.02	77.56±0.11	97.89±0.07	85.98±0.45	99.67±0.04	96.56±0.02	99.78±0.04
10	7.83±0.02	99.89±0.03	85.76±0.64	99.99±0.02	99.63±0.56	100±0.01	98.58±0.03	100±0.01
15	10.43±0.01	------	99.27±0.05	------	------	------	99.69±0.01	------
20	15.63±0.03	------	------	------	------	------	-------	------



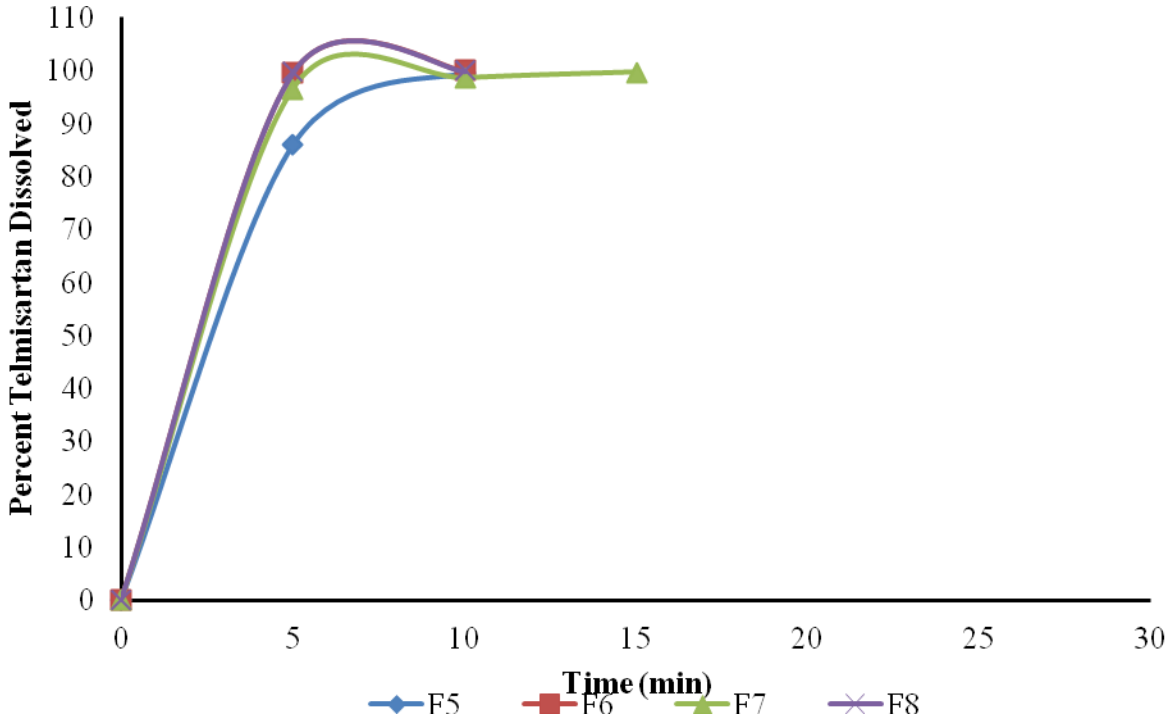


Fig.No.05 Dissolution Profiles of F_1 to F_8 Formulations

The dissolution parameters of the formulations from (F1-F8) which were made by direct compression method were shown in the **Table: 6**. The PD_5 (percent dissolved in 5 minutes) was more in F8 which consist of combination of 5% Starch Maleate, 5% Croscarmellose and 5% crospovidone. The same was in the case of DE_5% (dissolution efficiency in 5 minutes). The PD_5& DE_5% reveals that Starch Maleate was effective at 5% Croscarmellose at 5%, and crospovidone at 5%, when the formulations were made by direct compression using these superdisintegrants. The $k_1$also increased in all the formulations when compared to F1 formulation. The number of folds increase in DE_5% and number of folds increase in k_1 (min^{-1}) were given in the Table 5. From the results it was concluded that Starch Maleate (new superdisintegrant) could be used as a superdisintegrant in the formulation of fast dissolving tablets of Telmisartan.

Table 6: Dissolution Parameters of Telmisartan Fast Dissolving Tablets Employing Starch Maleate and Other Superdisintegrants.

Parameters	F1	F2	F3	F4	F5	F6	F7	F8
PD_5	5.67	96.87	77.56	97.89	85.98	99.67	96.56	99.78
DE_5 (%)	4.5	81.4	63.2	80	76.5	94.4	88.6	94.8
Increase in DE_5 (%) No of folds.	---	0.055	0.071	0.056	0.058	0.047	0.050	0.047
K_1 (min^{-1})	0.253	0.695	0.195	0.773	0.396	---	0.677	---
Increase in K_1(min^{-1}) No of folds.	---	0.364	1.297	0.327	0.638	---	0.373	---
Disintegration Time	4 sec	1 sec	1 sec	1 sec	1 sec	1 sec	1 sec	1 sec

Experimental design:

Optimization of the Telmisartan fast dissolving tablets was done using 2^3 factorial design in which 3 factors each at two levels were evaluated. To evaluate the individual and combined effects of Starch Maleate (factor A), Croscarmellose sodium (factor B) and Crospovidone (factor C), on dependent variables i.e., percent release in 5 min and dissolution efficiency in 5 min. The fast dissolving tablets were formulated using selected combinations of three

factors as per 2^3 factorial design. Formula of Telmisartan fast dissolving tablets was prepared as per 2^3 factorial design given in **Table:7.**

Table 7: Levels of The Three Factors Used In Experimental Design.

S.No	Factors Ingredients	Code	L_1	L_2
1	Starch Maleate	A	0	5
2	Croscarmellose sodium	B	0	5
3	Crospovidone	C	0	5

A polynomial regression algorithm was used to relate the independent variables to the response variables. The general first order model and equation they could be constructed from 2^n experimental design is indicated in the following equation

$$Y= \beta_0 + \beta_1A + \beta_2B + \beta_3C + \beta_1\beta_2AB + \beta_1\beta_3AC + \beta_2\beta_3BC + \beta_1\beta_2\beta_3ABC$$

Where, Y is the measured response, β_0 is the arithmetic mean response of 10 mins, $\beta1$, β_2, β_3, $\beta_1\beta_2$, $\beta_1\beta_3$, $\beta_2\beta_3$, $\beta_1\beta_2\beta_3$ are the coefficients for the corresponding factors and A, B, C, AB, AC, BC and ABC are the percentages of Starch Maleate, Croscarmellose sodium and crospovidone and interaction terms respectively. The coefficients were calculated accordingly to the general formula given in equation.

$$\beta= \Sigma XY/2^n$$

Where, βis coefficient, X is the corresponding variable (A, B, C) and Y is the response value (percent released in 5 minutes & dissolution efficiency in 5 minutes) n is the level.

The two levels of three factors employed in the experimental design are indicated in **Table: 7** and transformed design for analysis of responses of Telmisartan fast dissolving tablets is shown in **Table: 8.**

Table 8: Transformed Design For Analysis of Response of Telmisartan Fast Dissolving Tablets.

S.No	Formula Code	A (%)	B (%)	C (%)
1	F1	0	0	0
2	F2	5	0	0
3	F3	0	5	0
4	F4	5	5	0
5	F5	0	0	5
6	F6	5	0	5
7	F7	0	5	5
8	F8	5	5	5

The percent released in 5 minutes and dissolution efficiency in 5 min indicate that the dependent variables strongly depend on independent variables. The fitted equations relating the disintegration time percent release at the end of 10 minutes to the transform factors are shown in equations.

Final equation in terms of coded factors.

Percentage Dissolved in 5 min = + 82.50 + 16.06A + 10.45B + 13.00C – 10.17AB – 11.83AC – 7.78BC + 7.55ABC (R^2 = 1.000)

Percentage Dissolved in 5 min = + 72.93 + 14.73A + 8.72B +15.65C – 8.98AB – 8.70AC – 5.60BC + 6.05ABC (R^2 = 1.000)

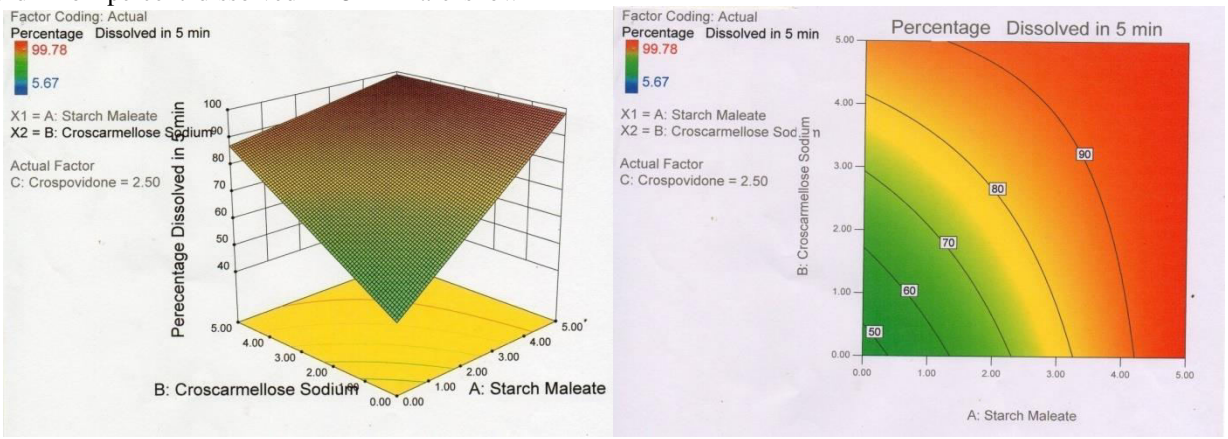
The value of the R^2 indicates the good fit. The polynomial equations can be used to draw a conclusion after considering the magnitude of coefficient and the mathematical sign it carries (Positive or Negative)

From the polynomial equations one can be deduce that the factor A, B, C and interaction of ABC have positive effect on percentage dissolved in 5 min of Telmisartan fast dissolving tablets. The interactions of AB, BC and AC have negative effect on the percentage dissolved in 5 min. Except the interaction of AB, AC and BC, all the other main interaction terms have positive effect on the dissolution E\efficiency in 5 min.

Once the polynomial equation, which relate the levels of each factor and their corresponding interactions with percent release in 5 minutes and dissolution efficiency in 5 min the surface response curves and contour plots were constructed using design expert software.

The response surface plots and contour plots reveal that as the concentration of Starch Maleate (A), Croscarmellose sodium (B), Crospovidone (C)

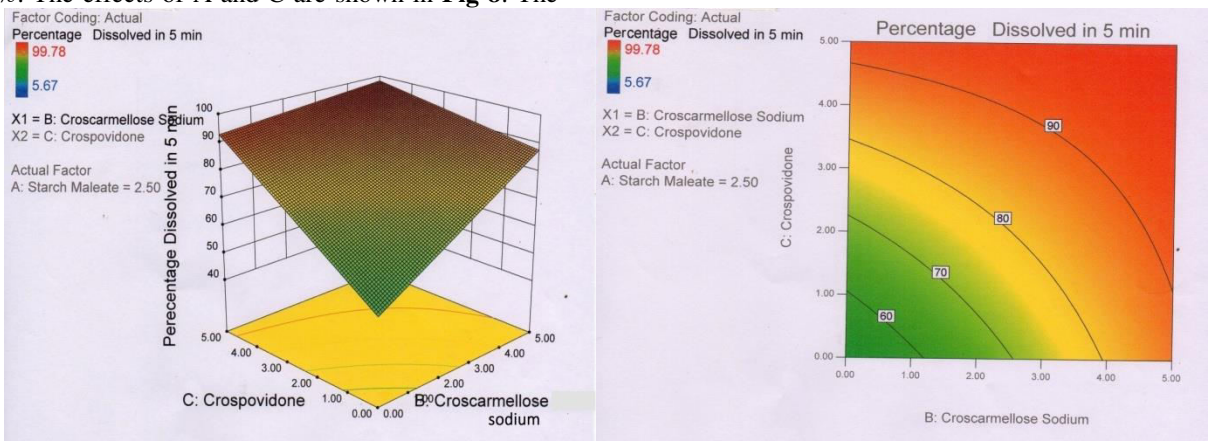
percent dissolved in 5 min increases. The effects of A and B on percent dissolved in 5 min are shown in **Fig: 6**.



(A)Response Plot **(B) Contour Plot**

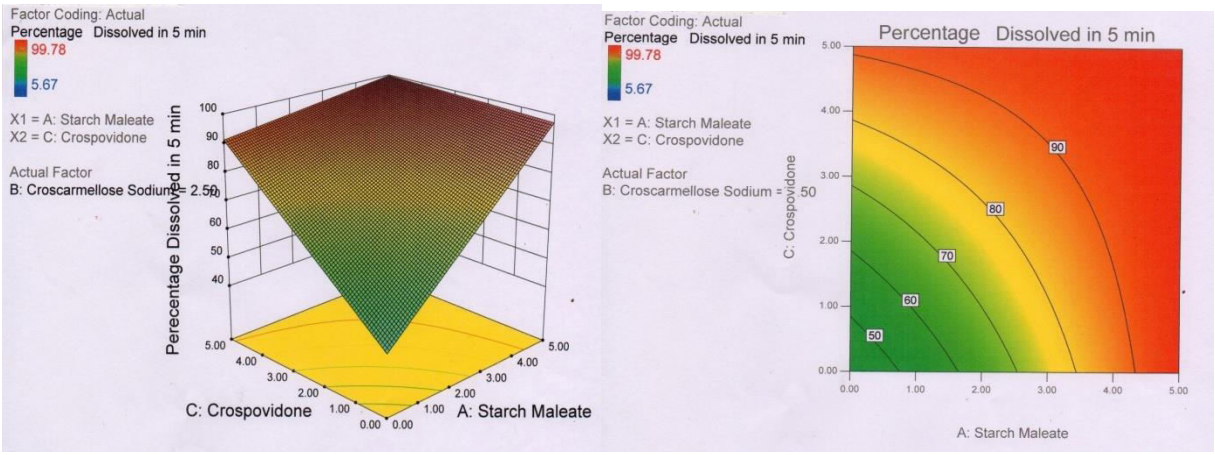
Fig. 6: (A) Response Plot (B) Contour Plot of Telmisartan Fast Dissolving Tablets (Effect of Croscarmellose sodium and Starch Maleate on Percentage Dissolved in 5min)

The contour plots were found to be linear. It was determined from contour plot (**Fig:6**) that a more percent dissolved in 5 min can be obtained with A level range between 3.5 and 4.5 and B level range from 4 to 5 %. The effects of B and C are shown in **Fig. 7**. The contour plots were found to be linear indicating linear relationship between B and C. It was determine from the contour plot (**Fig. 7**), more percentage dissolved in 5 min can be obtained with B level in between 4 to 5% and C level range from 4 to 5%. The effects of A and C are shown in **Fig 8**. The contour plots were almost found to linear indicating a linear relationship between A and C. It was determined from the contour plot, more percentage dissolved in 5 min can be obtained with A level in between 3.5 and 4.5% and C level between 4 to 5%. From this we can conclude that more percent dissolved in 5 min can be achieved when the factor (A) is used in the concentration range from 3.5 to 4.5%. B and C in the range of 4 to 5% of the total weight of the tablet.



(A)Response Plot **(B) Contour Plot**

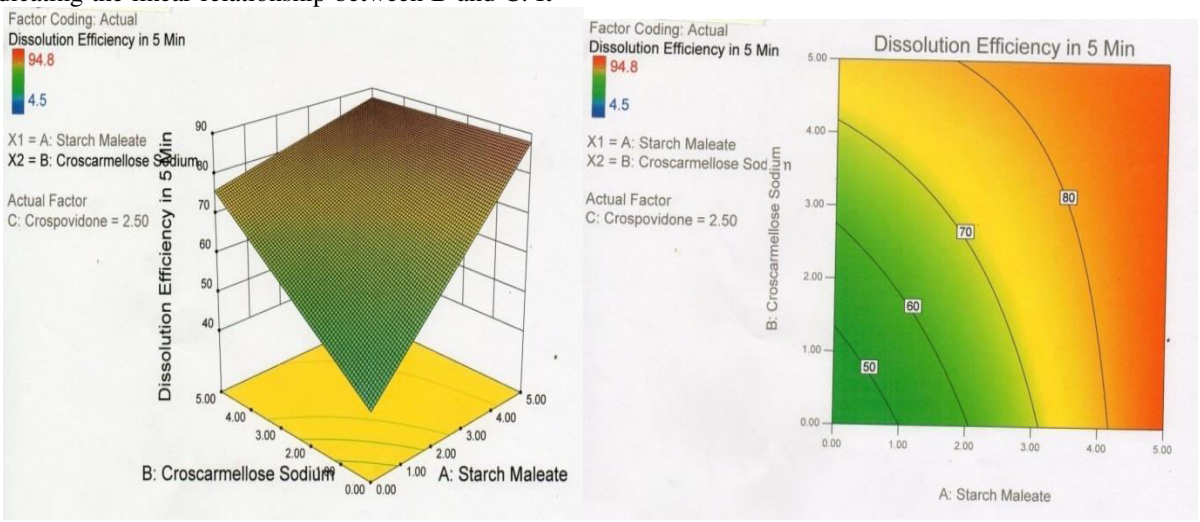
Fig. 7: (A) Response Plot (B) Contour Plot of Telmisartan Fast Dissolving Tablets (Effect of Croscarmellose sodium and Crospovidone on Percentage Dissolved in 5 min)



A)Response Plot **(B) Contour Plot**

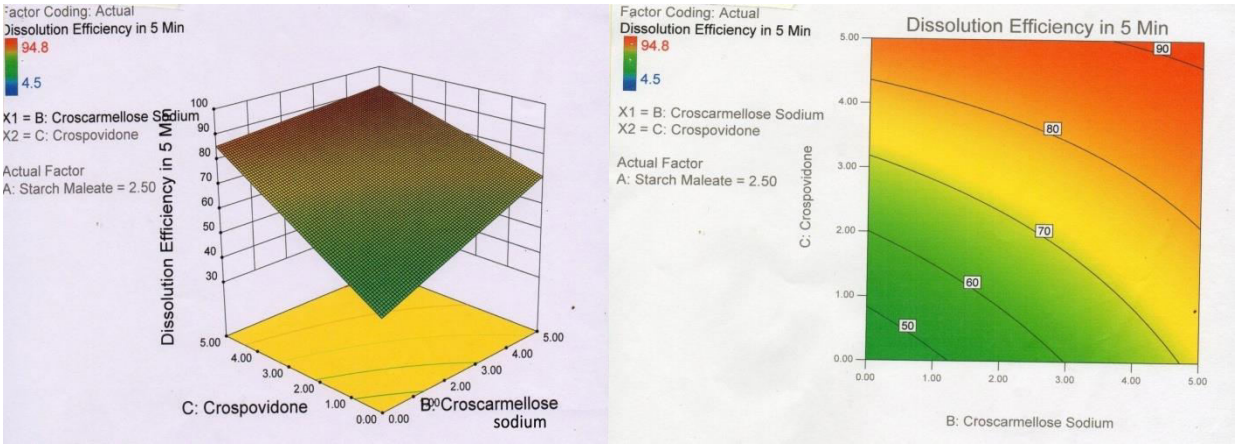
Fig. 8: (A) Response Plot (B) Contour Plot of Telmisartan Fast Dissolving Tablets (Effect of Crospovidone and Starch Maleate on Percentage Dissolved in 5 min)

The response surface plot and the contour plots reveal that as a concentration of A, B, C increases dissolution efficiency in 5 min increases. The effect of A and B on dissolution efficiency in 5 min are shown in **Fig 9**. The contour plots were found to be linear was determined from the contour plot **Fig 9** that more dissolution efficiency in 5 min obtained with A level range between 4 and 5% and B level range 4 to 5%. The effects of B and C are shown in **Fig 10**. The contour plots were found to be linear indicating the linear relationship between B and C. It was determined from the contour plot **Fig 10** that more dissolution efficiency in 5 min can be obtained with B level range between 4 and 5% and C level range 4 to 5%. The effects of A and C are shown in **Fig 11**. The contour plots were found to be linear indicating the linear relationship between A and C. It was determined from the contour plot more dissolution efficiency in 5 min can be obtained in A level range between 4 and 5% and C level range between 4 to 5%.



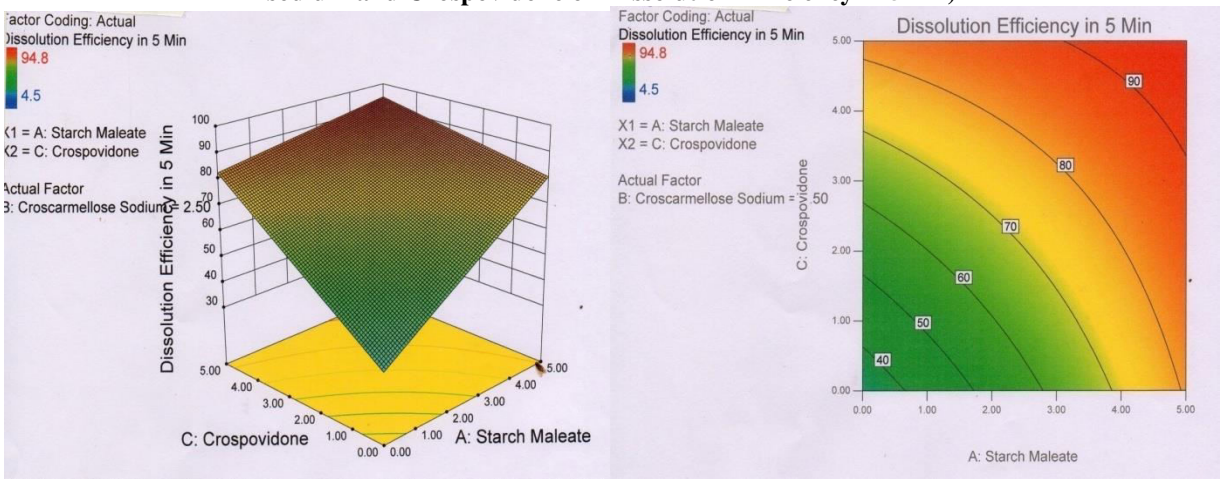
(A)Response Plot **(B) Contour Plot**

Fig. 9: (A) Response Plot (B) Contour Plot of Telmisartan Fast Dissolving Tablets (Effect of Starch Maleate and Croscarmellose sodium on Dissolution Efficiency in 5min)



(A)Response Plot **(B) Contour Plot**

Fig. 10: (A) Response Plot (B) Contour Plot of Telmisartan Fast Dissolving Tablets (Effect of Croscarmellose sodium and Crospovidone on Dissolution Efficiency in 5min)



(A)Response Plot **(B) Contour Plot**

Fig. 11: (A) Response Plot (B) Contour Plot of Telmisartan Fast Dissolving Tablets (Effect of Starch Maleate and Crospovidone on Dissolution Efficiency in 5min)

Stability Studies:

No visible changes were observed in the optimized fast-dissolving tablet of Telmisartan after storage. Drug dissolved from the fast dissolving tablet were evaluated before and after storage in each case. No significant difference (P> 0.05) was observed in the percent drug content before and after storage for 6 months. The drug dissolution profiles of the fast dissolving tablet before and after storage are shown in**Table:9** and **Fig 12**. The drug release characteristics of the formulation tested remained unaltered during the storage period. The results, thus, indicated that the drug content and drug release rate of the fast dissolving tablets formulated employing Starch Maleate were quite stable.

Table 9: Drug Releasing Profiles of Telmisartan Before and After Storage For 6 Months During Stability Testing

Time (Min)	Percent Telmisartan Dissolved (x ± s.d)	
	Before storage	After 6 months
1.	99.78±0.21	96.25±0.41

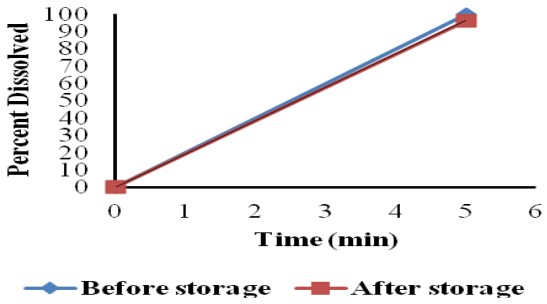


Fig.No.12 Stability Studies of Telmisartan Fast Dissolving Tablets

From the above data, the ideal concentrations of the superdisintegrants that are to be used in fast dissolving tablets to have more percent dissolved in 5 min and more dissolution efficiency in 5 min is factor (A) i.e., Starch Maleate 4%, factor (B) i.e., Croscarmellose sodium 5% and factor (C) i.e., Crospovidone 5% were found to be ideal.

CONCLUSION:

Fast dissolving drug delivery is a topic of current interest in pharmaceutical technology. In the present investigation Starch Maleate, a new polymer was prepared and evaluated for its application as superdisintegrant in fast dissolving dosage form. **Starch Maleate was found to be a better superdisintegrant with the Telmisartanand hence it could be used in the formulation of fast dissolving tablets** to provide fast dissolving release of the contained drug for 10 minutes. Drug release characteristics of the fast dissolving tablets formulated employing starch Maleate were quite stable and remained unaltered when subjected to accelerated stability testing at $40^0 \pm 2^0$ C and 75% RH for 6 months.

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