ISSN No:-2456-2165

Studies on Formulation and in-Vitro Evaluation of Mouth Dissolving Tablets Containing Telmisartan by using Box-Benkhen Design

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Abstract:- New era is an era of novel drug delivery systems. Pediatric, Geriatric and bed ridden patients have difficulties in swallowing tablets. The purpose of the present study was to develop and characterize mouth dissolving tablets of Telmisartan by using direct compression technique. Formulations were designed by factorial design technique. Sodium Saccharine, Cross povidone and Banana powder were used as a superdisintegrants while microcrystalline cellulose was used as diluents. The powder blends were prepared and evaluated for the properties such as angle of repose, loose bulk density, tapped bulk density, carr's compressibility index and hausner's ratio. Tablets were evaluated for hardness, friability, drug content, disintegration time, water absorption ratio, in vitro drug release in methanol. Formulation containing Crospovidone and Sodium Saccharine in higher concentration showed a rapid disintegration, wetting and in vitro drug release as compared to other formulations. Dispersion time indicate complete dispersion of formulation . Quick dispersion of formulations favours fast disintegration of formulations. The perturbation plot shows the super disintegration has the major contribution on prepared dosage form .

Keywords-*: Direct compression; Factorial design; Telmisartan; Mouth dissolving tablets; Super disintegrants*

I. INTRODUCTION

Drug delivery via the oral mucosa is a promising route, when one wishes to achieve a rapid onset of action or improved bioavailability for drugs with high first-pass metabolism. Nearly 35% of general, especially the elderly patients and children suffer from Dysphagia or difficulty in swallowing, which results in the incidence of non compliance and ineffective therapy. Box benkhen design is suitable for exploration of quadratic response surfaces and construction of second-order polynomial models, thus helping to optimize the process uusing a small number of experimental runs. Total of 13 runs one replicated center points of a cubical design region. During the run, the tablets were evaluated for physiochemical characterization and responses were recorded. In our study it measures the DT, and in response to that the polynomial regression equation was plotted and tested for the significance.

After generating the polynomial equations relating the dependent and independent variables, the process was optimized to obtain the levels of A,B, and C, which gives optimum values of Y at constrained conditions. To verify these values, a new formula was prepared according to the predicted levels of A,B, and C. Then, the tablet was prepared as per the optimized value and compared with the predicted value. Formulation of MDT includes formulation by box-behnken experimental design, procedure formulations.

Evaluation of MDT includes physic-chemical properties of tablets, wetting time, water absorption ratio, test for dispersion time, In-vitro dissolution studies and include stability studies.In the present study MDT of Telmisartan were prepared by using different superdisintegrants as cross povidone, sodium saccharine, banana powder in different concentration. Thirteen formulations were going to designed using higher and lower level of super disintegrants and employing combination of two superdisintegrants at a time. Tablets were prepared by direct compression technique.

A. Objective

The objective of the present work has to develop and evaluate the MDT in order to get rapid disintegration and dissolution.

To study the physio-chemical properties of natural banana powder.

To perform compatibility studies to investigate drug super disintegrants interaction by FT-IR.

II. MATERIALS AND METHODS

The chief material telmisartan were brought from salmirra pharmaceuticals where as cross povidone, sodium saccharin, mannitol, magnesium stearate, talc, mcc were brought from solistaa pharmaceuticals, and banana powder were self made. Electronic balance, bulk density apparatus, friability apparatus, etc.. were brought from different companies.

Year of experimentation : 2022

Site : Adhiparasakthi college of pharmacy

Methods implied for collection of data:

ISSN No:-2456-2165

III. PRE-FORMULATION STUDIES

A. Determination of absorption maximum of Telmisartan in methanol.

A stock solution of Telmisartan was prepared by dissolving 10 mg of drug in methanol and final volume was made upto 10 ml. A dilution of 10 micro gram per ml was kept in cuvette. The solution was scanned in the range of wavelength 200-400 nm. The UV spectrum showing lambda max was recorded using double beam UV-Visible spectrophotometer.

B. Preparation of standard curve of Telmisartan in methanol.

A stock solution of Telmisartan was prepared by dissolving 10 mg of drug in methanol and final volume was made upto 100 ml. The solutions in concentration range of 2-10 micro gram per ml were prepared by appropriate dilution of stock solution. The UV absorbance's of these solutions were determined spectrophotometrically at lamda max 296 nm using double beam UV-Visible spectrophotometer.

C. Drug superdisintegrants compatibilty studies

Fourier transform infra red spectroscopy (FT IR) study Drug superdisintegrants interaction studies are very important in designing a formulation. Telmisartan powder was mixed with various super disintegrants in the ratio of 1:1 and then afterwards the samples were scanned with FTIR (Perkin elmer-pharmaspec-1) over a wave number range of 4000-400 cm.

IV. FORMULATION OF MOUTH DISSOLVING TABLETS

Formulation by Box-Benkhen experimental design (Design expert, version 12)

Factor	Name	Unit	Low	High
A	Cross povidone (CP)	mg	4	10
B	Banana powder	mg	4	8
C	Sodium Saccharine (SS)	mg	0.4	1

Table 1: Formulation designing

V. PROCEDURE FOR FORMULATIONS DESIGNING

Box-Benkhen experimental design technique was used for formulation designing. Three formulation factors were found to have significant effect on the flowability, compressibility of powder prepared by direct compression method and hence the characters of the compressed tablets. These factors are present of the cross povidone was used in concentration of 2-5%, banana powder was used in 2-4%, sodium saccharine was used in 0.2-0.5%. Each formulation was composed with drug and excipients as shown in table.

During the run, the tablets were evaluated for physiochemical characterization and responses were recorded. In our study, it measured the DT, and in response to that the polynomial regression equation was plotted and tested for the significance. After generating the polynomial equations relating the dependent and independent variables, the process was optimized to obtain the levels of A,B, and C, which gives optimum values of Y at constrained conditions.

To verify these values, a new formula was prepared according to the predicted levels of A,B, and C. Then, the tablet was prepared as per the optimized value and compared with the predicted value.

VI. EVALUATION OF MOUTH DISSOLVING TABLETS .

A. Physico-chemical properties of tablets.

It includes appearance, dimension (thickness and diameter), weight variation test, hardness, friability tests.

B. In vitro dissolution studies .

In vitro drug release studies for the mouth dissolving tablets of Telmisartan was studied using dissolution test apparatus USP-Type II (Dissolution test apparatus paddle type) for the fabricated batches with the rotation speed of 50 rpm using phosphate buffer pH 6.8 as the dissolution medium maintained at a temperature of 37±0.5·C. Samples were withdrawn at predetermined time interval (02 mins) and filtered through whatman filter paper, diluted suitably and analyzed at 296 nm using a double beam UV-Visible spectrophotometer. The dissolution experiments were conducted in triplicate.

C. Disintegration time

The process of breakdown of a tablet into smaller particles is called as disintegration. One tablet in each of the 6 tubes of the basket is to be placed and the apparatus subjected to run. The assembly should be raised and lowered between 50 cycles per minute. The time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded.

D. Test for dispersion time

In vitro dispersion time was measured by dropping a tablet in a measuring cylinder containing 6 ml of phosphate buffer pH 6.8 (simulated saliva fluid). The time for the tablet to completely disintegrate into fine paricles was noted. Three tablets from each batch were randomly selected and in vitro dispersion time were performed.

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VII. RESULTS AND DISCUSSION :

A. *Pre-formulation studies*

Fourier-Transform Infra-Red spectroscopy.

I R spectrum of Telmisartan is shown in following graph.

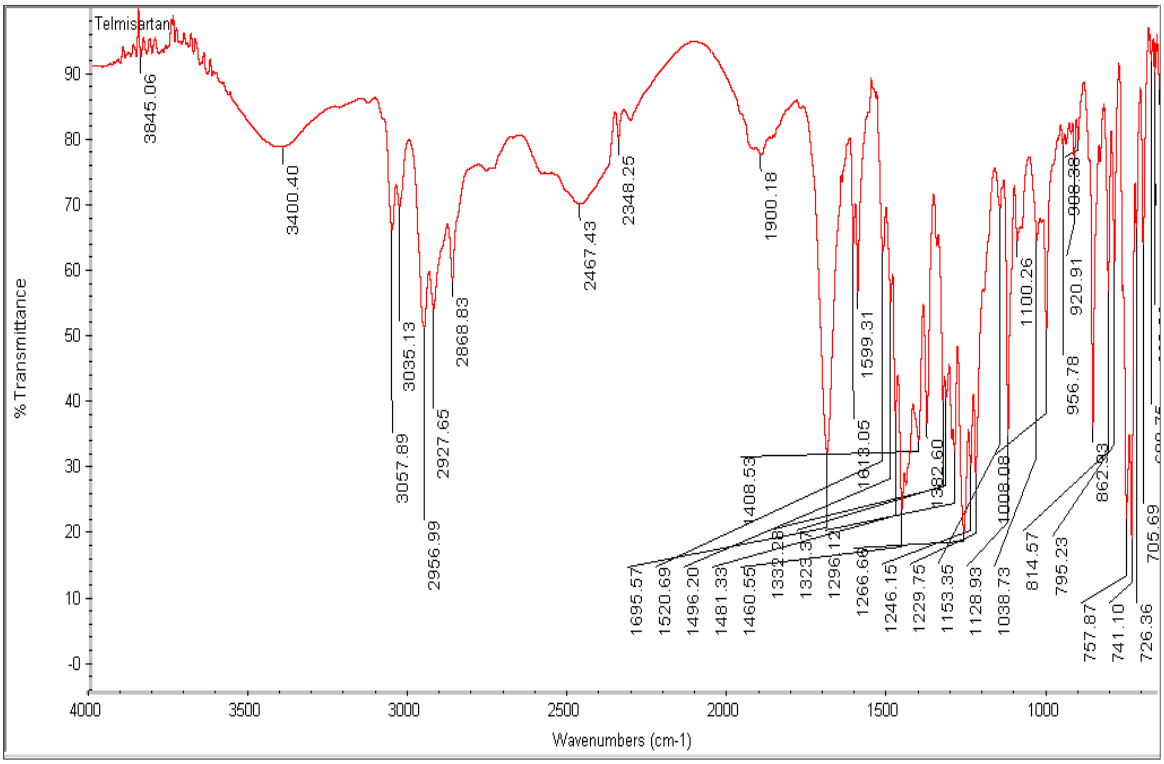

Fig. 1: FT-IR Spectrum of Telmisartan Drug super disintegration compatability studies

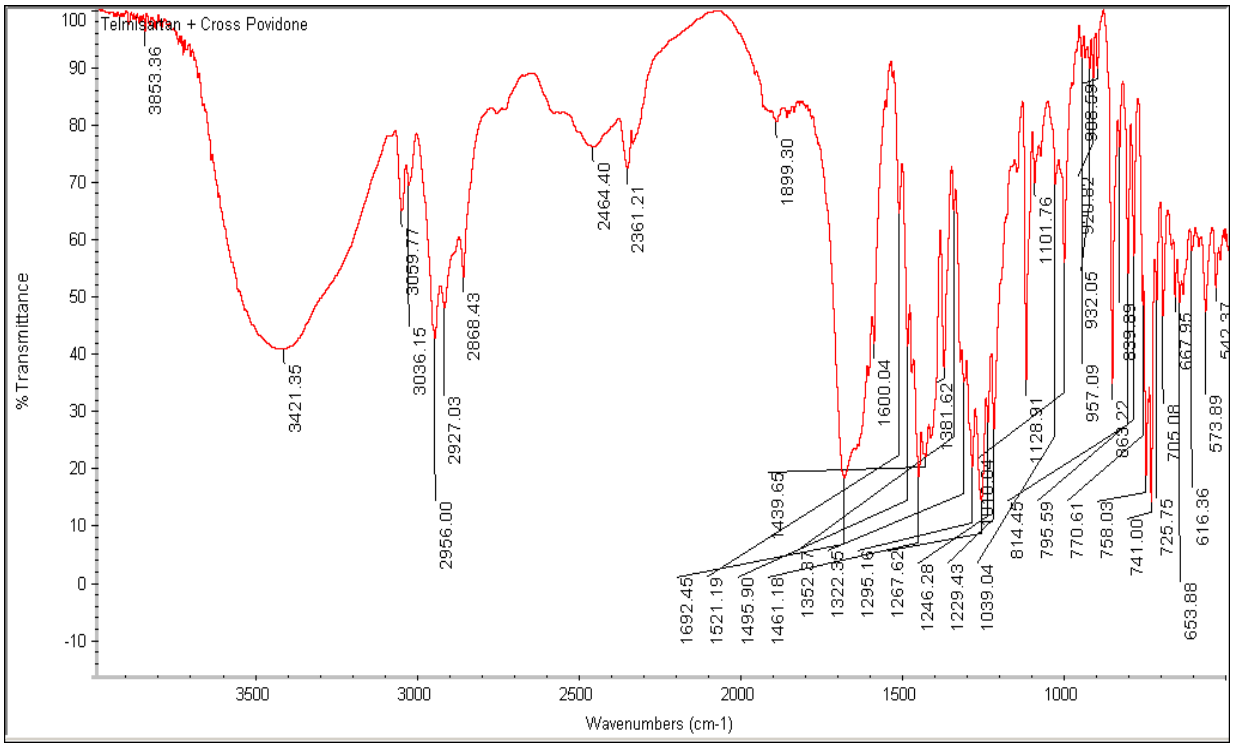

Fig 2: FT-IR spectrum of Telmisartan+ Crosspovidone

ISSN No:-2456-2165

B. Evaluation of Mouth Dissolving Tablets.

Formulation code	Thickness (Mm)	Weight Variation (%)	Hardness (Kg/cm^2)	Friability (%)	Drug Content (%)
F1	2.443±0.001	204.85±.1.46	3.1±0.06	0.22±0.01	99.79±0.80
F2	2.443±0.002	204.34±.0.94	3.16±0.08	0.22±0.00	99.46±0.90
F3	2.442±0.002	205.65±.0.56	3.13±0.06	0.21±0.01	99.18±0.85
F4	2.443±0.001	202.62±.1.22	3.07±0.04	0.22±0.01	99.94±0.41
F5	2.444±0.001	203.51±.1.34	3.06±0.03	0.22±0.01	100.33±0.84
F6	2.443±0.002	202.36±.1.36	3.17±0.07	0.22±0.00	100.63±0.08
F7	2.443±0.003	202.59±.0.87	3.22±0.05	0.21±0.01	99.81±0.45
F8	2.445±0.000	202.65±.2.29	3.20±0.05	0.22±0.01	99.54±0.96
F9	2.442±0.001	204.26±.0.86	3.09±0.08	0.22±0.01	100.1±0.73
F10	2.443±0.001	202.35±.0.49	3.14±0.11	0.21±0.00	100.2±0.09
F11	2.444±0.002	204.09±.1.23	3.12±0.02	0.21±0.01	100.25±0.25
F12	2.442±0.002	203.99±.1.77	3.12±0.02	0.22±0.01	100.41±0.37
F13	2.444±0.001	204.26±.0.48	3.10±0.09	0.20±0.00	99.85±0.33

Table 2 : Evaluation of Physico-chemical properties of tablets.

Formulation code	Time (sec)
F1	60±0.52
F2	55±0.53
F3	50±0.53
F4	40±0.00
F5	10±0.40
F6	12±0.53
F7	45±0.53
F8	51±0.52
F9	13±0.52
F10	14±0.53
F11	21±0.51
F12	24±0.55
F13	31±0.00

Table 3: Disintegrating time of mouth dissolving tablets

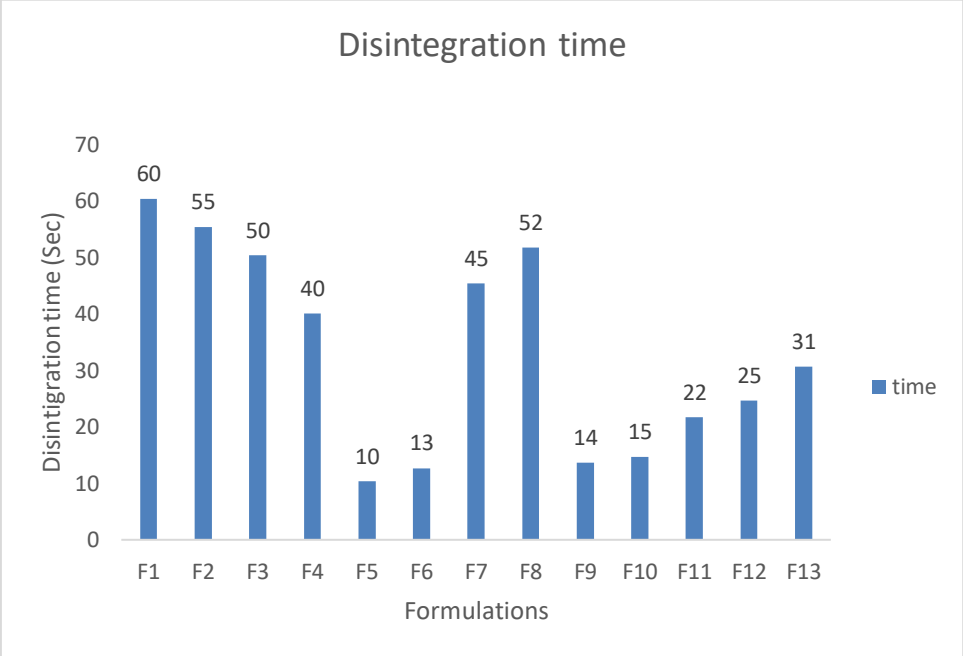

Fig. 3: Comparision of Disintegration time of Mouth dissolving Tablets.

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C. In-vitro dissolution profile of tablets.

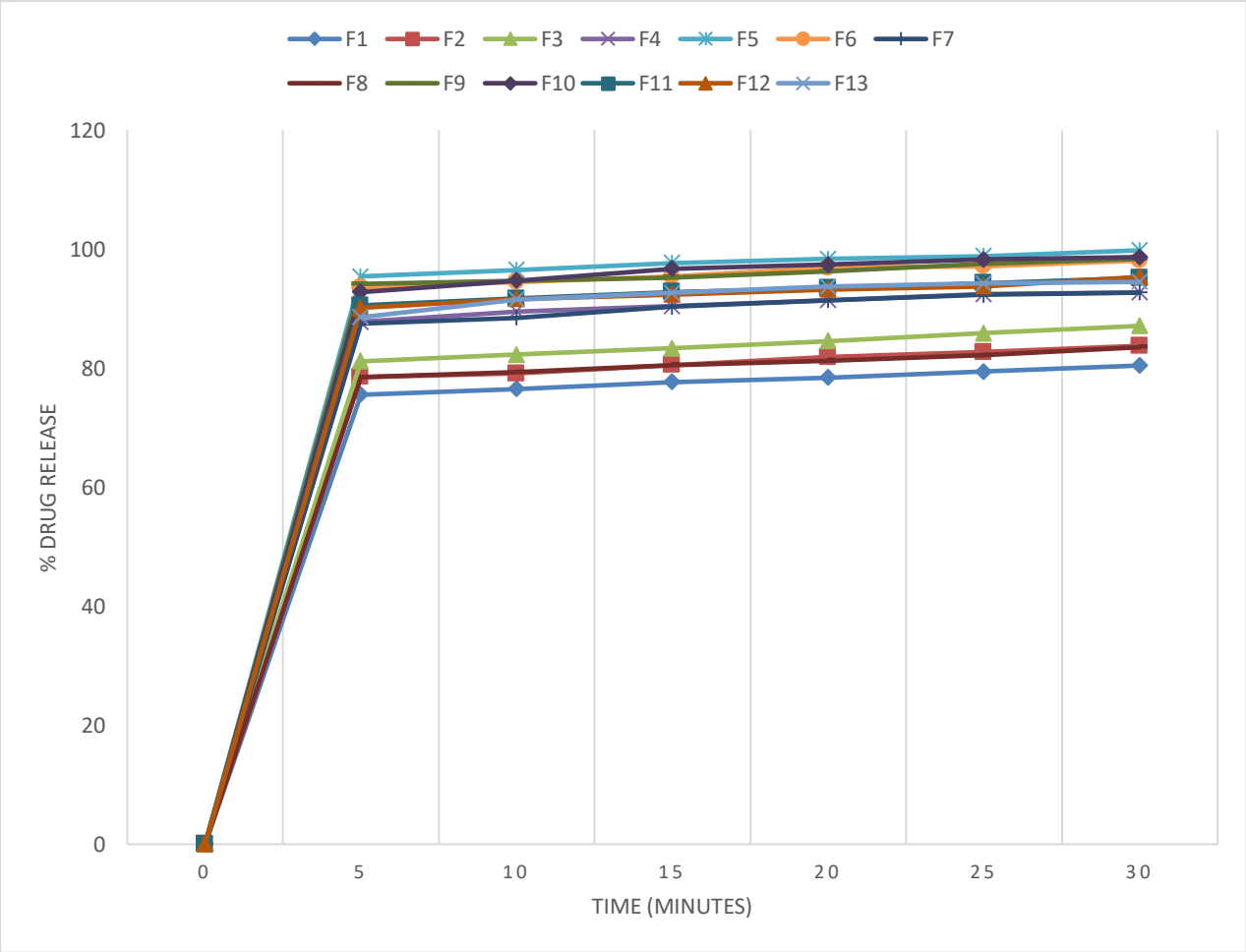

Fig. 4: Comparitive % release of Telmisartan from F1 to F13.

Dissolution study shows that almost all the drug released within the 15 minutes from all the formulations.

From dissolution data it can be observed that formulation F5 showed the highest percentage of drug release. This may be due to the optimum concentration of natural banana powder used in the formulations. The above figure shows the dissolution profile of MDT in the Ph 6.8 phosphate buffer as a dissolution medium.

D. Box-Benken Experimental Design

Run	Factor 1 A:Cross povidone (mg)	Factor 2 B:Banana (mg)	Factor 3 C:Sodium saccharine (mg)	Response 1 Disintegration time (sec)
1	4	4	0.7	60
2	4	6	0.4	55
3	4	8	0.7	50
4	7	4	1	40
5	10	8	0.7	10
6	10	6	1	13
7	7	4	0.4	45
8	4	6	1	52
9	10	6	0.4	14
10	10	4	0.7	15
11	7	8	1	23
12	7	8	0.4	25
13	7	6	0.7	31

Table 4: Experimental runs and observed value of response for BBD

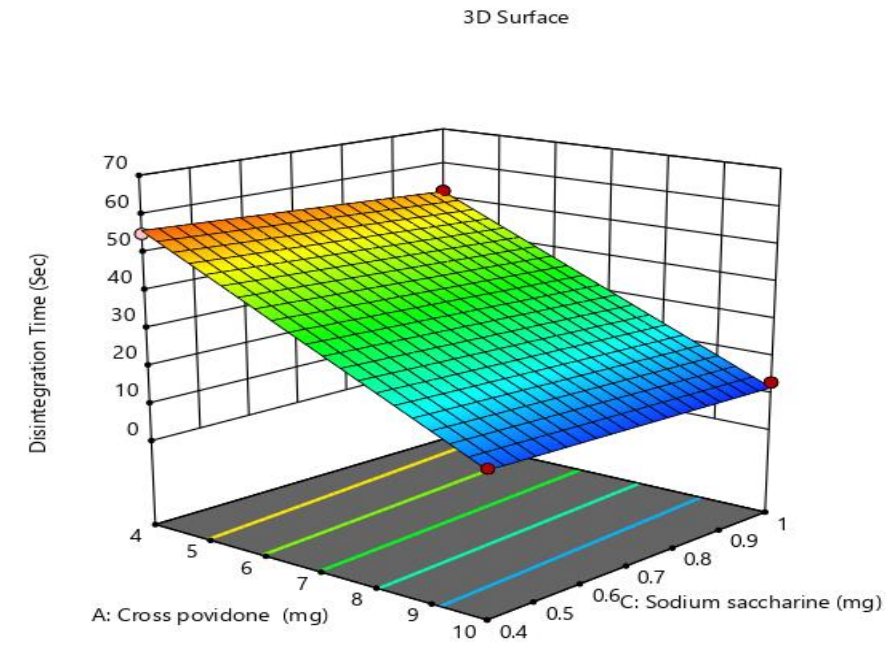

Fig. 5: 3D response surface plot showing the effect of A and C on response Y (disintegration time)

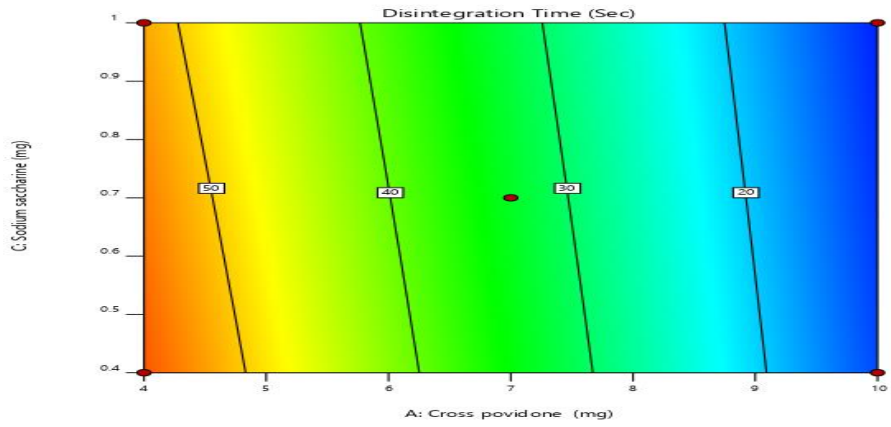

Fig. 6: Contour plot showing the effect of A and C on response Y (disintegration time)

E. Perturbation plot

The perturbation plot helps to compare the effects of all the factors at a particular point in the design space. The response is plotted by changing only one factor over it's range while holding all the other factors constant. The plot was plotted by design expert version 12 software. This plot provided the information releated to significant contribution and effect of factors to response. It observed that the effect of super disintegrant had major contribution on prepared dosage form as found in fig 6.

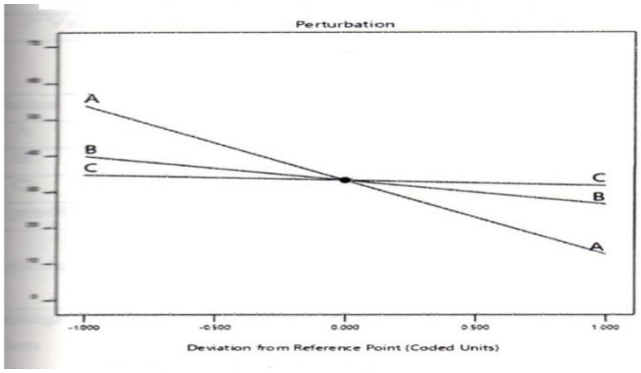

Fig. 7: Perturbation plot showing the deviation from the refrence point

ISSN No:-2456-2165

VIII. CONCLUSION

MDT's found to be brilliant drug delivery system for geriatric, pediatric, bed ridden, psychotic patients and those patients who are busy in travelling, has difficulty in swallowing and may not have access to water, MDT's offer many advantages over the conventional oral tablets. They require small amounts of active ingredients to be effective. The major advantages are quick absorption, rapid onset of action, improved bioavailability than regular tablet and capsule.

ACKNOWLEDGEMENTS

The authors are sincerely thankful to Adhiparasakthi college of pharmacy, Melmaruvathur, Kancheepuram, for providing us infrastructure facilities and moral support to carry out this research work. I sincerely express my gratitude to saimirra pharmaceutical private limited for providing telmisartan and solistaa pharmaceuticals private limited for providing cross povidone, sodium saccharine, mannitol, talc and magnesium stearate.

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