International Journal of PharmTech Research
CODEN (USA): IJPRIF, ISSN: 0974-4304, ISSN(Online): 2455-9563
Vol.14, No.02, pp 268-276, 2021

Formulation and Evaluation of Fenugreek Mucilage Based FastDissolving Tablet of TeneligliptinHydrobromide by Using 3^2 Factorial Design

Rahul Jodh*, Mukund Tawar, Monali Muneshwar, Sudarshan Behere

Department of Pharmacology, P.R.Pote College of Pharmacy, Amravati-444602 MH, India
Department of Pharmaceutics, P.R.Pote College of Pharmacy, Amravati-444602MH, India
Contact No: +91-9766938363, E-mail: jodhrahul@gmail.com

Abstract : Current research is focused on formulation and evaluation of natural gum based fast dissolving tablet of TeneligliptinHydrobromide by applying 3^2 factorial designs for the improvement of the drug absorption.Direct compression method was used. Two factors as independent variable (x_1) Fenugreek mucilage(x_2) sodium saccharin glycolate were taken with three level (+1, 0,-1). The level two factors were selected on basis of preliminary experiments conducted and their effect on dependent variable (disintegration time) was estimated. Formulated tablets were evaluated for parameters in which the values were found to be in the range of hardness 2.1-2.6 kg/cm^2, thickness 2.227-2.296 mm, weight variance 182-196 mg, wetting time 58-68 seconds, water absorption ratio 0.1628-0.2439, disintegration time 56 sec – 9 min, and friability 0.53-0.68 %. The software design expert (11.0) was used for getting experimental design, modeling the response surface and calculating the static evaluation.The tablet parameters tests of formulation (F1 to F10) were observed within prescribe limit. Disintegration time observed 56 seconds, % cumulative drug release 88.79 % to 98.90 %. Batch F6 was observed as promising batch.
Key Words : TeneligliptinHydrobromide, Fenugreekmucilage powder, Fast Dissolving tablets, Pharmaceutical excipients.

Introduction

A tablet is a pharmaceutical dosage form. Tablets could also be defined because the solid unit dose style of medicine or medicaments with or without appropriate excipients and prepared either by molding or by compression. Quick dissolving tablet is that the most generally used dosage type due to its convenience in terms of self- administration, compactness, and ease in producing. Beneficial in cases like nausea, suede episodes of allergic attack or coughing, wherever an extremist fast onset of action needed. An enhanced bioavailability,

DOI= http://dx.doi.org/10.20902/IJPTR.2021.140224

bioavailability, notably in cases of insoluble and hydrophobic medicine, because of fast disintegration and dissolution of that tablets[1-2]. Stability for extended length of time, since the drug remains in solid dose kind until it's consumed. So, it combines advantage of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability. Fenugreek Mucilage are used as thickeners and flavoring for different foods. These polysaccharides, when extracted in water, can result in a highly viscous solution with slimy appearance[3].

Material and Method:

TeneligliptinHydrobromide was procured from Yarrow Chem, Mumbai, Fenugreek Seeds were procured from the local market, Sodium starch glycolate Magnesium Stearate, Mannitol, Talc was procured from S.D. Fine Pvt.Ltd, Mumbai, Vanillin and Micro Crystalline Cellulose was procured from, Rankem, Mumbai. All other chemicals used were of analytical grade.

Method of Extraction:

Fenugreek seeds were collected from local market. Collected seeds were carefully washed and dried under shade for 24 h, further dried at 30– 40°C until constant weight was obtained. Size was reduced through grinder. Powdered seeds were passed through sieve no. #22 and stored it in air tight container for further use. Extraction of mucilage includes two steps[4-5].

Step1: Extraction of Mucilage:

Powdered seeds kept in 500ml of distilled water. Heated with continuous stirring at 60°C for approximately 4h. Concentrated solution was filtrated through muslin cloth and cool at 4°C-6°C.

Step2: Isolation of Mucilage:

Extracted mucilage was isolated in acetone. This allows filtration through muslin cloth. Washed with acetone and the mucilage filtrated through muslin cloth. Processed mucilage was further dried to constant weight at 35–45°C in hot air oven. Hard mucilage cake was grinded and sieved through sieve # 22, stored in desiccators for further used.

Characterization of Fenugreek Mucilage

Swelling Ratio:

One gram of mucilage was placed into a 25ml glass stopper measuring cylinder. 25 ml of water was added into the cylinder containing mucilage and mixture was shaken thoroughly at intervals of every 10 min for 1 h. The sample was allowed to stand for 3 hr at room temperature and volume occupied by mucilage was measured. The mean value was calculated, related to 1 g of mucilage[7].

Preparation of Fast Dissolving Tablet Using Drug TeneligliptinHydrobromide:

The superdisintegrant and gum in different ratios were used to prepare the tablets. All the ingredients were shown in Table 1 were passed through sieve no. 60.The total 10 formulations (F1–F10) were prepared using different concentrations of Fenugreek mucilageand sodium starch Glycol ate to study its effect on disintegration time[8-9].

Preparation of Factorial formulation with the corresponding formulation is outlined in Table 2 and 3. The effect of the independent variables, viz., Fenugreek mucilage(X_1) and SSG (X_2) on the dependent variable.Preparation of Factorial formulation with the corresponding formulation is outlined here.The effect of the independent variables, viz., Fenugreek mucilage(X_1) and SSG (X_2) on the dependent variable, Disintegration time range 11 to 58sec.

Data Analysis by Design Expert Software a 3^2 full factorial design was used. In this design 2 factors were evaluated, each at 3 levels and experimental trials were performed at all 9 possible combinations. The amount of Fenugreek mucilage(X_1) and the amount of SSG (X_2) was selected as independent variables. The disintegration time was selected as dependent variable. A polynomial term was used to evaluate the responses.

$Y = b0 + b1X_1 + b2X_2 + b11X_1X_1 + b22X_2X_2 + b12X_1$

Where, y is the dependent variable, b0 is the arithmetic mean response of the 9 runs, and b1 is the estimated coefficient for the factor X_1. The main effects (X1 and X2) the common results of dynamical one factor at a time from its low to high price. The interaction terms (X1X2) show however the response changes once 2 factors are at the same time modified.The polynomial terms (X_1X_1 and X_2X_2) are included to investigate nonlinearity.

Final Equations in Terms of Coded Factors

$DT = -0.00111 + 0.148333\ X_1 - 0.19833X_2 - 0.255(X_1X_2) + 0.351667(X_1)2 + 0.361667\ (X_2)^2$

Final equations in Terms of Actual Factors

$DT = -0.00111 + 0.148333Gum - 0.19833SSG - 0.255Gum*SSG + 0.351667(Gum)^2 + 0.361667\ (SSG)^2$

The above equation revealed the effect of independent variables on the desired response. The regression coefficient values are the estimates of the model fitting. The r^2 was high indicating the adequate fitting of the quadratic model. The polynomial equations can also be used to draw conclusions considering the magnitude of co-efficient and the mathematical sign it carries; i.e. positive or negative. The positive coefficient of variable X_1 i.e. Fenugreek mucilage, the response of disintegration time showed an increase in the A1 and A9 value with the increase in the gum concentration. The second variable X_2 i.e. SSG, responses showed positive coefficient for response A1 and A2, respectively.ANOVA for the dependent variables A1 and A 9 respectively are performed. ANOVA and Multiple regression analysis were done using Design Expert 11.0 software.The main effect of A and B represents the average result of changing variables at a time from its low level to high level. The interaction terms (AB, A^2, and B2) reveal the A1 and A10 changes when the two variables are simultaneously changed. The negative coefficient for the independent variable (B, B^2), (B, AB, A^2, B^2) and (B, B^2), (B, AB) indicate unfavorable effects on the Fast Dissolving Tablet (A1 and A9), respectively. The independent variables exhibit positive interaction which indicates the favorable effect on the Fast Dissolving[10].

The variance Inflation Factor (VIF) measures how much the variance of that model coefficient is inflated by the lack of orthogonality in the design and calculated for fast dissolving tablet (A1 and A9) respectively, which is found to be 1 indicating good estimation of coefficients. Similarly, Ri-squared is near to zero which is leading to good model. The model F value calculated for fast dissolving tablet (A1 and A9) respectively, are found to be 2.53, and there are only 5-10% chance of large lack of fit F value which could be due to noise and non significant lack of fit F value is good fit of model. In all cases "Pred R-squared" values are in reasonable agreement with the "Adj R-squared" values. The Adeq-Precision is the measures of the signal to noise ratio. A ratio> 4 is desirable. In the case of Fast Dissolving Tablet, the Adeq-Precision value is in range of 5.3670 which indicates an adequate signal[11].

Table 1: Preparation of Fast Dissolving Tablet

Ingredients (mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**
TeneligliptinHydrobromide	20	20	20	20	20	20	20	20	20	20
Gum	1	2	3	4	5	6	7	8	9	10
Sodium Starch Glycolate	10	9	8	7	6	5	4	3	2	1
Magnesium Stearate	5	5	5	5	5	5	5	5	5	5
Mannitol	25	10	10	10	10	10	10	10	10	10
Talc	5	5	5	5	5	5	5	5	5	5
Meglumine	2	2	2	2	2	2	2	2	2	2
MCC	67	67	67	67	67	67	67	67	67	67

Table 2: Variable with coded value in factorial design

Coded factor	Level	Factor	
		Factor (x_1) (%w/w)	**Factor (x_2) (%w/w)**
-1	Low	3	0.5
0	Intermediate	4	1.5
+1	High	15	2.5

Table 3: Preparation of Factorial Formulation

Ingredients (mg)	**A1**	**A2**	**A3**	**A4**	**A5**	**A6**	**A7**	**A8**	**A9**
TeneligliptinHydrobromide	20	20	20	20	20	20	20	20	20
Gum	6	6	6	8	8	8	10	10	10
Sodium Starch Glycolate	1	3	5	1	3	5	1	3	5
Magnesium Stearate	5	5	5	5	5	5	5	5	5
Mannitol	10	10	10	10	10	10	10	10	10
Talc	5	5	5	5	5	5	5	5	5
Meglumine	2	2	2	2	2	2	2	2	2
MCC	71	69	67	69	67	65	67	65	63

Direct Compression:

Direct compression technique is that the easiest method to manufacture tablets. Conversional equipment, commonly available excipients and a limited number of processing steps are involved in direct compression. The ingredients were weighted and passed through #60 mesh separately in these method drugs with other excipient is mixed in mortal pestle geometrically and the mixture thus obtained is compressed into tablets through 6mm flat faced punch on pilot pressed 10 station machine tablet[11-12].

Factorial Design:

A 3^2 full factorial design was used. In this style 2 factors were evaluated, each at 3 levels and experimental trials were performed at all 9 possible combinations. The amount of Fenugreek mucilage(X1) and the amount of SSG (X2) was selected as independent variables. The disintegration time was selected as dependent variable. A polynomial term was used to evaluate the responses.

$$Y = b0 + b1X1 + b2X2 + b11X1X1 + b22X2X2 + b12X1$$

Where, y is the dependent variable, b0 is the arithmetic mean response of the 9 runs, and b1 is the estimated coefficient for the factor X1. The main effects (X1 and X2) represent the typical results of dynamic one factor at a time from its low to high price. The interaction terms (X1X2) show however the response changes once pair of factors is simultaneously modified. The polynomial terms (X1X1 and X2X2) are included to investigate nonlinearity[13-14].

Evaluation of Prepared Tablet[15-20]

Hardness:

Hardness of tablet is outlined as the force applied across the diameter of the tablet within the order to break the tablet. It is done by using hardness tester like Pfizer hardness tester or Monsanto tablet hardness tester.

Thickness:

Thickness of tablets is determined using vernier caliper. An average value is calculated by using tablets in n=3 and then the mean (±) standard deviation values of thickness are noted.

Weight Variance:

According to Indian Pharmacopoeia procedure for the calculation of uniformity of weight, twenty tablets are taken and their weight is recorded individually and collectively on an electronic weighing balance. The mean of the weight of tablet was determined from the total weight.

Wetting Time:

A piece of tissue paper is folded twice and is placed in a small petri dish containing 6ml of distilled water. A tablet is rigorously placed on the surface of the folded tissue paper and the time required for water to reach the topmost surface of the tablet is noted as the wetting time. Less is the wetting time, indicates more porous the tablet.

Water Absorption Ratio:

To measure Water absorption ratio of the Tablet, a piece of tissue paper isfolded twice and was placed in a small Petri dish (Internal Diameter is= 6.5 cm) containing 5 ml of Distilled water. Thetablet is placed on the paper, and the time for complete wetting of the tablet was measured in seconds.

Water absorption ratio was determined using the equation:

$$R = \frac{Wb - Wa}{Wa} \times 100$$

Where,*Wa*is weight of tablet before water test and*Wb*is weight of tablet after the test

Disintegration Time:

The test is carried out using the disintegration apparatus. Distilled water is used as a disintegration media and the time taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus is measured.

Friability:

Friability is measured of mechanical strength of tablets. Roche friabilator is employed to see the crumbliness by following procedure. A reweighed tablet is placed in the friabilator. Friabilator comprises a plastic chamber that revolves at twenty five revolutions per minute, dropping the tablets at a distance of six inches with every revolution. The tablets are revolved within the friabilator for four minutes for one hundred revolutions. At the tip of check, tablets are reweighed; the loss within the weight of tablet is that the measure of crumbliness and is expressed in share as;

$$\% \text{ Friability} = \frac{\text{Loss in weight}}{\text{Initial Weight}} \times 100$$

Result and Discussion:

Standard Calibration Curve:

The results of standard calibration curve reveals that the drug obeys beers lamberts law as the equation obtained was liner y = 0.042x-0.004 with the regression value of 0.998.

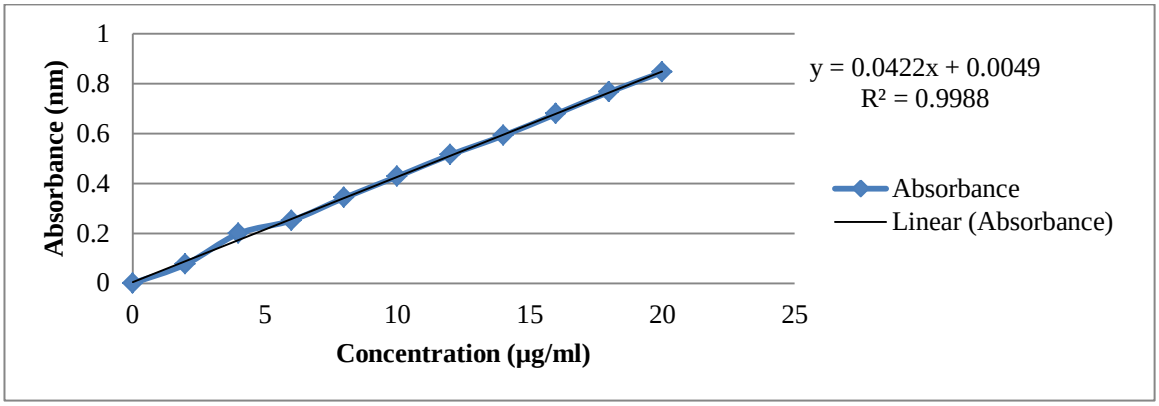

Fig 1: Standard Calibration Curve of Teneligliptin Hydrobromide

Evaluation Parameters of the Prepared Tablets:

The prepared tablets of TeneligliptinHydrobromide by direct compression were evaluated for the various parameters like Hardness in the range of 2.1-2.6 kg/cm^2, % Friability 0.53-0.68, Weight variance 182-196 mg, Thickness 2.227-2.296 mm, Wetting time 58-68 seconds, Water absorption ratio 0.1628-0.2439, Disintegration time 56 seconds – 9 minutes and % Drug content 79-99.87.

Evaluation of Tablets prepared by Factorial Design:

The prepared tablets of TeneligliptinHydrobromide by direct compression were evaluated for the various parameters like Hardness in the range of 2.1-2.6 kg/cm^2, % Friability 0.24-0.40, Weight variation 195.11-199.45 mg, Thickness 2.214-2.284 mm, Wetting time 0.23-1.6 seconds, Wetting absorption ratio 0.123-0.215, Disintegration time 0.11-0.58 seconds.

Table 4: Evaluation of Prepared Fast Dissolving Tablet

Formulation	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**
Hardness (kg/cm^2)	2.2	2.2	2.6	2.1	2.5	2.1	2.3	2.2	2.4	2.4
Friability (%)	0.61	0.68	0.59	0.53	0.63	0.25	0.64	0.58	0.67	0.56
Weight Variation (mg)	196	186	184	188	183	184	187	182	185	184
Thickness of Tablet(mm)	2.294	2.228	2.295	2.239	2.249	2.227	2.283	2.296	2.285	2.296
Wetting Time (second)	63 sec	64 sec	58 sec	66 sec	68 sec	60 sec	59 sec	58 sec	60 sec	64 sec
Water Absorption ratio	0.2436	0.2433	0.2251	0.2224	0.2223	0.2439	0.2228	0.2224	0.02235	0.1628
Disintegration Time	6 min	8 min	9 min	5 min	7 min	56 sec	3 min	9 min	6 min	59 sec
% Drug Content	98.15	95.47	93.5	97.56	93.58	99.87	93.47	94.53	98.41	97.54

Table 5: Evaluation of Factorial Formulation

Formulation	A1	A2	A3	A4	A5	A6	A7	A8	A9
Hardness (kg/cm^2)	2.2	2.6	2.1	2.5	2.3	2.2	2.4	2.2	2.1
Friability (%)	0.40	0.35	0.34	0.25	0.35	0.30	0.45	0.24	0.35
Weight Variation (mg)	199.31	195.12	196.53	199.31	196.45	199.32	199.45	197.32	195.11
Thickness of Tablet (mm)	2.229	2.236	2.254	2.244	2.284	2.276	2.214	2.234	2.248
Wetting Time (second)	1.6	0.23	0.52	0.39	0.23	0.26	1.26	0.39	0.51
Water Absorption ratio	0.154	0.123	0.154	0.215	0.184	0.154	0.184	0.153	0.153
Disintegration Time (sec)	0.56	0.19	0.58	0.32	0.29	0.11	1.5	0.22	0.50
% Drug Content	94.51	93.27	96.41	97.55	96.85	99.74	91.68	92.47	94.56

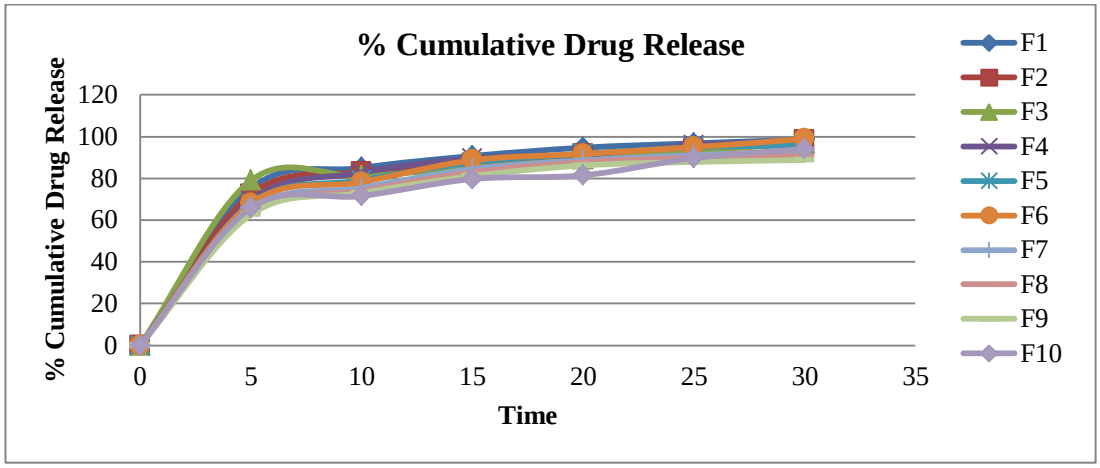

Fig 2: % Cumulative Drug Release of the Prepared Tablets

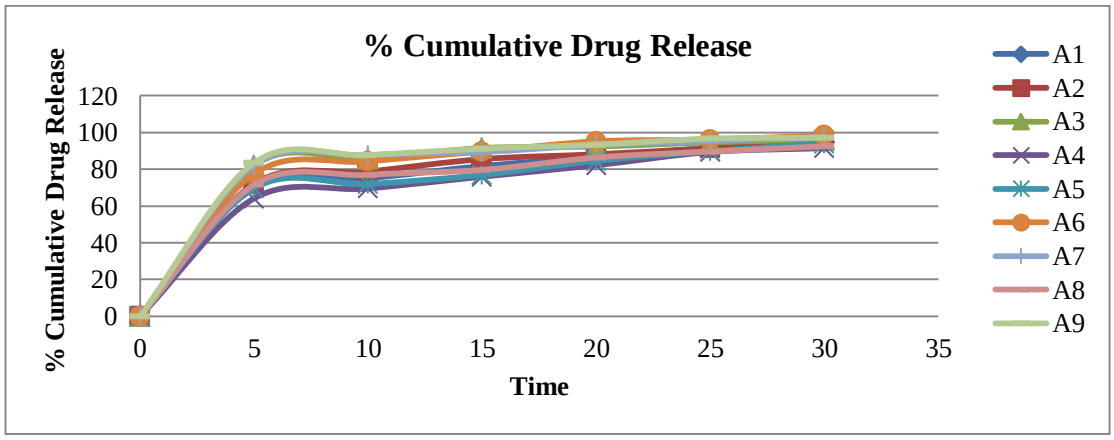

Fig 3: % Cumulative Drug Release of the prepared Factorial Batches

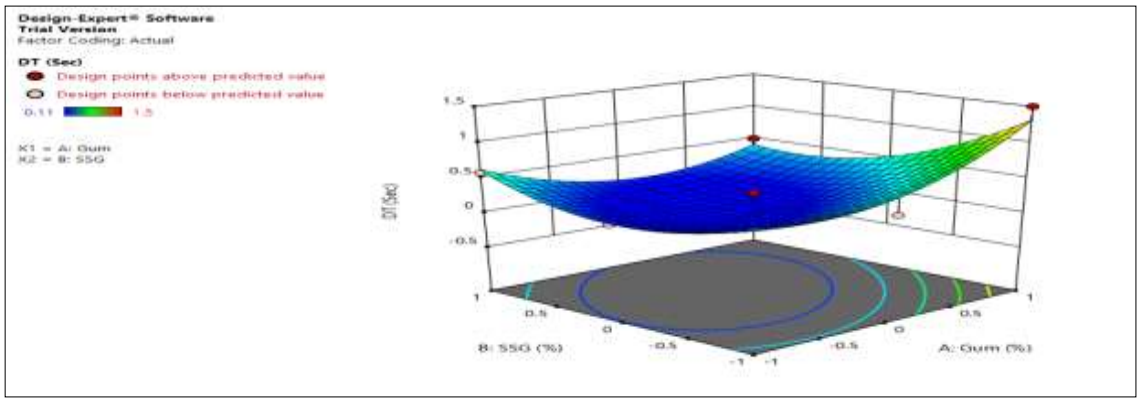

Fig 4: Response surface plot of Fast Dissolving Tablet on Disintegration Time

Discussion:

The prepared tablets of TeneligliptinHydrobromide with fenugreek mucilage powder as a superdisintegrant shows that the fenugreek mucilage can be a better alternative than the other synthetic disintegrants. The evaluation parameters of the tablets shows the satisfactory values as required in the terms of hardness, weight variation, friability, thickness, wetting time, water absorption ratio, drug content and the most important disintegration time was very low. The % drug release study shows that the drug release in the batch F6 was maximum i.e. 98.90 % and more than 50 % of the drug was released within 5 minutes with the maximum amount of drug content i.e. 99.87 with the disintegration time of 56 seconds. All these parameters shows that the batch F6 shows good results when compared to the other batches therefore, it was concluded that the batch F6 was the optimized batch.

Conclusion:

Preparation of fast dissolving tablet the superdisintegrant and gum in different ratios were used to prepare the tablets. The total 10 formulations (F1–F10) were prepared using different concentrations of Fenugreek mucilage and sodium starch glycolate to study its effect on,Hardness (kg/cm^2) 2.1 to 2.6, Friability (%) 0.53 to 0.68, Weight variation (mg) 182 to 196, Thickness of tablet (mm) 2.227 to 2.296, Wetting time (second) 58sec to 68sec, Water absorption ratio 0.1628 to 0.2439, Disintegration time range 56sec to 9min. The value of % cumulative drug release range 88.79% to 98.90%. From the present study, it can be concluded that natural super disintegrates like Fenugreek mucilage powder showed better disintegrating property than the most widely used synthetic super disintegrates like SSG in the formulations of FDTs and may be used as disintegrate in tablet formulations. The effect of different amount of complex and surfactant is used in different batches and the blending time for powder is also different for every batch.From this parameter the evaluation of tablet batches performed like wetting time, water absorption ratio, disintegration time, percent drug release.From the studies made it was found that batch F6 and F10 was having good disintegration time. The factorial design conclusively demonstrated use of response surface design of Fast Dissolving Tablet on Disintegration Time.

References:

1. Malviya V, Thakur Y, Gudadhe SS, Tawar M. Formulation and evaluation of natural gum based fast dissolving tablet of Meclizine hydrochloride by using 3 factorial design 2. Asian Journal of Pharmacy and Pharmacology. 2020;6(2):94-100.
2. Rajesh A, Manmeet K, Sangeeta A. Formulation and evaluation of fast dissolving tablet of Pioglitazone. Research Journal of Pharmacy and Technology. 2012;5(6):817-21.
3. Malviya VR, Pande SD, Bobade NN. Preparation and Evaluation of Sustained Release Beads of Zolmitriptan Hydrochloride. Research Journal of Pharmacy and Technology. 2019;12(12):5972-6.
4. Patel P, Kumar PA, Shah H, Patel N, Kheni P, Rao BS, Kulkarni SV, Babitha S. Formulation and Evaluation of Fast Dissolving Tablet of Telmisartan. Research Journal of Pharmacy and Technology. 2011;4(6):955-61.
5. Malviya VR, Pande SD. Road CKN. Preparation ad Evaluation of Zolmitriptan Hydrochloride

Lozenge. J Pharma Res. 2019;8(8):624-9.
6. Madoria N, Maheshwari Y. Formulation, Optimization and Characterization of Fast Dissolving Tablet of Celecoxib. Research Journal of Pharmacy and Technology. 2012;5(8):1085-8.
7. Malviya V, Ladhake V, Gajbiye K, Satao J, Tawar M. Design and Characterization of Phase Transition System of Zolmitriptan Hydrochloride for Nasal Drug Delivery System. International Journal of Pharmaceutical Sciences and Nanotechnology. 2020 May 31;13(3):4942-51.
8. Sharma S, Bharadwaj S, Gupta GD. Fast Dissolving Tablets of Promethazine Theoclate by Using Natural Superdisintegrants. Research Journal of Pharmacy and Technology. 2008;1(3):218-24.
9. Malviya VR, Tawar MG. Preparation and Evaluation of Oral Dispersible Strips of TeneligliptinHydrobromide for Treatment of Diabetes Mellitus. International Journal of Pharmaceutical Sciences and Nanotechnology. 2020 Jan 31;13(1):4745-52.
10. Kumar K, Chopra H, Sharma GK. Formulation and evaluation of fast dissolving tablet of montelukast by using co-processed excipients. Research Journal of Pharmacy and Technology. 2019;12(11):5543-8.
11. Malviya V, Manekar S. Design, Development and Evaluation of Aceclofenac and Curcumin Agglomerates by Crystallo Co-Agglomeration Technique. Research Journal of Pharmacy and Technology. 2021 Mar 18;14(3):1535-41.
12. Mahesh PG, Raman SG. Formulation and Evaluation of Fast Dissolving Tablet of Prasugrel. Research Journal of Pharmacy and Technology. 2021 Aug 1;14(8):4077-9.
13. Giri TK, Sa B. Formulation of rapidly disintegrating fast dissolving diazepam tablets using solid dispersions through a statistical approach. Research Journal of Pharmacy and Technology. 2010;3(4):1246-51.
14. Deshmukh SS, Quazi A, Saraf A. Formulation and Evaluation of Fast Dissolving Tablets of Chlorpromazine Hydrochloride Using Novel Co-processed Superdisintegrants. Research Journal of Pharmacy and Technology. 2012;5(9):1235-40.
15. Malviya V. Preparation and Evaluation of Emulsomes as a Drug Delivery System for Bifonazole. INDIAN JOURNAL OF PHARMACEUTICAL EDUCATION AND RESEARCH. 2021 Jan 1;55(1):86-94.
16. Ratnaparkhi MP, Karnawat GR, Andhale RS. Natural polymers in fast dissolving tablets. Research Journal of Pharmacy and Technology. 2021 May 1;14(5):2859-66.
17. Dave V, Yadav RB, Ahuja R, Yadav S. Formulation design and optimization of novel fast dissolving tablet of chlorpheniramine maleate by using lyophilization techniques. Bulletin of Faculty of Pharmacy, Cairo University. 2017 Jun 1;55(1):31-9.
18. Lal M, Priddy S, Bourgeois L, Walker R, Pebley W, Brown J, Desai J, Darsley MJ, Kristensen D, Chen D. Development of a fast-dissolving tablet formulation of a live attenuated enterotoxigenic E. coli vaccine candidate. Vaccine. 2013 Oct 1;31(42):4759-64.
19. Antonijoan R, García-Gea C, Puntes M, Pérez J, Esbrí R, Serra C, Fortea J, Barbanoj MJ. Comparison of inhibition of cutaneous histamine reaction of ebastine fast-dissolving tablet (20 mg) versus desloratadine capsule (5 mg): a randomized, double-blind, double-dummy, placebo-controlled, three-period crossover study in healthy, nonatopic adults. Clinical therapeutics. 2007 May 1;29(5):814-22.
20. Cilurzo F, Cupone IE, Minghetti P, Selmin F, Montanari L. Fast dissolving films made of maltodextrins. European Journal of Pharmaceutics and Biopharmaceutics. 2008 Nov 1;70(3):895-900.

*****