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Formulation and Optimization of Dicyclomine HCl mouth melt tablets by central composite design

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ABSTRACT

Dicyclomine HCl mouth melt tablets were formulated and optimized by Central composite design.
Method: Independent variables (concentrations of Dehydrated Banana powder DBP, X_1 and Orange peel pectin powder OPP, X_2) and dependent variables (*In vitro* dispersion time, Y_1 and percentage drug release, Y_2) were selected based on literature search. The model was found to be nonlinear and the curvature effect was significant. Therefore study resorted to composite design for optimization.
Results: DSC studies indicated drug and excipients were compatible. Precompression parameters indicated fairly good flow properties. By direct compression method all the tablets were formulated, evaluated for postcompression parameters and were found to be within specified limits. Drug release from all the formulations followed first order. Contour plots were used to decide most economical batch which were in desired range. The statistical model is mathematically valid as the experimental values and predicted values were relatively close to each other and suggested that the statistical model is mathematically valid.
Conclusion: The results demonstrated the effectiveness of the proposed design for development of Dicyclomine HCl Mouth melt tablets with optimized properties.

INTRODUCTION

The oral route is the best way for administration of drugs. Due to its ease of administration, manufacturing, precise dosing, stability and tamper proof tablet is one of the most chosen dosage form administered orally when compared with oral liquids (CheinYie, 2011). Paediatrics and geriatric patients, due to the physiological changes shows difficulty in swallowing which is a common problem associated with these groups. Improvement of a Mouth melt tablet a novel type of solid dosage form may reduce difficulty in swallowing, since they show faster disintegration and melts rapidly in saliva without the need of drinking water where the tablet disperses rapidly in the mouth before it is swallowed (Bi *et al*., 1996; Bi *et al*., 1999). Orodispersible tablets, fast dissolving tablets, melt-in-mouth tablets, rapid melts, porous tablets and quick dissolving tablets were categorized under mouth dissolving tablets (Sreenivas *et al*., 2005). In the treatment of smooth muscle spasm of the gastrointestinal tract an antispasmodic drug Dicyclomine HCl is widely used. It is rapidly absorbed orally but undergoes extensive first pass Metabolism. So the present study aimed at developing mouth-melt tablets of Dicyclomine HCl using natural superdisintegrants to reduce first pass metabolism and to increase the bioavailability of drug which may show faster onset of action in relieving spasms of the gastrointestinal tract as compared to conventional tablet dosage form. Superdisintegrants by water absorption and swelling in the formulations exhibits faster disintegration, promotes wettability & dispersibility through increased wetted surface by providing faster disintegration and dissolution.

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Based on a number of factors, their levels, and possible interactions Design of experiment (DoE) tool is used in R&D to formulate drugs of quality with fewer trials at low cost (Cavazzuti, 2013). Combination of factorial design or fractional factorial design and the star design, Central Composite design is developed by Box and Wilson. The model is validated using ANOVA. Combination and interaction of independent variables (e.g. material attributes) and dependent variables utilises design space to assure quality as per ICH Q8 (R2). In the present study, Dicyclomine HCl mouth melt tablets were formulated and optimized by central composite design to study the effect of independent variables (natural superdisintegrants) on *in vitro* dispersion time and *in vitro* drug release.

MATERIALS AND METHODS

Materials

Dicyclomine HCl (Indoco Remedies Ltd. Navi Mumbai, India), Aspartame, Mannitol, Talc, Magnesium stearate and microcrystalline cellulose were procured from S.D. Fine Chemicals, Mumbai, India.

Methods

Compatibility studies

Differential Scanning Calorimeter (DSC)

Accurately weighed 5 mg of drug alone and passed through the #60 sieve, transferred to DSC aluminium pan and scanned at 25-210°C temperature at heating rate of 10°C/min. The same procedure was carried out for optimized formulation also. The thermograms obtained were compared for any interaction with optimized formulation and pure drug alone (Bhargav *et al*., 2016).

Selection of excipients for formulation development of model drug

Natural Superdisintegrants as independent variables were selected for formulation development of model drug based on literature search, by experimentation done by authors in previous study (Haranath *et al*., 2016; Asha Latha *et al*., 2015) and Preformulation studies.

Preparation of Dehydrated Banana Powder

Bananas were purchased from local market of Ananthapuramu. Removed the peels and were sliced into pieces. Distilled water was added to remove the water-soluble contents in the pulp. Then preservative, 0.2% w/w methyl paraben was added and the pulp was grinded using domestic mixer. Transferred to hot air oven, dried at 45°C for 24 hours and sieved through Sieve No. 80 to get dehydrated Banana powder (Haranath *et al*., 2016).

Preparation of Orange peel pectin powder

Ripped oranges were procured obtained from from local market of Anantapuramu. Then peel was removed, washed carefully and driedby placing the peel under shade for 24 h. Then dried in a hot air oven at 60 °C. After drying it was made into pieces and powdered. Then sieved through sieve No. 20. 200 g of Peel powder was transferred to a solution of 1L water containing 1 g of citric acid maintained at pH 2. For extraction of pectin, it was subjected to reflux condensation at70 ºC for 6 h. A cheese cloth bag was taken and the concentrated juice was obtained by pressing hot acid extract and further cooled to 4 ºC followed by precipitation of pectin using ethanol: water (2:1 v/v) treatment with continuous stirring for 15 min and left aside for 2h. The obtained Pectin coagulate was filtered through cheese cloth, washed with 95 % alcohol and pressed. Further dried at 35 – 45 ºC to constant weight. The hard pectin cake was ground in domestic mixer and then passed through sieve No.60, for further use stored in desiccators (Asha Latha *et al*., 2015).

Characterization of Dehydrated banana powder and Orange peel pectin powder

Physiochemical evaluation like solubility, viscosity, swelling index, Bulk density, tap density, Angle of repose was done for dehydrated banana powder and Orange peel pectin powder (Arun Raj 2013).

In present investigation 2^2 factorial design with 4 replicates were selected for design of experimentation of tablets (Table 1). The model was found to be nonlinear and the curvature effect was significant. Therefore study resorted to central composite design for optimization (Table 2).

Table 1: Experimental design of tablets as per 2^2 Factorial Level.

Factor No.	Factor	Units	Low Level	High Level
1	Dehydrated Banana powder	mg	9 (-1)	15 (+1)
2	Orange peel pectin powder	mg	12.63 (-1)	16.32 (+1)

Table 2: Central composite design layout.

Formulation code	Combinations	DBP (X1) (mg)	OPP (X2) (mg)
F1	I	9 (-1)	12.63 (-1)
F2	X1	15 (+1)	12.63 (-1)
F3	X2	9 (-1)	16.32 (+1)
F4	X1X2	15 (+1)	16.32 (+1)
F5	Mid-point	12 (0)	14.475 (0)
F6	X1At-2L	6 (-2)	14.475 (0)
F7	X1At+2L	18 (+2)	14.475 (0)
F8	X1At-2L	12 (0)	10.785 (-2)
F9	X1At+2L	12 (0)	18.165 (+2)

Pre-compression parameters

Bulk density (BD)

By keeping the 100 ml graduated cylinder in a slanting position accurately weighed blend sample was transferred into it. Initial volume and weight were noted. Bulk density was calculated by the ratio of weight of the sample to the volume it occupied (Milind *et al*., 2010).

Tapped density (TD)

Accurately weighed blend sample was transferred into 100 ml measuring cylinder was used for determining tapped density (Electrolab Tapped Density Apparatus). Initial volume (V_0) of the cylinder was noted and then the cylinder was tapped for 10 times and the volume was measured. Further additional 500

tapings were made and the volume was noted. Continue the tapings to 1250 if the difference between the volume measured after 10 and 500 tapings was more than 2ml (Milind *et al*., 2010).

Compressibility index (CI)

Compressibility index (CI) is direct measurement of potential powder arch or the bridge strength and stability. It was calculated according to the equation given below (Milind *et al*., 2010).

$$CI = \left(TD - \frac{BD}{TD}\right) * 100$$

Hausner ratio

Flow of powder determined by Hausner ratio and determined using following formula (Milind *et al*., 2010)

Hausner ratio = Tapped density / Bulk density

Angle of repose

Funnel method was used to determine angle of repose (a). The blend was poured through a funnel that can be raised vertically to a maximum cone height (h). Angle of repose was calculated by measuring the radius of the heap (r) (Milind *et al*., 2010).

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

Blend of drug and excipients were mixed and convex faced tablets were compressed using 7 mm punch on "B" Tooling Rotary Tablet compression Machine.

Formulation of Dicyclomine blend by dry mixing

Direct compression was used for the formulation of Dicyclomine Mouth melt tablets (Table 3). All the required ingredients were weighed and sieved through mesh no. 60 separately. By using mortar and pestle drug, Mannitol and microcrystalline cellulose were mixed uniformly with gentle trituration to get a uniform mixture. Required weighed quantities of superdisintegrants and aspartame were taken for each specified formulation and mixed to the above mixture. Finally lubricated with magnesium stearate and talc.

Physical characterization of the tablets

Weight variation

20 tablets were selected randomly; the weight of individual tablet and the average weight of the tablets were noted (Pabari *et al*., 2012).

Tablet thickness

Twenty tablets were taken and their thickness was recorded using Vernier caliper scale (Pabari *et al*., 2012).

Hardness

Monsanto hardness tester was used to determine hardness of five tablets was from each formulation. The tablet was held between anvil and spindle. By applying constant force the knob was rotated until the tablet fractured (Pabari *et al*., 2012).

Friability

Roche friabilator was used to determine friability, rotated at 25 rpm/min for 4 min. Initial weight of 20 tablets was noted and loss in weight (%) was calculated (Pabari *et al*., 2012).

Friability = (W1 – W2) / W1 X 100

Weight of 40 Tablets = W1,

Weight of 40 Tablets after friability = W2

Drug content

Twenty tablets were weighed individually and powdered from each formulation. To 10 ml of methanol equivalent weight of 20mg of Dicyclomine HCl was added and volume was adjusted to 100ml with pH 6.8 buffer. 1 ml was taken from the above prepared solution and made up to 100 ml with pH6.8 buffer then analyzed at 217 nm by UV–visible spectrophotometer (Pathikkumar *et al*., 2013).

***In vitro* disintegration time**

The test was conducted for six tablets of each formulation at 37^0C ± 0.5^0C using disintegration apparatus. Distilled water was used as disintegration medium. A tablet was placed in each of six tubes of the apparatus and one disc was added to each tube, complete disintegration of the tablet with no mass remaining in the apparatus was measured in seconds (Pathikkumar *et al*., 2013).

Table 3: Formulation of Dicyclomine HCl mouth melt tablets

Ingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)	F9 (mg)
Dicyclomine HCL	20	20	20	20	20	20	20	20	20
Dehydrated Banana powder	9.0	15	9.0	15	12	6.0	18	12	12
Orange peel pectin powder	12.63	12.63	16.32	16.32	14.47	14.47	14.47	10.78	18.16
Mannitol	170.5	170.5	170.5	170.5	170.5	170.5	170.5	170.5	170.5
Micro crystalline cellulose	79.87	73.87	76.18	70.10	75.03	81.03	69.03	78.72	71.34
Aspartame	6	6	6	6	6	6	6	6	6
Magnesium stearate	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Talc	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Total weight (mg)	300	300	300	300	300	300	300	300	300

Wetting time

Five circular tissue papers of 10 cm diameter are placed in a Petri dish. To Ten millimetres of water, a water soluble dye Eosin was added and poured the prepared dye solution into Petri dish. A tablet is carefully placed on the surface of the tissue paper. Then wetting was noted, as the time required for water to reach upper surface of the tablet (Asha Latha *et al*., 2015).

Water absorption ratio

To a petri plate containing 6 ml of distilled water a piece of folded tissue paper was placed in to it. The time for complete wetting of the tablet was measured in seconds by placing pre weighed tablet on the paper. After wetting the tablet weight was noted. Water absorption ratio was calculated using the formula, (Milind *et al*., 2010)

$$R = (Wa-Wb)/Wa \times 100$$

Where R = Water absorption ratio, Wa= Weight of tablet after wetting, Wb= Weight of tablet before wetting.

***In vitro* dispersion time**

To a beaker with 10 ml of phosphate buffer solution (pH 6.8) maintained at 37±0.5°C a tablet was added and measured the time required for its complete dispersion (Milind *et al*., 2010).

***In vitro* drug release**

USP 24 method Type II apparatus, paddle (Electro lab) at 50 RPM was used for determining drug release from Dicyclomine HCl tablets. 900 ml of phosphate buffer (pH 6.8) maintained at 37 ± 0.5°C used as dissolution medium. At specified time intervals Five milliliters of the sample was withdrawn from the cylindrical vessel and replaced with 5ml of fresh media maintained at 37 ± 0.5°C. Whatman filter paper (no.41) was used for filtration of samples then suitably suitably diluted with phosphate buffer (pH 6.8) and analyzed at 217 nm using a UV-Visible spectrophotometer (Shimadzu) (Pathikkumar *et al*., 2013).

Statistical analysis and Optimization

Data obtained from all mouth melt tablet formulations were analyzed using Sigma Tech software (version 3.1) to generate the study design. Based on several statistical parameters provided by Sigma Tech software best-fit model was selected. Significant effects of independent variables on response regression coefficients were identified by Analysis of variance (ANOVA). Contour plots, a graphical optimization technique was used to study significant effected responses between factors & responses and to generate the new formulations with desired responses. The generated formulation (predict values) was evaluated for *In vitro* dispersion time and dissolution studies to verify closeness between predicted and experimental values. The predicted and experimental values were calculated for relative errors (%) (Reddy *et al*., 2016; Bansod *et al*., 2014).

Stability studies

Stability of optimized formulation was carried out at 40° C ±2°C /75% ± 5% RH for 3 months which was filled in HDPE containers. The optimized formulation was evaluated for *in vitro* dispersion time and *in vitro* drug release for 3 months respectively (Prusty *et al*., 2016).

RESULTS AND DISCUSSION

Compatibility studies

Differential Scanning Calorimeter (DSC)

DSC thermographs revealed that the melting point of the pure drug is 180.27^{o}C and that of the drug in the formulation is 144.51^{o}C. Presence of Dehydrated Banana powder and Orange peel pectin powder (Super disintegrants) reduced the melting point of Dicyclomine Hcl (pure drug) in optimized formulation and hence solubility is enhanced, as illustrated in Figure 1& 2.

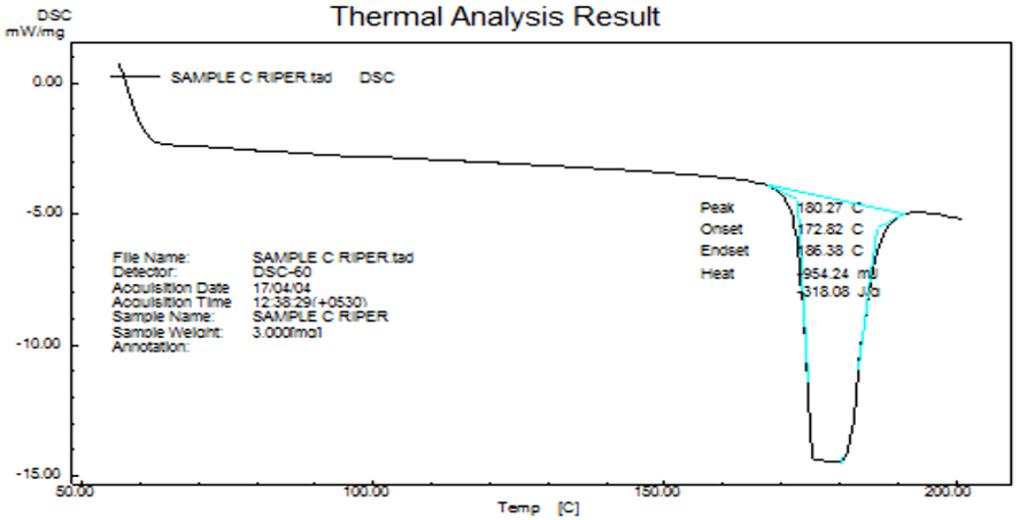

Fig. 1: DSC thermogram of Dicyclomine HCl pure drug.

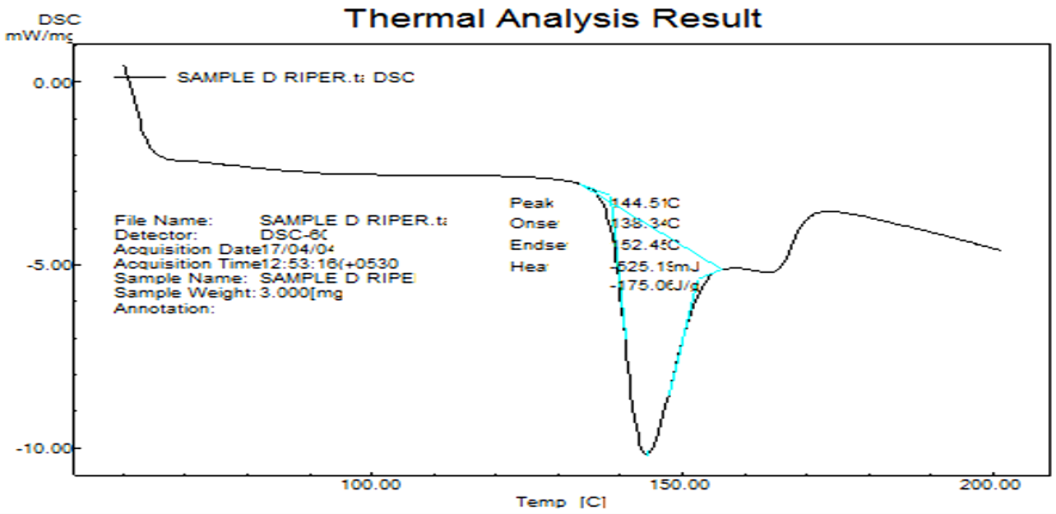

Fig. 2: DSC thermogram of optimized formulation.

Table 4: Evaluation of Pre compression parameters.

Formulation code	Bulk density (g/cm3)	Tapped density (g/cm3)	Compressibility Index (%)	Hausner's ratio	Angle of repose
F1	0.320± 0.041	0.408±0.0.35	21.56	1.27	28°.32±0.041
F2	0.335± 0.020	0.390±0.038	14.10	1.16	27°.51±0.020
F3	0.314±0.021	0.404±0.026	22.27	1.28	35°.63±0.021
F4	0.342±0.043	0.429±0.060	20.27	1.25	34°.03±0.043
F5	0.334±0.026	0.406±0.023	17.73	1.21	30°.95±0.026
F6	0.317±0.022	0.401±0.014	20.94	1.26	31°.39±0.035
F7	0.342±0.024	0.433±0.075	21.01	1.26	28°.25±0.047
F8	0.344±0.044	0.403±0.013	14.64	1.17	29°.21±0.026
F9	0.356±0.029	0.427±0.028	16.62	1.19	33°.01±0.031

All values are expressed as mean ±standard deviation (n=3).

Table 5: Evaluation of Dicyclomine HCl Mouth melt tablets -1.

Formulation code	Average weight (mg)*	Thickness (mm)*	Hardness (kg/cm2)**	Friability (%)*
F1	299±2.6	4.10±0.090	2.5±0.110	0.54±0.054
F2	300±1.6	4.18±0.023	2.3±0.108	0.23±0.112
F3	300±1.8	4.19±0.518	2.6±0.648	0.44±0.198
F4	300±1.3	4.21±0.603	2.5±0.751	0.21±1.163
F5	300±1.1	4.16±0.263	2.7±0.253	0.46±0.682
F6	301±0.8	4.13±0.648	2.7±0.612	0.33±0.263
F7	300±0.7	4.16±0.733	2.4±0.115	0.24±0.376
F8	300±2.7	4.18±0.756	2.3±0.130	0.41±0.358
F9	299±1.2	4.10±0.758	2.5±0.786	0.43±0.421

All values are expressed as mean ±standard deviation (n=20*, n=5**).

Characterization of Dehydrated banana powder and Orange peel pectin powder

Banana powder and orange powder were found to be soluble in water. An angle of repose found to be in the required range, 35.12 & 34.48 indicated a better flow property for banana powder and orange powder respectively. Angle of repose has been used to characterize the flow properties of powders, it also related to inter particulate friction or resistance to movement between particles.

Precompression parameters

The prepared dry blend for all formulations indicated good free-flowing property. Compressibility index (CI) and Hausners ratio was found to be in the range of 14.10 % to 22.17 % and range of 1.16 to 1.29 respectively, as shown in table 4.

Evaluation of compressed tablets

All the compressed tablets were evaluated for weight variation, thickness, friability hardness which were in compliance with pharmacopoeial (I.P) standards (Table 5). The percentage drug content of all the compressed tablets found to be in acceptable limits. The formulated and compressed tablets disintegrated within 25-90 Seconds. It was observed that increase in concentration of Dehydrated banana powder decreased disintegration time due to gel formation by its rapid capillary activity and pronounced hydration, the results are in consistent

Table 6: Evaluation of Dicyclomine HCl Mouth melt tablets-2.

Formulation code	Drug content (%)*	Disintegration time (sec)**	Wetting time (sec)***	Water absorption ratio(%)***
F1	99.37±0.24	40±0.31	46±0.78	92.48±0.19
F2	99.03±0.77	28±0.65	35±0.25	96.3±0.132
F3	97.31±0.31	48±0.28	62±0.55	85.25±1.05
F4	97.45±0.22	48±0.37	37±0.12	81.12±2.63
F5	98.90±0.63	40±0.60	51±0.33	93.41±3.12
F6	99.30±0.34	60±0.63	72±1.11	86.1±0.516
F7	98.36±0.67	25±0.68	29±1.28	98.1±0.662
F8	98.66±0.23	90±0.15	57±0.87	80.2±0.343
F9	97.40±0.71	47±1.32	49±0.77	94.23±3.82

All values are expressed as mean ±standard deviation (n=20*, n=6**, n=5***).

with wetting and water absorption time. Increase in disintegration time of Orange peel pectin due to reduction in solubility and increase in wetting time. The wetting time and water absorption ratio for all the compressed tablets was found to be in the range of 29 ± 1.28 to 72 ± 1.11 and 80.2± 0.343 to 98.1 ± 0.662 %. Among all formulations, formulation F7 showed highest water absorption ratio due to its more swelling and water penetration capacity (Table 6).

***In vitro* Dispersion time (Y_1)**

In vitro Dispersion time for all formulations was found to be 33 sec-130 sec (Table 7).

Final equation in terms of coded factors

$$Y_1 = 82.25 - 16.0\ X_1 + 1.6667\ X_2 - 24.5\ X_1X_2 - 3.15\ X_1^2 + 2.6\ X_2^2$$

Final equation in terms of actual factors

$$Y_1 = 82.25 - 16.0\ DBP + 1.6667\ OPP - 24.5\ DBP\ OPP - 3.15\ DBP^2 + 2.6\ OPP^2$$

In vitro dispersion data was analysed and found that X_1 was highest with SS ratio (66.93%) and a negative sign of the coefficient (-24.5). It indicated that the increase in the amount of X_1 decreased the dispersion time. R^2 model found to be significant hence this model has been used for predictions. Since the relationship between Y_1 Vs X (Independent variables) is nonlinear as shown by Sigma Tech software, the Central composite design has been applied. Magnitude of the coefficient and the mathematical sign (i.e., positive or negative) given by the polynomial equations were used to draw conclusions on responses. The multiple linear regression analysis revealed that dispersion time decreased with increase in Banana powder, dispersion time increased with increase in Orange peel powder. ANOVA was used to identify significant effect, Coefficient of determination R^2 = 0.995. The model was found to be significant at $p<0.05$ since the obtained F value is larger than critical F-value. The critical value of F is 4.95, obtained F value (i.e. 6.59) is larger than critical value and so it can be concluded that obtained F value is likely to occur by chance with a $p<0.05$ i.e. indicates significance at that level of probability. R^2 value of this quadratic model is 0.9128, found to be greater than 0.70 suggesting that this model is reliable for all CQAs Hence used to establish predictions and contours/design space for developing Robust method.

In vitro drug release (Y_2)

In vitro drug release for all formulations was found to be 83.5%-103.3% sec (Table 7).

Final equation in terms of coded factors

$$\text{Drug release } (Y_2) = 78.05 + 2.85\ X_1 - 2.65\ X_2 + 4.425\ X_1X_2 + 2.775\ X_1^2 - 4.075\ X_2^2$$

Final equation in terms of actual factors

$$Y_2 = 78.05 + 2.85\ DBP - 2.65\ OPP + 4.425\ DBP\ OPP + 2.775\ DBP^2 - 4.075\ OPP^2$$

In vitro drug release data was analysed and found that interaction of $X_1$was highest with SS ratio (54.44%) and a positive sign of the coefficient (4.425). It indicated that the increase in the amount of X_1 increased the drug release. Since the relationship between Y_2 Vs X is nonlinear as shown by Sigma Tech software, the Central composite design has been applied. The multiple linear regression analysis showed that drug release increased with increase in Banana powder, drug release decreased with increase in Orange peel powder. Dehydrated Banana powder due to its rapid capillary activity with faster wetting, highest water absorption time and pronounced hydration with little tendency to gel formation showed faster drug release. All the formulations followed First order model and followed fickian diffusion kinetics. ANOVA was used to identify significant effect, Coefficient of determination R^2 = 0.9023. The model was found to be significant at $p<0.05$ since the obtained F value is larger than critical F-value. The critical value of F is 4.95, obtained F value (i.e. 6.59) is larger than critical value and so it can be concluded that obtained F value is likely to occur by chance with a $p<0.05$ i.e. indicates significance at that level of probability. R^2value of this quadratic model is 0.851, found to be greater than 0.70 suggesting that this model is reliable for all CQAs Hence used to establish predictions and contours/design space for developing Robust method.

Table 7: Composition and Evaluation of the batches prepared by applying Central composite design.

S. No.	Combination redesigned	X_1	X_2	Y_1*	Y_2*
1	I	9	12.63	61±0.318	98.6±0.62
2	X1	15	12.63	39±0.206	99.5±0.18
3	X2	9	16.32	125±0.44	87.5±0.28
4	X1X2	15	16.32	45±0.88	103.3±0.67
5	Mid point	12.0	14.475	93±0.11	83.5±0.68
6	X1At-2L	6	14.475	130±028	85.9±0.34
7	X1At+2L	18	14.475	34±1.120	99.8±0.53
8	X1At-2L	12	10.785	77±0.991	96.6±0.87
9	X1At+2L	12	18.165	72±1.24	94.2±0.38

All values are expressed as mean ±standard deviation (n=6*).

Table 8: Comparison of experimental results with predicted responses of Dicyclomine HCl Mouth melt tablets formulation.

Ingredient	Composition (mg/tab)	Response	Predicted value	Experimental value	Standard error
DBP	18	Y_1 (DT)(sec)	35	33	1.0 %
OPP	12.63	Y_2(DR)(%)	100.2	99.7	0.25 %

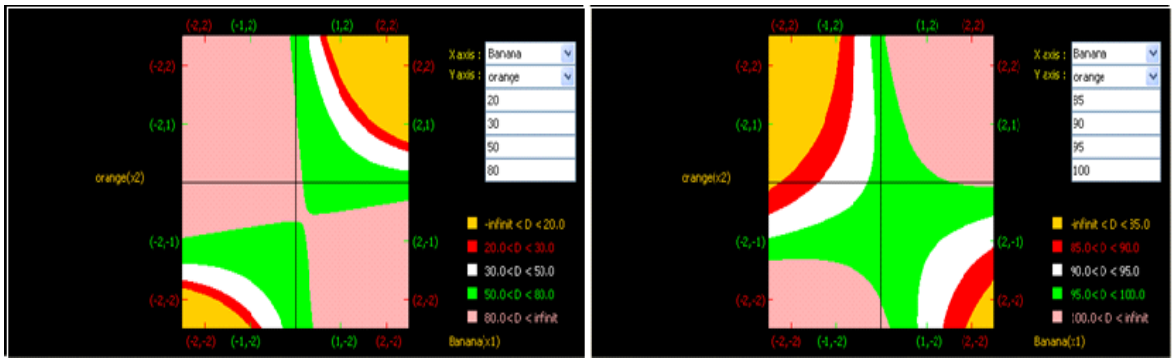

Fig. 3: Contour plots for Dicyclomine HCl Mouth melt tablets.

Establishing Design space

Total design space for dispersion time 20-80 min and for drug release 85-100% (Figure 3). Contour plots permitted the composition Dehydrated banana powder as 18 mg (+2) and orange peel powder 12.63 (-1). The optimized formulation exhibited closeness between experimental values and theoretical values which confirm validity of the model, the results were shown in table 8.

The optimized formulation showed no significant changes on dependent variables after 3 months and was within specifications.

CONCLUSION

In this study the statistical optimization technique, central composite design showed that the concentration of natural superdisintegrants have a profound and interactive effect on the dependent variables and showed that the experimental design was successfully applied to optimize the concentration of natural superdisintegrants to formulate mouth melt tablets with desirable properties of low dispersion time and high drug release. It can be concluded that central composite design could be successfully applied for the development of Dicyclomine HCl Mouth melt tablets with fewer numbers of trials and better quality attributes.

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REFERENCES

Prusty A, Mishra AK, Gupta BK. Development and evaluation of matrix tablet by taking new chemicals combination of chitosan and eudragit-I 100. J young Pharm. 2016; 8(3): 168-76.

Arun Raj. Comparative evaluation of potato starch and banana powder as disintegrating agents in Aceclofenac tablet formulation. International journal of pharmacy and pharmaceutical sciences 2013; 5(2): 2013.

Asha Latha MA, Padavala S, Bhargavi CH. Formulation and evaluation of fast dissolving tablets of Telmisartan using Natural Superdisintegrants. International journal of innovative drug discovery 2015; 5(1): 25-9.

Bhargav E, Harish P, Haranath C, Suryaprakash C. Formulation and Optimization of gastro retentiveextended-release floating tablets of Tramadol Hydrochloride. Inventi spreading knowledge. 2016;4:1-8.

Bi Y, Sunada H, Danjo K, Otsuka A. Preparation and evaluation of a compressed tablet rapidly disintegrating in the oral cavity. Chem Pharm Bull. 1996; 44(11):2121-7.

Bi Y, Sunada H, Danjo K, Yonezawa Y. Evaluation of rapidly disintegrating tablets prepared by a direct compression method. Drug Dev Ind Pharm. 1999; 25(5):571-81.

Cavazzuti M. Optimization Methods: From Theory to Design scientific and technological aspects. 1st ed: Springer-Verlag Berlin Heidelberg; 2013; 262.

Reddy C, Reddy YP, Devanna N. Formulation and Optimization of the extended release tablets of Dalfampridine by 2^3 factorial design. Journal of Pharmaceutical and Scientific Innovation. 2016; 5(1):27-37.

CheinYie W. Novel drug delivery systems. 2nded. Marcel Dekker. New York: 2011; 139.

Haranath C, Muralidhar P, Harish P, Surya Prakash reddy C. Comparative study of natural and synthetic superdisintegrating agents in the formulation of oral dispersible tablets of Escitalopram-IP. InventiRapid Novel excipients 2016; 3: 1-8.

Milind Wagh P, Chetan Yewale P, Santosh Zate U, Paresh Kothawade I, Ganesh Mahale H. Formulation and evaluation of Fast Dispersible tablets of Aceclofenac using different Superdisintegrants. Int J Pharm PharmSciInt J Pharm Pharm Sci. 2010; 2: 154-7.

Pabari RM, Ramtoola Z. Effect of disintegration mechanism on wetting, water absorption and disintegration time of Orodispersible tablets. J young Pharm. 2012; 4: 157-63.

Pathikkumar J, Maravaniya, Tanvee M. Deshpande, Ramesh Katedeshmukh. Development of Dicyclomine hydrochloride orally disintegrating tablet by superdisintegrantaddition method. International journal of universal pharmacy and biosciences. 2013; 2(3): 425-437.

Sreenivas SA, Dandagi PM. Orodispersible tablets: Newfangled drug delivery system-A review. Indian J Pharm Educ Res. 2005;39(4):177-81.

Bansod YD, Shirsat AE. Quality by Design approach to the development of Verapamil Hydrochloride floating matrix tablet. Am J Pharm Tech res. 2014; 4: 890-904.

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