Formulation Development and Evaluation of Mouth Dissolving Tablet of Aspirin by Using QbD Approach

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ABSTRACT: In the current investigations, mouth dissolving tablets (MDT) were developed by applying quality by design (QbD) approach. Direct compression method was applied for the preparation of MDT containing aspirin using 3^2 factorial design with quantity of drug, microcrystalline cellulose (MCC) and crosscarmellose sodium (CCS) as dependant variables. MCC and CCS were used as superdisintegrants. Sodium stearyl fumarate was used as lubricant. Developed MDT were evaluated for characteristics like hardness, friability, disintegration time (DT) and *in vitro* drug release . Design Expert 11.0 described adequately impact of selected variables (MCC and CCS) at various levels for response under study (DT and friability). The optimized batch showed disintegration time of 15-28 secs, friability within 1% and *in vitro* drug release of 75-98% after 30 mins, respectively. The present study of experimental design revealed that MCC and CCS are fruitful at low concentration to develop the optimized formulation. As per the results obtained from the experiments, it can be concluded that QbD is an effective and efficient approach for the development of quality into MDT with the application of QTPP, risk assessment and critical quality attributes (CQA).

Key words: quality by design, mouth dissolving tablets, QTPP, Aspirin, risk assessment

INTRODUCTION

"Quality by design (QbD) is well organised methodology for the development of any pharmaceutical formulation as per predefined objectives, proper understanding of product and process for control of process by considering science and quality risk management" (ICH Q8R2).[1,2] QbD is a potential methodology for development of assurance of product quality through robust manufacturing for patients. Consistent building of quality for pharmaceutical products as per guidelines of regulatory bodies is necessity for customer satisfaction which is a current requirement for pharmaceutical products as per guidelines of regulatory bodies is necessity for customer satisfaction which is a current requirement for industries in worldwide competition.[3,4] The qualitative drug product can be developed by maintaining safety, efficacy with application of quality target product profile (QTPP) which helped to detect critical quality attributes (CQAs). The possible risk factors are determined by using risk assessment in the product development/process development. Then, the multivariate experiments are carried out to obtain design space using design of experiments (DOE). DOE method can link the inputs to the outputs for continuous improvement of quality in product/process.[3]

As per USFDA, mouth dissolving tablets (MDT) is a medicament or API containing dosage form administered to disintegrate within seconds on putting on tongue without consumption of water which will be beneficial to pediatric, geriatric, Parkinson's disease, bedridden patients, psychotic patients, and during travelling.[4,5] QbD is applied to study influence of disintegrants and its combination

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at certain concentration for development of MDT at optimal level. Design of experiments (DOE) and response surface methodology (RSM) are applied input variables in few experiments to generate data with variation of one of the variable at every run.[6] In current research work, optimal settings of input variables such as mixtures of the disintegrants (MCC and CCS), spray dried lactose, sodium staryl fumarate, and microcrystalline cellulose were studied for formulation development of MDT at various compression pressures by direct compression technique to obtain optimal outcome.[7,8]

Thus, the objective of the current research work was to find out concentration range of superdisintigrants impact on the DT and friability of MDTs. 3^2 Factorial design was applied to evaluate utmost significant factors affecting composition of formulation. Central composite design (CCD) was applied to study exact relationship between CQAs and various factors.

MATERIALS AND METHODS

Materials. Aspirin was procured by Research Lab Fine Chem Industries, Mumbai, India. Gift sample of microcrystalline cellulose and sodium stearyl fumarate was gained from Glenmark Pharmaceutical Ltd. Sinner, Maharashtra, India. Analytical grade chemicals were applied for the research purpose.

Formulation of aspirin mouth dissolving tablet. Direct compression method was applied for the formulation of MDT containing aspirin using various excipients such as diluents and superdisintegrants and evaluated for different parameters like hardness, friability, disintegration time and dissolution profile to identify best combination further for preparation of MDT. As per the batches mentioned in Table.1, all ingredients like aspirin, cross carmellose sodium, spray dried lactose, microcrystalline cellulose and talc were sieved using sieve no. 40 individually. API was mixed with the superdisintigrants and other ingredients. Sodium stearyl fumarate was applied for lubricantion of the powder mix and this blend was compressed into tablet using 9.7 mm biconvex punch on a tablet compression machine (Minipress I, Karnavati, India).[7,8]

Table 1. Concentrations of API and excipients.

Experimental runs Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13
Aspirin (mg)	350	350	350	350	350	350	350	350	350	350	350	350	350
CCS (mg)	50	80	50	80	43.78	86.21	65	65	65	65	65	65	65
MCC (mg)	15	15	25	25	20	20	12.92	27.07	20	20	20	20	20
Sodium stearyl fumarate (mg)	10	10	10	10	10	10	10	10	10	10	10	10	105
Spray dried lactose (mg)	70	40	70	30	72	28	57	43	57	50	50	50	50
Talc (mg)	5	5	5	5	5	5	5	5	5	5	5	5	5

Design of experiment (DOE). Experiment was designed based on objectives of DOE that are: screening and optimization

Screening. Screening designs provide simple models with information about dominant variables and information about ranges. Screening is done with respect to DOE for selection of few input variables which will affect key responses. Screening with respect to DOE is an operation by which essential few input variables will be selected which will affect key responses. As per the literature study, CCS and MCC concentration influence the disintegration time and friability. Apart from this, there is no any statistical evidence which will prove uncertain

variable influence on key response. There may be possibility of unpredictable variable to have little influence on response which can be ignored without screening. Hence for the above stated reason screening is done for providing statistical evidence with respect to all input variables in order to study significant outcome of independent variable over dependent variable. The interaction effect between two or more input variables are also detected by screening. Here screening has been done for all formulation input variables (independent variables) and that are: cross carmellose sodium and microcrystalline cellulose. Above two variables were evaluated as independent variables for DT and friability as dependent variables.

Approaches for screenings. Limitation associated with Plackett-burman design is low resolution and two level full factorial design is useful only in case of low numbers of independent variables.[8] Hence fractional factorial design is selected for screening the experiment. Screening has been done by two level fractional factorial design i.e. 3^2 fractional factorial design. As per the outcome of the trail batches, MCC and CCS were used for further studies in concentration range of 50 to 80 mg and 15 to 25 mg respectively.[9,10]

Optimization of response surface methodology (RSM). Design of experiments (DOE) enclosed methods including application of a variety of types of experimental design, polynomial equations development and study of outcomes using experimental domain to establish optimal formulations.[11,12]

Central composite design:

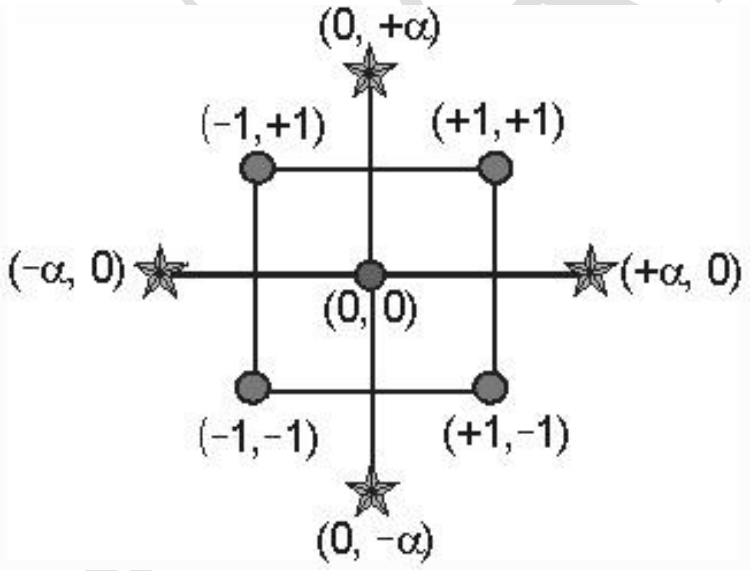

Figure 1. Central composite design for two factors.

A Box-wilson central design is also generally known as 'Central composite design' (CCD) encloses fractional factorial design with centre points is expand with a group of star points that allow estimation of curvature.[3,11] If the distance from the centre of the design space to a factorial point is ±1 unit for each factor, the distance from centre of the design space to a star point is $|\alpha| > 1$. The value of α depends on certain properties desired for the design and on the number of factors involved. Star points signify high and low extreme values for each factor present in the design. CCD is classified into circumscribed, inscribed, face centered.[12] For the optimization face centered design is used (Figure. 1). Design contains star points at each face of the

factorial space hence α= ±1. Thus here diversity needs 3 levels of selected factor.[11,13]

Determination of α,

α = (Number of factorial runs)$^{1/4}$

$\alpha = (2^k)^{¼}$…….(1)

Where,

k = Total number of factors involved experiment, k=2

$\alpha = (2^2)^{¼}$

α = 1.414

CCD is the type of RSM which is selected for optimization and investigation of variables beyond the experimental realm (-1.414 to + 1.414/very low to very high level). By using DOE, we selected CCS concentration 43.7868 mg to 86.2132 mg and MCC concentration of 12.9289 mg to 27.0711 mg (Table 2).

Table 2. 3^2 Central composite design layout.

Experimental run	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13
CCS (mg)	50	80	50	80	43.79	86.21	65	65	65	65	65	65	65
MCC (mg)	15	15	25	25	20	20	12.92	27.07	20	20	20	20	20

Pre-compression study of powder blend

Bulk density. Accurately weighed sample was filled in measuring cylinder to determine volume of the powder as Vo. The formula for calculation of bulk density as follows.[3,13]

Bulk density (ρo) = M/Vo…….. (1)

Where, M= mass of powder

Vo= apparent unstirred volume

Tapped density. The measuring cylinder tapped mechanically to determine tapped volume for calculation of tapped density using following formula.[3,13]

Tapped density (ρt) = M / Vt…… (2)

Where,

ρt = tapped density

M = weight of granules

Vt = tapped volume of granules in cm^3

Angle of repose. In funnel method for determination of angle of repose, accurately weighed mix was allowed to pass freely onto the surface and form heap of the powder to which tip of the funnel just touched. Diameter of cone by powder mix and pile height 'h' was applied for the calculation of angle of repose using following formula.[4,13]

Tan Θ = H /R……. (3)

Thus, $\Theta = \tan^{-1} H/R$…….(4)

Where, H= Pile height

R= Radius of pile

Compressibility index (Carr's index). Carr's index calculated by substituting bulk volume and tapped volume in the following formula[4,13],

Compressibility index= 100 (Vo-Vf)/Vo ×10 …. (5)

Where, Vo = Bulk volume

Vf = Tapped volume

Hausner's ratio. Hausner's ratio calculated by substituting bulk volume and tapped volume in the following formula [4,13],

Hausner's ratio = Vo/Vf …….. (6)

Where, Vo = Bulk volume

Vf = Tapped volume

Better flow property is detected from low values of Hausner's ratio and vice a versa.

Post compression study of aspirin MDT

Thickness. Five tablets of each formulation batch was subjected to Vernier Caliper (Dial Cappiler/Advance) for detection of thickness.

Average values in mm was considered for further study.[4,13]

Hardness. Tablets of each formulation batch were subjected to Monsanto hardness tester (Dolphin) for detection of hardness (kg/cm^2) and results were noted. [4,13]

Friability. Tablet strength was determined using Friability test apparatus, Roche Friabilator (META LAB). Pre-weighed sample of 20 tablets were subjected to 100 revolutions, followed by de-dusted and reweighed. A loss of less than 1 % in weight in generally considered acceptable.[4,13]

Weight variation test. Individual weight of each tablet and average weight for 20 tablets of each formulation batch were calculated. Single tablet weight against average tablet weight was applied to find the deviation in weight.[4,13]

***In-vitro* dissolution studies.** USP type-II apparatus (Electro lab, India) was applied to study *in-vitro* dissolution for developed formulation batches using 900 mL of phosphate buffer (pH 6.8) as the dissolution medium at 50 rpm and 37°C ± 0.5°C. Aliquot (10 mL) of the solution was pulled out at regular interval of 3 minutes and recharged with same volume of dissolution medium to retain constant volume. [4,13]

Fourier transforms infrared spectral studies. Physical mixture of Aspirin and all additives (1:1% w/w) was subjected to FTIR (Shimadzu FTIR 1800 crop, Japan) for evaluation of compatibility study and scanned at 4000 to 400 cm^{-1}. The obtained spectra were studied against standard spectra of aspirin for any modification.[12,13]

Differential scanning calorimetry. DSC- 60 (Shimadzu Corporation, Japan) was applied for evaluation of thermal behaviour of pure drug and developed batches where 10 mg of sample sealed in standard aluminium pans subjected for scanning in temperature range of 50°C to 300°C at a heating rate 10°C/min. [12,13]

Accelerated stability study. Developed formulation batches were subjected for stability study at 40 ± 2 ºC/ 75 ± 5 % relative humidity for three months. Once in a month, samples were evaluated for physicochemical properties.[6] At the end of 3 month, the comparative study was tabulated and any change in colour, appearance, hardness, DT and % drug release was evaluated.[7,8]

RESULTS AND DISCUSSION

Key elements for formulation development. On the basis of the trial batches outcome experiment was designed, so that all the formulations and process components satisfied all the criteria of QTPP for final dosage form.

Quality target product profile (QTPP). Desired quality standards w.r.t safety and effectiveness of the developed formulation can be ensured form quality characteristics of formulation by considering potential outcome as a QTPP.[10,11] For aspirin MDTs, at development commencement only target is set depending upon API characteristics such as physical attributes, identification, and assay, characterization of the RLD product (route of administration, dose strength, dosage form etc.).[12,13]

Components of drug product.

Drug substance (aspirin). After few trial runs, formulation is developed depending upon API's various physiochemical and biological characteristics such as particle size, water content, solubility, biological activity, permeability and stability etc. Thus, performance of the formulation and manufacturing process are enhanced using above mentioned charcteristics.[11]

Excipients

Croscarmellose sodium (CCS). The nature of CCS is a super disintegrant and hygroscopic which has 4-8 times swelling property in presence of water. CCS is free from any impurity and found no any chemical interaction between API and excipients.

Microcrystalline cellulose. For direct compression, Avicel PH 112 grade is used because of less % of moisture content as compared to other grades, free from interaction between API and MCC. As per literature, physical binding / adsorption

between the MCC and API is reported which is not found in studies of our formulation batches.

QTPP for aspirin MDTs.

Dosage form. As per the pharmaceutical equivalence requirement, dosage form of aspirin MDTs is same as reference listed drug (RLD).

Route of administration. To improve the ease of administration, the route of administration is similar to the RLD.

Stability. Stability of the product is important for safety and efficacy. Stability of aspirin MDTs is 36 months at room temperature and it should equivalent to or better than RLD shelf life.

Friability. As per the pharmacopoeial requirement, friability of the MDTs found to be less than 1.0%.

Dissolution: Bioavailability of any formulation depends upon results of dissolution specifications. Dissolution profile for MDTs was found to be more than 85% drug release at 30 minutes. [8,14]

Critical quality attributes of the aspirin MDTs. Desired quality in product can be ensured by maintaining physical, chemical, biological, or microbiological property or characteristic in appropriate limit, range which is known as critical quality attribute (CQA). Thus QTPP helps to identify CQA.[8]

For the aspirin MDTs, disintegration, dissolution, assay, friability were identified as CQAs (Tables 3 and 4).

Physical Attributes

Appearance. Colour, odour of aspirin MDTs are indirectly associated to safety and efficacy. Hence appearance was not considered as CQA for the aspirin MDT's (current product).

Odour. In current formulation batches, API and excipients are free from any unpleasant odour whereas manufacturing process did not applied any organic solvents. Hence odour is not considered as CQA for the Aspirin MDT's (current product).

Friability. An objective with not more than 1.0% as mean weight loss is fixed as per pharmacopoeial requirement. Hence, if it exceeds the standard limits (NMT 1%), it will cause impact on patient's safety, efficacy and product handling. Hence friability is considered as CQA for the aspirin MDT's (current product).

Identification. Identification test establish the identity of the drug in the product. The most conclusive test for identity is the infrared absorption spectrum. Identification test was found to be positive for the aspirin. Drug identification was not affected by formulation and process variables. So, identification test is not considered as CQA for the Aspirin MDT's (current product).

Dissolution. Drug release profile of aspirin MDTs was found to be same as RLD using predictive dissolution method. On the basis of trail batches, dissolution profile was dependent on variables of formulation and process. Hence, dissolution is considered as CQA for the Aspirin MDT's (current product).

Assay. Safety and efficacy of formulation get affected by assay variability. Variation in results of assay for any formulation depends upon process variables. Hence assay was evaluated throughout product and process development.

Disintegration test. As per compendial requirement, DT of MDT should not be more than 30s. Formulation or process variables affect on DT. Hence, disintegration test was considered as CQA for the aspirin MDT's (current product).

The particle size, shape and type of adherence of particles decide bulk density. The values for BD and TD are shown in table. 3. The results were found to be in range from 0.555 ± 0.03 to 0.652 ± 0.025 (BD) and 0.625 ± 0.001 to 0.785 ± 0.013 (TD) for powder blend respectively. The angle of repose and Carr's Index of powder blend was detected in between 22.55 ± 0.08 to 26.90 ± 0.07 and 8.02 ± 1.79 to 15.63 ± 1.31 respectively. Hausner's ratio was detected in between 1.050 ± 0.004 to 1.85 ± 0.007.

Table 3. 3^2 **Central composite design layout, experimental runs and their combinations.**

Experimental runs	Factor 1 MCC	Factor 2 CCS	Response DT(Sec)	Response 2 Friability (%)
F1	50	15	15 ± 3.00	0.2 ± 0.305
F2	80	15	19 ± 1.00	0.73 ± 0.159
F3	50	25	18 ± 4.00	0.28 ± 0.102
F4	80	25	15 ± 3.00	0.85 ± 0.133
F5	43.7868	20	16 ± 2.00	0.39 ± 0.189
F6	86.2132	20	19 ± 2.00	0.69 ± 0.253
F7	65	12.9289	17 ± 1.00	0.85 ± 0.165
F8	65	27.0711	16 ± 3.00	0.79 ± 0.220
F9	65	20	19 ± 5.00	0.8 ± 0.253
F10	65	20	19 ± 3.00	0.8 ± 0.253
F11	65	20	17 ± 1.00	0.8 ± 0.253
F12	65	20	19 ± 2.00	0.8 ± 0.253
F13	65	20	18 ± 4.00	0.8 ± 0.253

Table 4. Pre-compression properties of powder blend.

Batch No.	Angle of repose (°)	Bulk density (BD) gm/mL	Tapped density (TD) (gm/ml)	Carr's index	Hausner's ratio
F1	23.29±0.89	0.619±0.02	0.699±0.04	12.76±0.23	1.129±0.04
F2	24.61±1.18	0.606±0.01	0.714±0.02	15.15±0.46	1.178±0.006
F3	26.41±0.49	0.625±0.01	0.741±0.02	15.63±0.48	1.185±0.007
F4	25.10±0.51	0.626±0.03	0.691±0.03	9.39±0.49	1.103±0.006
F5	24.31±0.85	0.555±0.01	0.625±0.01	11.60±1.13	1.125±0.003
F6	23.44±1.56	0.601±0.03	0.661±0.04	9.02±0.58	1.098±0.007
F7	22.55±0.85	0.583±0.02	0.682±0.03	14.57±0.64	1.170±0.008
F8	25.02±0.76	0.571±0.01	0.645±0.02	11.92±0.90	1.129±0.004
F9	26.41±0.49	0.625±0.01	0.741±0.02	15.63±0.48	1.185±0.007
F10	23.65±1.56	0.652±0.03	0.678±0.04	8.02±0.75	1.050±0.004
F11	22.90±0.85	0.565±0.02	0.785±0.03	13.57±0.64	1.165±0.008
F12	25.45±0.76	0.590±0.01	0.629±0.02	10.92±0.85	1.155±0.004
F13	26.90±0.49	0.635±0.01	0.739±0.02	14.63±0.60	1.145±0.007

Table 5. Post compression properties of aspirin mouth dissolving tablet.

Formulation batches	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13
Hardness (kg/cm^2)	3.5± 0.126	2.5± 0.13	3.00± 0.16	4.05± 0.10	2.5± 0.10	4.00± 0.12	3.5± 0.13	4.00± 0.13	2.5± 0.12	2.00± 0.12	2.5± 0.13	2.00± 0.13	2.5± 0.12
Thickness (mm)	6.148± 0.05	6.218± 0.02	6.238± 0.06	6.44± 0.03	6.50± 0.01	6.362± 0.05	6.526± 0.05	6.488± 0.05	6.362± 0.05	6.362± 0.05	6.526± 0.05	6.488± 0.05	6.362± 0.05
% Friability	0.2± 0.305	0.73± 0.159	0.28± 0.102	0.85± 0.133	0.39± 0.189	0.69± 0.253	0.85± 0.165	0.79± 0.220	0.8± 0.253	0.8± 0.253	0.8± 0.253	0.8± 0.253	0.8± 0.253
Weight variation (mg)	500± 10	490± 15	510± 10	520± 05	480± 10	500± 20	490± 10	510± 10	500± 20	500± 20	500± 20	500± 20	500± 20
DT (second)	15± 3.00	19± 1.00	18± 4.00	15± 3.00	16± 2.00	19± 2.00	17± 1.00	16± 3.00	19± 5.00	19± 3.00	17± 1.00	19± 2.00	18± 4.00
% Drug release	98.58± 0.412	84.66± 0.314	95.09± 0.258	95.94± 0.954	97.67± 0.147	95.96± 0.156	95.95± 0.365	95.95± 0.321	96.82± 0.14	95.08± 0.365	95.09± 0.314	96.82± 0.364	96.81± 0.124

Hardness. Hardness of tablets was detected in between 2.5-4.05 kg/cm^2. The hardness of tablet varied although compression force was constant. The current outcome might be due to the increased concentration of the superdisintigrants in the formulations (Table 5).

Thickness. The tablets observed from 6.148 to 6.526 mm in thickness with minimum standard deviation values showed uniformity in the thickness respectively (Table 5).

% Friability. Friability was important to study weight loss of formulation. % Friability of tablets was found to be 0.20 to 0.80% which is within acceptable limit (Table 5).

Weight variation. All the formulation were varied from 490.00-500.00 mg which indicated that the uniform distribution of excipients and drug was found in the tablets (Table 5).

Disintegration time. High concentration of MCC in the formulation increases the hardness of the tablet. DT of all tablets were found to be in range of 15 to 19 secs (Table 5).

% Drug release. When MCC and CCS are used in low concentrations significantly gave higher drug release to 98.58%. Hence, % of drug release decreases with escalation of MCC concentration (Table 5).

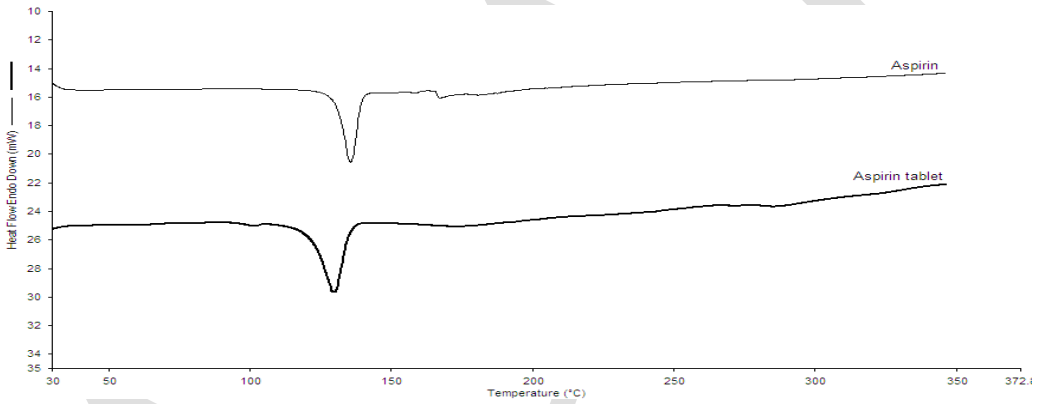

Figure 2. DSC of aspirin and aspirin tablet.

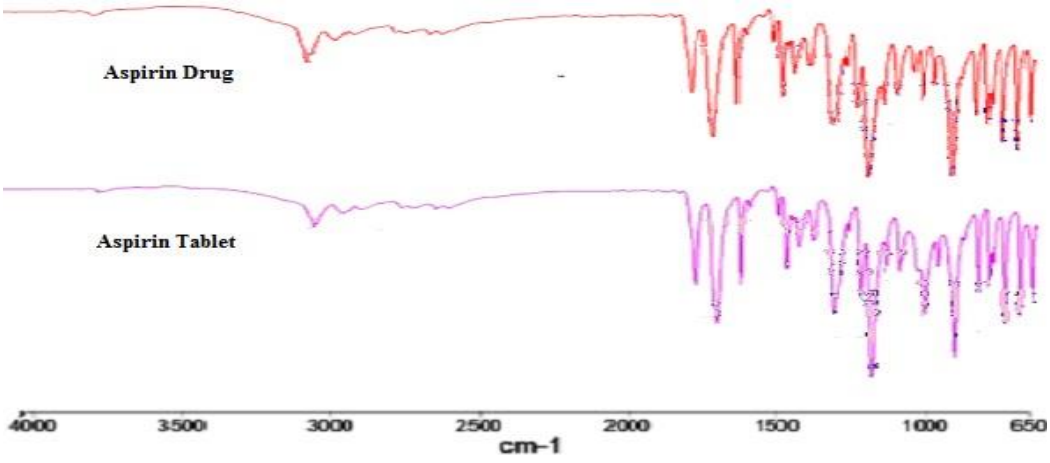

Figure 3. FTIR of aspirin and aspirin tablet.

Table 6. Stability study.

Parameter	Initial	1 Month	2 Month	3 Month
Color and appearance	White and smooth	White and smooth	White and smooth	White and smooth
Friability	0.20	0.25	0.30	0.24
Assay	99.50	99.25	99.35	99.25
DT	15s	15 s	18 s	18 s
% Drug Release	98.35 ± 0.425	98.28 ± 0.450	98.40 ± 0.425	98.10 ± 0.474

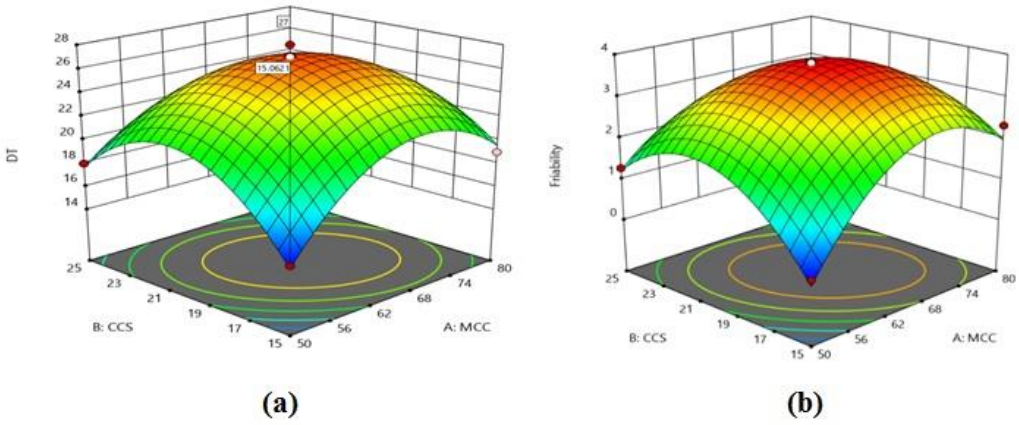

Figure 4. Response surface plot showing effect of (a) **MCC (A)** and **CCS (B)** on (a) DT, (b) **MCC (A)** and **CCS (B)** on (b) friability.

DSC of pure aspirin showed intense endothermic peak at 139.0˚C equivalent to melting point whereas aspirin tablet detected with sharp endothermic peak at 135.0°C. DSC curve of aspirin and aspirin tablet revealed with intense endothermic peak at 139.0°C and 135.0°C and indicated free from any interaction between API and excipients (Figure 2).

The studies were conducted on API and applied excipients. In figure 3 pure aspirin spectrum detected distinguished peaks at 2980.75 cm^{-1} and 1680.71^{cm-1} to O-H carboxylic acid and C=O (Figure 3).

Stability studies. Developed formulation batches were subjected for stability study 40 ± 2 ºC/ 75 ± 5 % RH for three months and monthly analysed for physicochemical parameters. At the end of 3 months, the comparative study was tabulated and change in color, appearance, friability, DT and % drug released were evaluated. As per the outcome of the study, there was no any significant various in the samples even after and during 3 months (Table 6).

DISCUSSION

The present study started with the aim of formulating aspirin MDTs which was comparable to marketed brand tablet also called reference listed drug (RLD) by quality by design approach. This included QTPP, CQA, DOE and control strategy for input variables. CQA for the current product selected such as physical attributes, assay, DT and % drug release. API qualities included particle size, solubility, hygroscopicity and solid state form. The screening was performed using 3^2 fractional factorial design with two independent variables as CCS and MCC and the dependent variables as DT and friability with the purpose of selection of vital few variables. The CCD was used as an optimization tool for analysis of predictive variables and found to be suitable for the current research work.

MCC and CCS were increased in DT when used at high concentrations. DT of all tablets were found between 15 to 19 s which was detected within acceptable limit as per USP. % Drug content in

developed MDT formulations was detected in range of 84.66% to 98.58%. *In-vitro* drug release profile for all developed batches (F1-F13) showed immediate release of aspirin within 30 minutes.

The developed MDTs were detected to be stable at 40±2^{o}C / 75%±5% RH and at room temperature 25^{o}C±2^{o}C with respect to DT, % friability, drug release and assay though there was little increase in viscosities of formulation.

As per the obtained 3D response surface plot of the experimental model, outcome of selected variables depends on DT and friability.

Figure 4 (a) and (b) shows the 3D plot which illustrates the effect of MCC and CCS on the DT and Friability. It is shown that both of the process input variables have a significant effect on the DT and Friability. It is demonstrated that the DT and friability of aspirin depends on the MCC and CCS meanwhile is the most significant factors. MCC and CCS showed less DT and % friability at their lower value.

DT= -49.222+0.9798*MCC+3.5563*CCS-MCC*CCS-0.0036*MCC^{2}-0.0525*CCS ^{2}……(7)

Above equation in terms of actual factors used to make predictions about the response for given levels of each factor. From equation 7, it was concluded that MCC (A), CCS (B) having an individual and combined effect on DT of the tablet.

Friability= +3.80+0.3209*MCC-0.0594*CCS-0.6375*MCC*CCS-1.45*MCC^{2}-1.39*CCS^{2}…….(8)

From equation 8, it was concluded that MCC (A), CCS (B) having an individual and combined effect on friability of the tablet.

Above equations in terms of actual factors used to make predictions about the response for given factor. From equations 7 and 8, it was concluded that positive coefficient indicate MCC significantly contribute to disintegration time and negative coefficient indicating CCS has no significant contribution on friability. As compared to medium and high level concentration both superdisintegrants were found to be effective at low level.[7,11]

CONCLUSION

MDTs incorporating active ingredients were evaluated for effect of various disintegrants on disintegration time and friability. DOE and RSM are proved as essential and beneficial tools for the investigation of effect of disintegrant concentrations and its combinations on DT and friability of MDTs. The current study claimed as an ideal tool for the development of product as per outline of QbD including specified limits of excipients in ranges within the designed acceptance space for product's optimum performance.

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Competing interest

Authors have declared no competing interest.

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