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Research article

Development and evaluation of therapeutically useful oral solid tablets containing natural extracts: a quality by design approach

Ujashkumar A Shah[1], Jayvadan K Patel[1], Tejas Vyas*[2], Govindarajan Raghavan[2]

[1] Faculty of Pharmacy, Nootan Pharmacy College, Sankalchand Patel University, Visnagar, Gujarat, India
[2] Zydus Wellness Institute, Zydus Wellness Research & Development, Ahmedabad, Gujarat, India

Corresponding author: Tejas Vyas, ✉ tejasb.vyas@zyduswellness.com, **Orcid Id**: https://orcid.org/0000-0002-1046-7769

Zydus Wellness Institute, Zydus Wellness Research & Development, Ahmedabad, Gujarat, India

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ABSTRACT

The quality target product profile was created for therapeutically useful oral solid tablets containing natural extracts. Important quality criteria were recognised. The risk priority no. was used to evaluate critical materials for initial risk assessment. Using Central Composite Design, the effects of critical parameters (croscarmellose sodium & PVP K-30) were investigated. The impact of the formulation variables X1: Croscarmellose sodium and X2: PVP K-30 on responses Y1: DT (Disintegration time in minutes) and Y2: Friability (%) were assessed. Factor X2: PVP K-30 was found to have a substantial impact on both the responses. The optimized formulation having Croscarmellose sodium-20mg/tab and PVP K-30 8 mg/tab meets the QTPP (quality target product profile) and essential requirements for oral solid tablets standards. Present research shows that QbD (quality by design) is an excellent method which comprehending the critical parameters for optimising therapeutically useful oral solid tablets containing natural extracts.

Keywords: QbD -Quality by Design, Oral solid tablets, Natural extracts, QTPP -Quality target product profile, DOE- Design of Experiments, CQA- Critical quality attributes.

INTRODUCTION

With increasing worldwide competitiveness and the expanding influence of information- technology, the Pharma sector must urgently enhance its efficiency of operation and overall quality of its products [1, 2, 3]. Time to launch in market, regulatory compliance, product quality, waste, cost optimisation, and cycle duration are main critical issues that has to be handled methodically [4, 5]. As a result of these criteria, as well as regulatory authorities' openness to adopt creative approaches that can provide higher quality and product safety standards, the pharmaceutical business is undergoing fast structural transition [4,5]. QbD has been recognised as a vital enabler in achieving the required performance exponential leap [6, 7].

The goal of QbD aims to effectively and consistently meet customer demands as a result [8, 9]. In contrast to the traditional Quality by Testing (QbT) method, which primarily verifies quality in the finished product, QbD proposes that quality be integrated into the process and product during development. [9, 10]. QbD emphasises that product and process understanding must be improved using exact scientific concepts and design efforts to fulfil stated goals [11]. A goal-driven approach to product development known as "Quality by Design" (QbD) promotes product and process control and comprehension while utilising sound science and effective risk management [12].

Natural Extracts as remedies is an ancient system that has been practised since the dawn of time [13]. Natural extracts remedies have been utilised as therapies for a wide range of ailments since ancient times. Despite recent improvements in modern medicine, importance of herbal supplements to world health has not changed and contributed significantly to health care [14].

80% of people around the world, according to the WHO (World Health Organisation), utilise herbs and other traditional medicines. These are safe to consume, effective, socially accepted with minimal side effects. The market's demand for herbal supplements has significantly increased during the past 20 years and there is a need to monitoring the safety, efficacy, and quality of herbal remedies [15].

Because safety and quality are regarded as important concerns while using herbal remedies, it is vital to implement suitable quality assessment measures for safety of consumer health by making sure that every herbal medications are harmless and of proper quality [16]. These requires to develop a systematic methodology and well-designed techniques for the production of products containing natural extracts.

The USFDA (United States Food and Drug Administration) recently presented QbD as a key model of pharmaceutical quality that should be taken into consideration while developing pharmaceutical processes & products [17]. Despite the widespread use of herbal pharmaceuticals, few cases of QbD application in herbal drug manufacturing have been identified. It is observed that methods developed based on experience are commonly applied in the production of herbal remedies, due to complex matrix and many process variables it fails to improvisation in the process understanding, it is crucial to build manufacturing processes within the context of QbD, which pushes finished products process to go far from trial and error strategies and towards predetermined processes so as to keep product quality within design space [18].

To make commercial herbal products as safe, effective, and high-quality as possible, it is necessary to employ a QbD methodology for the creation of herbal products [19, 20].

Semecarpus anacardium L.f. (SA) is being employed as a medicinal ingredient in several alternative therapies. Ayurvedic remedies containing Bhallataka (SA) include Bhallataka Vati (Bhaishaya Ratnaavali), Narasimha Ghrita (Ashtaanga Hridaya), which is used as a blood cleanser, Bhallataka Vati (Bhaishaya Ratnaavali), Tonics for the blood (hematinic) and Angaruya-e-kabir is used to treat neurological disorders [21, 22].

SA possesses anti-inflammatory and immunomodulatory properties. Semicarpol and bhilawanol, two phenolic compounds which have the ability to inhibit the initial tuberculin reaction as well as the initial phase of adjuvant arthritis. SA reduces nitrate/nitrite levels significantly, which may be linked to its antioxidant activity [21]. In India, "Chyavanprash" is a well-known and frequently employed traditional Ayurvedic formulation. It pertains to the Rasayana class of medications, which are renowned for their immune-enhancing and disease-preventative properties. Antioxidant-rich "Rasayana" medications have demonstrated hepatoprotective and immunomodulatory properties [23]. Amla (Emblica officinalis), the most noticeable and concentrated botanical in chyavanprash, is a blend of several others [24]. Chyavanprash has been the subject of extensive preclinical and clinical research for a variety of medicinal purposes, the most notable of which are its immune-enhancing properties. Additionally, Chyavanprash helps in balancing positive nitrogen, increases serum protein levels, and hastens weight increase, all while preserving a balanced adaptogenic activity and steroidal content [25, 26]. There are few studies reported for QbD and formulation importance for combination of these natural extracts. So in current research the focus was development of formulation having natural extracts by use of QbD technique.

MATERIALS & METHODS

Chyavanprash extract was procured from NJP healthcare Pvt Ltd (Mumbai) whereas amla extract and Semecarpus anacardium extract were purchased from Konark Herbal Health Care (Mumbai). Other excipients like PVP K-30, Croscarmellose Sodium, Lactose Anhydrous, Magnesium Stearate, and Colloidal Silicon Dioxide were purchased from local vendors of Pharmacopoeial grades.

QTPP (Quality Target Product Profile) of Therapeutically Useful Oral Solid Tablets

The International Council for Harmonisation (ICH) Q8 QTPP is a critical component of a QbD methodology. QTPP covers all product features required to verify comparable efficacy and safety [9]. The QTPP for oral solid tablet containing natural extracts was created after consideration of the essential quality standards of the products.

CQA (Critical Quality Attributes) of Therapeutically Useful Oral Solid Tablets

Early CQAs were derived based on QTPP in order to find desired product characteristics. Potential CQAs of excipients require to make oral solid tablet formulation containing natural extracts were established as having lowest disintegration time with maximum hardness and friability of maximum 1.0 %.

Risk Assessment

An assessment of the risk was carried out so that any pertinent high risk factors could be identified for the purpose of further study. Risk Priority Numbers (RPN) were assigned to three categories during the risk assessment process (low, medium, and high). Risk assessment was identified for essential input raw material and formulation, as well as their impact on product quality [29].

For the creation and optimisation of therapeutically useful oral solid Tablets, a CCD (central composite design) was applied. In the design, 2 parameters were examined at 3 levels, and formulation tests were performed. Croscarmellose Sodium (Disintegrant X1), PVP K-30 (Binder X2) were selected as variables which are independent and altered at three different levels, which were classified as lowest (-1), medium (0) and highest (+1) level. The response variables in this

study were disintegration time (Y1) and friability (Y2) in minutes and percentage respectively.

DOE-Design of Experiments

A systematic approach for discovering the interrelationship between elements which affects a process including output of that process which is organised and structured. Also known as "Design of Experiments" [17]. Design Expert (DE) ver.-13.0 (USA, Minneapolis, Stat-Ease Inc.) was used to create the experiments. Nine formulations were created and made with the help of software, as per Table-1. DOE-Design of Experiment programme was applied to determine the important values needed to get the appropriate response of the variables which are independent.

Table 1: Combinations of factors according to (3^2) factorial experiment of design.

	Coded values		Experiment-values (mg)	
	X1	X2	X1	X2
F-1	-1	0	10	16
F-2	1	0	30	16
F-3	-1	1	10	24
F-4	1	1	30	24
F-5	0	-1	20	8
F-6	0	1	20	24
F-7	-1	-1	10	8
F-8	0	0	20	16
F-9	1	-1	30	8

X1 Crosscarmellose Sodium is the concentration & X2 is the concentration PVP K30

Preparation of Therapeutically Useful Oral Solid Tablets Containing Natural Extracts

Oral solid tablets containing natural extracts was developed using the wet granulation process. The oral solid tablets were chosen based on a survey of the literature. Table 2 shows the formulation trials of oral solid tablets containing natural extracts that have been developed. All of the natural extracts, including Chyavanprash extract, amla extract and Semecarpus anacardium extract were precisely weighed out and passed it through sieve #.200 individually. The dose of the all the extracts were based on drug to extract ratio and based on literature search. Drug-excipients compatibility was keep in mind while selecting the excipients of the formulation.

All of the natural extracts, including Chyavanprash extract, amla extract and Semecarpus anacardium extract were accurately weighed and sieve # 200 used for sieving. Because of the hygroscopicity of all the above extract, they were triturated with an exactly weighed quantity of lactose anhydrous (dry combination). PVP K-30 was weighed and mixed with water to make a translucent granulating paste. The other ingredients like Croscarmellose-sodium, was mixed with the granulating paste to make it moist coherent paste. The generated moist coherent mass was run through sieve #10 to produce the granules. The granules were kept at 40-45°C in oven until absolutely dry. After appropriate drying, the granules were passed through sieve # 22 overlaid on sieve # 44 to separate fines from the granules.

The granules were properly combined with a dry mixture of Amla extract, Chyavanprash extract and Semecarpus anacardium extract and an exactly weighed quantity of magnesium stearate and colloidal silicon dioxide. Then free flowing granules were taken for the compression of tablet. Finally, the biconvex round tablets having an average total weight of 850 mg were prepared by use of a Compression CMD3 16 station D Tooling machine.

Table 2: Formulation trial batches of oral solid tablet containing natural extracts

Composition/Ingredients	F-1	F-2	F-3	F-4	F-5	F-6	F-7	F-8	F-9
Amla extract	500	500	500	500	500	500	500	500	500
Chyavanprash extract	160	160	160	160	160	160	160	160	160
Marking Nut tree dry extract (*Semecarpus anacardium*)	100	100	100	100	100	100	100	100	100
PVPK30	16	16	24	24	8	24	8	16	8
Crosscarmellose Sodium	10	30	10	30	20	20	10	20	30
Lactose Anhydrous	63	43	55	35	61	45	71	53	51
Magnesium Stearate	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Colloidal Silicon Dioxide (CSD)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Total (mg)	**850**	**850**	**850**	**850**	**850**	**850**	**850**	**850**	**850**

F-1 to F-9 represents total 09 formulation trials, amount of each excipients is shown in mg (milligram) per oral solid tablet

Physical Properties of the Oral Solid Tablet

The compressed oral solid tablets were tested for its physical properties such as disintegration time, thickness, weight variation, friability and hardness by Pharmacopoeial methodology [27]. The moisture value of the oral solid tablet was determined using the thermo-gravimetric method, often known as the loss on drying oven method [28].

Statistical Analysis

The ANOVA (analysis of variance) method was used to assess the significance of the fit model. The most effective model was choosen based on statistical evaluation such as the Sum of squares (SS), adjusted R2, R2 -coefficient of determination, Fischer's ratio (F value), Degrees of freedom (DF), Mean of square (MS) and probability (P) generated from Design of experiment software. To demonstrate the relationship between the independent and dependent variables, response surface plots such as 3-D surface and contour plots were employed. The plots previously mentioned were used to investigate the effects of different elements on the reaction at a specific time. At last, to identify the optimized formulation, a desirability approach and overlay plots were used [29].

Validation Study of Optimized Formulation Batch

To validate used optimization approach, optimized formulation batch of solid oral tablet with natural extracts with the predicted levels were developed. The experimental values' responses were quantitatively compared to the expected values' responses for the purpose to defend the selected experimental strategy.

Control - Strategy

A control strategy is created to make sure that the product is consistently produced with the desired quality. In light of product knowledge and existing process, a control-strategy provides a comprehensive picture of how quality is maintained. The metrics and qualities connected to active substance and excipients, as well as the corresponding techniques and control and constant monitoring frequency, are all part of the control -strategy [9].

Stability study

Stability studies for statistically optimized formulations were conducted in accordance with the guidelines of ICH (International council for harmonization) Q1A (R2) [. The samples of stability were kept in a proper Alu-Alu blister pack for 90 days at RT (room temperature) (30°±2°C/ RH 65±5 %) and at (40°±2°C/ RH 75±5 %) for accelerated conditions The formulation were examined for weight variation study, hardness, disintegration, and friability after 1 month & 3 months.

RESULTS & DISCUSSION

The QTPP summarises a drug product's quality requirements to ensure efficacy and safety. The solid oral tablet QTPP presented in (Table 3) includes data on dosage form and its design, administration mode, drug product quality attributes, dosage strength, packaging material information and its storage conditions.

CQAs were defined from QTPP to indicate satisfactory product quality. Table-3 summarises the CQAs of oral solid tablet, as well as the explanation for their criticality. CQAs of oral solid tablet formulation were considered to be disintegration time (min) (Y1) and friability (%) (Y2)

Table 3: CQA'S and QTPP for therapeutically useful oral solid tablet formulation

QTPP Parameters	Required Target	Justification of requirements
Dosage form of product	Tablet form	For patient ease of use
Dosage design of product	Conventional release tablet form	Patient compliance and acceptability.
Dosage strength	760 mg	Therapeutic dosage for effectiveness.
Route of Administration	Oral route	Dosage form intended for oral administration
Drug product Quality Attributes		
Description	Tablet description with desired size and shape.	Patient compliance
Friability	Maximum 1.0 %	As per Pharmacopoeial requirements
Hardness	3-10 kg/cm^2	To get desired release
Packaging material info	Packaging material suitable for the finished product quality criteria	Required to get the targeted expiry date with required product quality.
Disintegration time	Maximum 15.0 minutes.	To meet Pharmacopoeial requirement
Storage condition	Store in cool and dry place.	To keep product intact throughout the shelf life.
Critical Quality Attributes		
Friability	Maximum 1.0 %	In order to meet Pharmacopoeial requirement
Disintegration time	Maximum 15 min	Disintegration time is crucial for efficacy of the product
CQA- (Critical Quality Attributes) ; QTPP- (Quality Target Product Profile)		

Table 4: Initial risk assessment of critical material attributes (tablet)

Product CQA	Natural extracts					Excipients			
	Moisture level	Hygroscopicity level	Flow characteristics	Residual solvent amount	Impurity level	PVPK-30 content	CCS content	Lactose content	Colloidal silicon dioxide Content
Friability, Percentage	LL	LL	LL	LL	LL	HL	ML	LL	LL
Disintegration time	LL	LL	LL	LL	LL	HL	HL	LL	LL

LL- Low level, ML- Medium level, HL-High level

In light of previous scientific data and knowledge, an Initial Risk Assessment of active ingredient (natural extracts) and excipients was undertaken to reach the QTPP. The initial risk evaluation was conducted on all three plant extracts. Natural extracts were discovered to be a crucial input ingredient among them. Table-4 summarises the preliminary assessment of risk for this critical material and Table 5 summarises the preliminary assessment of risk for product variables and its logic.

Table 5: Preliminary risk assessment of formulation variables and its logic

Formulation-Variables	Product- CQA	Justification for formulation variables
PVP K-30 content	Disintegration time	PVP K-30 is employed as a binder, and changing its concentration can have a significant influence on disintegration time through hardness of tablet. It has high level risk.
	Friability	Due to its application as binder, it has high level risk on friability.
CCS content	Disintegration Time	Because CCS is employed as a disintegrant, changes in its levels can have a significant influence on disintegration time. It has high level risk.
	Friability	Its high amount can cause tablet friable; however, it can be mitigated by raising tablet hardness. It has medium level risk.
Lactose content	Disintegration time	Because it is employed as a filler, it has minimal effect on disintegration time or friability. It has low level risk.
	Friability	
Colloidal silicon dioxide Content	Disintegration time	Colloidal silicon dioxide has a lower effect on disintegration. It has low level risk.
	Friability	There is no effect of colloidal silicon dioxide on tablet friability. It has low risk.
Magnesium-stearate content	Disintegration time	Because it is used in such less concentrations, it has minimal effect on disintegration time or friability. It has low level risk.
	Friability	

CQA reflects selected quality requirements, while formulation -variables represent the content of each ingredients used.

Formulation elements that had a major impact on CQAs were thoroughly explored and exposed to design of experiments on basis of the preliminary risk assessment study and also crucial materials of the therapeutic ingredient (natural extracts) were exposed to the control method.

DoE comprised of two primary formulation variables whose deviations were deemed to be the most dangerous to the final product's quality profile. These variables were rated as high level risk depend on their RPN -Risk Priority Number. The key formulation factors for design of experimentation were croscarmellose sodium concentration (mg) (X1) and PVP K30 (mg) (X2). Oral solid tablets were developed and optimized using a randomised 3^2 central composite design.

Table 6 shows the experimental trials with variables which are independent and analysed responses for the proposed oral solid tablet formulation containing natural extract. Table 7 shows physical properties data.

Table 6: formulation details of oral solid tablet - responses and variables based on de-design expert

Standard	Run	Variable 1 A: CCS	Variable 2 B: PVP K-30	Response DT min.sec	Response Friability %
4	1	10	16	16.51	0.51
6	2	30	16	12.24	0.53
7	3	10	24	19.26	0.25
9	4	30	24	18.23	0.39
2	5	20	8	11.56	1.02
8	6	20	24	17.37	0.35
1	7	10	8	12.18	0.78
5	8	20	16	17.54	0.58
3	9	30	8	10.53	1.3

Table 7: Physical properties of oral solid tablet trials

Formulation- Batch	Hardness in kg/cm2	Thickness in mm	Weight variation in %	Friability in %	Disintegration time in min. sec	Moisture content in %
F-1	4.6	5.2	0.071	0.51	16.51	2.5
F-2	3.2	5.3	0.002	0.53	12.24	2.45
F-3	5.2	5.25	0.082	0.25	19.26	2.55
F-4	4.9	5.3	0.035	0.39	18.23	2.4
F-5	3.1	5.2	0.024	1.02	11.56	2.3
F-6	4.7	5.22	0.094	0.35	17.37	2.7
F-7	3.22	5.4	0.035	0.78	12.18	2.6
F-8	4.74	5.3	0.024	0.58	17.54	2.65
F-9	2.7	5.26	0.035	1.3	10.53	2.5

Physical characterisation was performed on formulation batches F-1 to F-9, and all physical parameters were confirmed to be suitable.

Oral solid tablet statistical optimisation was carried out by comparing many statistical parameters provided by Version 13 of Design-Expert Software. Table 8 represents various statistical data applicable to design. Variables which are independent and response were linked together using polynomial-equations and statistical characterisation using Software of Design-Expert. The regression findings of the measured responses are shown in Table 9. The influence of the factors indicated on the response is connected to the coefficients X1 and X2, as well as their quadratic terms and interaction. A synergistic influence on the reaction is shown by a positive value for the coefficient, whereas an antagonistic effect is indicated by a negative sign. The greater the coefficient, the stronger the independent variable's influence on the response. Contour plots and Response surface plots were created to graphically depict the influence of each component on responses (fig. 1-4).

Table 8: Statistical summary -anova (analysis of variance test)

Response	MS	SS	F value	DF	P value	R^2 value	Adjusted R^2 value	Model -Significance
Y1	39.35	78.71	20.38	2	0.0021	0.8717	0.8289	Significant
Y2	0.4095	0.8191	22.03	2	0.0017	0.8801	0.8401	Significant

MS is mean of squares, SS is sum of squares, F value is ratio of Fischer's, DF is degree of freedom, P value is probability, R^2 value is regression coefficient.

Response Y1 DT- Disintegration time: On basis of ANOVA study's regression- coefficient, as presented in Table 9, it was discovered that X1 which is independent variable has a negative sign, shows that it has an antagonistic impact on the Y1 response.

Table 9: Regression equation based on anova

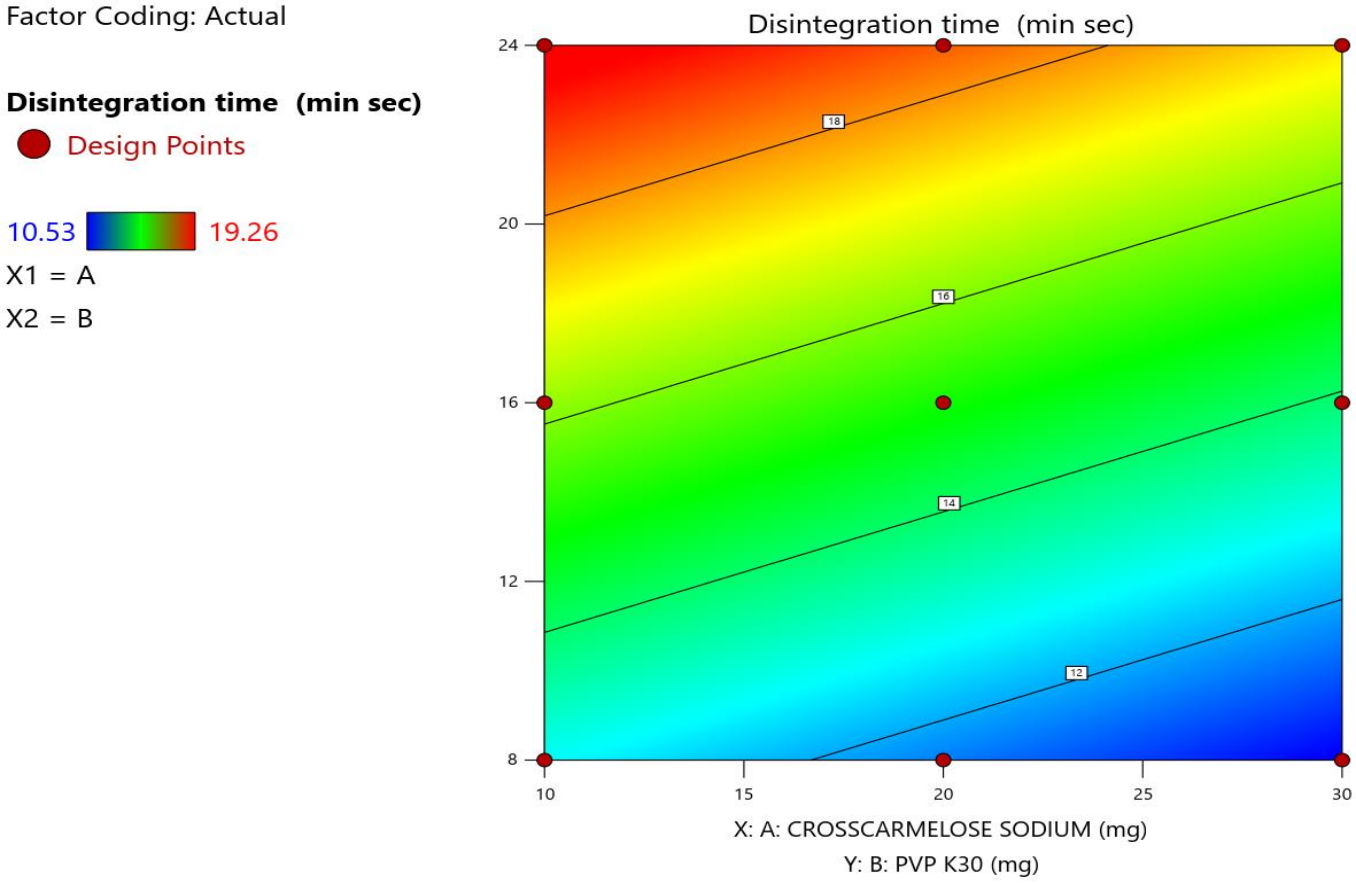
Response parameter	Regression-equation
Disintegration Time in min (Y1)	(+10.50- 0.115833X1 + 0.428958X2)
Friability (Y2)	(+1.11111+ 0.011333X1 - 0.043958X2)

X1 is amount of Croscarmellose Sodium, X2 is amount of PVP K-30, Y1 is Disintegration time in min, and Y2 is Friability in percentage

The coefficient of the variable X2 has a positive sign and exhibits a synergistic effect upon the response. The regression equation shows that X2 variable has high relevancy for response than X1 variable, because ANOVA revealed a negative coefficient for variable X1.

The Contour Plot and Response Surface Plot (Graphical demonstration), shows that raising the amount of X1 variable has very less effect on the Y1 response , in contrast to raising the amount of X2 variable increase the value of Y1 response. It means, as the quantity of PVP K-30 increases, so does the DT (min), in contrast to as the quantity of CCS increases, DT (min) not much impacted. Figures 1 and 2 show that X2 variable has a more substantial effect on Y1 response than X1 variable.

Figure 1: Contour-Plot -Response for Y1 DT (Disintegration Time in min sec)



Response Y2 Friability: On basis of regression coefficient derived from the study ANOVA, as presented in Table-9, it was revealed that X1 variable which is independent having positive sign, represent a synergistic influence on Y2 response, whereas variable has a negative sign, indicating that it has an antagonistic effect on the said response.

The Response Surface and Contour Plot shows that when the amount of variable X2 is high, the response value of Y2 falls means when the amount of PVP K-30 is high, the percentage of Friability reduces (Fig.-3 & 4).

Figure 2: RSP -Response Surface-Plot for Response Y1 - DT (Disintegration Time min sec)

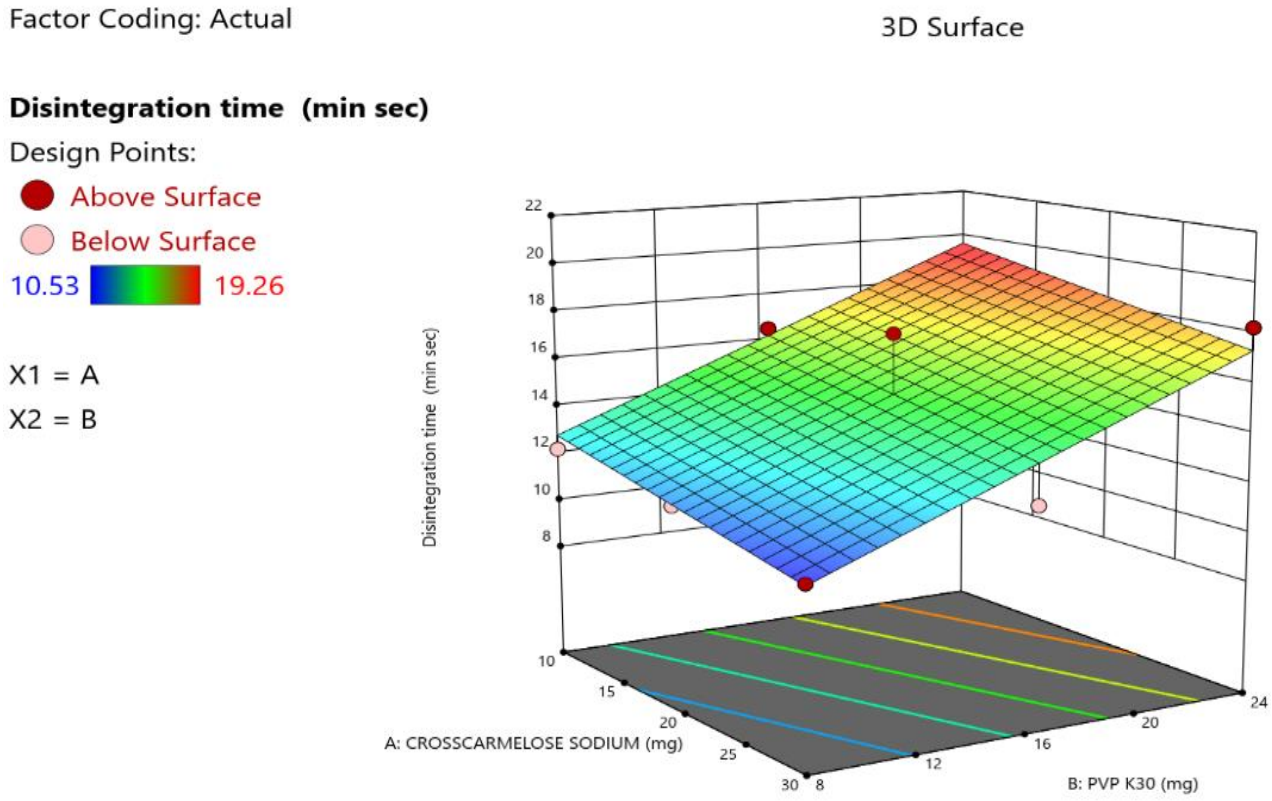


Figure 3: Contour-Plot for Response Y2- Friability

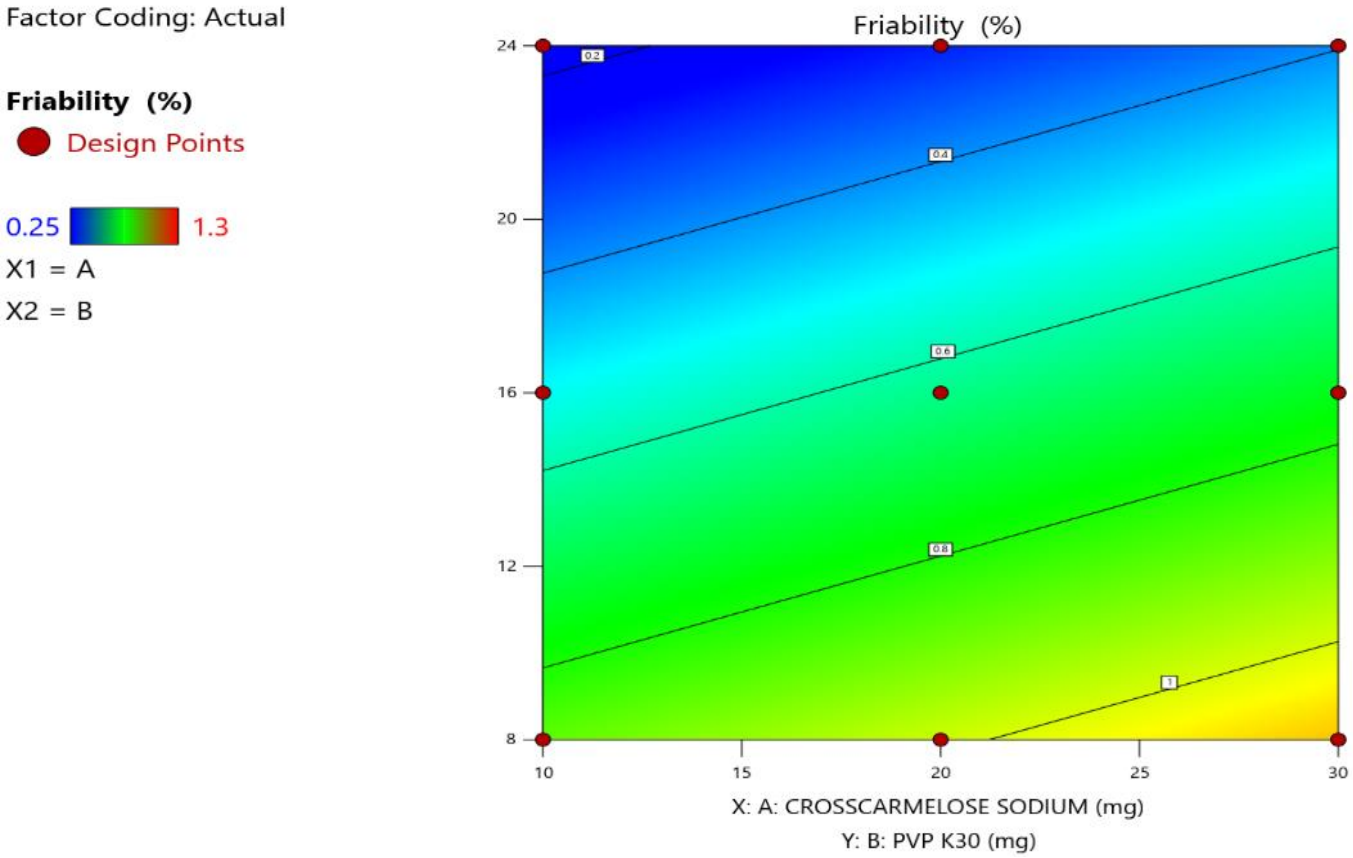
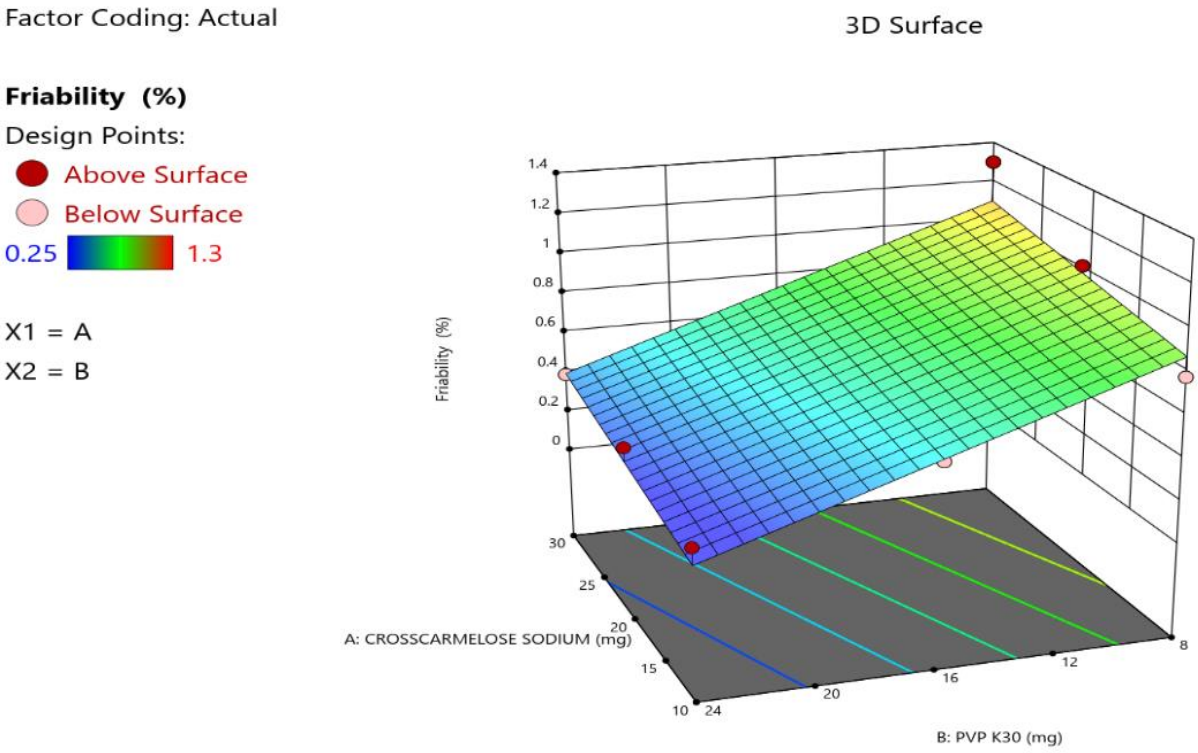


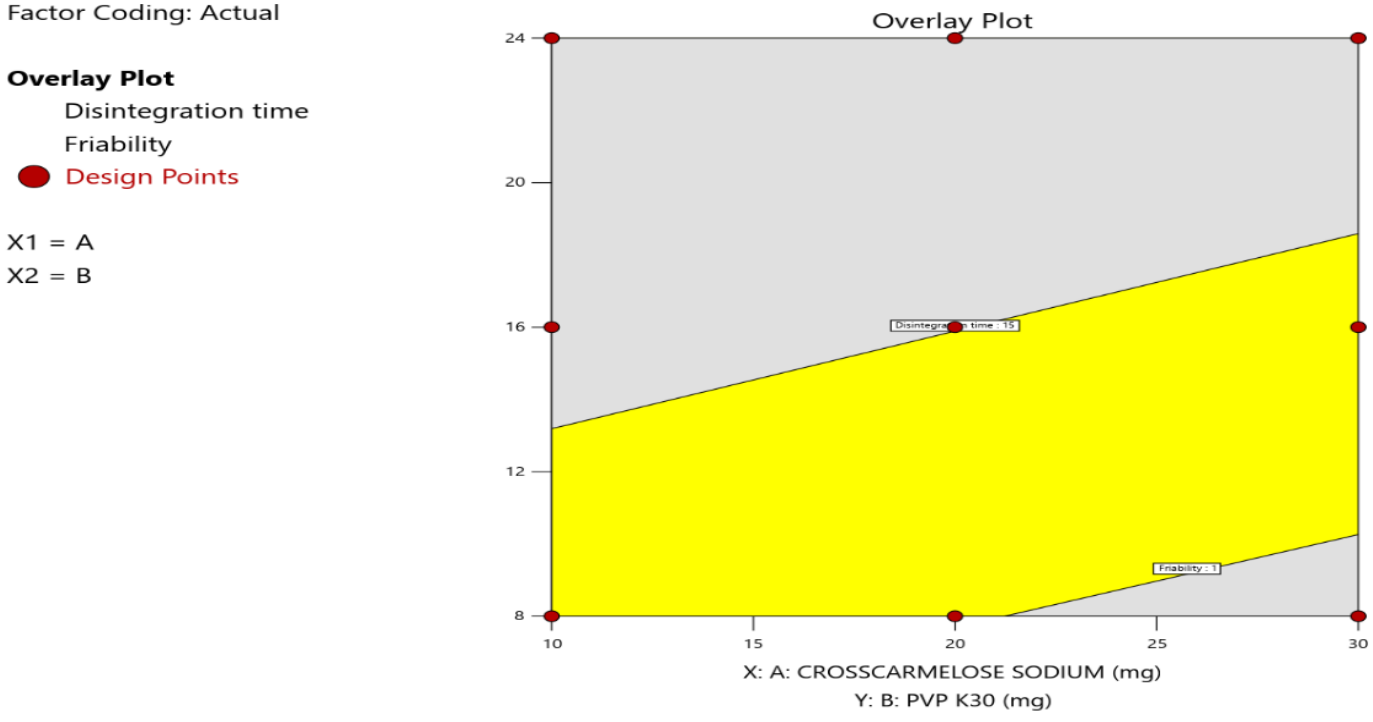
Figure 4: RSP- Response Surface- Plot for Response Y2- Friability



The concentration of Croscarmellose sodium has little effect on friability. As a result, it may be argued that X2 variable has a large influence on response Y2.

It was decided to create a design space for oral solid tablet formulation containing natural extracts. Based on product quality requirements, the parameters examined for establishing design-space include disintegration time (min) of maximum 15 minutes and Friability percentage of maximum 1. Bases on above criteria, it leads to a creation of design-space based on a multi-dimensional combination of ingredients, which leads to determination of right operating ranges for producing therapeutically useful oral solid tablets with respect to the target product profile. The shaded region with yellow hue in the design space (Overlay plot) depicted in Fig.-5 illustrates the space or area of optimum ranges of operation.

Figure 5: Overlay-plot with design-space shows that F-5 formulation trial (CCS-20 mg and PVP K-30 8 mg) falls in design-space region.



According to the Design-space, F-5 batch fall within the optimum operating ranges. As a result, formulations F-5 (PVP K-30 - 8 mg and CCS-20mg) meet the QTPP and CQA standards for oral solid tablet containing natural extract. As a result, F-5 was chosen as optimized formulation.

Table 10 shows the results. Predicted and measured values of the optimized formulation's (F-5) CQAs are practically identical. There is excellent agreement between experimental observations and model predictions. This implies that there is statistical equality between the experimental and anticipated values. This demonstrates the reliability of the formula-variables selected, their levels selected, and the techniques applied. 3^2 CCD- Central composite design was carried out for DoE-design of experiments. Formulation F-5 was further taken for accelerated stability study and evaluation.

Table 10: Predicted and experimental values comparison for F-5

Responses value	Predicted value	Actual value
Disintegration Time (Min)	11.62	11.56
Friability (%)	0.9861	1.02

To ensure that a consistent product of the required quality is manufactured, a control strategy has been developed. The control plan contained variables that were rated for high level risk in the original risk assessment & required to be managed within their permitted value ranges. CMAs of the drug material, i.e., plant extracts, are included in the Control-strategy of oral solid tablet formulation incorporating natural extracts, as are the measures used to limit the risk associated with these CMAs.

Table 11: Stability study for optimized formulation F-5

Evaluation	Initial	1 Month		3 Month	
		RT	Accelerated	RT	Accelerated
Parameters		30℃/75% RH	40℃/75% RH	30℃/75% RH	40℃/75% RH
Hardness (kg/cm^2)	03.1	03.05	03	03.08	03.04
Friability (%)	1.02	0.99	0.982	0.99	0.987
Disintegration (min)	11.56	12	12.5	12.2	13

Table 11 shows the findings of a stability study performed on the optimized batch (F-5) in accordance with ICH stability recommendations. The physical properties of formulation batch F-5 did not vary significantly. Hardness, friability, and disintegration time all changed slightly. However, these modifications remained within the parameters set. According to the research, the optimized formulation is stable for 3 months.

CONCLUSION

The results of this study demonstrated that the QbD technology may be successfully used to create oral solid tablets that contain natural extracts. The appropriate QTPP & CQAs were predefined so to get the desired final finished product quality. The study demonstrates that high level risk can be changed to low level risk by handling the formulation parameters within the suggested design-space. Additionally, it can be claimed that formulations created inside the design-space will be able to obtain CQAs in the finished product, delivering a product with the required QTPP.

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