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Fast Dissolving Tablets of Domperidone Using Natural Superdisintegrant: Formulation and Optimization

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ABSTRACT

Current research is focussed on development and optimization of fast dissolving tablets of Domperidone by applying 3^2 factorial design. Direct compression method was used. Two factors as independent variables (X_1- amount of β-cyclodextrin and X_2- amount of *LepidiumSativum* mucilage) were taken with three levels (+1,0,-1). The levels of two factors were selected on the basis of preliminary experiments conducted and their effect on three dependent variables (disintegration time, wetting time and *in vitro* drug release) was estimated.All the active blends were evaluated for precompression parameters (angle of repose, bulk density, carr's index, hausner's ratio) and formulated tablets were evaluated for post compression parameters (hardness, friability, weight variation, wetting time, disintegration time, water absorption ratio) and*In vitro* drug release studies. The software Design Expert (8.0.7.1) was used for generating experimental design, modeling the response surface and calculating the statistical evaluation. The optimised batch was further evaluated for SEM and accelerated stability studies. Tablet parametric tests of formulations (F1-F9) were observed within prescribed limits. DT was observed in the range from 15±2 to 42±4 sec and WT from 19±2 to 44±3 sec for formulation batches (F1-F9). Batch F6 was observed as promising batch with DT values of 15 sec and *in vitro* drug release (94%) in 15 min.No remarkable changes were observed in batch F6 (physicochemical properties and *in vitro*release profile)when kept for 3 months at 40ºC and 75% RH conditions. This indicates good stability of the formulation even after stressed conditions. Polynomial mathematical models, generated for various response variables using multiple regression analysis were found to be statistically significant ($p<0.05$). Conclusion: An optimized combination of *Lepidium Sativum* mucilage with β-cyclodextrin leads to successful development of fast dissolving tablets of Domperidone.

Keywords: β-cyclodextrin, direct compression, *Lepidium Sativum* mucilage, factorial design superdisintegrant

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INTRODUCTION

The admiration of oral dosage forms particularly tablets have not been obscured in spite of development of advanced drug delivery systems, because of its numerous advantages [1].However oral drug delivery systems faced many drawbacks such as dysphagia and delivery of unpalatable drugs, which may be a problem for mainly geriatric, pediatric, bedridden, nauseous or non-compliant patients[2].Difficulty in swallowing (dysphagia) is common among all age groups, especially in elderly, and is also seen in swallowing conventional tablets and capsules [3]. FDTs (fast dissolving tablets) are the most explored areas under development of alternate/ modified drug delivery systems for existing drug molecules. FDTs disintegrate or dissolve rapidly in the saliva without the aid of water. In clinical conditions like nausea and vomiting, administration of conventional dosage form with water is quite difficult. During emesis rapid peak plasma concentration is required to achieve desired pharmacological response[4]. FDTs serve the best fit for these physiological conditions. Fast dissolving/disintegrating dosage forms are also well established in the management of pain, inflammation, headache and hypertension. That is why the development of mouth dissolving with proper taste masking is among latest trends in pharmaceutical market[5]. Moreover if it is a BCS class II drug, there is a need to improve the dissolution rate of these drugs to maximize the therapeutic activity [6,7]. Valuable research reports for formulation of rapidly disintegrating tablets are available; also various technologies for improving dissolution property of poorly water soluble drugs have been documented to enhance bioavailability following oral absorption [5].The use of super disintegrants in FDTs plays a vital role in the disintegration and dissolution of tablet. Super disintegrants provide fast disintegration due to collective effect of swelling and water absorption by the tablet[8,9,10].The use of natural mucilage as super disintegrants[11]has been latest trends in research e.g. FDTs of nimesulide using *Lepidium Sativum*(LS) mucilage[12], FDTs of carvedilol by using *Plantago ovata* mucilage [13], FDT of poorly water soluble drug Glibenclamide using fenugreek, guar gum, modified locust bean gum and modified agar gum [14],FDTs of amlodipine besylate using Fenugreek seed mucilage and *Ocimumbasilicum* gum[15].The natural materials like gums and mucilages have been extensively used in the field of drug delivery for their easy availability, cost effectiveness, non-irritant nature, non-toxic, potentially degradable and compatible due to natural origin [11]. Domperidone is an antidopaminergic drug. It ischemically known as 1,3-dihydro-5-chloro-1-(1-(3-(2,3-dihydro2-oxo-1H-benzimidazol-1-yl)propyl)-4peridinyl)2Hbenzimidazol-2-one.

Domperidone does not readily cross the blood brain barrier. The low systemic bioavailability (13-17%) of the oral form of Domperidone is likely due to first pass hepatic metabolism and gut wall metabolism and significantly affected by the presence of food.

Present study involves the development of fast dissolving tablets of Domperidone based on a small number of experimental runs. Use of a 3^2factorial design was attempted to generate anoptimized region in the contour plots where the combination of β-cyclodextrin (β-CD) (solubility enhancer), and *Lepidium Sativum* (LS) mucilage (superdisintegrant) could provide hard and rapid disintegrating tablets which can release the drug maximally within 15 min.

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MATERIALS AND METHODS

Domperidone and Aspartame was kindly gifted by IPZAH Pharmaceutical Pvt. Ltd. Patiala, India. Mannitol, Talc and Magnesium stearate was procured from Loba Chemicals Pvt. Ltd. Ambala, India. Microcrystalline cellulose was obtained as a gift sample from Ontop Pharmaceutical Pvt. Ltd. Bangalore, India. β-CD and cross povidone was purchased from Signet Chemical Corporation, Mumbai. The seeds of *Lepidium Sativum* were purchased from local market.

METHODS:

Preformulation studies:

Isolation of mucilage from *Lepidium Sativum* (LS):

The seeds of *Lepidium Sativum* (LS) contain the mucilage around the outer layer. The seeds were boiled with distilled water for 15 min and the mass was filtered through buckner funnel without filter paper and the retained residues were boiled with distilled water for 15 min and the combined liquid was passed through eight folds of muslin cloth. Then the mucilage was precipitated from the filtrate by adding ethanol. The precipitated mucilage was dried in oven at 45°C till it was completely dried. The powder was passed through 80 mesh(#) and stored in dessicator. The dried powder was further evaluated for swelling studies[16].

Determination of Swelling Index:

Fine powdered LS mucilage (1 g) was placed into a 25 ml glass stoppered measuring cylinder. 25 ml of water was added into the cylinder containing material and mixture was shaken thoroughly at interval of every 10 min for 1 h and it was kept for 3 h at room temperature. Volume occupied by the plant material, including any sticky mucilage was measured.

Fourier Transform Infrared Spectroscopy (FTIR):

FTIR spectrum was recorded of pure drug, LSmucilage and mixture of drug with LS mucilage tocheck any interaction between the two. The samples were analysed by KBr pellet method. About 10 mg of the sample was mixed with dried potassium bromide of equal weight. Pellets were formed by compressing the mixture by using hydraulic press. The spectra are scanned over a frequency range 4000-400 cm^{-1}.

Preliminary batches of Fast Dissolving Tablets:

Various preliminary batches were formulated using different ratios (2-10%) of LS mucilage as super disintegrant and different ratios (5% and 10%) of β-CD, to observe the effect on disintegration/dissolution and wetting properties of tablets. Tablets of 200mg were compressed using single punch tablet machine. Good flow characteristics were observed in all

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active blends. A significant effect on disintegration, dissolution and wetting characteristics was observed by the presence of LS mucilage and β-CD.

Preparation of final batches using 3^2 factorial design (F1-F9):

From preliminary studies, 9 formulation batches were prepared by using 3^2 factorial design using two independent variables X_1 and X_2 where X_1-amount of β-CD and X_2- amount of LS mucilagewith three levels (-1, 0,+1).The composition of final formulation batches is depicted in table 1.

Table1: Composition of designbatches (F1-F9) of Domperidone Fast Dissolving Tablets

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Domperidone	10	10	10	10	10	10	10	10	10
Lepidium Sativum (LS) mucilage	4	8	12	4	8	12	4	8	12
β- CD	0	0	0	10	10	10	20	20	20
Mannitol	20	20	20	20	20	20	20	20	20
MCC	156	152	148	146	142	138	136	132	128
Talc	4	4	4	4	4	4	4	4	4
Mg stearate	2	2	2	2	2	2	2	2	2
Aspartame	4	4	4	4	4	4	4	4	4
Total weight	200	200	200	200	200	200	200	200	200

All the quantities are expressed in mg

Evaluation of Tablets (F1-F9):

Precompression parameters:

Bulk Density:

It was determined by pouring a weighed quantity of blend into graduated cylinder and measuring the volume and weight.

LBD (Loose bulk density) =Weight of powder/initial volume

Tapped Density:

It was determined by placing a graduated cylinder containing a known mass of active blend. The cylinder was allowed to fall under its own weight onto a hard surface from the

height of 10cm at 2 second intervals. The tapping was continued until no further change in volume was noted.

TBD (Tapped bulk density) =Weight of powder/volume of tapped packing

Angle of Repose:

Angle of repose was determined by using funnel method. The accurately weighed blend was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the head of blend. The drug-excipients blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder heap was measured and angle of repose was calculated using the following equation.

$$\tan \theta = h/r$$

Where h and r are the height and radius of the powder heap.

Hausner's Ratio:

Hausner's ratio is an indirect index of ease of powder flow. It was calculated by the following formula.

$$\text{Hausner's ratio} = D_t/D_b$$

Where D_t is the tapped density; $D_b$is the bulk density.

Carr's Index:

It indicates powder flow properties. It is expressed in percentage and is given by

$$I = \{D_t - D_b/D_t\} \times 100$$

Where, D_t is the tapped density and D_b is the bulk density of the powder.

Post compression parameters:

Weight Variation:

Total weight of 20 tablets from each formulation was determined and the average weight was calculated. The individual weight of the tablets was also determined accurately and the weight variation was calculated as specified in IP.

Thickness and Diameter:

It was measured by using Vernier Calipers. Three tablets were selected at random from each batch. It is expressed in mm.

Hardness:

Hardness or crushing strength was measured using Monsanto tablet hardness tester. It is expressed in kg/cm^2.

Friability test:

Friability test is carried out using Roche Friabilator, as specified in IP. The percentage of weight loss was calculated using the formula

$$\%Friability= [(W_1-W_2)100]/W_1$$

W_1 and W_2 is weight of tablet before and after test.

Wetting Time (WT):

Five circular tissue papers of 10cm diameter were placed in a petridish (10cm diameter). 10 ml of water containing Eosin, a water soluble dye, was added to petridish. A tablet was carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as wetting time.

Water Absorption Ratio:

A piece of tissue paper folded twice was placed in a small petridish (6mm) diameter containing 6ml of water. A tablet was put on the paper and the time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio, R, was determined using following equation:

$$R= 100\times(W_a-W_b)/W_b$$

Where W_b is weight of tablet before water absorption and W_a is weight of tablet after water absorption.

***In vitro* Disintegration Test:**

The USP disintegration test apparatus was used to determine disintegration time. The study was done in triplicate.

In vitro Drug Release Studies:

In vitro drug release was carried using USP II dissolution apparatus. The formulation batches were subjected to _in vitro_drug release in900ml of 0.1 N HClkept at 37± 0.5°C at a speed of 50 rpm. The aliquots were collected at specified time intervals (5, 10, 15, 30 and 45 min) and analyzed by UV spectroscopy. Cumulative drug release was then calculated. The study was done in triplicate.

Scanning Electron Microscopy (SEM):

The surface characteristics of optimum tablet formulation were evaluated by SEM studies. The micrographs were recorded using scanning electron microscope (**JEOL JSM-6100).** The sample was mounted on a double sided tape on aluminium stubs and was sputter coated with gold using fine coat ion sputter (**JEOL**).

Accelerated Stability Studies:

The stability studies of optimum tablet formulation were carried out in stability chamber (Remi Instruments, India) kept at 40° C and 75% RH conditions for three months. The effects of temperature and time on the physical characteristics of the tablet were evaluated for assessing the stability of the prepared formulations. The tablets were evaluated for their physicochemical parameters (such as hardness, thickness, diameter, friability, _in vitro_ disintegration time, wetting time, drug content and _in vitro_ dissolution) after 15days, 1 month, 2 month and 3 months.

RESULTS AND DISCUSSIONS

Determination of Swelling Index:

The swelling ratio of mucilage, determined in distilled water was observed to be 4.1± 0.563, indicated excellent swelling properties of mucilage.

Fourier Transform Infrared Spectroscopy (FTIR):

IR spectroscopy was carried out to evaluate chemical interaction between the drug and mucilage. The characteristics peaks of drug were observedat1680 cm^{-1},1485 cm^{-1},1125cm^{-1}representing stretching vibrations of N-H,C-N and C=O respectively (Figure 1).

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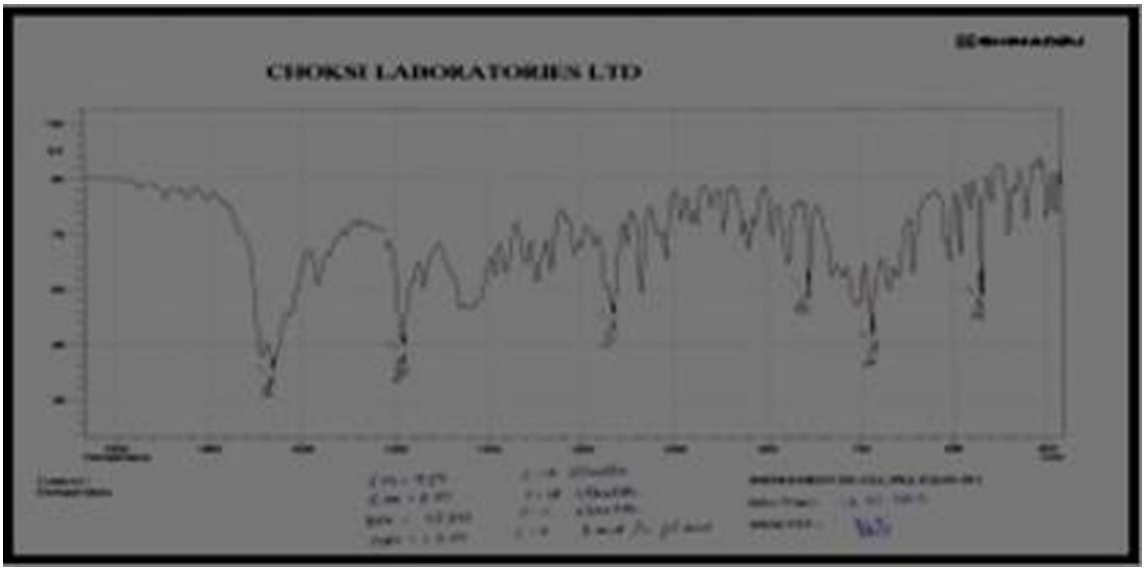

Figure 1

The IR spectra of LS mucilage suggested amorphous nature of polymer (Figure2).

Figure 2

The IR spectra of mixture revealed no difference in the position of absorption bands with respect toN-H,C-N,C=O indicating the absence of interaction between drug and mucilage (Figure 3).

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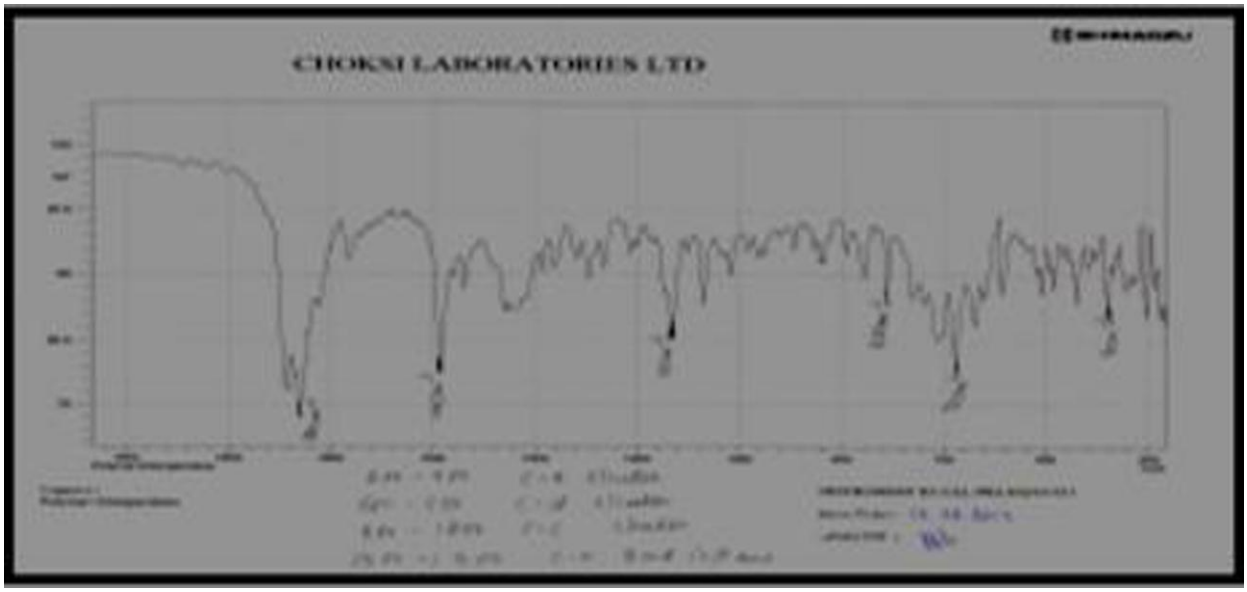

Figure 3

Evaluation of Tablets (F1-F9):

Pre compression Parameters:

The results of pre compression studies (bulk density, tapped density, angle of repose, Carr's index etc.) of active blends (F1-F9) are given in table 2. Good flow characteristics were observed to support further tableting.

Table 2: Evaluation of precompression parameters of design batches (F1-F9).

Parameter	F1	F2	F3	F4	F5	F6	F7	F8	F9
Bulk density(g/ml)	0.481± 0.023	0.484± 0.014	0.458± 0.021	0.514±0 .040	0.515± 0.041	0.504± 0.029	0.482± 0.025	0.484± 0.043	0.514±0 .009
Tapped density(g/ml)	0.584± 0.013	0.548± 0.023	0.550± 0.020	0.587±0 .009	0.589± 0.018	0.590± 0.021	0.570± 0.015	0.556± 0.019	0.605±0 .040
Angle of repose	20.30± 0.21	24.70± 0.13	21.30± 0.25	22.78±0 .32	22.79± 0.08	21.30± 0.15	22.29± 0.22	23.74± 0.09	25.64±0 .25
Carr's index	17.6	11.7	16.6	12.5	12.8	14.06	15.2	12.9	15
Hausner ratio	1.21	1.13	1.20	1.14	1.14	1.17	1.18	1.14	1.17

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Post compression Parameters:

The results of post compression studies are depicted in table 3.

Table 3: Evaluation of post compression parameters of design batches (F1-F9).

Parameters	F1	F2	F3	F4	F5	F6	F7	F8	F9
Weight of tablet (mg)	200.15	198.70	200.43	199.75	199.26	197.47	199.01	199.70	199.09
Thickness (mm)	3.42±0.04	3.52±0.04	3.59±0.03	3.46±0.04	3.51±0.03	3.34±0.04	3.47±0.03	3.55±0.03	3.54±0.03
Diameter (mm)	8.07±0.02	8.08±0.02	8.05±0.02	8.07± 0.02	8.08±0.01	8.05±0.02	8.07± 0.01	8.08±0.01	8.07±0.01
Hardness(kg /cm^2)	2.0±0.3	2.0±0.3	2.0±0.3	2.5±0.2	2.5±0.3	2.5±0.2	3.0±0.4	3.0±0.4	3.0±0.4
Friability (%)	0.9±0.05	0.9±0.04	0.9±0.04	0.62±0.03	0.65±0.03	0.69±0.04	0.31±0.03	0.33±0.03	0.38±0.03
Disintegration time (sec)	40±3	28±2	18±2	34±2	22±2	15±2	42±4	36±2	33±2
In vitro dispersion time (sec)	82±4	56±3	35±2	65±4	48±3	26±2	90±4	78±3	75±3
Wetting time (sec)	36±2	31±2	21±2	30±2	24±2	19±2	44±3	38±2	36±2
Water absorption ratio (%)	91.7	126	128	120	134	138	76	135	137

All nine formulations were uniform in dimensions, as well as exhibited sufficient hardness in the range of (2.0±0.3 kg/cm^2) to 3.0±0.4 kg/cm^2).The friability data (<1%) indicated sufficient resistance to abrasion. All the formulation batches passed weight variation test. The disintegration values less than 1 min was observed in all formulations. The super disintegrant (LS mucilage) alone has a significant impact on disintegration and wetting characteristics as seen in batch F1,F2 and F3.This may be due to enhanced swelling at higher mucilage concentration. The addition of β-CD in batches F4,F5 and F6 also improved the disintegration characteristics but not significantly. Higher amounts of β-CD in batches F7, F8 and F9 retard the disintegration and therefore drug release was also retarded. β -CD was added to enhance the dissolution characteristics which were observed in batch F6 (i.e. 100% drug release was observed within 30 min).F6 was observed as promising batch based upon disintegration and dissolution data.

***In vitro* Drug Release Studies:**

In vitro drug release of design batches (F1-F9) is shown in Figure 4.

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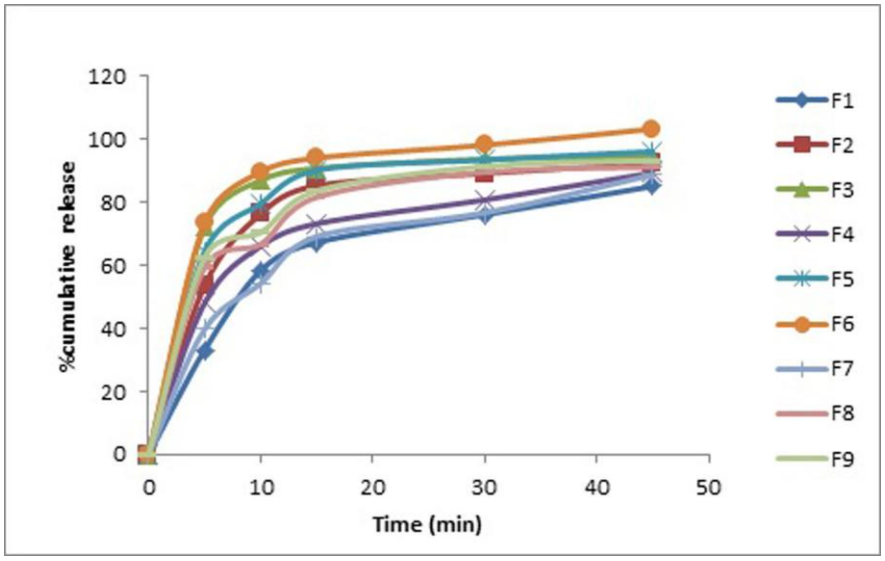

Figure 4

The increased concentration of LS mucilage leads to significantly enhanced drug release (90% in 30 min in batch F3).The addition of β-CD further improves dissolution of drug (batches F4-F6 in comparison to F1-F3) with maximum dissolution rate (94% in 15 min) in F6. This may be attributed to synergistic effect of rapid swelling action achieved with super disintegrant effect of mucilage and increased wet ability and thereby enhanced dissolution characteristics by β-CD. Higher amount of β-CD however retard drug dissolution which may be due to viscous polymeric networks.

Scanning Electron Microscopy (SEM):

The SEM photographs of optimised batch F6 are shown in Figure 5.

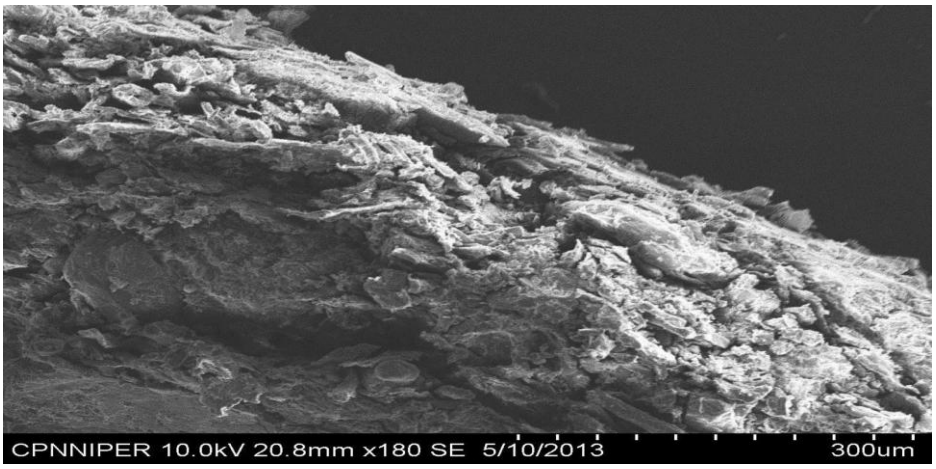

Figure 5

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Topological changes on tablet surface were observed which may be due to the presence of mucilage.

Accelerated Stability Studies:

Stability studies were carried out using optimum batch F6 as per ICH guidelines for 90 days at accelerated stability condition (40°C/75%RH). No remarkable changes were observed in batch F6 (as indicated by the results in table 4).This reveals stability of the formulation even after stressed conditions.

Table 4: Stability studies of optimised batch F6 at accelerated condition.

At Accelerated Condition(40°C and 75% RH)							
Parameter→ Time↓	**Weight Variation**	**Tablet Thickness (mm)**	**Tablet diameter (mm)**	**Hardness (kg/cm^2)**	**Wetting time (sec)**	**Friability (%)**	**Disintegration on time (sec)**
15 days	197.49	3.36±0.04	8.07±0.02	2.51±0.3	20±2	0.65±0.04	14±2
30 days	197.51	3.34±0.04	8.05±0.02	2.47±0.3	19±2	0.67±0.03	15±2
60 days	197.76	3.39±0.03	8.07±0.02	2.45±0.3	19±2	0.69±0.03	14±2
90 days	200.00	3.38±0.04	8.06±0.02	2.49±0.3	18±2	0.63±0.03	14±2

In vitro drug release was also carried out after 3 month stability testing and compared with initial F6 batch(before stability).The results indicated almost no change in drug release behaviour for F6 tablet after 3 month of stability testing (Figure 6).

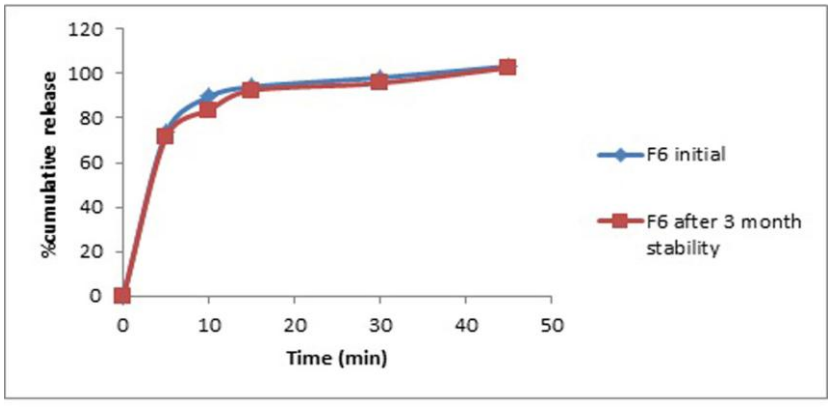

Figure 6

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EXPERIMENTAL DESIGN:

3^2 Full factorial design was applied to determine the effect of the amounts of β-cyclodextrin (X_1) and natural superdisintegrant (X_2) (as independent variables) on three response variables; disintegration time, wetting time and *in vitro* drug release respectively. Each factor was tested at three levels designated as-1, 0,+1. All other formulations and manufacturing variables were kept constant throughout the study. Table 5 summarizes the results of 9 experimental batches studied, their factor combinations and the translation of the coded levels of the experimental units employed during the study.

Table 5: Composition and Responses for 3^2 Factorial Design.

Batches	X_1	X_2	DT(sec) Mean±S.D.,n=3	WT (sec) Mean±S.D.,n=3	%cumulative drug release Mean±S.D.,n=3
F1	-1	-1	40±3	36±2	67.29
F2	-1	0	28±2	31±2	85.29
F3	-1	+1	18±2	21±2	90.81
F4	0	-1	34±2	30±2	73.22
F5	0	0	22±2	24±2	90.20
F6	0	+1	15±2	19±2	94.09
F7	+1	-1	42±4	44±3	69.136
F8	+1	0	36±2	38±2	81.61
F9	+1	+1	33±2	36±2	83.65

Translation of coded levels in actual units

Coded level	**-1**	**0**	**1**
X1: β-Cyclodextrin (mg)	**0**	**10**	**20**
X2: *Lepidium Sativum* (LS)mucilage (mg)	**4**	**8**	**12**

The results of ANOVA and regression analysis for three dependent variables are summarised in Table 6.

Table 6: Summary of results of Regression Analysis and ANOVA for measured response.

RESPONSE	b_0	b_1	b_2	b_{11}	b_{12}	b_{22}
			DT			
Full Model	281.47	114.4	-228.41	75.01	248.44	75.32
P value	0	0.0002	0	0.0011	0	0.0031
	Significant	Significant	Significant	Significant	Significant	Significant
Regression	DF	SS	MS	F	R^2	

	5	5.488E+.005	1.098E+.005	750.42	.9992	
WT						
Full Model	24.33	5	-5.67	1.75	10	0
P value	0.0047	0.0041	0.0029	0.1072	0.0027	1.000
	Significant	Significant	Significant	Significant	Significant	Significant
Regression	DF	SS	MS	F	R^2	
	5	554.92	110.98	47	.9874	
DR(15 min)						
Full Model	89.94	-1.5	9.82	-2.25	-6.21	-6
P value	0.0004	0.00178	0.0001	0.0102	0.0015	0.0016
	Significant	Significant	Significant	Significant	Significant	Significant
Regression	DF	SS	MS	F	R^2	
	5	761.03	153.21	253.52	.9976	

Mathematical Modelling:

The significance of the model and model terms were analyzed using ANOVA at 5% level of significance using statistical package Design Expert 8.0.4.7 (Stat-Ease Inc., Minneapolis, Minnesota, USA). The significance of model terms and a model fit comparison of response parameters are summarized in Table6.

The polynomial equation for DT, WT and DR (15min) was generated by multiple linear regression to quantitatively explain the effect of both factors on the responses. The various equations, in terms of coded factors, are as follows:

$$(DT)^{1.81} = 281.4 + 114.4\ X_1 - 228.4\ X_2 + 75.01\ X_1X_2 + 248.44\ X_1^2 + 75.32\ X_2^2$$

$$WT = 24.33 + 5\ X_1 - 5.6\ X_2 + 1.75\ X_1X_2 + 10\ X_1^2 - 1.57\ X_2^2$$

$$DR(15min) = 89.87 - 1.45\ X_1 + 9.8\ X_2 - 2.3\ X_1X_2 - 6.25\ X_1^2 - 6.05\ X_2^2$$

Disintegration Time (DT):

The Box-cox plot (Figure 7a) shows that data power law transformation with lambda 1.81 was required. This best lambda value was found at the minimum point of the curve generated by the natural log of the sum of squares of the residuals. Accordingly the equation represents the effect of two variables on DT. The polynomial equation indicates that there exists a significant inverse effect of concentration of β-CD and direct effect of LSmucilage on DT. In other words, as the concentration of LS mucilage is decreased and β-CD is increased, the value of DT decreases and the relationship follows power law.

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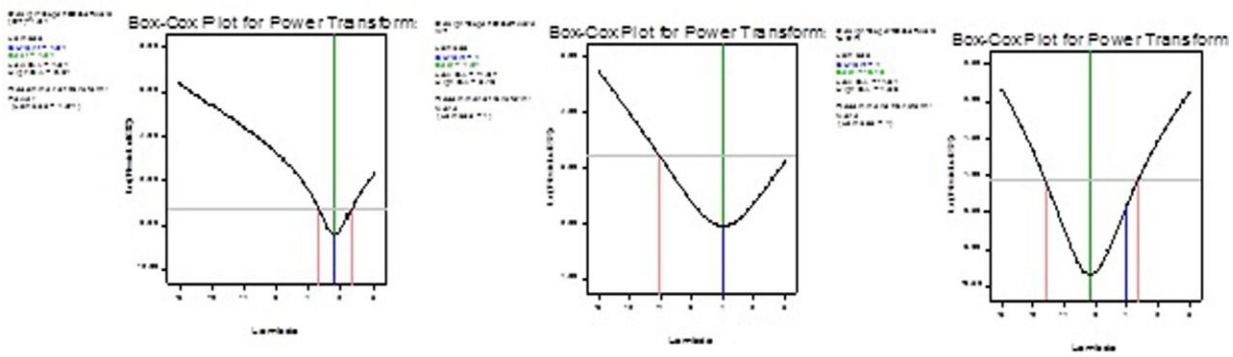

Figure 7(a,b,c)

The data indicates that disintegration time was decreased from 40±3 sec to 18±2 sec and from 42±4 sec to 33±2 sec at low and high level of β-CD respectively, as the concentration of the LS mucilage was increased. The DT value was increased from 40±3 sec to 42±4 sec and from 18±2 sec to 33±2 sec at low and high levels of LS mucilage respectively, as the concentration of β-CD was increased. Increased concentration of LS mucilage has significant effect on DT whereas β-CD exhibited minor effect on DT as indicated by coefficients in the equation. The response surface plot (Figure 8a) demonstrates the effect of amount of β-CD and LS mucilage on disintegration time (DT), which is in accordance with the observed data.

Wetting Time (WT):

The Box-cox plot indicates that transformation is not recommended to this data (Figure 7b).

The data indicates that wetting time was decreased from 36 ± 2 sec to 21 ± 2 sec and from 44 ± 3 sec to 36 ± 2 sec at low and high level of β-CD respectively, as the concentration of the LS mucilage increases. The wetting time value was first decreased from 36± 2 sec to 30 ± 2 sec and increased from 30 ± 2 sec to 44 ± 3 sec at low level of LS mucilage (with increasing amount of β-CD) and same random order in wetting time value was observed (i.e. 21sec→19 sec→36 sec) at high level of LS mucilage, as the concentration of β-CD was increased. Increased concentration of LS mucilage has significant effect on WT (as indicated in polynomial equation) whereas β-CD exhibited a random effect on WT. The response surface plot (Figure 7b) demonstrated the effect of amount of β-CD mucilage and LS mucilage on wetting time (WT).

Percent Drug Release (%DR) (15 min):

The Box-cox plot indicates that transformation is not recommended to this data (Figure 7c).

The response surface plot (Figure 8c) demonstrated the effect of amount of β- CD and LS mucilage on *in vitro* drug release. The data indicates that drug release was increased from

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(67.29 to 90.81%) and from (69.13 to 83.65%) at both low and high levels of β-CD with increasing concentration of LS mucilage.

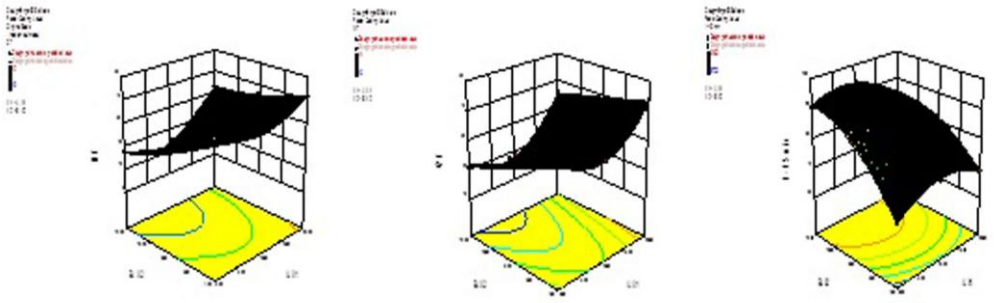

Figure 8(a,b,c)

The drug release was slightly increased from 67.29 to 69.136 % at low level of LS mucilage with increasing concentration of β-CD. At high level of LS mucilage, with increasing concentration of β-CD, the drug release was decreased from (90.80% to 83.65%). Increased concentration of LS mucilage has significant effect on *in vitro* release. β-CD showed random and negative effect on drug release.

OPTIMIZATION:

The pattern of variation of response parameters with two variables is the same. This indicates that middle levels of β-CD and high levels of LS Mucilage is desirable range to get optimized formulation as indicated in Table 7and Figure 9.

Table 7: Point Prediction

Factor	Name	Level	Low	Medium	High	Coding
X1	β- **cyclodextrin**	-0.i00	-1.00	0.00	1.00	Coded values
X2	LS mucilage	0.9	-1.00	0.00	1.00	Coded values

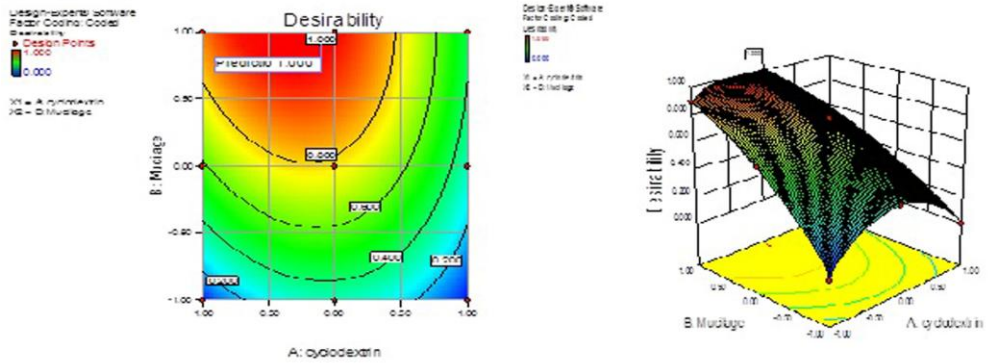

Figure 9

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CONCLUSION

Fast dissolving formulations of domperidone were developed by direct compression method and the effect of functionality differences of β-Cyclodextrin and LS mucilage on tablet properties was also elucidated using 3^2 Factorial design. The natural mucilage may act as an alternate carrier to synthetic super disintegrants. The amount of LS mucilage significantly affects the dependent variables (disintegration time, wetting time and *in vitro* drug release) and β-CD was observed to enhance the dissolution characteristics. Fast dissolving formulations of domperidone with enhanced solubility and bioavailability can be a successful drug delivery system.

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