

Formulation, Evaluation and Optimization of Fast Dissolving Tablets Containing *Amlodipine Besylate* by Sublimation Method

Narmada GY¹, Mohini K^{2*}, Prakash Rao B³, Gowrinath DXP⁴, kumar KS⁵

^{1, 2, 3} Department of Pharmaceutics, Visveswarapura Institute of Pharmaceutical Sciences, Bangalore, India

⁴ Nirmala college of pharmacy, kadapa, India

⁵ Cherran's college of pharmacy, coimbatore, India

Email: mohini.mpharm@gmail.com

ABSTRACT

The objective of this research was to formulate fast dissolving tablet of amlodipine besylate for rapid action. Sublimation method was adapted to prepare the tablets by using a 2³ full factorial design. FT-IR and D.T.A studies revealed that there was no physico-chemical interaction between amlodipine besylate and other excipients. All formulations are evaluated for pre-compression and post-compression parameters, wetting time, water absorption ratio. The results obtained showed that the quantity of starch potato, sodium starch glycolate, camphor significantly affect response variables. The results indicate that the optimized tablet formulation provides a short DT of 8 sec with sufficient crushing strength and acceptable friability. Stability studies of optimized formulation revealed that formulation is stable.

KEYWORDS: Amlodipine besylate, Camphor, Fast dissolving tablets, Sodium starch glycolate, Starch.

1. INTRODUCTION

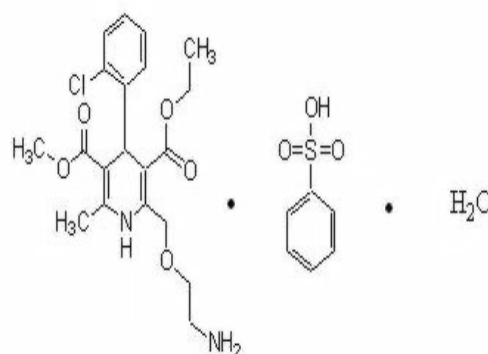
The concept of fast dissolving drug delivery system emerged from the desire to provide patient with conventional mean of taking their medication. Fast dissolving dosage forms can be disintegrated, dissolved, or suspended by saliva in the mouth. This fast dissolving tablet disintegrates instantaneously when placed on tongue and releases the drug dissolves or disperses in the saliva.¹ Fast dissolving tablets are useful in patients, ^{2, 3} like pediatric, geriatric, bedridden, or mentally disabled, who may face difficulty in swallowing conventional tablets or capsules⁴ leading to ineffective therapy, ⁵ with persistent nausea, sudden episodes of allergic attacks, or coughing for those who have an active life style. Fast dissolving tablets are also applicable when local action in the mouth is desirable such as local anesthetic for toothaches, oral ulcers, cold sores, or teething, ⁶ and to those who cannot

swallow intact sustained action tablets/capsules.⁷

Angina pectoris, commonly known as angina, is chest pain due to ischemia of the heart muscle, generally due to obstruction or spasm of the coronary arteries (the heart's blood vessels).⁸

The model drug selected was amlodipine besylate. Amlodipine besylate is chemically described as 3-Ethyl-5-methyl (±)-2-[(2-aminoethoxy) methyl] -4-(2-chlorophenyl)-1, 4-dihydro -6-methyl-3, 5-pyridinedicarboxylate, mono benzenesulphonate monohydrate.⁹

Figure 1: Structure of amlodipine besylate



Amlodipine is a dihydropyridine calcium antagonist (calcium ion antagonist or slow-channel blocker) that inhibits the transmembrane influx of calcium ions into vascular smooth muscle and cardiac muscle. Experimental data suggest that amlodipine binds to both dihydropyridine and non dihydropyridine binding sites. The contractile processes of cardiac muscle and vascular smooth muscle are dependent upon the movement of extra cellular calcium ions into these cells through specific ion channels. Amlodipine inhibits calcium ion influx across cell membranes selectively, with a greater effect on vascular smooth muscle cells than on cardiac muscle cells.¹⁰

Generally, the following points are considered for patient compliance in case of anti-angina patients, a rapid onset of action is necessary for immediate pain relief, patient has difficulty to swallow tablet or any another dosage form during pain, geriatrics has difficulty to swallow the dosage form. By considering the above points, patient convenience and compliance oriented research has resulted in bringing out safer and newer drug delivery systems one of such approach is fast dissolving drug delivery system. Conventional dosage forms for the anti-angina therapy includes tablets and injections. Injections provide effective rapid relief but, they are very painful and very expensive.

In this study, an attempt has been made to formulate fast dissolving tablet formulations of amlodipine besylate by using a 2³ factorial design by sublimation method.¹¹ The independent variables were selected as the quantities of starch potato, sodium starch glycolate (SSG)^{12, 13} and camphor, microcrystalline cellulose PH 102 (MCC)¹⁴ is used as diluent. Based on the preliminary studies, the ranges for formulation variables were selected. The dependent (response) variables were crushing strength, percentage friability and disintegration time (DT).

Camphor is a good subliming agent and in many formulations it is used as subliming agent.^{14, 15} In sublimation method, SSG is used as disintegrant and camphor as subliming agent.¹⁶

2. MATERIALS AND METHODS

2.1. Materials

Amlodipine besylate, aspartame, sodium stearyl fumarate(SSF) were received as gift samples from Strides Arco Lab Pvt. Ltd, Bangalore, India. Microcrystalline cellulose PH-102, starch potato, sodium starch glycolate, orange flavor was supplied by BIO PLUS Pvt. Ltd. Bangalore, India. Other materials used were analytical grade.

2.2. Experimental Design

In the present study a 2³ full factorial design was employed, containing 3 factors evaluated at 2 levels **Table 1**. The experimental trials were performed at 8 possible combinations and the three independent formulation variables evaluated included:

A= Amount of Starch Potato

B= Amount of Sodium Starch Glycolate

C= Camphor

Table 1: Level of formulation variables

Coded values	Independent variables		
	starch (A) (mg)	SSG (B) (mg)	camphor (C) (mg)
-1	19.2	8	8
1	30.4	12.8	11.2

2.3. Formulation by sublimation method:

In this study fast-dissolving tablet were prepared by using camphor. Eight formulations of Amlodipine besylate containing camphor^{17, 18} in different proportions were prepared by using MCC (PH102) as a diluent. All the ingredients were passed through # 60 mesh separately. The drug and the diluents was mixed in small portion of both each time and blending it to get uniform mixture and set aside. The other ingredients were weighed and mixed in geometrical order. Flavouring agent was added at the end and then mixed thoroughly with lubricant. The tablets of weight 160 mg were prepared by direct compression technique using 7 mm punch in 10-station rotary machine; Remake Minipress, Ahmedabad and the tablets are subjected to sublimation to attain the constant weight which indicates the complete removal of subliming agent. The composition of the factorial design batches is shown in **Table 2**.

Table 2: Formulation of amlodipine besylate tablets

INGREDIENTS	Starch	SSG	Camphor
F1(mg)	19.2	12.8	11.2
F2(mg)	30.4	12.8	11.2
F3(mg)	19.2	8	11.2
F4(mg)	30.4	8	11.2
F5(mg)	30.4	8	8
F6(mg)	19.2	12.8	8
F7(mg)	19.2	8	8
F8(mg)	30.4	12.8	8
FSP(mg)	20.97	12.8	9.07

3. COMPATIBILITY STUDIES

3.1. Fourier Transform Infrared Spectroscopy (FT-IR):

FT-IR spectroscopy was carried out for the following a) pure drug amlodipine besylate b) amlodipine besylate with starch c) amlodipine besylate with SSG d) amlodipine besylate with camphor e) amlodipine besylate with MCC f) amlodipine besylate with aspartame g) amlodipine besylate with aerosil h) amlodipine besylate with sodium stearyl fumarate (SSF) using Shimadzu FTIR model 8300 by taking KBr disc.

3.2. DIFFERENTIAL THERMAL ANALYSIS (DTA):

Amlodipine besylate and excipients were weighed and sealed in 40 ml aluminum crucibles with a pierced aluminum lid. Differential thermal analysis thermograms were obtained using a Mettler-Toledo STAR system and the DSC 822/700/1089 module (calibrated with indium). The analyses were performed under nitrogen (nitrogen flow rate 50 ml/min) in order to eliminate oxidative and pyrolytic effects at a standard heating rate of 15°C/minute over a temperature range of 30°C - 300°C. The melting range and other transitions of the drug substance and the individual excipient were determined previously and the representative thermograms were retained for comparison with the thermograms of mixtures.

DTA was carried out for the following a) pure drug amlodipine besylate b) amlodipine besylate with starch c) amlodipine besylate with SSG d) amlodipine besylate with camphor e) amlodipine besylate with MCC using a Mettler-Toledo STAR system

4. 3. EVALUATION PARAMETERS

4.1. Pre-compression Parameters

4.1.1. Flow properties

The tablet blends were evaluated for their bulk density, tapped density, carr's index

and flow properties. The tapping method was used to determine the tapped density, bulk density and percent carr's index.

4.2. Post-compression Parameters

4.2.1. Tablet Hardness

The strength of tablet is expressed as tensile strength (Kg/cm^2). The tablet crushing load, which is the force required to break a tablet into pieces by compression. It was measured using a tablet hardness tester (Monsanto hardness tester).¹⁹

4.2.2. Weight Variation Test

Randomly selected 20 tablets were weighed individually and together in a single pan balance. The average weight was noted and standard deviation was calculated. IP limit for weight variation in case of tablets weighting up to 120 mg is $\pm 10\%$, 120 mg to 300 mg is $\pm 7.5\%$ and more than 300 mg is $\pm 5\%$.

$$\text{PD} = (\text{W}_{\text{avg}}) - (\text{W}_{\text{initial}}) / (\text{W}_{\text{avg}}) \times 100$$

Where PD= Percentage deviation,

W_{avg} = Average weight of tablet,

$\text{W}_{\text{initial}}$ = Individual weight of tablet.

4.2.3. Friability

Roche friabilator was used for the purpose. This device subjects a number of tablets to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at a distance of 6 inches with each revolution. Pre-weighed 20 tablets were placed in the friabilator, which was then operated for 100 revolutions. Tablets were dusted and reweighed.

4.2.4. Drug Content

Ten tablets were powdered and the blend equivalent to 5 mg of amlodipine besylate was weight and dissolved in suitable quantity of pH 1.2 solutions. Solution was filtered and diluted and drug content analyzed spectrophotometrically at 239 nm using Shimadzu Corporation, UV-1601, Japan.

4.2.5. Disintegration Time

The disintegration time of tablet was measured in water (37°C) according to USP disintegration test apparatus. Three trials for each were performed.¹⁷

4.2.6. Wetting Time and Water Absorption Ratio

A piece of tissue paper folded twice was kept in a culture dish (internal diameter 5.5 cm) containing 6 ml of purified water. A tablet having a small amount of amaranth powder on the upper surface was placed on the tissue paper. The time required to develop a red color on the upper surface of the tablet was recorded as the wetting time. The same procedure without amaranth was followed for determining the water absorption ratio.²⁰ The wetted tablet was weighed and the water absorption ratio, R, was determined according to the following

equation,

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

Where, W_b and W_a were the weights of the tablet before and after study.

4.2.7. In vitro dispersion time

In vitro dispersion time was measured by dropping a tablet in a beaker containing 50 ml of Sorenson's buffer pH 6.8. Three tablets from each formulation were randomly selected and *in vitro* dispersion time was performed.^{21, 22}

4.2.8. Dissolution Studies of Formulated Tablets

The dissolution of amlodipine besylate tablets was carried out in basket type dissolution apparatus. The dissolution medium, 500 ml of 0.1 N HCL was taken and temperature is maintained at $37 \pm 1^\circ\text{C}$. The basket was rotated at 75 rpm for 30min.²³ The sample of 10 ml was withdrawn after every 5 min. and its absorbance was measured at 239 nm.

5. Results and discussion

5.1. Compatibility Studies

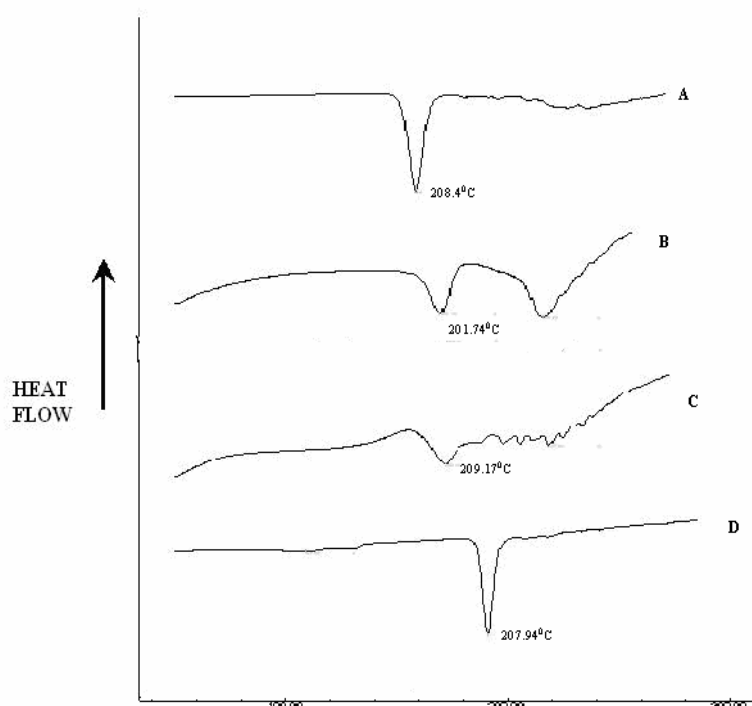
The FT-IR studies revealed that amlodipine besylate is compatible with the excipients used in the formulation. There were no extra peaks observed in the IR spectrum. The IR absorption band in cm^{-1} of the drug and excipients was found to be similar. This established that the drug amlodipine besylate and all the excipients used in the study showed no interaction and indicated that they were compatible with each other **Table 3**.

Table 3 FT-IR studies of amlodipine besylate alone and with excipients

COMBINATIONS	AMINE GROUP (cm^{-1})	ETHYLESTER OF ARYL ACID (cm^{-1})	SULFONIC SALTS (cm^{-1})	ALIPHATIC ETHERS (cm^{-1})
PURE DRUG	3194.23	1303.92	1184.33	1122.61
DRUG WITH SSG	3152.11	1325.01	1168.9	1120.68
DRUG WITH CAMPHOR	3108.21	1356.02	1156.06	1125.11
DRUG WITH MCC	3155.65	1303.92	1178.55	1118.75
DRUG WITH ASPARTAME	3118.02	1329.15	1158.31	1114.25
DRUG WITH AEROSIL	3125.16	1345.02	1165.13	1109.21
DRUG WITH SSF	3130.22	1335.21	1155.15	1125.07

In DTA, the chemical and physical changes of the substance are recorded as a function of temperature or time as substance is heated at a linear rate. DTA is useful in investigation of solid state interaction. In DTA, Thermograms are generated for the pure component and their physical mixture. In the absence of the any interaction, thermogram of mixture shows patterns corresponding to those of the individual components. DTA studies also revealed that amlodipine besylate is compatible with the excipients used in the formulation **Figure 2**.

Figure 2: D.T.A of amlodipine besylate and with excipients A) Pure drug, B) Drug with SSG, C) Drug with MCC and D) Drug with camphor



5.2. Pre-compression Parameters

Powders were prepared by using sublimation method having good flow properties and good compressibility index as indicated in **Table 4**.

Table 4. Pre compression Parameters of granules of Amlodipine Besylate by Sublimation Method

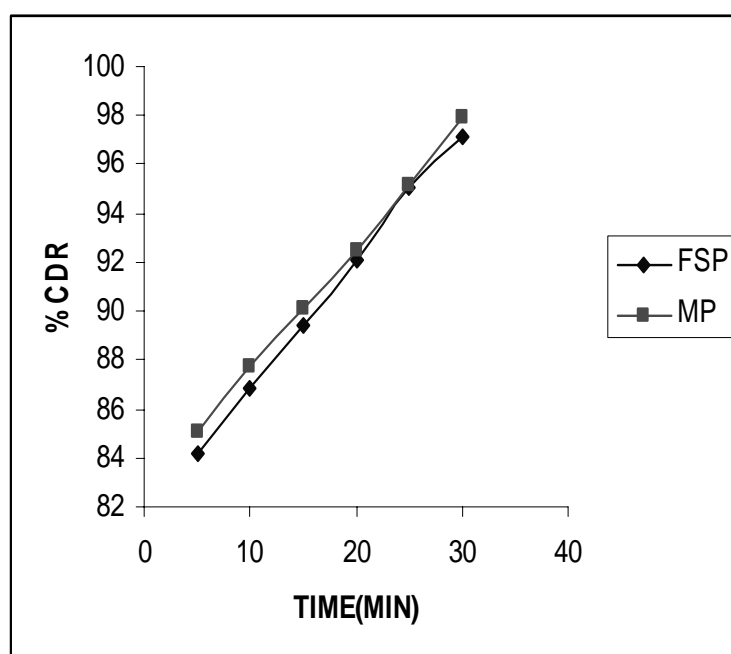
Formulations	BULK DENSITY (g/ml)	TAPPED DENSITY(g/ml)	ANGLE OF REPOSE (o)	MEAN CARR'S INDEX	HAUSNER'S RATIO
F1	0.467 ± 0.29	0.5914 ± 0.19	30.6 ± 0.28	21.9 ± 0.13	1.26±0.16
F2	0.478 ± 0.32	0.598 ± 0.27	29.1 ± 0.25	20 ± 0.17	1.25±0.17
F3	0.447 ± 0.39	0.573 ± 0.32	29.7 ± 0.23	21.9 ± 0.23	1.28±0.14
F4	0.469 ± 0.25	0.59 ± 0.19	29.3 ± 0.23	20.5 ± 0.31	1.25±0.14

F5	0.469 ± 0.27	0.577 ± 0.39	27.7 ± 0.35	18.5 ± 0.33	1.23 ± 0.12
F6	0.449 ± 0.31	0.555 ± 0.15	27.3 ± 0.25	18.9 ± 0.41	1.23 ± 0.16
F7	0.465 ± 0.42	0.552 ± 0.27	26.4 ± 0.55	15.7 ± 0.28	1.18 ± 0.13
F8	0.472 ± 0.4	0.589 ± 0.3	29.6 ± 0.43	19.8 ± 0.09	1.24 ± 0.19
FSP	0.470 ± 0.16	0.60 ± 0.22	27.2 ± 0.09	21.6 ± 0.31	1.27 ± 0.07

5.3. Post compression Parameters

The hardness of the tablet was found between 3.0 - 4.5 kg/cm² which have good mechanical strength. The tablet thickness was found to be 3.1-3.25 mm, weight variation the average percentage deviation of 20 tablets of each formula was less than $\pm 7.5\%$ **Table 5**, which provided good uniformity, friability of tablet was found below 1% indicating good mechanical resistance. The drug content found in the range of 97-102% (acceptable limit), disintegration time of all batches was found in the range of 6.5 – 9.7 sec. The wetting time of formulated tablets was found in the range of 9.3 – 22.5sec, water absorption ratio 77.5 – 83.1% , In vitro dispersion time 15.2 – 24 s,%CDR 96.0% - 97.7% and the %CDR of optimized formulation was compared with marketed product **Figure 3**.

Figure 3: Comparison of dissolution profiles of optimized formula (FSP) with marketed product



FSP - OPTIMIZED FORMULA OF SUBLIMATION

MP - MARKETING PRODUCT

Table 5. (a) Post Compression Parameters of Tablets (F1 – F4) of Sublimation Method

Parameters	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)
Weight Variation	0.603 ± 0.011	0.600 ± 0.009	0.602 ± 0.010	0.601 ± 0.135
Thickness (mm)	3.25 ± 0.07	3.2 ± 0.19	3.25 ± 0.14	3.25 ± 0.2
Hardness (kg/cm ²)	3 ± 0.09	3.5 ± 0.14	3 ± 0.12	3.75 ± 0.32
Friability (% w/w)	0.42 ± 0.21	0.3 ± 0.25	0.4 ± 0.13	0.28 ± 0.14
Disintegration time (sec)	6.52 ± 0.08	6.9 ± 0.21	7.2 ± 0.22	7.81 ± 0.14
Wetting time (sec)	9.3 ± 0.11	11.3 ± 0.32	12.5 ± 0.29	16.1 ± 0.21
Water absorption ratio (%)	82.3 ± 0.16	83.1 ± 0.21	81.6 ± 0.1	82 ± 0.15
In Vitro Dispersion Time (sec)	15.2 ± 0.07	15.8 ± 0.2	15.4 ± 0.16	17.8 ± 0.19
%Drug content	97 ± 0.31	100.6 ± 0.22	102 ± 0.2	101 ± 0.18
%CDR	96.0	96.7	97.5	97.1

(b) Post Compression Parameters of Tablets (F5 – F8, FSP) of Sublimation Method

F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)	FSP(mg)
0.602 ± 0.008	0.601 ± 0.010	0.602 ± 0.008	0.599 ± 0.008	0.602 ± 0.13
3.15 ± 0.05	3.1 ± 0.24	3.2 ± 0.1	3.15 ± 0.11	3.15 ± 0.07
4.5 ± 0.38	4 ± 0.25	4 ± 0.21	4.5 ± 0.33	3.75 ± 0.21
0.15 ± 0.11	0.25 ± 0.06	0.24 ± 0.21	0.19 ± 0.27	0.30 ± 0.24
9.71 ± 0.27	7.5 ± 0.16	8.5 ± 0.1	7.93 ± 0.36	8.0 ± 0.14
22.5 ± 0.19	16.4 ± 0.27	18 ± 0.19	16.7 ± 0.09	11.9 ± 0.32
77.5 ± 0.31	80.2 ± 0.22	81.4 ± 0.19	81.1 ± 0.17	84.7 ± 0.20
24 ± 0.19	17 ± 0.31	19 ± 0.26	18.4 ± 0.1	19 ± 0.13
98 ± 0.25	99 ± 0.3	102 ± 0.22	97 ± 0.15	102 ± 0.11
96.8	97.7	97.1	97.0	97.1

5.4. Optimization results

5.4.1. Effect of formulation variables on Hardness (R1)

The models were found to be significant with F value of 129.88 and P value of 0.0002. In this case A, C are significant model terms and The model describing the hardness (R1) can be written as :

$$R1 = +5.27214 + 0.042857 * A - 0.025000 * B - 0.24062 * C$$

As the conc of starch increases, hardness also increases. As the conc of SSG and camphor increases the hardness decreases. **Figure 4** represents the observed response values compared to that of predicted values. The effect of factors A, B and C can be further elucidated with the help of response surface plot **Figure 5**. In case of figure 5(a) factor A (starch) gave high value of R1 and in case of figure 5(b) high level of factor A gave high

value of R1 which indicates that the factor A have significant positive effect on hardness.

Figure 4: Correlation between actual and predicted values for hardness (R1)

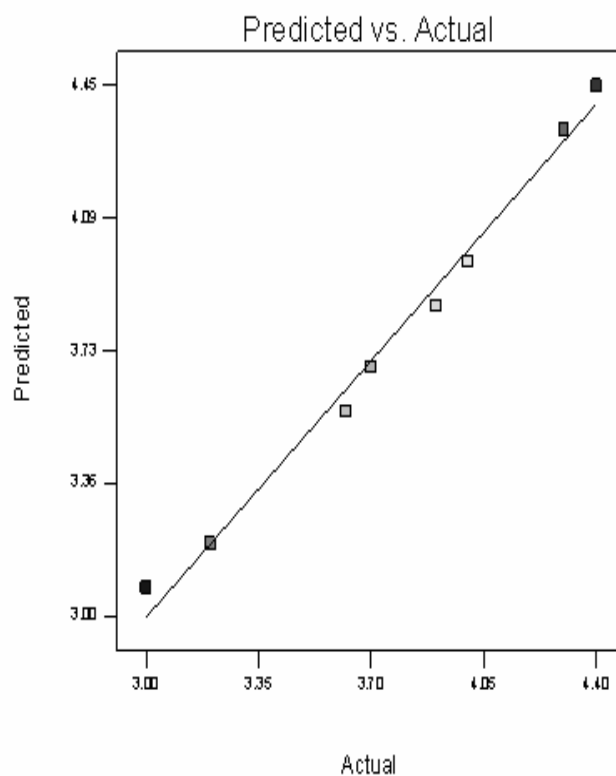
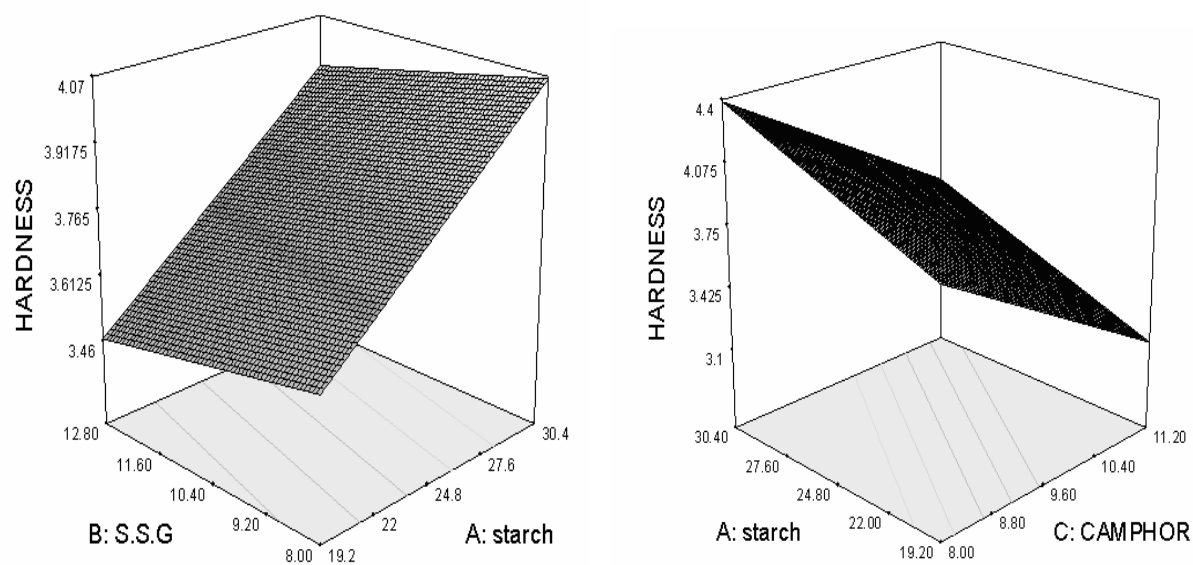


Figure 5: Response surface plots showing the effect of (a) SSG and starch (b) camphor and starch on hardness (R1)



5.4.2. Effect of formulation variables on Disintegration time

The terms R² of the model were found to be significant with an F value of 21.58 and P value of 0.0062. In this case A, B, C are significant model terms and The model describing the disintegration time (R²) can be written as :

$$R2 = +12.42262 + 0.060714 * A - 0.22292 * B - 0.40000 * C$$

As the conc of starch increases, D.T also increases, as the conc of S.S.G,L-H.P.C increases causes the decreases the D.T. **Figure 6** represents the observed response values compared to that of predicted values. The effect of factors A, B and C can be further elucidated with the help of response surface plot **Figure 7**. In case of figure 7(a) at high factor B (SSG) gave low value of R² at all levels of factor A (Starch) and in case of figure 7(b) high level of factor c(camphor) gave low value of R² at all the levels of factor A which indicates that the factor B,C have significant negative effect on disintegration time.

Figure 6. Correlation between actual and predicted values for disintegration time (R²)

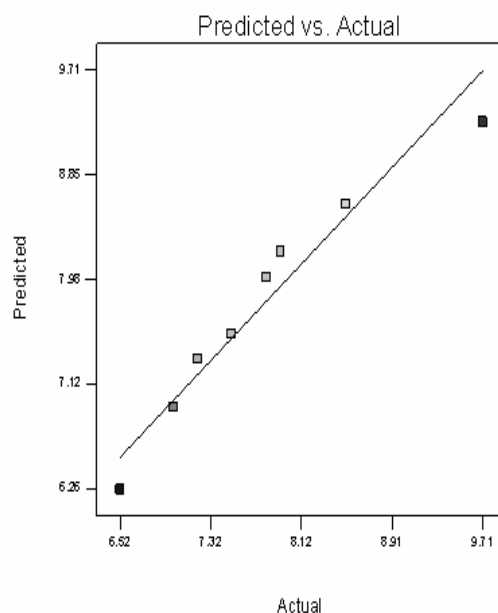
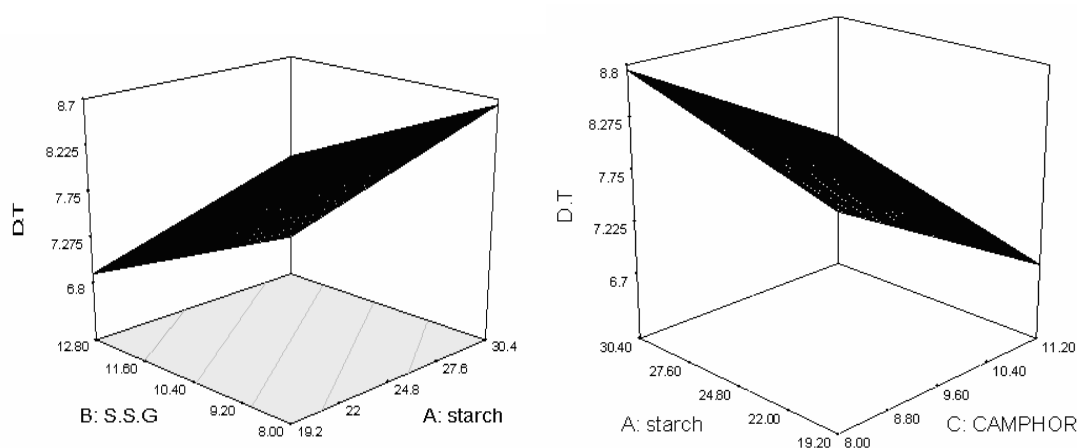


Figure 7: Response surface plots showing the effect of (a) SSG and starch (b) camphor and starch on disintegration time (R²)



5.4.3. Effect of formulation variables on Friability

The terms R3 of the model were found to be significant with an F value of 64.68 and P value OF 0.0008. In this case A, C are significant model terms. and The model describing the friability (R3) can be written as :

$$R3 = +0.018393 - 8.70536E003 * A + 4.68750E003 * B + 0.044531 * C$$

As the conc of starch increases, friability also increases, as the conc of S.S.G,L-H.P.C increases causes the decreases the friability. **Figure 8** represents the observed response values compared to that of predicted values. The effect of factors A, B and C can be further elucidated with the help of response surface plot **Figure 9**. In case of figure 9(a) factor A (starch) gave low value of R3 at all levels of factor B (SSG) and in case of figure 9(b) high level of factor A gave low value of R3 at all the levels of factor C (camphor) which indicates that the factor A have significant negative effect on friability.

Figure 8: Correlation between actual and predicted values for friability (R3)

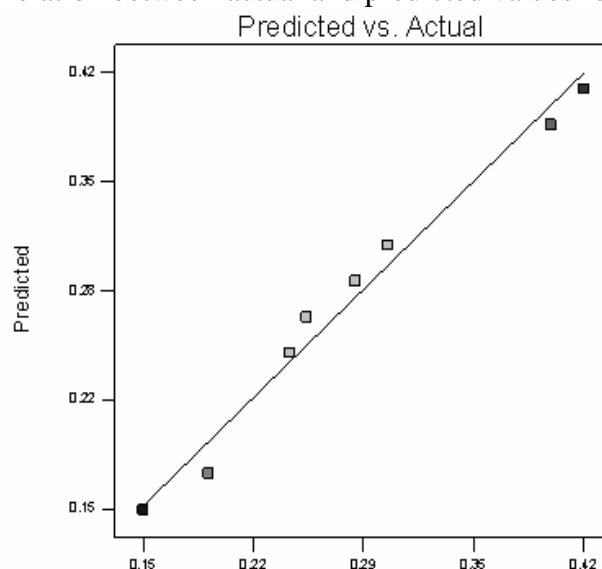
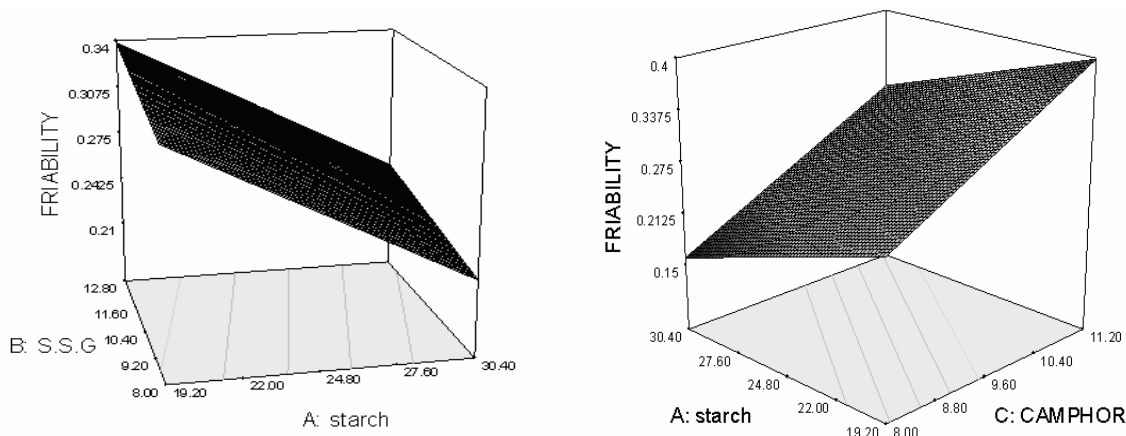


Figure 9: Response surface plots showing the effect of (a) SSG and starch (b) camphor and starch on friability (R3)



The ANOVA in **Table 6** for the dependent (response) variables demonstrates that the

model was significant for all response variables.

Table 6. Analysis of Variance for Dependent Variables from Factorial Design

Source	Sum square	d.f	Mean square	F value	Probability
Hardness kg/cm ²					
A- starch	0.46	1	0.46	107.16	R ² =0.9898 0.0005
B- S.S.G	0.029	1	0.029	6.7	0.0608
C-L-H.P.C	1.19	1	1.19	275.77	< 0.0001
Disintegration time sec					
A- starch	0.92	1	0.92	9.22	R ² =0.9418 0.0385
B- S.S.G	2.29	1	2.29	22.84	0.0088
C-L-H.P.C	3.28	1	3.28	32.69	0.0046
Friability (%)					
A- starch	0.019	1	0.019	60.84	R ² =0.9798 0.0015
B- S.S.G	1.01E-03	1	1.01E-03	3.24	0.1462
C-L-H.P.C	0.041	1	0.041	129.96	0.0003

Hence, the above results lead us to believe that concentrations of disintegrant and subliming agent have an important role to play, and optimal concentrations in fast dissolving tablets give rise to rapid disintegration times, good crushing strength values, and sufficiently low friability percentages, in order to successfully withstand the mechanical stress, during packing, transportation and handling.

6. Optimized formula:

A numerical optimization technique, focused on the desirability approach, was used to generate the optimum settings for the most effective formulation. The objective in the design of the process was to optimize the dependent (response) variables R1, R2, R3. The optimized formulation obtained was included in **Table 2**. The optimized formulation was prepared and evaluated for the various responses. The optimized results obtained were included in **Table 4**, **5**. The results in **Table 7** showed a good relationship between experimental and predicted values, which confirms the practicability and validity of the model.

Table 7. Comparison between the experimental (E) and predicted (P) values for the most probable optimal formulation

Optimized formulation	Dependable variables		
	Hardness R1 (kg/cm ²)	Disintegration time R2 (sec)	% friability R3 (% w/w)
Pred.	3.66	7.2	0.29
Exp.	3.75	8	0.3

7. Stability Studies

The stability studies of optimized formula were carried out at 40 °C and 75% RH using stability chamber for six months. The different parameters that were studied are disintegration time, hardness, friability, drug content and dissolution rate.^{24, 25} the optimized formulation was found to be stable in terms of physical appearance, drug content, disintegration time and *in vitro* drug release in **Table 8**.

Table 8. Stability Studies for optimized formula of Sublimation method (FSP)

Parameters	Initial	At 40 °C and 75% RH
Shape	Round	Round
colour	White	White
Odor	Orange	Orange
Weight Variation	0.602 ± 0.13	0.597 ± 0.05
Thickness(mm)	3.15 ± 0.07	3.15 ± 0.15
Hardness (kg/cm ²)	3.75 ± 0.21	3.75 ± 0.08
Friability (% w/w)	0.30 ± 0.24	0.30 ± 0.07
Disintegration time (sec)	8.0 ± 0.14	8.4 ± 0.10
Wetting time (sec)	11.9 ± 0.32	12.0 ± 0.08
Water absorption ratio (%)	84.7 ± 0.20	84.9 ± 0.31
In vitro dispersion time (sec)	19 ± 0.13	19.5 ± 0.10
% Drug content	102 ± 0.11	102 ± 0.05
%CDR	97.1	97.1

8. Conclusion

The results of a 2³ full factorial design revealed that the amount of camphor, starch and sodium starch glycolate significantly affect the dependent variables such as disintegration time, hardness and percentage friability. Thus it is concluded that by adopting a systematic formulation approach, an optimum point can be reached in the shortest time with minimum efforts. Sublimation technique would be an effective alternative approach compared with the use of more expensive adjuvant in the formulation of fast dissolving tablets.

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