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FORMULATION AND EVALUATION OF FAST DISSOLVING TABLETS OF CHARANTIN USING TWO DIFFERENT TECHNUQUES

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ABSTRACT

Fast dissolving tablets considered as an innovative dosage form to avoid the problem of swallowing and to provide quick onset of action. Here Charantin containing fast dissolving tablets were prepared by using two different techniques i.e., direct compression and sublimation method. All the formulations in both methods prepared by using three different superdisintegrants viz Crospovidone, Croscarmellose sodium and sodium starch glycolate in 5% and 10% concentration. And in sublimation technique Camphor used as sublimating agent. Then all the prepared formulation was evaluated for certain pre formulation parameters and also post formulation parameters. Comparative study of two different methods shows that sublimation method is a better alternative to direct compression technique.

KEYWORDS: Charantin, Crospovidone, Croscarmellose sodium, Sodium starch glycolate, Direct compression method, Sublimation method.

INTRODUCTION

Oral route is most preferred route among the different conventional dosage forms and it remains as most acceptable route because of low cost of therapy and ease of administration. To increase patient compliance and convenience fast dissolving tablets system emerged as newer drug delivery system. Nowadays fast dissolving drug delivery system increasing its popularity and acceptance too for reason of rapid disintegration and dissolution without need of water or chewing. And this system emerged as good alternative for many class of patients who find difficulties in swallowing tablets and capsules. Swallowing problems usually common in children due to underdeveloped muscular and nervous system.[1,2]

Charantin is a main constituent of Momordica Charantia which belongs to family of Cucurbitaceae. It is steroidal glucoside which contains equal mixture of sitosteryl glucoside and stigmasteryl glucoside.[3] It is soluble in methanol, sparingly soluble in water, slightly soluble in polar solvents like chloroform etc. It reveals various activities such as anti-tumor, antioxidant, anti-ulcer activities etc., And Charantin mainly optimize the blood glucose level by enhancing the glucose uptake and glycogen synthesis in liver, fat cells and muscles. It also helps in insulin release from pancreatic beta cells by repairing and increasing the new beta cell production. It exhibits the sugar lowering property equivalent to insulin.[4,5]

In the present work, an attempt has been made to develop fast dissolving tablets containing Charantin by direct compression and sublimation methods using suitable superdisintegrants and subliming agents.

MATERIALS AND METHODS

Charantin used was bought from Shreedha phytochemicals, Jaipur, India and β- Cyclodextrin was obtained from Rolex chemicals, Mumbai. Crospovidone, Croscarmellose sodium, sodium starch glycolate were obtained from Shreeji chemicals, Mumbai, India. Camphor was obtained from Thomas baker pvt.ltd, Mumbai. Microcrystalline cellulose obtained from SD fine chemical ltd, Mumbai, India. All other chemicals used were of analytical grade.

PREPARATION OF FAST DISSOLVING TABLETS

1. Direct compression method[6,7]

Fast dissolving tablet containing Charantin were prepared by using direct compression method by using different ratios of superdisintegrants. Accurately weighed ingredients were separately passed through #60. Then excipients and drug were thoroughly mixed in a geometric ratio and obtained blend is finally compressed into 500mg tablets. The detailed composition of formulation shown in table 1.

Table 1: Formulation details of fast dissolving tablet of Charantin by direct compression method.

Sl.no	Ingredients (Mg/Tab)	Fd1	Fd2	Fd3	Fd4	Fd5	Fd6
1	Charantin	100	100	100	100	100	100
2	B-cyclodextrin	300	300	300	300	300	300
3	Crospovidone	25	50	-	-	-	-
4	Croscarmellose sodium	-	-	25	50	-	-
5	Sodium starch glycolate	-	-	-	-	25	50
6	Microcrystalline cellulose	55	30	55	30	55	30
7	Magnesium stearate	5	5	5	5	5	5
8	Talc	5	5	5	5	5	5
9	Saccharin sodium	10	10	10	10	10	10

2. Sublimation method[8,9]

Fast dissolving tablets containing Charantin were prepared by sublimation technique using camphor as sublimating agent along with different ratios of superdisintegrants. Accurately weighed quantity of ingredients were passed through #60 separately and then mixed. Then the obtained blend directly compressed into 500mg tablets, and after compression the tablets were subjected to sublimation in hot air oven at 60^0 C, which produces porous structure due to removal of volatizable component. The detailed composition of formulation shown in table 2.

Table 2: Formulation details of fast dissolving tablets of Charantin by sublimation method.

SL.NO	INGREDIENTS (mg/tab)	FS1	FS2	FS3	FS4	FS5	FS6
1	Charantin	100	100	100	100	100	100
2	B-cyclodextrin	300	300	300	300	300	300
3	Camphor	15	15	15	15	15	15
4	Crospovidone	25	50	-	-	-	-
5	Croscarmellose sodium	-	-	25	50	-	-
6	Sodium starch glycolate	-	-	-	-	25	50
7	Microcrystalline cellulose	40	15	40	15	40	15
8	Magnesium stearate	5	5	5	5	5	5
9	Talc	5	5	5	5	5	5
10	Saccharin sodium	10	10	10	10	10	10

PRE-FORMULATION TESTS[10,11]

1. Angle of repose

It indicates the flow property of the powder and it was performed by using fixed funnel method. The blend was poured through funnel and by using radius and height of heap, the angle of repose was calculated. Values were tabulated in table 3 and 4.

$$\mathbf{Tan\ \theta = h/r}$$

Where, θ = the angle of repose

h = height of the heap of the powder

r = radius of the heap of the powder

2. Bulk density

Bulk density is ratio of total mass to bulk volume of powder. The weighed quantity of powder was poured to graduated measuring cylinder, then initial and final volume was noted. Values were tabulated in table 3 and 4.

$$\mathbf{BD=M/V_b}$$

Where, BD indicated bulk density

M indicates the mass of powder

V_b indicates bulk volume of powder

3. Tapped Density

Tapped density is ratio of total mass to tapped volume of powder. The measured volume of powder was transferred to graduated measuring cylinder, then initial volume noted and final volume was noted after the tapping cylinder for 200 times. Values were tabulated in table 3 and 4.

$$\mathbf{TD=M/V_t}$$

Where, TD indicated tapped density

M indicates mass of powder

V_t indicates tapped volume of powder

4. Carr's index

Compressibility of the powder blend can be determined. Calculated by using formula given below. Results were tabulated in table 3 and 4.

$$\mathbf{Carr's\ index=(TD-BD/TD)\ *100}$$

Where, TD is tapped density

BD is bulk density

5. Haunser's ratio

It is ratio of tapped density to bulk density. Ease of powder flow can be determined. Values were tabulated in table 3 and 4.

Haunser's ratio=TD/BD

Where, TD is tapped density

BD is bulk density

EVALUATION[12,13]

1. Hardness

It is defined as force required to break a tablet. Monsanto hardness tester was used and randomly 3 tablets from each batch selected for the test. Values were tabulated in table 5 and 6.

2. Thickness

3 tablets were randomly selected from each batch of formulation and measured thickness by using Vernier calipers. Then values were tabulated in table 5 and 6.

3. Friability

Friability was measured by using Roche friabilator. 20 tablets of known weight was selected from each batch and transferred to chamber to rotate at 20 rpm for 4min then weighed again. Percent friability was calculated by using formula given below. Results were tabulated in table 5 and 6.

$$\%\text{Friability} = [(W_1 - W_2)/W_1] * 100$$

Where, W_1 is the weight of tablets before test

$W_{2\ is}$ weight of tablets after test

4. Weight variation

Randomly 10 tablets were selected from each batch and noted the individual and average weight of tablets. By using average weight of tablets the percent deviation of each tablets were calculated. Values were tabulated in 5 and 6.

5. Wetting time[14,15]

Wetting time was calculated by using given procedure. Petridish with distilled water containing amaranth solution was prepared and later 3 tablets from each batch of formulations were selected randomly. Then selected tablet was kept at centre of petridish.

Then calculated the time taken for tablet surface to become completely red. Values were tabulated in table 7 and 8.

6. Water absorption ratio

Randomly selected 3 preweighed tablets from each formulation taken and placed in distilled water taken in petridish. Then after wetting of tablet weighed again. By using formula given below the water absorption ratio was calculated. Values were tabulated in table 7 and 8.

$$R=[(W_b-W_a)/W_a] *100$$

Where, W_a is weight of tablet before absorption

W_b is weight of tablet after absorption

7. Drug content uniformity[16,17]

Powder equivalent to 100mg of Charantin dissolved in methanol and filtered. The filtrate was measured at 281nm in UV-Visible spectrophotometer. By using standard calibration curve the drug content was calculated. Results obtained was tabulated in table 7 and 8.

8. *In vitro* disintegration test[18,19,20]

Disintegration test apparatus was used to perform *in vitro* disintegration test. Randomly tablets were selected for test and introduced to test apparatus containing water as a medium with temperature 37±2^{0}C. Then time taken for complete disintegration of tablets was noted. Values were tabulated in table 7 and 8.

9. *In vitro* dissolution test

The USP dissolution apparatus was used to determine drug release pattern from each formulation. 900ml of pH 7.4 phosphate buffer was used as a dissolution medium and maintaining temperature at 37±0.5^{0}C and allowed to run the apparatus at 50rpm speed. By maintaining sink condition, the samples were withdrawn at 10 min interval for 1hour. Then all collected samples were analyzed at 281nm using spectrophotometer later cumulative percentage of drug release was calculated. Results were tabulated in table 9 and 10.

10. Stability studies

As per ICH guidelines the accelerated stability studies was conducted at 40^{0}C/75%RH for optimized formulations (FD2 and FS2) for 3 months in a ambered colour bottles. Then formulations were evaluated again for any changes in characteristics at 1-month interval.

RESULTS AND DISCUSSION

Fast dissolving tablets of Charantin, an effective antidiabetic formulation were prepared by two methods direct compression method and sublimation method, by varying concentrations of superdisintegrants and using 5% camphor as sublimating agents.

In present work Charantin containing fast dissolving tablet was prepared by using Crospovidone, Croscarmellose sodium and sodium starch glycolate as superdisintegrants in direct compression method and by using camphor as sublimating agent in sublimation method. Totally 12 formulations were prepared and evaluated for various pre and post formulation parameters.

Various pre-formulation parameters like angle of repose, bulk density, tapped density, carr's index and haunser ratio were performed for all 12 formulations prepared by direct compression and sublimation method and results were found to be within the acceptable limits. Hence all 12 batches of powder blend exhibit good flowing property.

Table 3: Pre-formulation parameters of powder blend - Direct compression method.

Formulation code	Angle of repose (degree)	Bulk density (g/cc)	Tapped density (g/cc)	Haunser's ratio	Carr's index (%)
FD1	23.13±0.58	0.50±0.009	0.57±0.014	1.13±0.051	11.29±3.53
FD2	22.79±0.59	0.48±0.0014	0.583±0.028	1.22±0.087	16.57±5.402
FD3	21.63±0.51	0.513±0.009	0.606±0.018	1.19±0.014	15.63±1.418
FD4	24.30±0.36	0.5±0	0.593±0.018	1.196±0.037	14.72±1.324
FD5	23.66±0.99	0.47±0	0.56±0.014	1.203±0.032	16.013±2.083
FD6	23.26±0.65	0.493±0.02	0.593±0.014	1.21±0.056	15.706±3.086

Table 4: Pre-formulation parameters of powder blend - Sublimation method.

Formulation code	Angle of repose (degree)	Bulk density (g/cc)	Tapped density (g/cc)	Haunser's ratio	Carr's index (%)
FS1	23.9±0.59	0.53±0.02	0.65±0.04	1.21±0.06	15.21±3.29
FS2	23.58±0.59	0.55±0.04	0.68±0.04	1.22±0.05	15.84±2.59
FS3	23.41±0.82	0.59±0.03	0.71±0	1.19±0.06	13.77±0.87
FS4	23.87±0.85	0.54±0.05	0.62±0	1.16±0.11	17.47±2.65
FS5	24.05±1.03	0.57±0.03	0.72±0.85	1.24±0.09	13.70±1.71
FS6	23.76±0.81	0.55±0.04	0.75±0.05	1.23±0.08	13.22±1.27

Then the prepared tablets evaluated for various parameters, firstly prepared tablets of all formulations possessed good mechanical strength with hardness range of 2.3±0.08 kg/cm^2 to 2.46±0.04 kg/cm^2 (direct compression method) and 2.43±0.12 kg/cm^2 to 2.86±0.04 kg/cm^2 (sublimation method). Then all formulations with percent friability < 1% indicating that

tablets were stable. The formulations prepared by direct compression method were more friable than sublimation method. Formulations prepared by both methods passed the weight variation test, and the percent deviation was not more than ±5%.

Table 5: Evaluation results of Charantin fast dissolving tablets - Direct compression method.

Code	Hardness (Kg/cm^2)	Thickness (mm)	Friability (%)	Weight variation (mg)
FD1	2.36±0.04	3.29±0.03	0.35±0.04	499.8±1.29
FD2	2.3±0.08	3.32±0.08	0.4±0.01	499.3±1.55
FD3	2.43±0.04	3.55±0.05	0.42±0.02	500.46±1.55
FD4	2.36±0.09	3.13±0.12	0.47±0.01	500.56±1.10
FD5	2.46±0.04	3.40±0.04	0.36±0.01	499.26±1.65
FD6	2.40±0.08	3.36±0.09	0.47±0.01	500.1±1.34

Table 6: Evaluation results of Charantin fast dissolving tablets - Sublimation method.

Code	Hardness (Kg/cm^2)	Thickness (mm)	Friability (%)	Weight variation (mg)
FS1	2.43±0.12	3.29±0.02	0.55±0.10	499.83±0.98
FS2	2.66±0.09	3.46±0.07	0.73±0.05	499.36±1.56
FS3	2.73±0.04	3.37±0.09	0.57±0.05	499.9±1.60
FS4	2.6±0.08	3.32±0.05	0.61±0.07	500.6±1.14
FS5	2.86±0.04	3.39±0.06	0.74±0.05	498.6±1.34
FS6	2.80±0.08	3.36±0.03	0.62±0.09	500.3±0.98

And then prepared tablets were evaluated for wetting time, then results were found to be in range of 70±1.63 sec to 97.66±2.05 sec (direct compression method) and 57.66±3.29 sec to 65.33±8.17 sec (sublimation method). The water absorption ratio was found to be in range of 14.69±0.31% to 15.81±0.51% (direct compression method) and 13.98±0.77% to 16.56±0.76% (sublimation method). Further tablets were subjected to *in vitro* disintegration test and all formulations shows disintegration time less than 3min.Formulations prepared by sublimation method disintegrate more rapidly than tablets prepared by direct compression method.

Table 7: Post formulation parameters of Charantin fast dissolving tablets - Direct compression method.

Code	Wetting time (sec)	Water absorption ratio (%)	Disintegration time (sec)	Drug content uniformity (%)
FD1	83.33±3.85	14.69±0.31	91±4.54	97.9±0.42
FD2	70±1.63	15.81±0.51	77.66±2.05	99.7±0.51
FD3	92.66±3.29	15.57±0.64	101.66±2.49	98.3±0.81
FD4	86.66±1.24	15.06±0.79	97.66±2.05	98.9±0.94

FD5	97.66±2.05	15±0.31	105±2.44	99.1±1.12
FD6	92.66±2.05	15.18±0.43	99±2.94	97.6±0.75

Table 8: Post formulation parameters of Charantin fast dissolving tablets - Sublimation method.

Code	Wetting time (sec)	Water absorption ratio (%)	Disintegration time (sec)	Drug content uniformity (%)
FS1	63±4.54	14.81±1.71	72±3.26	97.4±0.73
FS2	57.66±3.29	13.98±0.77	65±2.86	99.2±0.68
FS3	64±5.09	16.56±0.76	73.66±4.64	98.6±0.95
FS4	59±6.97	14.62±0.92	69.66±7.40	97.8±0.44
FS5	65.33±8.17	16.06±1.74	75±9.62	98.9±1.05
FS6	61.66±2.86	14.82±0.46	71.66±3.68	98.3±1.3

The percentage of drug content of the tablets prepared by direct compression method and sublimation method were found to be 97.6±0.75% to 99.7±0.51% and 97.4±0.73% to 99.2±0.68% respectively. Then formulations were subjected to *in vitro* dissolution test and drug release at end of 1 hour was found to be in range of 84.35% to 98.86%. Optimized formulation FD2 prepared by direct compression method releases 96.71% and FS2 prepared by sublimation method release 98.86% at end of 1 hour.

Table 9: Dissolution profile - Direct compression method.

Time (min)	Cumulative drug release(%)					
	FD1	FD2	FD3	FD4	FD5	FD6
5	23.91	29.82	20.68	25.52	21.76	22.29
10	38.41	44.32	36.26	42.44	34.92	37.07
20	46.47	55.34	43.79	52.11	42.44	48.35
30	57.76	64.20	56.14	60.44	52.92	58.91
40	68.77	77.64	64.20	73.611	61.25	67.43
50	80.68	86.50	77.64	83.01	74.14	79.52
60	92.68	96.71	88.11	93.76	84.35	90.80

Table 10: Dissolution profile - Sublimation method.

Time (min)	Cumulative drug release(%)					
	FS1	FS2	FS3	FS4	FS5	FS6
5	29.28	32.50	25.52	27.40	24.71	23.91
10	41.91	47.82	38.14	44.32	38.14	43.52
20	52.65	61.79	52.92	56.95	47.01	56.41
30	63.13	70.65	58.83	71.73	58.56	64.74
40	77.10	84.35	68.77	78.98	69.58	73.34
50	88.38	92.68	83.28	87.31	79.79	87.31
60	94.29	98.86	91.61	96.44	89.19	94.56

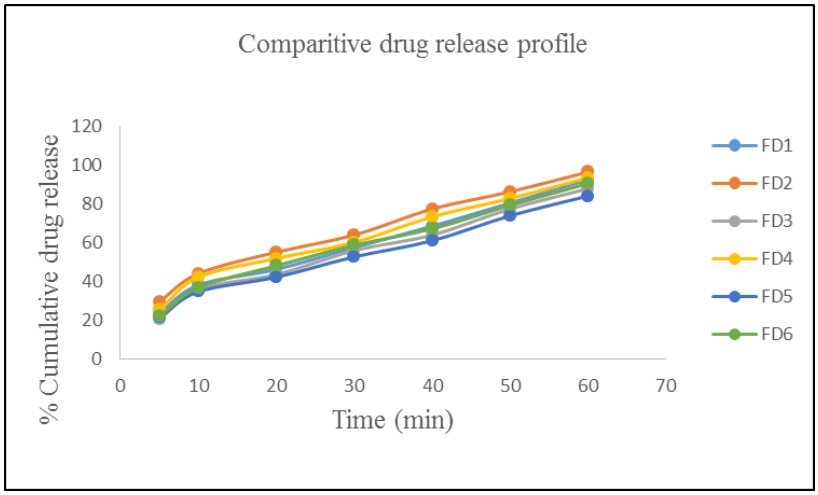

Figure 1: *In vitro* cumulative drug release - Direct compression method.

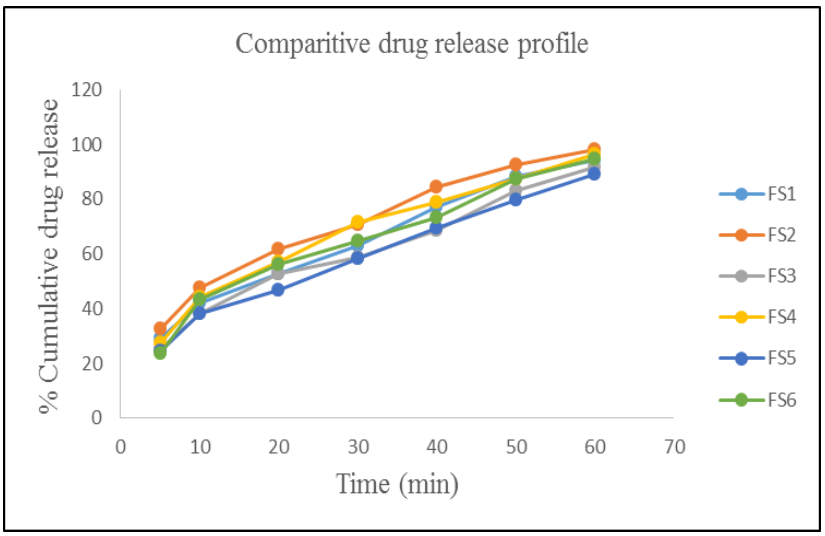

Figure 2: *In vitro* cumulative drug release - Sublimation method.

FTIR spectroscopic study was performed to determine the compatability between the drug and superdisintegrants used for preparation of tablets. IR studies performed for pure drug, polymer along with physical mixture of drug and superdisintegrants. Then studies reported that drug and superdisintegrants were compatible. The characteristic peaks present in Charantin pure drug sample also exist in mixture sample, report indicates that drug and superdisintegrants were compatible. Hence IR studies concludes that no changes in chemical integrity of the drug.

Accelerated stability studies was performed for optimized formulation FD2 and FS2 and reported that no significant changes in chemical and physical parameters of formulations during stability period. Thus, concluded that optimized formulations were stable.

CONCLUSION

The present research work, Charantin fast dissolving tablet were prepared by using various superdisintegrants concentrations in direct compression method and using camphor as sublimating agents in sublimation method. The prepared formulations evaluated for various parameters. The FD2 formulation was found to optimized in direct compression method and FS2 formulation was found to be optimized in sublimation method. And by comparing both optimized formulation the FS2 formulation disintegrate more rapidly and releases more drug than compared to FD2 formulation. Hence, it can be concluded that sublimation method showed better disintegration and drug release as compared to direct compression method.

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