CHARANTIN FAST DISSOLVING TABLET- AN EFFECTIVE ANTIDIABETIC TREATMENT

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ABSTRACT

Charantin fast dissolving tablets were formulated by using sublimation method to reduce the bitter taste and first pass hepatic metabolism with a view to enhance patient compliance. Three different superdisintegrants, viz., Crospovidone, Croscarmellose sodium and sodium starch glycolate used in different ratios (5% and 10%) along with camphor, beta cyclodextrin, microcrystalline cellulose and saccharin sodium. Camphor used as sublimating agent and saccharin sodium used as taste masking agent. The preformulation tests were performed for different batches of powder blends and also the formulated tablets were evaluated for post formulation parameters. FTIR studies indicates that the drug and excipients are compatible and also the stability studies indicate that there were no significant changes in the formulation.

KEYWORDS : *Charantin, Crospovidone, Croscarmellose sodium, Fast dissolving tablets, Sodium starch glycolate*.

INTRODUCTION

Among the various advancement in drug delivery system the oral route remains as the most acceptable route of drug administration, because of patient convenience, low cost of therapy and easy administration. In oral drug delivery system, the major portion were occupied by tablets and capsules and also well accepted by patients. But the majority of the patient groups such as pediatrics, geriatrics, nauseated, mentally retarded and also the patients with reduced water intake diet expresses the difficulty in swallowing the dosage form. The main aim of fast dissolving tablet concept was to supply patient with convenient mean of taking medication. Due to dysphagia and tremors many patients face difficulty in swallowing oral dosage form. Because of underdeveloped muscular and nervous system, children also face problem of swallowing. Due to rapid disintegration, self-administration without need of water or chewing, the fast dissolving drug delivery system gaining much importance and acceptance in recent years [1,2].

Charantin is one of the major active constituent of Momordica charantia which belongs to the family of cucurbitaceae. Charantin belongs to the group of steroidal glucoside which constitutes equal mixture (1:1) of sitosteryl glucoside ($C_{35}H_{60}O_6$) and stigmasteryl glucoside ($C_{35}H_{58}O_6$). It is characterized by sparingly soluble in water, slightly soluble in polar solvents like chloroform etc., and soluble in methanol. It exhibits the antihyperglycemic activity by regenerating pancreatic β cells, increasing insulin secretion, enhancing glucose uptake by adipose or muscle tissues and inhibit glucose absorption from intestine and glucose production from liver. It posses sugar lowering activity equal to insulin and also expresses other activities like anti-tumor, immune modulator, antioxidant, anti-ulcer properties etc., [3].

MATERIALS AND METHODS

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

PREPARATION OF FAST DISSOLVING TABLET

Charantin fast dissolving tablet were prepared by sublimation technique using camphor as sublimating agent along with various superdisintegrants ratios. All the ingredients were accurately weighed and were passed through #60 sieve separately. The resultant mixture is directly compressed into 500mg tablets, then tablets were subjected to sublimation by placing in a hot air oven at 60^0C to generate porous structure, due to removal of volatilizable component**.** The detailed composition of the formulation is shown in table 1[4,5].

INGREDIENTS (mg/tab)	FD1	FD2	FD3	FD4	FD5	FD6
Charantin	100	100	100	100	100	100
B-cyclodextrin	300	300	300	300	300	300
Camphor	15	15	15	15	15	15
Crospovidone	25	50	-	-	-	-
Croscarmellose sodium	-	-	25	50	-	-
Sodium starch glycolate	-	-	-	-	25	50
Microcrystalline cellulose	40	15	40	15	40	15
Magnesium stearate	5	5	5	5	5	5
Talc	5	5	5	5	5	5
Saccharin sodium	10	10	10	10	10	10

Table1: Formulation details of fast dissolving tablet of Charantin.

PREFORMULATION STUDIES[6,7,8]:

1. **Angle of repose:**

It is an indication of the frictional forces existed between granule particles. It is defined as the maximum angle possible between the surface of the pile of granules and the horizontal plane and test was carried by using fixed funnel method. Values were expressed in table 2

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

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:**

It is the ratio of total mass to the bulk volume of powder. Then accurately weighed quantity of the powder blend was transferred into the graduated measuring cylinder, initial and final volume was noted. Then results were expressed in g/ml. Values were expressed in table 2.

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

Where, M indicates the mass of powder

V_b indicates bulk volume of powder

3. **Tapped density:**

It is the ratio of total mass to tapped volume of powder. Then measured quantity of powder blend was transferred to graduated measuring cylinder, then initial and final volume was noted by tapping the cylinder for 200 times. Then results were expressed in g/ml. Values were expressed in table 2.

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

Where, M indicates mass of powder

V_t indicates tapped volume of powder

4. **Carr's index:**

This parameter interprets the compressibility character of powder. Calculated by using the given formula. Values were expressed in table 2.

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

Where, TD is tapped density

BD is bulk density

5. **Haunser's ratio:**

It indicates the flow ability of powder blend. It is defined as ratio of tapped density to the bulk density. Values were expressed in table 2.

$$\mathbf{Haunser's\ ratio=TD/BD}$$

Where, TD indicates tapped density

BD indicates bulk density

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

Table 2: Pre-compression parameters of powder blend

EVALUATION

1. **Hardness:**[9,10,11]

   It indicates strength of tablet. From each batch of formulation 3 tablets were randomly selected and evaluated for hardness by Monsanto hardness tester. Values were given in table 3.

2. **Thickness:**

   From each batch of formulation 3 tablets were selected randomly and subject to evaluate thickness by using Vernier calipers. Values were given in table 3.

3. **Friability:**

   It indicated the physical strength of tablet, upon mechanical shock or attrition. Roche friabilator was used to measure friability. From each batch of formulation 10 tablets were randomly selected and rotated at 25rpm for 4min in friability chamber and weighed again. Then calculated the percent friability. Values were given in table 3.

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

   Where, W_1 is the weight of tablets before test

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

4. **Weight variation:**

   From each batch of formulation ten tablets were randomly selected, then individual weight and average weight of tablets were noted. Then from average weight of tablets the percent deviation of each tablet was calculated. Results were given in table 3.

5. **Wetting time and water absorption ratio:**

The wetting time was measured by following procedure. A petridish with 10ml of distilled water containing amaranth solution, then randomly selected tablets placed in centre of petridish. Then time required for surface of tablet to become red completely was determined.

Water absorption ratio was determined by placing preweighed tablets in petridish containing distilled water and then tablets were reweighed after water absorption. Calculated by using following formula.

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

Where, W_a is weight of tablet before absorption

W_b is weight of tablet after absorption

6. Drug content uniformity [12,13]:

Ten tablets were randomly selected from each batch of formulation and powder equivalent to 100mg of Charantin was dissolved in methanol and then filtered. The drug content present in filtrate measured by using UV-Visible spectrophotometer at 281nm after accurate dilution. Then by using standard calibration curve the percentage of drug present in solution was determined. Results were given in table 4.

7. *In vitro* disintegration test [14]:

Performed by using disintegration test apparatus. 6 tablets were selected randomly and then taken to disintegration tester by using water as a medium and maintaining temperature at 37 ± 2^0 C. And time taken for complete disintegration of tablets were noted. Results were given in table 4.

8. *In vitro* dissolution test [15,16]:

By use of USP dissolution apparatus (paddle type) the drug release pattern of the formulation were determined. 900ml of phosphate buffer of pH 6.8 used as a medium and by maintaining temperature at 37 ± 0.5^0C at 50 rpm. At interval of 10min samples were withdrawn upto 120min by maintaining sink condition. The samples collected were analyzed by using UV-Visible spectrophotometer at 281nm, and cumulative drug release pattern were calculated. Results were given in table 5.

9. Stability studies [17,18]:

Accelerated stability studies were carried out on optimized formulation (FS2) as per ICH guidelines at 40^0C/75%RH by storing the tablets in amber coloured bottles for a period of 3 months. Then tablets were examined for any significant changes in formulation characteristics at interval of 1month.

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

Table 3: Post formulation results of Charantin fast dissolving tablets

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

Table 4: Post formulation results of Charantin fast dissolving table

Time (min)	**Cumulative drug release(%)**					
	F1	**F2**	**F3**	**F4**	**F5**	**F6**
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

Table 5: Dissolution profile of Charantin fast dissolving tablet

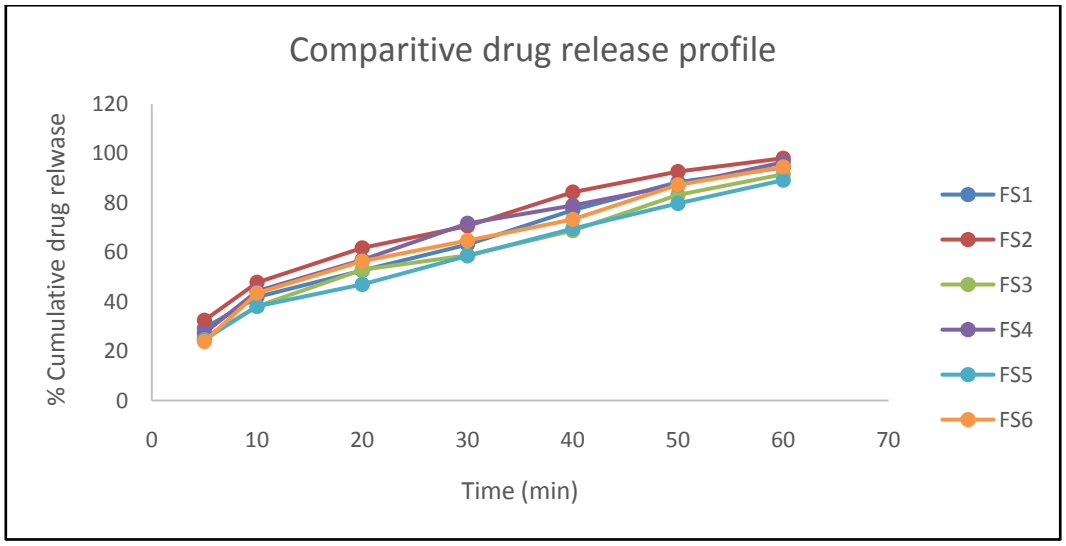

Figure 1:*In vitro* cumulative drug release from Charantin fast dissolving tablets formulations

RESULTS AND DISCUSSION:

Charantin fast dissolving tablet, and effective antidiabetic drug were prepared by sublimation technique using camphor as sublimating agent, with varying the superdisintegrants concentration.

In this current work Charantin fast dissolving tablets were prepared by using Crospovidone, Croscarmellose sodium and sodium starch glycolate as superdisintegrants in the concentration of 5% and 10% by sublimation technique using camphor as sublimating agent,

Before compression the powder blend of all the batches were subjected to preformulation parameters like angle of repose, bulk density, tapped density, Haunser's ratio and carr's consolidation index. The parameters were found to be within the limits for all powder batches hence concluded with good flow properties. Then after the compression of tablets, formulations were subjected to post formulation evaluation parameters.

The prepared formulations were found to be with hardness range of 2.43±0.12 to 2.86±0.04 Kg/cm^2,indicating good mechanical strength of tablets. And then all the batches of formulation were taken for weight variation test, and found that the percentage deviation was not more than ±5%.Then wetting time was carried out and result was found to be in range of 57.66±3.29 to 65.33±8.17 sec. The water absorption ratio was found to be in range of 13.98±0.77 to 16.56±0.76 %. Then the drug content uniformity test and *in-vitro* disintegration parameters were carried out and the result were found to be in range of 97.4±0.73 to 99.2±0.68 %

and 65±2.86 to 75±9.62 sec respectively. The in-vitro dissolution studies exhibit the drug release patterns for 60min in range of 91.61 to 98.86 %.

FT-IR spectroscopy study was carried out separately to check the compatibility between the drug (Charantin) and superdisintegrants (Crospovidone, Croscarmellose sodium, sodium starch glycolte) used for preparation of fast dissolving tablet. FT-IR was performed for drug, superdisintegrants and physical mixture of drug and superdisintegrants. IR spectroscopic studies reported that the drug and superdisintegrants were compatible. The characteristic peaks of Charantin pure drug also exist in drugsuperdisintegrants mixture, hence indicating drug and superdisintegrants are compatible. Thus, IR studies concludes with no significant changes in the chemical integrity of drug.

Accelerated stability studies for the optimized formulation (FS2) was carried out and results reveals that there were no significant changes in physical and chemical parameters of the formulation during the study period. Hence, concluded that the optimized formulation was stable.

CONCLUSION

The present research work, fast dissolving tablet containing Charantin using Crospovidone, Croscarmellose sodium and sodiumstarch glycolate as superdisintegrants at 5% and 10% concentration by sublimation technique using camphor as sublimating agent. All the prepared formulation were subjected to different pre and post formulation parameters and all results were found to exist within the acceptable limits. Among the above prepared formulations, the FS2 formulation i.e. formulation with 10% Crospovidone exhibits good result with less disintegration time of 65±2.86 sec with high drug release upto 98.86 %. Thus concluded that the fast dissolving tablets containing Charantin prepared by using 10% concentration of Crospovidone was proved to be optimized formulation among the all other preparations with different superdisintegrants ratios.

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