ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Formulation and evaluation of fast dissolving tablets of hydrocortisone sodium succinate

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ABSTRACT

Hydrocortisone sodium succinate is the most common and useful anti-inflammatory drug of the adrenocortical steroids category. It is most widely use in the treatment of asthma, endocrine disorders, dermatological disorders, allergic states, etc. The objective of the present was to prepare FDTs containing hydrocortisone sodium succinate using various superdisintegrants such as crospovidone, croscarmellose sodium and sodium starch glycolate by direct compression method in different concentrations. The simple lattice design was applied to evaluate the effect of single or mixture of the above superdisintegrants. The superdisintegrants such as crospovidone, croscarmellose sodium and sodium starch glycolate were considered as independent variables. The final blend was evaluated for Bulk density, Tapped density, Carr's index, Angle of repose and Moisture content. The prepared FDTs were evaluated for appearance, hardness, friability, *in vitro* disintegrating time, wetting time, water absorption ratio, drug content, *in vitro* drug release studies and *in vitro* diffusion study using pig buccal mucosa. Among the formulations; F2 showed wetting time (46.5 ± 0.42 s), minimum disintegration time (15.3 ± 0.51 s), *in vitro* dissolution study (98 % release in 7 min.), and *in vitro* diffusion study (98 % in 5 min.). FT-IR studies revealed the absence of drug polymer interaction. Short term accelerated and intermediate stability studies indicated no significant changes in hardness, friability, *in vitro* disintegration time, drug content and *in vitro* drug release studies.

Keywords: FDTs; Hydrocortisone sodium succinate; Asthma; Best formulation; Simple lattice design.

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ISSN: 0975-8585

INTRODUCTION

Hydrocortisone sodium succinate is the most common and useful anti-inflammatory drug of the adrenocortical steroids. It is most widely used in the treatment of asthma, endocrine disorders, dermatological disorders, allergic states, etc. It is practically very soluble in water and alcohols [1]. The present investigation was to prepare fast dissolving tablet (FDTs) of hydrocortisone sodium succinate to increase its dissolution by its faster disintegration. Fast dissolving tablets also lead to an increased patient compliance, as it can be swallowed without the use of water. This characteristic helps the patient to get relief from the asthmatic attack even though when they are travelling, when no experts person are available for I.V administration or when no water is available and when the patients is in not a condition to reach the hospital for the treatment. The drug-hydrocortisone sodium succinate is highly soluble in water and saliva which lead to rapid absorption of the drug through the highly versatile area of the mouth. This newer formulation of anti-inflammatory can offer advantages over older formulation in terms of enhance convenience, less side effect profile, improved efficacy, and/or fast onset of action as it bypasses the first pass metabolism. A dosage form which is in solid state and get dissolve or disintegrate rapidly in the oral cavity, resulting into the solution or suspension without the need of water is termed as fast dissolving tablets. Oral dosage forms like tablets and capsules possessing great problem of swallowing mainly by pediatrics, geriatrics, bedridden, nauseous or non complaint patients [2]. Orally disintegrating dosage forms has to be placed in mouth, where it gets dispersed in saliva without the need of water. US Food and Drug Administration and Central for Drugs Evaluation and Research define in the 'Orange Book' that an fast dissolving tablet as "a solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue [2]. Disintegrants are substance or agents added to the tablet formulation facilitate the breakup or disintegration of tablet or capsule into smaller fragments in an aqueous environment, thereby increasing the larger surface area and promoting a more rapid release of the drug substance that dissolve more rapidly than in absence of disintegrants. In recent years, several disintegrants have been developed, often called as "superdisintegrants" [3].Superdisintegrants are generally used at a low level in the solid dosage form, typically in concentration of 1-10 % by weight relative to the total weight of the dosage unit [4]. Examples of superdisintegrants are croscarmellose sodium, crospovidone and sodium starch glycolate which represent example of cross linked cellulose, cross linked polymer and cross linked starch respectively[4]. The tablets formulated by using these disintegrants were disintegrated within 2 min. The higher dissolution rates observed with superdisintegrants may be due to rapid disintegration and fine dispersion of particles formed after disintegration [5]. Mechanisms of tablet disintegrants follow are swelling, porosity and capillary action, due to disintegrating particle/particle repulsive forces and due to deformation [3]. The various technologies are being utilized or adopted to prepare fast dissolving tablets are direct compression method, sublimation method, humidity treatment method, sintering method, wet granulation method, dry granulation method, melt granulation method, spray drying method, moulding method, freeze drying method and cotton candy method [6].

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MATERIAL AND METHODS

EXPERIMENTAL

Materials

Hydrocortisone sodium succinate, Aarti drugs limited; Microcrystalline cellulose, Central drug house Pvt. Ltd; Crospovidone (CP), Micro Labs; Sodium starch glycolate (SSG), Micro Labs; Croscarmellose sodium (CCS), Micro Labs; Mannitol, Merck Specialist Ltd; Magnesium stearate, Rolex Laboratory Reagent; Talc, Rolex Laboratory Reagent.

Table 1 List of materials used in work.

Materials	Suppliers
Hydrocortisone sodium succinate	Aarti Drugs Limited, Mumbai-400022
Microcrystalline cellulose	Central drug house Pvt. Ltd., Bombay
Crospovidone	*Micro Labs, Bangalore*
Sodium starch glycolate	*Micro Labs, Bangalore*
Croscarmellose sodium	*Micro Labs, Bangalore*
Mannitol	Merck Specialties Ltd., Mumbai
Magnesium stearate	Rolex Laboratory Reagent

Preformulation Study

Drug-Excipient compatibility studies by using FT-IR spectroscopy

The FT-IR study of pure drug-Hydrocortisone sodium succinate with crospovidone, croscarmellose sodium, sodium starch glycolate alone and in mixture were carried out. The peaks were recorded in the range of 1000 to 3600 cm^{-1}[7].(Figure 1-4).

Angle of repose

Table 2 Angle of repose

Angle of repose (in degrees)	Type of flow
< 25	Excellent
25 – 30	Good
30 – 40	Satisfactory
> 40	Very poor

The angle of repose of powder was determined by funnel method. The accurately 1.2 g weighed powder were 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 heap of the powder. The powder was allowed to flow through funnel freely onto the surface. The diameter of the powder cone was

ISSN: 0975-8585

measured and angle of repose was calculated using the following equation [8]. Shown in table 2.

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

$$\text{Therefore, } \theta = \text{Tan}^{-1}\, h/r$$

Where, θ = angle of repose,
h = height of cone,
r = radium of the cone

Bulk Density

Both, loose bulk density (LBD) and tapped bulk density (TBD) were determined. A quantity of 9 g of powder from each formulation, previously lightly shaken to break any agglomerates formed was introduced into 25 ml measuring cylinder. After the initial volume was observed, the cylinder was allowed to tap by using the Tap density tester (USP) for the 100 taps and than final volume was observed [9].

Bulk density is calculated by using formula:
Bulk density = Weight of the powder/Bulk volume of the powder
Tapped density is calculated by using formula:
Tapped density = Weight of the powder/Tapped volume of the powder

Carr's Index

Table 3 Carr's Index values

Carr's index (%)	Type of flow
5 – 15	Excellent
12 – 18	Good
18 – 23	Satisfactory
23 – 35	Poor
35 – 38	Very poor
> 40	Extremely poor

The Carr's index of the powder mix was determined by using formula [9]:
Carr's index (%) = [(TBD – LBD) * 100] / TBD
Where, LBD = weight of the powder/volume of the packing
TBD = weight of the powder/tapped volume of packing
Shown in table 3

Hausner ratio

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

Hausner ratio = Tapped density / Bulk density

Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25) [3].

Moisture Content

The moisture content of the powder is carried out by thermo-gravimetry method using IR moisture balance. The 4 g powder is placed over the plate and distributed uniformly. The panel must be adjusted to zero before the process. The lid of the IR moisture balance must be closed. Now the IR lamp of 250 watt is switch on and adjusts the temperature to 100°C by the help of controlling knob. The temperature should be maintained until the color of the white powder changes to light brown or off white. Then, the percentage amount of the moisture present in the powder is observed at the reading panel [10].

Direct compression method for tablet preparation

Drug, selected superdisintegrants, microcrystalline cellulose, magnesium stearate and talc were taken in required quantities and passed through sieve # 44 separately. In dry state, the drug with other ingredients was mixed for the period of 10 min in mortar to get uniformly mix powder. These powders were lubricated with magnesium stearate and talc. The lubricated powder was compressed into tablets in 7 mm die cavity of rotary tablet punching machine.

Evaluation of physicochemical parameters

The tablets were evaluated for the parameters mentioned in Indian Pharmacopoeia and other special parameters for FDTs as mentioned here:

Thickness

The thickness of tablets was important for uniformity of tablet size. Thickness was measured using screw gauge on randomly selected samples [11].

Hardness

The resistance of tablet for shipping or breakage, under conditions of storage, transportation and handling, before usage, depends on its hardness. The hardness of tablet of each formulation was measured by Pfizer hardness tester. Tablets from each batch were selected and evaluated, and the average value with standard deviation was recorded [11].

Friability

Friability is the measure of tablet strength. Roche friabilator was used for testing the friability using the following procedure. Tablets were weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of six

inches with each revolution. After 4 min. the tablets were weighed and the percentage loss in tablet weigh was determined. The equation of the friability is shown below [11].
% Friability = [(initial weight – final weight)/initial weight]*100
Standards:Compressed tablets that loose less than 1.0 % of their weight are generally considered acceptable.

Weight Variation

Table 4 Weight variation specification as per IP

Average weight of tablet (mg)	Percentage deviation
80 mg or less	10
More than 80 mg but less than 250 mg	7.5
250 mg or more	5

Twenty Tablets were weighed individually and the average weight was determined. The % deviation was calculated and checked for weight variation as per Indian Pharmacopoeia [12].Shown in table 4

Estimation of drug content

Estimation of drug content test as describe in the IP was followed. Tablets were weighed and average weight is calculated. All tablets were crushed and powder equivalent to 5 mg drug was dissolved in 10 ml of 6.8 pH phosphate buffer. Solution was filtered and absorbance was measured by using UV-Visible spectrophotometer at 248.5 nm against reagent blank. Percentage amount of drug present in one tablet was calculated [12]

Wetting time

A piece of tissue paper folded twice was placed in a small petri-dish (internal diameter of 5 cm.) containing 6 ml of water. A tablet was placed on the paper and the time required for complete wetting was measured. It is measured in the unit of second [13]

Water absorption ratio

Before keeping the tablet for the wetting time the initial weight of the tablet has been measured which is denoted by Wa. After the completion of the wetting time the wetted tablet was then weighted that is denoted by Wb. Water absorption ratio 'R' was determined using the equation [13].

$$R = 100 (Wb – Wa)/Wa$$

Where, Wa is weight of tablet before water absorption
Wb is weight of tablet after water absorption

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Modified disintegration test

For *in vitro* dispersion time, one tablet was placed in a beaker containing 10 ml of 6.8 pH phosphate buffer at 37 ± 0.5°C and the time required for complete dispersion was determined [13]

***In vitro* drug release study**

The *in vitro* release rate of hydrocortisone sodium succinate from fast dissolving tablets was determined using USP dissolution testing apparatus II (paddle type). The dissolution test was performed using 900 ml of 6.8 pH phosphate buffer, at 37 ± 0.5°C and 50 rpm. Aliquots were withdrawn from the dissolution apparatus and the sample was replaced with fresh dissolution medium. After filtration, the amount of drug released was determined from the standard calibration curve of pure drug [14].

Dissolution test:

- Apparatus : USP Type II
- Volume of medium : 900 ml
- Temperature : 37 ± 0.5°C
- Paddle speed : 50 rpm
- Dissolution medium used : 6.8 pH phosphate buffer
- Aliquots quantity withdrawn : 2 ml
- Sampling interval time (min) : 1, 2, 3, 4, 5, 6, 7, 8, 9, 10

***In vitro* Diffusion study**

The pig buccal mucosa should be cut properly so that it can fit to the mouth of the franz diffusion cell. The fast dissolving tablet is kept above the buccal mucosa in the donor compartment of the franz diffusion cell and pour the sufficient amount of the 6.8 pH phosphate buffer solution above the fast dissolving tablet till it disintegrant totally. The fast dissolving tablet disintegrates into the donor compartment and releases the drug which diffuses through the buccal mucosa and enters into receptor compartment. The time required for the maximum amount of the drug from the donor to receptor compartment is observed. During the entire process, the constant stirring by the use of magnetic stirrer and the constant temperature of 37.5 ± 2°C is maintained [15].

Stability studies of the most satisfactory formulation

Stability testing of drug products begins as a part of drug discovery and ends with the demise of the compound or commercial product. To access the drug and formulation stability, stability studies were done according to ICH guidelines. The stability studies were carried out on the optimized formulation as per ICH guidelines. The most satisfactory formulation sealed in aluminum packaging and kept in humidity chamber maintained at 30 ± 2°C/65 ± 5 % RH and 40

ISSN: 0975-8585

± 2°C/75 ± 5 % RH for 2 months. The samples were analyzed for the drug content, *in vitro* dissolution studies, disintegration time and other physicochemical parameters after 30 days and 60 days [16].

RESULT AND DISCUSSION

Preformulation study results

Standard calibration curve:

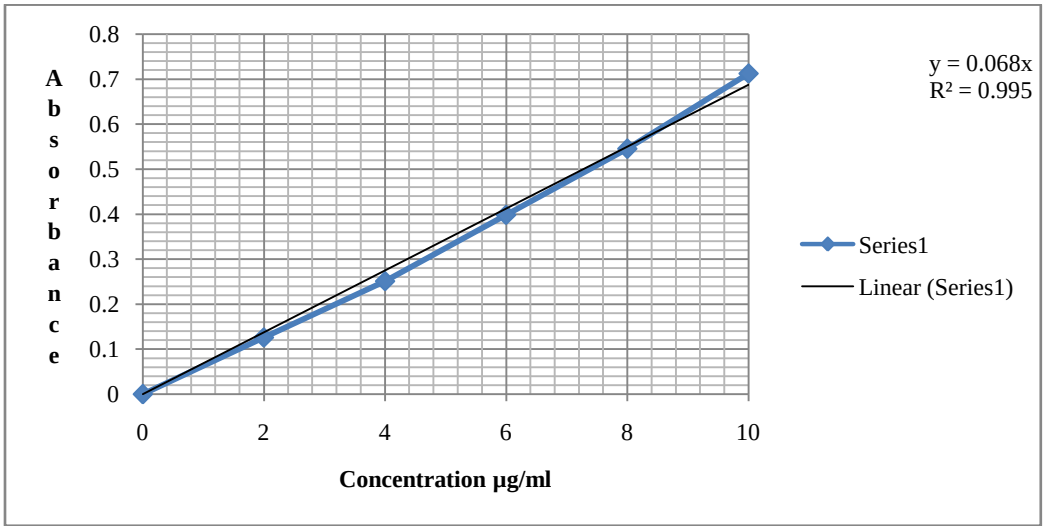

Figure 1: Standard calibration curve of hydrocortisone sodium succinate

The standard calibration curve is measure in 6.8 pH phosphate buffer by using the UV/Visible spectrophotometer. The details are mention in table and figure 1 and table 5 Table 5 Standard

Table-5: calibration curve of hydrocortisone sodium succinate

Sr. No.	Concentration(µg/ml)	Absorbance
1	0	0
2	2	0.126 ± 0.002
3	4	0.251 ± 0.002
4	6	0.398 ± 0.001
5	8	0.545 ± 0.002
6	10	0.712 ± 0.001

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FT-IR of pure drug and polymer mixture:

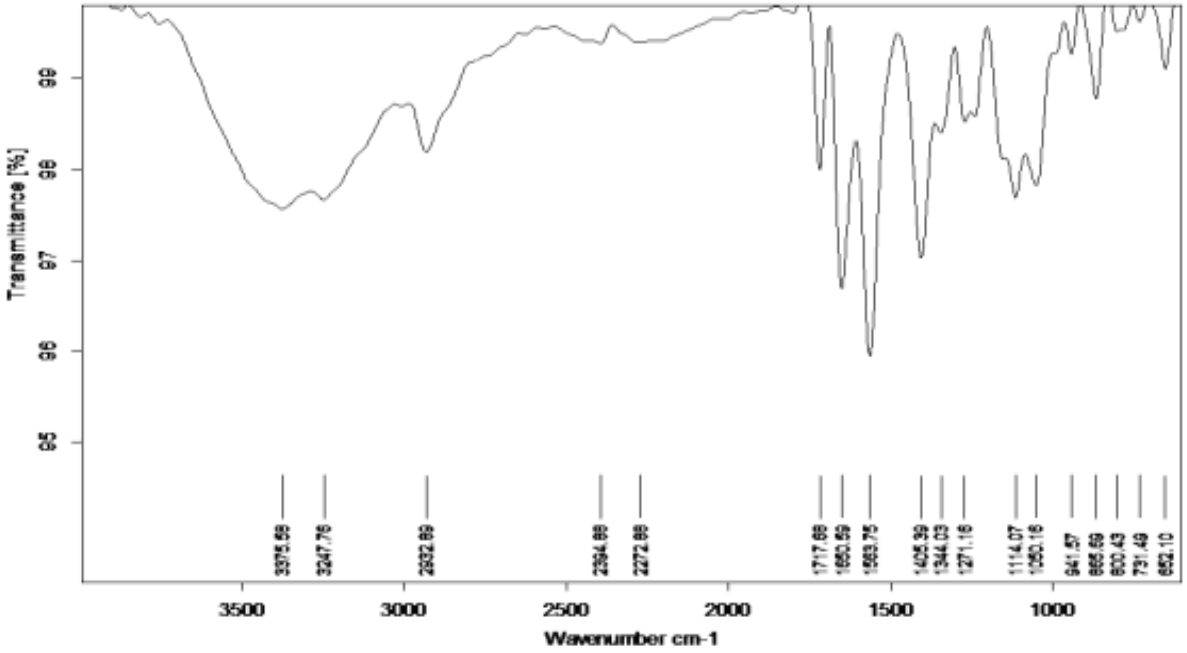

Figure 2: FT-IR spectra of pure hydrocortisone sodium succinate

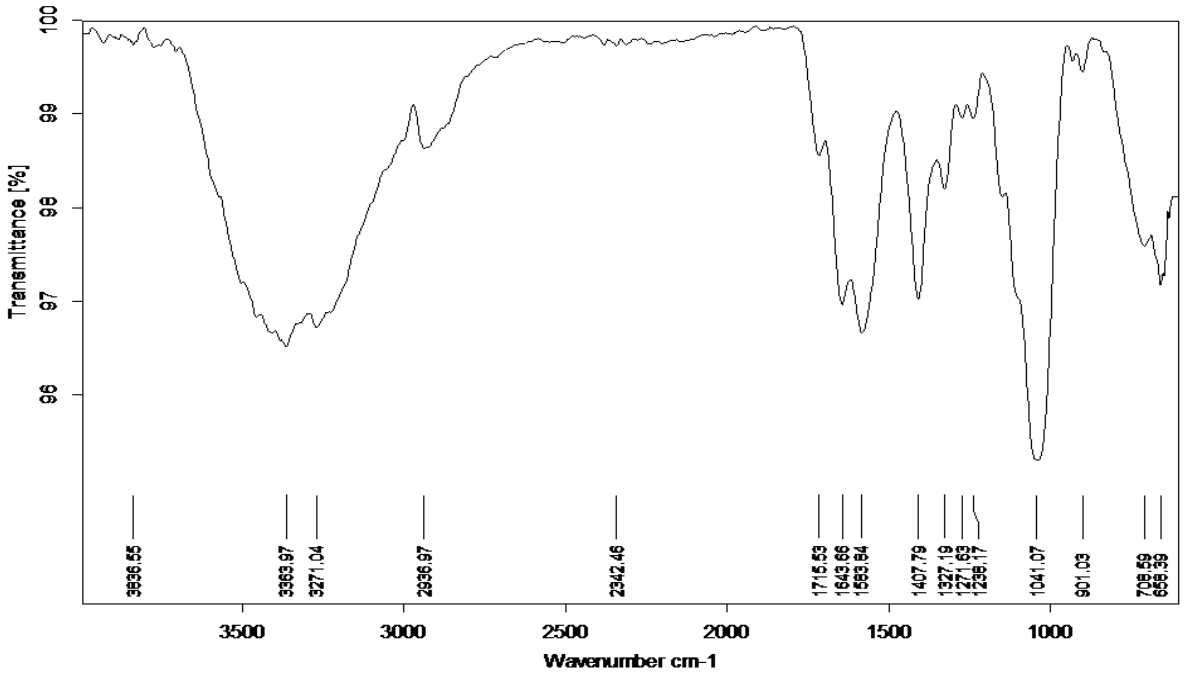

Figure 3: FT-IR spectra of pure hydrocortisone sodium succinate + Crospovidone

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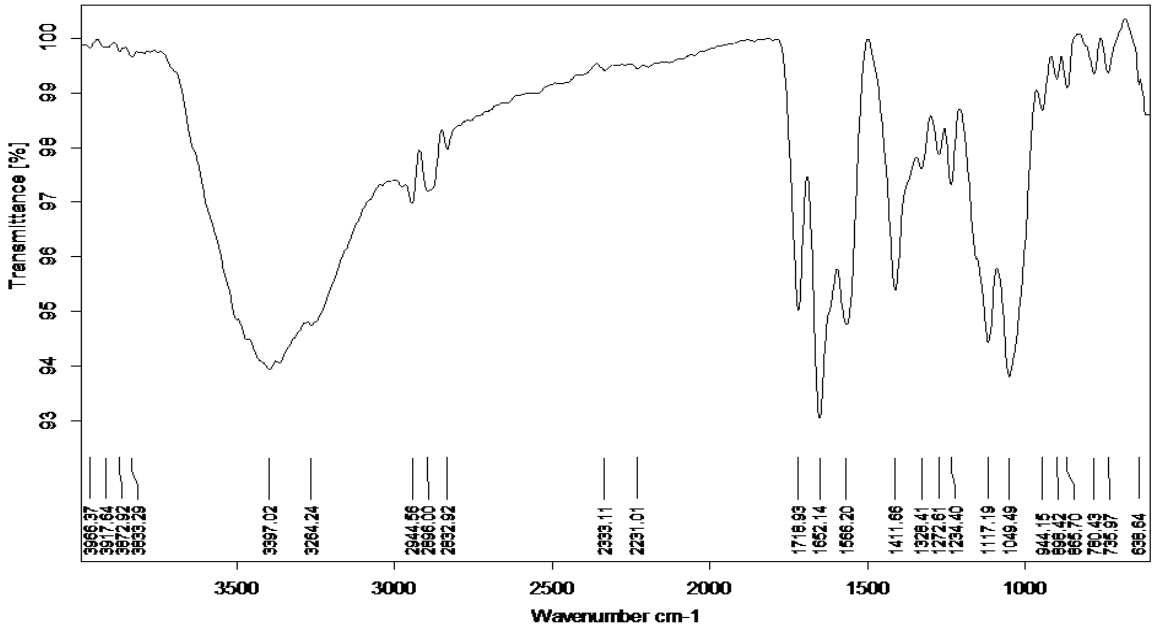

Figure 4: FT-IR spectra of pure hydrocortisone sodium succinate + croscarmellose sodium

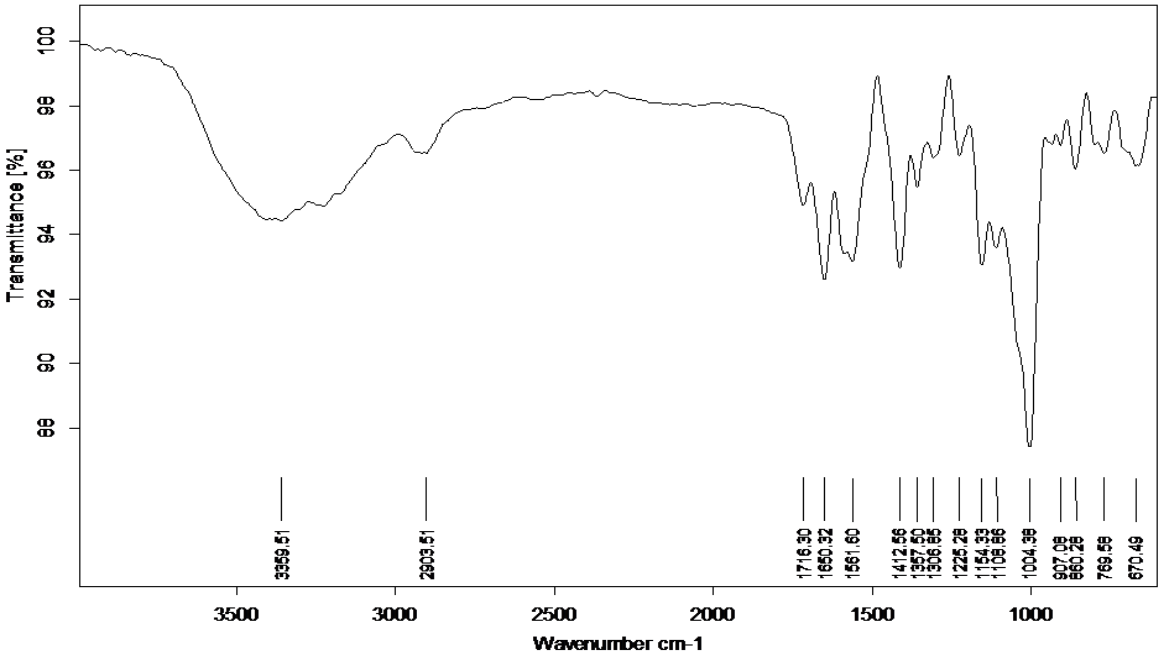

Figure 5: FT-IR spectra of pure hydrocortisone sodium succinate + sodium starch glycolate

The compatibility studies of the drug alone and along with the different superdisintegrants are carried out by using FT-IR, Tensor 27, Bruker. The data of studies are shown in table [7]. Shown In table 6 and figure 2 to 5.

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Table 6 Peak of hydrocortisone sodium succinate in FT-IR Spectra

Frequency (cm^{-1}) Pure drug	Frequency (cm^{-1}) Pure drug + CP	Frequency (cm^{-1}) Pure drug + CCS	Frequency (cm^{-1}) Pure drug + SSG	Description
2900-3600	2900-3600	2900-3600	2900-3600	O-H stretch
2932	2936	2944	2903	Aliphatic C-H stretch
1650,1717	1643,1715	1662,1718	1650,1716	C=O stretch
1050	1041	1049	1004	C-O-C bending

Formulation design and chart:

The formulation chart has been design by simplex lattice design using expertx8 software. The data of the formulation chart has been mention in tablet and table. Shown in table 7 and 8.

Table 7 Simplex lattice design for formulation of hydrocortisone sodium succinate.

Formulation code	Ingredients		
	Sodium starch glycolate	Crospovidone	Croscarmellose sodium
F-1	1.000	0	0
F-2	0	1.000	0
F-3	0	0	1.000
F-4	0.333	0.333	0.333
F-5	0.545	0.227	0.227
F-6	0.227	0.545	0.227
F-7	0.227	0.227	0.545
F-8	0.500	0.500	0
F-9	0.500	0	0.500
F-10	0	0.500	0.500
Each formulation contains 5 mg of hydrocortisone sodium succinate, 11 mg of superdisintegrants, 9 mg of microcrystalline cellulose, 124 mg of mannitol, 0.5 mg of magnesium stearate and 0.5 mg of talc. Total weight of tablet 150 mg.			

Table 8 factors and their corresponding levels implemented for formulation of fast dissolving tablets of hydrocortisone sodium succinate

Independent variable (Factor)	0.000	0.227	0.333	0.500	0.545	1
Crospovidone (mg)	0	2.5	3.6	5.5	6	11
Croscarmellose sodium (mg)	0	2.5	3.6	5.5	6	11
Sodium starch glycolate (mg)	0	2.5	3.6	5.5	6	11

Angle of repose:

The angle of repose value ranged from 16.10 ± 0.74° to 20.74 ± 1.07° which indicate the excellent flow properties of powder [8]. Thevalues of entire formulations are mention in table 9.

Bulk density and Tapped density:

The value of bulk density and tapped density were ranged from 1.15 ± 0.005 g/ml to 1.21 ± 0 g/ml and 1.30 ± 0 g/ml to 1.52 ± 0.025 g/ml respectively [9]. The details of entire formulations are mention in table 9.

Carr's Index:

The Carr's Index values ranged from 10.39 ± 0.17 % to 24.27 ± 0.91 %. These values indicate that the powder mixture of all the batches exhibited satisfactory characters and hence, they are suitable for direct compression for preparation of fast dissolving tablets [9]. The values of entire formulation are mention in table 9.

Hausner's ratio:

The Hausner's ratio vales ranged from 0.79 to 1.32. These values show that maximum number of formulation showing the good flow properties [3]. The hausner's ratio for all the formulations is shown in table9.

Moisture content:

The moisture content values ranged from 2.7 ± 0.17 % to 2.1 ± 0.14 %. These values indicate that the powder mixture of all batches exhibited moisture content within the limits of IP i.e. should not exceed 5 %. Hence, they are suitable for direct compression for preparation of fast dissolving tablets [10]. The entire values of moisture content have been shown in table 9.

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Table 9 Micromeritic properties of fast dissolving tablet of hydrocortisone sodium succinate
***Average of 3 determination ± standard deviation**

Formulation code	Angle of repose* (º) ± S.D.	Bulk density* (gm/ml) ± S.D.	Tapped density* (gm/ml) ± S.D.	Carr's index* (%) ± S.D.	Moisture content* (%) ± S.D.	Hausner's ratio
F1	19.30 ± 1.21	1.16 ± 0.020	1.34 ± 0.045	13.36 ± 1.51	2.5 ± 0.42	1.15
F2	17.24 ± 1.98	1.19 ± 0.011	1.33 ± 0.011	10.39 ± 0.17	2.1 ± 0.14	1.11
F3	18.93 ± 0.78	1.15 ± 0.005	1.30 ± 0	11.27 ± 0.44	2.3 ± 0.39	1.13
F4	18.55 ± 0.99	1.66 ± 0.011	1.32 ± 0.011	12.05 ± 1.41	2.4 ± 0.34	0.79
F5	20.74 ± 1.07	1.19 ± 0.011	1.40 ± 0.011	15.16 ± 0.77	2.2 ± 0.45	1.17
F6	16.69 ± 0.19	1.15 ± 0.005	1.41 ± 0.011	18.35 ± 0.53	2.1 ± 0.20	1.22
F7	19.05 ± 0.57	1.21 ± 0	1.49 ± 0.017	18.78 ± 0.95	2.7 ± 0.17	1.23
F8	16.43 ± 0.84	1.15 ± 0	1.44 ± 0.025	20.48 ± 1.38	2.3 ± 0.95	1.25
F9	16.10 ± 0.74	1.15 ± 0.005	1.52 ± 0.025	24.27 ± 0.91	2.2 ± 0.26	1.32
F10	17.56 ± 1.70	1.18 ± 0	1.48 ± 0.028	20.42 ± 1.59	2.4 ± 0.22	1.25

Tablet evaluation study:

Thickness:

The thickness of all the formulation was in the range of 3.20 ± 0.021 mm to 3.22 ± 0.021 mm [11]. The values of thickness for all the formulation are mention in the table10.

Weight variation:

The average weight of tablets was calculated for each formulation and it varies from each from 150.0 ± 0.85 mg to 150.4 ± 1.07 mg which complied with the official limit of the IP [12]. The result of the weight variation for all the formulation is mention in table10.

Hardness:

The hardness for all the formulations ranges between 1.2 ± 0 to 1.3 ± 0.11 kg/cm^2[11]. The result for hardness for all the formulation is mention in table 10.

Friability:

The friability for all the formulation varied from 0.039 % to 0.149 % which is less than 1 % as per official requirement of IP [11]. The result for friability for all the formulation is mention in table10

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Disintegration time:

The disintegration time, for all the formulation ranges between 15.3 ± 0.51 seconds to 35.8 ± 0.98 seconds. Increased disintegration time was observed with increase in level of croscarmellose sodium than sodium starch glycolate and crospovidone. The disintegration time decrease with increase in the amount of crospovidone so the disintegration time varies as follows croscarmellose sodium > sodium starch glycolate > crospovidone [13]. The result for disintegration time for all the formulation is mention in table 10 and figure 6.

Table 10 Characterization of developed fast dissolving tablet of hydrocortisone sodium succinate
***Average of 3 determination ± standard deviation**

Formulation code	Hardness* ± S.D. (Kg/cm^2)	Friability (%)	Weight variation* (mg)	Estimation of drug content (%)	Wetting Time* (s) ± S.D.	Disintegration time* (s) ± S.D.	Water absorption* ± S.D. (%)	Thickness* ± S.D. (mm)
F1	1.22 ± 0.057	0.063	150.4 ± 1.07	89.65	58.3 ± 0.38	23.80 ± 0.75	113.9 ± 0.37	3.22 ± 0.021
F2	1.20 ± 0	0.11	150.0 ± 0.98	98.00	46.5 ± 0.42	15.30 ± 0.51	111.8 ± 0.40	3.21 ± 0.019
F3	1.20 ± 0	0.102	150.2 ± 1.26	96.16	54.5 ± 0.23	35.80 ± 0.98	113.2 ± 0.81	3.21 ± 0.023
F4	1.25 ± 0.11	0.039	150.4 ± 0.92	95.83	53.5 ± 0.22	15.66 ± 0.81	113.8 ± 1.01	3.21 ± 0.024
F5	1.27 ± 0.09	0.056	150.1 ± 0.85	95.33	52.4 ± 0.25	22.83 ± 0.75	113.8 ± 0.35	3.21 ± 0.026
F6	1.20 ± 0	0.073	150.0 ± 0.85	96.00	48.4 ± 0.21	15.50 ± 0.54	111.8 ± 0.78	3.21 ± 0.023
F7	1.30 ± 0.11	0.059	150.2 ± 1.00	96.14	51.6 ± 0.31	17.33 ± 0.51	113.4 ± 0.34	3.20 ± 0.022
F8	1.25 ± 0.10	0.149	150.2 ± 1.50	94.82	52.7 ± 0.28	16.50 ± 1.04	113.5 ± 0.57	3.20 ± 0.21
F9	1.22 ± 0.05	0.093	150.4 ± 0.92	94.48	54.3 ± 0.25	21.00 ± 1.26	113.4 ± 0.29	3.20 ± 0.023
F10	1.20 ± 0	0.14	150.3 ± 0.98	96.48	49.4 ± 0.23	20.60 ± 0.81	113.1 ± 0.42	3.21 ± 0.021

ISSN: 0975-8585

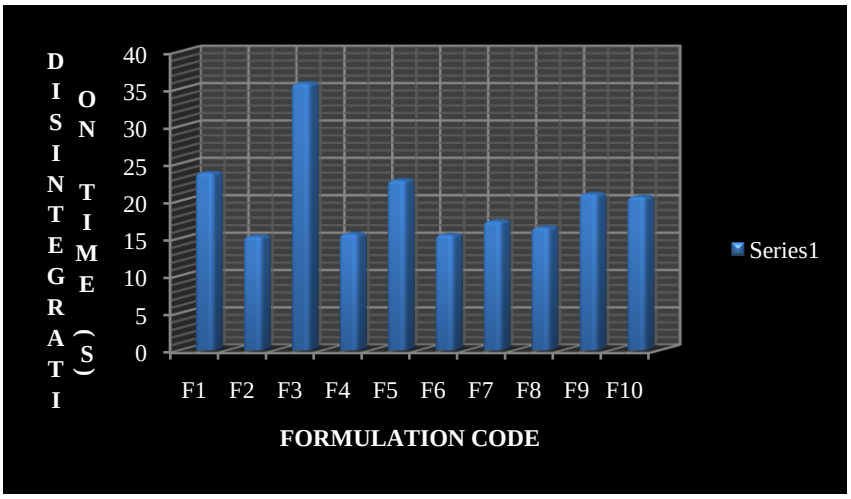

Figure 6: disintegration time of formulation F1 to F10

Wetting time:

The values of wetting time were found in the range of 46.5 ± 0.42 seconds to 58.3 ± 0.38 seconds. It indicates that as the amount of sodium starch glycolate increases, the wetting time is also increases. The wetting time is least for formulation containing crospovidone, so it will release the drug faster than formulation containing sodium starch glycolate and croscarmellose sodium. The wetting time is as follows: sodium starch glycolate > croscarmellose sodium > crospovidone [13]. The result for wetting time is mention in the table10 and figure 7.

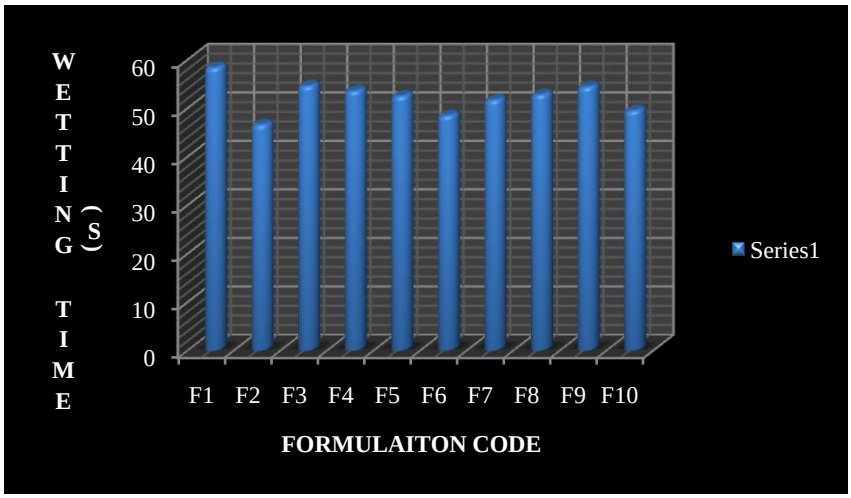

Figure 7: wetting time of formulation F1 to F10

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Water absorption ratio:

The values for water absorption ratio were found in the range from 111.8 ± 0.40 % to 113.9 ± 0.37 %. It indicates that the formulation containing sodium starch glycolate having higher water absorption ratio as compared to croscarmellose sodium and crospovidone. Formulation containing crospovidone has least water absorption ratio than sodium starch glycolate and croscarmellose sodium. The rate of water absorption is as follows: sodium starch glycolate > croscarmellose sodium > crospovidone [13]. The result of water absorption ratio for all the formulation is mention in table10 and figure 8.

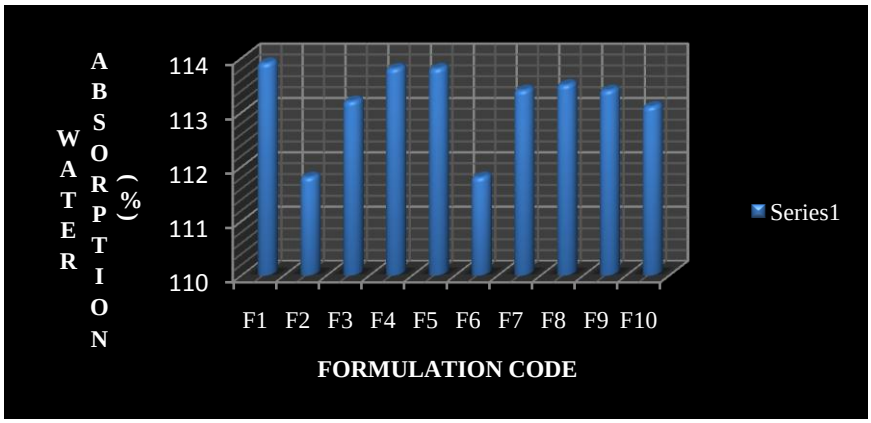

Figure 8: Water absorption ratio of formulation F1 to F10

Estimation of drug content:

The amount of drug present in all the formulation varies from 89.65 % to 98.00 % [12]. The result of drug content for all the formulation is mention in table10.

***In vitro* drug release profile study:**

All the formulation releases maximum amount of drug within 8 min [14]. The result of *in vitro* drug release study for all the formulation is mention in table12(a) and 12(b), figure 10 to 12.

Table 12(a): Drug release profile of various formulations of developed fast dissolving tablets F1 to F5

***Average of 3 determination ± standard deviation**

e N)	1 (%)*	F2 (%)*	F3 (%)*	F4 (%)*	F5 (%)*
	46 ± 0.53	79 ± 0.55	.47 ± 0.55	20 ± 0.55	.5 ± 0.40
	86 ± 0.40	.8 ± 0.15	.85 ± 0.53	94 ± 0.81	38 ± 0.46
	21± 0.40	28 ± 0.15	.39 ± 0.70	83 ± 1.36	53 ± 0.45
	16 ± 0.70	62 ± 0.15	.08 ± 0.66	84 ± 1.22	23 ± 0.40
	45 ± 0.95	04 ± 0.40	5.5 ± 0.77	46 ± 1.48	15 ± 0.81
	01 ± 0.26	17 ± 0.15	.53 ± 0.53	06 ± 0.27	32 ± 0.55
	58 ± 0.15	39 ± 0.15	.18 ± 0.15	27 ± 0.27	33 ± 0.55
	7 ± 0.26		21 ± 0.005		45 ± 0.46

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Figure 12(b): Drug release profile of various formulations of developed fast dissolving tablets F6 to F10
***Average of 3 determination ± standard deviation**

Time (MIN)	F6 (%)*	F7 (%)*	F8 (%)*	F9 (%)*	F10 (%)*
1	27.85 ± 0.53	27.85 ± 0.79	28.2 ± 0.55	28.55 ± 0.30	28.47 ± 0.30
2	40.11 ± 0.53	37.64 ± 1.07	39.14 ± 0.55	38.88 ± 0.61	38.79 ± 0.53
3	54.62 ± 0.40	56.11 ± 1.40	55.5 ± 1.55	56.74 ± 0.40	57.89 ± 0.15
4	67.20 ± 0.55	66.41 ± 0.55	67.38 ± 1.22	68.09 ± 0.40	68.27 ± 0.55
5	81.50 ± 0.30	79.46 ± 0.27	80.8 ± 1.40	83.72 ± 0.53	85.49 ± 0.40
6	96.01 ± 0.15	93.79 ± 0.66	94.77 ± 0.54	95.49 ± 0.30	95.41 ± 0.15
7	96.13 ± 0.15	94.89 ± 0.38	94.89 ± 0.56	96.41 ± 0.31	96.59 ± 0.27
8	96.17 ± 0.15	95.27 ± 0.30	94.83 ± 0.56		

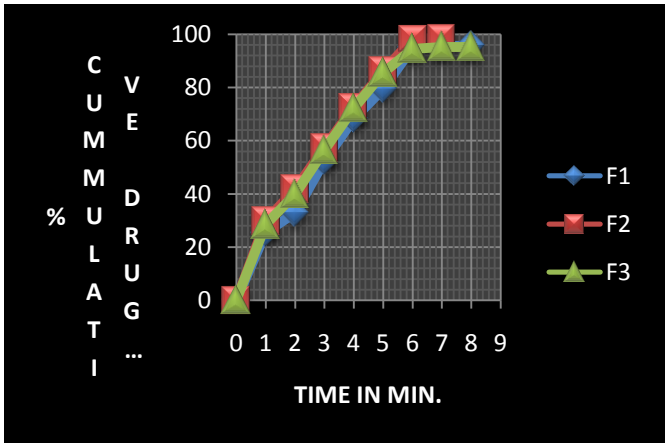

Figure 10: Drug release profile F1, F2 & F3

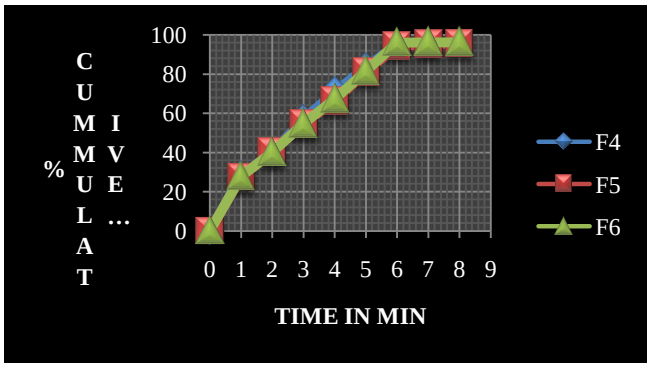

Figure 11: Drug release profile F4, F5 & F6 formulation

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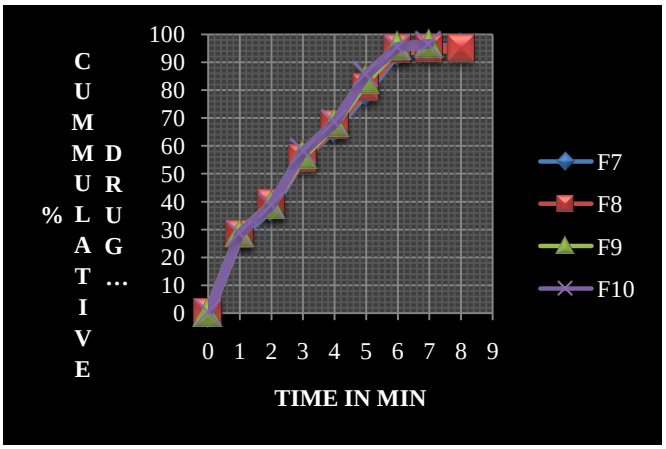

Figure 12: Drug release profile F7, F8, F9 & F10 formulation

In vitro drug diffusion study through buccal mucosa:

All the formulation diffuse maximum amount of the drug through buccal mucosa within 7 min [15]. The result of *in vitro* diffusion study is mention in the table11 and figure 9.

Table 11 *In vitro* diffusion study of hydrocortisone sodium succinate

SL. NO	TIME (MIN)	% Concentration of HSS diffuse across the buccal mucosa									
		F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
1	1	24.40	31.57	28.52	33.52	30.88	30.29	32.94	32.35	29.70	33.23
2	2	31.35	50.72	31.76	45.88	42.05	51.17	50.88	49.41	36.47	44.41
3	3	52.65	69.95	57.35	61.47	58.23	61.17	62.94	63.82	56.17	60.00
4	4	71.33	80.91	71.17	79.11	65.00	82.05	80.29	80.58	64.11	72.64
5	5	83.96	97.98	86.17	95.00	84.11	95.88	88.52	94.70	83.82	86.47
6	6	89.17		94.41		94.41		96.17		94.11	96.47
7	7			96.10							

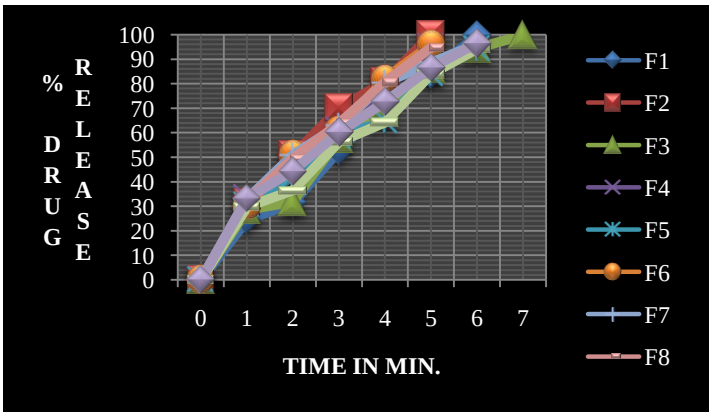

Figure 9: Drug diffusion study of formulation F1 to F10

ISSN: 0975-8585

Stability studies:

Stability studies were carried out on the best formulation F2 at 30 ± 2°C/65 ± 5 % RH and 40 ± 2°C/75 ± 5 % RH for two months to assess their long term stability and accelerated stability studies as per ICH guidelines. Table 13 and 14 showed that there is no significant change in disintegration time, hardness, friability, drug content and *in vitro* drug release of F2 after stability studies. Shown in figure 13 and 14.

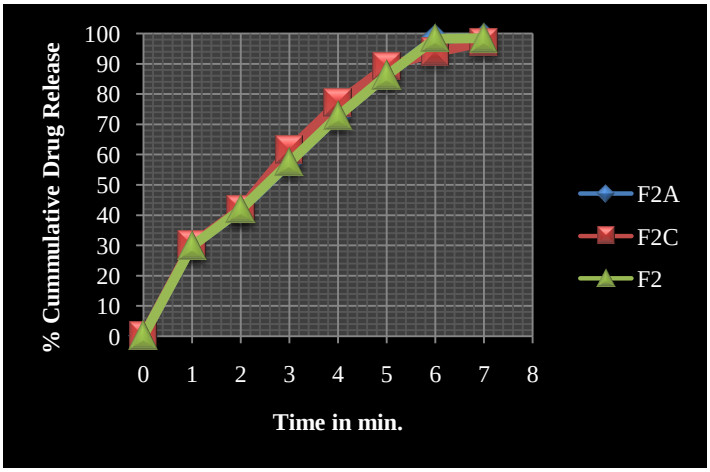

Figure 13: % cumulative drug release of F2 during stability studies

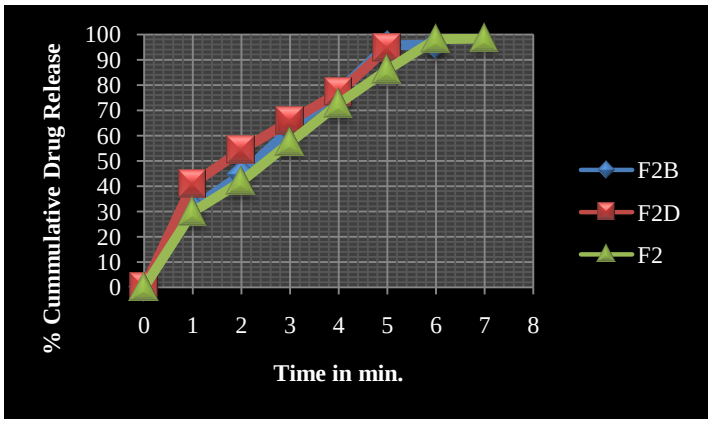

Figure 14: % cumulative drugrelease of F2 during stability studies

***F2A, F2C = 30 ± 2°C / 65 ± 5 % RH**

***F2B, F2D = 40 ± 2°C / 75 ± 5 % RH**

ISSN: 0975-8585

CONCLUSION

In the present study, an attempt was made to prepare FDTs of hydrocortisone sodium succinate in order to increase its dissolution by its faster disintegration and patient compliance, as it can be swallowed without the use of water.

The FDTs of hydrocortisone sodium succinate were prepared by direct compression method using simplex lattice design. In these dosage form three super disintegrating agent were used namely crospovidone, crosocarmellose sodium and sodium starch glycolate in order to decrease the disintegration time. The process was carried out and the formula was prepared by the observed response and desirable values. The best formulation was found to be best in terms of cost effectiveness as one super disintegrant was used, disintegration time was found to be 15 s with sufficient hardness, friability and release the maximum amount of the drug in 7 min. It showed no significant change in physicochemical properties, drug content, disintegrate properties and *in vitro* dissolution pattern after storage at 30 ± 2°C/65 ± 5 % RH and at 40 ± 2°C/75 ± 5 % RH during stability studies for two months. Thus, the objective of the present investigation to design and prepared FDTs of hydrocortisone sodium succinate was achieved

SUMMARY

The present study was carried out to prepare FDTs of hydrocortisone sodium succinate for asthmatic patient.

UV spectrophotometric method was used for the determination of hydrocortisone sodium succinate in 6.8 pH phosphate buffer at 248.5 nm

FDTs of hydrocortisone sodium succinate were prepared by direct compression method using simplex lattice design.

The prepared formulation were evaluated for various physicochemical parameters like thickness, hardness, friability, weight variation, estimation of drug content, wetting time, water absorption ratio, *in vitro* disintegration time, *in vitro* diffusion study and *in vitro* drug release studies.

The best formulation was selected by considering the best points such as cost effectiveness as only one polymer is used, less disintegration time, maximum release in less time, etc.

The best formulation F2 fulfills the every point for being best as mention above. Stability study of F2 formulation was preformed and that showed no major change in physicochemical parameters, *in vitro* disintegration time and *in vitro* drug release profile.

ISSN: 0975-8585

ACKNOWLEDGMENTS

The author thanks Aarti Drugs Ltd., for providing the gift sample of hydrocortisone sodium succinate, Micro Labs, for providing the gift sample of superdisintegrants such as croscarmellose sodium, sodium starch glycolate and crospovidone. The author is also thankful to Chairman, Principal and Staff members of Acharya and B.M. Reddy College of Pharmacy, Bangalore for providing required facilities to carry out this research work.

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