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EXPLORING "*SAMUDRA-FEN*"AS AN ALTERNATIVE EXCIPIENT IN THE MANUFACTURING OF FAST DISINTEGRATING TABLET.

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ABSTRACT

Salbutamol Sulphate is a short acting, selective β2 adrenergic receptor agonist widely used as a bronchodilator which is used for the treatment of asthma. The purpose of this research was to explore "samudra-fen" as alternative excipient in the manufacturing of fast disintegrating tablet. Recently fast disintegrating drug delivery system have started gaining popularity and acceptance as a new drug delivery system because they are easy to administer and lead to better patient compliance. In present work an attempt has been made to formulate and evaluate fast disintegrating tablets of Salbutamol Sulphate. Samudra-fen, Croscarmellose sodium, Sodium starch glycolate and crospovidone were used as super disintegrating agents. Direct compression technique was used as it is economical process. The prepared tablets were evaluated for precompressional as well post compressional parameters. Formulations containing combination of 3% Samudra-fen and 3% Crospovidone as super disintegrating agent show rapid disintegrating time as compared to other formulations.

KEYWORDS: Salbutamol Sulphate, Samudra-fen, Croscarmellose sodium, Sodium starch glycolate, crospovidone, Direct compression, Fast disintegrating tablet.

INTRODUCTION

Oral routes of drug administration have wide acceptance than other dosage forms up to 50-60%. Fast disintegrating tablets are those when put on tongue disintegrate instantaneously releasing the drug which dissolve or disperses in the saliva. Faster the dissolution and dispersion of drug into saliva, quicker the absorption as well as onset of action. Fast disintegrating tablet format is designed to allow administration of an oral solid dose form without water or fluid intake. Such tablets readily dissolve or disintegrate in the saliva

generally within less than 60 seconds. This advantage of fast dissolving tablet can be successfully employed developing dosage forms for the treatment of asthma. As in most of symptoms of asthma there is need of suitable rapidly acting drug therapy.

The basic approach in development of FDTs is the use of superdisintegrants like cross linked carboxymethyl cellulose (croscarmellose), sodium starch glycolate (primogel, explotab), polyvinylpyrolidone (polyplasdone) etc, which provide rapid disintegration of tablet. Earlier reported work reveals that varieties of superdisintegrants were tested in the preparation of FDT from natural to synthetics. Out of all tested superdisintegrants many of them are costlier and having some lacunae. By keeping this in mind, "Samudra-fen" (*Sepia officinalis shell*) powder is tested as an economic superdisintegrant. This excipient is not tested earlier as superdisintegrant, but it has usefulness in common household remedies. Hence to give a scientific background to its traditional utility, this work is undertaken. The samudrafen powder is tested alone as superdisintegrant and to see its effect with other superdisintegrants combinations are also tried out.

The main objective of present work was to develop FDT by direct compression method and to explore "Samudra-fen" as an alternative excipient in the manufacturing of Fast Disintegrating Tablet.

Asthma is a respiratory illness marked by recurrent episodes of airway obstruction, an exaggerated bronchoconstriction response to environmental stimuli, and varying degrees of airway inflammation. Asthma is common, affecting at least 5% of the adult population and often arising in childhood. Asthma can also be severe and is a major cause of morbidity and even mortality in children and young adults. Salbutamol sulphate is a short-acting, selective beta2-adrenergic receptor agonist used in the treatment of asthma and COPD. Salbutamol is generally used for acute episodes of bronchospasm caused by bronchial asthma, chronic bronchitis and other chronic bronchopulmonary disorders such as chronic obstructive pulmonary disorder (COPD) where rapid treatment with suitable drug is always needed and salbutamol sulphate is the highly preferred drug or typically used drug in treatment of above mentioned disorders. FDT of salbutamol sulphate would assure rapid onset of action relieving the symptoms of asthma.

MATERIALS AND METHODS

Salbutamol sulphate was gifted by Cure Medicines Ltd. Pune. Directly compressible Microcrystalline cellulose, Croscarmellose sodium, Sodium starch glycolate, crospovidone were obtained from Cipla Ltd. Kurkumbh. Samudra-fen was gifted by Mankarnika Aushdhalaya, Pune.

METHODOLOGY

Identification of Pure Salbutamol Sulphate

Description

Salbutamol sulphate is a white or almost white odorless powder. Freely soluble in water, slightly soluble in ethanol (95%).

Solubility

The solubility of Salbutamol sulphate was determined by using shake flask method.

Melting Point of Pure Salbutamol Sulphate

Melting point of was determined by Micro controlled based melting point apparatus (Chem. Line). A small amount of drug was taken in one end closed capillary tube and placed in then the capillary was inserted in bath of silicone oil which was heated in controlled manner with the help of electrical heating coil and the temperature at which the drug melts was noted. Average of triplicate readings was noted and compared with the IP 2007 standards.

UV Spectroscopy of Pure Salbutamol Sulphate

Accurately weighted 100 mg of salbutamol sulphate was transferred in to the 100 ml volumetric flask and volume was made up to 100 ml with 0.1 N HCl. From this solution, 1 ml was withdrawn and added to the 10 ml volumetric flask and diluted to 10 ml with 0.1 N HCl. Finally, volume was scanned in the range of 200-400 nm. The wavelength of the maximum absorption was noted and UV spectrum was taken.

Study of IR Spectrum of Pure Salbutamol Sulphate

IR spectroscopy is one of the most powerful analytical techniques, which offers the possibility of detecting chemical interaction. The IR spectra analysis of salbutamol sulphate was taken to ascertain the purity of the compound. IR spectra of salbutamol sulphate were recorded by using Fourier transform Infrared spectrophotometer.

Standard Curve of Pure Salbutamol Sulphate

Standard Curve of Pure Salbutamol Sulphate In 0.1 N Hcl

Accurately weighted 100 mg of salbutamol sulphate was added to the 100 ml volumetric flask. Volume was made up to 100 ml with 0.1 N HCl (1000 µg/ml). From this solution 1 ml was withdrawn and added into 10 ml volumetric flask and volume was made to 10 ml with 0.1 N HCl (100 µg/ml). This solution was used as stock solution. From the stock solution 0.2, 0.4, 0.6, 0.8, 1.0, 1.2, ml were withdrawn and added to 10 ml volumetric flask and finally diluted to 10 ml with 0.1 N HCl to get the solution with concentration of 2-12 µg/ml respectively. The absorbance was measured for each solution at 276 nm using UV-visible spectrophotometer. The graph was plotted for absorbance Vs concentration.

Preparation of Stock Solution

Accurately weighed 100 mg of salbutamol sulphate was transferred to the 100 ml volumetric flask containing 0.1 N HCl. From resulting solution 10 ml was pipetted out anddiluted to 100 ml with 0.1 N HCl separately for stock solution of 100 µg/ml

Preparation of Working Solution

From above stock solution, aliquots of 0.2ml, 0.4ml, 0.6ml, 0.8ml, 1.0ml, 1.2ml were withdrawn and transferred to the 10 ml volumetric flask each containing 0.1 N HCl to get the concentration of 2 µg/ml, 4 µg/ml, 6 µg/ml,8 µg/ml, 1.0 µg/ml, 1.2 µg/ml, respectively. Finally the absorbance of prepared solution was measured against blank 0.1 N HCl at 276 nm using UV visible spectrophotometer and calibration curve graph was plotted for concentration vs. absorbance.

Powder Characterization

Physical parameter of bulk drug like Angle of repose, bulk density, tapped density (BD and TD), carr's index and hausner's ratio was measured.

Angle of Repose

Angle of repose (θ) is the maximum angle between the surface of a pile of powder and horizontal plane. It is usually determined by Fixed Funnel Method and is the measure of the flowability of powder.

The accurately weighed powder was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the powder. The powder was allowed to flow through the funnel freely onto the surface. The diameter of the

powder cone was measured and the angle of repose was calculated using the following equation.

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

Therefore; $\theta = \tan^{-1}(h/r)$

Where,

h= Height of pile, r= Radius of the base of the pile ,θ= Angle of repose

DENSITY

Powder density may influence compressibility, tablet porosity, dissolution and other properties.

Bulk Density (BD)

Largely depends on particle shape. As the particle become more spherical in shape, bulk density decreases. The smaller granules are able to form close, more intimate packing than larger granules. The term bulk density refers to measure used to describe a packing or granules. It is the weight the volume ratio of the substance expressed in gm/cm^3 and calculated by using the following equation.

$$\mathbf{B_d = W/V_I}$$

Where,

$B_{d=}$ Bulk density, W= Weight of sample in gram, $V_{I=}$ Initial volume of sample in cm^3

Tapped Density (TD)

It is a limiting density attained after "tapping down," usually in a device that lifts and drops a volumetric measuring cylinder containing the powder from a fixed distance.The tapped density is the weight by tapped volume ratio expressed in gm/cm^3 and calculated by using the following equation.

$$\mathbf{T_d = W/V_T}$$

Where, $T_{d=}$ Tappeddensity, W= Weight of sample in gram,$V_{T=}$ Final tapped volume of sample in cm^3.

Carr's Compressibility Index

Compressibility is the ability of powder to decrease in volume under pressure. Compressibility is a measure that is obtained from density determinations. The compressibility index of the powder was determined by Carr's compressibility index.

$$Carr's\ Index = [(TD - BD) \times 100 / TD]$$

Hausner's Ratio

Hausner's found that the ratio tapped density/bulk density was related to inter particle friction as such, and could be used to predict powder flow properties.

Hausner's Ratio = Tapped Density / Bulk Density.

Preparation of Tablets of Salbutamol Sulphate By Direct Compression Technique

Tablet blend was prepared using formulae given in table no.10, 11, and 12. The amount of superdisintegrants was varied from 2% to 6% for study of effect of superdisintegrants. The sodium starch glycolate, croscarmellose sodium, and crospovidone, *Sepia officinalis* were used as superdisintegrants. Aspartame was used as sweetener. Magnesium stearate was used as lubricant. Aerosil was used as glidant and microcrystalline cellulose was used as polymer. The drug and other ingredients were mixed with trituration. The tablets were prepared with direct compression using 6 mm punch.

The Composition of F1 – F21 Batch Is Shown Below

Ingredients	Formulations																				
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15	F16	F17	F18	F19	F20	F21
Salbutamol Sulphate	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
Sodium Starch Glycolate	2	4	6	--	--	--	--	--	--	--	--	--	1	2	3	--	--	--	--	--	--
Croscarmellose Sodium	--	--	--	2	4	6	--	--	--	--	--	--	--	--	--	1	2	3	--	--	--
Crospovidone	--	--	--	--	--	--	2	4	6	--	--	--	--	--	--	--	--	--	1	2	3
Sepia officinilis	--	--	--	--	--	--	--	--	--	2	4	6	1	2	3	1	2	3	1	2	3
Microcrystalline Cellulose	28	26	24	28	26	24	28	26	24	28	26	24	28	26	24	28	26	24	28	26	24
Mannitol	58	58	58	58	58	58	58	58	58	58	58	58	58	58	58	58	58	58	58	58	58
Aspartame	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Flavour	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Aerosil	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Magnesium Stearate	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Total Weight (mg)	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100

All quantities are in mg, Formula for one tablet is shown in table**.**

***In Vitro* Evaluation of Formulated Fast Dissolving Tablets of Salbutamol Sulphate**

Thickness and diameter

Tablet thickness was controlled within 5% or less of a standard value. The thickness and diameter of the tablets were determined using a verniercaliper.

Hardness

The mechanical strength of the tablet was determined by using Monsanto hardness tester. This tester has a graduated scale which gives the reading in Kg/cm^2. The tablet to be tested was placed between the spindle and anvil. The desired pressure needed to hold the tablet in position is applied by moving the screw knob in clockwise direction. The scale was moved so that the indicator rested at zero. The pressure was applied till the tablet breaks. The reading was noted.

Weight Variation

It is desirable that every individual tablet in a batch should be uniform in weight, but a small variation in the weight of the individual tablet is liable to occur. Therefore a little variation is allowed in the weight of the tablet by the pharmacopoeia.

To study weight variation test IP procedure was followed. 20 tablets of each formulation were weighed individually and collectively using an electronic balance and average weight was calculated. From the individual tablet weight, the range and percentage standard deviation was calculated.

Determination of Drug Content

Drug content from the tablets was determined by taking tablets from each formulation. Five tablets from each formulation were accurately weighed and powdered. Powder equivalent to 20 mg of the drug was weighed and transferred to a volumetric flask and added to it 100 ml of 0.1N HCl. The resultant solution was shaken for 20 minutes on sonicator. Then solution was diluted with a sufficient quantity of 0.1N HCl to achieve concentration up to 12µg/ml of Salbutamol sulphate. The absorbance was then measured at 276 nm. The content of Salbutamol was estimated in triplicate using calibration curve constructed in the same solvent.

Percent Friability

Friability test was performed to evaluate the ability of the tablet to withstand wear and tear in packing, handling and transportation. The friability of tablet was determined by using Roche Friabilator. It is expressed in percentage (%). Thirty three tablets were initially weighed (initial wt.) and transferred into friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again (final wt.). The percentage friability was then calculated by using following formula.

% Friability = [(Initial wt. – Final wt.) ÷ Initial wt.] 100

% friability of tablet less than 1% is considered acceptable.

Disintegration Time

A disintegration test was performed to determine the time required to break the tablet into fine aggregates/particles. In the present study disintegration test was carried out on six tablets using the apparatus specified in IP (Electrolab disintegration apparatus). The 0.1 N HCl at 37^0c ± 2^0c was used as a disintegration medium and time in second taken for complete disintegration of the tablet with no palpable mass remaining in apparatus was measured.

Wetting time and water absorption ratio

Wetting time is closely connected to the inner structure of tablets and to hydrophilicity of the excipients. According to the following equation planned by washburn E.W, the water penetration rate into the powder bed is proportional to the pore radius and affected by the hydrophilicity of the powders.

$$dl/dt = r\,\gamma\cos\theta/(4\eta l)$$

Where, l is length of penetration ,r is capillary radius ,γ is surface tension ,η is liquid viscosity, t is time ,θ is contact angle. A portion of the tissue paper folded twice was placed in a small petri plate (internal diameter = 6.5cm) containing 6ml of water. A tablet was located on the paper and time for complete wetting of the tablet was measured in seconds. The method was slightly modified by maintaining water at 37°C. The same procedure was followed for determining the water absorption ratio. The wetted tablet was weighed and water absorption ratio, R was determined according to the following equation,

$$R = \{(Wa-Wb)/Wb\}\times 100$$

Where, Wb and Wa were the weights of the tablet before and after study.

9.9.8. *In Vitro* Dissolution Study

In vitro dissolution of Salbutamol sulphate fast dissolving tablets was studied using USP type II tablet dissolution apparatus. The dissolution was carried out in 900ml 0.1 N HCl at 37±0.5˚c, at 50 RPM. 5 ml aliquots were withdrawn at specific time interval, and filtered using Whatman filter paper. Absorbance of the filtered solution was checked UV spectrophoto metrically at 276nm and the drug content was determined. Sink conditions were maintained throughout the study.

Stability Studies

Stability studies for the developed formulations were carried out by storing the selected formulation at 40^0C /75% RH up to one month.

RESULT AND DISCUSSION

Characterization of drug

Description

Salbutamol sulphate powder was found to be white or almost white odorless and as per the description given in official book.[33]

Solubility: Salbutamol sulphate Powder was found to be soluble in water, slightly soluble in ethanol and chloroform.

Taste: Salbutamol sulphate was slightly bitter in taste

MELTING POINT

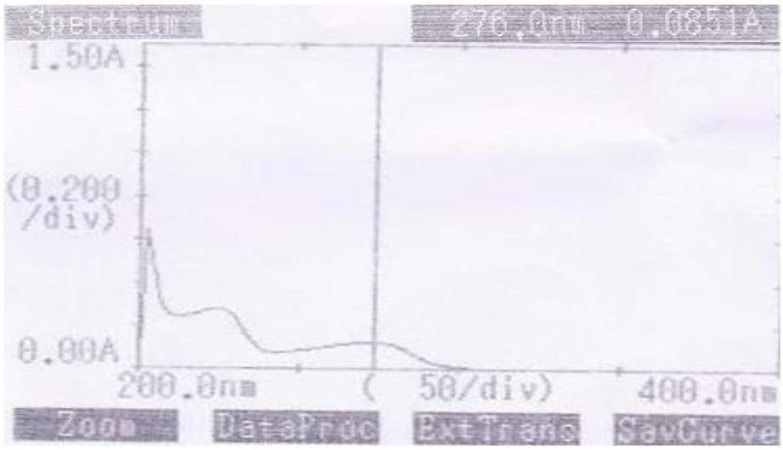
Table1: Melting Point of Salbutamol Sulphate

Sr. No	Parameters	Salbutamol Sulphate
1	Melting point (°C)	205^0C

UV Spectroscopy

Λmax Determination

The optimal absorbance was found to be 0.0851 at 276 nm. λmaxof Salbutamol Sulphate was found to be at 276 nm in 0.1 N HCl



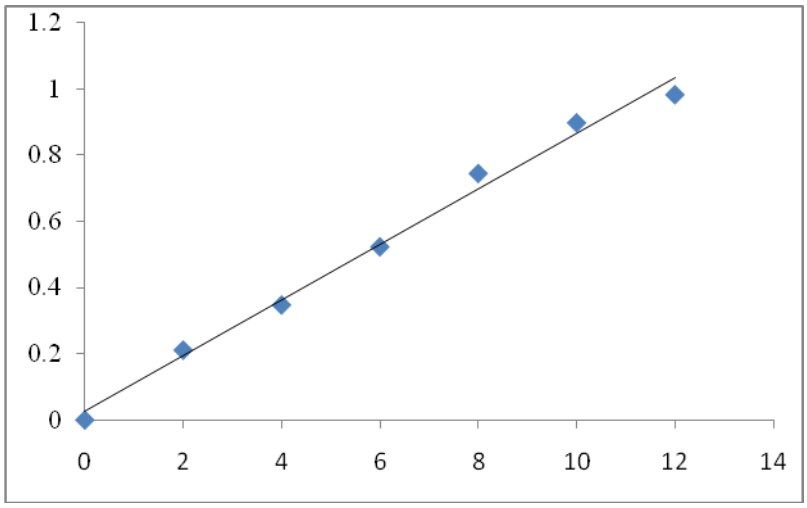
UV Spectrum of Salbutamol Sulphate

Calibration CURVE oF Salbutamol Sulphate IN 0.1 N Hcl

The results of absorbance shown at various concentrations of Salbutamol Sulphatein 0.1 N HCl given in Table 15.

Table2: Absorbance Value At Various Concentration of Salbutamol Sulphate.

Sr. No.	Concentration (µg/ml)	Absorbances
1	0	0.0000
2	2	0.2112
3	4	0.3476
4	6	0.5237
5	8	0.7452
6	10	0.8985
7	12	0.9833



Calibration Curve of Salbutamol Sulphate In 0.1N HCL

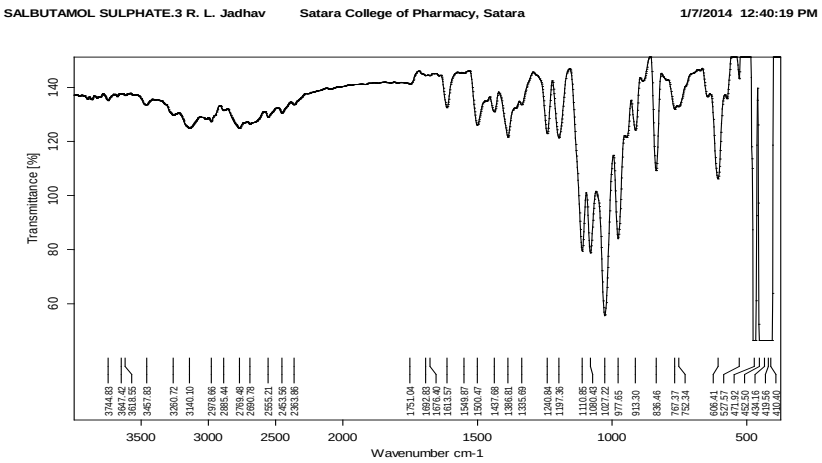
The standard calibration curve exhibited good coefficient of correlation as shown in Table .

Table3: Standard Curve Statistics

Sr. No.	Parameters	Values
1.	Slope (m)	0.008698
2.	Intercept (c)	0.001482
3.	Correlation coefficient	0.991
4.	λ_{max}	276

FTIR Spectra

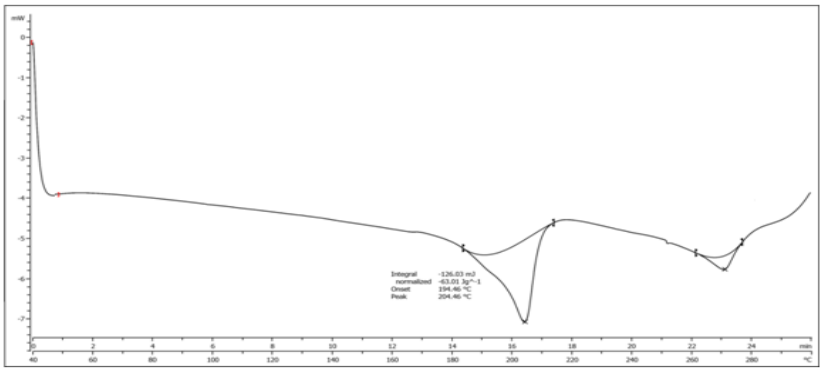
An FTIR spectrum of Salbutamol Sulphate is shown in Figure 5. FTIR peaks of Salbutamol Sulphate are given in Table.



FTIR Spectra of Salbutamol Sulphate

Thermal Analysis

Differential Scanning Calorimetry (DSC)



Powder Characterization

Characterization of each formulation was carried out and results obtained were shown in Table 4.

Table 4: Flow Properties of Formulation Powder.

Formulation Code	Bulk density (g/cc)	Tapped Density (g/cc)	Carr's index	Hausner's Ratio	Angle of repose(^{0})
F1	0.51±0.78	0.60±01.04	13.64±1.71	1.15±1.02	29.20±0.85
F2	0.50±0.89	0.62±0.78	16.09±0.54	1.19±0.57	31.25±1.31
F3	0.53±1.02	0.61±0.45	16.72±1.16	1.19±0.29	28.83±0.93
F4	0.42±1.07	0.60±0.67	14. 21±1.07	1.16±0.45	29.13±0.52
F5	0.50±0.98	0.59±0.97	15.04±0.72	1.17±0.67	32.68±0.72
F6	0.51±0.53	0.63±1.01	14.19±0.67	1.16±0.95	28.83±0.67
F7	0.53±0.95	0.61±0.89	15. 91±1.6	1.18±1.04	29.05±0.45
F8	0.52±0.45	0.60±0.84	14. 3±0.68	1.15±0.67	28.22±1.02
F9	0.51±0.74	0.60±0.39	15.38±0.81	1.18±0.89	29.44±0.86
F10	0.45±0.94	59±0.65	15.14±0.25	1.15±0.65	29.84±0.85
F11	0.51±0.87	61±0.69	16.05±0.49	1.19±0.94	28.15±0.65
F12	0.52±0.45	62±0.97	13.62±0.75	1.16±0.74	31.24±1.5
F13	0.51±0.95	58±0.25	14.36±0.85	1.17±0.75	27.45±0.19
F14	0.50±1.05	63±0.78	15.52±0.68	1.16±0.36	28.85±0.56
F15	0.42±0.77	61±1.05	17.45±0.36	1.14±0.68	23.56±0.89
F16	0.47±0.87	60±0.48	16.12±0.23	1.16±0.65	31.45±0.16
F17	0.55±0.36	62±0.64	14.45±1.23	1.19±0.38	29.45±0.56
F18	0.51±0.25	59±0.94	15.98±0.36	1.15±0.46	27.65±1.12
F19	0.52±0.64	60±0.65	16.85±0.25	1.19±0.94	29.45±0.85
F20	0.49±0.64	63±0.94	13.06±0.64	1.17±0.74	27.15±0.49
F21	0.51±0.33	61±0.68	15.64±0.39	1.12±0.35	29.25±0.65

All values are expressed as mean± SD, n=3

Bulk density of the powder blends of different formulations was found to be in the was found to be less than 1.5. Both these values indicate good flow property and good compression characteristics.

EVALUATION OF TABLETS

Tablet Thickness and Diameter

Thickness of Tablet was determined by using micrometer screw gauge. The thickness of the prepared Tablet was found to be between3.032 to 3.061mm and diameter of tablet was found in the range of 5.93 to 7.16 mm. There was no marked variation in the thickness of tablet within each formulation indicating uniform behavior of powder throughout the compression process. The result of measured thickness and diameter of each formulation was as shown in the Table 5.

Table 5: Tablet Thickness And Diameter

Formulations	Tablet thickness(mm)	Tablet Diameter(mm)
F1	3.057 ± 0.57	6.16 ± 0.78
F2	3.035 ± 0.12	6.15 ± 0.92
F3	3.032 ± 0.41	5.96 ± 0.23
F4	3.038 ± 0.52	6.18 ± 0.78
F5	3.042 ± 0.42	6.17 ± 0.86
F6	3.048 ± 0.15	7.16 ± 0.82
F7	3.037 ± 0.73	6.18 ±0.56
F8	3.036 ± 0.92	6.16 ± 0.87
F9	3.034 ± 0.81	6.17 ± 0.68
F10	3.054 ± 0.57	6.19 ± 0.64
F11	3.037 ± 0.58	6.16 ± 0.54
F12	3.032 ± 0.56	5.93 ± 0.25
F13	3.042 ± 0.45	6.14 ± 1.02
F14	3.061 ± 1.05	6.16 ± 0.69
F15	3.059 ± 1.09	5.10 ± 0.58
F16	3.038 ± 0.25	7.12 ± 0.15
F17	3.036 ± 0.98	6.13 ± 0.89
F18	3.048 ± 0.67	6.18 ± 0.65
F19	3.033 ± 0.74	6.12 ± 0.25
F20	3.053 ± 0.25	6.14 ± 0.98
F21	3.058 ± 0.87	6.18 ± 1.05

All values are expressed as mean± SD, n=10

Hardness: Hardness values of the formulation ranged from 2.18to 3.50 kg/cm^2, which indicate good strength of tablet. The measured hardness of each formulation was shown in the Table 6.

Table 6: Tablet Hardness

Formulations	Hardness (kg/cm^2)
F1	3.45 ± 1.08
F2	2.48 ± 1.12
F3	3.22 ± 1.08
F4	3.22 ± 0.87
F5	3.18 ± 0.89
F6	2.66 ± 1.05
F7	2.34 ± 1.08
F8	2.32 ± 0.16
F9	2.53 ± 0.84
F10	3.50 ± 0.45
F11	3.61 ± 0.65
F12	3.45 ± 0.24
F13	2.48 ± 1.08
F14	2.68 ± 0.21

F15	2.54 ± 0.25
F16	2.31 ± 1.09
F17	2.18 ± 0.18
F18	3.12 ± 0.73
F19	2.51 ± 0.26
F20	2.59 ± 0.95
F21	2.50 ± 0.54

All values are expressed as mean± SD, n=10

Friability

Weight loss was calculated and represented in the terms of % friability. Friability values of all the formulation were observed less than 1%, indicating good strength of tablet.Results were shown in Table 7.

Table 7: Tablet Friability

Formulations	Friability (%)
F1	0.34 ± 0.98
F2	0.34 ± 0.74
F3	0.44 ± 1.05
F4	0.58 ± 1.01
F5	0.51 ± 0.67
F6	0.66 ± 0.76
F7	0.76 ± 0.53
F8	0.54 ± 0.67
F9	0.86 ± 1.14
F10	0.35 ± 0.64
F11	0.26 ± 0.74
F12	0.38 ± 1.68
F13	0.54 ± 0.54
F14	0.58 ± 0.87
F15	0.51 ± 0.65
F16	0.68 ± 0.78
F17	0.63 ± 0.25
F18	0.64 ± 1.05
F19	0.59 ± 0.64
F20	0.61 ± 0.54
F21	0.76 ± 0.23

All values are expressed as mean± SD, n=3

Weight Variation Test

During weight variation test none of the tablet was found to deviate by permissible percentage as per Indian Pharmacopoeia 1996 (7.5%) from the mean value of the 20 tablets. Thus it was found that all the formulations were found to comply the weight variation test.

Table 8: Average Weight of Tablets

Formulations Code	Weight variation
F1	Passes
F2	Passes
F3	Passes
F4	Passes
F5	Passes
F6	Passes
F7	Passes
F8	Passes
F9	Passes
F10	Passes
F11	Passes
F12	Passes
F13	Passes
F14	Passes
F15	Passes
F16	Passes
F17	Passes
F18	Passes
F19	Passes
F20	Passes
F21	Passes

All values are expressed as mean± SD, n=20

Wetting Time and Water Absorption Ratio

The data for wetting time and water absorption ratio of Fast dissolving tablets of Salbutamol sulphate was shown in Table 9.

Table9: Data for Wetting Time and Water Absorption Ratio.

Formulation Code	Water absorption ratio (%)	Wetting time(Sec.)
F1	20.99 ± 2.34	57.4 ± 0.89
F2	25.92 ± 1.15	52.4 ± 0.54
F3	32.56 ± 0.47	48.6 ± 0.53
F4	35.78 ± 0.92	40.0 ± 0.70
F5	39.71 ± 1.37	33.0 ± 1.14
F6	46.15 ± 0.93	34.6 ± 0.89
F7	49.35 ± 1.75	25.6 ± 0.54
F8	53.8 ± 1.30	25.0 ± 0.70
F9	56.28 ± 1.21	23.4 ± 1.14
F10	84.32 ± 0.87	95.5 ± 0.98
F11	79.12 ± 0.24	91.5 ± 0.54
F12	86.45 ± 0.94	85.6 ± 1.09
F13	27.94 ± 1.16	71.9 ± 0.94

F14	31.26 ± 1.08	64.5 ± 0.84
F15	39.85 ± 0.95	59.4 ± 0.67
F16	42.78 ± 0.68	55.6 ± 1.61
F17	43.6 ± 0.84	50.6 ± 0.56
F18	51.78 ± 0.79	47.6 ± 0.94
F19	61.45 ± 1.23	47.4 ± 1.12
F20	59.12 ± 0.84	41.9 ± 1.18
F21	63.58 ± 0.93	38.5 ± 0.36

All values are expressed as mean± SD, n=3

Wetting time and water absorption ratio were found to decrease and increase respectively with the corresponding increase in the concentration of superdisintegrant. It may be due to the hydrophilic nature of superdisintegrant. These things might have resulted into increased capillary action which has resulted into decreasing the wetting time and increasing the water absorption ratio of all the formulations.

Disintegration Time

The data for in vitro disintegration time of fast dissolving tablets of Salbutamol sulphate was shown in Table 10.

Table10: Disintegration Time

Formulation Code	Disintegration time in sec.
F1	76 ± 0.57
F2	69 ± 1.15
F3	65 ± 1.15
F4	52 ± 0.57
F5	49 ± 1.00
F6	51 ± 0.57
F7	45 ± 0.58
F8	32 ± 1.00
F9	28 ± 1.02
F10	645 ± 0.75
F11	594 ± 0.48
F12	561 ± 0.65
F13	247 ± 1.12
F14	243 ± 0.25
F15	221 ± 1.06
F16	168 ± 0.94
F17	141 ± 0.86
F18	94 ± 0.78
F19	79 ± 0.56
F20	61 ± 1.09
F21	53 ± 0.78

All values are expressed as mean± SD, n=3

Determination of Drug Content

The drug content was found to be uniform among all formulation and ranged from 95.56±01.23 % to 99.89±0.54%. The content of active ingredient in each formulation was as shown in the Table 11.

Table 11: Drug Content

Formulations Code	Drug Content (%)
F1	97.66±0.87
F2	98.45±0.96
F3	95.56±1.23
F4	97.0±0.98
F5	98.65±0.87
F6	97.43±1.27
F7	96.24±0.78
F8	98.78±0.55
F9	99.85±0.67
F10	95.61 ± 0.57
F11	97.63 ± 0.95
F12	92.84 ± 0.42
F13	93.42 ± 1.15
F14	98.53 ± 0.98
F15	95.67 ± 1.07
F16	96.72 ± 0.68
F17	98.18 ± 0.94
F18	95.76 ± 0.35
F19	97.42 ± 1.19
F20	96.32 ± 0.52
F21	99.89 ± 0.54

All values are expressed as mean± SD, n=3

***In Vitro* Dissolution Study**

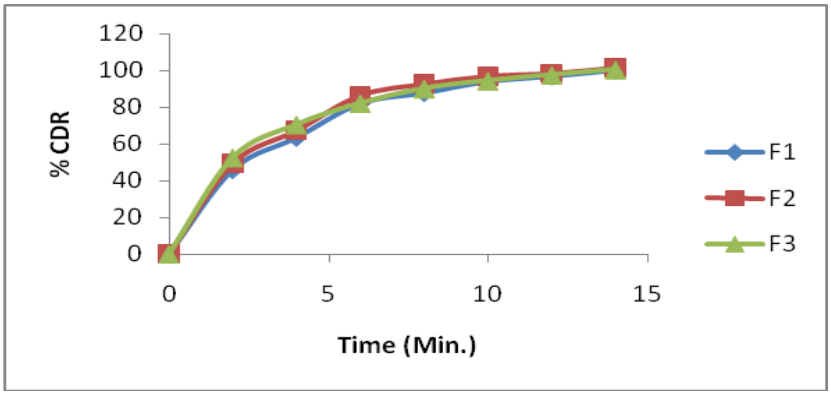
During *in vitro* dissolution study, it was found that 10 min. time was required for the complete drug release from the formulations F21. It was also observed that the increasing concentration of sodium starch glycolate, croscarmellose sodium, crospovidone in alone and in combination with *sepia officinalis* caused increase in drug release.

This may be attributable to superdisintegrants with the increase in concentration of superdisintegrants the capillary action might have increased which might have resulted into reducing the time required for wetting and disintegration of tablets and finally the dissolution of the drug.

Table 12: *In Vitro* Dissolution Profile of Formulation F1-F3

Time in min	F1	F2	F3
2	46.05 ± 0.98	49.36 ± 1.4	52.5 ± 0.21
4	63.61 ± 1.2	67.24 ± 0.85	70.51 ± 0.71
6	82.25 ± 0.55	86.31 ± 0.31	82.19 ±0.23
8	88.01 ± 1.6	92.53 ± 1.3	90.19 ± 0.18
10	94.25 ± 1.26	96.83 ± 0.63	94.48 ± 0.63
12	97.09 ± 2.03	98.35 ± 1.23	97.59 ± 0.83
14	100.41± 1.05	101.45 ± 0.83	100.53 ± 0.79

All values are expressed as mean± SD, n=3

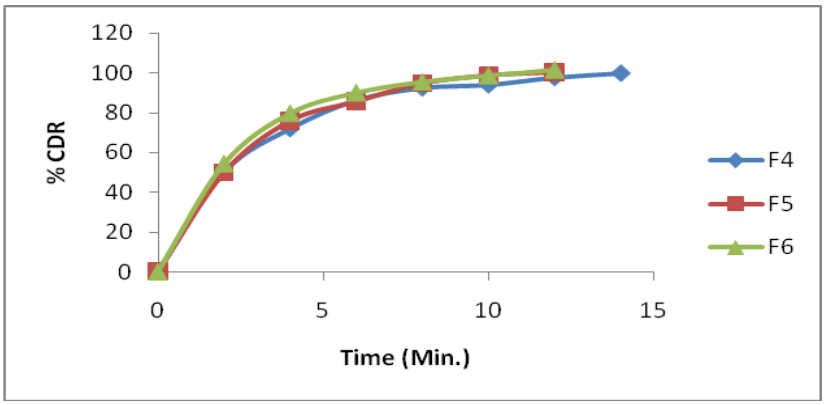


***In Vitro* Dissolution Profile of Formulation F1-F3**

Table 13: *In Vitro* Dissolution Profile of Formulation F4-F6

Time in min	F4	F5	F6
2	50.17 ± 1.6	49.83 ± 0.56	54.35 ± 0.69
4	72.04 ± 1.6	75.86 ± 0.33	79.74 ± 0.56
6	86.38 ± 0.62	85.59 ± 0.76	90.11 ± 1.4
8	92.56 ± 1.35	94.73 ± 0.56	95.55 ± 1.5
10	94.13 ± 1.6	98.76 ± 0.43	98.75 ± 0.28
12	97.78 ± 0.96	100.28 ± 0.72	101.63 ± 0.92
14	99.94 ± 0.63	_	_

All values are expressed as mean± SD, n=3

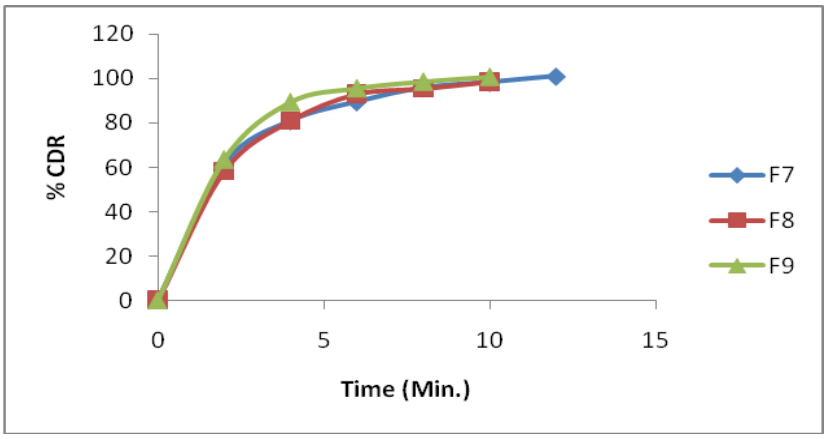


***In Vitro* Dissolution Profile of Formulation F4-F6**

Table14:*In Vitro* Dissolution Profile of Formulation F7-F9

Time in min	F 7	F 8	F9
2	61.15 ± 1.23	58.15 ± 0.96	63.58 ± 0.42
4	80.92 ± 0.42	80.82 ± 1.2	89.51 ± 1.2
6	89.49 ± 1.14	92.85 ± 1.1	95.74 ± 0.73
8	95.82 ± 0.63	95.29 ± 0.44	98.75 ± 0.42
10	98.29 ± 0.46	98.45 ± 0.92	100.9 ± 1.23
12	101.03 ± 0.87	_	_

All values are expressed as mean± SD, n=3

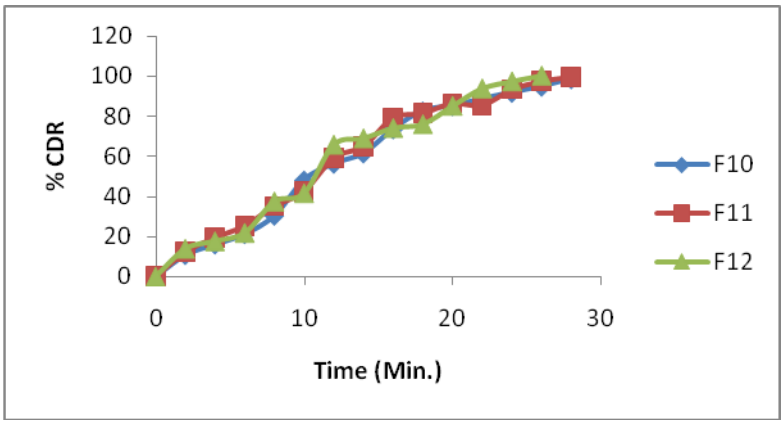


***In Vitro* Dissolution Profile of Formulation F7-F9**

Table 15: *In Vitro* Dissolution Profile of Formulation F10-F12

Time in min	F10	F11	F12
2	10.64±0.94	12.19±0.94	17.36±0.65
4	15.92±1.78	19.74±0.87	21.75±0.98
6	21.12±0.98	24.34±1.32	37.94±0.74
8	30.35±2.12	35.23±0.58	41.58±1.05
10	48.32±0.65	42.78±0.47	62.34±2.45
12	56.45±0.89	59.58±0.89	68.65±0.98
14	61.49±0.57	64.32±0.65	74.84±0.56
16	73.25±1.56	79.84±1.56	76.47±0.89
18	82.35±1.98	81.25±2.15	85.45±0.98
20	85.45±1.25	86.14±0.85	93.38±1.91
22	88.68±0.25	87.89±0.69	95.21±0.95
24	91.45±2.15	93.56±1.56	98.31±0.67
26	94.65±1.05	97.65±1.25	100.25±1.34
28	98.78±0.96	99.35±0.69	-

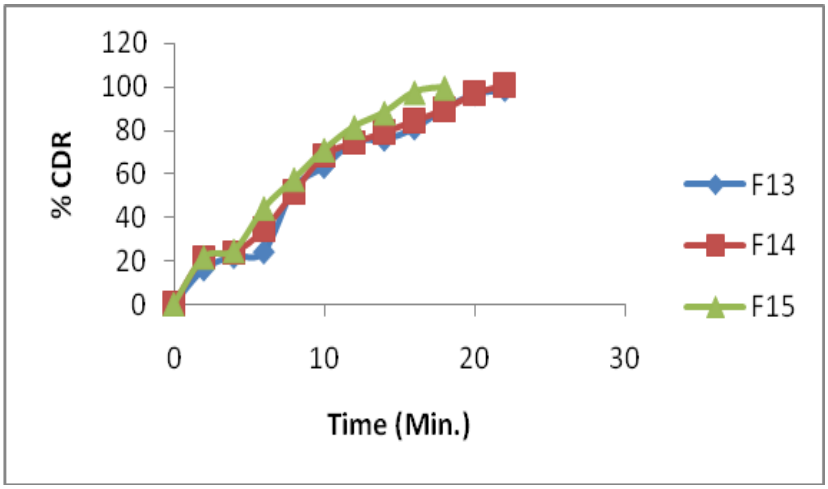
All values are expressed as mean± SD, n=3



***In Vitro* Dissolution Profile of Formulation F10-F12**

Table16: *In Vitro* Dissolution Profile of Formulation F13-F15

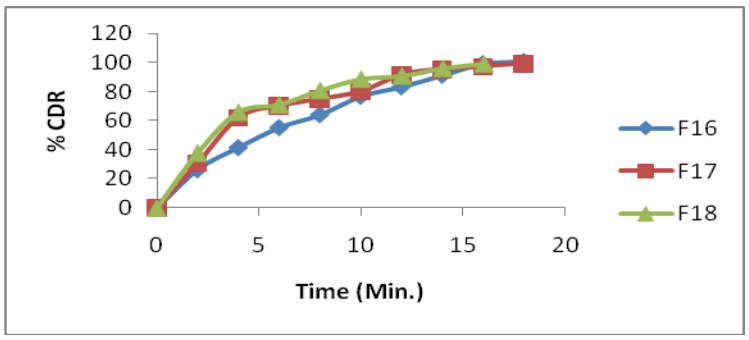
Time in min	F13	F14	F15
2	16.08± 0.55	21.35 ± 1.22	21.55 ± 1.66
4	21.92± 1.98	29.65 ± 0.88	28.17 ± 1.06
6	24.04± 0.23	34.16 ± 1.71	44.11 ± 2.14
8	53.36± 1.06	51.49 ± 2.1	57.42 ± 2.04
10	63.42± 1.48	68.26 ± 2.12	70.99 ± 1.81
12	74.93± 1.33	74.07 ± 1.18	81.52 ± 1.2
14	75.95± 1.57	78.9 ± 1.66	88.06 ± 1.83
16	81.08± 1.05	84.14 ± 2.88	97.45 ± 0.67
18	90.15± 2.12	89.43 ± 2.03	99.65 ± 0.71
20	96.83± 0.27	96.56 ± 1.81	-
22	98.78± 1.39	100.61 ± 0.83	-



***In Vitro* Dissolution Profile of Formulation F13-F15**

Table 17: *In Vitro* Dissolution Profile of Formulation F16-F18.

Time in min	F16	F17	F18
2	26.44±1.55	30.97±1.22	37.9±1.03
4	41.62±0.34	62.29±1.81	65.95±1.02
6	55.36±1.89	70.3±1.53	71.12±2.0
8	64.11±2.61	74.97±1.58	80.84±077
10	76.79±1.14	80.2±1.38	88.64±2.45
12	83.36±2.14	91.75±2.04	90.8±1.02
14	91.33±1.06	95.39±1.46	96.01±1.72
16	99.13±1.13	97.27±1.3	99.14±0.81
18	100.69±0.76	99.55±1.49	-

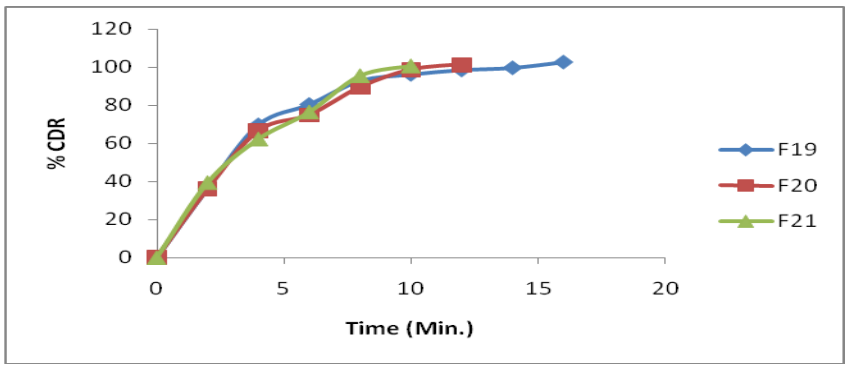


***In Vitro* Dissolution Profile of Formulation F16-F18**

Table 18: *In Vitro* Dissolution Profile of Formulation F19-F21.

Time in min	F19	F20	F21
2	36.28 ± 0.94	36.22 ± 1.09	39.45 ± 0.79
4	69.61 ± 2.10	66.59 ± 2.04	62.36 ± 1.49
6	80.29 ± 0.28	74.87 ± 1.098	76.55 ± 1.38
8	92.65 ± 0.73	89.49 ± 2.07	95.64 ± 1.17
10	96.04 ± 1.21	98.6 ± 1.25	100.78 ± 1.4
12	98.37 ± 1.66	101.32 ± 1.96	-
14	99.5± 0.69	-	-
16	102.49 ± 1.08	-	-

All values are expressed as mean± SD, n=3



***In Vitro* Dissolution Profile of Formulation F19-F21**

Stability Studies

Stability studies for the optimized formulation were carried out by storing the formulation at 40^0c /75% RH up to one month. The formulation F21 was selected on the basis of their high cumulative percentage drug release within lower time(10 min). This formulation showed no significant changes in the values after performing stability study. The data obtained was given in table 18.

Table 18: Stability Studies of Optimized Formulation (F21)

Formulation 21	% CDR	*In vitro* isintegration time (sec)	Drug content
Before stability	100.78 ± 1.23	53± 0.78	99.89± 0.54
After stability	98.75 ± 1.34	49 ± 1.2	96.82 ± 1.74

All values are expressed as mean± SD, n=3

CONCLUSION

Sepia officinalis shell powder, crosscarmellose sodium, sodium starch glycolate, crospovidone were tested for disintegration effect in FDTs of Salbutamol sulphate. The study reveals that all tested superdisintegrants have effect on disintegration time of prepared tablets. The tested superdisintegrants shows different effect on disintegration when tested alone and in combination.

Sepia officinalis shows effervescence when it comes in contact with acids, this concept was used as hypothesis and explored for its effect on disintegration time. When *Sepia officinalis* shell powder alone was used as superdisintegrants, it doesn't show remarkable results in lowering disintegration time. But when it is tested in combination with other superdisintegrants it shows good results. Final result revealed that batch F21 that consist of 3% crospovidone and 3% *Sepia officinalis* shell powder lower the disintegration time up to 53 sec. Hence this combination of superdisintegrants can be used in fast disintegrating tablet. Evaluation studies performed in present investigations revealed that the formulation F21 was found to be optimum. The disintegration test revealed shortest time required to the formulation F21 when tested in combination of superdisintegrants. Further dissolution profile for the formulation F21 was found to be 100.78%. Other evaluation parameters like hardness, friability was found to be 2.50 kg/cm^2 and 0.76% respectively for the formulation F21.

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