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Formulation and Evaluation of Fast Dissolving Levosalbutamol Sulphate Tablet

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Mr.Shetkar M.A, Mr.More R.R, Mr.Mahapure D.A, Dr.Patil.S.S, Dr. Poul B.N.

Maharashtra College of Pharmacy, Department Of Quality Assurance, Nilanga-413521, Dist. Latur (MS) India.

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ABSTRACT

The oral route of administration is the most preferred route to its many advantages like ease of administration, accurate dosage, self medication, pain avoidance, versatility and patient compliance. Tablet and capsules are the most popular dosage forms. But one important drawback of such dosage form is Dysphasia or difficulty in swallowing. To solve the above mentioned problem, pharmaceutical technologists have put best efforts to develop a fast dissolving drug delivery, i.e. Fast Dissolving Tablet that disintegrates and dissolves rapidly in the saliva, within a few second without the need of drinking water or chewing, a mouth dissolving tablet usually dissolves in the oral cavity within 15 sec to 4 min. The demand for Fast Dissolving Tablets (FDTs) has been growing during the last decade especially for elderly and children who swallowing difficulties. Levosalbutamol (LVS) is the R - enantiomer of short acting β2-adrenergic receptor agonist of Salbutamol. Chemically it is 4[(1R)-2-(tert-butylamino)-1-hydroxyethyl]-2-(hydroxymethyl) phenol and its molecular formula $C_{13}H_{21}NO_3$, Molecular wt. 239.311 g/mol. As a bronchodilator, it is used to treat asthma and COPD (Gilman AG and Limbird LE, 2001; Milgrom H, 2006). Literature survey reveals that, only few spectrophotometric (Dave HN et al., 2007; Basavaiah K et al., 2007; Arun. K et al., 2010; Thulasamma. P et al., 2011) and bio-analytical methods by HPLC was found using human plasma (Ghulam Murtaza et al., 2009; McCarthy et al., 1993), urine (De Groof. J et al., 1991) , blood (Black SB and Hansson RC, 1999) and biological fluids (Girault J et al., 1991) for the quantitative estimation of Levosalbutamol sulphate in bulk and pharmaceutical formulations have been developed.

INTRODUCTION

Solid dosage forms like tablet and capsule are most popular and preferred drug delivery system because they have high patient compliance, relatively easy to produce, easy to market, accurate dosing, and good physical and chemical stability.

The concept of fast dissolving drug delivery system emerged from the desired to provide patient with conventional means of taking their medication. Fast dissolving dosage form can be disintegrated, dissolved or suspended by saliva in mouth. The fast dissolving tablets disintegrates instantaneously when placed on tongue and releases the drug, dissolve or disperses in saliva[1]. The fast dissolving tablets are useful in patients[2,3] like pediatric, geriatric, bedridden or mentally disabled, who may face difficulty in swallowing conventional tablet or capsule leading to ineffective therapy[5], most pharmaceutical forms for oral administration are formulated for direct ingestion or for chewing or for prior dispersion/dissolution in water. Some of them are absorbed in mouth (sublingual or Buccal tablet) to obviate the problem associated with conventional dosage forms orally fast dissolving tablets have been developed which combine hardness, dosage uniformity, stability and other parameters, since no water is required for swallowing the tablets and they are thus suitable for geriatric, pediatric and travelling patients[6].

The demand for Fast Dissolving Tablets (FDTs) has been growing during the last decade especially for elderly and children who have difficulties in swallowing. Levosalbutamol (LVS) is the R - enantiomer of short acting β2-adrenergic receptor.

The fast dissolving tablet formulation is defined by the food and drug administration (FDA) as, "A solid dosage form containing medicinal substances which disintegrates rapidly, usually within matter of seconds, when placed upon the tongue"[7]. It is difficult for many patient to swallow tablets and hard gelatin capsule hence they do not comply with prescription, which results in high incidence of non compliance and ineffective therapy. Such problem can be resolved by mean of fast dissolving tablet. These FDT are designed to dissolve or disintegrates rapidly in saliva generally within <60 second.

Tablet is most popular among all dosage forms existing today because of its self administration, and easy manufacturing; however in case of hand tremors, dysphasia geriatric patients the problem of swallowing is common which leads to poor patient compliance. To overcome these

drawbacks, mouth dissolving tablets or orally disintegrating tablets have emerged as alternative oral dosage form. These tablets disintegrate, dissolve and disperse in saliva within few seconds [2]. Fast dissolving tablets are useful in patients [3] like pediatric, geriatric, bed ridden or mentally disabled.

Desired criteria for mouth disintegration drug delivery system [12-13]

- Not require water to swallow, but it should dissolve or disintegrate in the mouth in a matter of seconds.
- Have a pleasing mouth feel.
- Should compatible with masking.
- Should be potable without fragility concern.
- Exhibit low sensitivity to environmental condition such as humidity and temperature.
- Allow the manufacturing of tablet using conventional processing and packaging equipment at low cost.

Benefit of Fast dissolving tablet

- Administered without water, anywhere, any time.
- Suitable for geriatric and pediatric patient, who experience difficulties in swallowing and for the other groups that may experience problem using conventional oral dosage form, due to being mentally ill, the developmentally disable and the patient who are un-cooperative, or are on reduced liquid intake plans or are nauseated.
- Beneficial in case such as motion sickness, suede episodes of allergic attack or coughing, where an ultra rapid onset of action required.
- An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs , due to rapid disintegration and dissolution of these tablets.
- Stability for longer duration of time, since the drug remains in solid dosage form till it is consumed. So, combines advantage of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability.

Salient features of fast dissolving drug delivery system

- Ease of Administration to the patient who refuses to swallow a tablet as pediatric geriatric patient and psychiatric patient.
- Consentience of administration and accurate dosing as compared to liquids.
- No need of water to swallow the dosage form, which is highly convenient especially for patient who are traveling and do not have immediate access to water.
- Good fast feel property of FDDS help to change to basic view of medication as better pill particularly for pediatric patient.
- Rapid dissolution and absorption of drug, which may produce quick onset of action.
- Some drugs are absorbed from the out, pharynx and esophagus as the saliva passes down into the too much; in such cases bioavailability of drugs is increased.
- Ability to provide advantages of liquid medication in the form of solid form.
- Pre-gastric absorption can result in improved bioavailability and as a result of reduced dosage, improved clinical performance through a reduction of unwanted effects.

Limitation of Fast Dissolving Tablets

- FDT is hygroscopic in nature so must be kept in dry place.
- Sometime it possesses mouth feeling.
- It is also showing the fragile, effervescence granules property.
- FDT requires special packaging for proper stabilization & safety of stable product.

Superdisintegrants

Disintegrants are agents added to tablet (and some encapsulated) formulation to promote the breakup of the tablet (and capsule "slugs') into smaller fragments in an aqueous environment thereby increasing the available surface area and promoting a more rapid release of the drug substance. They promote moisture penetration and dispersion of the tablet matrix. In recent years, several newer agents have been developed known as "superdisintegrants'. These newer substances are more effective and mechanical strength. On contact with water the superdisintegrants swell, hydrate, change volume or form and produce a disruptive change in the tablet.

Effective superdisintegrants provide improved compressibility, compatibility and have no negative impact on the mechanical strength of formulation containing high-dose drugs. Tablet disintegration has received considerable attention as an essential step in obtaining fast drug release. The emphasis on the availability of drug highlights the importance of the relatively rapid disintegration of tablet as a criterion for ensuring uninhibited drug dissolution behavior. Number of factors affects the disintegration behavior of tablets. The development of fast dissolving or disintegration tablets provides an opportunity to take an account of tablet disintegrates. Recently new materials termed as superdisintegrant have been developed to improve the disintegration process. Selecting appropriate formulation excipients and manufacturing technology can obtain the design feature of fast disintegrating tablet. The disintegrants have the major function to oppose the efficiency of the tablet binder and the physical forces that act under compression to form the tablet.

The stronger the binder, the more effective must be the disintegrating agents in order for the tablets to release its medication. Ideally, it should cause the tablet to disrupt, not only into the granules from which it was compressed, but also into powder particles from which the granulation was prepared. Disintegrants are an essential component to tablets formulation. While rapidly disintegrating tablets do not necessarily ensure fast bioavailability, slowly disintegrating tablets assure slow bioavailability. The ability to interact strongly with water is essential to disintegrant function.

Combinations of swelling and/or wicking and/or deformation are the mechanisms of disintegrant action. Superdisintegrants offer significant improvements over starch. But hygroscopicity may be a problem in some formulation, a disintegrant used in granulated formulation processes on more effective if used both “intra-granularly’ and “extra-granularly” thereby acting to break up the tablet into granules and having the granules further disintegrant to release the drug substance into solution. However, the portion of disintegrants added intra-granularly (in wet granulation processes) is usually not as effective as that added extra-granularly due to the fact that it is exposed to wetting and drying (as part of the granulation process) which reduces the activity of the disintegrant. Since a compaction process does not involve its exposure to wetting and drying, the disintegrant used intra-granularly tends to retain good disintegration activity.

MATERIALS AND METHODS

Materials

Levosalbutamol, Croscarmillose Sodium, Crosprovidone, Sodium Starch Glycolate, Microcrystalline cellulose, Magnesium stearate and Aerosil gift sample were obtained from Research Lab Fine Chem, Mumbai.

Pre-formulation Parameter powder blends:

- Angle of repose
- Bulk density
- Tapped density
- Compressibility index (%)
- Hausner's ratio

Angle of repose:

Angle of repose was determined by fixed height method to characterize the flow property of powder blend. A funnel with 10 mm diameter of stem was fixed at a height of 2 cm over the platform. Sample was slowly passed along the wall of the funnel till the tip of pile formed touches the stem of the funnel. A rough circle was drawn around pile base and the radius of powder cone was measured. Relationship between angle of repose (Ø) and flow ability are shown in Table No. 2. Angle of repose was calculated from the average radius using following formula.

$$\text{Tan } Ø = h / r$$

$$Ø \tan^{-1}(h / r)$$

Where,

Ø =Angle of repose

h=height of the pile

r= average radius of the powder cone

The relationship between Angle of repose and powder flow:

Powder flow	Angle of repose
Excellent	25-30
Good	31-35
Fair-aid not needed	36-40
Passable-may hang up	41-45
Poor-must agitate, vibrate	46-55
Very poor	56-65
Very-very poor	66

Bulk Density:

Bulk density is defined as the mass of a powder divided by the bulk volume. The bulk density of powder depends primarily on particle size distribution, particle shape, and the tendency of the particles to adhere to one another. Both bulk density (BD) and tapped density (TD) were determined. A quantity of accurately weighted powder (bulk) from each formula, previously shaken to break any agglomerate's formed was introduced into a 25 ml measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2 sec interval. The taping was continued no further change in volume was noted LBD and TBD was calculated using following formula;

$$BD = \frac{\text{Weight of the powder}}{\text{Volume of the packing}}$$

$$TP = \frac{\text{weight of the powder}}{\text{Tapped volume of the packing}}$$

Tapped density:

The measuring cylinder containing a known mass of blend was tapped for a fixed time. The minimum volume (V1) occupied in the cylinder and weight (M) of the blend was measured. The tapped density (ρ1) was calculated using the following formula.

$$\rho 1 = \frac{M}{V1}$$

Tapped density = weight of sample/volume occupied by the sample

Compressibility Index:

In recent years the compressibility index and the closely related Hausner's ratio have become the simple, fast and popular method of predicting powder flow characteristics. The compressibility index and Hausner's ratio are determined by measuring the bulk density and tapped density of powder. Grading of the powders for their flow properties according Carr's index is given in Table No. 3. The flow ability of powder can be evaluated by comparing the bulk density (Do) and tapped density (Df) of powder and the rate at which it packed down. Compressibility index is calculated by –

$$\textbf{Compressibility index (\%)} = \frac{\textbf{Df-Do X 100}}{\textbf{Df}}$$

Where,

Do = Bulk density

D f = Tapped density

Grading of the powders for their flow properties according to Carr's index

Consolidation index (Carr %)	Flow
5-15	Excellent
12-16	Good
18-21	Fair-aid to passable
23-35	Poor
33-38	Very poor
>40	Very very poor

Hausner's ratio:

It is the ratio of tapped density to bulk density.

Hausner's ratio = Df / Do

Where, Do = Bulk density, Df = Tapped density

Method of preparation of fast dissolving tablets:

Direct compression Method

Preparation of fast dissolving tablets by direct compression technique:

Method:

Fast dissolving tablets of Levosalbutamol sulphate were prepared by direct compression method according to the formula given in Table No. 1.

All the ingredients were passed through 60 mesh sieve separately. The drug and microcrystalline cellulose was mixed by small portion each time of both, blending it to get a uniform mixture and kept side. Then the ingredients were weighted and mixed in geometrical order and tablets were compressed of 8 mm sizes flat capsule type punch to get tablet using Rimek Compression Machine.

Post -compression properties:

- Hardness
- Friability
- Weight variation
- Uniformity of thickness
- Drug content uniformity
- Wetting time
- *In-vitro* disintegration test
- *In-vitro* dissolution Test

Hardness Test:

Although hardness test is not an official, tablet should have sufficient handling during packing and transportation. Hardness of tablet was measured using digital hardness tester. It is the pressure requires for fracturing diametrically placed tablets by applying the force. The hardness of 5 tablets from each batch was determined and average of reading in triplicate was calculated, which was expressed in kg/cm².

Friability Test (F):

Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at height of 6 inches in each revolution. Reweighed sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula.

$$F = \frac{\text{W initial} - \text{W final}}{\text{W initial}} \times 100$$

% of Friability of tablets less than 1% is considered acceptable.

Weight Variation Test:

With a tablet designed to contain a specific amount of drug in a specific amount of formula, the weight of a tablet being made is routinely measured to ensure that a tablet contains proper amount of drug**.**

Procedure:

Weight of 20 tablets was determined and average weight was calculated. Then individual tablets were weighed and the individual weight was compared with an average weight.

Shows the weight variation tolerance for tablets

Average weight of tablet (mg)	Maximum percent deviation allowed
130 mg or less	10%
More than 130 mg and less than 324 mg	7.5%
324 mg or more	5%

Uniformity of Thickness:

The crown thickness of individual tablet may be measured with a micrometer which permits accurate measurements and provides information on the variation between tablets. Other technique employed in production control involves placing 5 or 10 tablets in holding try, where

their total crown thickness may be measured with a sliding calliper scale, the tablet thickness was measured using screw gauge.

Drug content uniformity:

The test is applicable for tablets that contain less than 10 mg or less than 10% w/w of active ingredients. The test for uniformity of content should be carried out only after the content of active ingredient in a pooled sample and tablets have been shown within acceptable limits of the started content. Ten tablets were taken and their content was determined by UV spectrophotometry.

Wetting Time:

The method was applied to measure tablet wetting time. A piece of tissue paper folded twice was placed in a small Petri dish (i.d. = 6.5 cm) containing 10 mL of water to a tablet was placed on the paper, and the time for complete wetting was measured three trials for each batch were performed and standard deviation was also determined. The method was reported by Yunxia Bi et al.

Disintegration Time:

The process of breakdown of a tablet into smaller particles is called as disintegration. The *in-vitro* disintegration time of a tablet was determined using disintegration test apparatus as per I.P. specifications

I.P. Specification place one each of the basket. Add a disc to each tube and run the apparatus using distilled water maintained at 37º±2ºC as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in the tablet with no palpable mass remaining in the apparatus was measured and recorded.

***In vitro* dissolution studies:**

Dissolution rate was studied by using USP type-II apparatus (US XXIII Dissolution Test Apparatus at 50 rpm) using 900 mL of phosphate buffer pH (6.8) as dissolution medium. Temperature of the dissolution medium was maintained at 37±0.5ºC, aliquot of dissolution of filtered was withdrawn at every 1 min interval and filtered, the absorbance of filtered solution

was measured by UV spectrophotometer method at 276 nm and concentration of the drug determined from standard calibration.

***In Vitro* Release Studies Details:**

Apparatus Used	:	USPXXIII dissolution test apparatus
Dissolution medium	:	6.8 Phosphate buffer solutions
Dissolution medium volume	:	900 mL
Temperature	:	37±0.5ºC
Speed of basket paddle	:	50 rpm
Sampling intervals	:	1 min
Sample withdraw	:	5 mL
Absorbance measured	:	276 nm

RESULTS AND DISCUSSION

Pre-compression parameters:

Powder ready for compression containing drug and various excipients were subjected for pre-compression parameters (micrometric properties) to study the flow properties of granules, to achieve uniformity of tablet weight. The results of all the pre-formulation parameters are given in Table No. 2.

Angle of repose (Ɵ):

The data obtained from angle of repose for all the formulations were found to be in the range of 25.78º and 30.50º. All the formulations prepared by all three methods showed the angle of repose less than 30º which reveals good flow property as mentioned earlier in the literature. (Table No. 2)

Bulk Density:

Bulk density (BD) and tapped density (TD) for the blend was performed. The loose bulk density and tapped bulk density for the entire formulation blend varied from 0.50 gm/cc to 0.54 gm/cc (direct compression method) respectively (Table No-2).

Carr's consolidation index:

The result of Carr's consolidation index or compressibility index (%) for the entire formulation blend ranged from 13.02% to 17.01% (Table No-2).

Hausner's ratio:

Hansner's ratio of entire formulation showed between 1.18 to 1.20 indicates better flow properties.

Post-compression parameters:

Hardness:

The hardness of the tablets prepared was determined by Monsanto Hardness tester and found to be within the range of 2.5 kg/cm^3 to 3.3kg/cm^3. (Table No-3)

Friability test:

The friability was found in all designed formulation in the range 0.36% to 0.44% to be well within the approved range (<1%) (Table No. 3).

Weight variation test:

The weight variation was found in all designed formulation in the range 199.6 to 203.1 mg and % deviation was in a range of 0.03 to 1.22. All the tablets passed weight variation test as the average percentage weight variation was within 7.5% i.e. in the pharmacopoeia limits. (Table No. 3).

Thickness:

The mean thickness was (n=3) almost uniform in all the formulations and values ranged from 4.20 mm to 4.65 mm. Standard deviation values indicated that all the formulations were within the range (Table No. 3).

Disintegration time:

The *in-vitro* disintegration time was measured by the time taken to undergo complete disintegration. Rapid disintegration within 3 minutes was observed in all the formulation. The disintegration time of all the formulation is checked & is found within the range of 15 sec-20 sec.

Wetting time:

Wetting time is closely related to the inner structure of the tablets. The wetting time of Levosalbutamol Sulphate tablets prepared were found to be in the range of 34-40 sec (Table No. 3).

Drug Content:

The uniform drug content was performed for all the formulations. The average value and standard deviation of the entire tablets were found to be in between 97.23 +1.26 to 100+1.84

***In-vitro* dissolution study**:

Dissolution studies for all formulations were determined by USP type-II apparatus (DR-6, Campbell Instruments, Dissolution Test Apparatus 50 rpm). The dissolution profile of Levosalbutamol sulphate from the tablets was shown in Fig. 2, 3 & 4 at the time 30 min.

It was observed from the result that, CCS formulation showed maximum dissolution rate with more than 92.14% of drug released in 25 min.

CP formulation released more than 85.24% of drug release in 25 min and SSG formulation released more than 83.11% of drug release in 30 min.

DISCUSSION

In the present work, an attempt has been made to prepare fast dissolving tablets (FDT) of Levosalbutamol Sulphate with ingredients such as synthetic superdisintegrants by using direct compression.

Melting Point: Melting point was noted triplicate and was found to be 120 to 126ºC

UV-Spectroscopy: The UV spectrum obtained at the wavelength of maximum absorbance (λ_{max}) was found to be 276 nm (A. R. grade) and phosphate buffer pH 6.8.

Methods of preparation of fast dissolving tablet:

Fast dissolving tablets of levosalbutamol sulphate were successfully prepared by Direct Compression.

Result of pre-compression parameter for tablet prepared by direct compression.

Angle of repose (Ɵ): The data obtained from angle of repose for all the formulations were found to be in the range of 28.01 to 29.16.

Bulk density: The lose bulk density and tapped bulk density for all the formulations blend varied from 0.54 gm/cc to 0.59 gm/cc.

Carr's consolidation index: The result of Carr's consolidation index or compressibility index (%) for the entire formulation blend ranged from 17.32% to 23.10%

Hausner's ratio: Hausner's ratio of entire formulations showed between 1.18 to 1.20.

Result of Post-compression Parameters for tablet prepared by direct compression:

Hardness: The hardness of the tablet prepared by method was determined by Monsanto Hardness tester and found to be within the range of 2.5 kg/cm² to 3.2 kg/cm².

Friability Test: The friability was found in all designed formulations in range 0.55% to 0.85% to be well within the approved range (<1%).

Weight variation test: The weight variation was found in all designed formulation in the range 196 to 205 mg.

Thickness: The mean thickness was almost uniform in all the formulation and values ranged from 4.20 mm to 4.85 mm.

Disintegration time: The *in-vitro* disintegration time of fast dissolving tablets were prepared by direct compression method, were found to be in the range of 40 to 60 sec.

Wetting time: The wetting time of Levosalbutamol sulphate tablets prepared by direct compression method were found to be in range of 38 to 50 sec.

Drug content: The percentage drug content of the tablet was found to be in range between 95.18 to 99.1%.

CONCLUSION

In present study, oral bioavailability of LS is around 40% this study results revealed that it is possible technique to enhance dissolution rate by using direct compression technique using different concentration as superdisintegrants three types of superdisintegrants in different concentration differed in their ability to disintegrate the Levosalbutamol Sulphate tablets.

The flow properties of excipients and drug were good. The tablets prepared were found to be good without any chipping, capping and sticking.

Formulated tablets gives satisfactorily result for various physicochemical evaluation *in vitro* dispersion time, wetting time, water absorption ratio and drug content.

FTIR studies revealed that there is no chemical interaction between Levosalbutamol sulphate and the excipients used in the study.

Formulated tablets gives satisfactorily result for various physicochemical evaluations of tablets like tablet dimension, hardness, friability and weight variation.

From the above study, **F9** formulation was concluded as an optimized formulation due to its better disintegration time and better *in-vitro* dissolution profile. From the above data, it can be concluded that superdisintegrants croscarmillose sodium has better disintegrant property than other disintegrants namely, sodium starch glycolate and crospovidone.

In-vitro drug release of fast dissolving tablets of levosalbutmol sulphate was found to be in following order **F9** > **F3** > **F2** > **F7**. Among all formulation **F9** was to be the best formulation as it released **95.05%** of drug, in 25 minutes. In comparison CCS is greater than CP and SSG.

The faster drug dissolution rate will lead to improve bioavailability, effective therapy, improve patient compliance and satisfies all the criteria as fast dissolving. The result concluded that fast dissolving tablet of levosalbutamol sulphate showing enhanced dissolution will improve bioavailability and effective therapy.

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Table No. 1. Formulation of Levosalbutamol sulphate Fast dissolving tablets by direct compression method

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8	F9
Levosalbutamol sulphate	5	5	5	5	5	5	5	5	5
Croscarmellose sodium	---	---	---	---	---	---	6	12	18
Crospovidone	---	---	---	6	12	18	---	---	---
Sodium Starch glycolate	6	12	18	---	---	---	---	---	---
Lactose	70	70	70	70	70	70	70	70	70
Microcrystalline cellulose	114	108	102	114	108	102	114	108	102
Magnesium Stearate	3	3	3	3	3	3	3	3	3
Aerosil	2	2	2	2	2	2	2	2	2
Total Weight (mg)	200	200	200	200	200	200	200	200	200

All quantities are in milligrams (mg).

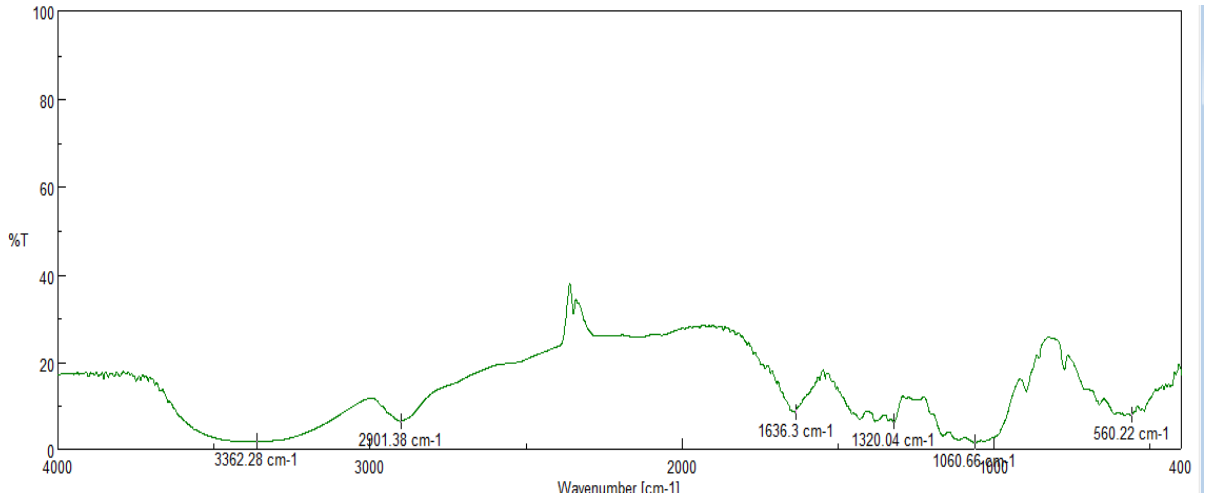

Fig. No 1. IR Spectrum of Pure drug + Excipients

Table No. 2. Pre-compression parameters of direct compression method

Formulation Code	Angle of repose (ɵ)	Bulk density (g/cc)	Tapped density (g/cc)	Hausner's Ratio	Compressibility Index (%)
F1	28.01	0.51	0.62	1.18	16.02
F2	29.00	0.52	0.63	1.19	17.01
F3	28.04	0.50	0.62	1.20	15.0
F4	30.02	0.51	0.60	1.20	16.02
F5	28.00	.052	0.60	1.21	17.01
F6	28.45	0.53	0.61	1.18	13.0
F7	28.85	0.50	0.63	1.20	15.02
F8	29.72	0.51	0.62	1.18	17.00
F9	29.16	0.52	0.62	1.20	15.05

Table No. 3. Post Compression parameter of tablets prepared by direct Method

Formulation Code	Hardness (kg/cm^2)	Friability (%)	Weight variation (mg)	Thickness (mm)	Wetting Time (in sec)	*In-vitro* Dispersion time (in sec)	Drug Content (%)	*In-vitro* Drug Release (%)
F1	2.5	0.58	200	4.25	42	45	95.99	80.60
F2	2.7	0.60	200	4.55	49	49	95.90	89.80
F3	2.8	0.66	201	4.44	43	51	97.69	90.44
F4	3.0	0.64	198	4.54	48	46	95.98	70.48
F5	3.4	0.68	199	4.60	46	44	95.50	72.58
F6	3.5	0.63	198	4.25	48	49	94.71	87.00
F7	3.1	0.69	200	4.65	40	52	94.65	75.33
F8	2.9	0.70	201	4.60	49	57	98.00	88.15
F9	3.0	0.62	199	4.61	42	60	99.95	95.05

Table No. 4. Percent Drug Release Profile

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	00.00	00.00	00.00	00.00	00.00	00.00	00.00	00.00	00.00
2	20.38	20.98	21.75	21.98	15.57	22.67	17.86	20.15	24.05
4	23.58	25.65	29.33	25.41	22.43	28.83	27.27	25.41	28.63
6	26.79	31.83	45.30	29.99	30.45	40.98	34.11	33.84	45.12
8	41.21	43.74	54.94	35.94	37.32	50.60	41.44	40.98	56.57
10	51.97	50.04	66.62	47.39	45.10	59.07	48.31	48.77	67.33
12	61.54	76.94	70.97	52.43	56.32	70.52	57.47	57.01	80.62
14	71.44	80.15	80.35	61.59	62.96	75.78	67.08	68.23	87.03
16	80.60	89.80	90.44	70.48	72.58	87.00	75.33	88.15	95.05

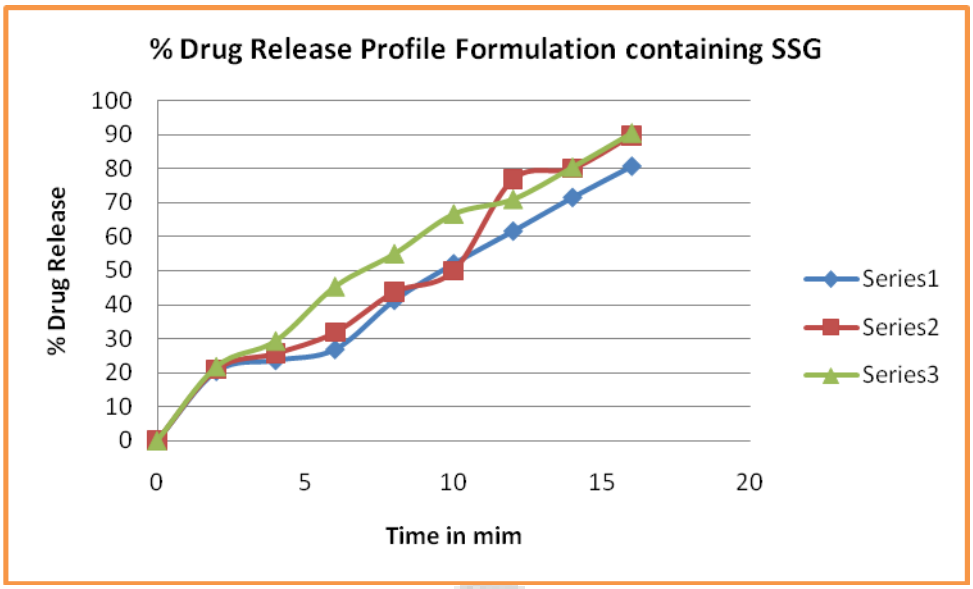

Fig. No 2. Profile of Formulation containing SSG (F1-F3)

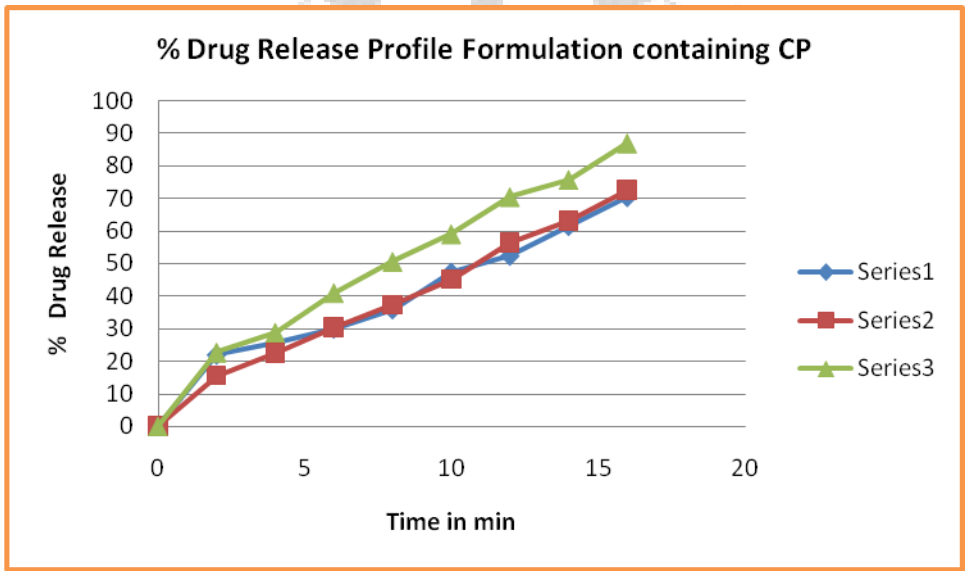

Fig. No. 3. Profile of Formulation containing CP (F4-F6)

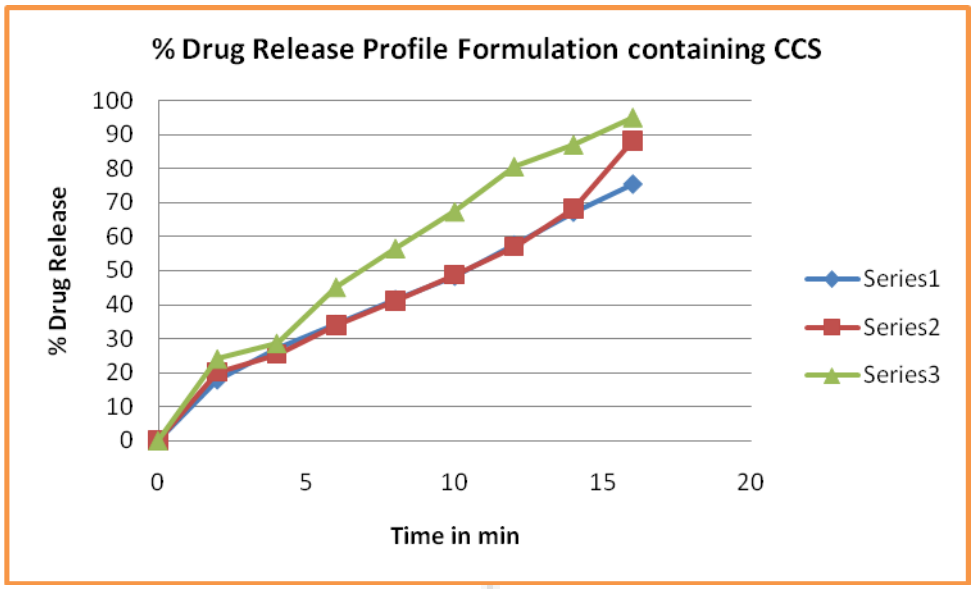

Fig. No. 4. Profile of Formulation containing CCS (F7-F9)

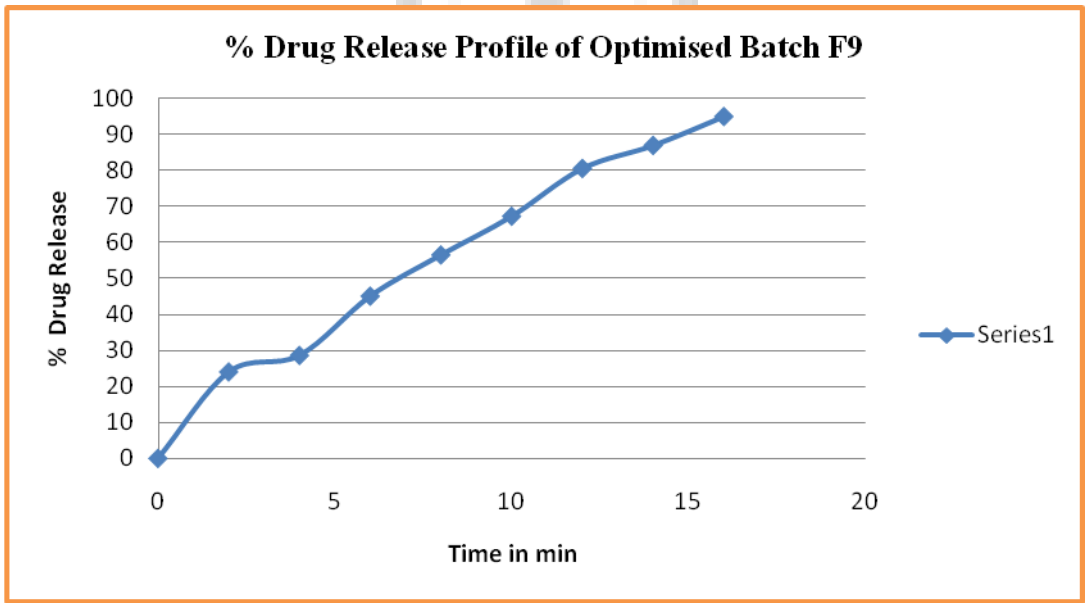

Fig. No. 5. Profile of optimized Formulation Batch F9