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Research Article

DESIGN AND CHARACTERIZATION OF PULSATILE DRUG DELIVERY SYSTEM OF TERBUTALINE SULPHATE

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ABSTRACT

Objective: The present work was aimed to design & characterize an oral dosage form to release Terbutaline sulphate following a programmed time period (pulsed release system).Pulsatile release tablet comprises a drug containing core and pH sensitive polymeric coating capable of delaying drug release and providing gastric resistance.

Methods: The core tablets of terbutaline sulphate were prepared for the treatment of nocturnal asthma .The core tablets were prepared by direct compression method using different disintegrating agents. The cores were coated with pH sensitive polymers (Eudragit S-100, Eudragit L-100) at different coating levels to develop a suitable dosage form which should show minimum drug release in upper regions of gastrointestinal tract (GIT).

Results: Prepared tablets were characterized for various physical parameters such as hardness, thickness, weight variation disintegration test drug content and ***invitro*** drug release characteristics. All the parameters were found to be in the standard range. The dissolution of best formulation F_4S_3, F_7S_3 and $F_{11}S_3$ have shown the lag phase of 5 hrs at 10% coating level and almost complete drug release was achieved after 11hrs . The kinetic study data for best formulation followed zero order kinetics. Stability study of the best formulation indicates no significant difference in release profile after a period of 3 months

Conclusion :From this study it was concluded that a pH dependent pulsatile drug delivery of Terbutaline sulphate for some formulations has a lag time of 5 and 4 hours. Tablet is taken at bed time and expected to release the drug in early morning hours, when the symptoms of asthma are morae prevalent

Keywords: Pulsatile drug delivery, lag time, Nocturnal asthma, Terbutaline sulphate, Eudragit.

INTRODUCTION

Asthma is a disorder that causes the airways of the lungs to swell and narrow, leading to wheezing, shortness of breath, chest tightness, and coughing. The coughing often occurs at night or early in the morning. An inflammation to the airways makes them swollen and verya sensitive. They tend to react strongly to certain inhaled substances. When the airways react, the muscles around them tighten. This narrows the airways, causing less air to flow into the lungs. The swelling also can worsen, making the airways even narrower. Cells in the airways may make more mucus than normal. Mucus is a sticky, thick liquid that can further narrow your airways. This chain reaction can result in asthma symptoms. Symptoms can happen each time the airways are inflamed[1,2].

Oral controlled drug delivery systems represent the most popular form of controlled drug delivery systems for the obvious advantages of oral route of drug administration. Such systems release the drug with constant or variable release rates. These dosage forms offer many advantages, such as nearly constant drug level at the site of action, prevention of peak-valley fluctuations, reduction in dose of drug, reduced dosage frequency, avoidance of side effects, and improved patient compliance However, there are certain conditions for which such a release pattern is not suitable. These conditions demand release of drug after a lag time. In other words, it is required that the drug should not be released at all during the initial phase of dosage form administration. Such a release pattern is known as pulsatile release. A pulsatile drug delivery system is characterized by a lag time that is an interval of no drug release followed by rapid drug release[3,9].

In chronopharmacotherapy (timed drug therapy) drug administration is synchronized with biological rhythms to produce maximal therapeutic effect and minimum harm for the patient. By basing drug delivery on circadian patterns of diseases drug effect can be optimized and side effects can be reduced. If symptoms occur at daytime a conventional dosage form can be administered just prior the symptoms are worsening. If symptoms of a disease became worse during the night or in the early morning the timing of drug administration and nature of the drug delivery system need careful consideration[11,12]. Terbutaline is a selective β2 adrenoceptor agonist. At therapeutic doses it acts on the β-2 Adrenoreceptors of bronchial muscle, with little or no action on the β-2 adrenoreceptors of the heart. It is suitable for the management and prevention of attack of asthma

Mechanism of action

Terbutaline is given as the sulfate for its bronchodilating properties in the management of disorders with reversible airways obstruction such as in asthma and in certain patients with chronic obstructive pulmonary disease. The mechanism of the antiasthmatic action of short acting β-adrenergic receptor agonists is undoubtedly linked to the direct relaxation of airway smooth muscle and consequent bronchodilator. Stimulating these receptors leads to activation of adenyl cyclase, increase in cellular cyclic AMP, and consequent reduction of muscle tone. β2-adrenergic receptors agonists have also been shown to increase the conductance of potassium channels in airway muscle cells leading to membrane hyperpolarisation and relaxation. This occurs, in part, by mechanism independent of adenylyl cyclase activity and cyclic AMP production[10].

MATERIALS AND METHODS

Materials

Terbutaline sulphate was a gift sample from Shimoga Chemical, Sangali. EudragitS-100, EudragitL-100,From Evonik, polymer pvt Ltd., Mumbai Croscarmellose sodium, crospovidone, and sodium starch glycolate from Wallace Pharma Pvt. Ltd. Goa . All other reagents used were of analytical grade.

Methods

Preformulation study

Calibration of Terbutaline sulphate

A stock solution of Terbutaline sulphate is prepared by dissolving 100 mg drug in 100 ml of pH1.2,PH 6.8,and pH 7.4 phosphate buffer. From this stock solution, suitable dilutions were prepared using the same solvent in the range of 2 to 12µg/ml. The λ max of the drug was determined by scanning one of the dilutions between 400 and 200 nm using a UV-visible spectrophotometer (simadzu-1800).And it was found to be 276nm. The absorbance of all the other solutions is measured in 0.1 N HCl and phosphate buffer PH 6.8. Standard curve between concentration and absorbance was plotted and intercept and slope values were noted[13,14].

Preparation of core tablet:

Tablets of terbutaline sulphate were made by direct compression method. All ingredients were weighed accurately and blended homogeneously for 15 minutes by trituration using glass mortar and pestle. Microcrystalline cellulose was used as direct compressing agent. Crospovidone, Croscarmellose Sodium and Sodium Starch Glycolate were used as disintegrating agents. Magnesium stearate and Talc were used as lubricants. Tablets were compressed in Minipress Tablet Compression Machine using 10 mm round concave punches. (Proton Engineeer, Ltd., Ahmadabad, India).

Preparation of coating:

Coating was made using different pH sensitive polymers like EudragitS-100 and Eudragit L-100.

Drug - Polymer Compatibility Studies:

A successful formulation of a stable and effective solid dosage form depends on careful selection of excipient that are added to facilitate administration, promote the consistent release and bioavailability of the drug and protect it from degradation. If the excipient are new and not been used in formulation containing the active substance, the compatibility studies are of paramount importance. Compatibility of Terbutaline sulphate with the respective polymers that is Eudragit -S100, Eudragit L-100, and super disintegrants was established by Infrared Absorption Spectral Analysis (FTIR)[15].

Table 1: List of Ingredients in Formulation

INGREDIENTS (mg) /Formulation	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Terbutaline sulphate	8	8	8	8	8	8	8	8	8	8	8	8
Croscarmellose sodium	1	2	3	4	-	-	-	-	-	-	-	-
Crospovidone	-	-	-	-	3	4	5	6	-	-	-	-
Sodium starch glycolate(SSG)	-	-	-	-	-	-	-	-	2	3	4	5
Starch	20	20	20	20	20	20	20	20	20	20	20	20
Microcrystalline cellulose	167	166	165	164	165	164	163	162	166	165	164	163
Talc	2	2	2	2	2	2	2		2	2	2	2
Magnesium stearate	2	2	2	2	2	2	2	2	2	2	2	2
TOTAL WT.	200	200	200	200	200	200	200	200	200	200	200	200

EVALUATION OF CORE TABLETS:

Hardness

Tablets were evaluated for their hardness using Monsanto hardness tester. The experiment was performed in triplicate and average value was calculated.

Weight variation

Ten tablets from each formulation were weighed using an electronic digital balance (Shimadzu) and the average weight was calculated. The experiment was performed in triplicate and average value was calculated.

Thickness

Tablets were evaluated for their thickness using digital Varnier callipers. The experiment was in triplicate and average value was calculated. The experiment was performed in triplicate and average value was calculated[16].

Friability

The friability test was done using Roche's Friabilator. Ten tablets were selected and weighed individually. Then the friability test was carried out at 25 rpm for 4 min. These tablets were then again weighed and percentage loss in weight was calculated. The experiment was performed in triplicate and average value was calculated.

$$\% \text{ of Loss} = \frac{\text{Initial Weight} - \text{Final Weight}}{\text{Initial Weight}} \text{ X } 100$$

***In vitro* Disintegration test for tablet:**

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[11,12].

Place one tablet in each of the 6 tubes of the basket. Add a disc to each tube and run the apparatus using pH 6.8 SIF (simulated intestinal fluid) and pH 7.4 SCF (simulated colonic fluid) maintained at $37^0 \pm 2^0$C as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in the pH 6.8 maintained at $37^0 \pm 2^0$C. The time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded. The experiment was carried out in triplicate[17].

Dissolution Studies of the Coated Tablets: Drug release studies of coated tablets were carried out using USP XXIII dissolution test apparatus I. Initially tablets were placed in 900 ml of 0.1 N HCl for 2 hours maintained at 37 ± 0.5^0C, 75 rpm followed by pH 6.8 phosphate buffer for 3 hours and pH 7.4 for 5 hours. Aliquots of predetermined quantity were collected manually at definite time intervals replacing with fresh buffer to maintain sink condition and analysed for drug content using a UV-visible spectrophotometer at λ max of 276 nm[18].

RESULTS AND DISCUSSION

Identification of Drug: The IR spectrum obtained of pure drug shows characteristic absorption peaks as given below and depicted in (Figure 4 to 9).

Calibration of Terbutaline sulphate –

Calibration of Terbutaline sulphate was carried out in three pH ie 0.1NHcl, 6.8 pH,& 7.4pH the graph was showed from (Figure 1 to 3).

Drug - excipient Compatibility Studies:

Compatibility studies of pure drug Terbutaline sulphate with polymers were carried out prior to the preparation of tablets. I.R spectra of pure drug Terbutaline sulphate and that with polymer were obtained, which are depicted in (Figure Nos.4 to 9). All the characteristic peaks of Terbutaline sulphate were present in spectra at respective wavelengths, indicates compatibility between drug and Polymer. It shows that there was no significant change in the chemical integrity of the drug.

Precompressional parameters:

Blend of formulation was subjected for precompressional evaluations such as angle of repose, bulk and tapped density, compressibility index and Hausner's Ratio.Results of the pre-compression parameters performed on the blend for batch F_1 to F_{12} are tabulated in (Table No.2).

Angle of repose values for batches from F_1 to F_{12} were found to be in the range 28.94±0.85, to 30.64±0.20 . Compressibility index was found to 13.38±1.17, to 15.31±1.29, for batch F1, to F12 The results of Hausner's ratios were found to be in the range,1.15±0.013, to 1.18±0.018, for batch F1, to F12 . The results of angle of repose (<30) indicate good flow properties of the powder based on (Table No. 2). This was further supported by lower compressibility index values. Generally, compressibility index values up to 15% results in good to excellent flow properties.

Post-compressional parameters:

The formulated tablets were subjected for evaluation according to official specifications for shape, thickness, hardness, friability, weight variation, drug content and *in vitro* disintegration time.

Physical appearance:

Tablets were white in color, having concave surface with circular shape.

Uniformity of thickness:

The results of thickness for tablets are tabulated in (Table No.3). The mean thickness of tablets (n=3) of batches F1to F12 were found to be in the range of 3.96±0.11 to 4.22±0.09,. The standard deviation values indicated that all the formulations were within the range.

Weight variation test:

The weight variations of all formulations are tabulated in (Table No.3). All the tablets passed the weight variation test, i.e., average percentage weight variation was found within the pharmacopoeial limits of ±7.5%.

Hardness test:

Hardness or crushing strength of uncoated tablets for all the formulations was found to be in the range 4.2 to 4.9 kg/cm^2 and for coated tablets the hardness was found to be in the range 5.0 to 5.4 kg/cm^2 which is tabulated in Table No.3. The low standard deviation values indicated that the hardness of all the formulations was almost uniform and the tablets possess good mechanical strength with sufficient hardness.

Friability test:

Friability values for batch F1 to F12 were found to be in the range 0.200±0.09, to 0.338±0.05, respectively. The obtained results were found to be well within the approved range (<1%) in all the prepared formulations. That indicated tablets possess good mechanical strength. The results are tabulated in Table No.3.

Drug Content:

The formulated tablets were assayed in triplicate. The average value and standard deviations were calculated. The tablets of batch F1, to F12 showed drug content in the range 93.22±0.42 to 98.5±0.72, The results are tabulated in Table No.3.

The results were within the limit (90% to 110%) specified in pharmacopoeia. The cumulative percentage drug released from each tablet in the *in vitro* release studies was based on the average drug content present in the tablet.

***In vitro* Disintegration time:**

In vitro disintegration for batch F1 to F12 was found to be in the range as follows in pH 1.2 it was 2.53±0.05 to 8.83±0.25 in pH 6.8 it was 2.13±0.02 to 4.39±0.01 and in 7.4 pH it was 2.27±0.07 to 5.09±0.01 min. The results are tabulated in (Table No.4). Batch F4, F7 & F11 was showed least disintegration time. Hence further study was planned using formulation F4, F7 & F11 as core tablet.

***In vitro* drug release studies:**

The *in vitro* drug release of all formulation before coating (F_1 to F_{12}) was carried out in pH1.2, pH 6.8, & pH 7.4

The selected formulation F_4, F_7, & F_{11} were coated with pH sensitive polymers (Eudragit S-100, Eudragit L-100) showed small amount of drug release in the first two hrs in the gastric environment.

Formulation coated with Eudragit S 100 as pH sensitive polymer:

- Selected Formulation were Coated with Eudragit S-100 of different concentration and the formulation was named as F_4S_1, F_4S_2, F_4S_3,F_7S_1, F_7S_2, F_7S_3, & $F_{11}S_1$, $F_{11}S_2$,$F_{11}S_3$
- At 2.5% Coating (F_4S_1, F_7S_1, $F_{11}S_1$,) there was no lag phase was observed & within 5hrs complete drug release was seen ie.87.46%, 89.88%, & 82.49% respectively.
- At 5% coating concentration the formulations F_4S_2, F_7S_2, $F_{11}S_2$. The complete drug release was observed 91.35%, 93.22%, & 85.67% respectively after 10hrs and around 8 to 10% drug was released within 3hrs. This Concentration is not enough to elicit pharmacological action (concentration less than therapeutic range).
- At 10% coating concentration i.e. Formulation F_4S_3, F_7S_3, $F_{11}S_3$.the complete drug released was observed within 11 hrs i.e. 95.24%, 93.00%, 89.29% respectively. Around 8 to 14 % drug was released within 5hrs. This concentration is not enough to show pharmacological action (concentration is sub therapeutic range).
- **Formulation coated with Eudragit L 100 as pH sensitive polymer:**
- Selected formulation were coated with Eudragit S-100 of different concentration and the formulation was named as F_4L_1, F_4L_2, F_4L_3, F_7L_1, F_7L_2, F_7L_3, & $F_{11}L_1$, $F_{11}L_2$, $F_{11}L_3$
- At 2.5% coating (F_4L_1, F_7L_1, $F_{11}L_1$,) there was no lag phase was observed & within 5hrs complete drug release was seen i.e. 84.62%, 87.13%, & 81.57% respectively.
- At 5% coating concentration the formulations F_4L_2, F_7L_2, $F_{11}L_2$.The complete drug release was observed 91.43%,85.02%,83.65% respectively after 10hrs and around 9 to 15% drug was released within 2hrs.This Concentration is not enough to elicit pharmacological action (concentration less than therapeutic range).
- At 10% coating concentration i.e. Formulation F_4L_3, F_7L_3, $F_{11}L_3$.the complete drug released was observed within 11 hrs i.e. 91.43%, 85.02%,& 83.65% respectively.& Around 13 to 18 % drug was released within 4hrs. This Concentration is not enough to show pharmacological action (concentration is sub therapeutic range).

The results of in vitro drug release studies indicated that less amount of drug was released in first few hours for all the formulation. This course of drug released was in sub therapeutic range, this release was unavoided as loosely adhered or superfacial drug may enter in the dissolution fluid.

CONCLUSION

The aim of this study was to explore the feasibility of time and pH dependent colon specific, pulsatile drug delivery system of Terbutaline sulphate to treat Asthma. A prompt attempt was made to develop pulsatile release tablets using pH sensitive polymers (Eudragit S100, Eudragit L100) and evaluated for *In vitro* characterization. From the results obtained in the present research work, it can be concluded that-

- From IR, Studies and physical observation it was observed that there was no significant Drug- Excipient interaction. So it can be concluded that drug and other excipients are compatible with each other.
- Based on disintegration time, Crospovidone was selected as a disintegrant in the formulation of core tablets and found satisfactory in terms of hardness, thickness, weight variation, *In vitro* disintegration, and content uniformity.
- To achieve colonic delivery, core tablets were coated at different coating level of pH sensitive polymers and evaluated for lag time and *in vitro* drug release.
- The lag time is directly proportional to the coating level applied of all the polymer solutions
- The release profiles of drug from all formulations followed zero order and first order kinetics.
- At the coating level of 10% Eudragit S 100 (F_4S_3, F_7S_3, and $F_{11}S_3$) provided the most appropriate polymer for pulsatile drug delivery.
- Difference in drug release was observed in different pH and different coating level
- Stability studies proved that the formulation was quite stable.

From this study it was concluded that a pH dependent pulsatile drug delivery of Terbutaline sulphate for some formulations has a lag time of 5 and 4 hours. Tablet is taken at bed time and expected to release the drug in early morning hours, when the symptoms of asthma are more prevalent

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Chan WA, Boswell CD, Zhang Z. Comparison of the release profile of a water soluble drug carried by Eudragit-coated capsules in different *in-vitro* dissolution liquids. Powder Technology 2001; 119: 2632.

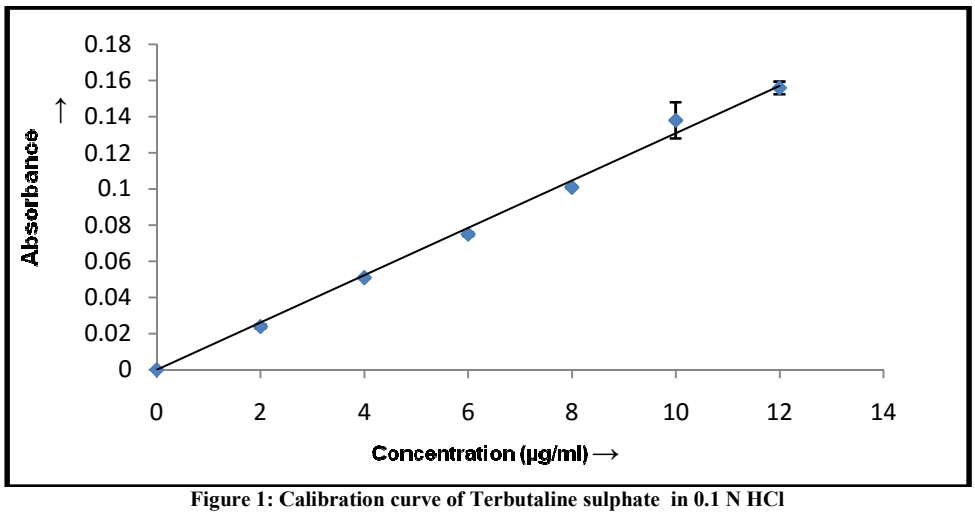

Figure 1: Calibration curve of Terbutaline sulphate in 0.1 N HCl

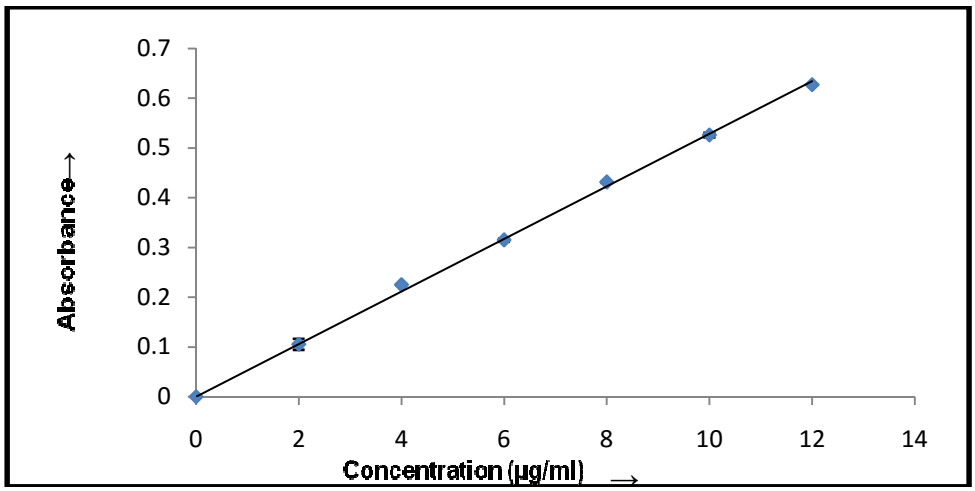

Figure 2: Calibration curve of Terbutaline sulphate in pH 6.8 phosphate buffer

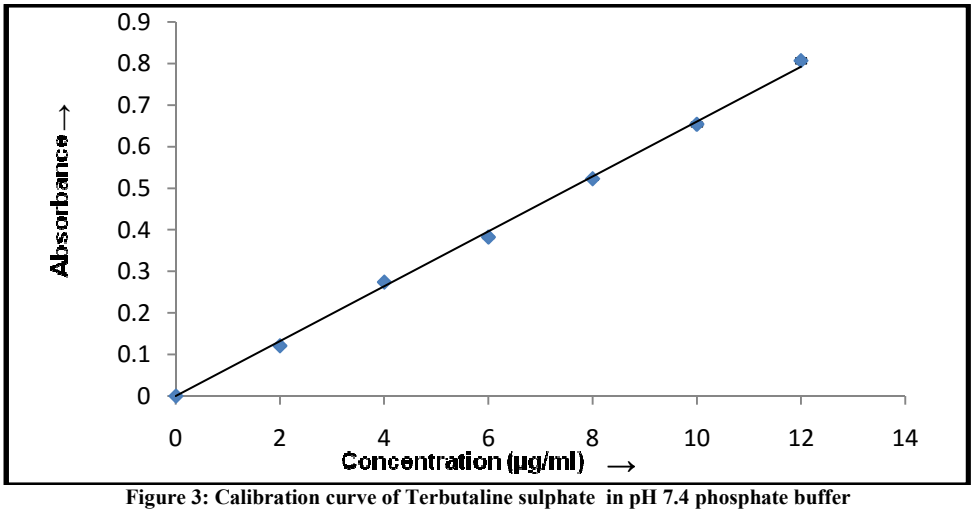

Figure 3: Calibration curve of Terbutaline sulphate in pH 7.4 phosphate buffer

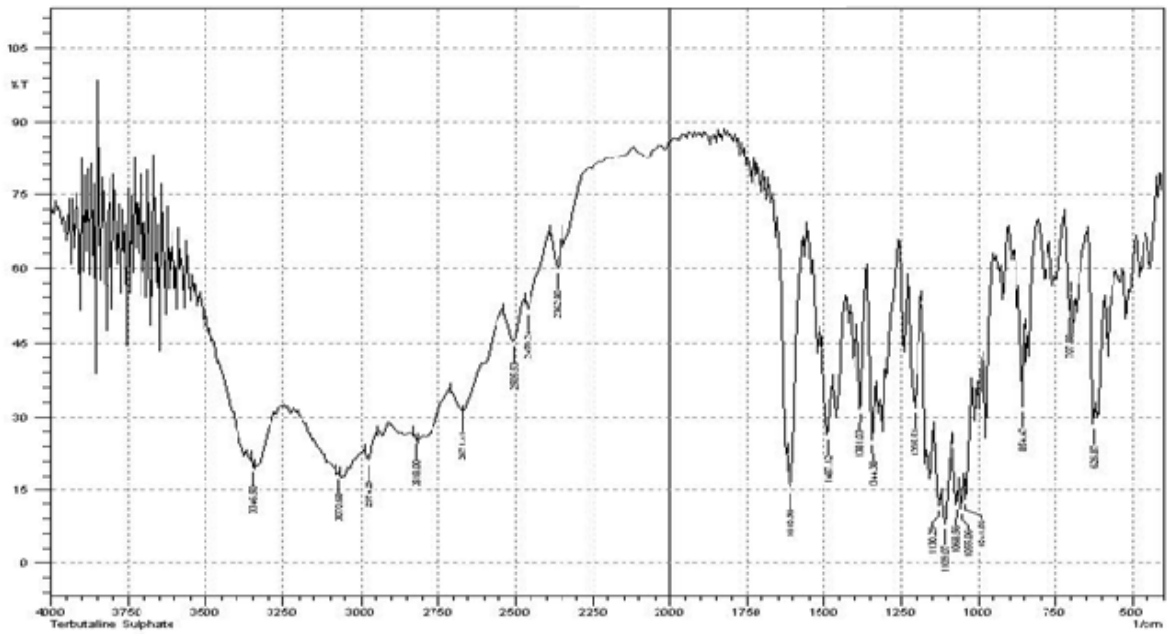

Figure 4: FT-IR Spectra of Terbutaline sulphate

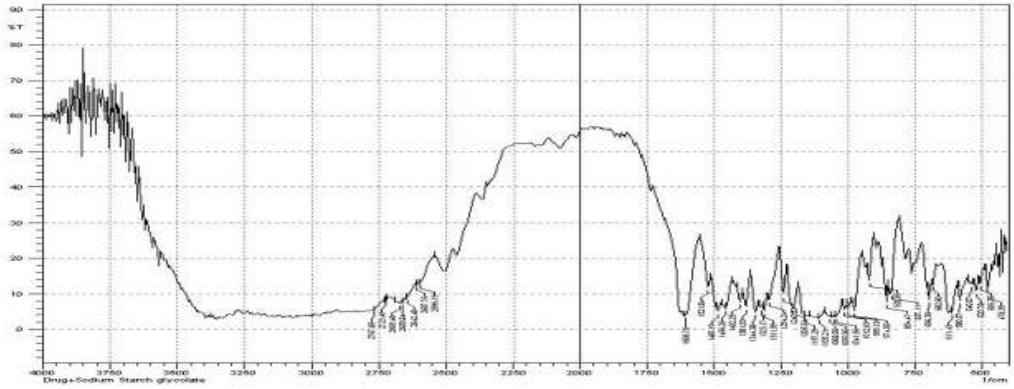

Figure 5: FT-IR Spectra of Terbutaline sulphate and Sodium starch glycolate

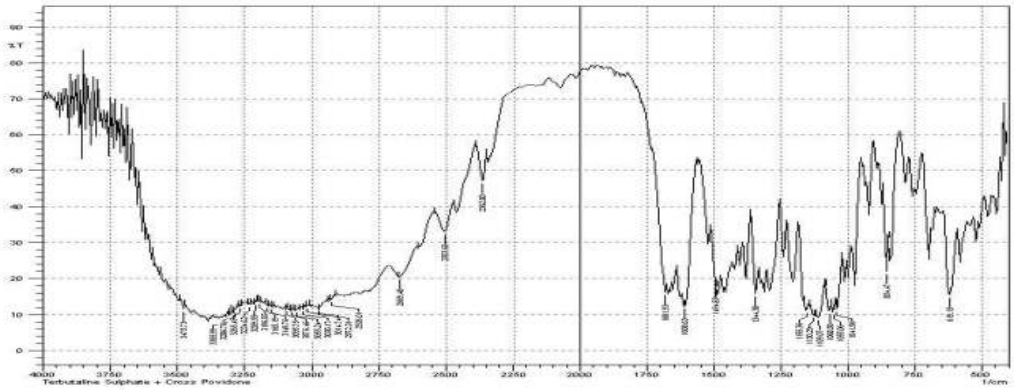

Figure 6: FT-IR Spectra of Terbutaline sulphate and Cross Povidon

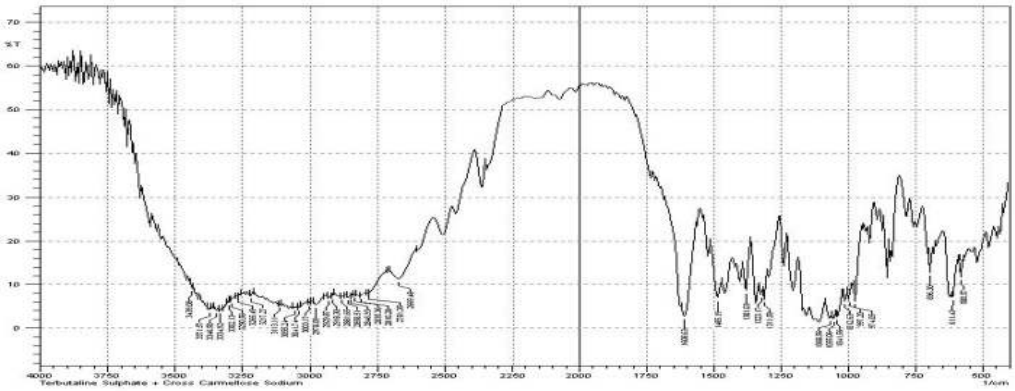

Figure 7: FT-IR Spectra of Terbutaline sulphate and Cross carmellose Sodium

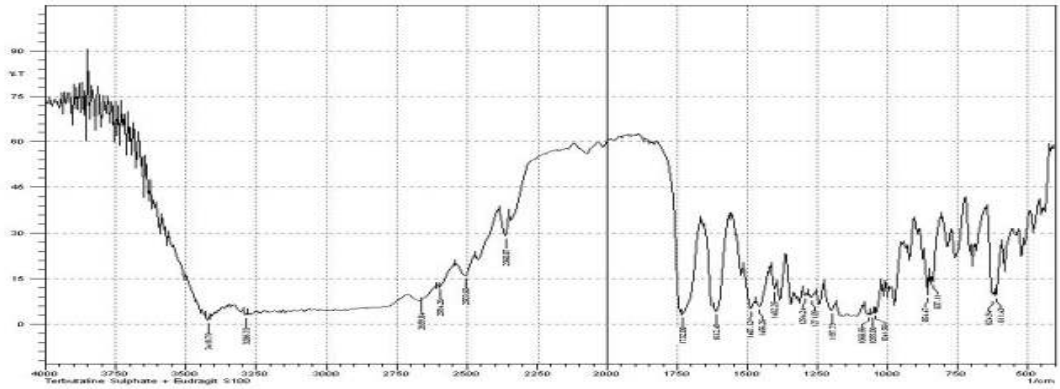

Figure 8: FT-IR Spectra of Terbutaline sulphate and Eudragit S-100

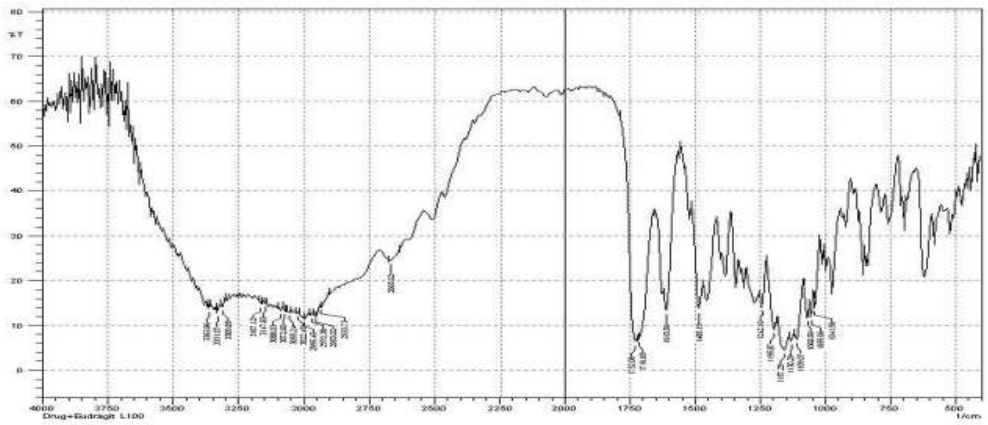

Figure 9: FT-IR Spectra of Terbutaline sulphate and Eudragit L-100

Characteristic	Frequency (Cm-1)
O-H stretch	3330
Aromatic C-H stretch	3050
Secondary amine salt stretch	2720-2900,2660,2500
Aromatic ring stretch	1610,1485

Table 2: Pre-compression evaluation of the blend

Batch	Bulk Density (gm/cc)	Tapped density (gm/cc)	Carr's Index	Hausner's Ratio	Angle of Repose
F_1	0.2396±0.0023	0.279±0.0040	14.29±0.41	1.16±0.005	29.99±0.77
F_2	0.2376±0.0023	0.275±0.0034	13.57±0.98	1.15±0.013	28.94±0.85
F_3	0.2363±0.0028	0.272±0.0017	13.43±0.91	1.15±0.012	29.71±0.30
F_4	0.2346±0.0023	0.273±0.0034	14.03±0.24	1.16±0.003	29.84±0.79
F_5	0.2396±0.0028	0.281±0.0040	14.90±1.13	1.17±0.015	29.23±1.27
F_6	0.2393±0.0028	0.276±0.0040	13.38±1.17	1.15±0.015	29.84±0.51
F_7	0.2383±0.0028	0.275±0.0005	13.43±0.97	1.15±0.013	29.82±0.90
F_8	0.2366±.0023	0.276±0.0034	14.24±0.24	1.16±0.003	29.67±0.83
F_9	0.2336±0.0028	0.275±0.0040	15.22±1.15	1.17±0.016	28.99±0.91
F_{10}	0.2373±0.0023	0.280±0.0065	15.31±1.29	1.18±0.018	29.85±0.57
F_{11}	0.2346±0.0023	0.271±0.0040	13.50±1.13	1.15±0.015	30.64±0.20
F_{12}	0.2343±0.0028	0.272±0.0034	13.84±0.03	1.16±0.0004	29.37±0.31

Table 3: Post-compression evaluation of the prepared Core Tablets

Batch	Uniformity of thickness (mm)	Weight variation of uncoated tablet (mg)	Weight variation of coated tablet (mg)	Hardness of Uncoated Tablet (kg/cm^2)	Hardness of Coated Tablet (kg/cm^2)	Friability (%)	% Drug Content
F_1	4.15±0.13	197.8±2.16	219±2.0	4.2±0.2	5.4±0.1	0.231±0.11	94.49±0.42
F_2	4.11±0.13	201.2±1.92	220.2±1.64	4.5±0.3	5.0±0.2	0.236±0.05	94.06±0.42
F_3	4.04±0.16	200±1.58	219.8±3.03	4.7±0.2	5.2±0.2	0.303±0.17	93.22±0.42
F_4	4.06±0.08	200.4±2.79	221.2±3.49	4.5±0.3	5.2±0.2	0.267±0.05	94.12±0.81
F_5	3.96±0.11	198±2.0	218.8±1.92	4.9±0.2	5.1±0.3	0.332±0.15	95.33±0.42
F_6	4.01±0.15	201.4±2.30	220.8±1.78	4.5±0.3	5.2±0.3	0.200±0.09	95.05±0.88
F_7	4.20±0.09	198.4±1.81	219±1.58	4.6±0.1	5.4±0.3	0.338±0.05	98.5±0.72
F_8	3.97±0.06	199±1.87	218.6±2.07	4.9±0.1	5.0±0.3	0.302±0.10	94.35±0.64
F_9	4.22±0.09	201.6±2.88	220.6±3.36	4.2±0.2	5.1±0.05	0.335±0.05	95.19±0.64
F_{10}	4.15±0.13	198.8±2.16	218±2.0	4.3±0.3	5.3±0.12	0.267±0.15	93.78±0.64
F_{11}	4.11±0.13	205.2±1.92	220±1.64	4.8±0.4	5.2±0.3	0.201±0.10	94.62±0.81
F_{12}	4.04±0.16	203±1.58	218±3.03	4.9±0.4	5.4±0.2	0.266±0.15	94.20±1.29

Table 4: Disintegration Time study of core tablet

Batch	Disintegration Time (min)		
	1.2pH	6.8pH	7.4pH
F_1	7.72±0.375	4.39±0.01	5.08±0.015
F_2	6.6±0.2	3.36±0.04	4.32±0.025
F_3	4.87±0.26	2.49±0.015	3.55±0.035
F_4	4.19±0.005	2.42±0.07	2.21±0.014
F_5	4.13±0.03	2.27±0.33	3.25±0.07
F_6	4.60±0.15	2.54±0.04	3.13±0.015
F_7	2.53±0.05	2.13±0.02	2.27±0.07
F_8	3.17±0.025	2.49±0.06	3.08±0.035
F_9	8.97±0.61	3.4±0.02	5.09±0.01
F_{10}	8.17±0.15	4.27±1.85	3.50±0.015
F_{11}	7.66±0.35	3.12±0.03	3.38±5.43
F_{12}	8.83±0.25	4.14±0.025	4.09±0.015

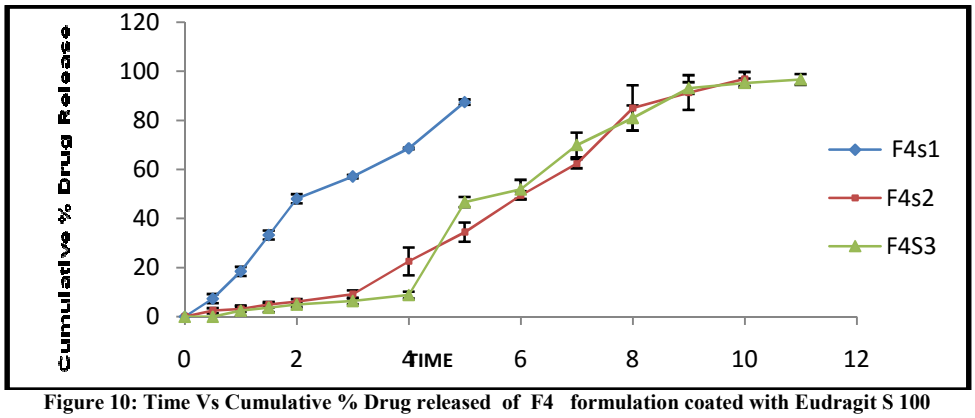

Figure 10: Time Vs Cumulative % Drug released of F4 formulation coated with Eudragit S 100

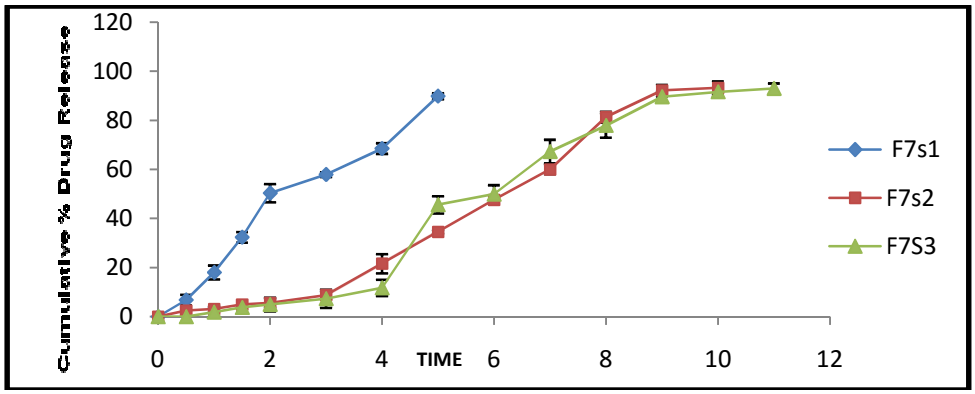

Figure 11: Time Vs cumulative % drug released of F_7 formulation coated with Eudragit S 10

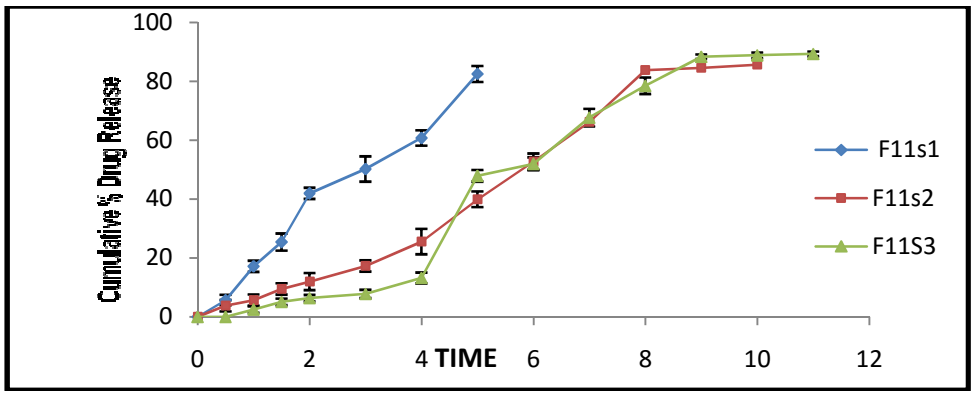

Figure No *12* Time Vs cumulative % drug released of formulations F_{11} coated with Eudragit S 100

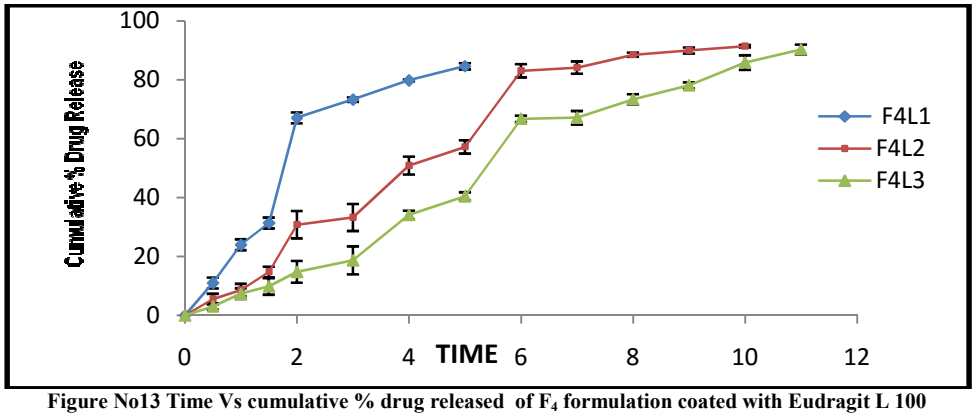

Figure No13 Time Vs cumulative % drug released of F_4 formulation coated with Eudragit L 100

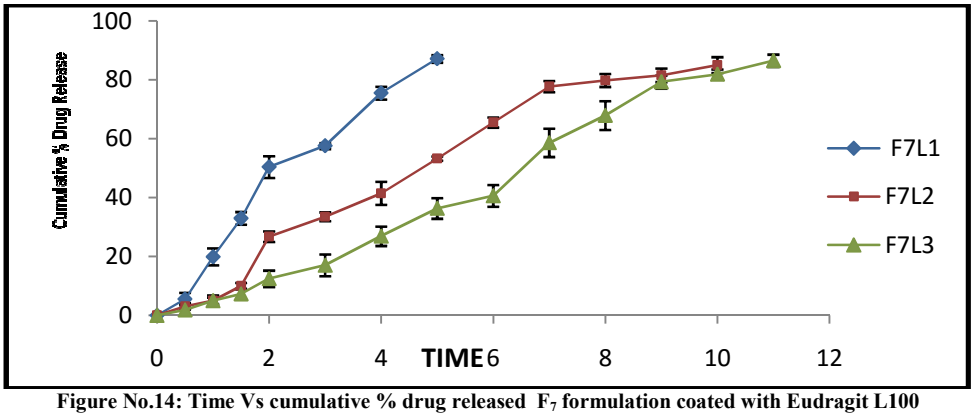

Figure No.14: Time Vs cumulative % drug released F_7 formulation coated with Eudragit L100

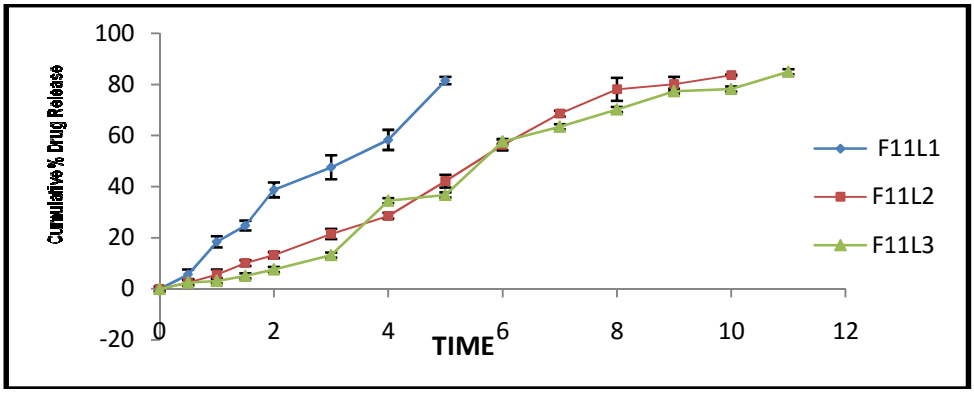

Figure No.15 Time Vs cumulative % drug released of F_{11} formulation coated with Eudragit L 100

Table 5: Release kinetics data of all the formulations coated with Eudragit S 100

Formulation code	% CDR	Zero order	First order	Higuchi	Korsmeyer-peppas	
		R^2	R^2	R^2	n	R^2
F_4S_1	87.46	0.972	0.940	0.933	1.81	0.614
F_4S_2	91.35	0.958	0.885	0.847	1.77	0.970
F_4S_3	95.24	0.944	0.758	0.827	1.91	0.953
F_7S_1	89.88	0.967	0.912	0.923	1.27	0.809
F_7S_2	93.22	0.957	0.842	0.815	1.62	0.929
F_7S_3	93.00	0.951	0.915	0.838	1.90	0.962
$F_{11}S_1$	82.49	0.980	0.929	0.914	1.84	0.648
$F_{11}S_2$	85.67	0.973	0.914	0.867	1.53	0.915
$F_{11}S_3$	89.29	0.948	0.930	0.846	1.84	0.956

Table 6: Release kinetics data of all the formulations coated with Eudragit L 100

Formulation code	% CDR	Zero order	First order	Higuchi	Korsmeyer-peppas	
		R^2	R^2	R^2	n	R^2
F_4L_1	84.62	0.878	0.932	0.905	1.749	0.558
F_4L_2	91.43	0.946	0.962	0.931	1.426	0.813
F_4L_3	90.31	0.974	0.956	0.913	1.469	0.894
F_7L_1	87.13	0.968	0.975	0.931	1.324	0.762
F_7L_2	85.02	0.963	0.981	0.936	1.336	0.920
F_7L_3	86.47	0.986	0.937	0.894	1.40	0.962
$F_{11}L_1$	81.57	0.983	0.917	0.971	1.80	0.637
$F_{11}L_2$	83.65	0.983	0.959	0.898	1.56	0.907
$F_{11}L_3$	85.00	0.971	0.971	0.896	1.66	0.957

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