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Formulation and Evaluation of Floating Microbeads of Terbutaline Sulfate

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A B S T R A C T

The objective of the present study is formulation and evaluation of Terbutaline sulfate microbeads to improve drug oral bioavailability. Terbutaline sulfate microbeads were prepared by ionotropic external gelatation technique using sodium alginate, locust bean gum in different ratios, various formulations were prepared with these polymers. The Terbutaline sulfate microbeads were characterized with respect to IR, DSC, XRD, swelling studies, angle of repose, bulk density, tapped density, Carr's index Hausner's ratio, and stability studies and all the results indicated that the microbeads were having good flow nature. By the invitro dissolution studies it was concluded that the formulation (F4) was showing better result of 98.97% drug release. FTIR and DSC studies showed that there is no incompatability between the drug and polymers. The data was subjected to Zero order, first order, Higuchi, Korsmeyer and Peppas diffusion model and the optimized formulation followed peppas order of release kinetics.

Keywords: Terbutaline sulphate, Floating microbeads.

A R T I C L E I N F O

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1. Introduction

Asthma is a chronic disease involving the airways in the lungs. These airways, or bronchial tubes, allow air to come in and out of the lungs. For many asthma sufferers, timing of these symptoms is closely related to physical activity. And, some otherwise healthy people can develop asthma symptoms only when exercising. This is called exercise-induced bronchoconstriction (EIB), or exercise-induced asthma (EIA). Staying active is an important way to stay

healthy, so asthma shouldn't keep you on the sidelines. Your physician can develop a management plan to keep your symptoms under control before, during and after physical activity. People with a family history of allergies or asthma are more prone to developing asthma. Many people with asthma also have allergies. This is called allergic asthma. Childhood asthma impacts millions of children and their families. In fact, the majority of children who develop asthma do so before the age of five. There is no cure for asthma, but once it is properly diagnosed and a treatment plan is in place you will be able to manage your condition, and your quality of life will improve.

Asthma Symptoms

According to the leading experts in asthma, the symptoms of asthma and best treatment for you or your child may be quite different than for someone else with asthma. The most common symptom is wheezing. This is a scratchy or whistling sound when you breathe. Other symptoms include:

- Shortness of breath
- Chest tightness or pain
- Chronic coughing
- Trouble sleeping due to coughing or wheezing

Asthma symptoms, also called asthma flare-ups or asthma attacks, are often caused by allergies and exposure to allergens such as pet dander, dust mites, pollen or mold. Non-allergic triggers include smoke, pollution or cold air or changes in weather. Asthma symptoms may be worse during exercise, when you have a cold or during times of high stress. Children with asthma may show the same symptoms as adults with asthma: coughing, wheezing and shortness of breath. In some children chronic cough may be the only symptom. one or more of these common symptoms, make an appointment with an allergist immunologist:

Patterns in asthma symptoms are important and can help your doctor make a diagnosis. Pay attention to when symptoms occur:

- At night or early morning
- During or after exercise
- During certain seasons
- After laughing or crying
- When exposed to common asthma triggers

Floating Drug Delivery System

Floating drug delivery system is also known as hydrodynamically balanced system (HBS). While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration.

Approaches to design floating drug delivery system

Practical approaches in designing FDDS

The concept of FDDS was first described in the literature as early as 1968, when Davis (1968) disclosed a method to overcome the difficulty experienced by some persons of gagging or choking after swallowing medicinal pills. The author suggested that such difficulty could be overcome by providing pill having a density of less than 1.0g/cm3, so that pill will float on water surface. Since then several approaches have been used to develop an ideal floating drug delivery system.

Pharmaceutical Microbeads

Microbeads are uniform polymer particles, typically 0.5 to 1000 micrometres in diameter. Bio-reactive molecules can be adsorbed or coupled to their surface, and used to separate biological materials such as cells, proteins, or nucleic acids. Sodium alginate has been used as a matrix material to achieve controlled-release drug delivery due to its hydrogel-forming properties. Alginate salts are known to form a reticulated structure when in contact with calcium ions and their characteristic has been used to produce sustained release particulate systems for a variety of drugs. The ability of alginate sodium salt, to rapidly form viscous solutions and gels on contact with aqueous media has been exploited by the pharmaceutical industry in sodium alginate's wide application as a carrier in hydrophilic matrix controlled release oral dosage forms. Ionotropic gelation is based on the ability of polyelectrolytes to cross link in the presence of counter ions to form hydrogels. Microencapsulation by ionotropic gelation is one of the widely used method for preparation of calcium-alginate microspheres/beads which has ability to form gels reaction with calcium salts. Recently the use of calcium-alginate gel beads as a vehicle for controlled drug delivery system has attracted considerable attention because of their property of reswelling which is susceptible to environment pH. Consequently, acid sensitive drugs incorporated into beads would be protected from gastric juice. However, major disadvantages of alginate beads are their fast disintegration in simulated intestinal fluid and high porosity, which result in rapid drug release.

2. Materials and Methods

This chapter describes materials used, preformulation studies, methods of formulations and experimental techniques adopted for the development of different floating microbeads of Terbutaline Sulfate.

Materials

Terbutaline Sulfate was obtained as a gift sample from Micro labs limited, Bengaluru Karnataka. The purity assays of thesedrug, as given in the certificate of analysis, were about 99% to 101%. All the mentioned excipients are USP/NF, EP, JP grade procured as a gift samples from respective manufacturer suppliers and other reagents, solvents were used of analytical grade satisfying pharmacopoeias specifications.

Experimental methods

Preformulation studies

In the present study, several preformulation parameters such as calibration curve development, solubility of drugs with different solvents and drug-polymer compatibility were evaluated to observe the drugs compatible with other excipients in the manufacturing process.

Development of calibration curve

A stock solution of Terbutaline Sulfate was prepared by dissolving 100mg of pure drug in little quantity of methanol, magnetically stirred at 50 rpm for 30 minutes.

Then the volume was adjusted up to 100 ml with pH 1.2 acidic buffer, pH 6.8 and pH 7.4 phosphate buffers in a 100 ml volumetric flask to obtain the concentration 1000 µg/ml. From the stock solution, prepare different concentration of aliquots which are diluted with respective buffers and subjected to scanning between 200 - 400 nm in a UV-Visible spectrophotometer (Shimadzu 1201, Japan). The absorption maxima of Terbutaline Sulfate were obtained at λ max 275 nm. Accurately measured 10 ml of the above stock solution was further diluted up to 100 ml with corresponding buffers to obtain a working standard solution containing 100µg/ml. The different aliquots of working standard solution were diluted serially with sufficient buffers to obtain the concentration below Beer's range of 2 – 20µg /ml. A calibration curve for Terbutaline Sulfate was obtained by measuring the absorbance at λ max 275 nm. The procedure was performed in triplicate to validate the development of calibration curve. Calibration graphs of Terbutaline Sulfate was plotted by taking concentration on x-axis and absorbance on y-axis to obtain a straight line. The certain parameters such as the slope, intercept, coefficient of correlation, standard deviation were calculated.

Saturation solubility studies:

The saturation solubility of Terutaline sulfate was determined in the following: double distilled water and 0.1N hydrochloric acid containing 0.5, 1.0, 1.5 and 2% w/v of sodium lauryl sulfate [SLS] and 1% w/v of calcium chloride, pH 4.5 acetate buffer, pH 6.8 and pH7.4 phosphate buffers at 37^0C. An excess quantity of Terbutaline Sulfate was added to 100 ml of dissolution medium in a conical flask and agitated continuously at room temperature for 8 hours on a mechanical shaker. The solutions were kept aside for 2 hours until the equilibrium was achieved and then filtered through No-41 Whatman filter paper. The filtrate suitably diluted with respective media and analyzed at λ max 275 nm by UV- Visible spectrophotometer (Shimadzu 1201, Japan). The quantity of Terbutaline Sulfate present in the sample was calculated by using the equation of the standard curve.

Fourier transforms infrared (FTIR) spectra

The drug polymer interactions were studied by using FT-IR spectrophotometer (Shimadzu 1700S). The samples were prepared by adopting KBr pellet technique and scanned from 4000 to 450 cm^{-1} taking air as the reference

Differential scanning calorimetry (DSC): The thermal behavior of Terutaline sulfate in the formulations was performed by using differential scanning calorimetry (Shimadzu, Tokyo, Japan). The samples were heated in sealed aluminum pans under nitrogen flow (30ml / minutes) at a scanning rate of 5 ^{0}C/ minutes from 24±1 to 250^0C. Empty aluminum pan was taken as reference and the heat flow as a function of temperature was measured for the drug and drug -polymer mixture.

X-Ray Powder Diffractometry (XRPD)

The crystalline nature of drug and polymer in the manufacturing process was performed by using Philips X-ray powder diffractometer (model; PW 1710) with copper target. The X-ray diffraction patterns of pure drug and the optimized drug loaded formulations were recorded using the radiation at 30 kv and $25mA^0$, scanning speed at $20/min^{-1}$ and 40 to 400 diffraction angle (2θ) ranges.

Preparation of drug loaded microbeads

The Terbutaline Sulfate microbeads were prepared by ionotropic external gelation technique. Sodium alginate (1-3%) was dissolved in deionized water at a temperature 45^0C using magnetic stirrer. On complete solution, an accurately weighed quantity of Terbutaline Sulfate was added and dispersed uniformly. The dispersion was sonicated for 30 minutes to remove any air bubbles formed during the stirring process. The bubbles free sodium alginate-drug dispersion (50 ml) was added drop wise through a 24-guage hypodermic needle fitted with 10 ml glass- syringe into 50 ml of calcium chloride solution (1-5%w/v) and stirred at 200 rpm for 30 minutes The droplets from the dispersion instantaneously gelled into discrete matrices on contact with the solution of calcium chloride. The drug loaded microbeads were further stirred in the solution of calcium chloride for an additional 0.5 - 2.5 hours. After the specified stirring time and stirring speed the gelled beads were separated by filtration, washed three times with deionized water, finally dried at 80 ^{0}C for 2 hours in a hot air oven. The dried microbeads were immediately preserved in air-tight containers. The batch details of process and formulation variables are given in table below

Process and formulation variables study

Eight batches of Terbutaline Sulfate loaded microbeads were prepared to investigate the effect of certain formulation and process variables, such as drug to polymer ratio, concentration of cross-linking agent, cross-linking time and stirring speed on mean particle size, yield, actual drug content, drug entrapment efficiency and in-vitro drug release. To study the effect of these variables, each time one variable was varied, keeping the others constant.

Evaluation of drug-loaded microbeads [7,8]

Yield of microbeads

The yield of formulated microbeads was evaluated by comparing the practical yield with that of the theoretical yield. The percentage of yield was calculated by using the following formula;

$$\text{Percentage of yield} = \frac{\text{Practical weight}}{\text{Theoretical weight}} \times 100$$

Measurement of micromeritic properties of microbeads

i) Flow properties (angle of repose)

The flow characteristics of the drug loaded microbeads were measured by determining their angle of repose using fixed-base cone method. A glass funnel was secured with its tip positioned at a fixed height (H) above graph paper placed on a horizontal surface. The sample was poured through the funnel until the apex of the conical pile touched to the tip of the funnel. The height and radius of the heap was measured. The experiment was repeated in triplicate, the angle of repose (tan θ) was calculated using the formula;

$$\text{Angle of repose}[\theta] = \tan^{-1}(h/r)$$

H = cone height, r = radius of circular base formed by the microbeads on the ground.

Table 1: Relationship between angle of repose (θ) and powder flow

Angle of Repose (θ) in degrees	Flow properties
< 25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

ii) Bulk density and tapped densities

The bulk and tapped densities of the formulated granules or powder blends were evaluated by using the bulk density apparatus. Known weights of microbeads were transferred into a 50cc graduated measuring cylinder. The cylinder was fixed on bulk density apparatus and the timer knob was set for 100 tapings. Then, the initial bulk volume and final volume after 50 tapings were noted. The experiment was repeated in triplicate.

Table 2: Grading of the granules/powders for their flow properties

Consolidation index (Carr's %)	Flow properties
5-15	Excellent
12-16	Good
18-21	Fair to passable
23-35	Poor
>40	Very poor

Determination of particle size of drug loaded microbeads: The average particle size of drug loaded microbeads was determined by optical microscopic technique. The Olympus model (SZX-12) having resolution of 30 xs was used for this purpose. Eyepiece of the microscope was fitted with a micrometer. The instrument was calibrated at 1unit of eyepiece micrometer equal to 1/30mm (33.33µm). Thirty microbeads were suspended in small quantity of liquid paraffin oil. The sample was spread over a clean glass slide placed on mechanical stage of the microscope. Estimate the size of each bead with the help of eyepiece. In all measurements at least 20 particles in five different fields were examined[140]. Each experiment was carried out in triplicate.

Scanning electron microscopic analysis (SEM)

The shape and surface characteristics were determined by scanning electron microscopy (model-JSM, 35CF, jeol, Japan) using gold sputter technique. Photographs were scanned within a range of 50-5000 magnifications

Estimation of drug content and drug entrapment efficiency:

Accurately weighed quantity of crushed Terbutaline Sulfate loaded microbeads were suspended in 100 ml of phosphate buffer containing 10 ml of methanol. The resulting solution was transferred into a stoppered conical flask and the flask was shaken for a period of 12 hours by using a mechanical shaker at room temperature. Next day it was stirred for 15 minutes. The solution was filtered, after suitable dilution; the drug content in the filtrate was analyzed at λ max 275 nm for Terbutaline Sulfate against a reagent blank prepared with dummy microbeads using UV-Visible spectrophotometer (Shimadzu 1201). The obtained absorbance was plotted on the standard curve to get the exact concentration of the entrapped drug. Each experiment was carried out in triplicate (n=3). The actual drug content and percentage of drug entrapment efficiency (DEE)

Determination of swelling properties of drug loaded microbeads: The swelling properties of the drug loaded microbeads were determined in various pH ranges. Thirty uniform size dried microbeads were placed in small beakers containing 50 ml of pH 1.2 acidic buffer allowed to swell at 37^0C. After 2 hours interval, the equilibrium of swollen beads was observed and measured by Optical microscopy (Olympus model SZX-12). The magnitude of swelling was presented by the ratio of the mean diameter of swelling beads to the mean diameter of the dried beads before the test. Each experiment was carried out in triplicate (n=3). Swelling ratio was determined from the following relation;

$$\text{Swelling ratio (\%)} = \frac{\text{Mean diameter at time (t) - Initial diameter (µm)}}{\text{Initial diameter (µm)}} \text{ X } 100$$

Weighed 50 mg of terbutaline sulfate loaded microbeads were placed in a small basket, soaked in pH 1.2, pH 4.8 and pH 6.8 buffer solutions and then shaken occasionally at room temperature. After a predetermined time to remove excess water, the swollen beads were immediately weighed on digital balance (GE-412 Sartorius).The experiment was performed in triplicate. The fresh samples were used for each individual time point. The percentage of weight gain by the sample corresponding to swelling was calculated by using the formula.

$$\text{Swelling Index (\%)} = \frac{Wt - W0}{W_0} \text{ X } 100$$

Where; Wt is the weight of wetted microbeads at time (t) and W_0 is the initial weight of the microbeads at zero time (t)

***In-vitro* drug release studies**

The drug release studies were carried out using USP XIII rotating basket dissolution apparatus, (Model-TDT-08L, Electrolab Mumbai, India). The drug release profile from microbeads was examined in three different buffer solutions to mimic the various physiological regions of GI-tract. The drug loaded microbeads filled in empty hard gelatin capsule shells and put into the basket rotated at a constant speed 75 rpm and maintained temperature 37^0C. The 900 ml dissolution medium of pH 0.1NHCl was used for dissolution for 12 hours. Samples (5ml) were withdrawn at different time intervals over a period of 12 hours. After each sampling, equal volume of the medium was replaced with same volume of fresh medium. The sample was filtered through 0.45µ membrane filter and diluted with appropriate dilution with respective medium.

Then estimate the Terbutaline Sulfate concentration at λ max 275 nm (Shimadzu 1201, Japan)

Mechanism of drug release kinetics studies

Application of Release Rate Kinetics to Dissolution Data

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

Zero order release rate kinetics:

To study the zero–order release kinetics the release rate data ar e fitted to the following equation.

$$F = K_o t$$

Where, 'F' is the drug release at time't', and 'K_o' is the zero order release rate constant. The plot of % drug release versus time is linear.

First order release rate kinetics: The release rate data are fitted to the following equation

$$Log (100-F) = kt$$

A plot of log cumulative percent of drug remaining to be released vs. time is plotted then it gives first order release.

Higuchi release model:

To study the Higuchi release kinetics, the release rate data were fitted to the following equation.

$$F = k\ t1/2$$

Where, 'k' is the Higuchi constant.

In higuchi model, a plot of % drug release versus square root of time is linear.

Korsmeyer and Peppas release model:

The mechanism of drug release was evaluated by plotting the log percentage of drug released versus log time according to Korsmeyer- Peppas equation. The exponent 'n' indicates the mechanism of drug release calculated through the slope of the straight Line.

$$M_t/ M_\infty = K\ t^n$$

Where, M_t/ M_∞ is fraction of drug released at time 't', k represents a constant, and 'n' is the diffusional exponent, which characterizes the type of release mechanism during the dissolution process.

For non-Fickian release, the value of n falls between 0.5 and 1.0; while in case of Fickian diffusion, n = 0.5; for zero-order release (case I I transport), n=1; and for supercase II transport, n > 1. In this model, a plot of log (M_t/ M_∞) versus log (time) is linear.

Hixson-Crowell release model:

$$(100-Q_t)^{1/3} = 100^{1/3} – K_{HC}.t$$

Where, k is the Hixson-Crowell rate constant. Hixson-Crowell model describes the release of drugs from an insoluble matrix through mainly erosion. (Where there is a change in surface area and diameter of particles or tablets).

3. Results and Discussion

The present study was aimed to develop Terbutaline sulfate microbeads. All the formulations were evaluated for physicochemical properties, *In-vitro* drug release and Stability studies.

Analytical Method

Graphs of Terbutaline sulfate was taken in Simulated Gastric fluid (pH 1.2) at 300nm.

Table 3: Observations for graph of Terbutaline sulfate in 0.1N HCl (275nm)

Conc [µg/l]	Abs
0	0
5	0.163
10	0.314
15	0.438
20	0.563
25	0.719
30	0.842

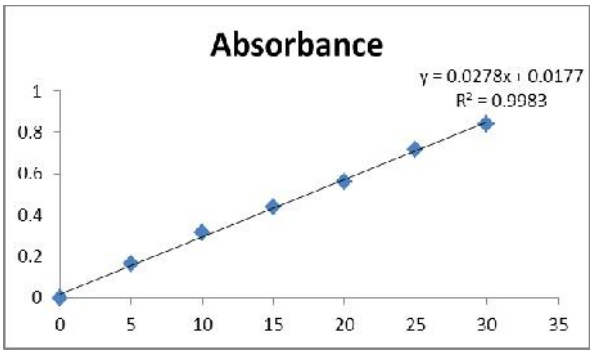

Figure 1: Figure 6: Standard graph of Terbutaline sulfate in 0.1N HCl

Figure 2: FTIR Spectrum of Pure Drug

Figure 3: FTIR Spectrum of Optimized Formulation

Observation: by observing the above data obtained there seems no interactions between the pure drug and the selected polymers.

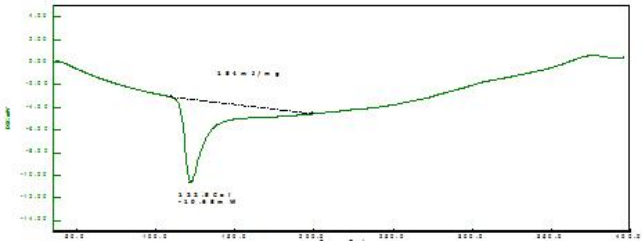

Figure 4: DSC of pure drug

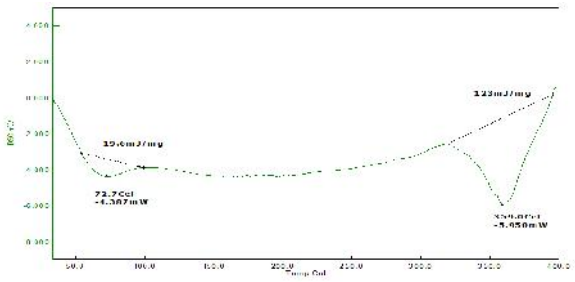

Figure 5: DSC of optimized formulation

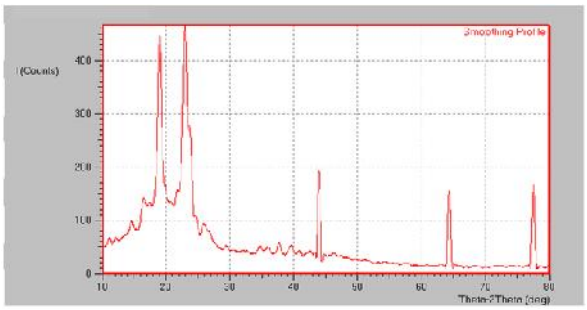

Figure 6: XRD Spectrum of Pure drug

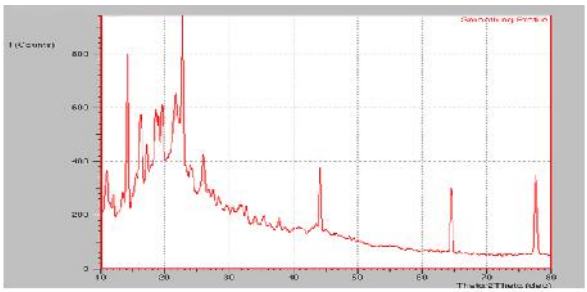

Figure 7: XRD Spectrum of Optimized formulation

Observation: By observing the above XRD data it was concluded that there is no change in the crystal form of the pure drug when it was mixed with the selected polymers.

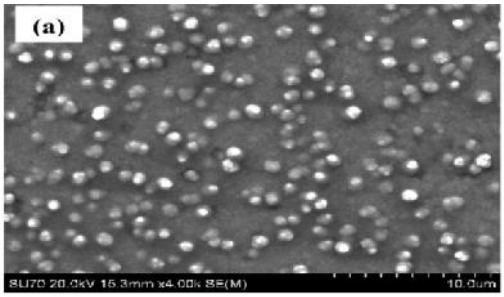

Figure 8: Optimized formulation

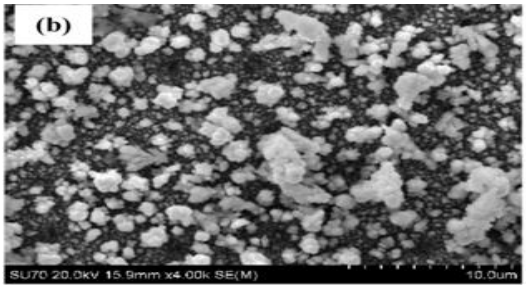

Figure 9: Terbutaline sulfate +locust bean gum

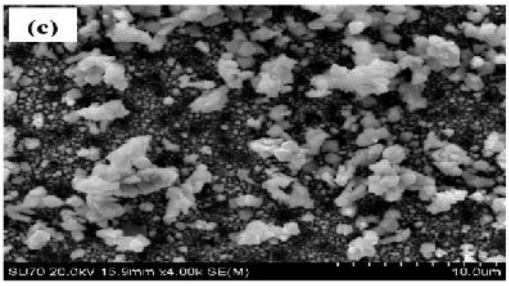

Figure 10: Terbutaline sulfate +sodium alginate

Microbeads were subjected to various pre-formulation parameters. The angle of repose values indicates that the microbeads have good flow properties. The bulk density of all the formulations was found to be in the range of 0.43 to 0.58(gm/cm3) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.57 to 0.69 showing the powder has good flow properties. The compressibility index of all the formulations was found to be ranging between 16 to 18 which shows that the powder has good flow properties. All the formulations has shown the hausner ratio ranging between 0 to 1.2 indicating the powder has good flow properties.

Table 4: Percentage yield

S.No	Formulation code	Percentage yield
1	F1	92.5±0.07%
2	F2	87.5±0.08%
3	F3	82.5±0.06%
4	F4	93.75±0.05%
5	F5	91.5±0.03%
6	F6	88.75±0.04%
7	F7	87.5±0.02%
8	F8	82.5±0.05%

n=3, Mean±SD values

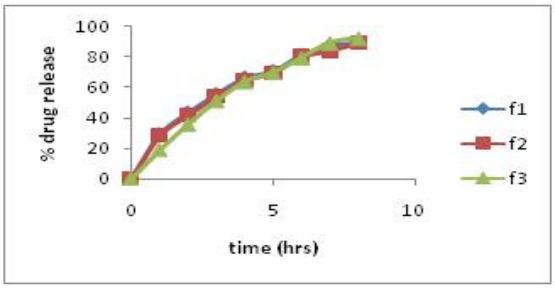

Figure 11: Dissolution profile of terbutaline sulfate microbeads (F1, F2, F3 formulations).

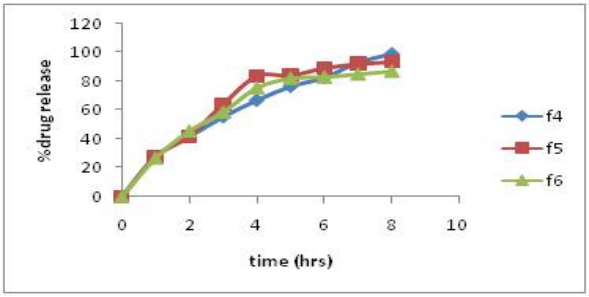

Figure 12: Dissolution profile of Terbutaline sulfate microbeads (F4, F5, F6 formulations).

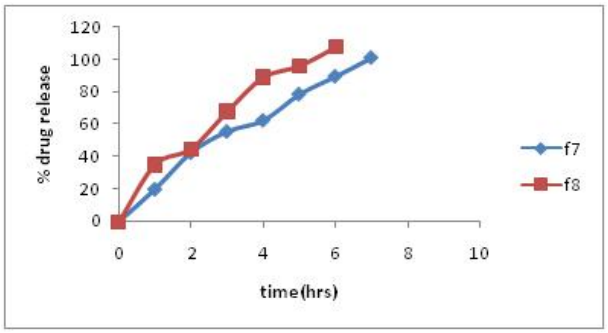

Figure 13: Dissolution profile of Terbutaline sulfate microbeads (F7, F8 formulations).

Application of Release Rate Kinetics to Dissolution Data: Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

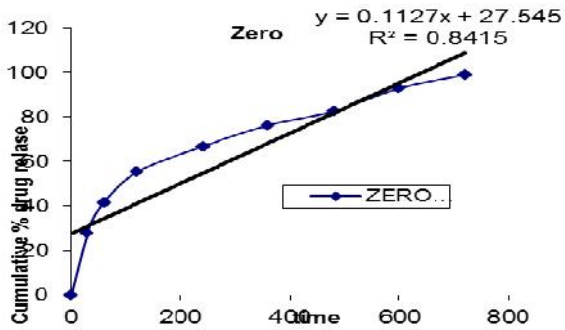

Figure 14: Zero order plot

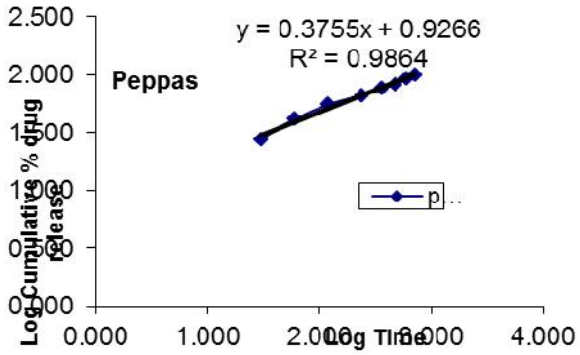

Figure 15: Peppas plot

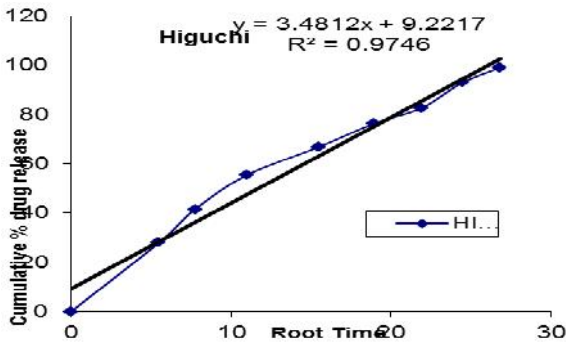

Figure 16: Higuchi plot

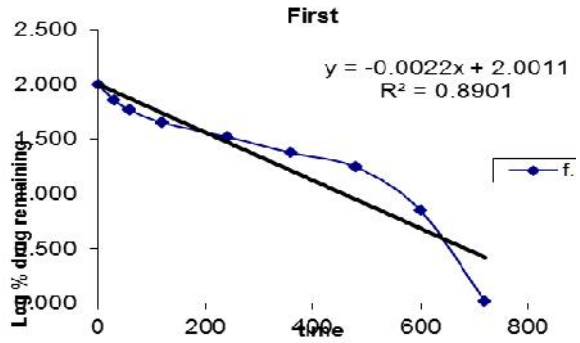

Figure 17: First order plot

4. Conclusion

The objective of the present study is formulation and evaluation of Terbutaline sulfate microbeads to improve drug oral bioavailability. Terbutaline sulfate microbeads were prepared by ionotropic external gelatation technique using sodium alginate, locust bean gum in different ratios. various formulations were prepared with these polymers. The Terbutaline sulfate microbeads were characterized with respect to IR, DSC, XRD, swelling studies, angle of repose, bulk density, tapped density, Carr's index Hausner's ratio, and stability studies and all the results indicated that the microbeads were having good flow nature. By the invitro dissolution studies it was concluded that the formulation (F4) was showing better result of 98.97% drug release. FTIR and DSC studies showed that there is no incompatability between the drug and polymers. The data was subjected to Zero order, first order, Higuchi, Korsmeyer and Peppas diffusion model.and the optimized formulation followed peppas order of release kinetics.

Table 5: Saturation solubility studies

S.No	Sample	Microbeads	Drug		Reading	
					Blank	Sample
1	F1	Sodium alginate		0.H_2O	0.000	0.440
2	F2	Sodium bicarbonate		0.01N HCl	0.000	0.108
3	F3	Locust bean gum		0.01N HCl	0.000	0.307
4	F4	Acetic acid		0.H_2O	0.000	0.499
5	F5		Terbutaline sulfate	0.H_2O	0.000	0.125
6	F6		Terbutaline sulfate	0.01N HCl	0.000	0.639
7	F7	Calcium chloride		0.01N HCl	0.000	0.355
8	F8	Sodium alginate	Terbutaline sulfate	0.01N HCl	0.000	0.499

Table 6: Rheological parameters of microbeads

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
F1	26.01±0.02	0.49±0.05	0.57±0.07	16.21±0.05	0.86±0.02
F2	24.8±0.05	0.56±0.02	0.62±0.05	16.87±0.02	0.98±0.05
F3	22.74±0.07	0.52±0.09	0.68±0.02	17.11±0.05	0.64±0.07
F4	25.33±0.02	0.54±0.02	0.64±0.05	17.67±0.02	1.12±0.09
F5	26.24±0.09	0.53±0.05	0.67±0.02	16.92±0.07	1.2±0.02
F6	26.12±0.05	0.56±0.02	0.66±0.07	17.65±0.02	1.06±0.09
F7	24.54±0.03	0.55±0.04	0.56±0.02	17.67±0.05	1.22±0.09
F8	25.65±0.02	0.57±0.06	0.57±0.04	16.92±0.07	1.42±0.02

n=3, Mean±SD values

Table 7: The drug content of the optimised microbeads was found to be

Formulation	F1	F2	F3	F4	F5	F6	F7	F8
Actual Drug Content	89.95 ± 0.25	64.90 ± 0.78	69.54 ± 0.64	98.76±0.06%	67.87 ± 0.86	66.20 ± 0.75	64.90 ± 0.78	88.35 ± 0.93
Drug Entrapment Efficiency	62.90 ± 0.78	89.95 ± 0.25	87.44 ± 0.90	97.96 ± 0.98	88.35 ± 0.93	89.95 ± 0.25	90.56 ± 0.35	67.87 ± 0.86

n=3, Mean±SD values

Table 8: Swelling studies in 0.1n Hcl

Time (hrs)	F1	F2	F3	F4	F5	F6	F7	F8
1	1.09±0.02	0.87±0.05	0.80±0.07	0.72±0.02	0.68±0.05	2.12±.08	2.86±0.09	3.41±0.09
2	1.28±0.05	1.16±0.02	1.14±0.05	1.12±0.08	0.86±0.09	2.95±0.02	3.75±0.05	4.52±0.08
3	2.92±0.08	2.48±0.07	1.72±0.02	1.63±0.05	1.46±0.02	12.68±0.09	10.90±0.02	9.65±0.05
4	3.18±0.07	3.55±0.08	1.77±0.09	1.82±0.02	1.98±0.05	16.24±0.02	15.87±0.09	14.32±0.02
5	4.78±0.09	3.33±0.09	2.58±0.08	2.32±0.09	2.27±0.07	22.32±0.05	20.33±0.02	18.68±0.07

n=3, Mean±SD values

Table 9: Dissolution Data of Terbutaline sulfate microbeads

Time(hrs)	F1	F2	F3	F4	F5
0	0	0	0	**0**	0
1	29.02±0.02	28.04±0.05	18.87±0.02	**27.86±0.01**	27.73±0.06
2	43.32±0.05	41.65±0.02	35.66±0.05	**41.45±0.02**	42.04±0.01
3	55.28±0.01	53.81±0.05	51.06±0.02	**55.25±0.05**	64.33±0.02
4	66.08±0.06	64.53±0.02	63.63±0.01	**66.73±0.06**	83.84±0.05
5	70.44±0.05	69.43±0.01	69.71±0.05	**76.34±0.02**	84.32±0.08
6	80.9±0.02	79.98±0.05	79.27±0.02	**82.52±0.05**	89.44±0.02
7	87.27±0.08	83.98±0.02	89.02±0.08	**92.97±0.01**	92.34±0.09
8	88.80±0.02	89.00±0.04	92.24±0.02	**98.97±0.02**	93.71±0.04

n=3, Mean±SD values

Table 10: Dissolution Data of Terbutaline sulfate microbeads

Time(hrs)	F6	F7	F8
0	0	0	0
1	26.75±0.02	20.04±0.02	35.05±0.04
2	45.55±0.06	42.55±0.07	44.85±0.02
3	58.66±0.02	55.56±0.04	67.84±0.07
4	75.54±0.05	62.42±0.02	88.98±0.04
5	82.11±0.01	78.52±0.04	95.96±0.07
6	83.12±0.08	89.50±0.07	107.54±0.02
7	85.11±0.02	101.05±0.02	-
8	87.02±0.02	-	-

n=3, Mean±SD values

Table 11: Application of rate release kinetics for optimised formulation

Cumulative (%) Release Q	Time (T)	Root (T)	Log (%) Release	Log (T)	Log (%) Remain
0	0	0			2.000
27.86	30	5.477	1.445	1.477	1.858
41.45	60	7.746	1.618	1.778	1.768
55.25	120	10.954	1.742	2.079	1.651
66.73	240	15.492	1.824	2.380	1.522
76.34	360	18.974	1.883	2.556	1.374
82.52	480	21.909	1.917	2.681	1.243
92.97	600	24.495	1.968	2.778	0.847
98.97	720	26.833	1.996	2.857	0.013

Table 12: Stability studies data for optimized formulation

S.No	Optimised formulation(F3) duration	25^0C(75%RH)	37^0C (75%RH)
1	1 Month	98.55%	98.10%
2	2 Month	98.27%	97.80%
3	3 Month	98.20%	97.75%

n=3, Mean±SD values

By observing the stability studies it is concluded that the optimised formulation is stable through the entire period of 3 months and the drug release profile is also intact throughout the time being.

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