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Research/Review

Formulation development and *in vitro* evaluation of terbutaline floating tablets

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Abstract

The present study outlines a systematic approach for designing and development of Terbutaline floatingtablets to enhance the bioavailability and therapeutic efficacy of the drug. Floating tablets of Terbutaline haveshown sustained release thereby proper duration of action at a particular site and are designed to prolong thegastric residence time after oral administration. Different formulations were formulated by using direct compression method. A floating drug delivery system (FDDS) was developed by using sodium bicarbonate asgas-forming agent and HPMC E5, Eudragit RLPO and Sodium carboxy methylcellulose as polymers. The prepared tablets wereevaluated in terms of their physical characteristics, precompression parameters, *in vitro* release and buoyancylag time. The results of the *in vitro*release studies showed that the optimized formulation (T7) could sustaindrug release for 12 hrs by using Sodium carboxy methylcellulose in the concentration of 5mg. The *in vitro* drug release followed zero order kinetics.

Keywords: Terbutaline, HPMC E5, Eudragit RLPO and Sodium carboxy methylcellulose and Floating tablets.

INTRODUCTION

Oral controlled release drug delivery have recently been of increasing interest in pharmaceutical field to achieve improved therapeutic advantages, such as ease of dosing administration, patient compliance and flexibility in formulation. Drugs that are easily absorbed from gastrointestinal tract (GIT) and have short half-lives are eliminated quickly from the systemic circulation. Frequent dosing of these drugs is required to achieve suitable therapeutic activity. After oral administration, such a drug delivery would be retained in the stomach and release the drug in a controlled manner, so that the drug could be supplied continuously to its absorption sites in the gastrointestinaltract (GIT).[1] Prolonged gastric retention improves bioavailability, increases the duration of drug release, reduces drug waste, and improves the drug solubility that are less soluble in a high pH environment[2]Gastroretentive drug delivery is an approach to prolong gastric residence time, thereby targeting site-

specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effects. Gastroretentive dosage forms can remain in the gastric region for long periods and hence significantly prolong the gastric retention time (GRT) of drugs. Over the last few decades, several gastroretentive drug delivery approaches being designed and developed, including: high density (sinking) systems that is retained in the bottom of the stomach[3] , low density (floating) systems that causes buoyancy in gastric fluid[4,5,6], mucoadhesive systems that causes bioadhesion to stomach mucosa[7], unfoldable, extendible, or swellable systems which limits emptying of the dosage forms through the pyloric sphincter of stomach[8,9],superporous hydrogel systems[10] magnetic systems[11]etc. The current review deals with floating type gastroretentine drug delivery system.

Basic gastrointestinal tract physiology

The stomach is divided into 3 regions anatomically: fundus, body, and antrum pylorus. The proximal part is the fundus and the body acts as a reservoir for undigested material, where as the antrum is the main site for mixing motions and acts as a pump for gastric emptying by propelling actions. Gastric emptying occurs during fasting as well as fed states but the pattern of motility is distinct in the 2 states. During the fasting state an interdigestive series of electrical events take place, which cycle through both stomach and intestine every 2 to 3 hours. This is called the interdigestivemyloelectric cycle or migrating myloelectric cycle (MMC), which is divided into following 4 phases.[12]

Phase I: This period lasts about 30 to 60 minutes with no contractions.

Phase II: This period consists of intermittent contractions that increase gradually in intensity as the phase progresses, and it lasts about 20 to 40 minutes. Gastric discharge of fluid and very small particles begins later in this phase.

Phase III: This is a short period of intense distal and proximal gastric contractions (4-5 contractions per minute) lasting about 10 to 20 minutes these contractions, also known as ‘‘house-keeper wave,’’ sweep gastric contents down the small Intestine.

Phase IV: This is a short transitory period of about 0 to 5 minutes, and the contractions dissipate between the last part of phase III and quiescence of phase

Need For Gastroretention

- Drugs that are absorbed from the proximal part of the gastrointestinal tract (GIT).
- Drugs that are less soluble or that degrade at the alkaline pH.
- Drugs that are absorbed due to variable gastric emptying time.
- Local or sustained drug delivery to the stomach and proximal small intestine to treat certain conditions.
- Particularly useful for the treatment of peptic ulcers caused by H.Pylori infections.[12]

Factors controlling gastric retention of dosage forms

There are several factors that can affect gastric emptying of an oral dosage form which include density, size and shape of dosage form, feeding state, biological factors such as age, gender, posture, body mass index, disease state etc.

Effect Of Dosage Form Size &Shape

Small size tablets are emptied from the stomach during the digestive phase while large size units are expelled during the house keeping waves found that floating unit with a diameter equal or less than 7.5 mm had larger gastric residence time (GRT) compared to nonfloating units but the GRT was similar for floating and non-floating units having a large diameter of 9.9 mm. They found that GRT of nonfloating units were much more variable and highly dependent on their size which are in the order of small < medium < large units. Moreover, in supine subjects, size influences GRT of floating and non- floating form. Tetrahedron and ring shaped devices have a better GRT as compared with other shapes.[13,14]

Density

The density of a dosage form also affects the gastric emptying rate and determines the location of the system in the stomach. Dosage forms having a density lower than the gastric contents can float to the surface, while high density systems sink to bottom of the stomach [16]. Both positions may isolate the dosage system from the pylorus. A density of < 1.0 gm/ cm3 is required to exhibit floating property.[15]

Gender, Posture & Age

Generally females have slower gastric emptying rates than male. The effect of posture does not have any significant difference in the mean gastric retention time (GRT) for individuals in upright, ambulatory and supine state. In case of elderly persons, gastric emptying is slowed down.[16]

Effect of Food & Specific Gravity

To float FDDS in the stomach, the density of dosage form should be less than gastric content i.e.1.0 g/cm3. Since, the bulk density of a dosage form is not a sole measure to describe its buoyant capabilities because the magnitude of floating strength may vary as a function of time and gradually decrease after immersing dosage form into fluid as a result of development of its hydrodynamic equilibrium. Various studies have shown the intake of food as main determinant of gastric emptying rather than food. Presence of food is the most important factor effecting GRT than buoyancy. GRT is significantly increased under fed condition since onset of MMC is delayed. Studies show that GRT for both floating and non-floating single unit are shorter in fasted subjects (less than 2 hour), but significantly prolonged after meal (around 4 hour).[12]

Nature of Meal & Frequency of Food

Feeding of indigestible polymers or fatty acid salts can change the motility pattern of the stomach to fed state, to increase gastric emptying rate and prolonging the drug release. Diet rich in protein and fat can increase GRT by 4-10 hours.[12]

Type of Formulation

Multiple unit formulation show a more predictable release profile and insignificant impairing of performance due to failure of units, allow co-administration of units with different release profile or containing incompatible substances and permit a large margin of safety against dosage form failure compared with single unit dosage form.[13]

Future Potential

Floating dosage form offers various future potential as evident from several recent publications. The reduced fluctuations in the plasma level of drug results from delayed gastric emptying. Drugs that have poor bioavailibility because of their limited absorption to the upper gastrointestinal tract can be delivered efficiently thereby maximizing their absorption and improving their absolute bioavalability.

Buoyant delivery system considered as a beneficial strategy for the treatment of gastric and duodenal cancers.

- The floating concept can also be utilized in the development of various anti-reflux formulations.
- Developing a controlled release system for the drugs, which are potential to treat the Parkinson's disease.
- To explore the eradication of Halico-bector pylori by using the narrow spectrum antibodies.[14]

Classification Of Gastroretentive Drug Delivery System

The main approaches that have been examined for gastroretentive dosage forms (GRDFs) are: low density of GRDF that cause buoyancy above gastric fluid (Floating system), high density which retain the dosage form in the body of stomach, concomitant administration of drugs or excipients which slow the motility of the GIT, bioadhesion to gastric mucosa, swelling to a large size which prevents emptying of dosage form through the pyloric sphincter.

Floating Drug Delivery Systems

A floating dosage form is useful for drugs acting locally in the proximal gastrointestinal tract. These systems are also useful for drugs that are poorly soluble (or) unstable in intestinal fluids. The floating properties of these systems help to retain in the stomach for a long time. Various attempts have been made to develop floating systems, which float on the gastric contents and release drug molecules for the desired time period. After the release of a drug, the remnants of the system are emptied from the stomach. Based on the mechanism of buoyancy, two different technologies have been used in development of floating drug delivery systems.

These include:

a) Effervescent system.

b) Non- Effervescent system.

Effervescent Systems

Effervescent systems10 include use of gas generating agents, carbonates (e.g. Sodium bicarbonate) and other organic acid (e.g. citric acid and tartaric acid) present in the formulation to produce carbon dioxide (CO2) gas, thus reducing the density of the system and making it float on the gastric fluid. An alternative is the incorporation of matrix containing portion of liquid, which produce gas that evaporate at body temperature. These effervescent systems further classified into two types:

1) Gas generating systems.

2) Volatile liquid or Vacuum containing systems.

Gas Generating Systems

Tablets Intragastric Single layer Floating Tablets or Hydrodynamically Balanced System (HBS)

These formulations have bulk density lower than gastric fluids and thus float in the stomach that increases the gastric emptying rate for a prolonged period,[19] (Fig.3). These are formulated by intimately mixing the gas (CO2) generating agents and the drug within the matrix tablet. The drug is released slowly at a desired rate from the floating system and the residual system is emptied from the stomach after the complete release of the drug. This leads to an increase in the gastric residence time (GRT) and a better control over fluctuations in plasma drug concentration.

- Immediate release layer and
- Sustained release layer.

Floating Capsules

These floating capsules[20] are formulated by filling with a mixture of sodium alginate and sodium bicarbonate. The systems float as a result of the generation of CO2 that was trapped in the hydrating gel network on exposure to an acidic environment.

Multiple Unit Type Floating Pills

These multiple unit type floating pills20are sustained release pills, known as seeds, which are surrounded by two layers (Fig.5). The outer layer is of swellable membrane layer while the inner layer consists of effervescent agents. This system sinks at once and then it forms swollen pills like balloons which float as they have lower density, when it is immersed in the dissolution medium at body temperature. The lower density is due to generation and entrapment of CO2 within the system. Key: (a) conventional SR pills; (b) effervescent layer; (c) swellable layer; (d) expanded swellable membrane layer; (e) surface of water in the beaker (370C).

Floating System with Ion-Exchange Resins

Floating system using bicarbonate loaded ion exchange resin was made by mixing the beads with 1M sodium bicarbonate solution, and then the semi-permeable membrane is used to surround the loaded beads to avoid sudden loss of CO2. On contact with gastric contents an exchange of bicarbonate and chloride ions takes place that results in generation of CO2 that carries beads towards the top of gastric contents and producing a floating layer of resin beads.

Volatile liquid or Vacuum Containing Systems

Intragastric Floating Gastrointestinal Drug Delivery System

This system floats in the stomach because of floatation chamber, which is vacuum or filled with a harmless gas or air, while the drug reservoir is encapsulated by a microporous compartment.

Inflatable gastrointestinal delivery systems

Inflatable chamber are incorporated, which contains liquid ether that gasifies at body temperature to inflate the chamber in the stomach. These systems are fabricated by loading the inflatable chamber with a drug reservoir, which can be a drug, impregnated polymeric matrix, then encapsulated in a gelatin capsule, [19](Fig.7). After oral administration, the capsule dissolves to release the drug reservoir together with the inflatable chamber. The inflatable chamber automatically inflates and retains the drug reservoir compartment in the stomach. The drug is released continuously from the reservoir into gastric fluid.

Intragastric Osmotically Controlled Drug Delivery System

It is comprised of an osmotic pressure controlled drug delivery device and an inflatable floating support in a biodegradable capsule. In the stomach, the capsule quickly disintegrates to release the intragastirc osmotically controlled drug delivery device. The inflatable support inside forms a deformable hollow polymeric bag that contains a liquid that gasifies at body temperature to inflate the bag. The osmotic pressure controlled drug delivery device consists of two components; drug reservoir compartment and an osmotically active compartment. The floating support is also made to contain a bioerodible plug that erodes after a predetermined time to deflate the support. The deflated drug delivery system is then emptied from the stomach.

Non-Effervescent Systems

Non-effervescent floating drug delivery systems are normally prepared from gel-forming or highly swellable cellulose type hydrocolloids, polysaccharides or matrix forming polymers like polyacrylate, polycarbonate, polystyrene and polymethacrylate. In one approach, intimate mixing of drug with a gel forming hydrocolloid which results in contact with gastric fluid after oral administration and maintain a relative integrity of shape and a bulk density less than unity within the gastric environment[21] The air trapped by the swollen polymer confers buoyancy to these dosage forms. Excipients used most commonly in these systems include hydroxypropyl

methylcellulose (HPMC) polyacrylates, polyvinyl acetate, carbopol, agar, sodium alginate, calcium chloride, polyethylene oxide and polycarbonates [22]. This system can be further divided into the sub-types:

MATERIALS

Terbutaline-Procured from Astra geneca Ltd, Bangalore, India. Provided by SURA LABS, Dilsukhnagar, Hyderabad, HPMC E5-Degussa India Ltd. (Mumbai, India), Eudragit RLPO-Arvind Remedies Ltd, Tamil nadu, India, Sodium carboxy methylcellulose-Merck Specialities Pvt Ltd, Mumbai, India, Citric acid-Laser Chemicals, Ahmedabad, India, Sodium bicarbonate-Merck Specialities Pvt Ltd, Mumbai, India, Micro crystalline cellulose-Merck Specialities Pvt Ltd, Mumbai, India, Magnesium Stearate-Apex Chemicals, Ahmedabad, India,Talc-S.D. Fine Chem., Mumbai, India.

METHODOLOGY

Analytical method development

Determination of absorption maxima

A solution containing theconcentration 10 µg/ mL drug was prepared in 0.1N HCL UV spectrum was taken using Double beam UV/VISspectrophotometer. The solution was scanned in the range of 200 – 400 nm.

Preparation calibration curve

10mg Terbutaline pure drug was dissolved in 10ml of methanol (stock solution1) from stock solution 1ml of solution was taken and made up with10ml of 0.1N HCL (100µg/ml). From this 1ml was taken and made up with 10 ml of 0.1N HCL (10µg/ml). The above solution was subsequently diluted with 0.1N HCL to obtain series of dilutions Containing 5, 10, 15, 20, 25µg /ml of per ml of solution. The absorbance of the above dilutions was measured at 220 nm by using UV-Spectrophotometer taking 0.1N HCL as blank. Then a graph was plotted by taking Concentration on X-Axis and Absorbance on Y-Axis which gives a straight line Linearity of standard curve was assessed from the square of correlation coefficient (R^2)which determined by least-square linear regression analysis.

Preformulation parameters

The quality of tablet, once formulated by rule, is generally dictated by thequality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characteristics of blends produced. The various characteristics of blends tested as per Pharmacopoeia.

Angle of repose

The frictional force in a loose powder can be measured by the angle of repose. It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles producing a surface angle, is in equilibrium with the gravitational force. The fixed funnel method was employed to measure the angle of repose. A funnel was secured with its tip at a given height (h), above a graph paper that is placed on a flat horizontal surface. The blend was carefully pored through the funnel until the apex of the conical pile just touches the tip of the funnel. The radius (r) of the base of the conical pile was measured.

Table 1: Angle of Repose values (as per USP)

Angle of Repose	Nature of Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Bulk density

Density is defined as weight per unit volume. Bulk density, is defined as themass of the powder divided by the bulk volume and is expressed as gm/cm^3. The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together. Bulk density is very important in the size of containers needed for handling, shipping, and storage of raw material and blend. It is also important in size blending equipment. 10 gm powder blend was sieved and introduced into a dry 20 ml cylinder, without compacting.

Tapped density

After carrying out the procedure as given in the measurement of bulk densitythe cylinder containing the sample was tapped using a suitable mechanical tapped density tester that provides 100 drops per minute and this was repeated until difference between succeeding measurement is less than 2 % and then tapped volume, V measured, to the nearest graduated unit.

Measures of powder compressibility

The Compressibility Index (Carr's Index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is. As such, it is measures of the relative importance of interparticulate interactions. In a free- flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value.

For poorer flowing materials, there are frequently greater interparticle interactions, and a greater difference between the bulk and tapped densities will be observed.

Table 2: Carr's index value (as per USP)

Carr's index	Properties
5 – 15	Excellent
12 – 16	Good
18 – 21	Fair to Passable
2 – 35	Poor
33 – 38	Very Poor
>40	Very Very Poor

Formulation development of floating Tablets

Procedure for direct compression method

1) Drug and all other ingredients were individually passed through sieve no ≠ 60.
2) All the ingredients were mixed thoroughly by triturating up to 15 min.
3) The powder mixture was lubricated with talc.
4) The tablets were prepared by using direct compression method by using 6mm punch.

Formulation of tablets

Table 3: Formulation composition for Floating tablets

INGREDIENTS (MG)	FORMULATION CODE								
	T1	T2	T3	T4	T5	T6	T7	T8	T9
Terbutaline	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
HPMC E5	5	10	15	-	-	-	-	-	-
Eudragit RLPO	-	-	-	5	10	15	-	-	-
Sodium carboxy methylcellulose	-	-	-	-	-	-	5	10	15
Citric acid	10	10	10	10	10	10	10	10	10
Sodium bicarbonate	20	20	20	20	20	20	20	20	20
Micro crystalline cellulose	54.5	49.5	44.5	54.5	49.5	44.5	54.5	49.5	44.5
Magnesium Stearate	5	5	5	5	5	5	5	5	5
Talc	3	3	3	3	3	3	3	3	3
Total Weight	100	100	100	100	100	100	100	100	100

All the quantities were in mg

RESULTS AND DISCUSSION

Analytical Method

Determination of absorption maxima

The standard curve is based on the spectrophotometer. The maximum absorption was observed at 220nm.

Calibration curve

Graphs ofTerbutaline was taken in 0.1N HCL (pH 1.2)

Table 4: Observations for graph of Terbutaline in 0.1N HCL

Conc [µg/mL]	Abs
0	0
5	0.176
10	0.332
15	0.481
20	0.637
25	0.789

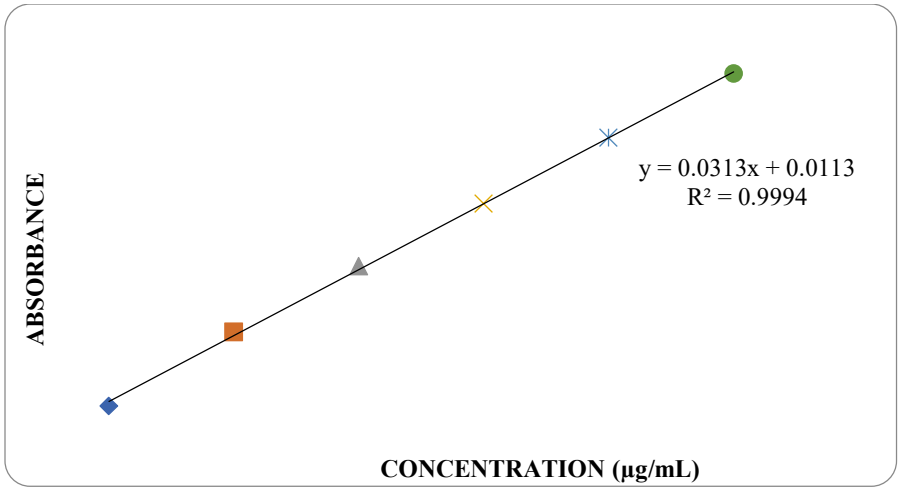

Fig 1: Standard graph of Terbutaline in 0.1N HCL

Standard graph ofTerbutaline was plotted as per the procedure in experimental method and its linearity is shown in Table 8.1 and Fig 8.1. The standard graph of Terbutaline showed good linearity with R^2 of 0.999, which indicates that it obeys "Beer- Lamberts" law.

Preformulation parameters of powder blend

Table 5: Pre-formulation parameters of blend

Formulation Code	Angle of Repose	Bulk density (gm/mL)	Tapped density (gm/mL)	Carr's index (%)	Hausner's Ratio
T1	29.35	0.538	0.649	17.10	1.20
T2	30.30	0.546	0.665	17.89	1.21
T3	31.65	0.576	0.672	14.28	1.16
T4	29.98	0.524	0.657	20.24	1.25
T5	29.66	0.564	0.677	16.69	1.20
T6	29.98	0.536	0.635	15.59	1.18
T7	30.32	0.576	0.650	11.38	1.12
T8	27.33	0.547	0.657	16.74	1.20
T9	30.62	0.567	0.678	16.37	1.19

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.524to 0.576 (gm/ml) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.635to 0.678showing the powder has good flow properties. The compressibility index of all the formulations was found to be below 20.24 which show that the powder has good flow properties.All the formulations has shown the hausners ratio ranging between 1.12to 1.25 indicating the powder has good flow properties.

Quality control parameters for tablets

Tablet quality control tests such as weight variation, hardness, friability, thickness, Drug content and drug

release studies were performed for floating tablets.

Table 6: *Invitro* quality control parameters

Formulation codes	Weight variation (mg)	Hardness (kg/cm^2)	Friability (%loss)	Thickness (mm)	Drug content (%)	Floating lag time (sec)	Total Floating Time(Hrs)
T1	98.59	4.18	0.24	3.94	96.83	56	11
T2	96.32	4.92	0.58	3.20	99.67	43	10
T3	99.20	4.35	0.36	3.86	98.31	39	12
T4	97.45	4.12	0.18	3.42	96.40	32	11
T5	98.24	4.91	0.73	3.75	98.37	25	12
T6	97.69	4.18	0.62	3.59	99.13	20	12
T7	98.48	4.69	0.70	3.82	98.89	18	12
T8	99.14	4.17	0.46	3.14	98.11	28	12
T9	98.93	4.56	0.34	3.73	97.32	34	12

All the parameters for SR layer such as weight variation, friability, hardness, thickness, drug content were found to be within limits.

***In vitro* drug release studies**

Table 7: Dissolution data of Floating tablets

TIME (HR)	CUMULATIVE PERCENTAGE OF DRUG RELEASE								
	T1	T2	T3	T4	T5	T6	T7	T8	T9
0	0	0	0	0	0	0	0	0	0
1	28.92	15.58	13.29	20.99	15.82	11.34	16.50	10.29	06.91
2	36.34	28.25	18.13	26.63	20.90	18.26	21.32	15.72	10.30
3	40.68	38.71	23.96	38.24	28.35	22.54	28.11	22.90	18.61
4	58.15	43.90	28.14	42.81	37.45	28.87	35.08	28.38	23.52
5	67.76	50.65	35.20	56.60	45.76	36.93	40.96	35.27	28.81
6	76.50	59.12	42.87	64.32	50.81	45.27	48.60	40.12	37.32
7	90.31	65.08	49.73	70.41	57.96	50.71	56.14	46.90	45.60
8	96.83	78.70	56.51	87.88	66.75	59.56	61.73	54.63	51.97
9		89.36	68.09	96.59	71.31	66.81	75.69	61.28	58.82
10		97.18	76.80		85.85	73.04	83.82	67.12	64.35
11			88.66		98.91	77.10	91.09	76.30	70.82
12			93.37			90.17	99.59	89.27	78.99

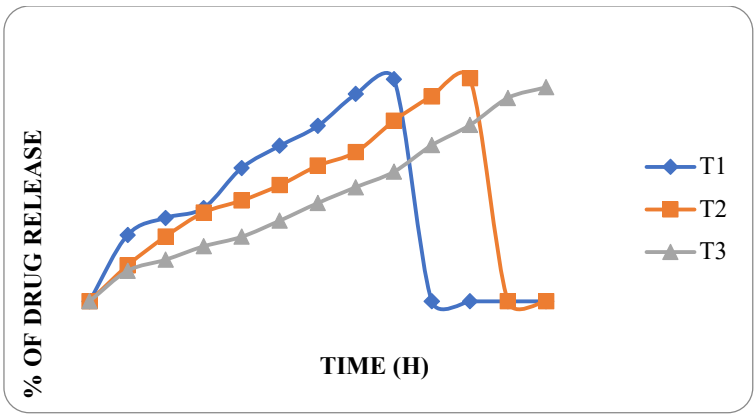

Fig 1: Dissolution data of Terbutaline floating tablets containing HPMC E5

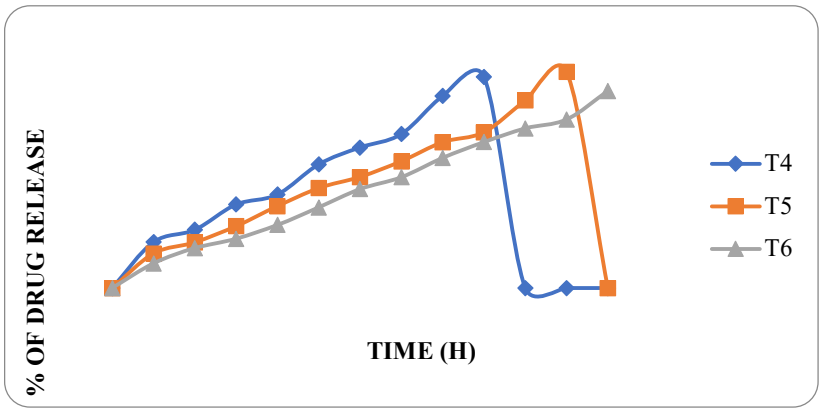

Fig 2: Dissolution data of Terbutaline floating tablets containing Eudragit RLPO

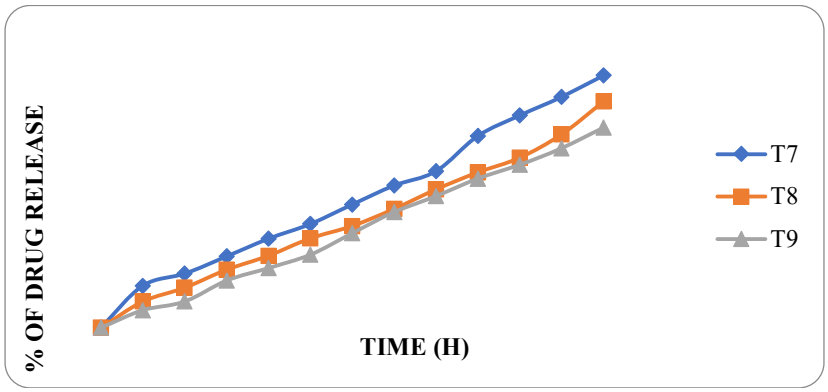

Fig 3: Dissolution data of Terbutaline Floating tablets containing Sodium carboxy methylcellulose

From the dissolution data it was evident that the formulations prepared with HPMC E5as polymer wereretarded the drug release12 hours. In low concentration of the polymer the drug release was unable to retarded up to 12 hours. Whereas the formulations prepared with higher concentration of Eudragit RLPO retarded the drug release up to 12 hours in the concentration 15 mg. In lower concentrations the polymer was unable to retard the drug release up to 12 hours. Whereas the formulations prepared with Sodium carboxy methylcellulose were retarded the drug release in the concentration of 5 mg (T7 Formulation) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 99.59 % in 12 hours with good retardation.

Hence from the above dissolution data it was concluded that T7 formulation was considered as optimised formulation because good drug release (99.59%) in 12 hours.

Application of release rate kinetics to Dissolution data for optimised formulation

Table 8: Application kinetics for optimised formulation

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG(%) RELEASE	LOG (T)	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE / t)	1/CUM% RELEASE	PEPPAS log Q/100	% Drug Remaining	Q01/3	Qt1/3	Q01/3-Qt1/3
0	0	0			2.000				100	4.642	4.642	0.000
16.5	1	1.000	1.217	0.000	1.922	16.500	0.0606	-0.783	83.5	4.642	4.371	0.271
21.32	2	1.414	1.329	0.301	1.896	10.660	0.0469	-0.671	78.68	4.642	4.285	0.357
28.11	3	1.732	1.449	0.477	1.857	9.370	0.0356	-0.551	71.89	4.642	4.158	0.484
35.08	4	2.000	1.545	0.602	1.812	8.770	0.0285	-0.455	64.92	4.642	4.019	0.623

40.96	5	2.236	1.612	0.699	1.771	8.192	0.0244	-0.388	59.04	4.642	3.894	0.748
48.6	6	2.449	1.687	0.778	1.711	8.100	0.0206	-0.313	51.4	4.642	3.718	0.923
56.14	7	2.646	1.749	0.845	1.642	8.020	0.0178	-0.251	43.86	4.642	3.527	1.115
61.73	8	2.828	1.790	0.903	1.583	7.716	0.0162	-0.210	38.27	4.642	3.370	1.272
75.69	9	3.000	1.879	0.954	1.386	8.410	0.0132	-0.121	24.31	4.642	2.897	1.745
83.82	10	3.162	1.923	1.000	1.209	8.382	0.0119	-0.077	16.18	4.642	2.529	2.112
91.09	11	3.317	1.959	1.041	0.950	8.281	0.0110	-0.041	8.91	4.642	2.073	2.568
99.59	12	3.464	1.998	1.079	-0.387	8.299	0.0100	-0.002	0.41	4.642	0.743	3.899

Optimised formulation T7 was kept for release kinetic studies. From the above graphs it was evident that the formulation T7 was followed Zero order release kineticsmechanism.

Drug – Excipient compatability studies
Fourier Transform-Infrared Spectroscopy

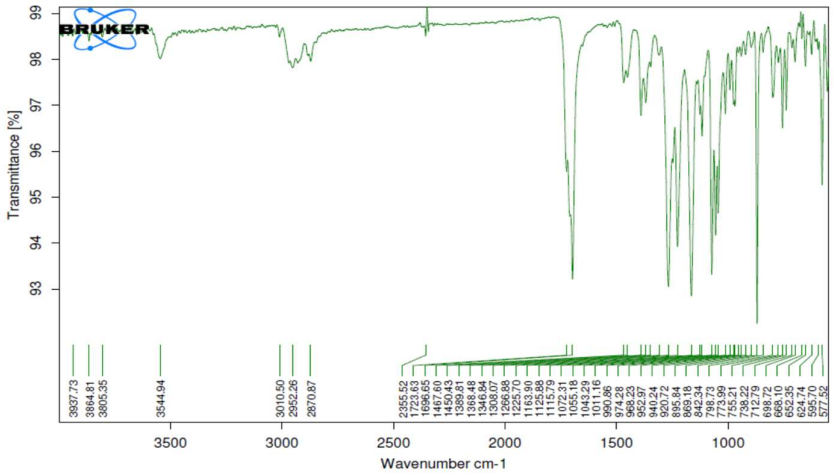

Fig 4: FTIR Spectrum of pure drug

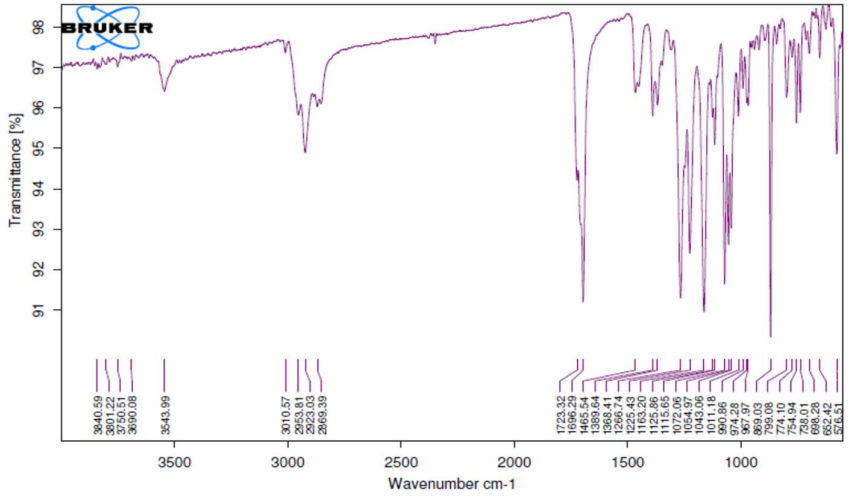

Fig 5: FTIR Spectrum of optimised formulation

There was no disappearance of any characteristics peak in the FTIR spectrum of drug and the polymers used. This shows that there is no chemical interaction between the drug and the polymers used. The presence of peaks at the expected range confirms that the materials taken for the study are genuine and there were no possible interactions. Terbutaline are also present in the physical mixture, which indicates that there is no interaction between drug and the polymers, which confirms the stability of the drug.

CONCLUSION

Floating tablets were formulated and evaluated using Terbutaline by using HPMC E5, Eudragit RLPO and Sodium carboxy methylcellulose use as polymers, by varying drug to polymer ratio. All the formulations were prepared by using direct compression method. The pre compression parameters of all formulations show good flow properties and these can be used for tablet manufacturing. The post compression parameters of all formulations were determined and the values were found to be satisfactory. Sodium bicarbonate is used as gas generating agent. Citric acid is used to achieve buoyancy effect under the elevated pH, which results an enhancement in drug release. The shapes of the tablets of all the formulations were found to be white, smooth, flat faced circular with no visible cracks. The tablets prepared with low viscosity grade Sodium carboxy methylcellulose (i.e.T7) exhibited short Floating Lag Time and longer Floating Time, when compared with the formulations containing high viscous grade. It is concluded that the formulations prepared with low viscous Sodium carboxy methylcellulose (T7) showed desirable buoyancy time. It is observed that, in all the formulations as the concentration of polymer increases, the amount of drug release was found to be decreased, because the amount of drug binded in the polymer could be more. From the drug content and *in vitro* dissolution studies of the formulations, it was concluded that the formulation T7 shown best result i.e., the formulation prepared with Sodium carboxy methylcellulose, sodium bicarbonate, microcrystalline cellulose, magnesium stearate, talc retarded the drug release up to 12 hours in the concentration of 5mg of Sodium carboxy methylcellulose. *In-vitro* dissolution data was fitted to Zero order kinetics models to check the release kinetics. The best fit release was achieved with Zero order kinetics.

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