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FORMULATION AND EVALUATION OF GASTRO RETENTIVE TABLETS OF ITOPRIDE

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ABSTRACT

Itopride is a gastro prokinetic. It is a dopamine D2 antagonist with acetylcholine sterase inhibitory actions. Floating tablets of itopride formulated to increase gastric residence and there by improve its therapeutic efficacy. By using different polymers such as hydroxy propylmethyl cellulose, sodium alginate and eudragit prepare formulations F1, F2, F3, F4, F5, F6, F7, F8, F9. Formulated tablets showed satisfactory results for various post compression evaluation parameters like Thickness, Hardness, Weight Variation, Floating Lag Time, Total Floating Time, Content Uniformity and in vitro drug release. Formulation F4 gave better controlled drug release and floating properties incomparison to the other formulations.

Keywords: D2antagonist, Acetylcholinesterase Inhibitor and Increase Gastric Resistance.

INTRODUCTION

Oral route is the most convenient and extensively used route for drug administration. This route has high patient acceptability, primarily due to ease of administration. Over the years, oral dosage forms have become increasingly sophisticated with major role being played by controlled release drug delivery systems (CRDDS) release drug at predetermined rate.

Drug delivery technologies are advanced enough to design any dosage form that can deliver drugs at a constant rate for extended periods of time ranging from days to years. And yet most oral controlled release dosage forms deliver drugs for only 12hrs. Oral delivery for 24 hrs is possible for some drugs; such are absorbed well throughout Gastro Intestinal Tract (GIT). Thus, the real issue in the development of oral controlled release dosage forms is how to extend the time for drug absorption from final intestine.

1.1 Conventional Drug Delivery System

Oral drug delivery is the most widely utilized route of administration among all the routes that have been explored for systemic delivery of drugs via pharmaceutical products of different dosage forms. Oral route is considered most natural, uncomplicated, convenient and safe due to its ease of administration, patient acceptance and cost-effective manufacturing process. Pharmaceutical products designed for oral delivery are mainly conventional drug delivery systems, which are designed for immediate release of drug for rapid or immediate absorption (Robinson JR Lee, 1987).

The conventional dosage forms like solutions, suspensions, capsules, tablets and suppository etc. have some limitations such as

1. Drugs with short half-life require frequent administration, which increases chances of missing the dose of drug leading to poor patient compliance.
2. A typical peak-valley plasma concentration-time profile is obtained which makes attainment of steady state condition difficult.
3. The unavoidable fluctuations in the drug concentration may lead to under medication or over

medication as the steady state concentration values fall or rise beyond the therapeutic range.
4. Thefluctuatingdruglevelsmayleadtoprecipitationofadverseeffectsespeciallyofadrugwithsmall therapeutic index, whenever overdosing occurs

1.1 Controlled Drug Delivery Systems

Controlled drug delivery systems have been developed which are capable of controlling the rate of drug delivery, sustaining the duration of therapeutic activity or targeting the delivery of drug to a tissue controlled drug delivery or modified drug delivery systems are conveniently divided into different categories.

1. Delayed release
2. Sustained release

Oral Controlled Drug Delivery Systems

Oralcontrolledreleasedrugdeliveryisasystemthatprovidescontinuousoraldeliveryof drugs at predictable and reproducible kinetics for a predetermined period throughout the course of GI transit and also the system that target the delivery of a drug to a specific region within the GI tract for either a local or systemic action (Vora et al.), 1996

Classification of Oral Controlled Release Systems

The majority of oral controlled release systems rely on dissolution, diffusion, or a combination of both mechanisms, to generates low release of drug to gastro intestinal milieu

Diffusion controlled system

The nature of the membrane determines the rate of drug release. The characteristics of reservoir diffusion systems are

1. Zero order drug release is possible.
2. The drug release rate is dependent on the type of polymer.
3. High molecular weight compounds are difficult to deliver through the device. Coating and micro encapsulation technique can be used to prepare sub devices.

I. Matrix Devices

It consists of drug dispersed homogeneously in a matrix. The characteristics of the matrix
Diffusion system is

1. Zero order release cannot be obtained.
2. Easy to produce than reservoir devices.
3. High molecule weight compounds are delivered through the devices.

A) Dissolution controlled system

The common forms of dissolution controlled systems fall into two categories.

Matrix Dissolution Controlled System

The common forms of dissolution controlled systems fall into two categories.
In this the drug is compressed along with the slowly dissolving carrier of some sort into a tablet form. Here the rate of drug availability is controlled by the rate of penetration of the dissolution fluid into the matrix. The techniques used in the preparation of these systems are Aqueous dispersions, congealing, spherical agglomeration etc. The materials used are hydrated methylcellulose, carnauba wax, carbopol, silicone, glyceryl tristearate, methyl acrylate- methyl methacrylate, polyvinyl chloride etc.

Encapsulation Dissolution Control System

These are prepared by giving coating to Particles, seeds or granules by using the technique such as microencapsulation. The materials used for coating are shellacs, glyceryl monostearate, ethyl cellulose, acrylic resins, cellulose acetate butyrate, di-polylactic acid, polyvinyl chloride, sodium carboxy methyl cellulose, etc.

Diffusion and Dissolution Controlled System

In a bio erodible matrix, the drug is homogenously dispersed in a matrix and it is released either by swelling controlled mechanism or by hydrolysis or by enzymatic attack.

The development process of oral controlled drug delivery system is precluded by several physiological difficulties, such as an ability to restrain and localize the drug delivery system with in desired region of the gastrointestinal tract and the highly variable nature of gastric emptying process. Therefore the scientific frame work required for the successful development of an oral drug delivery system consists of basic understanding of(i)physicochemical, pharmacokinetic and pharmacodynamic characteristics of the drug; (ii) the anatomic and physiologic characteristics of the gastrointestinal tract and(iii) physic chemical characteristics and the drug delivery mode of the dosage form to be designed (BankerandRhodes,2002).

The main areas of potential challenge in the development of oral controlled drug delivery systems are

1.2 Development of Drug Delivery System

To develop a viable oral controlled release drug delivery system capable of delivering a drug at a therapeutically effective rate to a desirable site for required duration for optimal treatment is obtained by optimizing the following two parameters.

Modulation of Gastrointestinal Transit Time

To modulate the GI transit time so that the drug delivery system developed can be transported to a target site or to the vicinity of an absorption site and reside there for a prolonged period of time to maximize the delivery of a drug dose.

Minimization of Hepatic First Pass Elimination

If the drug to be delivered is subjected to extensive hepatic first-pass elimination, preventive measures should be devised to either by pass or minimize the extent of hepatic metabolic effect (Streubelet al.,) 2003

Gastro retentive Drug Delivery Systems

The development of oral CRDDS has been hindered by the inability to localize the system in the selected regions of the GIT. There has been considerable research over the last decade on the possibility of controlled and site specific delivery to the GIT by controlling the gastrointestinal transit of orally administered dosage forms using Gastro Retentive Drug Delivery Systems (GRDDS). Such GRDDS possess the ability of retaining the drug in GIT particularly in the stomach for long periods (S. S.Davis 2005).The idea of gastro retention stems from the need to localize drugs at specific region of GIT such as stomach in the body. Often the extent of drug absorption is limited by the residence time of the drug at absorption site. The transit time in GIT i.e., from the mouth to anus, varies from one person to another. It also depends upon the physical properties of the object in gested and the physiological conditions of the alimentary canal. In addition, the relatively brief G.I. transittime(8-12hr) for most of the drugs impedes the formulation of once daily dosage form. Many drugs show poor bioavailability (BA) in the presence of intestinal metabolic enzymes like cytochrome P450(CYP3A), abundantly present in the intestinal epithelium. Their activity decreases longitudinally along the small intestine, with levels risings lightly from the duodenum to the jejunum and declining in the ileum and colon. This nonuniform distribution of CYP3A causes regional variability in the absorption of drugs that are the substrates of those enzymes S. S.Davis 2005.

The therapeutic window of many drugs is limited by their short circulating half-life and absorption via a defined segment of the intestine. Such pharmacokinetic limitations lead in many cases to frequent dosing of these medications to achieve the required therapeutic effect. This results in "pill burden" and consequently decreased patient compliance. The phenomenon of absorption via a limited part of the GI tract has been termed the "narrow absorption window" once the dosage form passes the absorption window, the drug will be neither bioavailable nor effective. In extreme cases, drugs that are insufficiently absorbed due to narrow absorption cannot be delivered entirely, and are either given by a parental route or the development of Novel Techniques or by GRDDS.

A rational approach to enhance bioavailability and improve pharmacokinetic and pharmacodynamic profiles is to retain the drug reservoir above its absorption area, i.e., in the stomach and to release the drug in a controlled manner, so as to achieve a zero order kinetics (i.e., "oral infusion") for a prolonged period of time. The need for gastro retentive dosage forms (GRDFs) has led to extensive efforts in both academia and industry towards the development of such drug delivery systems (S. S.Davis 2005). GRDFs extend significantly the period of time over which the drugs may be released.

Various approaches have been pursued to increase the retention of an oral dosage form in the

stomach [3,4]. These systems include: Floating systems, bio adhesive systems, swelling and expanding systems, high density systems. Floating Drug Delivery System (FDDS) has a bulk density lowerthangastricfluidsandthusremainbuoyantinthestomachforaprolongedperiodof time, without affecting the gastric emptying rate [5-7]. . While the system is floating on the gastric contents, the drug is released slowly at a desired rate from the system. After the release of the drug, the residual system is emptied from the stomach. This, results in an increase in the GRT and a better control of the fluctuations in the plasma drug concentration[8-10].

Formulation considerations for GRDDS

1. It must show effective retention in the stomach to suit for the clinical demand.
2. It must be convenient for intake to facilitate the patient compliance.
3. It must have sufficient drug loading capacity,
4. It must control the drug release profile,
5. It must have full degradation and evacuation of the system once the drug release is completed.
6. It should not have effect on gastric motility including emptying pattern.
7. It should not have other local adverse effects

1.5.5.1. Floating DDS (FDDS)

Floating systems, first described by Davies in 1968, have a bulk density lower than the gastric content. They remain buoyant in the stomach for a prolonged period of time, with the potential for continuous release of drug. Eventually, the residual system is emptied from the stomach. Gastric emptying is much more rapid in the fasting state and floating systems rely heavily on the presence of food to retard emptying and provide sufficient liquid for effective buoyancy. In 1985, Mojaverian et al. reported that the amount, nature and caloric content of the food and the frequency of feeding profoundly affect gastric retention (P Mojaverian et al) 1988.

Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. 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. However, besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal. To measure the floating force kinetics, a novel apparatus for determination of resultant weight (RW) has been reported in the literature.

1.5.5.1.1. Classification of FDDS

Based on the mechanism of buoyancy, floating systems can be classified into two distinctcategories

A. Non-effervescentsystems.[11-14].
B. Effervescent systems.

The gelatinous polymer barrier formation results from hydrophilic polymer swelling. Drug isreleasedby diffusion and erosion of the gel barrier.

The HBS must comply with three manor criteria L.J. Caldwell etal 1988

1. It must have sufficient structure to form a cohesive gel barrier
2. It must maintain an overall specific gravity lower than that of gastric contents i.e.,1.004-1.01 g/ml
3. It should dissolve slowly enough to serve as a reservoir for the delivery system

A bilayer tablet can also be prepared to contain one immediate-release and other sustained-release layer. Immediate-release layer delivers the initial dose where as SR layer absorbs gastric fluid and forms a colloidal gel barrier on its surface Sheth et al 1978.

Bilayer formulations in which one layer conferred the buoyancy and the other controlled the drug release. Oth et al. produced a bilayer formulation of misoprostol against gastric ulcers (Oth.M1992).Both layers contained swellable polymers and only one contained drug(Fig.4) so that buoyancy and drug release could be optimized independently. They observed a mean gastric residence time >3 hrs after a single meal (breakfast) and >10 hrs after a succession of meals. Mitrapatenteda multilayered floating laminate

1. Intragastric floating drug delivery device

The device comprised of a drug reservoir encapsulated in a microporous compartment having pores along its top and bottom surfaces. The peripheral walls of the drug reservoir compartment were completely sealed to prevent any physical contact of the undissolved drug with the stomach walls. The floatation chamber caused the system to float in the gastric fluid [Yuasa.Hetal1996], developed intragastric floating SR granules of diclofenac sodium using polymer solutionof hydroxypropyl cellulose L grade (HPC-L) and ethylcellulose, and calcium silicate as a floating carrier, which has a characteristically porous structure with numerous pores and a large individual pore volume. The coated granules acquired floating ability from the air trapped in the pores of calcium silicate when they were coated with a polymer(Singh. Brahma N., KwonH.Kim 2000).

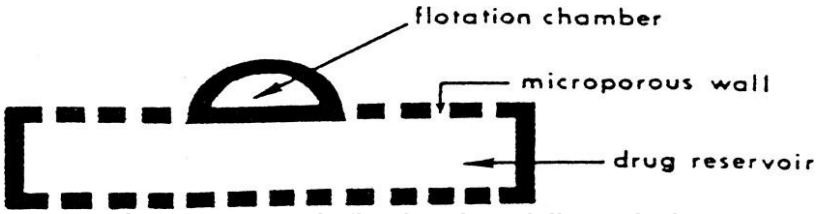

Fig. 1: Intragastric floating drug delivery device

2. Floating tablets

Single-unit floating tablets prepared based on polypropylene foam powder and matrix-forming polymer. Incorporation of highly porous foam powder in matrix tablets provided density much lower than the density of the release medium. A 17% wt/wt foam powder (based on mass of tablet) was achieved *in vitro* for at least 8 hours. It was concluded that varying the ratios of matrix-forming polymers and the foam powder could alter the drug release patterns effectively (Shweta Aroraet al 2005 & Streubel A et al 2003)

3. Floating Microspheres

Conventionally, the drug-loaded microspheres have been developed by emulsification and solvent-evaporation method. Example was preparation of hollow microspheres (micro balloons), loaded with ibuprofen in their outer polymer shell. The ethanol-dichloromethane solution of the drug and an enteric acrylic polymer was poured into an agitated aqueous solution of PVA that was thermally controlled at 40^{o}C. The gas phase generated in dispersed polymer droplet by evaporation of dichloromethane formed an internal cavity in microspheres of polymer with drug. The micro balloons floated continuously over the surface of acidic dissolution media containing surfactant for greater than 12hr *invitro*. The drug release was higher in pH7.2 than in pH 6.8.

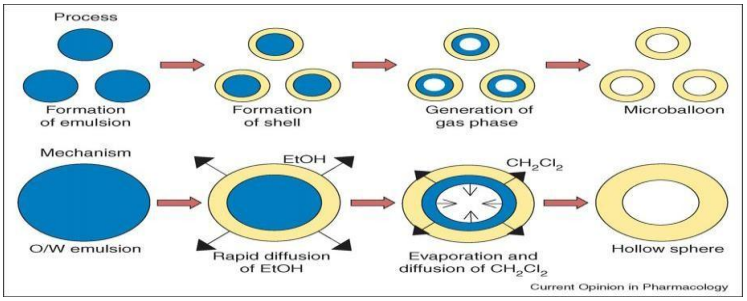

Fig. 2: Floating Microsphere

B. Effervescent systems or Gas generating systems

A DDS can be made to float in the stomach by incorporating a floating chamber with may be filled with vacuum, air or inert gas. The gas in the floating chamber can be introduced either by the effervescent reaction between organic acids and bicarbonate salts or by the volatilization of an organic solvent.

1. Effervescent reaction Tablets

Floatability can also be achieved by generation of gas bubbles. CO2 can be generated in situ by incorporation of carbonates or bicarbonates, which react with acid—either the natural gastric acid or co-formulated as citric or tartaric acid. The optimal stoichiometric ratio of citric acid and sodium

bicarbonate for gas generation is reported to be 0.76:1 (Bardonn. P.L et al2006 &,Garg. S., S. Sharma 2003). The generated CO2 which gets entrapped in the gellified hydrocolloid layer of the system, thus decreasing its specific gravity and making it float over chime. These tablets may be either single layered (Hashim, H., Liwan, A 1987), wherein the CO2 generating components are intimately mixed with in the tablet matrix, or bilayered.

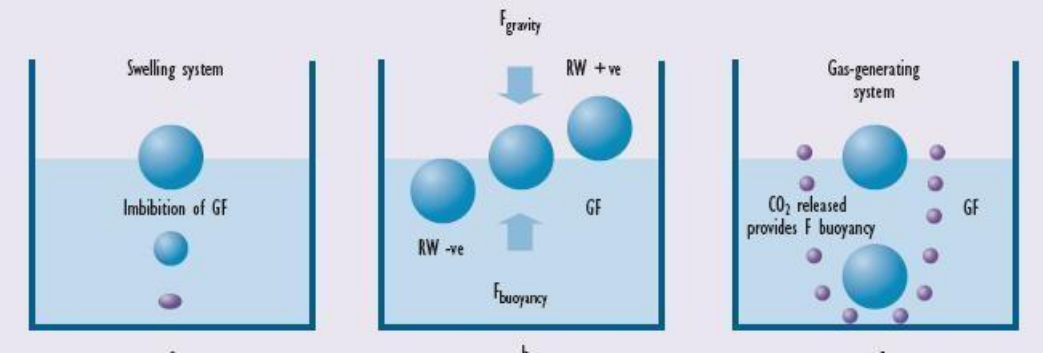

Fig. 3: Formation of CO2 in gas generating systems

2. Volatile liquid containing systems

The GRT of a DDS can be sustained by incorporating an inflatable chamber, which contains a liquid i.e., ether, cyclopentane, that as gasifies at body temperature to cause the inflation of the chamber in the stomach.

Two patents on FDDS issued to the Alza Corporation disclosed drug delivery devices for the controlled and continuous administration of medicinal agents.

These ***Gastro-inflatable drug delivery devices*** are osmotically controlled floating systems containing a hollow deformable unit that can convert from a collapsed to an expanded position, and returns to the collapsed position after an extended period. The deformable system consists of two chambers separated by an impermeable, pressure-responsive, movable bladder. The first chamber contains the drug and the second chamber contains the volatile liquid.

The device inflates, and the drug is continuously released from the reservoir into the gastric fluid. The device may also consist of a bioerodible plug made up of PVA, polyethylene etc. that gradually dissolves causing the inflatable chamber to release gas and collapse after a predetermined time to permit the spontaneous ejection of the inflatable system from the stomach. **Intragastric osmotically controlled *DDS*** consists of an osmotic pressure-controlled drug delivery device and an inflatable floating support in a bioerodible capsule, when the device reaches the stomach, bioerodible capsule quickly disintegrates to release the DDS. The floating support is made up of a deformable hollow polymeric bag containing a liquid that gasifies at a body temperature to inflate the bag. The osmotic-pressure controlled drug delivery device consists of two compartments

- A drug reservoir compartment
- An osmotically active compartment

The drug reservoir compartment is enclosed by a pressure-responsive collapsible bag, which is impermeable to vapors and liquids and has a drug delivery orifice. The osmotically active compartment contains an osmotically active salt and is enclosed within a semi permeable housing.

In stomach, the water in the gastric fluid is continuously absorbed through the semi-permeable membrane into the osmotically active compartment to dissolve osmotically active salt. The osmotic pressure is thus created, which acts as a collapsible bag, and in turn forces the drug reservoir compartment to reduce its volume and activate the release of the drug solution formulation through the delivery orifice. The floating support is also made to contain a bioerodible plug that erodes after a predetermined time to deflate the support. The deflated DDS is then excreted from the stomach (Michaels).

C. Raft- forming systems

Here, a gel-forming solution (e.g. sodium alginate solution containing carbonates or bicarbonates) swells and forms a viscous cohesive gel containing entrapped CO2 bubbles (Fig. 4) on contact with gastric fluid. Formulations also typically contain antacids such as Aluminum hydroxide or Calcium carbonate to reduce gastric acidity. Because raft-forming systems produce a layer on the top of gastric fluids, they are often used for gastro-esophageal reflux treatment (Washington. N1987,

Foldager. Jetal 1991, Fabregas.J. Let al 1994.

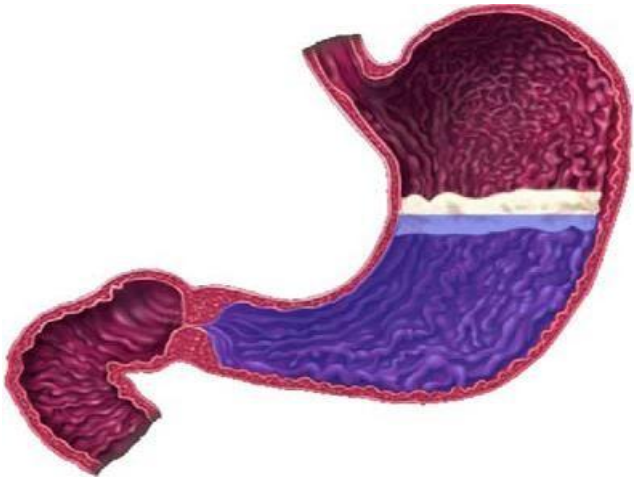

Fig. 4: Schematic illustration of the barrier formed by a raft-forming system

D. Low-density systems

Gas-generating systems inevitably have a lag time before floating on the stomach contents, during which the dosage form may undergo premature evacuation through the pyloric sphincter. Low-density systems (<1 g/cm3) with immediate buoyancy have therefore been developed. They are made of low-density materials, entrapping oil or air. Most are multiple unit systems, and are also called ‘‘micro balloons’’ because of the low-density core

METHODOLOGY

Table 1: LIST OF MATERIALS AND SUPPLIERS

S.NO	INGREDIENTS	SUPPLIERS
1	Itopride	SuppliedByPharmaTrain
2	HPMC K100M	SD FineChemicals,Mumbai
3	Eudragit RS100	SD FineChemicals,Mumbai
4	Sodium alginate	SD FineChemicals,Mumbai
5	Sodium Bicarbonate	SD FineChemicals,Mumbai
6	Citric Acid	SD FineChemicals,Mumbai
7	MCC	SD FineChemicals,Mumbai
8	Aerosil	SD FineChemicals,Mumbai
9	Magnesium Stearate	SD FineChemicals,Mumbai

Table 2: Formulation Table

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Itopride	100	100	100	100	100	100	100	100	100
HPMC K100M	50	100	150	-	-	-	-	-	-
EudragitRS100	-	-	-	50	100	150	-	-	-
Sodiumalginate	-	-	-	-	-	-	50	100	150
Sodium bicarbonate	60	60	60	60	60	60	60	60	60
Citricacid	30	30	30	30	30	30	30	30	30
MCC	140	90	40	140	90	40	140	90	40
Aerosil	10	10	10	10	10	10	10	10	10
Mg.Stearate	10	10	10	10	10	10	10	10	10
Totalweight	**400**	**400**	**400**	**400**	**400**	**400**	**400**	**400**	**400**

Table 3: List of Equipment's

S.NO	Name of The Equipment	Model
1	Electronic weighing balance	Scale-tec
2	Friabilator	Roche Friabilator Electrolab, Mumbai
3	Laboratory oven	Dtc-00r
4	Compression machine	Cmd (Cadmach)
5	Tablet hardness tester	Pfizer Hardness Tester, Mumbai
6	UV	LabindiaUv3000+
7	Dissolution apparatus	ElectrolabTDT-08L
8	Vernier calipers	Cd-6"Cs

RESULTS AND DICUSSION

1. Construction of Standard calibration curve of Itopride in 0.1N HCL:

The absorbance of the solution was measured at 257nm, using UV spectrometer with 0.1N HCl as blank. The values are shown in table. A graph of absorbance Vs Concentration was plotted which indicated in compliance to Beer's law in the concentration range 2 to 10µg/ml

Table 4: Standard Calibration
Graph values of Itopride in 0.1NHcl

Concentration (µg / mL)	Absorbance
0	0
2	0.136
4	0.248
6	0.355
8	0.462
10	0.581

Standard plot of Itopride plotted by taking absorbance on Y–axis and concentration (µg/ml) on X–axis, the plot is shown figure

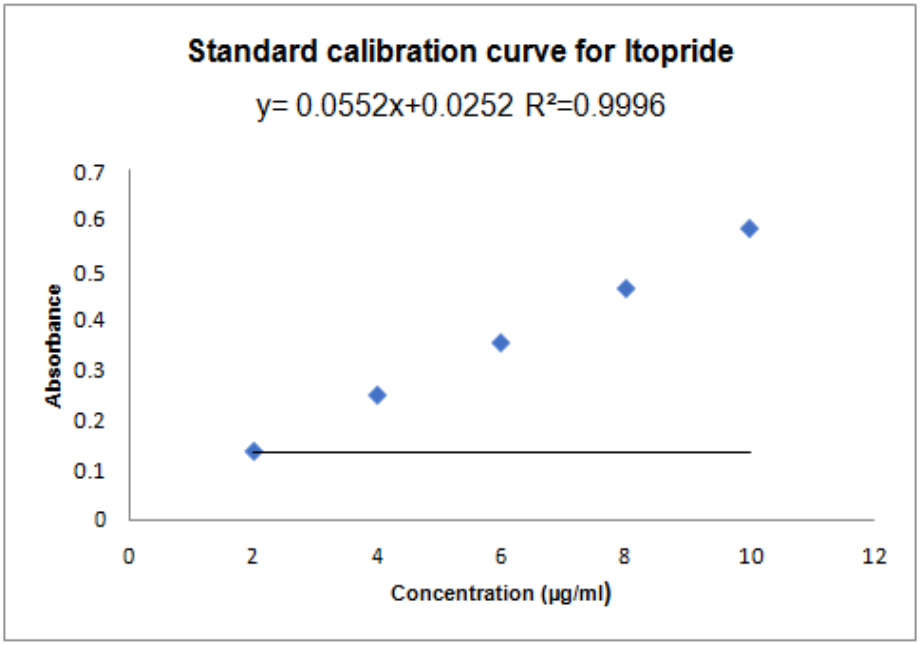

Fig. 5: Standard calibration curve of Itopride in 0.1 NHcl

Inference

The standard calibration curve of Itopride in 0.1NHCl showed good correlation with regression value of 0.999.

I. Evaluation of Tablets

Pre compression studies of Itopride Floating tablets

Table 5: Pre compression studies of Itopride Floating tablets

Formulation Code	Bulk density	Tapped density	Cars index	Hausners ratio	Angle of repose(˚)
F1	0.515	0.522	13.15	1.10	22.17
F2	0.471	0.476	16.23	1.21	31.11
F3	0.505	0.527	14.26	1.15	25.71
F4	0.522	0.519	12.36	1.09	23.31
F5	0.496	0.499	17.42	1.12	28.27
F6	0.481	0.511	18.09	1.07	24.67
F7	0.500	0.581	13.12	1.16	22.32
F8	0.441	0.510	13.27	1.25	27.37
F9	0.401	0.462	13.10	1.5	23.17

- The Itopride floating tablets were evaluated for their flow properties; the results for the blends of compression tablets were shown in Table.
- The bulk density and the tapped density for all formulations were found to be almost similar.
- The Carr's index and Hausner's ratio were found to be in the range of ≤18 and 1.07 to 1.5 respectively, indicating good flow and compressibility of the blends.
- The angle of repose for all the formulations was found to be in the range of 22.17-31.11˚ which indicating passable flow (i.e. incorporation of glidant will enhance its flow).

Table 6: In-vitro Dissolution results for formulation trails

Time (hrs)	%Drug released								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0	0	0	0	**0**	0	0	0	0	0
1	45	37	35	**19**	16	13	40	30	15
2	57	47	47	**25**	22	21	52	43	24
4	80	69	55	**46**	43	35	75	65	42
6	99	80	75	**67**	55	48	88	79	63
8	100	100	91	**77**	63	54	96	91	79
10	100	100	98	**89**	77	67	100	98	86
12	100	100	100	**100**	83	74	100	100	95

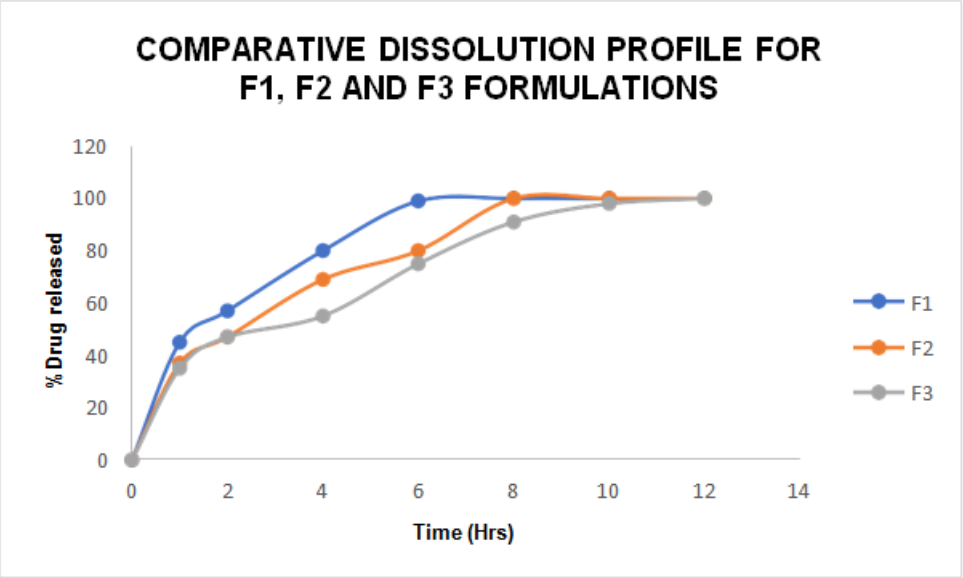

Fig. 6: Comparative dissolution profile for F1, F2 and F3 formulations

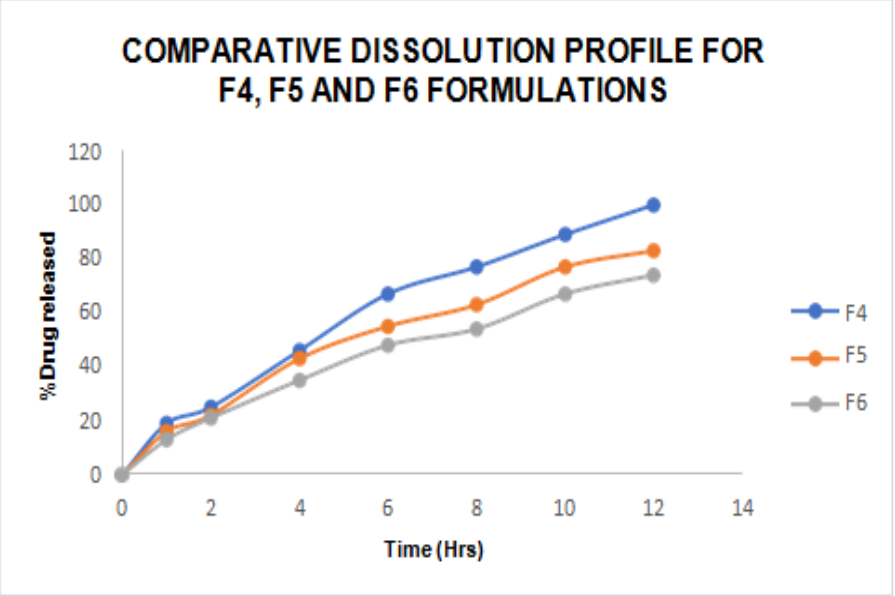

Fig. 7: Comparative dissolution profile for F4, F5 and F6 formulations

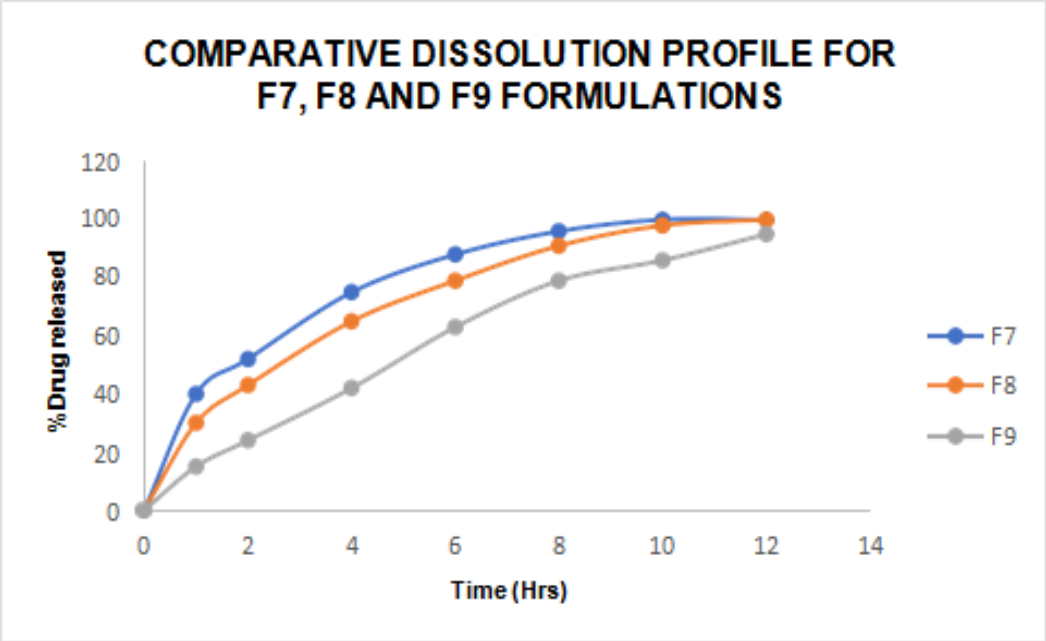

Fig. 8: Comparative dissolution profile for F7, F8 and F9 formulations

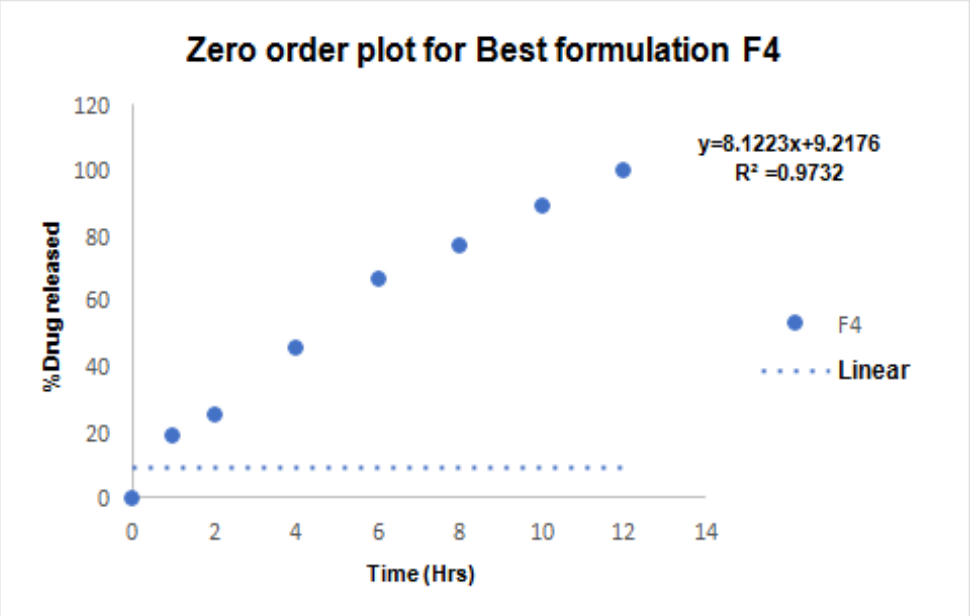

Fig. 9: Zero order plot for best formulation F4

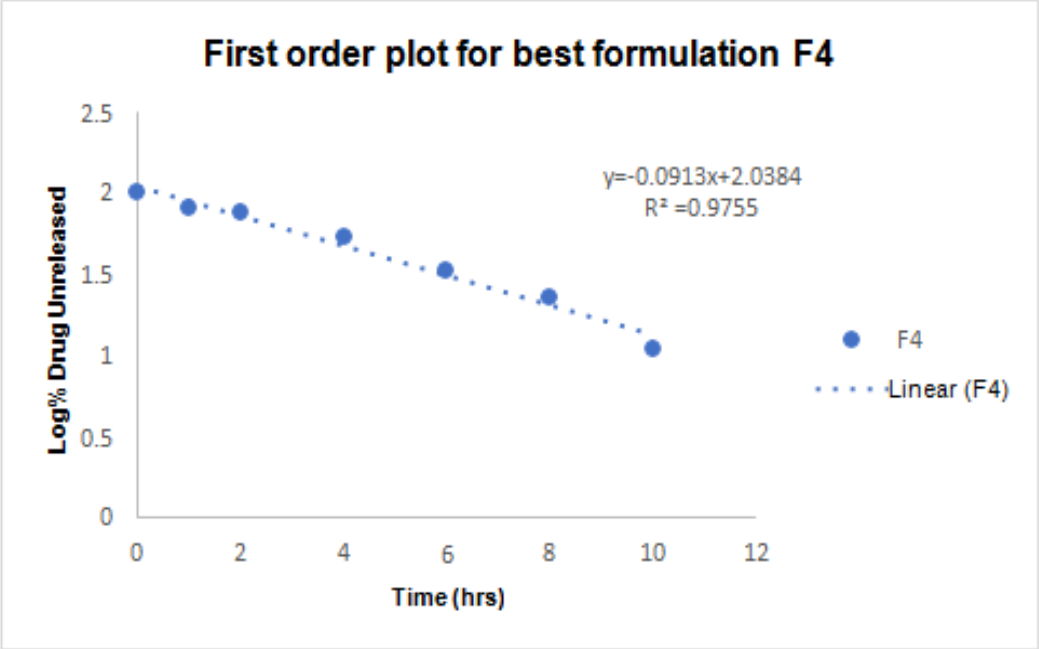

Fig. 10: First order plot for best formulation F4

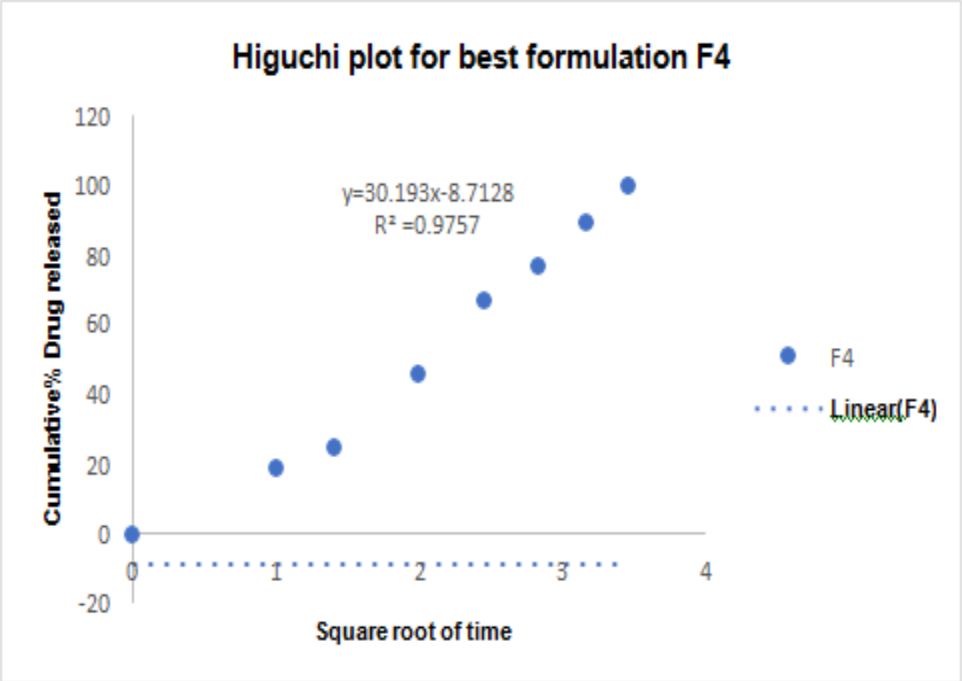

Fig. 11: Higuchi plot for best formulation F4

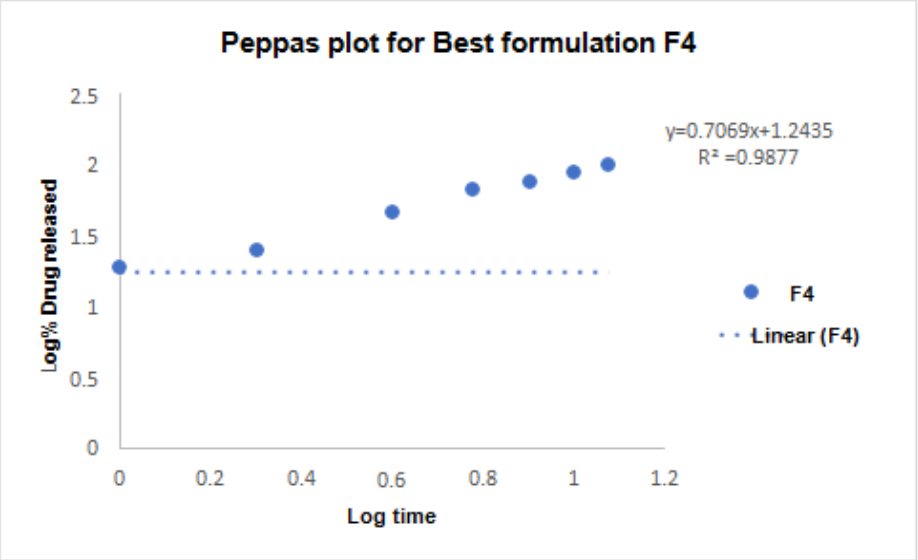

Fig. 12: Peppas plot for best formulation F4

Table 7: R^2value and N result table

Formulation Code	r^2values (Regression coefficient)				n value
	Zero order	First order	Higuchi	Peppas	
F4	0.973	0.975	0.975	0.987	0.706

Inference

1. Among the different control release polymers Eudragit RS100 was showing highest drug release retarding capacity.
2. Formulation F4 was showing the satisfactory results.
3. F4 formulation diffusion exponent n value is in between 0.45 to 0.89 so both formulations was following non fickian anmolous diffusion model.
4. Higuchi plots for F4 formulations are having good correlation values so the drug is releasing diffusion mechanism.

CONCLUSION

From the experimental data, it can be concluded that

- Floating Tablets of Itopride are formulated to increase gastric residence time and there by improve its therapeutic efficacy.
- Eudragit RS 100 was respectively showed better Sustained drug release of Itopride.
- When drug: polymer concentration increases the release rate decreases this is because of reason when the concentration of polymer increases the diffusion pathlength increases
- Formulated tablets showed satisfactory results for various Post compression evaluation parameters like: tablet thickness, hardness, weight variation, floating lag time, total floating time, content uniformity and *in vitro* drug release.
- Formulation F4 gave better-controlled drug release and floating properties in comparison to the other formulations.
- The release pattern of the F4 formulations was best fitted to Korsmeyer-Peppas model, Higuchi and first-order model.
- The most probable mechanism for the drug release pattern from the formulation was non-Fickian diffusion or anomalous diffusion.

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