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Research Article

GASTRO RETAINTIVE DRUG DELIVERY SYSTEM: A REVIEW

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A B S T R A C T

Purpose: To make a review by focusing upon various criterias and concepts of Gastro Retaintive Drug delivery System. Methods: This review is prepared by focusing on recent literatures on needs, advantages and disadvantages, factors affecting, suitable and unsuitable drugs, pharmacokinetic aspect, mechanism, approaches, list of polymers and other ingredients used, in vitro and in vivo evaluation, literature survey, marketed products, patented formulations, applications, limitations, and future aspect of Gastro Retaintive Drug Delivery system. **Result:** It is an Hydrodynamically Balanced System (H.B.S) or Low Density system (LDS) which improve the controlled delivery of drug that have an absorption window by continuously releasing the drug for prolonged period of time at desired rate before it reaches at absorption site and improve the bioavailability. **Conclusion:** The GRDDS can be considered as a Controlled Drug Delivery System (CDDS) in which ideal doses form attains the desired therapeutic concentration of drug in plasma and maintains constant frequency for entire duration of treatment.

INTRODUCTION

Oral route of administration is one of the most reliable method of drug administration must produce better plasma drug [1]concentration and must produce better bioavailability,[2] easy of intake, and increase patient compliance. The oral drug delivery system is of two types. 1- First release 2-Prolonged release. The fast release form of tablet lead to fluctuation in plasma drug level and require multiple dose. The prolonged release (Controlled Drug Delivery System) is divided into four types.1-Delayed release (Enteric coated) 2- Extended release (Zero order, First order, Biphasic release) 3- Programmed release (Pulsatile, triggered), 4- Site specific or timed release (Colonic delivery, Gastric retention).[3.] Control release implies the predictability and reproducibility to control the drug release in the body with lower and less frequent dose.[1]

Gastro retentive drug delivery system (GRDDS) can remain in gastric region for several hours and hence prolong the gastric residence time of drug. It improve bioavailability, reduce drug waste, and improve solubility of drug. That are less soluble in a high pH environment. It has application for local drug delivery to the stomach and proximal small intestine.[4]

The objective of the present research to make a detailed review upon Gastro retentive drug delivery system (GRDDS) , its criterias and concepts

Need of Grdds

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produce incomplete drug release from various dosage form in absorption zone (Stomach or upper part of small intestine) and produce less bioavailability[5]

To achieve prolong Gastric Resistance Time and to Gastric Emptying Time to be able to withstand the forceful peristaltic wave in stomach, constant contraction, grinding, churning the GRDDS is developed .[3,6]

***Advantages of Grdds*:[7,6,8]**

1. The drugs absorb through stomach at definite pH condition.
2. These are not restricted for medicaments which are principally absorb in stomach.
3. It produce independent site of absorption.
4. They remain buoyant on gastric fluid due to lower bulk density than gastric fluid.
5. They produce better bioavailability
6. These are implemented for drugs having narrow absorption window
7. They stabilise the therapeutic level for prolonged period of time.
8. They produce better Gastric Retention Time and Gastric Emptying Time.
9. They produce site specific drug action in stomach and small intestine related problems.
10. They provide systemic and controlled drug delivery system.
11. They minimise over use of drug at disease site.
12. They minimise the variance in concentration of drugs effect.

13. They reduce counter activity by body and provide higher efficiency.
14. They provides control rate of fluctuation.
15. They provide selective receptor activation.

***Disadvantages of Grdds*:[7,6,8]**

1. May irritate in stomach lining.
2. Required level of fluid in the stomach should present.
3. On multiple administration increasing the dose size may cause hazard.
4. Drugs may cause problems in gastric solubility.
5. The drug efficacy depend upon upright movement .
6. Drug release at particular site of stomach is more beneficial.
7. It is not suitable for drugs with stability or solubility problems in the stomach .
8. Sufficient water (200-250 ml) to be taken with dosage form.

***Factors Affecting Grdds*: [7,9]**

Table 1 Factors controlling GRDDS and their normal range.

Sl no	Factors controlling grdds	Normal range
1	Particle size	1-2 mm
2	Density	1gm/cm^3 to 2.5gm/cm^3
3	Size	7.5 in diameter
4	Shape of dosage form	Round or spherical shape
5	Single or multiple formulations	Multiple formulations are preferable.
6	Food intake	GRT is longer in fed state
7	Nature of meal	Presence of fatty acid and indigestible polymer shows less gastric retention time.
8	Frequency of intake	Increase 400 times due to low frequency of MIMigrating Myoelectric Reflex.(MMC)
9	Posture	Varies between spine and upright ambulatory tract.
10	Gender	Male having better GRT than female
11	Age	Age >70 shows longer GRT
12	Nature of Drugs	Drug must be gastric acid friendly
13	Disease state	GRT decreases in diabetic, hypothyroidism, duodenal ulcer
14	Body mass index	More obesity can cause less GRT
15	Lypophilicity of drug	Lypophilic drugs are better absobable
16	Specific gravity	Must lower than Gastric contents (1.004-1.01 gm/cm^3)

***Drug Suitable for Grdds*:[7,5]**

Table 2 Drug suitable for GRDDS

Sl no	Conditions	Examples
1	That disturb colonic microbes(Helicobacter pylori)	Antibiotics,Metoprostol
2	Drug that degrade the colon	Ranitidine,MetforminHcl
3	Drugs absorbe rapidly in GIT	Metronidanzole,Tetracycline
4	Drugs with narrow absorption of window	Cyclosporin,Methoxitrate
5	Drugs which are poorly soluble in alkaline pH	Forosemide,Diazepam,Veraprimil
6	Drugs that primarily absorb in stomach	Amoxilline
7	Drugs acting locally in stomach	Antacid

***Drugs Not Suitable for Grdds*:[7,5,9]**

Table 3 Drug not suitable for GRDDS

SL No	CONDITIONS	EXAMPLES
1	Drugs with very limited acid solubility	Phenytoin
2	Drugs that suffer instability in GIT pH	Erythromycin,Rebiprazole,Clarithromycin
3	Drug that selectively release in colon	Corticosteroids

***Pharmacokinetic Aspects of Grdds*:[10]**

Absoption Window

The candidates for GRDDS are molecules that have poor colonic absorption but are characterized by better absorption properties at upper part of GIT.

Enhance Bioavailability

Compound having narrow absorption window having the possibility of continuous administration of the compound at specific site.

Enhance first Pass Biotransformation

Pre-systemic metabolism of the tested compound is increased when the drug is presented to metabolic enzyme (Cytochrom p450) in a sustained manner

Improve Bioavailability due to Reduced P-Glycoprotein Activity in t6he Duodenum

The drugs that P-gp substrate do not undergoes oxidative metabolism. GRDDS may elevate absorption compaired to immediate and CR dosage form.

Reduce Frequency of Dosing

For drugs with relatively short biological half life ,sustained and slow input from GRDDS result flip-flop pharmacokinetic and enable reduced dosing freequency.

Targeted Therapy for local Elements in upper GIT tract

The prolonged and sustained administration of the drug from GRDDS to the stomach may produce local therapy in the stomach and small intestine.

***Pharmacodynamic Aspects of Grdds*:[21]**

Reduce Fluctuation of Drug Concentration

The fluctuations in drug effects are minimized and concentration dependent adverse effects that are associated with peak concentration can be prevented.

Improved Selectively in Receptor Activation

Minimization of fluctuation in drug concentration also make it possible to obtain certain selectively in the elicited pharmacological effect of drugs that activate different type of receptors at different concentration.

Reduced Counter Activity of the body

Slow input of drug into the body was shown to minimize the counter activity leading to higher drug efficiency.

Extended Time over Critical (Effective) Concentration

Clinical response is not associated with peak concentration. but rather with duration of time over critical therapeutic concentration.

Minimize Adverse Activity of Colon

The pharmacodynamnic aspect provide the rationale for GRDDS formulation for beta-lactum antibiotics that are only absorbed from the small intestine and due to presence at colon it develop of microorganism's resistance,

Mechanism of Grdds

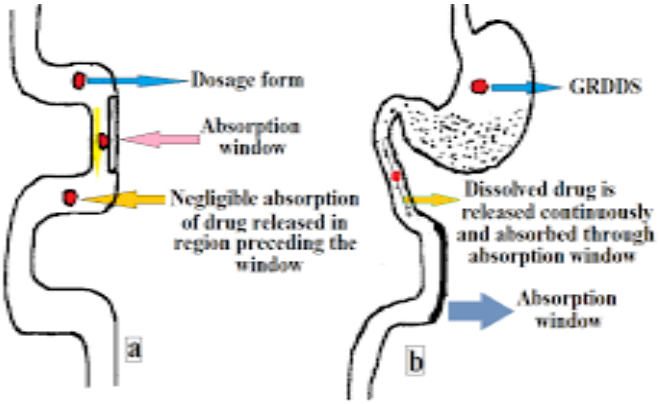

Figure 1 Mechanism of Grdds. [12]

(a)Conventional drug delivery systems
(b) Gastro retentive drug delivery systems.

Common Difference Between Conventional Drug Delivery System And Gastro Retentive Drug Delivery System:[40,43]

Table 4 Common difference between Conventional Drug Delivery System and Gastro Retentive Drug Delivery System

Sl No	Parameters	Conventional Drug Delivery System	Gastro Retentive Drug Delivery System
1	Patient compliance	Poor	Better
2	Dose dumping	High risk	No risk
3	Drug having low absorption in small intestine	Not appropriate	Appropriate
4	Drug acting locally in stomach	Not very much use full	Much useful
5	Toxicity	Greater susceptibility towards toxicity	Low susceptibility
6	Drug with poor solubility at higher pH	Not much beneficial	Much beneficial
7	Drug that undergoes degradation in colon	Not much beneficial	Much beneficial
8	Drug that have fast GIT Absorption	Not much beneficial	Much benifical

List of Polymers and Other Ingredients Used In Grdds:[10,13,15]

Table 6 List of polymers and other ingredients used in GRDDS

Sl no	Category	materials
1	POLYMERS	**Cellulose polymers**-HPMC K4M,HPMCK15,HPMC K 100, HPMC 4000,HPMC K4,HPC-M,HPC-L,HPC-H,HPC-M,Ethyl cellulose. Methyl cellulose. **Eudragit**- Eudragit s 100,Eudragit RL, Eudragit-s,Eudragit-RS **Alginates**- Calcium alginate, Sodium alginate etc **Others**-Propylean foam, Poly methyl Metha crylate ,PVA, Polycarbonate, Metolose S.M 100,PVP, Polyox, Acrylic polymer, Carbopol, Pectine.
2	INERT FATTY MATERIALS (5% TO 75%)	Bees wax ,Long chain fatty alcohols,Gelucires39/01and 43/01
3	EFFERVESCENT AGENTS	Sodium bicarbonate, Citric acid, Tatraric acid, Di Sodium Glycin carbonate, Citric Acid, Citroglycin,
4	LOW DENSITY MATERIALS	Glycin palmitosterate, Glyceryl behenate, Polypropelene low powder(Accurel MP 1000)
5	BUOYANCY INCREASING AGENTS (UPTO 80%)	Ethyl cellulose
6	RELEASE RATE ACCELERANTS (5% TO 60%)	Lactose, Mannitol, etc
7	RELEASE RATE RETARDANTS(5 % TO 60%)	Di-calcium phosphate, Talc, Magnesium stearate,

Charecterstics of Suitable Drugs For Grdds:[3,7]

Table 6 Characteristics of suitable drugs for GRDDS

	Type of dosage forms	Drugs Used
1	Floating Tablets	,Cephalexin,Ziduvudine,Losartan, Cho Pentoxyfillin,Chlorpheniramine milate, Thiophyline, Furosemide,Ciprofloxacin, Captopril,Acetyl salicylic acid, Nimodipine,Amoxycilin trihydrate, Deltiazem, Floro uracil, Predinsolon, Metformin hydrochloride, PABA,Veraprimil HCL,Isoserbide nitrate, Atenolol, Sotalol,Aceraminophane, Ampiciline
2	Floating Microspheres	Aspirin,Griseofulvin,P-Nitroaniline,Ibuprofen, Terfinadine,Tranilast , Veraprimil, Aspirin,Gresofolvin, Ibuprofen,Terfenadine,Piroxicam, Theophiline,Nifedipine, Diperidamol, Orlistat.
3	Floating Capsules	Veraprimil HCL,Chlorodiazepoxide HCL, Diazepam, Furosemide,Levodopa, Misoprostol, Propranolol HCL, Nicardipine, Pepstatin , Celiprolol HCL
4	Floating granules	Indomethacin, Diclofenac sodium,Predinsolon,Cinnarizine, Deltizem, Florouracil, Isosorbide mononitrate, Isosorbide dinitrate, Ranitine HCL
5	Floating films	Albendazole, P-Aminobenzoic acid, Piretanide, Predinsolon, Quinidine gluconate.
6	Floating powders	Riboflovin,Sotalol,Theophylline
7	Floating beads	Ranitidine HCL, Loratadine, Deltizem HCL
8	Floating In situ Gel	Aluminium Hydroxide,or Calcium Carbonate.

Evaluation of Gastroretentive Dosage Form [15]

Evaluation of a drug product is a tool to ensure

1. Performance characteristics
2. Control batch to batch quality

Apart from routine tests like general appearance, hardness and friability, drug content, weight variation, uniformity of content, disintegration time, drug release, etc., GRDDS need to be evaluated for gastroretentive performance by carrying out specific tests.

In Vitro Evaluation[47]

Floating systems

Floating lag time: It is determined in order to assess the time taken by the dosage form to float on the top of the dissolution medium, after it is placed in the medium. These parameters can be measured as a part of the dissolution test

Floating time: Test for buoyancy is usually performed in SGF Simulated Gastric Fluid maintained at 370C.The time for which the dosage form continuously floats on the dissolution media is termed as floating time.

Specific Gravity or Density: Density can be determined by the displacement method using Benzene as displacement medium.

Resultant weight: Now we know that bulk density and floating time are the main parameters for describing buoyancy. But only single determination of density is not sufficient to describe the buoyancy because density changes with change in resultant weight as a function of time. For example a matrix tablet with bicarbonate and matrix polymer floats initially by gas generation and entrapment but after some time, some drug is released and simultaneously some outer part of matrix polymer may erode out leading to change in resultant weight of dosage form.

The magnitude and direction of force or resultant weight (up or down) is corresponding to its buoyancy force (Fbuoy) and gravity force (Fgrav) acting on dosage form

Swelling Systems

Swelling Index: After immersion of swelling dosage form into SGF at 370C, dosage form is removed out at regular interval and dimensional changes are measured in terms of increase in tablet thickness or diameter with time.

Water Uptake: It is an indirect measurement of swelling property of swellable matrix. Here dosage form is removed out at regular interval and weight changes are determined with respect to time. So it is also termed as Weight Gain. Water uptake = WU = (Wt – Wo) * 100 / Wo Where, Wt = Weight of dosage form at time t; Wo = Initial weight of dosage form II)

In Vitro Dissolution test

In vitro dissolution test is generally done by using USP apparatus with paddle and GRDDS is placed normally as for other conventional tablets.

But sometimes as the vessel is large and paddles are at bottom, there is much lesser paddle force acts on floating dosage form which generally floats on surface. As floating dosage form not rotates may not give proper result and also not reproducible results. Similar problem occur with swellable dosage form, as they are hydrogel may stick to surface of vessel or paddle and gives irreproducible results. In order to prevent such problems, various types of modification in dissolution assembly made are as follows

To prevent sticking at vessel or paddle and to improve movement of dosage form, method suggested is to keep paddle at surface and not too deep inside dissolution medium.

Floating unit can be made fully submerged, by attaching some small, loose, non- reacting material, such as few turns of wire helix, around dosage form. However this method can inhibit three dimensional swelling of some dosage form and also affects drug release.

Other modification is to make floating unit fully submerged under ring or mesh assembly and paddle is just over ring that gives better force for movement of unit

In previous methods unit have very small area, which can inhibit 3D swelling of swellable units, another method suggest the change in dissolution vessel that is indented at some above place from bottom and mesh is place on indented protrusions, this gives more area for dosage form. In-spite of the various modifications done to get the reproducible results, none of them showed correlation with the in vivo conditions. So a novel dissolution test apparatus with modification of Rossett-Rice test apparatus was proposed

In Vivo Evaluation [15]

Radiology: X-ray is widely used for examination of internal body systems. Barium Sulphate is widely used Radio Opaque Marker. So, BaSO4 is incorporated inside dosage form and X-ray images are taken at various intervals to view gastric residence (GR).

Scintigraphy: Similar to X-ray, emitting materials are incorporated into dosage form and then images are taken by scintigraphy. Widely used emitting material is Tc99.

Gastroscopy: It is peroral endoscopy used with fiber optics or video systems. Gastroscopy is used to inspect visually the effect of prolongation in stomach. It can also give the detailed evaluation of GRDDS.

Magnetic Marker Monitoring: In this technique, dosage form is magnetically marked with incorporating iron powder inside, and images can be taken by very sensitive bio-magnetic measurement equipment. Advantage of this method is radiation less and so, not hazardous.

Ultrasonography: Used sometimes, not used generally because it is not traceable at intestine.

13C Octanoic acid Breath test: In stomach due to chemical reaction, octanoic acid liberates CO2 gas which comes out in breath. The important Carbon atom which will come in CO2 is replaced with 13C isotope. So time up to which 13CO2 gas is observed in breath can be considered as gastric retention time of dosage form. As the dosage form moves to intestine, there is no reaction and no CO2 release. So this method is cheaper than other.

literature Survey [16-49]

Table 7

Sl No	Formulations	Drugs	Polymers	Techniques	Results	References
1	Floating tablets	Norfloxacin	HPMC K 4M,HPMC K 100M,Xantham gum	Wet granulation technique	The tablet remain in remain in stomach for 180 +/- 30 minutes in fasting then bioavilability increases at absoption window	16
2	bilayer floating tablet	Captopril	HPMC K ,Citric acid, Sodium bicarbonate	Direct compession technique	Approx 95% drug release in 24 hrs in vitro, while the floating lag time was 10 min and produce better in vitro dissolution rate	17
3	Floating tablets	5- Floro Uracil	Carbopol,Citric acid, sodium bicarbonate	Wet granulation technique	Produce sustained release for 24 hrs and remain buoyant for 16 hours.	18
4	Oral floating matrix tablet	Aceclofenac	HPMC K 15 M, Ethyl cellulose,Bees wax, sodium bicarbonate, Glycerin Monosterate	Melt granulation techniques	Produce floating lag time for 4 minutes,Floating duration 12 hours, drug release is 90% at the end of 12 hours.	19
5	Effervence floating tablet	Famotidine	Sodium Bicarbonate, HPMC ,Carbopol	Effervence Techniques	Produce drug release 98% for 24 hrs & remain buoyant for 24 hrs at proper storage and humidity condition.	20
6	Floating tablets	Famotidine	Methocel K 100M, Methocel K 15M	Effervence Techniques	Produce in vitro buoyancy (6to 10 hrs),produce sufficient sustained release and better physical properties.	21
7	Floating matrix tablet	Domperidone	HPMC k 4m,carbopol 943P,Sodium Alginate	Wet granulation technique	Produce desired floating tablet and prolonged drug release for 24 hrs	22
8	Hot melt extruded tablet	Chloropheniramin Acetohydroximine	Eudragit RSPO,Eudragit EPO,Sodium bicarbonate	Hot melt extruded techniques	The HME tablet showed a porous strucrutrs due to CO2 release where The DC tablet show no buoyancy and rapid release .	23
9	Floating matrix tablet	Domperidone	HPMC K4M,Carbopol934P, Sodium Alginate	Direct compression techniques	No significant effect of Sod alginate on floating property was observed but it is important for gel formation.	24
10	Floating drug	Cefuroxime axetile	HPMC K4M,HPMC K 100LV,SLS	Direct compression techniques	Polymer blend and SLS effect the time required for 50% drug release, produce rate constant for 12 hrs	25
11	Floating tablets	Theophyline	Methocell K 100M, Methocel K 15MR	Direct compression techniques	Polymer content & amount of floating agent significantly affect the mean dissolution time & % of drug release after 8 hrs.	26
12	Effervence floating tablet	Amlodipine besylate	HPMCK100M,HPMCK15M,Carbopol,Citric Acid	Direct compression techniques	The maximum floating time is 24 hrs.	27
13	First dissolving tablet	Valsartan	Crosspovidone,Ac-Di-Sol,SSG,MCC	Direct compression techniques	The drug release from FDT increase with increasing conc of Superdisintigrant ; crosspovidone.	28
14	Floating tablets	Deltiazam	HPMC K4M,HPMC K 15M,Citric acid, Naco3 ,Talc, EC, Sodium bicarbonate, Magnesium Stearate	Direct compression techniques	The obtain drug release upto 99.81%, at 12 hrs.	29
15	Floating tablets	Itopride HCL	HPMCK100M,HPMCK15M,Carbopol,Citric Acid	Direct compession technique	Better release action for 24 hours and improve Bioavilability .	30
16	Floating matrix tablet	Ranitidine	HPMC K14M,HPMC K 100M,Ca,NaHCo3,Algin ate Sesbania Gum, & Gum acacia	Direct compession technique	Excellent in-vitro floating behaviorof the tablat at the concentration of 15% (W/W)	31
17	Hemidrate floating tablet	Levofloxacin	Gelucire43/01,HPMC,	Direct compession technique	The drug release was a function of the ratio of hydrophobic and hydrophilic matrix tablet.	32
18	Gastroretentive floating matrix tablets	Domperidone Maleate		Direct compession technique	No compatability problem with the excipients. drug release from most of the formulations follows Fickian diffusion. From in-vivo X-ray studies, it was clearly observed that the floating tablets showed a gastric residence of nearly 4.5 hrs in fed state.	33
19	Hollow microsphere	Pyroxicam	HPMC K4M, HPMC K15M and HPMC 100M. polycarbonate	Solvent evaporation technique	Encapsulation efficiency is 95%.Phamacokinetic anyalysis provide better bio avilability.	34
20	Floating granules	Deltizam HCL	Gelurice 43/01	Melt granulation techniques	Retain in stomach for 6 hrs. 65% to 85 % drug was released over 6 hrs.	35
21	Hollow microsphere	NicradipineHCL, Veraprimil HCL	PVA,Ethyl acetate,	Non solvent diffusion techniques	The microsphere intended to flot over the gastric media of more than 12 hrs	36

22	Floating microparticulate	Veraprimil HCL	EC, Udragit RS-100	Solvent diffusion evaporation technique	Max ratio of component in organic phase affect size and size distribution	37
23	Floating microsphere	Veraprimil HCL	Celluloseacetate, acrycoat S100, Eudragit S100	Solvent diffusion evaporation technique	Prolong bioavilability	38
24	Floating microsphere	Deltiazam HCL,	Calcium silicate as porous carrier	Emulsion solvent diffusion technique	Prolonged release,and remain buoyant for more than 10 hrs	39
25	Hollow microsphere	Deltizam HCL , Nifedipine	PVP,EC,	Solvent diffusion evaporation technique	It flot in release medium for more thar 24 hrs.	40
26	Floating microparticulate	Metoprolol tartarate	Eudragit RSPO,Polypropelene foam powder	Non aquous emulsification S.E Technique	It became enable quantitative estimation of gastric emptying rate	41
27	Floating matrix tablet	Nifedipine	HPMC K 100 M, Sodium bicarbonate,	Wet granulation technique	The release of drug depends upon propotion of polymer present in the formulation.	42
28	Floating tablets	Atenolol	Sodiumbicarbonate	Direct compession technique	It is approach to achive in vitro buoyancy and improve absorption of Atenolol	43
29	Floating tablets	Deitizam HCL	HPMC K 4M,HPMC k 100M,	Wet granulation techniques	The drug release is 99.87 % and prolong release for the time period about 12 hrs	44
30	Floating sustained tablet	Nimodipine	HPMC,PEG 6000	Direct compression techniques	Increasing the HPMC and decresing the PEG 6000 content a decline in vitro relese.	45
31	OptimizedSustained release floating capsule	NicradipineHCL	Hydrocolloid, Sodiumbicarbonate	Capsule filling technique	Drug duration increases after administration compairing to MICARD capsule.	46
32	Floating and bioadheshive tablet	Sotalol HCL	NaCMC,HPMC,EC, Crosspovidone	Wet granulation techniques	Bioadhesive capacity is more	47
33	Floating tablets	Captopril	HPMC K 100 M, K15M,K4M,	Direct compression techniques	HPMC at 35% shows better bioavilaility ,and retain in dosage form on the desired site for effective period of time.	48
34	Alginet gel bead	Nicradipine HCL	CACL2,Sodium alginate	23 factorial design	Release occours due to diffusion and irrosion mechanism.	49

Marketed Products [3,7]

Table 8

SL No	Brand Name	Drugs	Dosage Form	Dose	Company
1	Medopar	Levodopa,& bencerazide	Floating ,CR Capsules	100mg&25mg	Roche products ,USA
2	Cifran OD	Ciprofloxacin	Tablet	500mg,1gm	Ranbaxy , India
3	Valrelease	Diazepam	Floating capsule	15mg	Hoffman -Laroche,USA
4	Topalkan	Al-Mg Antacid	Floating liquid Alginate	-	Pierrefibre drug,France
5	Convirone	Ferrus Sulphate	Colloidal gel forming FDDS	-	Ranbaxy ,India
6	Cytotec	Mesoprostol	Bilayer floating capsule	100mcg/200mcg	Pharmaacia,USA
7	Liquid Gaviscon	Al-Mg Antacid	liquid	95mg&358mg	Glaxosmithkline, India

Patented Drugs [31]

Table 9

SL No	Patent App No	IIssue/Publication date	Patent title	PATENT OWNER
1	US Patent 2013/0078,290	March 28 ,2013	Gastroretaintive dosage Form of GABA analogs	Rubicon reserch Private Limited
2	US Patent 2013/0022/654	June 24 ,2013	Control release pharmaceutical composition of Tapendatol	Lupin Limited
3	US Patent 2013/0004,434	June 03 ,2013	Gastroretaintive extend release composition of theraputic agents	Council of scientific and industrial reserch
4	US Patent 2012/0321,706	Dec20,2012	Novel gastoretaintive dosage form of poorly soluable drugs	Intech pharma limited
5	US Patent 2012/0269,866	October 25 ,2012	Gastro retaintive composition on the basis of water soluable reaction product from venyl group	Best corporation
6	US Patent 2012/0021,051	Jan 16 ,2012	Zaeplon Gastro retaintive Delivery system	Intech pharma Ltd
7	US Patent 2012/0268,666	Nov 3,2011	Novel gastroretaintive delivery system	Intech pharma Ltd
8	US Patent 2011/0171,275	July 14,2011	Gastro retaintive drug delivery system, Preparation and use	Teamacademyof Pharmaceutical sciences
9	US Patent 2007/0128,276	June 07 ,2007	Control release composition comprising Nimusilide	Pancea biotech Ltd
10	US Patent 2006/0121,106	June 08 ,2006	Theraputic system comprising Amoxicilline and Calvulinic acid	Lec Pharmaceutical DD
11	US Patent 2004/6658/962	Feb o3 ,2004	Gastro retaintive controlled release pharmaceutical dosage form	YissumReserch developmentand company
12	Us Patent 2003/0021,545	Jan 30,2003	Gastro retaintive Controll release pharmaceutical dosage form	YissumReserchdevelopment and company

1. Enhance bioavilability.
2. Sustained drug Delivery.
3. Site specific drug delivery system.
4. Absorption enhancement.
5. Minimized adverse activity at the colon.
6. Reduce fluctions of drug concentration.

Limitation [13]

1. Adequate amount of fluid (200-250 ml) must be present in stomach to retain buoyancy outcome effect of the formulation.
2. The proteinous drug having solubility incompatibility in gastric fluid.
3. Drug having good absorption capacity in whole GIT is not acceptable.

Future Aspect: [10]

1. It can produce better balance of clinical advantages of GRDDS.
2. It can produce benefit for treatment of gastric ulcer.
3. More research can be done on H-Pyroli The causative of chronic gastric and peptic ulcer.

CONCLUSION

The above study conclude that the GRDDS is a efficient technique to maintain better bioavailability by providing sustained action. GRDDS is the most safer dosage form which help for treatment of chronic disease like ulcer and carcinoma of GIT. Due to sustained action it reduce dose frequency. Minimise contra indication ,systemic toxicity[10] ,and drug dependence. A lot of researches are going on to develop new concept and to provide new prarcotherapies .It also provide many approaches with use of different polymers and other constituents can produce different range of gastroretaintive system[1,13].So it is proved that it can overcome the different physiological and pharmaceutical barrier to develop the more effective gastroretaintive dosage form.

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