ISSN: 2320 - 4230

Journal of Drug Discovery and Therapeutics

Available Online at www.jddt.in

CODEN: - JDDTBP (Source: - American Chemical Society)

Volume 5, Issue 2, February: 2017, 01-16

Review Article

AN OVERVIEW OF GASTRO RETENTIVE DOSAGE FORMS (GRDFS)

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ABSTRACT

Gastro retentive 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. Prolonged gastric retention improves bioavailability, reduces drug waste and improves solubility for drugs that are less soluble in a high pH environment. Gastro retention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patients. The goal of any drug delivery system is to provide a therapeutic amount of drug to proper site in the body to achieve promptly and then maintain a desired drug concentration. Various dosage alternatives found by recent development can be administered via different routes of administration. Various routes that are used include oral, topical, nasal, rectal, vaginal and ocular, etc. The oral delivery of drugs is considered to be the most appealing route of administration. This belief has led to the identification of many very successful drugs, but also saw the downfall of some promising therapeutics that failed to meet criteria required for sufficient oral bioavailability. The use of solid dispersion technologies for improving the dissolution characteristics of poorly water-soluble drugs and in turn their oral bioavailability has become a major point of attraction. Formulation of drugs as solid dispersion offers a variety of processing and excipient options that allow for flexibility when formulating oral delivery systems for poorly water-soluble drugs. Much of the research that has been reported on solid dispersion technologies involves drugs of class III of BCS classification. Hence, the hypothesis has been that the rate of absorption *in vivo* will be concurrently accelerated with an increase in the rate of drug dissolution.

Keywords: gastric residence time, bioavailability, oral delivery of drugs, solid dispersion technologies, BCS classification.

INTRODUCTION

The goal of any drug delivery system is to provide a therapeutic amount of drug to proper site in the body to achieve promptly and then maintain a desired drug concentration. Recent development in technology has provided viable dosage alternatives that can be administered via different routes of administration. Various routes that are used include oral, topical, nasal, rectal, vaginal and ocular, etc. [1]

The oral delivery of drugs is considered by decision-makers in the pharmaceutical industry to be the most appealing route of administration. This belief has led to the identification of many very successful drugs, but also to the downfall of some promising therapeutics that failed to meet criteria required for sufficient oral bioavailability. [2]

Nearly half of the new drug candidates that reach formulation scientists have poor water solubility, and oral delivery of such drug is frequently associated with low bioavailability to overcome these problems, various formulation strategies have been exploited, such as the use of surfactant, lipids, permeation enhancers, micro-ionization, salt formation, comlexation with cyclodextrin, nanoparticles and solid dispersion. [3]

The use of solid dispersion technologies to improve the dissolution characteristics of poorly water-soluble drugs and in turn their oral bioavailability has become a major point of attraction. Formulation of drugs as solid dispersion offers a variety of processing and excipient options that allow for flexibility when formulating oral delivery systems for poorly water-soluble drugs. Much of the research that has been reported on solid dispersion technologies involves drugs of class III of BCS classification. Hence, the hypothesis has been that the rate of absorption in vivo will be concurrently accelerated with an increase in the rate of drug dissolution. [4]

1.1 Gastro retentive Dosage Forms (GRDFs)

Gastro retentive 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. Gastro retentive tablet is

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defined as solid unit dosage form that can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs.

Prolonged gastric retention improves bioavailability, reduces drug waste and improves solubility for drugs that are less soluble in a high pH environment. It has applications also for local drug delivery to the stomach and proximal small intestines. Gastro retention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patients. [5]

1.1.1 Drug Candidates Suitable for GRDFs

The therapeutic interest to prolong the gastric residence time of a pharmaceutical dosage form with time-controlled release kinetics can be used, especially in the case of drugs, which [6]:

- Are locally active in the stomach (e.g. Misoprostol, Antacids and antibiotics against *Helicobacter pylori).*
- Have an absorption window in the stomach or in the upper small intestine (e.g. L-DOPA, P-Amino benzoic acid, Furosemide and riboflavin).
- Are weakly basic drugs exhibiting low solubility at high pH values (e.g. diazepam, Cefpodoxime Proxetil, Chlordiazepoxide and Verapamil HCl).

Drugs targeting to the stomach can also be attractive for several other reasons:

1. For drugs which have poor stability in the colon. [6,7]
2. Drugs with narrow window of absorption. (e.g. Cyclosporine, Methotrexate and Levodopa).
3. Drugs those are unstable in the intestinal or colonic environment (e.g. Captopril, Ranitidine HCl and Metronidazole).
4. Drugs that disturb normal colonic microbes (e.g. antibiotics used for the eradication of Helicobacter pylori, such as Tetracycline, Clarithromycin and Amoxicillin).[1]

1.1.2 Drugs those are unsuitable for GRDFs:

- Drugs with limited acid solubility e.g. Phenytoin etc.
- Drugs that suffers instability in the gastric environment e.g. Erythromycin, Rabeprazole, Clarithromycin, Esomeprazole etc.
- Drugs intended for selective release in the colon e.g. 5-amino salicylic acid and corticosteroids etc.[5-7]

1.1.3 Advantages of Gastro retentive Delivery Systems:

- The Floating systems are advantageous for drugs absorbed through the stomach. E.g. Ferrous salts, antacids.
- GRDFs provide advantages such as the delivery of drugs with narrow absorption window in the small intestinal region. [1]
- Better patient compliance is achieved due to its ease of administration.
- Compared to all other oral routes, these are microbiologically and chemically stable.
- Better suited for large scale production.
- These are the most lighter and compact.[8]
- Improvement of bioavailability and therapeutic efficacy of the drugs and possible reduction of dose. e.g. Furosemide.
- Maintenance of constant therapeutic levels over a prolonged period and thus reduction in fluctuation in therapeutic levels minimizing the risk of resistance especially in case of antibiotics. E.g. Beta-lactam antibiotics (Penicillin's and Cephalosporin's).
- Gastrointestinal transit time thereby increasing bioavailability of sustained release delivery systems intended for once-a-day administration. e.g. Ofloxacin. [9]
- They also have an advantage over their conventional system as it can be used to overcome the adversities of the gastric retention time (GRT) as well as the gastric emptying time (GET). As these systems are expected to remain buoyant on the gastric fluid without affecting the intrinsic rate of employing because their bulk density is lower than that of the gastric fluids.
- The controlled, slow delivery of drug from gastro retentive dosage form provides sufficient local action at the diseased site, thus minimizing or eliminating systemic exposure of drugs. This site-specific drug delivery reduces undesirable effects of side effects.
- Gastro retentive dosage forms minimize the fluctuation of drug concentrations and effects. Therefore, concentration dependent adverse effects that are associated with peak concentrations can be prevented. This feature is of special importance for drug with a narrow therapeutic index.[8]

1.1.4 Disadvantages of GRDDS

- Floating system is not feasible for those drugs that have solubility or stability problem in G.I. tract.

- The drugs that are significantly absorbed throughout gastrointestinal tract, which undergo significant first pass metabolism, are only desirable candidate.
- Some drugs present in the floating system causes irritation to gastric mucosa.[1]
- Increased fluid levels are required in the stomach so that the system float properly.
- Due to low density and amorphous nature of some drugs compacts do not form because they resist Compression.
- Swallowing problem in case of children and unconscious patients.
- Bioavailability problem occurs in case of poor wetting and less dissolution properties.
- Sometimes encapsulation or coating is required for the drugs that are oxygen sensitive, bitter tasting and with bad odor. [8]
- These systems do not offer significant advantages over the conventional dosage forms for drugs, which are absorbed throughout the gastrointestinal tract e.g Nifedipine. [7]

1.1.5 Drugs that would benefit from GRDDS

- CNS drugs (for Parkinson disease, epilepsy, Alzheimer and migraine)
- Anti-viral products (for HIV, herpes and hepatitis) and certain antibiotics,
- Anti-hypertension drugs,
- Anti-diabetic agents for Type-2 diabetes,
- Drugs for local treatment of GI infections and gastric enzyme replacement. **[7]**

1.1.6 Formulation considerations for GRDFs

- It must have effective retention in the stomach to suit for the clinical demand
- It must have sufficient drug loading capacity.
- It must control the drug release profile.
- It must have full degradation and evacuation of the system once the drug release is over.
- It should not have effect on gastric motility including emptying pattern.
- It should not have other local adverse effects. [9]

1.1.7 Factors Affecting Gastric Retention:

Gastric residence time of an oral dosage form is affected by several factors-

- **P^H of the stomach:-**To pass through the pyloric valve into the small intestine the particle size should be in the range of 1 to 2 *mm*. The pH of the stomach in fasting state is ~1.5 to 2.0 and in fed state is 2.0 to 6.0. A large volume of water administered with an oral dosage form raises the pH of stomach contents to 6.0 to 9.0. Stomach doesn't get time to produce sufficient acid when the liquid empties the stomach; hence generally basic drugs have a better chance of dissolving in fed state than in a fasting state.
- **Density: -** The density of a dosage form also affects the gastric emptying rate. A buoyant dosage form having a density of less than that of the gastric fluids floats. Since it is away from the pyloric sphincter, the dosage unit is retained in the stomach for a prolonged period. Density of the dosage form should be less than the gastric contents (1.004*gm/ml*).
- **Size and shape of dosage unit: -** Size and shape of dosage unit also affects the gastric emptying. Several reports show that tetrahedron and ring-shaped devices have a better gastric residence time as compared with other shapes. The diameter of the dosage unit is also equally important as a formulation parameter. Dosage forms having a diameter of more than 7.5 *mm* show a better gastric residence time compared with one having 9.9 *mm*.
- **Fed or Unfed State:-** Under fasting conditions, the GI motility is characterized by periods of strong motor activity or the migrating myoelectric complexes (MMC) that occurs every 1.5 to 2 hours. The MMC sweeps undigested material from the stomach and if the timing of administration of the formulation coincides with that of the MMC, the GRT of the unit can be expected to be very short. However, in the fed state, MMC is delayed and GRT is considerably longer.
- **Nature of the meal: -** Feeding of indigestible polymers of fatty acid salts can change the motility pattern of the stomach to a fed state, thus decreasing the gastric emptying rate and prolonging the drug release. **[6,8]**
- **Frequency of feed: -** The GRT can increase by over 400 minutes when successive meals are given compared with a single meal due to the low frequency of MMC.

- **Gender: -** Mean ambulatory GRT in meals (3.4±0.4 *h*) is less compared with their age and race-matched female counterparts (4.6±1.2 *h*), regardless of the weight, height and body surface.
- **Age: -** Elderly people, especially those over 70 years have a significantly longer GRT.
- **Miscellaneous: -** Biological factors such as age, body mass index (BMI), gender, posture, and diseased states (diabetes, Chron's disease) influence gastric emptying.[9, 10]

Table 1: Regional specific characteristics of GIT influencing gastro retention [10]

Region	Surface area(m^2)	Liquid secretion (*ml/min*)	Reaction P^H	Transit time (*h*)
Oral cavity	About 0.05	0.5-2	5.2-6.8	short
Stomach	0.1-0.2	2-4	1.2-3.5	0.5-3
Duodenum	About 0.04	1-2	4.6-6	1-10
Small intestine	4500	0.2	4.7-6.5	1-2
Large intestine	0.5-1	0.2	7.5-8	4-20

1.1.8 Approaches of GRT

Various attempts have been made to develop gastro retentive delivery systems. For example, floating, swelling, mucoadhesive and high-density systems have been developed to increase gastric retention time of the dosage forms.

1.1.8.1 Mucoadhesive Systems

The mucoadhesive systems are intended to extend the GRT by adhering them to the gastric mucous membrane. Bioadhesion on soft tissues of certain natural or synthetic polymers has been exploited to control as well as to prolong the gastric retention of the delivery systems. The adhesion of the polymers with the mucous membrane may be mediated by hydration, bonding, or receptor mediated. In hydration mediated adhesion, the hydrophilic polymers become sticky and mucoadhesive upon hydration. Bonding mediated adhesion may involve mechanical or chemical bonding. Chemical bonds may involve covalent or ionic bonds or Vaan der Waals forces between the polymer molecules and the mucous membrane. Receptor mediated adhesion takes place between certain polymers and specific receptors expressed on gastric cells. [9]

1.1.8.2 Swelling Systems

The presence of polymers in the system promotes their swelling to a size that prevents their passage through pyloric sphincter resulting in prolonged GRT. However, a balance between the rate and extent of swelling and the rate of erosion of the polymer is crucial to achieve optimum benefits and to avoid unwanted side effects. Polymeric coating system formed an outer membrane on the conventional tablets. In the dissolution media the membrane detached from the core and swelled to form a balloon that kept the unit floating. The size of the unit is increased by three to six folds. Thus, the floating ability as well as the increased dimension offered the system gastro retentive property. Swelling systems are also referred to as plug type systems.

1.1.8.3 High-Density Systems

High-density systems are intended to lodge in the rugae of the stomach withstanding the peristaltic movements. Systems with a density of 1.3 *g/ml* or higher are expected to be retained in the lower part of the stomach. The formulation of heavy pellets is based on the assumption that the pellets might be positioned in the lower part of the antrum because of their higher density. The pellets with density of at least 1.5 *g/ml* have significantly higher gastric residence time both in fasted and fed state. [11]

1.1.8.4 Floating drug delivery systems

Floating drug delivery systems is one of the important approaches to achieve gastric retention to obtain sufficient drug bioavailability. These delivery systems are desirable for drugs with an absorption window in the stomach or in the upper small intestine. These have a bulk density less then gastric fluids and so remain buoyant in the stomach without affecting gastric emptying rate for a prolonged period and the drug is released slowly as a desired rate from the system. After release of drug, the residual system is emptied from the stomach. This result in an increased gastric retention time (GRT) and a better control of the fluctuation in

plasma drug concentration. These following approaches have been used for the design of floating dosage forms of single and multiple-unit systems. Recently a single-unit floating system was proposed consisting of polypropylene foam powder, matrix forming polymers, drug and filler. [12]

Floating systems can be classified as effervescent and non-effervescent systems.

1.1.8.5 Effervescent systems

Flotation of a drug delivery system in the stomach can be achieved by incorporating a floating chamber filled with vacuum, air, or an inert gas. Gas can be introduced into the floating chamber by the volatilization of an organic solvent (e.g. ether or cyclopentane) or by the CO_2 produced as a result of an effervescent reaction between organic acids and carbonate–bicarbonate salts. These devices contain a hollow deformable unit that converts from a collapsed to an expanded position and returns to the collapsed position after a pre-determined amount of time to permit the spontaneous ejection of the inflatable system from the stomach.

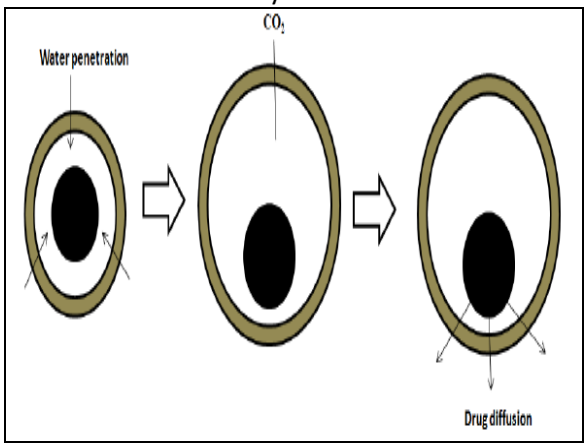

Figure 1: Drug release mechanism from gastro retentive tablet [12]

1.1.8.6 Non-effervescent systems

Non-effervescent systems incorporate a high level (20–75% w/w) of one or more gel-forming, highly swellable, cellulosic hydrocolloids (e.g. hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, and sodium carboxymethylcellulose) polysaccharides or matrix-forming polymers (e.g. polycarbophil, polyacrylates, and polystyrene) into tablets or capsules. penetration into the device and consequent drug release. As the exterior surface of the dosage form dissolves, the gel layer is maintained by the hydration of the adjacent hydrocolloid layer. The air trapped by the swollen polymer lowers the density and confers buoyancy to the dosage form. [5]

On contact with gastric fluid, these gel former polysaccharides and polymers hydrate and form a colloidal gel barrier that controls the rate of fluid **super porous hydrogel**

Although these are swellable systems, they differ sufficiently from the conventional types to warrant separate classification. With pore size ranging between 10 *nm* to 10 *μm*, absorption of water by conventional hydrogels is a very slow process and several hours may be needed to reach an equilibrium state during which premature evacuation of the dosage form may occur. Super porous hyrdrogel, average pore size > 100 *μm*, swell to equilibrium within a minute, due to rapid water uptake by capillary wetting through numerous interconnected open pores. Moreover, they swell to a large size and are intended to have sufficient mechanical strength to withstand pressure by the gastric contraction.

1.1.8.6 Magnetic systems

The magnetic dosage forms contain a small internal magnet and an extra-corporal magnet that controls the gastrointestinal transit of the dosage form. Although these systems seem to work, the external magnet must be positioned with a degree of precision that might compromise patient compliance. [7]

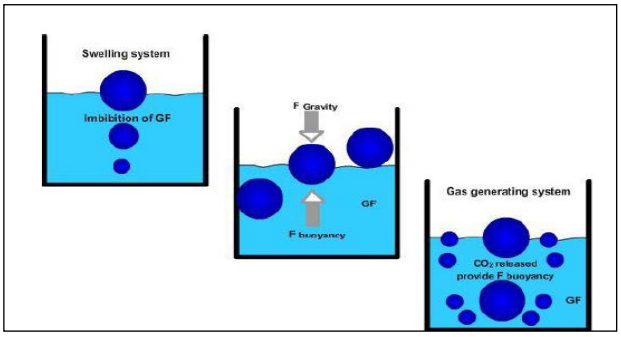

Figure 2: Images showing the different Approaches of GRDFs [12]

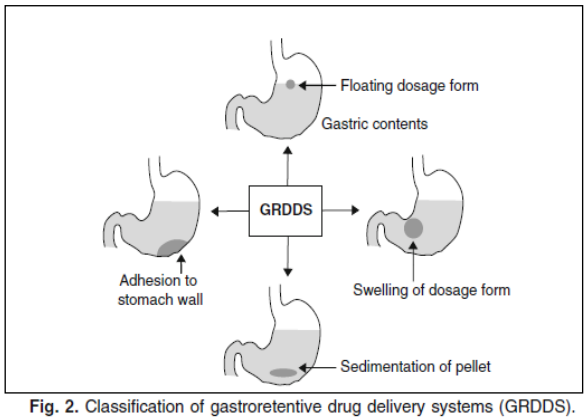

Fig. 2. Classification of gastroretentive drug delivery systems (GRDDS).

Figure 2: Images showing the different Approaches of GRDDs [12]

Table 2: List of Commercially Available Gastro retentive Tablet [11, 12]

Product	Remarks/technology	Active ingredient
Zanocin OD	Effervescent floating system	Ofloxacin
Riomet OD	Effervescent floating system	Metformine HCl
Cifran OD	Effervescent floating Form	Ciprofloxacin
Inon Ace Tablets	Foam based floating system	Simethicone
Gabapentin GR	Polymer based swelling technology	Gabapentin
ProQuin XR	Polymer based swelling technology	Ciprofloxacin
Glumetza	Polymer based swelling technology	Metformine HCl
Metformin GR	Polymer based swelling technology	Metformine HCl
Prazopress XL	Effervescent and swelling-based floating system	Prazosin HCl
Cipro XR	Erodible matrix based system	Ciprofloxacin hydrochloride
Baclofen GRS	Coated multi-layer floating and swelling system	Baclofen
Coreg CR	Gastro retention with osmotic system	Carvedilol
Madopar	Floating, CR capsule	Levodopa and Benserzide
Valrelease	Floating capsule	Diazepam
Cytotec	Bilayer floating capsule	Misoprostol (100mcg/200mcg)
Topalkan	floating liquid alginate	Aluminum magnesium antacid
Conviron	Colloidal gel forming FDDS	Ferrous sulphate

1.2 Definition of Solid Dispersions

The term solid dispersion refers to a group of solid products consisting of at least two different components, generally a hydrophilic matrix and a hydrophobic drug. The matrix can be either crystalline or amorphous. The drug can be dispersed molecularly in amorphous particles (clusters) or in crystalline particles. [13]

1.2.1 Applications of Solid Dispersions

- To increase the solubility of poorly soluble drugs thereby increase the dissolution rate, absorption and bioavailability.
- Stabilize unstable drugs against hydrolysis, oxidation, recrimination, isomerisation, photo oxidation and other decomposition procedures.
- Masking of unpleasant taste and smell of drugs.
- Improvement of drug release from ointment creams and gels.
- To avoid undesirable incompatibilities.
- To obtain a homogeneous distribution of a small amount of drug in solid state.
- To dispense liquid (up to 10%) or gaseous compounds in a solid dosage.
- To formulate a fast release primary dose in a sustained released dosage form.
- To formulate sustained release regimen of soluble drugs by using poorly soluble or insoluble carriers.
- To reduce pre systemic inactivation of drugs like morphine and progesterone. [14]

1.2.2 Common methods used for preparation of solid dispersion

1.2.2.1 Fusion method

The fusion method is sometimes referred to as the melt method, which is correct only when the starting materials are crystalline. Therefore, the more general term fusion method is preferred. The first solid dispersions created for pharmaceutical applications were prepared by the fusion method.

1.2.2.2 Hot melt extrusion

Melt extrusion is essentially the same as the fusion method except that intense mixing of the components is

induced by the extruder. When Solid Dispersions: Compared to melting in a vessel, the product stability and dissolution are similar, but melt extrusion offers the potential to shape the heated drug-matrix mixture into implants, ophthalmic inserts, or oral dosage forms.

1.2.2.3 Solvent evaporation

The drug and carriers are dissolved or dispersed in common solvent (or solvent mixture) and then solvent is evaporated with the help of heat, with or without vacuum. The dried solid mass is crushed, pulverized and stored in desicator. There are several factors which may affect the dispersion characteristic, some are listed as: drug-to-carrier ratio, carrier type, solvent composition, rate of evaporation, temperature of evaporation. [4]

1.2.2.4 Melting solvent method

In this method drug is first dissolved in a suitable liquid solvent Solution is then incorporated directly into the melt of polyethylene glycol obtainable below 70°*C*, without removing the liquid solvent. It has been shown that 5-10 % (*w/w*) of liquid compound could be incorporated into polyethylene glycol 6000 without significant loss of its solid property.

1.2.2.5 Lyophillization Techniques

Lyophillization has been thought of a molecular mixing technique. The drug and carrier are co- dissolved in a common solvent, Frozen and sublimed to obtain a lyophilized molecular dispersion.

1.2.2.6 Melt agglomeration method

This technique has been used to prepare where in the binder acts as a carrier. In addition, are prepared either by Heating binder, drug and excipients to a temperature above the melting point of the binder or by spraying a dispersion of drug in molten binder on the heated excipients by using a high shear mixer. [14]

1.2.2.7 Kneading

The physical mixture of drug and carrier is triturated to thick paste using small volume of solvent. The solvent used can be organic (alcohol, dichloromethane, acetone) or aqueous (water) or mixture thereof. The kneaded paste is dried in oven or vacuum oven and the dried mass is pulverized and stored in desiccators. Kneading process is economical but residual solvent may be an issue.

1.2.2.8 Spray drying

In conventional spray drying process, the drug and carrier are dissolved or dispersed in a common solvent and atomized in a drying chamber with hot drying gases. The properties of SD prepared by spray drying method are influenced by solvent composition (organic or aqueous or mixture thereof), atomization efficiency, consistency of feed material, rate of drying, drying gas flow rate, inlet temperature and size of atomized droplets. The physicochemical properties of drug and carrier also influence the characteristics of SD.

1.2.2.9 Kinetic Sol Dispersing

KSD is a new fusion-based process where no external heat is applied. The mixture of drug and carrier is subjected to high shear and frictional forces where it gets melted. In KSD, a circular processing chamber is fitted with a rotating shaft having blades protruded toward the chamber wall. The composition is loaded into chamber at room temperature, and allows the blades to rotate at high speed. These rotating blades generate heat through friction and shear, and temperature within chamber is increased.

1.2.2.10 Agitation granulation

The drug and binder solution (granulation fluid) is added to the carrier or mixture of carriers and then the mixture are granulated in high-speed agitation granulator. The resulting granules are dried in a fluid-bed dryer and dried granules are passed through sieve. [15]

1.3 Analytical Method Development

The principle of validation of quantitative procedures is widely spread today with simple question of acceptability or not of an analytical procedure for a given application, relating to good practices (GLP, GMP, etc.) and other documents of normative character (ISO, ICH, EMEA, FDA, etc.).[16] Since the adoption of the International Conference on Harmonization quality Chapter-8 concerning a Quality by Design (QbD) approach, there have been many discussions on the opportunity for analytical method developments to follow a similar approach. A key component of the QbD paradigm is the definition of the Design Space (DS) of analytical methods where assurance of quality is provided.[17] As per USP, validation of an analytical method is the process by which laboratory studies establish that the performance characteristics of the method meet the requirements for the intended analytical application which ensure that every result of the routine analysis should be close enough to its unknown but true value is the samples.[18] There has been greater emphasis on method validation because most organizations develop methods of analysis and incorporate them into legislation. Analysts are allowed a greater freedom of choice of analytical method which meets certain pre-defined criteria.[19]

There are key parameters that are determined and used for validation of steps to ensure that the validation data generated under conditions are equivalent to the final procedure, which includes-

- Detection of all compounds of interest (purity control).
- Separation of all compounds of interest.
- Quick method development.
- Short analysis time.
- Reduced need for sample pretreatment.
- High reproducibility of migration time.
- High reproducibility of peak area, relative peak area (main component assay).
- Accuracy (main component assay).
- Ruggedness.
- Low costs. [20]

1.3.1 Accuracy and recovery

The accuracy of an analytical procedure is the closeness of agreement between the conventional true value or an accepted reference value and the value found. This is sometimes termed trueness, which is stated quantitatively in terms of bias. The ICH document on validation methodology recommends accuracy to be assessed using a minimum of nine determinations over a minimum of three concentration levels covering the specified range (for example, three concentrations with three replicates each). Accuracy should be reported as percent recovery by the assay of known added amount of analyte in the sample or as the difference between the mean and the accepted true value, together with the confidence intervals. The expected recovery depends on the sample matrix, the sample processing procedure and the analyte concentration. [21]

1.3.2 Robustness

The robustness of an analytical procedure is the measure of its capacity to remain unaffected by small but deliberate variations in method parameters and provides an indication of its reliability during normal usage. It can be demonstrated by showing that operational or environmental influences have no significant effect on test results. [22]

1.3.3 Precision

The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogenous sample under the prescribed condition. At least five determinations of three concentrations at low, medium and high range of calibrations are performed and the percent relative standard deviation (RSD) is calculated which is less than 2%.

1.3.4 Limit of Detection

The limit of detection (LOD) is the smallest measured concentration of an analyte from which it is possible to deduce the presence of the analyte in the test sample with acceptable certainty. [19] The limit of detection (LOD) of an individual analytical procedure is the lowest amount of analyte in a sample which can be detected but not necessarily quantifies as an exact value. LOD is the point at which a measured value is larger than the uncertainty associated with it. [21]

1.3.5 Limit of Quantitation

The LOQ is the smallest measured content of an analyte above which the determination can be made with the specified degree of accuracy and precision [19] The limit of Quantitation (LOQ) is the lowest amount of analyte in a sample that can be quantitatively determined with suitable precision and accuracy. LOQ is a Parameter of quantitative assays for low levels of compounds in sample matrices, and is used particularly for the determination of impurities and/or degradation products. [20]

1.3.6 Linearity

The linearity of an analytical procedure is its ability (within a given range) to obtain test results which are directly proportional to the concentration (amount) of analyte in the sample. [23]

1.3.7 Ruggedness

Ruggedness is the ability of the method to produce similar result for a given sample when it is used in a variety of normal test conditions, such as different equipment, different analysts, different laboratories or different days. Having the method evaluated by another analyst, preferably in another laboratory provides a means to evaluate the ruggedness of the method. [24]

2. REVIEW OF LITERATURE

2.1 Oral route for drug administration and tablets as oral solid dosage form

It is well accepted fact that oral route of drug administration is one of the most important methods of administrating drugs for systemic effect. Advantages associated with oral route like simplicity, safety, convenience, noninvasive nature and cost effective has made oral dosage form one of the most widely used routs for drug administration.

It is found probable that at least 90% of the drugs used to produce systemic effects are administered by the oral route. [25] Its importance is highlighted in case like in treatment of chronic disease where oral route is a major route for drug delivery. [26]

Among the various oral dosage forms that are administered via oral route, tablet, a solid oral dosage form represents most common and preferred one.[27] Owing to the advantages like better patient compliant, least tendency for "hang up" above the stomach, easy modifiable drug release profile, better suited to large scale production, easiest and cheapest dosage form to package and shipment and better chemical, mechanical and microbiological stability has made tablet superior of all the oral dosage forms. [28]

2.2 Drug solubility, permeability and bioavailability in oral route

For therapeutic effectiveness of any drug, it needs to reach its site of action and stay there long enough to exert its pharmacological effect. Availability of drug at site of action principally depends upon its bioavailability or the rate at which relative amount of an administered drug reaches systemic circulation in intact form. For 100% bioavailability of orally administered drug it must completely release from the dosage form, fully dissolved in Gastro Intestinal Fluid (GIF), remain stable in GIF, pass through the GI-barrier into the mesenteric circulation without being metabolized and pass through the liver into the systemic circulation unchanged. Anything that adversely affects mentioned criteria influences the bioavailability of the drug. Physiological factors, physiochemical properties associated with drug, dosage form and dosage form associated formulation and production related factors are the major factors that influence bioavailability. Thus, for a drug to be seen in systemic circulation after administration of the drug *via* oral route it must pass through various physiological, biological and physiochemical barriers. Owing to the nature of human physiology, after oral administration of drug, it must dissolve in the GIF followed by drug transport through biological membrane. Since, the GIF is aqueous in nature whilst the biological membrane lippophilic, drug needs to satisfy various physiochemical properties like aqueous solubility, dissolution rate, $P^{ka,}$ lipid solubility, chemical stability and Complexation in order to increase its bioavailability. [29]

2.3 Biopharmaceutical classification of drugs

A biopharmaceutics drug classification was introduced to correlate *in vitro* drug product dissolution and *in vivo* bioavailability proposed for drug dissolution and gastrointestinal permeability are the fundamental parameters controlling rate and extent of drug absorption. This analysis uses a transport model and human permeability results for estimating *in vivo* drug absorption to illustrate the primary importance of solubility and permeability on drug absorption. Based on this classification scheme very rapidly dissolving high solubility drugs, e.g. 85% dissolution in less than 12 minutes, a simple one point dissolution test, is all that may be needed to insure bioavailability.

Owing the compounds solubility and intestinal permeability characteristics these drugs can be classified as below:

Table 3: Biopharmaceutic Drug Classes [30]

Class	Solubility	Permeability
I	High	High
II	Low	High
III	High	Low
IV	Low	Low

Of the 130 0rally administered drugs on the WHO list, 61 could be classified with certainty. 21 (84%) of these belong to class I (highly soluble, highly permeable), 10% (17%) to class II (poorly soluble, highly permeable), 24 (39%) to class III (highly soluble, poorly permeable) and 6 (10%) to class IV (poorly soluble, poorly permeable). [31]

2.4 Approaches for improving bioavailability of poorly water soluble drugs

Several methods have been employed to enhance the solubility, dissolution and bioavailability of poorly soluble drugs. Some of these methods are particle size reduction, cyclodextrin complexation, solubilization, co-solvency, solid dispersion (SD), salt formation, polymorphs, solvates or hydrates, pro-drugs, microparticulates (liposomes, microspheres, etc.). But each of these methods has some particles limitations. All drugs cannot be reduced to desired particles size, or on size reduction it is not necessary to enhance dissolution rate. Further, the micronized particles may start agglomeration or develop surface charge which leads to less active surface area and poor wettability. The particle size reduction is an energy-dependent process which may not be suitable for stress labile (thermo labile, compaction sensitive) drugs. Cyclodextrin complexation is commonly used to enhance solubility and dissolution rate. But it involves an expensive process, excipients and even it fails some time

to complex with many drugs. The solubilization and co-solvency are used for liquid formulations. The patient compliance and commercial viability of liquid formulations are low. Further, the liquid formulations are difficult to handle and their self-life is also less when compared with solid formulations. Salt formation has been proved to be a good option for solubility enhancement. The limitations of this method are neutral drugs, weakly acidic or basic drugs and chemical reactions to prepare suitable and stable salt. Micro particulates formulations are in recent trend for improving bioavailability of poorly soluble drugs. These formulations are difficult to scale-up with uniformity and consistency. Along with high production cost, the solubility of micro particulates is of big concern. The pro drugs have shown limited scope in bioavailability enhancement by increasing g the solubility of drugs. [32]

2.5 Solid dispersion technique

The phase solubility behavior of Gliclazide in presence of various concentrations of PEG 6000 in 0.1 N HCl was obtained at 37°*C*. The solubility of Gliclazide increased with increasing amount of PEG 6000 in water. Gibbs free energy values were all negative, indicating the spontaneous nature of Gliclazide solubilization and they decreased with increase in the PEG 6000 concentration, demonstrating that the reaction conditions became more favorable as the concentration of PEG 6000 increased. The SDs of Gliclazide with PEG 6000 exhibited enhanced dissolution rate of Gliclazide, and the rate increased with increasing concentration of PEG 6000 in SDs. Mean dissolution time (MDT) of Gliclazide decreased significantly after preparation of SDs and physical mixture with PEG 6000. [33]

Solid dispersions of Fenofibrate were prepared using PEG 6000, Poloxamer 407 and a mixture of PEG 6000 and Poloxamer 407(1:1 mixture). The effect of melt and solvent methods of preparation of solid dispersion on dissolution behavior was also investigated. Dissolution studies indicated a significant increase in dissolution of Fenofibrate when dispersed in PEG6000 and Poloxamer 407. Physical mixtures containing PEG and Poloxamer 407 also showed improved dissolution of Fenofibrate as compared with that of pure drug, indicating the solubilizing effect of PEG6000 and Poloxamer 407. [34]

Solid dispersions of poorly water soluble drug meloxicam was prepared by using Hydroxyethyl cellulose (HEC), mannitol and polyethylene glycol (PEG) 4000 and to develop a dosage form for geriatric Population. Higher in *vitro* dissolution of solid dispersions was recorded compared to their corresponding physical mixtures and the pure drug. PEG 4000 in 1: 9 drugs to carrier ratio exhibited the highest drug release (100.2%), followed by mannitol (98.2%) and HEC (89.5%) in the same ratio [12]
Solid dispersion for carvedilol was prepared by using spray-drying method. Solid dispersions were formulated with carvedilol and Eudragit RS and hydroxyl propyl methyl cellulose to control the dissolution rates of carvedilol. The release behavior of solid dispersion analyzed at simulated gastric fluid (pH 1.2) in *in* vitro study. The dissolution rate of carvedilol was higher than active pharmaceutical ingredient. In conclusion, we can control the dissolution rate by solid dispersion using biomedical polymers. [35]

2.6 Use of water soluble polymer

Tablets containing Hydroxy propyl methylcellulose (HPMC), drug and different additives were compressed. The investigation shows that tablet composition and mechanical strength have the greatest influence on the floating properties and drug release. With the incorporation of a gas-generating agent together with microcrystalline cellulose, besides optimum floating (floating lag time of 30 sec); duration of floating (>8 *h*), the drug content was also increased. The drug release from those tablets was sufficiently sustained (more than 8 *h*) and non-Fickian transport of the drug from tablets was confirmed. Radiological evidence suggests that, that the formulated tablets did not adhere to the stomach mucus and that the mean gastric residence time was prolonged (>4 *h*). [36]

An anti-ulcer drug, ranitidine hydrochloride, is delivered through a gastro retentive ethyl cellulose based microparticulate system capable of floating on simulated gastric fluid for 4-12 *h*. Preparation of microparticles is done by solvent evaporation technique with modification by using an ethanol co-solvent system. The formulated microspheres were free flowing with good packability and encapsulation efficiencies were up to 96%. Scanning electron microscopy confirmed porous, spherical particles in the size range 300–750 mm. Microspheres showed excellent buoyancy and a biphasic controlled release pattern with 12 h. In vivo bioavailability studies performed on rabbits and Tmax, Cmax, AUC were calculated and confirmed significant improvement in bioavailability. [37]

The effervescent-based floating drug delivery was a promising approach to achieve *in vitro* buoyancy. The addition of gel-forming polymer HPMC K4 M, HPMC K15 M, carbopol 934P and gas-generating agent sodium bicarbonate was essential to achieve *in vitro* buoyancy. The *in vitro* drug release profiles obtained for tablets

made with combinations of HPMC K4 M, HPMC K15 M, carbopol 934P showed lesser FLT (30 *Sec*) and a prolonged floating duration (> 24*h*) which was a controlled release characteristic (98%) for 24 *h.* [38]
Floating matrix tablets of Cefpodoxime Proxetil were prepared by direct compression technique, using polymer such as Hydroxy propyl methyl cellulose (HPMC K4M), sodium CMC and carbopol 934P in different combinations with other standard excipients like sodium bicarbonate, lactose and Magnesium stearate used as gas generating agent, as filler and as lubricant respectively. The effect of polymer concentrations on buoyancy and drug release pattern was also studied. *In-vitro* drug release mechanism was evaluated by PCP V-3 software. All the matrix tablets showed significantly greater swelling index and exhibited controlled and prolonged drug release profiles and some floated over the dissolution medium for more than12 hr. [39]

2.7 Research carried on gastro retentive formulation

Patel et al investigated gastro retentive tablet of Verapamil hydrochloride using different hydrocolloid polymers including carbopols, hydroxyl propyl methyl cellulose and Xanthan gum by direct compression techniques. Selected tablets containing Xanthan gum along with citric acid showed buoyancy more than 24 hr. [40]

Dave et al developed gastro retentive delivery system of ranitidine HCl. Guar gum, Xanthan gum and HPMC were used as gel forming agents. Sodium carbonate was incorporated as gas generating agent. The effects of citric acids and Xanthan gum on drug release profile and floating properties were investigated. [41]

Renuka et al prepared floating controlled release tablets of carvedilol. The gastro retentive drug delivery is a promising approach to achieve *in vitro* buoyancy and thereby longer gastric retention time by using natural polymers like Xanthan and guar gum and gas generating agent sodium bicarbonate. The *in vitro* evaluation of drug delivery system showed that floating tablets containing natural polymers like both Xanthan and guar gum exhibited more controlled release than Xanthan gum alone. [42]

Mohammed Muqtader et al buoyant delivery systems are promising dosage forms which could be a better alternative to conventional oral dosage forms in order to improve bioavailability by increasing the gastric retention time of the drug. Natural polymers such as Xanthan gum and guar gum can be used to prepare floating drug delivery systems like Famotidine which has higher absorption at low pH. [43]
N. Narang et al floating drug delivery has become the most popular method for controlling the drug release. Stavudine floating tablets were prepared by blending the drug, polymers (Xanthan gum, guar gum, HPMC); Gas generating agent and diluents followed by slugging. These tablets swelled while coming in to contact with the aqueous medium. The formulation containing Xanthan gum and guar gum exhibited good drug retaining capability. [44]

Chaudhary et al formulate and evaluate floating drug delivery system containing Theophylline as a model drug, because theophylline, a methyl xanthine derivative used in the treatment of chronic asthma as an adjunct to β-2 agonist and corticosteroid therapy. It is rapidly absorbed after oral administration with a half-life 4-8 hours and no difference in the amount of absorption between the stomach, ileum and colon. Hence the floating form was developed. However, it is prepared by direct compression method. Direct compression method of theophylline tablet containing HPMC (K100), Xanthan gum, carbopols 934P, aerosol and sodium bicarbonate, PVP K30, lactose and MCC. [45]

Iqwal Siddiqui Aslam et al in vitro study revealed that floating tablet of Diltiazem hydrochloride was adequately float on the medium and release the drug in sustained manner. The concentration of different grades HPMC and Xanthan gum have great impact on the in vitro drug release of diltiazem hydrochloride and Xanthan gum has more drug release retarding property than HPMC. [46]

Marella Radhakrishna et al designed to formulate and evaluate balanced floating drug delivery system as controlled release module, which prolongs the release rate of the drugs and found that promising controlled release by gastro retentive floating tablet of Amoxicillin trihydrate using HPMC K4M, HPMC K15M, HPMCK100 and Xanthan gum by taking single polymer in the formulation in which gave better controlled release and floating properties comparison to other formulation. [47]

Nappinnai M et al objective of the present work is to improve bioavailability of Cefpodoxime proxetil (CP) through gastro retentive mucoadhesive microspheres because of its good absorption profile in acidic pH values of stomach. Microspheres were prepared by simple emulsification e phase separation technique using Cefpodoxime proxetil, Chitosan, Dioctyl sodium sulfo succinate (DOSS), Petroleum Ether, Liquid paraffin and Glutaraldehyde. In vivo studies indicated that prolonged

gastric retention of microspheres improves the bioavailability of CP. [48]

Karthikeyan D et al developed floating microsphere of Cefpodoxime proxetil in order to achieve extended retention in upper GIT for 12 hours. The microsphere were prepared by non-aqueous solvent evaporation method using different ratios of CP, HPMC K4M, and Ethyl cellulose in the mixture of dichloromethane and ethanol with tween-80 as surfactant. The *in vitro* drug release was studied for 12 hours and the floating microspheres showed better result and it may be useful for prolonging the drug release in stomach and improve the bioavailability. [4]

Voosre SK et al the present investigation concerns the development of Hydro dynamically balanced tablets of Ciprofloxacin Hydrochloride that were designed to prolong the gastric residence time after oral administration and thereby increasing drug bioavailability. Floating tablets of Ciprofloxacin HCl were prepared by direct compression using HPMC K4M and HPMC K15M as polymers along with Sodium bicarbonate as gas generating agent. Tablets were evaluated for in-vitro release characteristic for 12 hrs. It is found that the hardness of the tablets affects the Buoyancy characteristics of the dosage form. The in-vitro release studies indicated that the floating tablets of Ciprofloxacin HCl containing HPMC K15M showed sustained release when compared with the marketed product and provides a better option for controlled release action and improved bioavailability. [49]

Chinthala C.S.K. et al attempted to formulate and evaluate gastro retentive floating drug delivery system containing Gabapentin in the form of tablets using polymers like HPMC K100M, HPMC K15M, Polyox WSR 303 and sodium bicarbonate as gas generating agent. The tablets were prepared by direct compression method. The in-vitro dissolution studies were carried out in a USP type-II apparatus in 0.1 N HCl. At all the strengths of the polymer tested combination of HPMC K100M and POLYOX WSR 303 (2:1) gave relatively slow release of Gabapentin over 24 h when compared to other formulations and showed buoyancy lag time 6 sec. [50]

Keservani R.K. et al Microballoons of Cefpodoxime proxetil were formulated by solvent evaporation and diffusion method employing hydroxypropylmethyl cellulose (HPMC) and ethyl cellulose (EC) polymers. Most of formulations remained buoyant maximum for more than 12 hrs indicating good floating behavior of microballoons. *In Vitro* studies suggest that microballoons may be potential delivery system for Cefpodoxime proxetil with improvement in bioavailability in comparison to conventional dosage forms. [51]

2.8 Research on Cefpodoxime proxetil

Effervescent Floating GR dosage form was developed for CP and evaluated in rats. The GR dosage form improved the oral bioavailability of CP significantly by 75%, hence providing a proof- of-concept. [52]

Once daily, sustained release tablet of CP were prepared by using hydrophilic polymer HPMC.

In vitro dissolution studies indicated a sustained-release pattern throughout 24 hours of the study that was comparable to the theoretical release profile. Drug release kinetics indicated that drug release was best explained by Higuchi's equation, as these plots showed the highest linearity (R^2 = 0.9734), but a close relationship was also noted with zero-order kinetics (R^2 = 0.9708). Decreasing the dose frequency of Cefpodoxime proxetil increases patient compliance; patients prefer to take the drug once daily. It also improves the rate of bacterial killing and hastens the cure from the indications, and therefore increases compliance. [53]

Floating Microspheres of Cefpodoxime Proxetil with Eudragit E100 plus HPMC and Eudragit E100 plus PEG were prepared by the emulsion solvent diffusion method to mask the bitter taste of an antibiotic. The effect of different polymers with different drug–polymer ratios on the taste masking and the characteristics of the microspheres were investigated. It was found that Eudragit E100 mask the taste but retard the drug release whereas combination of Eudragit E100 with PEG and with HPMC showed the better result for masking the unpleasant taste of Cefpodoxime Proxetil with floating ability as well as provide good drug release. Further dry powder for reconstitution was prepared from microspheres with respect to its use in pediatric population. [54]

The cefpodoxime proxetil -hydroxypropyl-β-cyclodextrin (CP–HP-β-CD) complex was prepared by kneading method in the presence of Sodium carboxymethyl cellulose (Na CMC). The solubility method was used to investigate the effect of hydroxypropyl-β-cyclodextrin (HP-β-CD) and Na CMC on the solubility of CP. The complex tablets were prepared using direct compression method. Dissolution studies were performed with complex tablets and commercial tablets in pH 1.2, 4.5, 6.8 and 7.4 buffer solutions. It was observed that Complexation occurred in all formulations, and HP-β-CD is able to increase CP solubility and dissolution rate of CP was improved from complex tablets, when compared

with commercial tablets. Furthermore, the antimicrobial activity studies revealed that the CP–HP-β-CD complex and complex tablets were shown to have more effective antimicrobial activity than commercial tablets. [55]

2.9 Analytical methods of Cefpodoxime proxetil

A simple, rapid, accurate and precise Spectrophotometric method has been developed for simultaneous estimation of Cefpodoxime proxetil and Ofloxacin from tablet dosage form. Proposed method involves formation of 'simultaneous equations' at 235 nm and 298 nm, using methanol: water (70:30), as a solvent. The linearity was observed in the concentration range of 4 - 24 µg/ml for Cefpodoxime proxetil and 4 - 20 µg/ml for Ofloxacin. The results of analysis have been validated statistically and by recovery studies. [56]

UV-Spectrophotometric method for the analysis of Cefpodoxime proxetil by using different hydrotropic agents was developed. The Spectrophotometric analysis of Cefpodoxime proxetil by utilizing different hydrotropic agents such as ammonium acetate (6M), sodium citrate (1.25 M), sodium glycinate (1M), Sodium chloride)1M), and urea (1M) were carried out. From different hydrotropic agents, urea showed best aqueous solubility of Cefpodoxime proxetil. The linearity was observed in the concentration range of 10-120 µg/ml. The method was validated and found to be precise. Accuracy (percent recovery) for Cefpodoxime proxetil was found to be 99.82 ± 0.106. [57]

Three simple, sensitive, accurate, and rapid UV/visible Spectrophotometric methods have been developed for the estimation of Cefpodoxime proxetil in bulk drug and in pharmaceutical dosage form. Method A involves the determination of Cefpodoxime proxetil in bulk drug and pharmaceutical formulations, which shows maximum absorbance at 235 *nm* in methanol, while method B is based on ion-pair complex between Cefpodoxime proxetil and Bromocresol purple in acidic medium and the subsequent extraction of the ion pair in chloroform. The yellow colored ion pair complex shows maximum absorption at 415 *nm*, while method C is based on ion-pair Complex between Cefpodoxime Proxetil and bromocresol green in acidic medium and the subsequent extraction of the ion pair in chloroform. The yellow colored ion pair complex shows maximum absorption at 425 nm. Beer's law was obeyed in the concentration range of 5-25 *µg/ml* in method A, 5-25 *µg/ml* in method B and 5-25 *µg/ml* in method C respectively. Results of the analysis were validated statistically and by recovery studies. The percent recovery obtained (99.9± 0.36-99.8± 0.69 for method A, 100.3± 0.45-99.75± 0.87 for method B and 100.1±0.36-99.6± 0.57 for method C) indicates noninterference from the common excipients used in the formulations. [58]

A new simple**,** precise, accurate and selective RP-HPLC method has been developed and validated for simultaneous estimation of Cefpodoxime proxetil and Ambroxol hydrochloride in tablet dosage form. The method was carried out on a Qualisil RP C-8 (250 *mm* x 4.6 mm, 5 *µm*) column with a mobile phase consisting of acetonitrile: 0.025 M potassium dihydrogen phosphate buffer (70:30 *v/v*) pH adjusted to 4.0 with *ortho*phosphoric acid and flow rate of 1.0 mL/min. Detection was carried out at 248 nm. Diclofenac sodium was used as an internal standard. The retention time for Cefpodoxime proxetil, Ambroxol hydrochloride and Diclofenac sodium was found to be 3.89, 2.69 and 5.52 min, respectively. The Cefpodoxime proxetil and Ambroxol hydrochloride followed linearity in the concentration range of 3 - 21 *µg/mL* (R^2 = 0.9981) and 2 – 12 *µg/mL* (R^2 = 0.9980), respectively. [59]

High performance liquid chromatographic (HPLC) method for the determination of Cefpodoxime proxetil (CP) as bulk drug and as pharmaceutical formulation. Both R and S isomers of the drug were separated using Phenomenex (250 × 4.6 mm, 5 *µ*m particle size) ODS column with a flow rate of 1mL min−1 and an SPD 20A UV detector to monitor the eluate at 252 nm. The isocratic method used a mobile phase consisting of methanol and phosphate buffer of pH4.0 in the ratio 65: 35.Thelinear regression analysis data for the calibration plots showed good linear relationship with R^2 = 0.9999 in the working concentration range of 5–100 *µ/ml*. The LOD and LOQ were 53 and 160 *ng/ml*, respectively. [60]

Simple, accurate, precise and sensitive UV-Spectrophotometric and reversed-phase high-performance liquid chromatographic (RP-HPLC) methods for simultaneous estimation of clavulanate potassium (CLA) and Cefpodoxime proxetil (CP) in combined tablet dosage form have been developed and validated. Beer's law is obeyed in the concentration range of 15-150 *µg/ml* in methanol at 270 nm and 235nm for CLA and CP, respectively for simultaneous equation method. The RP-HPLC method uses a Shimadzu LC10 AT VP system with Luna C18 column and methanol: acetonitrile: water: tetrahydrofuran (THF) (40:30:20:10 V/V/V/V) as the mobile phase. The detection was carried out using a diode array detector set at 220 nm. Linearity of LC method in the concentration range of 15-200 and 5-50 *µg/ml* for CLA and CP respectively. The recoveries were in the range of 99.56±0.32 and 99.67±0.46 for CP and

99.89±0.27 and 99.70±0.45 for CLA in simultaneous equation method and HPLC method, respectively. [61]

Conclusion:

Gastro retentive 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. Prolonged gastric retention improves bioavailability, reduces drug waste and improves solubility for drugs that are less soluble in a high pH environment. Gastro retention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patients. The goal of any drug delivery system is to provide a therapeutic amount of drug to proper site in the body to achieve promptly and then maintain a desired drug concentration. Various dosage alternatives found by recent development can be administered via different routes of administration. Various routes that are used include oral, topical, nasal, rectal, vaginal and ocular, etc. The oral delivery of drugs is considered to be the most appealing route of administration. This belief has led to the identification of many very successful drugs, but also saw the downfall of some promising therapeutics that failed to meet criteria required for sufficient oral bioavailability. The use of solid dispersion technologies for improving the dissolution characteristics of poorly water-soluble drugs and in turn their oral bioavailability has become a major point of attraction.

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