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Comparative evaluation of quantification of gastroretentive drugs through ultraviolet spectrophotometer and high-performance liquid chromatography

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ABSTRACT

Quantification is a major step in the pharmaceutical industry for determining the quantity and quality of a specific Active Pharmaceutical Ingredient in each drug formulation. This step is major step for commercializing and marketing of the drug. Several methods have been developed for the quantification of the drug but the most used are UV and HPLC methods. In this study we try to review the various quantification methods by UV and HPLC and accomplish that which method is better for the Quantification for Gastroretentive drugs. Gastroretentive drug delivery system is a type of drug which retains foe a prolonged time in the Gastrointestinal tract and do not get disintegrated immediately. One type of Gastroretentive drugs is Gastroresistant drugs which do not disintegrate regardless the acidic pH of the stomach but gets absorbed in the surface of the intestines at a basic pH. This is possible because these types of drugs are enteric coated. Spectrophotometry techniques can be used as an alternative method for HPLC for the quantification of Gastroretentive drugs.

Keywords *– Gastroretentive drugs, Gastro-resistant, HPLC, UV-Spectrophotometer*

1. INTRODUCTION

Oral route drug administration is one of the most common and most preferred administration methods of drugs in the body of a human. Drugs such as Gastrointestinal drugs which are easily absorbed in the Gastrointestinal tract have very short half-lives and are excreted out from the systemic regulation quickly. So, the drug should be administered in the body frequently to achieve a desired therapeutic effect. Therefore, development of a dosage form of the drug which would avoid this problem and slowly release the drug into the GI tract in a controlled manner in a target specific way and have a higher retention time in the body was mandatory. The advantages of prolonged gastric retention of the drug includes – improves bioavailability, the duration of the drug release is prolonged, the drug wastes are reduced, and it improves the solubility of the drug. So, this kind of drug approach is known as Gastroretentive drug delivery system. The gastroretentive dosage forms can stay in the GI tract for long periods of time as compared to the normal dosage forms and significantly increase the retention time of the drug in the body.[1] In the testing of the drugs the quantitative and qualitative analysis of the drug is an important step in the commercialization of drugs. To carry out the same many methods is being used to carry out the qualitative and quantitative analysis of the drug – the most common of them used is High Performance Liquid Chromatography (HPLC) and Ultraviolet Spectrophotometer methods (UV). The main aim of HPLC analysis of any specific drug is to correctly identify, generate accurate quantitative results and to monitor the progress of the therapy of the disease that is being addressed by the drug.[2] Another commonly used method for the quantification of rugs is UV spectroscopy. UV methods are comparatively cheaper, easier and less time consuming than HPLC. But the method for the analysis of drug is determined by identifying the nature of the drug and its physical and chemical properties. Depending on the nature of the drug the appropriate method is being chosen for the analytical study of the drug.[3] Drugs like Omeprazole, Pantoprazole, Rabeprazole are the drugs which comes under the category of delayed release capsules or tablets which are enteric coated or have a gastric resistant coating. The gastric retention of the drug can be achieved by several ways like – Coating of the tablets or capsules, Floating delivery systems, Swelling systems etc.

2. GASTRORETENTIVE DRUG DELIVERY SYSTEM

There are several administration methods that can be implied to administer the drug into the body of an individual but the most preferred one remains the oral administration route. The oral routes are widely preferred due to its easy administration, inexpensive,

and flexibility in formulation which leads to higher level of patient compliance. Out of all the drugs that are available in the market 50% of the drugs are orally administered.[4] Although its highly effective but there originate a few problems with oral administration. The difficulties include the drug has decreased therapeutic effect which has a lower absorption ability, the drug delivery is not controlled, and the delivery of the drug is not site specific in cases it is needed for a targeted drug delivery. So, to encounter all these problems it was mandatory to formulate an orally administered drug which is site specific and increase its retention time in the Gastrointestinal tract to increase its therapeutic index.[5] The gastroretention of the drug can be achieved in many ways, some of those include:

2.1 Floating Dosage forms

These dosage forms are useful in the administration of the drug into local targets of the stomach such as Antacids. It is also advantageous in cases of high intestinal movement in the GI tract in disorders like diarrhea. The main disadvantage of this system is that it requires high level of fluids in the stomach to keep the drug floating and work efficiently.[6]

2.2 Coating of the drug for site specific action of the drug

Drugs that remain in the GI tract for a prolonged period and perform a site-specific action are generally enteric coated like – Omeprazole, Rabeprazole, Pantoprazole etc.

2.3 Bio adhesive and Mucoadhesive systems

In this kind of systems bio adhesive polymers are used which sticks to the epithelial surface of GIT. Bio adhesive kind of systems are generally used for specific targeted drug delivery and helps in increasing the absorption of the drug. [7]

Other than these three approaches there are many other approaches to enhance the working of the gastroretentive molecules. The human stomach is divided into three major regions – the Fundus, Body and Pylorus (Antrum). The movement of the Gastric region is divided into four major patterns generally known as the Migrating Motor Complex. The duration of each cycle is approximately 90-120 minutes. The four phases of the MMC are depicted in Table 1.

Table 1- The four phases of the Motor Migrating Complex (MMC)[8]

Phase	Description	Duration
Phase 1	No contractions are observed	30-60 minutes
Phase 2	Intermittent contraction is observed	20-40 minutes
Phase 3	Contractions at maximum frequency which results in the migration of the material distally	10-20 minutes
Phase 4	The transition period between Phase 3 and Phase 1	0-5 minutes

Drug absorption from the GI tract is a complex procedure and depends on various parameters. So, the Gastroretentive Drug delivery systems can be widely used for increasing the retention time of the drug in the GI tract, increasing the bioavailability of the drug, and helps in increasing the solubility of the drug in a high pH condition.

3. GASTRORESISTANT DRUGS

The role of a good dosage form is to ensure the correct release of the drug into the specific site and generate the desired therapeutic effects in the body. Also, the drug should be chemically and physically stable to produce a good therapeutic effect. Gastroresistant tablets in general means that the tablets which do not degrade in the gastric system and are resistant to the acidic pH of the stomach. The Gastroresistant tablets are designed to be absorbed in the intestines rather than in the stomach. These tablets are enteric coated which helps the drug to resist the low acidic pH of the stomach and are disintegrated in the basic or higher pH of the intestinal fluid.[9] These drugs generally come under the category of delayed dosage forms as they are modified to delay their release in the GI tract and are also cite specific. The enteric coated tablets also help in targeted drug delivery i.e., the drugs only release in the specific site for which it is designed for. Some of the common examples of Gastroresistant tablets are- Omeprazole, Pantoprazole, Rabeprazole, Lansoprazole etc.

4. HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

High Performance Liquid chromatography is a technique used to separate the individual constituents in a liquid-liquid mixture. There are two phases in the HPLC system – i) Mobile phase and the ii) Stationary phase. The mobile phase is incorporated into the stationary phase which is generally porous silica packed column and by the process of differential migration the individual components of the liquid mixture gets separated. As the components are separated one by one from the column a detection unit detects the analytes after leaving the column, it delivers a voltage response as a function of time which is known as a Chromatogram. Each peak emerges at a specific time which identifies the specific constituent, and the area of the peak determines the quantity of the constituent that is present in the mixture.

4.1 Components

The basic components which comprises the HPLC are – a Solvent Degasser, a HPLC pump, an Autosampler, Detector and Column oven.

4.2 Elution modes

The two types of elution modes in HPLC include – Isocratic elution (a single solvent or mobile phase is used) and Gradient (two different types of solvent or mobile phases are used in the elution process).

4.3 Column that should be used
Porous tightly packed Silica column (C18, C8, C4, Phenyl-Hexyl, Biphenyl)

4.4 Column size
100 x 3mm, 2.7 to 5 µm particles

4.5 Detectors that are commonly used
UV/Vis detectors, Photo Diode Array detectors, Refractive index detectors, Fluorescence detectors etc. [10] HPLC being a highly sensitive technique to separate out the components from the liquid mixtures it plays an important role in the pharmaceutical industry. The quantitation of an API in particular drug formulation is a very important process before the commercialization, marketing and ensuring the adequate quality of the drug. HPLC helps in the quantitation of the API of the drug formulation in the Pharmaceutical industry.

5. UV- SPECTROPHOTOMETRY
Ultraviolet spectrophotometry uses the light for absorption of the specific regions of the ultraviolet spectral region. Generally, UV-spectrophotometer is used in determining the concentrations of a particular particle dissolved in a solution. This instrument is also used in the quantitation of a particular API present in a specific drug formulation in the pharmaceutical industry.

Principle: The UV- Spectrophotometer works on the principle of Beer-Lambert Law which states that 'the absorbance of a particular solution is directly proportional to the absorbent and the path length'.

$$A= \varepsilon bC$$

Where,
A= Absorption
ε=Molar absorptivity
b=Length of light path
C=Concentration

5.1 Components
A light source, monochromator, two sample holders, detector, and the interpreter. Although both UV and HPLC can be used for the quantification of drug, but it depends on the drug that which method will be the best suitable way to quantify it.

6. MATERIALS AND METHODS
HPLC machine with a detector, UV Spectrophotometer, Omeprazole, Pantoprazole, Lansoprazole, Rabeprazole and Esomeprazole reference standards, All the chemicals were acquired required for the analysis for each of the drug. Extensive Literature survey was done and the most appropriate methods for the quantification for Gastroretentive drugs were found out and the results were noted down for each of the method both for UV-Spectrophotometer and High-Performance Liquid Chromatography.

7. Comparison of quantification of Gastroretentive drugs through HPLC and UV

S. no.	Drug Name	Method by UV-Spectroscopy	Method by HPLC	Results
1.	Omeprazole	Material and methods- UV spectrophotometer Solvent mixture - Phosphate buffer -pH=6.8 Standard solution- 20mg in 10 ml buffer. Further diluted to obtain a stock solution of 200µg/ml. Then 1,2,3…,10ml of std. solution transferred to 10 ml flasks. UV range -200-400nm	Phosphate buffer pH=7.4 Mobile phase – 70:30(buffer: Acetonitrile) Flow -1.5ml/min Column – RP-C18 column Wavelength- 280 nm Solutions were made from 10.0-30.0 µg/ml	UV- Spectrophotometry results- Peak maxima observed at -298 nm Showed good linearity HPLC results- Retention time of omeprazole was observed at 5 minutes with symmetrical peaks.
2.	Esomeprazole	Material and methods – UV spectrophotometer Solvent Mixture – 20% methanol was used as solvent Standard solution- 10 mg of ES drug in 100 ml volumetric. Volume made up by solvent mixture	0.025MAmmonium dihydrogen phosphate buffer (pH- 6.1) Mobile Phase- Buffer: methanol (35:65) Flow- 0.8 ml/min Wavelength – 302nm Column – Luna C18 column (250mm x 4.6 mm x 5 µm) 55.7 mg standard dissolved in 50 ml methanol (1mg/ml)	UV results- Peak Maxima at 275 nm Showed excellent linearity within the concentrations of – 5-30µg/ml HPLC results- Retention time of Esomeprazole was observed at 6 minutes.

3.	Pantoprazole	Diluent – Distilled Milli Q water Linearity range – 5-35µg/ml Wavelength – 290 nm Standard solution- 0.02 g of Pantoprazole in 100 ml volumetric and the volume made up by distilled water	Buffer – 6.8 gm of Potassium dihydrogen orthophosphate and 1 gm of hexane sulphonic acid in 1000 ml water (pH=7.3) Mobile phase – Buffer: Acetonitrile (50:50) Flow rate -1.5 ml/min Wavelength- 290 nm Injection volume- 10 µl Column – C18 column (250mm x 4.6mm x 5µm)	UV results- The method showed linear results and was effective HPLC results- Retention time of Pantoprazole was observed at 8 minutes
4.	Rabeprazole	Diluent- 0.1 N Hydrochloric acid Linearity range- 2-10 µg/ml Wavelength- 278 nm	Solvent mixture – Methanol: Water:Diethylamine (80:20:0.1) Buffer- 0.15% Potassium dihydrogen Phosphate (pH= 6.0) Mobile Phase- Buffer: Acetonitrile (65:35) Flow rate – 1.0 ml/min Wavelength- 280 nm Column – 250 mm x 4.6 mm x 5 µm	UV results – The calibration graph of the specific wavelength considered was found to be linear HPLC results- The retention time of Rabeprazole was found to be 5.6 minutes
5.	Lansoprazole	Solvent Mixture- 0.01 M Phosphate buffer (pH= 6.8) Linearity range- 5-30µg/ml Wavelength – 298 nm	Solvent mixture- Water: Acetonitrile: Triethylamine (60:40:1) Mobile Phase – Water: Acetonitrile: Triethylamine (60:40:1) pH= 7.0 Flow rate – 1 ml/min Wavelength- 285 nm Injection volume- 10 µl	UV results – The graph constructed on the basis of the wavelength was found to be linear HPLC results – The retention time of Lansoprazole was observed at 8.8 minutes

*Methods in the table are w.r.t IP

8. RESULTS AND DISCUSSION

From the extensive literature survey that was conducted for the comparison of the UV and the HPLC methods it was observed that both methods were accurate and generated a desired response. The HPLC methods were more sensitive as compared to the UV methods. Both methods are reliable and appropriate for the analysis and quantification of the gastroretentive drugs.

9. CONCLUSION

HPLC is more sensitive over UV when carrying out the analysis of the drug formulation at lower concentrations. But the advantage of UV method over HPLC is that all the UV methods are much easier than the HPLC method and require less labor. Also, the UV methods are much more inexpensive and require less optimization of parameters as that of HPLC. Although the results indicate that both the UV and HPLC methods are appropriate to quantify the GRDs but the HPLC methods are more accurate and precise. For the accurate and precise quantification of GR drugs HPLC has proven to be a better method than UV as it can be used for other purposes also and not just quantification such as identification of the drug, separation purposes etc. UV samples can also get contaminated with other chemicals which absorbs the same wavelength as the drug to give a false result. So, we conclude that although both methods are simple, specific and reliable they may be successfully used as routine methods for the quantification of GR drugs but HPLC is a better method to quantify a specific drug in order to generate accurate and correct results.

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Appendix

S.no.	Abbreviations	Full Forms
1.	HPLC	High Performance Liquid Chromatography
2.	UV	Ultraviolet
3.	GIT	Gastrointestinal Tract
4.	MMC	Motor Migrating Complex
5.	API	Active Pharmaceutical Ingredient
6.	IP	Indian Pharmacopeia
7.	GRD	Gastroretentive Drugs

