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Research Article

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Formulation and Evaluation of Gastro Retentive Floating tablet of Atorvastatin Calcium: A review

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Abstract

Oral solid dosage forms are most taking routes for many drugs and are still the most widely used formulations for new and existing modified release products. Howsoever the drug or the active moiety must be absorbed well throughout the Gastrointestinal Tract (GIT) in order to produce an optimized therapeutic effect. Absorption may be hindered, if there is a narrow absorption window for drug absorption in the GIT or if the drug is unstable in the GI fluids. the main challenge is to develop an oral controlled release dosage form not only to prolong the delivery but also to prolong the retention of the dosage form in the stomach or small intestine until the entire drug is released. One of the most important approaches to control the retention of drug delivery system in GIT is by adopting Gastro Retentive Drug Delivery Systems (GRDDS). Such retention systems are important for drugs that are drugs undergo rapid clearance in intestine like Atorvastatin calcium. Gastro Retentive Drug Delivery System of Atorvastatin calcium could be successfully formulated by direct compression technique, using different viscosity grades of HPMC, as binder used as Avicel PH102, sodium bicarbonate as gas generating agent, talc as glidant, magnesium stearate as lubricant and lactose as diluent. The optimized tablet formulation had showed 99.74% of drug release in 24 h. Therefore, the optimized formulation containing HPMC K100M with Avicel PH102 sustained the drug release for a period of 24 h and remains buoyant throughout the studies. Among the different grades of HPMC, HPMC K100M showed the maximum retardation in drug release. The in *vitro* dissolution profile of drug release from the tablets followed zero order kinetics. From the higuchi plot of dissolution profile, that the drug was released by diffusion mechanism and from the peppas plot we concluded that the release mechanism was found to be non Fickian release. The optimized formulation undergoes stability study at 25◦C / 60% RH, 30◦C / 65% RH, 40◦C / 75% RH.

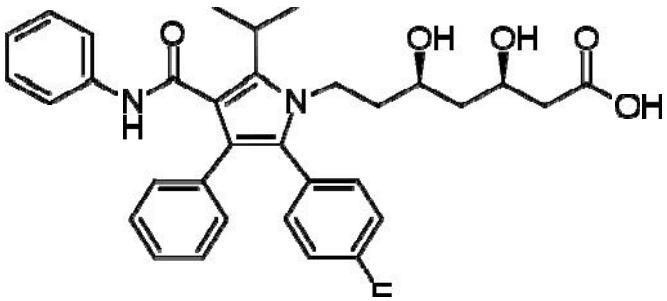
Keywords

Formulation, Evaluation, Gastro Retentive Floating Tablet, Atorvastatin Calcium.

Introduction

Oral solid dosage forms are the preferred routes for many drugs and are still the most widely used formulations for new and existing modified release products. The benefits offered by modified release systems include reducing dosing frequency with improved patient compliance, better and more uniform clinical effects with lower incidence of side effects and possible enhanced bio-availability. The rational design of modified release systems where, biological, physicochemical and physico-mechanical considerations have been taken into account during formulations of modified release dosage form, has alleviated the risk of dose dumping in vivo[1]. Among the different type of formulation, gastric emptying of dosage forms is an extremely variable process and ability to prolong and control the emptying time is a valuable asset for dosage forms, which reside in the stomach for a longer period of time than conventional dosage forms. Several difficulties are faced in designing controlled release systems for better absorption and enhanced bioavailability. One of such difficulties is the inability to confine the dosage form in the desired area of the gastrointestinal tract. Gastro Retentive drug delivery systems can be retained in the stomach for a long time. Such retention systems are important for drugs that are degraded in intestine or for drugs like antacids or certain antibiotics. The main objective of developing these systems is to increase the safety of a product, to extend its duration of action and decrease the side effects of drugs[2]. FDDS are preferred as they are economic and has improved patient compliance and they are advantageous for drugs absorbed from the stomach e.g.: ferrous salts and for drugs meant for local action in the stomach e.g.: antacids, drugs with narrow absorption window in the small intestine region e.g.: L-Dopa. When there is a vigorous intestinal movement and a short transit time as might occur in certain type of diarrhoea, poor absorption is expected. Under such circumstances also it may be advantageous to keep the drug in floating condition in stomach to get a relatively better response[3]. In this regarding, Atorvastatin calcium gastro retentive floating tablets were prepared by direct compression technique using polymers such as using different viscosity grades of HPMC, as binder used as Avicel PH102, sodium bicarbonate as gas generating agent, talc as glidant, magnesium stearate as lubricant and lactose as diluent. Direct compression technique using to enhance gastric retention and to increase its bioavailability and duration of action[4].

Molecular Structure of Atorvastatin[5]:



IUPAC Name:

(3R,5R)-7-[2-(4-fluorophenyl)-3-phenyl-4-(phenylcarbamoyl)-5-propan-2-ylpyrrol-1-yl]- 3,5-dihydroxyheptanoate

Atorvastatin identifiers:

CAS number: 134523-00-5
Category: Anti-Hyperlipidemic
Bio-Pharmaceutical Classification System: Class-II

Chemical data:

Formula: $\mathbf{C_{33}H_{35}FN_2O_5}$

Mol. Mass: 558.64 g/mol

Atorvastatin was first synthesized in1985 by Bruce Roth while working at Parke-Davis Warner-Lambert Company (now Pfizer). Atorvastatin is a member of the drug class known as statins, used for lowering blood cholesterol. It also stabilizes plaque and prevents strokes through anti-inflammatory and other mechanisms. Like all stations, atorvastatin works by inhibiting HMG-CoA reductase, an enzyme found in liver tissue that plays a key role in production of cholesterol in the body[6].

Materials and Methods

Materials:

Atorvastatin calcium was procured from Morepen laboratories Ltd., Avicel PH102 order from Medreich, Banglore, HPMC (K15M, K100M) were purchased from colorcon Asia Pvt. (Goa, INDIA), sodium bicarbonate and other excipients were procured from Ranbaxy laboratory Ltd, Guragaon, India.

Pre-formulation of sustained released tablet of Atorvastatin Calcium [7]

All ingredients were collected and weighed accurately. Atorvastatin calcium, HPMC, avicel PH102, sodium bicarbonate and lactose was shifted and passed through #40 mesh. And Magnesium stearate, talc was passed through #60 mesh. Then the major raw materials were mixed with the lubricant. Lubricated blend was compressed using 7mm flat round shaped punches plain on both sides in 16 station compression machines with average weight of 150mg.

Evaluation of Formulations [8]

Pre compression parameters [10]:

It includes Angle of repose, Bulk density, Tapped density, Cars index, Hausner's ratio.

Table: 1 Pre-formulation study data of the pure drug:

Sr. No	Parameters	Values obtained
1.	Angleofrepose(θ)	22°57'0.1332
2.	Bulk density(gm/ml)	0.3463□0.007
4.	Tap density(gm/ml)	0.4544□0.009
5.	Hausner'sratio	1.312□0.002
6.	Carr'sindex	23.55□0.212

Post-compression parameters [10, 11,]:

It includes Weight variation, Hardness, Friability, Thickness and diameter, Drug content, In-vitro buoyancy studies, and In-vitro dissolution studies [12].

Results and Discussion

The present study was undertaken to formulate Atorvastatin calcium floating tablets. Controlled release dosage forms deliver the drug at a slow release rate over an extended period of time. The drug Atorvastatin calcium is formulated as a floating tablet due to its rapid absorption in acidic pH, high intestinal clearance and maintains required drug concentration in blood. The tablets prepared in the present study by direct compression technique have advantages over those prepared by wet granulation in terms of time and energy consumption, thus making it possible to formulate tablets at a lower cost because of their flexibility, hydrophilic polymer matrix systems are widely used in oral controlled drug delivery. The study involved pre-formulation of drugs and granules, formulation and processing development along with evaluation of the tablets.

Conclusion

Gastro Retentive Drug Delivery System of Atorvastatin calcium could be successfully formulated by direct compression technique, using different viscosity grades of Hydroxy Propyl Methyl Cellulose, Avicel PH102 was used as binder, sodium bicarbonate as gas generating agent, talc as glidant, magnesium stearate as lubricant and lactose as diluent. Therefore, the optimized formulation containing HPMC K100M with Avicel PH102 sustained the drug release for a period of 24 h and remains buoyant throughout the studies. Among the different grades of HPMC, HPMC K100M showed the maximum retardation in drug release. The *in vitro* dissolution profile of drug release from the tablets followed zero order kinetics. From the higuchi plot of dissolution profile, we found that the drug was released by diffusion mechanism and from the peppas plot we concluded that the release mechanism was found to be non Fickian release. The optimized formulation undergoes stability study at 25 / 60% RH, 30◦C / 65% RH, 40◦C / 75% RH. There was a slight change in physical characteristics, buoyancy study and dissolution study. Finally, it was concluded that Gastro Retentive Drug Delivery System of Atorvastatin calcium prepared with higher viscosity grade HPMC K100M, which sustain the release of the drug in the GIT. It is a promising approach as it can able to release the required quantity of drug to the body, which results in minimizing the major side effect as rhabdomyolysis by minimizing the drug concentration in blood and also the entire dose was released in acidic medium, where atorvastatin having more absorption and ultimately leads to better patient therapy.

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