



POLYMER-BASED FLOATING MATRIX TABLETS FOR IMPROVED DELIVERY OF ACECLOFENAC

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ABSTRACT

For medications like aceclofenac that have limited solubility and poor bioavailability, the creation and testing of floating matrix tablets shows great potential for improving therapeutic effectiveness and patient compliance. Developing aceclofenac-based floating medication delivery devices was the focus of this investigation. By bouncing on the contents of the stomach, the medicine is gradually and at the correct pace eliminated from the system. When taken as directed, rather than with frequent, excessive dosages, these floating tablets may enhance the medication's bioavailability in addition to reducing lag time and releasing the medicine up to 12 hours after manufacture. Sodium bicarbonate, carbpol, xanthun-gum, guar-gum, microcrystalline cellulose, cellulose acetate phthalate, polyvinyl phthalate, and other polymers were used in the research to make floating tablets.

Keywords: Aceclofenac, Floating tablets, Matrix, Polymer, Cellulose

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I. INTRODUCTION

The pharmaceutical industry places a significant emphasis on the development of effective drug delivery systems as a means of improving treatment results and increasing patient compliance. Among the many different approaches to drug administration, floating matrix tablets have attracted a lot of interest because of their capacity to extend the amount of time that they spend in the stomach. This allows them to guarantee a continuous release of the medication and leads to an increase in its bioavailability. Aceclofenac is a nonsteroidal anti-inflammatory medicine (NSAID) that is often used for the therapy of a variety of painful and inflammatory illnesses. These disorders include rheumatoid arthritis, osteoarthritis, and ankylosing spondylitis. Aceclofenac is

renowned for its powerful analgesic and anti-inflammatory characteristics. In spite of this, its therapeutic efficiency is restricted due to its low solubility and poor stomach retention, which therefore requires frequent dose intervals throughout treatment. The formulation of dosage forms that demonstrate buoyancy in the gastric fluid is the core idea behind floating drug delivery systems. This technique ensures that the medicine is retained in the stomach for a longer period of time. This extended stomach residency duration not only makes it easier to release the medicine continuously, but it also reduces the number of times that the drug has to be administered, which ultimately leads to an increase in patient compliance and therapeutic effectiveness. As a medication that belongs to the BCS class II and has a poor



solubility, aceclofenac is confronted with difficulties that are associated with its unpredictable absorption and restricted bioavailability. Floating matrix tablets have controlled release characteristics, which allows them to sustain therapeutic drug levels in the systemic circulation for a longer length of time. This makes them a feasible answer to the issues that have been presented.

Additionally, gas-generating agents are included into the formulation of aceclofenac floating matrix tablets in order to provide buoyancy to the dosage form. This is accomplished by the introduction of both hydrophilic and hydrophobic polymers. Sodium alginate and hydroxypropyl methylcellulose (HPMC) are examples of hydrophilic polymers that contribute to the creation of the matrix and offer prolonged drug release. On the other hand, hydrophobic polymers, such as ethyl cellulose and Eudragit[®], slow down the release of the medication by building a barrier surrounding the dosage form. As an additional point of interest, gas-generating compounds like sodium bicarbonate react with stomach juice to produce carbon dioxide. This carbon dioxide then becomes trapped inside the gel matrix, which results in the buoyancy of the tablet. As a result of the synergistic combination of these excipients, aceclofenac is able to maintain its presence in the stomach for an extended period of time and be released gradually, which guarantees that its therapeutic advantages are maximized.

Assessment of the quality, performance, and efficacy of aceclofenac floating matrix tablets is accomplished via the use of a number of different assessment factors. Physicochemical characterization, in vitro drug release studies, buoyancy studies, swelling studies, compatibility studies, and pharmacokinetic investigations are some of the factors that are included in this category. In order to guarantee that the tablet complies with pharmacopeial requirements, physicochemical characterisation comprises evaluating the tablet's appearance, size, weight fluctuation, hardness, friability, and drug content consistency. The release kinetics of aceclofenac from floating matrix tablets

over a predetermined amount of time may be better understood via the use of in vitro drug release experiments. These studies are carried out under settings that replicate the environment of the stomach. Researchers are able to understand the release mechanism and kinetics of the formulation by measuring drug release at predefined time intervals. This allows them to guide future optimization efforts.

II. REVIEW OF LITERATURE

Dr, Rajentran et al., (2016) The aim of this study was to develop a regiospecific medication delivery system for Zidovudine. Zidovudine floating tablets were created using the direct compression method with varying concentrations of various polymers and a combination of xanthan gum and chitosan using the effervescent process. Sodium bicarbonate was used as a gas-generating agent. The floating tablets underwent assessment for weight consistency, hardness, fragility, drug concentration, swelling characteristics, in vitro floating ability, and dissolution behavior. An investigation was conducted on how varying concentrations of polymers affect medication release profile and floating qualities. The tablets that were manufactured showed acceptable physico-chemical properties. All the produced batches exhibited satisfactory in vitro buoyancy. The tablet expanded both outward and inward while being tested for buoyancy in a laboratory setting. The tablet floated for almost 12 hours. Higher levels of Chitosan reduced the time it took for the tablets to float, but they remained buoyant for a longer period. Formulations with a 1:1 ratio of medication to polymer floated for a longer period compared to formulations combining xanthan gum and chitosan. The medication was released from the tablets in a sustained manner, and non-Fickian drug transport from the tablets was verified.

Kumar, Sunil et al., (2012) This research aims to assess how natural gums impact the drug release profile in matrix systems for once daily sustained release tablet formulations. Aceclofenac, a nonsteroidal anti-inflammatory medication (NSAID), was used as a model compound to assess its release properties

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from various matrices. Matrix tablets of Aceclofenac were created using direct compression method with natural gums (xanthan gum and karaya gum) in various drug to gum ratios of FX, FK, and FXK (FX and FK in 1:1 ratios). The tablets underwent assessment for physical properties such as hardness, weight variation, friability, swelling index, and drug content. In-vitro drug release was conducted in Phosphate buffer at pH 7.4 for 24 hours. All the physical characteristics of the produced tablet were within acceptable parameters. Aceclofenac is released from a gelatinous swelling mass, which regulates the diffusion of drug molecules through the polymeric components into an aqueous media. The FXK matrices exhibit a more controlled release of prices compared to FX and FK matrices due to the burst effect and rapid release in the case of FX and FK matrices, respectively. FTIR investigations indicated that there was no chemical interaction between the medication and polymers in the FXK formulation. The release process was elucidated using zero-order, first-order, Higuchi, and Korsmeyer equations, considering swelling and non-Fickian diffusion mechanisms. The FXK matrices provide a greater number of pricing outcomes compared to FX and FK individually by leveraging the synergistic interaction between two biopolymers and ensuring consistency in the hydration layer in dissolution fluid.

Mayee, R.V. &Shinde, P.V. (2012) This research aimed to create and assess a floating tablet pulsatile medication delivery system for managing early morning stiffness and providing symptomatic relief from pain in rheumatoid arthritis patients. Aceclofenac was used as a model medication with different ratios of polymers including HPMC K4 M and Ethyl cellulose. Eight formulations were created, and formulation F8 exhibited excellent floating characteristics with a total floating time of 470. It also demonstrated a pulsatile drug distribution pattern. The tablets underwent examination for hardness, friability, and other in vitro testing. All parameters met the IP restrictions. The research found that combining hydrophilic polymers with hydrophobic polymers is

effective for optimizing the formulation of aceclofenac for pulsatile drug release.

Garg, Shiv (2011) Tablets may be used for the purpose of delivering pharmaceuticals in a precise manner and lowering the concentrations of drugs at locations other than the organ that is being targeted. In the current research, floating tablets of aceclofenac were used as a model medication, and their production and assessment were carried out. For the purpose of extending the duration of the gastric residence period. Floating effervescent tablets were created using a variety of materials, including hydroxypropyl methylcellulose (HPMC) K 4M and K 15M, psyllium husk, swelling agents such as crospovidone and micro crystalline cellulose, and gas generating agents such as sodium bicarbonate and citric acid. These tablets were then evaluated for their floating properties, swelling characteristics, and drug release studies. The preparation of floating non-effervescent tablets was accomplished by using polypropylene foam powder in conjunction with a variety of matrix forming polymers, including HPMC K 4M, Carbopol 934P, xanthan gum, and sodium alginate. In vitro drug release tests were carried out, and the linear regression approach was used to examine drug release kinetics. The results of these investigations revealed that the Higuchi equation and the Korsmeyer and Peppas equation were simultaneously followed. In the majority of the formulations, the kind of drug release mechanism that was discovered was fickian. In the clinic, floating tablets of aceclofenac might be used to provide sustained drug release for at least twenty-four hours. This would result in an increase in both the bioavailability of the medication and the patient's compliance with its usage.

Yadav, I.K. et al., (2010) In the current investigation, the purpose was to manufacture oral sustained release matrix tablets of aceclofenac by using both hydrophilic and hydrophobic polymers throughout the formulation process. Aceclofenac is a non-steroidal anti-inflammatory medication that is utilized in the treatment of symptomatic conditions such as



rheumatoid arthritis, osteoarthritis, and ankylosing spondylitis. Its biological half life is four hours. To investigate the nature of the interaction between the medication and the polymer, FTIR investigations were carried out. Through the use of the direct compression technique, controlled release formulations of aceclofenac (200 mg) were created. In vitro drug release and stability tests were performed on the tablets, as well as physicochemical and stability inspections. An investigation into the impact of the drug-to-polymer ratio on drug release was carried out in order to better optimize the formulation. According to the findings of FTIR investigations, there was no interaction identified between aceclofenac and polymers. The pills were determined to have physicochemical parameters that were within the acceptable range. The duration of time that the medicine was released from the improved formulations F1, F4, and F7 was prolonged for a dozen hours. The kinetic treatment applied to optimized formulations revealed that the release of drug follows the zero order model and Super Case II transport for F1 and F7. On the other hand, the drug release of F4 was best characterized by Higuchi's model and Super Case II transport. An increase in the concentration of the polymer resulted in a delay in the release of the medication. The formulations that were optimized underwent stability experiments for a period of three months at a temperature of 45 degrees Celsius and a relative humidity of 75±5%. The results demonstrated that the formulations exhibited stability with regard to the physicochemical parameters and release pattern. Based on the findings of the current research, it was determined that both hydrophilic and hydrophobic polymers are suitable for use in the formulation of a matrix-based sustained release formulation of aceclofenac.

Kumar, Ravi et al., (2009) Aceclofenac was going to be administered by a floating matrix drug delivery system, which was the objective of this research. In order to extend the amount of time that aceclofenac stays in the stomach and to boost its bioavailability, floating matrix tablets of the medication were

produced. There is a possibility that rapid gastrointestinal transit might lead to an incomplete release of the medication from the drug delivery system above the absorption zone, which would result in a reduction in the effectiveness of the dosage that was provided. Different combinations of bees wax were utilized in the development of floating matrix tablets that contained 100 milligrams of aceclofenac. Polymers such as hydroxypropylmethylcellulose (HPMC K15M), ethyl cellulose, bees wax, cetyl alcohol, glycerin monostearate alone or in combination, and other common excipients were utilized in the preparation of the tablets through the use of the melt granulation process. As an agent that generates gas, sodium bicarbonate was introduced into the mixture. Investigations were conducted to determine how sodium bicarbonate influences the medication release profile as well as the floating qualities. Tablet qualities that were deemed acceptable, floating lag time, and the overall period of floating and in vitro drug release were taken into consideration throughout the formulation optimization process. Monolithic tablets with optimal hardness, uniform thickness, constant weight homogeneity, and minimal friability were generated as a consequence of the formulation that was developed after the experiment. Based on the findings of dissolving experiments and floating lag time, it was determined that formulations F9 demonstrated a regulated and effective release of therapeutic agents. After using the linear regression analysis and fitting the model, it was discovered that the formulation F9 that was chosen had a drug release mechanism that was characterized by diffusion combined with erosion, and it followed first order kinetics.

III. RESEARCH METHODOLOGY

Preparation of calibration curve of Aceclofenac

To begin, a 100 ml stock solution of 0.1 (N) HCl and 100 mg of Aceclofenac is prepared. We used 10 milliliters of the stock solution and diluted it with 100 milliliters of 0.1 (N) hydrochloric acid. A volume of 100 ml was prepared by diluting 1, 2, 3, 4, 5, and 6 ml of



this solution with 0.1 (N) HCl, respectively. Afterwards, a UV spectrophotometer operating at 224 nm was used to measure the absorbances.

Preparation of floating matrix tablets of Aceclofenac

After the appropriate ratios of different excipients were mixed, Aceclofenac floating matrix tablets were manufactured using the direct compression method. Before combining, each component was completely blended and passed through a 40-mesh screen, with the exception of talc and magnesium stearate.

For each batch of fifty tablets, the ingredients (including 25 mg of aceclofenac) were well mixed before being compressed using 9 mm round and concave punches on a single punch tablet machine.

In vitro floatation study

Dissolution equipment type-II, USP (Campbell electronics, India) was used to assess the in vitro floating ability of the produced tablets. Three tablets from every batch of formulation were added to the dissolving vessels together with 500 cc of simulated gastric fluid (SGF, pH 1.2). The system was then programmed to rotate at 50 rpm and maintain a temperature of $37 \pm 0.5^\circ \text{C}$. We determined the buoyancy duration and the time it took to float on top of the dissolving media (lag-time).

In vitro release study

The test was conducted using a dissolving equipment type- II, USP, to determine the in vitro release of Aceclofenac floating matrix tablets. The tablets were mixed with 900 ml of SGF (pH 1.2), which was kept at a temperature of $37 \pm 0.5^\circ \text{C}$ with a rotating paddle speed of 50 rpm. To keep the sink condition throughout the experiment, 5 ml of aliquots were taken at regular intervals and

the same quantity of new dissolving media was added to the dissolution vessel. The filtered and appropriately diluted samples were prepared for analysis by means of a UV-VIS spectrophotometer at 224 nm in comparison to a blank.

Statistical analysis

For the analysis of all of the data, basic statistics were used. BioStat version 2009 for Windows, which was developed by Analyst-Soft Inc., was utilized in order to carry out the straightforward statistical analysis.

IV. RESULTS & DISCUSSION

In vitro floatation

In accordance with Table 1, all of the floating matrix tablets of Aceclofenac were floated thoroughly over an extended period of time (not less than six hours), with a minimum floating lag time of fourteen to thirty seconds. Effervescent agents include sodium bicarbonate and citric acid, both of which were present in these floating tablets. Effervescent agents are often capable of producing carbon dioxide (CO_2), which contributes to a decrease in the density of the system and causes it to float atop the aqueous medium. It is also possible that the HPMC K4M and tamarind gum that are included in these tablet matrixes might give buoyancy, which could result in fast hydration and swelling of the polymeric matrices, so forming a floating mass in the stomach pH (1.2). An increase in the viscosity of the polymer might cause the swelling of the polymeric chains to become more pronounced; nevertheless, the extremely viscous polymers generated a constant hydrogel that was able to prevent the solvent from penetrating further into the core of the tablet matrix system.

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Table 1: Results of in vitro floatation of floating tablets of Aceclofenac

Floatation results	F1	F2	F3	F4	F5	F6	F7	F8
Floating lag time(sec)	30	36	14	21	16	18	20	16
Floating duration(hrs)	6 ≤	6 ≤	6 ≤	6 ≤	6 ≤	6 ≤	6 ≤	6 ≤

In vitro drug release

The release of Aceclofenac from floating matrix tablets was evaluated in simulated gastric fluid (pH 1.2) using dissolving equipment type-II, USP. The Aceclofenac tablets floated and released the medication steadily in simulated gastric fluid (pH 1.2) for 4 hours. Tamarind gum-HPMC K4M-calcium alginate blends were utilized as release retardants in the floating tablets. The increased viscosity from combining tamarind gum, HPMC K4M, and calcium alginate may lead to the creation of thick gels when exposed to water. This would slow down the medication release rate from these floating pills. Siepmann and Peppas proposed that the drug release from HPMC matrices follows a sequential pattern.

Initially, strong concentration gradients of water are created at the interface between the polymer and water, causing water to be absorbed into the matrix. HPMC expands as

water is absorbed, causing significant changes in polymer properties, drug concentrations, and system size. as in contact with water, the medication dissolves and diffuses from the device owing to a concentration gradient. As water content rises, the drug's diffusion coefficient experiences a significant increase. The drug release from these floating systems was seen to be delayed when the amount of hydrophilic polymer blends (tamarind gum-HPMC K4M-calcium alginate) increased.

The increased viscosity caused by a higher concentration of hydrophilic polymer blends like tamarind gum-HPMC K4M-calcium alginate may lead to the creation of thick gels when in contact with water in the dissolution medium. This can result in the formation of a uniform hydrogel on the tablet's surface, hindering the solvent from penetrating deeply into the tablet core and consequently slowing down the release of Aceclofenac from these floating tablets.

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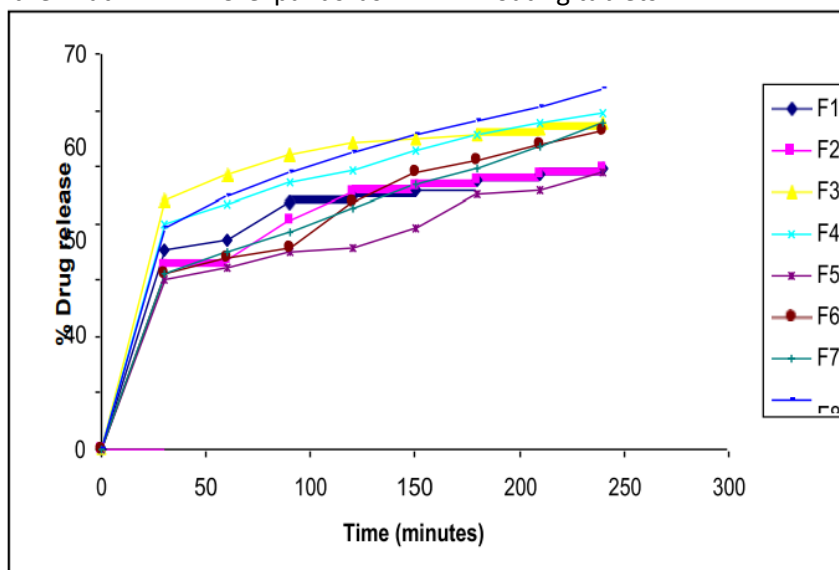


Figure 1: In vitro drug release from various floating tablets of Aceclofenac in SGF (pH 1.2)



V. CONCLUSION

The creation of aceclofenac floating matrix tablets shows potential in enhancing patient adherence and treatment effectiveness by reducing dose frequency and ensuring consistent medication levels in the bloodstream. Aceclofenac floating tablets were created by direct compression by blending hydrophilic polymers (tamarind gum-HPMC K4M-calcium alginate) and effervescent additives. The Aceclofenac floating pills exhibited prolonged buoyancy for at least 6 hours with a minimal delay in floating of 14 to 30 seconds. Prepared floating tablets of Aceclofenac were examined for in vitro release in simulated gastric fluid (pH 1.2) and demonstrated sustained drug release over a period of 4 hours.

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