

# Ciprofloxacin Swellable Tablet: A review of formulation strategies and evaluation

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## ABSTRACT:

Ciprofloxacin, a broad-spectrum fluoroquinolone antibiotic, is often used to treat bacterial infections. Swellable tablet formulations of ciprofloxacin are gaining interest for their potential to improve drug release profiles, bioavailability, and controlled therapeutic effects. This review discusses various formulation strategies, focusing on the use of hydrophilic and hydrophobic polymers, including hydrogels, starch derivatives, and cellulose-based materials, to control swelling and drug release. Factors like excipient choice, compression force, buffering agents, and particle size affect tablet performance. Evaluation involves *in vitro* tests such as dissolution studies, swelling index measurements, and stability assessments. Challenges, including drug release variability and stability issues, are addressed with proposed solutions. Overall, ciprofloxacin swellable tablets offer enhanced patient adherence and therapeutic outcomes.

**Keywords:** Ciprofloxacin, swellable, Hydrogel, Bioavailability

## I. INTRODUCTION

Drugs are active chemical substances employed for the diagnosis, prevention, and treatment of disease; they also alter the physiological state of the body. Oral administration of drugs is the most significant mode of administering drugs for systemic action. Oral administration of drugs has widespread acceptability up to 50-60% of total dosage forms. Solid dosage forms are well-accepted and the most preferred route because of their benefits. Tablets are solid dosage forms with medicinal agents with or without appropriate diluents. They provide a safe and convenient means of active pharmaceutical ingredients (API) administration with good physiochemical stability compared to some other dosage forms and ensure precise dosing. The regulation of gastrointestinal transit of orally taken dosage forms by gastro retentive drug delivery systems (GRDD) can enhance the bioavailability of drugs with site-

specific absorption. Gastric retention for an extended period can be attained using floating, swelling, bio-adhesive, or high-density systems [1]. For medications with a low plasma half-life, oral sustained-release dosage forms help produce the therapeutic effect for 24 hours and deliver the drug longer. Drugs with a limited window for absorption in the gastrointestinal tract (GIT) will not be well absorbed [2], [3]. Gastro retentive drug delivery systems (GRDDSs) are used for these medications, have been created. For medications absorbed from the upper gastrointestinal tract and those that are less soluble or unstable in an alkaline pH, oral sustained-release dosage forms with extended stomach residence time aid in absorption [4].

## Mechanism of swelling in drug delivery

Both hydrophilic and hydrophobic medications can be released in a tuneable and sustained manner thanks to innovative polymeric materials for examining the evolution of swellable polymeric materials into effective delivery systems for therapeutic agents. Within the sub-classes of swelling devices, swellable matrices, and superdisintegrants, the discussion of swellable controlled drug delivery devices and systems focuses on their structures, properties, and swelling mechanisms. Major factors influencing the manner of drug release will also be investigated, as will mathematical models used to predict drug release characteristics. In the final section, the potential drawbacks of swellable controlled drug delivery systems will be discussed. [5] In the case of polymers, swelling is the alternative drug delivery mechanism frequently employed to regulate the drug release from a device. Chain mobility is impacted by swelling because water is absorbed, lowering the glass transition temperature. Drugs with enhanced diffusivity and release rate are enclosed in a hydrogel, a polymer matrix. The primary process influencing water uptake on the swollen polymer surface is diffusion, and the release of drugs. [6]

## Formulation Strategies

### Selection of Polymers

Using a hydrophilic polymer (various grades of HPMC), gas-producing agent, and swelling agents in each formulation, ciprofloxacin HCl tablets are made by the wet granulation process. One-half of the swelling agents are applied intragranularly, and the other half is applied extragranularly.[7] When choosing a polymer material for a product, there are numerous considerations to take into account. Choosing the appropriate polymer requires a thorough grasp of the product's intended application and purpose. The working environment of the product must also be taken into account, including the temperature range it will be subjected to, UV exposure, and the substances it will come into contact with while in use.

Determining the product's intended lifespan is also crucial because it will affect the durability of the polymer that is chosen. By carefully weighing these variables, you may choose the polymer that will work best and last the longest for your application.[8]

### Role of excipients

Pharmacologically inert ingredients known as excipients are purposefully added to a drug product (DP) for a variety of functional purposes, including improving the size or volume of the dosage form, dissolving solid dosage forms, binding particles, lubricating the product during processing, masking taste, or altering drug release. The design and development of dosage forms heavily rely on excipients. One: When designing a high-quality DP, the choice of excipients is crucial and is determined by both the drug's and the excipients' compatibility as well as their functioning. The choice of excipient type, grade, and concentration in formulation is made via excipient-compatibility testing and formulation development research.[9]

### Techniques for Tablet Preparation

The active pharmaceutical ingredient (API) and a variety of excipients that serve as fillers, binders, disintegrants, lubricants, glidants, colorants, and flavor modifiers are commonly found in compressed tablets. Excipients such as coating polymers, plasticizers, and colors must be included in the final list of formulation ingredients because the compressed tablet is frequently coated. Compressed tablets are one of the most popular oral solid dose forms, although making

them can be difficult. Choosing an appropriate manufacturing process and the formulation's excipients from a variety of options that can support the intended therapeutic effect by maximizing the release kinetics, stability, and API solubility is an essential first step.[9], [10]

### Wet granulation

The most popular granulation method in the pharmaceutical industry for making tablets is wet granulation. Additionally, the granular formulation enhances the end product's content consistency and lessens segregation. It will be easier to comprehend how formulation and process variables affect the behaviour of the powder in the granulator after the primary granulation-related phenomena are identified. The most often used medicine delivery method is the tablet. According to reports, factors such as the type and quantity of liquid binder and its characteristics, such as viscosity, density, wettability, solid-liquid contact angle, and liquid droplet size, have an impact on wetting and nucleation and, consequently, granule attribution.[11]

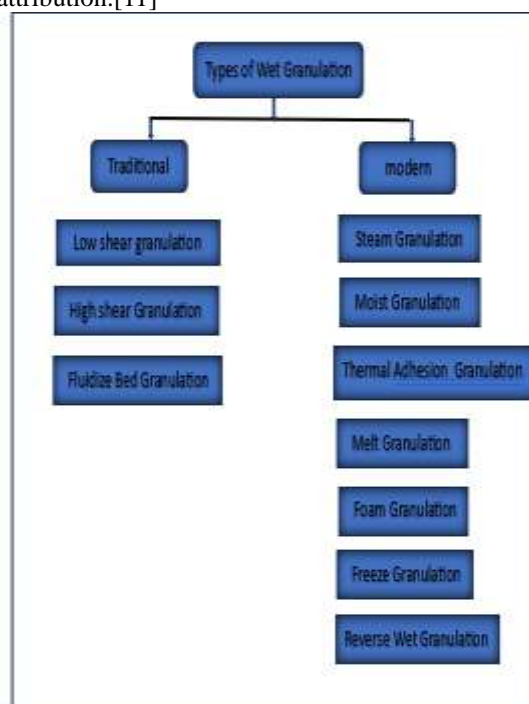


Fig: 01

### Direct compression

Direct compression is a preferred option since it offers the quickest, most efficient, and least complicated method of producing tablets. The product is easy to process because the maker can combine an API with the lubricant and excipient,

and then compress the mixture. There is no need for further processing. This kind of method can also use chemicals that are sensitive to heat or moisture, which would not be appropriate for wet granulation. In contrast to granulation procedures, it necessitates a very selective selection of excipients because its operation depends on the raw materials exhibiting good flowability and compressibility.[12]

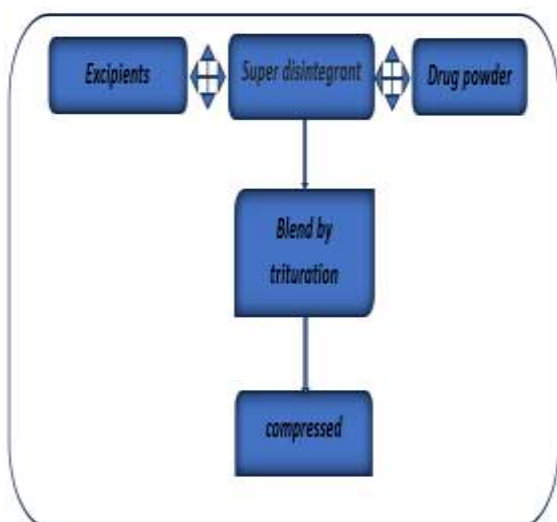


Fig:02

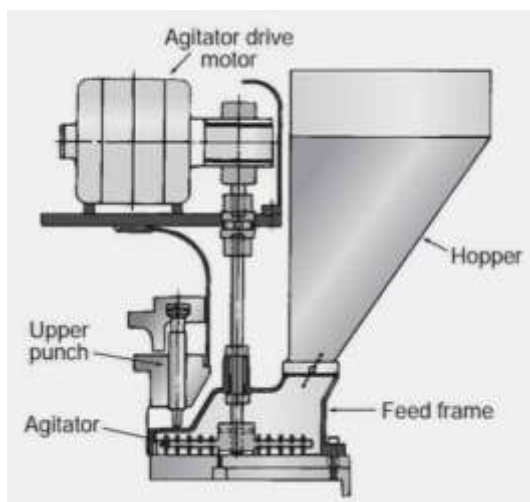


Fig:03[13]

In this regard, both high and low API dosages pose difficulties. The quality of tablets is impacted if the formulation asks for a significant amount of API because most APIs have poor compressibility. However, there may also be issues if low concentrations of active ingredients must be added to tablets, since it can be challenging to

precisely mix a small amount of active ingredient with a large volume of excipient to get the required homogeneity and consistency.[12]

### Optimization of Formulation

The definition of optimization is "to make perfect," meaning to use various methods and procedures to make anything perfect. Various medicine formulations use optimization approaches to assist in creating high-quality products. It includes several kinds of pharmaceutical products and their manufacturing methods. Numerous difficulties in the pharmaceutical process and product, including formulation, manufacturing, excipient selection, novel drug development, and other pharmacy-related challenges, are solved through the application of optimization techniques. We look at the several issues that arise throughout research because of the optimization technique. Pharmaceutical product and process formulation can be made easier with the use of optimization techniques.[14]

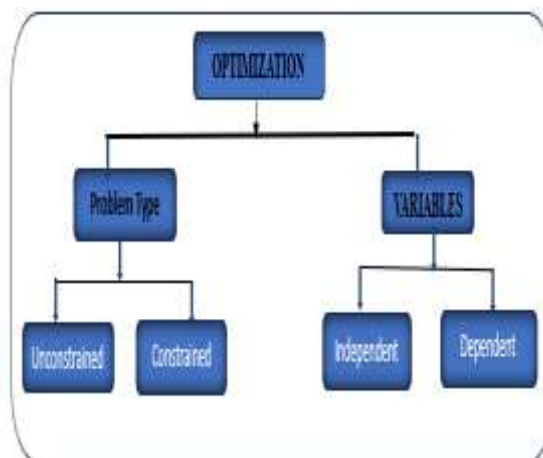


Fig:04

### Design of Experiments (DoE)

Design of experiments (DOE) is a systematic, efficient method that enables scientists and engineers to study the relationship between multiple input variables (aka factors) and key output variables (aka responses). It is a structured approach for collecting data and making discoveries.[15]

Process variables are initially "screened" using the design of experiment (DOE) approach to identify those that are crucial to the result: kind, proportion, disintegration time (DT), and other

excipients. The second phase is "optimization," which involves figuring out the ideal parameters for the crucial variables. It entails modifying the composition of the mixture and investigating the effects of these modifications on the combination's characteristics through the use of "mixture designs." [16]

#### DOE is useful:

- In driving knowledge of cause and effect between factors.
- To experiment with all factors at the same time.
- To run trials that spans the potential experimental region for our factors.
- To enable us to understand the combined effect of the factors,

#### Influence of Polymer Ratio and Drug Load

The ratio of polymer to drug and the drug load are crucial factors in the development of drug delivery systems, particularly in controlled release formulations. The polymer ratio directly affects the release profile of the drug, as it determines the matrix's structural integrity and the rate at which the drug is released. A higher polymer ratio often leads to a slower release due to the dense network formed by the polymer, which limits the diffusion of the drug. Conversely, a lower polymer ratio can result in a faster release, as the matrix may be less restrictive. The drug load also plays an essential role. Increasing the drug load can enhance the therapeutic effect by providing a higher dose, but it can also impact the release characteristics. High drug loads might cause the formulation to become unstable, leading to uneven drug release or reduced control over the release rate. Balancing the polymer ratio and drug load is key to ensuring the drug is delivered predictably and effectively, avoiding either too rapid or too slow a release. By adjusting these parameters, pharmaceutical formulators can tailor drug delivery systems to achieve optimal therapeutic outcomes.

#### Evaluation Parameters

Weight homogeneity, which guarantees a constant dosage in every tablet, is a crucial criterion for tablet evaluation. Tablet strength is measured by hardness, which ensures the tablets dissolve well and don't break easily. Friability measures how well tablets withstand mechanical stress and how long they last while being transported. How soon a pill dissolves in the body for efficient absorption is determined by its

disintegration time. The rate at which the active component dissolves is measured. Each pill has the right amount of medication because of content homogeneity. Finally, to guarantee both quality and visual appeal, the look is examined for flaws like cracks or discoloration.

#### Pre-Compression Parameters

Once an active ingredient has been discovered, the pre-compression evaluation of tablets can concentrate on the formulation and administration method of the product. Increased chemical instability and bioavailability could result from these changes. There should be a real possibility of a successful drug development process for the molecular form of the medicine that advances from the pre-compression evaluation of tablets. [17]

#### Bulk Density

The mass of a loose powder bed per unit volume is known as its bulk density. The envelope volumes of the individual particles, as well as the gaps between them, are included in the unit volume. The process of packing the material into that volume can have an impact on how compressed the powder is, which in turn can affect the bulk density value.

$$\text{Bulk Density (g/mL)} = M/V_o$$

A crucial factor in the development of processes and the production of solid dosages is bulk density. It is employed in figuring out how much powder can fit in a container, like a blender or a tablet press or capsule filler's hopper. The amount of powder that can fit within a capsule is also ascertained using it. [18]

#### Tapped Density

The mass of a powder divided by the volume it occupies after being tapped for a predetermined amount of time is known as the powder's "tapped density." A powder's random dense packing is represented by its tapped density.

$$\text{Tapped Density (g/mL)} = M/V_f$$

The bulk density of the granules following a particular compaction procedure is referred to as "tapped density." According to the US Pharmacopeia (USP), a device that raises and lowers a volumetric measuring cylinder filled with the powder a predetermined distance can be used to estimate tapped density.[19]

### Angle of Repose

A conical pile is created when large amounts of granular material are deposited onto a level surface. The angle of repose, which is the internal angle between the pile's surface and the horizontal surface, is influenced by the material's density, surface area, particle shapes, and coefficient of friction. Compared to materials with a high angle of repose, those with a low angle of repose create flatter piles.

$$\theta = \tan^{-1}(\mu)$$

### Compressibility Index (Carr's Index)

Carr's Index is a measure of a powder's tendency to consolidate or decrease in volume under pressure, calculated using bulk and tapped densities, and is used to assess powder flowability.

$$\text{Compressibility Index (\%)} = \left[ \frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Tapped Density}} \right] * 100$$

### Post-Compression Parameters

Post-compression parameters are essential for evaluating tablet quality and physical characteristics after compression.

### Tablet Hardness

"Tablet hardness" refers to the amount of force needed to shatter a tablet when it is subjected to a bending or tension load in a testing device. A tablet's hardness significantly impacts its effectiveness and general performance, particularly when it comes to patient use, packaging, and shipping. Additionally, it is a crucial component of tablet quality assurance.[20]

### Types of hardness testers

There are two types of hardness testers: manual and electronic. The manual hardness testers require the individual placement of each tablet and manual recording of the results. Electronic testers automatically measure and record the hardness.

- **Monsanto**

The Monsanto tester was developed 50 years ago. The design consists of "a barrel containing a compressible spring held between 2 plungers". The tablet is placed on the lower plunger, and the upper plunger is lowered onto it.[21]



Fig: 05[22]

- **Pfizer**

The Pfizer tester compresses a tablet between a holding anvil and a piston connected to a force-reading gauge when its plier-like handles are gripped.[21]



Fig: 06[23]

### Friability

Friability, or the state of being friable, is a term used in materials science to characterize a solid's propensity to fracture into smaller pieces when subjected to stress or contact, particularly rubbing. Induritate is the opposite of friable.

$$\text{Friability (\%)} = \frac{W_1 - W_2}{W_1} \times 100$$



Fig:07[24]

#### Weight Variation

The difference between the average weight of a sample batch and the actual weight of individual units (such as pills or capsules) is known as weight variation. It is a quality control test used to guarantee dosage unit homogeneity in pharmaceutical manufacturing.

$$\text{Weight Variation (\%)} = \frac{\text{Individual Weight} - \text{Average Weight}}{\text{Average weight}} \times 100$$

#### Drug Content Uniformity

One pharmaceutical analysis criterion for tablet quality control is the uniformity of content. Several capsules or tablets are chosen randomly, and the specific amounts of the active component in each tablet are assayed using an appropriate analytical technique.[25]

#### Swelling Index

The Swelling Index is a measure used to determine the capacity of a material, typically a pharmaceutical or polymer substance, to absorb liquid and expand. This property is crucial for evaluating the performance of tablets, gels, or other dosage forms. A higher swelling index often indicates better water uptake, enhancing drug release. It helps develop formulation, especially for sustained or controlled drug delivery systems.

$$\text{Swelling Index (SI)} = \frac{W_t - W_0}{W_0} \times 100$$

#### Water Uptake Studies

Water uptake studies assess how much water a substance, such as a polymer or tablet, can absorb over time. These studies help understand the hydration behaviour and stability of materials in different environments. By measuring weight gain after exposure to moisture, researchers can predict performance in drug delivery or packaging. Such evaluations are essential for developing effective, reliable formulations with controlled-release or moisture-sensitive properties.

$$\text{Water Uptake (\%)} = \frac{W_t - W_0}{W_0} \times 100$$

#### In-Vitro Drug Release Studies

Using a tablet dissolution tester [Dissolution Tester (USP), type 1 (basket technique)] in 900 cc of pH 6.8 phosphate buffer at 37.5±0.5 °C, the release rate for each of the developed formulations was examined for up to 24 hours. One hundred rpm was the agitation speed. A 10 ml sample was taken out and replaced with new dissolving media at prearranged intervals. Following the proper dilution, the samples were examined.[26]



Fig: 08

### Release Kinetics Models

Drug release dissolution media is one or more mechanisms that rely on the matrix's composition, geometry, preparation technique, and other factors that control the drug release kinetics. This can be described by mathematical models based on the model's accuracy and desired or necessary forecasting capacity.

### RELEASE MODELS

#### Zero-order release kinetics

It describes the continuous, concentration-independent release of a drug from a drug delivery system. At its most basic level, zero-order release can be shown as

$$Q = Q_0 + K_0 t$$

#### First-order release kinetics

The initial release order from a system where the rate of release is concentration-dependent is described by the following equation:

$$\frac{dC}{dt} = -Kt$$

#### Higuchi Model

Higuchi created the first mathematical model in 1963 that attempted to explain drug release from a matrix system. This model is suitable for researching the release of medications that are integrated into semisolid and solid matrices and are both water soluble and low soluble. The following equation provides the model expression:

$$Q = A [D (2C - C_s) C_s t]^{1/2}$$

#### Korsmeyer - Peppas Model

Using a straightforward relationship to explain drug release from a polymeric system, an empirical equation to examine drug release from swelling and nonswelling polymeric delivery systems, including Fickian and non-Fickian. The first 60% of drug release data was fitted in the Korsmeyer–Peppas model to determine the mechanism of drug release.[27]

$$M_t / M_\infty = K t^n$$

### Stability Studies

The degree to which a drug substance or product maintains the same qualities and attributes that it had when it was manufactured, within predetermined bounds and during its storage and usage, is referred to as drug stability.[28]

### Future Prospects

Ciprofloxacin swellable pills have bright futures, especially when it comes to improving patient compliance and therapeutic efficacy. By generating a hydrogel layer upon contact with gastric fluids, swellable drug–polyelectrolyte matrices (SDPM), which are used in these tablets, allow for controlled and prolonged drug release. Ciprofloxacin can be released gradually, thanks to this process, which keeps therapeutic medication levels stable for long periods. Formulations with effervescent ingredients, such as sodium bicarbonate, can improve absorption in the stomach and proximal small intestine and increase gastric retention, extending the duration of the medication's action. These developments are especially helpful in avoiding side effects, decreasing the frequency of doses, and treating illnesses that call for constant antibiotic levels. Ciprofloxacin tablets greatly improve drug delivery systems by providing focused therapy, controlled release, and increased bioavailability, which improves patient adherence and treatment results.

## II. CONCLUSION

Ciprofloxacin swellable tablets are a major development in controlled drug delivery systems, especially for medications like ciprofloxacin that have a limited window of absorption. When these formulations come into contact with gastric fluids, hydrophilic polymers like hydroxypropyl methylcellulose (HPMC) generate a gel-like matrix that allows for targeted and prolonged drug release in the stomach and proximal small intestine. By producing carbon dioxide, effervescent chemicals such as sodium bicarbonate improve gastric retention by increasing buoyancy and extending the tablet's duration in the stomach. According to studies, these pills can greatly increase bioavailability and therapeutic efficiency by achieving a mean stomach retention period of almost 320 minutes. Furthermore, non-Fickian diffusion mechanisms are frequently followed by

the release kinetics, enabling controlled and predictable drug release profiles. Ciprofloxacin swellable pills are a viable alternative in contemporary pharmacotherapy because of these developments, which also lessen systemic side effects and improve patient compliance by lowering the frequency of administration.

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