PRELIMINARY ANALYSIS INTO THE FORMULATION OF PROMPT DISINTEGRATING CIPROFLOXACIN TABLETS USING PECTIN EXTRACTED FROM CITRUS SINENSIS PEEL AS A DISINTEGRANT

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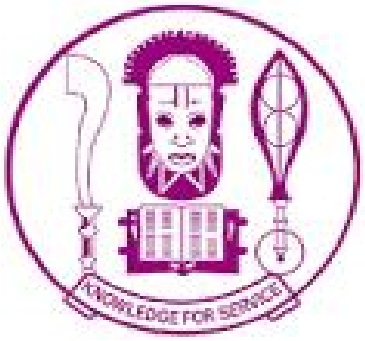

DEPARTMENT OF PHARMACEUTICS AND PHARMACEUTICAL TECHNOLOGY,

FACULTY OF PHARMACY
UNIVERSITY OF BENIN
BENIN CITY

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A PROJECT SUBMITTED TO THE DEPARTMENT OF PHARMACEUTICS AND PHARMACEUTICAL TECHNOLOGY IN PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE AWARD OF DOCTOR OF PHARMACY (PHARM.D) DEGREE OF FACULTY OF PHARMACY, UNIVERSITY OF BENIN, BENIN CITY, NIGERIA.

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CERTIFICATION

This is to certify that this project was successfully carried out by IGBINEWEKA DANIEL in the Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmacy, University of Benin, Benin City, Nigeria.

IGBINEWEKA DANIEL (STUDENT)	DATE
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DEDICATION

This work is dedicated to Almighty God for making this project a success, my mother, Mrs. OMORUYI MABEL for her support and care and my Spiritual Father, Pastor Emmanuel Ubiebi, thank you sir for making me who I am today.

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ABSTRACT

Introduction: Disintegrating agents are used to speed up the breakdown of solid dosage forms, such as tablets and capsules, after administration. Pectin is a complex polysaccharide composed of galacturonic acid units commonly used in the pharmaceutical industry as a disintegrant due to its ability to absorb water and swell leading to the disruption of tablet structure and promoting rapid disintegration.

Objective: To investigate the feasibility of incorporating pectin obtained from citrus sinensis peel as a fast acting disintegrant and assessing its impact on tablet disintegration and dissolution profile and to compare the performance of the locally obtained pectin based-formulations with other disintegrants.

Method: Pectin was extracted using the hot acid extraction method and various batches of ciprofloxacin tablets (F1-F7) were prepared by wet granulation technique. The granules produced were subjected to pre-compression (bulk and tapped densities, angle of repose, Hausner's ratio and Carr's index) and post compression (hardness, friability, weight uniformity and dissolution) evaluations respectively.

Results: The granular mixtures of the various batches had angle of repose between 22.53° to 28.60° indicating excellent flow. The Hausner's ratio ranged from 1.12 to 1.22 while the Carr's index was between 11.69% and 17.20%. The bulk and tapped densities were found to be between 0.41gm/cm3 to 0.58gm/cm3 and 0.42gm/cm3 to 0.60gm/cm3 respectively. The seven batches had uniform weight with low standard deviation values of less than ±5% which are within the B.P limits. The hardness values ranged from 7.2 to 10.0 kg/cm2 while the friability values of 0.60 - 0.98% were found to be less than 1%. The disintegration time of the pectin formulation F2-F6 ranged from 11.5-26.4min as compared with those of the standards F1 and F7 whose disintegration time value were 8.2 and 13.5 respectively. The in vitro dissolution result showed that F6 had the best dissolution profile among the formulations containing pectin.

Conclusion: Pectin obtained from Citrus sinensis at a concentration of 15% showed excellent disintegrating property when compared with sodium starch glycolate and maize starch which are super disintegrants and conventional disintegrants respectively.

CHAPTER ONE

1.0 INTRODUCTION

1.1. BACKGROUND

Tablets are one of the most popular and practical medication administration methods; however, they might provide problems for some patients, such as those with dysphagia or those who require a fast onset of action (Gerhard et al, 2003). Orally disintegrating tablets (ODTs), which don't require chewing or water to dissolve or disintegrate in the mouth in a matter of seconds, have been created as a solution to these problems. ODTs have a number of benefits over traditional tablets, including better patient compliance, increased bioavailability, and quicker drug absorption.

But when producing ODTs, excipients must be carefully chosen, notably disintegrants, which are substances that encourage the tablet to break up into tiny pieces when it comes into contact with saliva.

1.1.1. JUSTIFICATION

- The disintegration duration, dissolving rate, and mechanical strength of ODTs are significantly influenced by disintegrants. The disintegration of tablets employing natural disintegrants, which are sourced from plant or animal sources, must therefore be improved.
- Natural disintegrants are non-toxic, biodegradable, biocompatible, readily obtainable, and affordable, which are advantages over synthetic ones. Natural disintegrants can also serve as nutritional supplements and improve the solubility of medications that aren't very water-soluble. Starches, gums, mucilage’s, and dried fruits are a few examples of natural disintegrants.

COMPARATIVE STUDY

The following are a few recent research on the use of natural disintegrants to speed up pill disintegration:

The disintegration and dissolution characteristics of ODTs made with various natural super disintegrants, including banana powder, orange peel pectin, and fenugreek seed mucilage, were compared in a study by Singh et al. (2022). They observed that fenugreek seed mucilage, and banana powder were the next two most efficient natural super disintegrants. Additionally, banana powder enhanced the ODTs' flavor and texture.

In a study by Kumar et al. (2021), the impact of natural disintegrants on the formulation of ODTs using paracetamol as a model medication was assessed. These disintegrants included aloe vera gel, papaya latex, and pineapple juice. They noticed that all of the natural disintegrants sped up the dissolution and decreased the disintegration time.

In a study by Patel et al. (2020), the utilization of natural disintegrants in the production of ODTs containing metformin hydrochloride as an anti-diabetic medication was examined. These disintegrants included the peel of a mango powder, apple peel powder, and lemon peel powder. They found that mango peel powder had the fastest disintegration time and the highest rate of dissolution, making it the best natural disintegrant for metformin hydrochloride ODTs.

According to these findings, natural disintegrants can be employed as efficient substitutes for synthetic ones when creating ODTs with different medications. However, more study is required to maximize the formulation parameters for higher quality and stability of ODTs and to investigate the possibilities of other natural sources.

1.1.1.2 Definition and Classification of Pharmaceutical Dosage Forms

Dosage form is referred to the physical mold of a dose of a chemical compound used as a treatment or medication intended for administration for ingestion. (PharmalQ Glossary, 2023). Pharmaceutical dosage forms play a crucial role in the effective delivery of drugs to patients. They are designed to ensure accurate and convenient administration of medications while maximizing therapeutic outcomes.

Based on their physical characteristics, they can be divided into a number of groups, including dosage forms that are solid, liquid, semi-solid, and gaseous. Each category includes distinct formulations made to fit the demands of the patient and the properties of the medicine.

1.1.1.3. SOLID DOSAGE FORMS

- **Tablets**: These are compressed solid preparations containing the active drug and excipients, designed for oral administration. (Ansel's et al., 2014)
- **Capsules**: Gelatin shells enclosing powdered or granulated drugs, facilitating oral administration.
- **Powders**: These are finely divided drug substances used for internal or external administration after reconstitution or dilution.
- **Granules**: These are agglomerates of fine particles, often used for oral administration or in the preparation of suspensions.

1.1.1.4. LIQUID DOSAGE FORMS

a. **Solutions**: Homogeneous mixtures of one or more drugs dissolved in a suitable solvent.

- ❖ Suspensions: Dispersions of finely divided solid particles in a liquid medium, requiring shaking before administration.
- ❖ **Emulsions**: They are two-phase systems comprising immiscible liquids, stabilized by emulsifying agents, often used for topical applications.(Encyclopaedia Britannica, 2023)

b. **Semi-solid Dosage Forms:**

- ❖ **Ointments**: These are Semisolid preparations for topical application, typically containing a drug and a hydrophobic base.
- ❖ **Creams**: Semisolid emulsions used for external applications, consisting of oil and water phases.
- ❖ **Gels**: Semi-solid systems containing a network of solid particles dispersed in a liquid medium, suitable for topical and oral administration.

c. **Gaseous Dosage Forms:**

- ❖ **Inhalation Aerosols**: Pressurized systems delivering drugs in fine particles or droplets for inhalation therapy e.g, salbutamol inhaler.
- ❖ **Gases**: Medicinal gases administered through inhalation or injection, such as oxygen or nitrous oxide.

1.1.1.5. Advantages of solid dosage forms includes,

a. **Tablets**:

- ❖ Convenient and portable: Tablets are compact, easy to handle, and convenient for patients to carry and administer.
- ❖ Accurate dosing: Tablets offer precise dosing due to standardized formulations and uniform drug distribution.
- ❖ Shelf stability: Tablets have good chemical and physical stability, allowing for extended shelf life
- ❖ Controlled release: They can be formulated as immediate-release or modified-release tablets, enabling controlled drug release profiles.
- ❖ Identification: Tablets can be easily identified through shape, color, and markings, aiding in proper medication administration.

b. **Capsules**:

- ❖ Ease of swallowing: Capsules, particularly soft gelatin capsules, are generally easier to swallow than tablets, making them suitable for patients who have difficulty swallowing solid dosage forms.
- ❖ Masking taste and odor: Capsules can help mask unpleasant tastes or odors associated with certain drugs, improving patient acceptance.

- ❖ Formulation flexibility: Capsules can accommodate a wide range of drug formulations, including powders, granules, liquids, and even combinations of multiple drugs.
- ❖ Customized release profiles: Capsules can be formulated with immediate-release, delayed-release, or extended-release properties to meet specific therapeutic needs.
- ❖ Protection from atmospheric conditions: Hard-shell capsules provide protection to drugs sensitive to atmospheric oxygen and moisture.

c. **Powders**:

- ❖ Rapid dissolution and absorption: Powders typically exhibit faster dissolution rates, leading to quicker drug absorption and onset of action.
- ❖ Versatility in administration: Powders can be administered orally, reconstituted with a liquid for oral or topical use, or used for inhalation.
- ❖ Adjustable dosing: Powders offer flexibility in dosing adjustments, allowing precise customization according to patient needs.
- ❖ Improved stability: Compared to liquid formulations, powders often have increased stability and longer shelf life.
- ❖ Ease of storage and reconstitution: Powders can be stored in a dry form, reducing space requirements, and reconstituted into a liquid when needed.

d. **Granules**:

- ❖ Improved flow and handling characteristics: Granules have better flow properties than powders, facilitating accurate measurement and dispensing during manufacturing and compounding.
- ❖ Uniformity in dosing: Granules with consistent particle sizes provide more uniform dosing, reducing the risk of dose variation.
- ❖ Ease of administration: Granules are suitable for oral administration, as they can be swallowed easily with water or mixed into food or beverages.
- ❖ Taste masking: Granules can be formulated with taste-masking agents to improve palatability, making them suitable for pediatric and geriatric populations.
- ❖ Enhanced stability: Granules offer improved stability compared to powdered formulations, reducing the risk of degradation or changes in drug potency over time.

Advantages of Liquid Dosage Forms:

a. **Solutions**:

- ❖ Rapid drug absorption: Drugs in solution form are readily absorbed by the body, resulting in faster onset of action.
- ❖ Accurate dosing: Solutions allow precise and accurate dosing as the drug is uniformly dissolved.
- ❖ Suitable for patients with swallowing difficulties: Solutions are ideal for patients who have difficulty swallowing tablets or capsules.

- ❖ Versatile routes of administration: Solutions can be administered orally, topically, intravenously, or by other parenteral routes, offering flexibility in drug delivery.
- ❖ Immediate release: Solutions provide immediate drug release, which is advantageous for drugs requiring rapid action.

b. **Suspensions**:

- ❖ Drug stability: Suspensions can maintain drug stability for drugs that are not easily soluble or are prone to degradation in solution form.
- ❖ Dose flexibility: Suspensions allow for flexible dosing adjustments, making them suitable for pediatric and geriatric populations.
- ❖ Extended release: Suspensions can be formulated as sustained-release formulations, providing prolonged drug release and reducing dosing frequency.

1.1.2.0. PHARMACEUTICAL TABLETS

A pharmaceutical tablet is defined as a compressed solid dosage form containing medicaments with or without excipients. (Leon et al.,1990). They vary in shape and differ greatly in size and weight, depending on the number of medicinal substances and the intended mode of administration.

1.1.2.1. METHOD OF TABLET MANUFACTURING

Manufacturing tablets involves a series of steps and processes to transform a formulation into a solid dosage form. They include,

A. **Pre-Formulation and Formulation Development:** The first step in tablet manufacturing involves pre-formulation studies, which include the selection of active pharmaceutical ingredients (APIs), excipients, and the development of a suitable formulation. Factors such as drug properties, desired release profile, and patient requirements are considered during this stage (Gohel et al, 2007).

B. **Weighing and Blending:** Once the formulation is established, the individual components, including APIs and excipients, are accurately weighed according to the desired dosage strength. These materials are then blended together using appropriate blending equipment to achieve a uniform mixture (Lachman et al, 2012).

C. Granulation: Granulation is often employed to improve flow properties, compressibility, and content uniformity of the formulation. Granulation methods includes,

1.1.2.2. Wet granulation: It is a widely used method in tablet manufacturing that involves the formation of granules by agglomerating and binding powdered materials using a liquid binder.

Wet granulation typically involves the following steps:

- ❖ Blending the powdered ingredients.

- ❖ Adding a liquid binder to form a wet mass.
- ❖ Wet massing or agitating the mixture to achieve uniform distribution.
- ❖ Screening or drying the wet mass to obtain granules.
- ❖ Final blending and compression of the granules into tablets (Kumar et al., 2013)

Binder Selection: The choice of binder is crucial in wet granulation. Binders can be water-soluble (e.g., polyvinylpyrrolidone, hydroxypropyl cellulose) or water-insoluble (e.g., ethyl cellulose, hydroxypropyl methylcellulose). The binder should exhibit good binding properties, appropriate viscosity, and compatibility with the active ingredients and other excipients. (Lachman et al, 2012).

1.1.2.3. ADVANTAGES OF WET GRANULATION

a. Improved Flow and Compression Characteristics: Wet granulation enhances the flow properties of powders, facilitating uniform distribution and reducing segregation during tablet compression. It also improves compressibility, leading to tablets with consistent hardness and reduced friability.
b. Uniform Drug Distribution: Wet granulation allows for uniform distribution of active ingredients throughout the granules, ensuring consistent drug content in each tablet and minimizing dose variability
c. Enhanced Stability: The process of wet granulation can improve the stability of moisture-sensitive drugs by reducing their exposure to moisture during tablet manufacturing and storage. Masking of Unpleasant Tastes: Wet granulation offers the opportunity to incorporate taste-masking agents or flavors into the granules, making the resulting tablets more palatable (Kumar et al., 2013).

1.1.2.4. CHALLENGES AND CONSIDERATIONS OF WET GRANULATION

a. Process Optimization: Wet granulation parameters, such as binder concentration, mixing time, and drying conditions, need to be optimized to achieve desired granule characteristics and tablet properties (Kumar et al., 2013).
b. Moisture Sensitivity: Since the process involves the addition of a liquid binder, it is essential to control moisture levels during wet granulation to prevent unwanted moisture-induced changes, such as degradation or loss of drug potency.
c. Increased Manufacturing Time and Cost: Wet granulation is a more time-consuming and resource-intensive process compared to direct compression, as it involves additional steps such as wet massing, drying, and milling of granules (Kumar et al., 2013).

1.1.2.5. Dry granulation*:* Dry granulation is a tablet manufacturing process that involves the compaction of powdered materials without the use of a liquid binder.(Kertesz & Szabo, 2006). Instead of adding a liquid binder to form granules, dry granulation relies on the application of mechanical pressure to compress the powders into compacted masses, which are then milled and sieved to obtain granules.

Dry granulation typically consists of the following steps:

- ❖ Blending the powdered ingredients.
- ❖ Compaction of the blend into slugs or ribbons using a tablet press or roller compactor.
- ❖ Milling the slugs or ribbons to produce granules.
- ❖ Final blending and compression of the granules into tablets (Gohel et al., 2007).

1.1.2.6. Advantages of Dry Granulation*:*

a. Avoidance of Liquid Binders: Dry granulation eliminates the need for liquid binders, which can be beneficial for moisture-sensitive drugs or formulations that require stability in the absence of moisture.
b. Enhanced Chemical Stability: The absence of moisture during the granulation process helps maintain the chemical stability of moisture-sensitive drugs, reducing the risk of degradation.
c. Improved Flow and Compression Characteristics: Dry granulation can improve the flow properties of the blend, resulting in uniform granule distribution and improved compressibility during tablet compression (Kamble et al., 2018).
d. Cost-Efficient: Dry granulation can be a cost-effective option as it eliminates the need for expensive liquid binders and drying processes associated with wet granulation.

1.1.2.7. **Challenges and Considerations:**

a. Powder Flow and Compression Behavior: Proper selection of excipients and optimization of the formulation are crucial to ensure satisfactory powder flow and compaction behavior during dry granulation.
b. Granule Size Distribution: Achieving a uniform granule size distribution can be challenging in dry granulation. Proper milling and sieving techniques should be employed to obtain granules with the desired particle size range (Gohel et al, 2007).
c. Limited Applicability: Dry granulation may not be suitable for all drug substances and formulations. It is typically preferred for materials that exhibit adequate compressibility and flow properties (Lachman et al, 2012).

D. Compression: The granulated or directly compressed powder blend is then fed into a tablet compression machine. Compression involves the application of mechanical force to transform the powdered material into solid tablets of the desired shape, size, and hardness

E. Coating (optional): Tablets can undergo a coating process, primarily for aesthetic purposes, to provide a protective layer or to modify drug release characteristics. Coating can be performed using various coating materials and techniques, including film coating, sugar coating, or enteric coating (Gohel et al., 2007).

F. **Packaging:** The final step involves packaging the manufactured tablets into suitable containers, such as blister packs, bottles, or foil pouches, ensuring product stability,

protection, and ease of administration. Proper labeling and product information are included on the packaging.

G. It is important to note that the tablet manufacturing process can vary depending on the specific requirements of the formulation and the equipment used. Additional steps, such as milling, drying, and quality control tests, may also be involved in tablet production.

1.1.2.8. TYPES OF TABLETS.

Tablets can be classified according to;

1. **Tablets ingested orally**
   a) Standard compressed tablets
   b) Multiple compressed tablets. Consistent of;

- Sugar coated tablet
- Film coated tablet
- Gelatin coated tablet
- Enteric coated tablet
- Layered tablet
- Inlay tablet

2. **Tablets used in oral cavity.**
   a) Buccal tablet
   b) Sublingual tablet
   c) Troches and lozenges

3. **Tablets administered via other routes**

   a) Implant tablets
   b) Vaginal tablets

4. **Tablets used to prepare solution**

   a) Effervescent tablet
   b) Dispensing tablet
   c) Hypodermic tablet
   d) Tablet Triturate or Molded tablet

1.1.3.0 DISINTEGRANTS/DISINTEGRATING AGENTS.

When making pharmaceutical formulations, disintegrants and disintegrating agents are used to speed up the breakdown or disintegration of solid dosage forms, such as tablets and capsules, after administration. These substances make it easier for the active pharmaceutical ingredient (API) to dissolve and release in the body, resulting in more efficient drug absorption and bioavailability. Disintegrating agents are broadly divided into two types;

1. **Normal Disintegrant**: Corn starch, partially pregelatinized starch, microcrystalline cellulose, and low substituted hydroxypropyl cellulose are examples of starch- and cellulose-based excipients that fall within the category of "normal" disintegrants (Parind et al, 2016). As disintegrants, a variety of clays, such as Vee gum HV, gums, such as agar, guar, tragacanth, and alginate, resins, such as polacrilin potassium, and finely divided solids, including colloidal silicon dioxide and magnesium aluminum silicate, have also been used. Normal disintegrants are often hydrophilic but insoluble in water or digestive secretions (Uebbing et al, 2017).
2. **Super disintegrants**: Super disintegrants are more effective disintegrants that are capable of good disintegration action at much lower concentrations in the tablet formulations as a result of chemical modification of starch, cellulose, and povidone. Croscarmellose sodium, crospovidone, and sodium starch glycolate are examples of super disintegrants (Dushyant et al,2023).

1.1.3.1. MECHANISM OF ACTION OF DISINTEGRANTS

The mechanism of action of disintegrants involves promoting the breakup of a tablet or capsule into smaller particles, facilitating drug dissolution and subsequent absorption. Disintegrants function through different mechanisms, such as swelling, wicking, and deformation.

- Swelling disintegrants, such as cross-linked polymers, absorb water, leading to an increase in volume and subsequent tablet disintegration. The swelling process generates internal stress within the tablet, causing it to disintegrate into smaller fragments or particles. These fragments, with increased surface area, dissolve more readily, allowing for faster drug release and subsequent absorption in the gastrointestinal tract. Factors such as particle size, degree of cross-linking, and polymer concentration can influence the

swelling behavior and, consequently, the disintegration time of the tablet. (Sharma et al, 2019).

- Wicking disintegrants, like microcrystalline cellulose, rapidly absorb water, creating channels that disrupt the tablet structure and aid in disintegration. These channels created by the wicking action of disintegrants allow for faster penetration of water into the tablet, promoting its breakdown into smaller particles (Sodhi et al, 2015).
- Deformation disintegrants, such as starches and clays, deform upon exposure to water, generating pressure and mechanical forces that cause tablet disintegration. The deformation of disintegrants upon contact with water leads to the generation of pressure within the tablet, facilitating its breakup into smaller fragments (Gohel et al, 2011).

1.1.3.2. LOCALLY SOURCED DISINTEGRANTS

Locally sourced disintegrants are natural substances that can be obtained from local plants or mineral sources, providing an alternative to commercially available disintegrants. These natural disintegrants offer potential advantages in terms of cost-effectiveness, sustainability, and compatibility with the environment.

Commonly used local disintegrants include.

1. **Starches**: Starches derived from various plant sources, such as corn, potato, or rice, are commonly used as disintegrants in tablet formulations. Starches possess swelling properties, and upon exposure to water, they absorb moisture, leading to an increase in volume and subsequent tablet disintegration (Kamble et al, 2018). The granules of starch disintegrants swell and disrupt the tablet structure, promoting rapid dissolution (Chavhan et al, 2015).
2. **Guar gum:** Guar gum is a natural polysaccharide derived from the seeds of the guar plant. It has been used as a disintegrant due to its water-absorbing and swelling properties (Rajalakshmi & Remya, 2018). When exposed to water, guar gum forms a viscous gel, contributing to tablet disintegration and drug release (El-Menshawe et al, 2019).
3. **Locust bean gum:** Locust bean gum, also known as carob gum, is extracted from the seeds of the carob tree. It is a galactomannan polysaccharide that exhibits swelling properties upon hydration (Patel et al, 2016). Locust bean gum promotes tablet disintegration by absorbing water and forming a gel-like structure, facilitating the breakup of the tablet (Rajalakshmi & Remya, 2018).
4. **Tamarind seed polysaccharide:** Tamarind seed polysaccharide is derived from the seeds of the tamarind tree. It is a natural polysaccharide with excellent water absorption and swelling capabilities (Chowdary et al., 2013). Tamarind seed polysaccharide disintegrants rapidly imbibe water, leading to the formation of a swollen mass that aids in tablet disintegration and dissolution.

1.1.3.3. ADVANTAGES OF LOCALLY SOURCED DISINTEGRANTS

Locally sourced disintegrants offer several advantages in pharmaceutical formulations. These advantages include cost-effectiveness, sustainability, potential availability, and come with the environment.

a. Cost-effectiveness: Locally sourced disintegrants can be more cost-effective compared to commercially available disintegrants. Natural materials obtained from local sources are often less expensive and more accessible, reducing manufacturing costs (Kamble, Kuchekar, & Mahajan, 2018). This advantage can contribute to cost savings in pharmaceutical formulation development.
b. Sustainability: Utilizing locally sourced disintegrants aligns with sustainability initiatives as it reduces the dependence on synthetic disintegrants and promotes the use of renewable resources (El-Menshawe, Soliman, & El-Kamel, 2019). Natural materials are typically biodegradable and have a lower environmental impact compared to synthetic alternatives.
c. Potential availability: Locally sourced disintegrants have the potential for greater availability in regions where the source material is abundant. This can reduce supply chain complexities and ensure a consistent supply of disintegrants for pharmaceutical manufacturing (Rajalakshmi & Remya, 2018).
d. Compatibility with the environment: Natural disintegrants sourced locally are often biocompatible and have a reduced risk of adverse effects or allergic reactions compared to synthetic counterparts (El-Menshawe et al., 2019). This advantage can improve patient safety and acceptability of the medication.

   These advantages make locally sourced disintegrants an attractive option in pharmaceutical formulation development, providing a sustainable and cost-effective alternative to commercially available disintegrants.

1.1.3.4. DISADVANTAGES OF LOCALLY SOURCED DISINTEGRANTS

Locally sourced disintegrants, despite their advantages, may also present some disadvantages in pharmaceutical formulations. Here are some potential disadvantages,

a. Variability in composition: Locally sourced disintegrants derived from natural materials may exhibit variability in their composition, which can affect their performance and consistency in tablet formulations (El-Menshawe, Soliman, & El-Kamel, 2019). Differences in growing conditions, harvesting methods, and processing techniques can lead to variations in the chemical composition of the disintegrant, potentially impacting its functionality.
b. Batch-to-batch inconsistency: The use of locally sourced disintegrants may result in batch-to-batch inconsistency due to the natural variability of the source material

(Rajalakshmi & Remya, 2018). This variability can affect the disintegration time and overall performance of the tablets, leading to challenges in maintaining product quality and uniformity.

c. Allergenic potential: Locally sourced disintegrants derived from natural sources may carry a risk of allergenicity in susceptible individuals. Natural materials can contain allergenic proteins or other components that may trigger allergic reactions in certain individuals (El-Menshawe et al., 2019). It is important to consider the potential allergenicity of locally sourced disintegrants and conduct appropriate safety evaluations.

d. Limited availability: While locally sourced disintegrants may be readily available in certain regions, their availability can be limited in other geographical areas or during specific seasons (Kamble, Kuchekar, & Mahajan, 2018). This can create challenges in ensuring a consistent and reliable supply of the disintegrant, especially for large-scale pharmaceutical manufacturing.

1.1.3.5. SOURCES OF NATURALLY USED COMMON DISINTEGRANTS.

- **Agar**: It has a mucilage-like flavor and appears yellowish, grey, or colorless. It takes the form of dried gelatinous substance derived from many species, including Pterocladia (red algae), Gracilaria, and Gelidiumamansii. Agarose and agaropectin are two polysaccharides found in agar. The former is the cause of the gel strength, and a high gel strength makes it suitable for use as a disintegrant in the creation of tablets that dissolve when taken orally (Anand N et al., 2013).
- **Pectin from Mango peel:** Mango peel contains pectin, a hydrophilic colloid formed of a collection of heteropolysaccharides. Although pectin cannot be utilized to predict super disintegrant behavior, it can be used to create or dispersible tablets due to its high swelling index and biological fluid solubility (Malviya R et al., 2008).
- **Chitin and chitosan**: The shells of crabs and shrimp contain chitin. It contains an amino group that is covalently joined to the acetyl group, unlike chitosan. Chitin, a structural component of crustacean exoskeletons (crab and shrimp shells) and fungal cell walls, is deacetylated to produce chitosan. According to Goel H. et al. (2010), chitosan appears to be an improved disintegrating agent than maize starch and is suitable for use as a super disintegrant in tablets.
- **Soy Polysaccharide**: It belongs to the class of super disintegrants that have natural origins. It is produced from soybeans. High molecular weight carbohydrate polymers including xylose, galactose, mannose, and arabinose make up this substance. In the direct compression of tablets, it functions as a super disintegrant (Hosny KM et al., 2015).
- **Guar gum:** It is extracted from the endosperms of the Leguminosae family plant Cyamopsis tetragonolobus. By means of glycoside connections, it is constructed of galactan and mannan units. According to Rowe R et al. (2009), it can be employed as a

disintegrant, binder, stabilizing, thickening, and suspending agent in the pharmaceutical industry.

- **Gum from Mangifera indica:** It is a member of the Anacardiaceae family and is frequently referred to as mango. The powder has a look that ranges from white to off-white in color. According to Nayak RK et al. (2011), it can be utilized as a disintegrant, binder, suspending agent, and emulsifying agent.
- **Gum karaya:** The exudate that can be obtained from plants associated with sterility is known as gum karaya. Its constituent polysaccharides are galactose, rhamnose, and galacturonic acid. As an alternative super disintegrant, gum karaya can Due to its low cost, biocompatibility, and other advantages, gum karaya can be employed as a super disintegrant substitute for other super disintegrants (Shirwaikar A et al., 2008).
- **Carob gum (locust bean gum): I**t is gum made from Ceratonia siliqua seeds that have been extracted. It can be utilized as a bio-adhesive, thickening, and gelling agent. It seems to be an odorless, yellowish-white powder (Malik K et al., 2011).

1.1.4. PECTIN

Pectin is a natural disintegrant derived from plant sources, particularly from the peels or cell walls of fruits like apples and berries. It is a complex polysaccharide composed of galacturonic acid units, with varying degrees of methylation and acetylation (Rajalakshmi & Remya, 2018).

Pectin is commonly used in the pharmaceutical industry as a disintegrant due to its ability to absorb water and swell, leading to the disruption of tablet structure and promoting rapid disintegration. When exposed to water, pectin forms a gel-like matrix by absorbing and retaining water molecules. This swelling and gel formation contribute to the breakup of the tablet into smaller particles, facilitating drug release and dissolution. Pectin disintegrants are particularly effective in formulations with low to moderate tablet hardness and provide controlled disintegration within a specified time frame.

In both hot and cold alkaline water, pectin is soluble. Pectin can be utilized as a stabilizer in acidic protein beverages as well as to enhance the mouth feel and pulp stability in beverages made from juice. Additionally, pectin boosts the gel strength of low-calorie jams and decreases syneresis in jams and marmalades. In confectionary jellies, pectin is employed to provide a solid gel structure and a clean bite. Pectin is a naturally occurring polysaccharide that is biocompatible, biodegradable, renewable, and used as an emulsifier, gelling agent, stabilizing agent, and thickening.

1.1.4. CLASSIFICATION OF PECTIN

Pectin is a complex polysaccharide that can be classified into different types based on its source, degree of esterification, and behavior under different pH and temperature conditions. It is classified into,

i. **High Methoxy Pectin (HM pectin):** High methoxy pectin refers to pectin with a high degree of esterification, typically above 50%. This type of pectin forms gels in the presence of sugar and low pH conditions, such as those found in jams, jellies, and fruit-based products (Ebringerová & Hromádková, 2010). HM pectin gels are thermally reversible and can be disrupted upon heating and re-gelled upon cooling.

ii. **Low Methoxy Pectin (LM pectin):** Low methoxy pectin refers to pectin with a low degree of esterification, typically below 50%. LM pectin requires the presence of calcium ions and a specific pH range for gel formation (Ebringerová & Hromádková, 2010). The gels formed by LM pectin are thermally irreversible and remain stable even upon heating.

iii. **Amidated Pectin:** Amidated pectin is a modified form of pectin where some of the carboxylic acid groups are replaced by amide groups. This modification alters the gelation properties of pectin, making it more resistant to calcium-induced gelation (Ebringerová & Hromádková, 2010). Amidated pectin is used in applications where stability to calcium ions is desired, such as in dairy products or acidic beverages.

iv. **Modified Pectin:** Modified pectin refers to pectin that has undergone various chemical or enzymatic modifications to alter its functional properties. Examples of modified pectin include partially depolymerized pectin, enzymatically hydrolyzed pectin, and chemically crosslinked pectin (Voragen, Coenen, & Verhoef, 2009). These modifications can affect the gelation behavior, solubility, viscosity, and other properties of pectin, making it suitable for specific applications.

1.1.4.1. SOURCES OF PECTIN

Pectin, a complex polysaccharide, is primarily derived from plant sources, particularly from the peels or cell walls of fruits. It is found in various fruits and vegetables, with some sources being more abundant in pectin than others. The following are common plant sources of pectin:

- **Citrus Fruits**: Citrus fruits, such as oranges, lemons, and grapefruits, are known for their high pectin content. Pectin is mainly derived commercially from orange peels. The peels of these fruits are particularly rich in pectin, making them a valuable source for pectin extraction (Cui et al., 2016).
- **Apples**: Apple pomace, which includes the peels, cores, and residues after juice extraction, is another significant source of pectin. Apple pomace contains a substantial amount of pectin, making it a suitable raw material for pectin production (Wang et al., 2017).

- **Berries**: Various berries, including strawberries, raspberries, and blackberries, contain pectin in their cell walls. These fruits can be used as sources of pectin, either individually or in combination with other pectin-rich materials (Cui et al., 2016).
- **Other Fruits and Vegetables:** Pectin can also be obtained from other fruits and vegetables, such as peaches, apricots, plums, carrots, and sugar beets. These sources may have different levels of pectin content, requiring specific extraction methods for optimal yield (Cui et al., 2016; Wang et al., 2017).

1.1.4.2. APPLICATIONS OF PECTIN

1. Pectin and its derivatives are used in diarrheal disorder and constipation.

2. Pectin lowers the blood cholesterol level by increasing the fecal cholesterol, fecal fat.

3. In medicine, pectin increases viscosity and volume of stool.

4. In cosmetic products pectin acts as stabilizer

5. Pectin is used in confectionery jellies to give a good gel structure and a clean bite.

6. Pectin can be used to improve the mouthfeel.

7. Pectin also reduces syneresis in jams and marmalades.

8. Pectin reduces the rate of digestion by immobilizing food components in the intestine.

9. It is used in hair tonics, body lotions and shampoos.

10. It is also used in deodorants and toothpastes.

11. Specialty medical adhesives and preparations for wound healing both utilize pectin.

12. Pectin hydrogels have been used as a binding agent in tablet formulations.

13. It has been applied to the delicate removal of heavy metals from biological systems.

14. As a demulcent, pectin is also utilized in throat lozenges.

15. Pectin serves as a natural preventative measure against toxic cation poisoning.

16. Pectin is utilized to keep syrups from losing their viscosity.

17. To prevent ulcerated mouth and throat ulcers, pectin and kaolin are combined.

18. Diabetes and gastric reflux disease are additional uses for it.

19. It is utilized to create synthetic cherries.

20. Pectin stops cancer cells' angiogenesis, which kills the cancer cell. (Bhavesh et al., 2022).

1.1.4.3. CITRUS SINENSIS AS A PLANT SOURCE OF PECTIN.

Citrus sinensis, commonly known as sweet orange, is a species of citrus fruit belonging to the Rutaceae family. It is one of the most widely cultivated citrus fruits worldwide, valued for its sweet and juicy flavor.

Citrus sinensis is a tropical and subtropical fruit tree native to China and is now extensively grown in various parts of the world. It is characterized by its round or oval-shaped fruits with a bright, orange-colored peel and segmented pulp (Baldwin, 2019). The fruit is known for its high vitamin C content, as well as other nutrients and bioactive compounds, making it a popular choice in the food and beverage industry (Chen et al., 2019). In terms of cultivation, *Citrus sinensis* prefers a warm and humid climate, typically found in regions with mild winters and long periods of sunlight. The tree can reach a height of 6 to 9 meters and has glossy, evergreen leaves (Baldwin, 2019). It is commonly propagated through grafting onto rootstocks for optimal growth and fruit production (Chen et al., 2019).

The sweet orange fruits of *Citrus sinensis* are not only consumed fresh but also used in various processed forms such as juices, jams, marmalades, and desserts. The fruit is prized for its refreshing taste and nutritional benefits. It contains a range of bioactive compounds, including flavonoids,carotenoids, and essential oils, which contribute to its antioxidant and potential health-promoting properties (Chen et al., 2019).

In addition to its culinary and nutritional value, *Citrus sinensis* has also been explored for its potential medicinal properties. Various studies have highlighted the potential health benefits of *Citrus sinensis* and its bioactive compounds, including anti-inflammatory, antimicrobial, antidiabetic, and anticancer properties (Chen et al., 2019; Nour et al., 2018). Overall, *Citrus sinensis*, or sweet orange, is a popular citrus fruit known for its delightful flavor, nutritional value, and potential health benefits. Its cultivation and utilization have significant economic and cultural importance worldwide.

Pectin is primarily obtained from the peels of *Citrus sinensis* fruits, which are a by-product of the juice industry (Kertesz & Szabo, 2006). The peels of Citrus sinensis contain a significant amount of pectin, making them a valuable raw material for pectin extraction.

Pectin extraction from *Citrus sinensis* peels involves various methods which includes.

1. The hot acid extraction method involves treating the peels with acid, typically dilute hydrochloric acid or citric acid followed by heating and filtration to separate the pectin from other components (Hussain et al., 2017).

2. Enzymatic extraction, on the other hand, utilizes enzymes, such as pectinase, to break down the pectin-containing cell walls and release pectin (Kertesz & Szabo, 2006). Enzymatic extraction depends on concentration of enzyme, reaction temperature, time, the particle size of the plant material, and type of enzyme. The enzymatic treatment interferes with the glycosidic bonds of the pectin and ensures their breakage. This action decreases the viscosity of the solution, facilitating filtration and centrifugation. This extraction method has the advantage of being less polluting as compared to others. Also, pectinases have specific reactivity to pectin. However, enzymatic production remains expensive and the reaction is difficult to control. Finally, this method can lead to a degradation of the pectin and a loss of its properties.
3. Microwave-assisted extraction (MAE): A developing method called microwave-assisted extraction (MAE) uses two oscillating perpendicular fields—electric and magnetic—to help polar solvents absorb microwave radiation. Rapid extraction methods such as MAE use microwave-frequency electromagnetic radiation to produce thermal energy in solvent inside the sample. Here, EDTA and naoh are utilized as the solvent. While dipole rotation is caused by the alternating displacement of polar molecules, electrophoretic transfer of ions and electrons initiated by microwave energy creates an electric field that drives particle motion. (Harshada et al, 2014)
4. DIELECTRIC BARRIER DISCHARGE PLASMA EXTRACTION (DBD): DBD plasma, generated through atmospheric cold plasma, can alter biomacromolecules like pectin chains by releasing positive ions and electrons. This process can also degrade biopolymers like proteins and polysaccharides. However, pectin extraction using DBD plasma has received limited attention, and further research is needed to modify its structure.(Anissa et al 2021).

The utilization of *Citrus sinensis* as a plant source of pectin provides not only a sustainable solution for pectin production but also adds value to the by-products of the citrus juice industry.

1.1.4.4. THE RATIONAL OF THE STUDY.

Pectin, derived from *citrus sinensis* peel, can serve as an effective disintegrant in tablet formulations. Disintegrants play a crucial role in promoting tablet disintegration and subsequent drug release. Pectin possesses swelling and water absorption capabilities, allowing it to rapidly absorb moisture upon contact with saliva or other dissolution media. This swelling property facilitates the breakup of the tablet into small particles, enhancing drug dissolution and absorption (Dixit et al., 2012).

Rapid dissolving tablets, also known as fast-disintegrating or orally disintegrating tablets, are designed to disintegrate or dissolve quickly in the oral cavity without the need for water or

chewing. These tablets offer several advantages, such as ease of administration, improved patient compliance, and enhanced drug absorption due to increased surface area and direct absorption through oral mucosa (Gupta et al., 2013). By formulating a rapid dissolving tablet using pectin as a disintegrant, the following benefits can be achieved:

a. Enhanced Disintegration: Pectin's swelling property aids in the rapid disintegration of the tablet, ensuring quick drug release.
b. Improved Drug Dissolution: The rapid disintegration of the tablet facilitated by pectin allows for faster drug dissolution, leading to rapid onset of action and improved therapeutic efficacy.
c. Patient Convenience: Rapid dissolving tablets offer a convenient dosage form for patients, particularly those who have difficulty swallowing conventional tablets or have limited access to water.
d. Community-Sourced Pectin: Utilizing pectin obtained from community-acquired *citrus sinensis* peel as a disintegrant promotes sustainable and locally sourced ingredients, contributing to community engagement and economic development.

In this regard, using pectin from locally sourced citrus sinensis peel as a disintegrant in the formulation of a rapid-dissolving tablet combines pectin's special qualities with the requirements of a rapid-dissolving tablet for improved drug dissolution, increased patient compliance, and the utilization of locally sourced materials.

1.1.4.5. Aims and Objectives of the study.

1. To investigate the feasibility of incorporating pectin obtained from citrus sinensis peel as a disintegrant and assessing its impact on tablet disintegration and drug release.
2. To compare the performance of the locally obtained pectin-based formulation with other disintegrants.

CHAPTER TWO

2.0 MATERIALS AND METHODS

2.1 MATERIALS

A. CIPROFLOXACIN

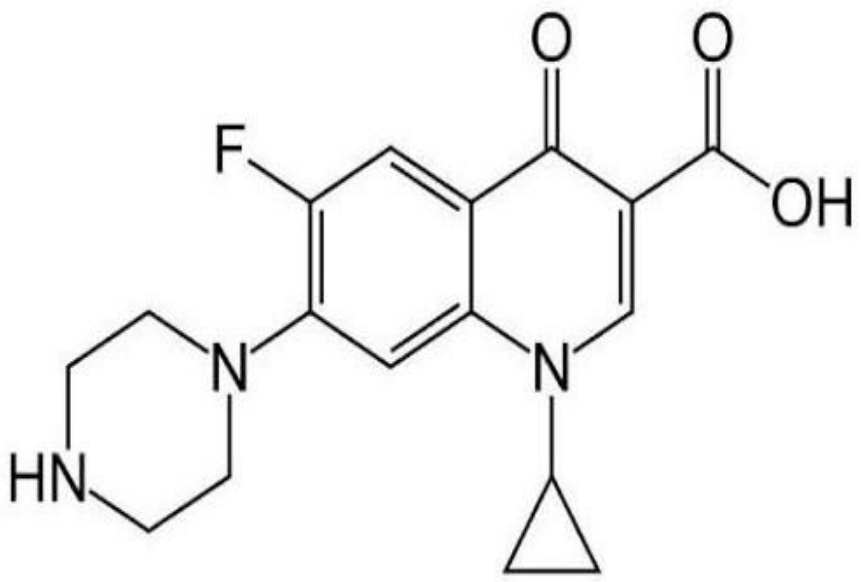

Figure 2.1: Structure of Ciprofloxacin

Ciprofloxacin is a fluoroquinolone antibiotic of the second generation used to treat a variety of bacterial illnesses, including pneumonia, gonorrhea, urinary tract infections, prostate infections, and eye and ear infections (Alodokter, 2023). Additionally, it can be used to treat plague and anthrax (Drugs.com, 2021). Ciprofloxacin kills bacteria by inhibiting specific enzymes that the bacteria utilize to grow and repair their DNA (GoodRx, 2023).

According to Pietsch F et al. (2017), bacterial topoisomerase II (DNA gyrase) and topoisomerase IV are inhibited by the antibiotic ciprofloxacin. Because ciprofloxacin targets DNA gyrase's alpha subunits, it can't supercoil bacterial DNA, which inhibits DNA replication (LeBel M et al., 1988).

PHYSICO-CHEMICAL PROPERTIES OF CIPROFLOXACIN

Chemical Name: Ciprofloxacin hydrochloride

Synonym:

Molecular formula: C17H18FN3O3

Molecular weight: 331.4 g/mol

Melting Point: 313°C to 322°C

Storage temperature: Room temperature
Solubility: Soluble in water (3.5 g/100 ml), ethanol (1.6 mg/ml).

Form: White to slightly yellowish color with bitter taste

Water solubility:

PHARMACOLOGICAL PROPERTIES

Bioavailability: 70%

Metabolism: Ciprofloxacin is mainly metabolized by the liver, through the enzyme CYP1A2. CYP1A2 is responsible for converting ciprofloxacin into four major metabolites: oxo ciprofloxacin, sulfociprofloxacin, desethylene ciprofloxacin, and formylciprofloxacin

Half-Life: 4hours

Excretion: About 40% to 50% of ciprofloxacin is eliminated unchanged in the urine, and another 15% is excreted as metabolites.

A. LACTOSE

The food and pharmaceutical sectors use lactose, a natural sugar obtained from cow's milk, for a variety of purposes. Its molar mass is 342.297g/mol and its chemical formula is C12H22O11. It has a pleasantly sweet flavor and is a white, water-soluble, non-hygroscopic solid (Gerrit M, 2014).

Some of the applications of lactose are:

1. Due to its abilities as a filler, binder, coating agent, and stabilizer, lactose is utilized as an excipient in the formulation of tablets, capsules, inhalation products, and lyophilized goods.
2. In the food sector, it serves as a carrier and enhancer of flavors and smells.
3. It is a sweetener used in dairy products, particularly infant formula, where it closely resembles the chemical makeup of human milk.
4. Microorganisms use it as a substrate to produce lactic acid, ethanol, and other fermentation products.

B. MAIZE STARCH

A typical excipient in the pharmaceutical industry is maize starch. Depending on the application, maize starch can serve as a diluent, a disintegrant, or a binder. By acting as a diluent, it enhances the medication formulation's volume and makes it simpler to handle and measure. It functions as a disintegrant, aiding the drug's breakdown and release of the active component within the body. It functions as a binder, securing the drug particles in a cohesive mass. Its many benefits include being organic, secure, biodegradable, biocompatible, and reasonably priced. In wet and dry granulation operations as well as direct compression, maize starch can be utilized as a diluent. One of the oldest and most adaptable excipients used in solid dose formulations is maize starch. It is natural, safe, biodegradable, biocompatible, and affordable, among other benefits.

C. MAGNESIUM STEARATE

A synthetic soap known as magnesium stearate is composed of a variety of fatty acid salts of magnesium, primarily stearic acid and palmitic acid. It is one of the excipients that the pharmaceutical industry uses the most frequently, particularly for the production of tablets and capsules. As a pharmaceutical excipient, magnesium stearate has several functions and benefits, such as:

- The friction and adhesion between the powder particles and the tablet press or capsule filling machine are decreased as a result of its acting as a lubricant and release agent. These speeds up the manufacturing process and guards against harm to the machinery and dosage forms.
- It enhances the uniformity and stability of the dosage forms by improving the flowability and compressibility of powders. It shields the active components against oxidation, light, and moisture-related deterioration.
- By creating a hydrophobic layer on the dosage forms' surface, it can alter the rate of drug disintegration and bioavailability. The chosen medication release profile will determine whether this is advantageous or detrimental.

D. TALC

Talc is a natural mineral that has various applications in the pharmaceutical industry. It is used as an excipient, which is a substance that helps to improve the quality and performance of the drug product. Some of the functions of talc as an excipient are:

1. Lubricant and diluent: Talc reduces the friction between the particles and the equipment during the tablet compression process. It also helps to increase the bulk volume of the powder mixture and make it easier to handle.
2. Glidant: Talc improves the flowability of the powder into the capsule shell. It prevents the powder from sticking to the capsule machine and ensures a uniform filling.
3. Dissolution retardant: Talc slows down the release of the drug from the tablet or capsule by forming a protective layer on the surface. This can be useful for controlled release formulations that require a sustained drug delivery. Adsorbent and stabilizer: Talc absorbs moisture and prevents the growth of microorganisms in the formulation. It also stabilizes the suspension of insoluble drug particles and prevents them from settling or caking

E. MANNITOL

Mannitol is a pharmaceutical excipient and food additive that functions as a tablet diluent, sweetening agent, therapeutic agent, and plasticizer. It is a polyol (hexahydric alcohol) that has a sweet taste and a cooling sensation in the mouth. It is chemically similar to mannose and an isomer of sorbitol. It has low hygroscopicity, inertness with respect to active pharmaceutical ingredients (APIs), good compatibility, and the ability to produce robust tablets. It is also suitable for the formulation of orally disintegrating tablets and moisture sensitive APIs. Mannitol can also be used in other tableting methods such as dry granulation, roller compaction, and wet granulation. It can improve the bulk density, flow properties, and content uniformity of powders. It can also act as a plasticizer and reduce the brittleness of tablets.

2.2 METHODS

2.2.1. EXTRACTION OF PECTIN

Orange Peel Preparation

In the initial phase of the extraction process, fresh orange fruits were sourced from a local market in Benin City. The orange fruits were carefully examined to ensure they were free from contaminants or pesticide residues. Subsequently, the orange fruit peels were meticulously separated from the fruit pulp, and thorough cleaning was carried out to eliminate any residual fruit remnants or impurities. Following the cleaning process, the orange fruit peels were cut into

smaller pieces to in order to increase it's surface area. To enhance the extraction process, the cleaned and prepared orange fruit peels were dried under shade for 24 hours and further dried at 45°C in a conventional oven until constant weight was obtained. The dried peels were then weighed and 100g of the orangefruit peels was weighed and available for further processing.

Extraction with Citric Acid

For the pectin extraction phase, 100g of the weighed orange peel was placed into a 1000ml conical flask containing 200ml of citric acid with a pH of 1.9.were Subsequently, the mixture was heated in a controlled water bath at a temperature of 90°C for a duration of 2 hours. This process aimed to facilitate the extraction of pectin from the orange fruit peels. The utilization of citric acid at a specific pH played a critical role in this phase to ensure efficient extraction of pectin.

Ethanol Precipitation

Following the completion of the extraction step, ethanol precipitation was employed to recover the extracted pectin. A total of 100ml of ethanol was used. After ethanol addition, the mixtures were allowed to stand for 1hour. During this period, the pectin precipitated out of the solution and formed a gel-like substance or pectin cake at the bottom of the flask.The pectin gel was left for some time to allow the gel to float after which it was removed from the extracts by using filter cheese cloth. The percentage yield of the pectin was calculated.

PERCENTAGE YIELD OF PECTIN

The pectin yield was calculated by equation.

$Y\ (\%) = P/Bi \times 100$

Where Y is the extracted pectin yield in percent (%)

P is the amount of extracted pectin in gram and Bi is the initial weight of orange peel.

Fig 1: Photo of orange peel in water bath

Fig 2: Photo of pectin gel

2.2.2. MANUFACTURE OF TABLETS

Wet granulation process was used to produce seven distinct batches of tablets. Table 1 lists the chemical makeup of each tablet in a batch. 250 mg of the medication, the binder, the filler and pectin were combined uniformly to make the calculated amount needed to create 500 mg ciprofloxacin tablets. Wet mass was prepared by progressively incorporating enough of the granulating agent (10% maize starch). By utilizing a 20# sieve and the sifting process, granules were created. Additionally, granules were dried at 35 to 45 °C for an hour. Until the compression of tablets, the dry granules were kept in desiccators. The flow properties of the dry granules were

tested before compression. Using a single punch tablet press, the necessary granule quantities were weighed and compressed. The compressed tablets of each batch were stored in air tight containers at room temperature for further study.

Table 2.0: Composition of Ciprofloxacin tablets (mg)

Ingredients	F1	F2	F3	F4	F5	F6	F7
Ciprofloxacin	250	250	250	250	250	250	250
Talc	20	20	20	20	20	20	20
Magnesium stearate	15	15	15	15	15	15	15
Mannitol	70	70	70	70	70	70	70
Lactose	120	120	107.5	95	82.5	70	107.5
Pectin(%)	-	17.75	26.63	35.5	44.38	53.25	-
Maize Starch	-	-	-	-	-	-	37.5
Sodium starch Glycolate	25	-	-	-	-	-	-
Total	500	500	500	500	500	500	500

2.2.3. EVALUATION OF GRANULES

Granules were evaluated for all pre-compression parameters like bulk density, tapped density, Hausner's ratio, compressibility index and angle of repose as shown in table 3.1. The evaluation was carried out using the methods specified in official pharmacopoeias. All the determinations were carried out in triplicate and averages reported.

ANGLE OF REPOSE

The angle of repise is an indicator of the flowability of granules. It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. The Angle of repose was determined by the following formula.

Tan Θ = h/r
Where h = height of cone
r= radius of cone base
Θ = angle of repose

BULK DENSITY

The measured weight of granules was poured into a clean, dry 50ml measuring cylinder and the volume occupied by the granules was determined. The ratio of the mass of granules to the volume occupied was determined using the equation.

Db = M/Vb

Where Db = Bulk density

M = Mass of granules

Vb = Volume occupied by granules

TAPPED DENSITY

A measure of the granules was placed in a clean, dry 50ml measuring cylinder and the volume occupied by the granules after 100 taps was determined. The ratio of the mass to granules to the the tapped volume was determined using the following equation.
Dt = M/Vt
Where Dt = tapped density

M = weight of granules

Vt = volume occupied by granules after tapping

COMPRESSIBILITY (CARR'S) INDEX (CI)
This was determined by using the bulk and tapped densities earlier obtained. CI was determined using the equation below.
C.I (%) = Dt - Db/Dt ×100
Where C.I = compressibility index

Dt = tapped density
Db = bulk density

HAUSNER'S RATIO
The Hausner's ratio was also determined using the following equation:
Hausner's ratio (%) = Tapped density (Dt)/ Bulk density (Db)

FLOW RATE

A glass funnel was clamped to the retort stand. Different batches of ciprofloxacin granules were allowed to pour through the orifice of the funnel while recording the time taken for it to completely pour out using a stopwatch. The flow rate was calculated using this formula.

Flow rate = m/t
Where m = weight of powder
t = time of flow

2.2.4. PHYSICAL PROPERTIES OF TABLETS

WEIGHT VARIATION TEST

Ten (10) tablets were randomly chosen from each batch and weighed on an automated scale. Additionally, the weight's mean and relative standard deviation were calculated.

FRIABILITY

Friability testing was determined using Roche Friabilator with readings in triplicate. 10 tablets were weighed and allowed for 100 revolutions in 4 min at 25rpm. The percentage weight loss was calculated by reweighing the tablets. The percentage friability was then calculated by:

%F = Wo – Wt x 100/ Wo

Where,
%F= percent friability, Wo= initial weight of 10 tablets, Wt = final weight of 10 tablets.

HARDNESS

Hardness of all batches was determined using Mosanto Hardness tester. The test was carried out in triplicate for all batches.

THICKNESS

Thickness was measured by vernier caliper. The readings were carried out in triplicate and average value was noted (Malviya R, 2010).

DISINTEGRATION TEST

The test was carried out on six tablets using a tablet disintegration tester. Distilled water at 37ºC ± 2ºC was used as a disintegration media and the time in minutes taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured.

IN VITRO DRUG RELEASE STUDIES

In-vitro drug release was studied using a Dissolution Apparatus Electro Lab TDT 08L taking 900ml of 0.1M HCL buffer as a dissolution medium maintained at 37 ± 2ºC for 5 hrs at 50 rpm. 5ml of sample was withdrawn at 10minutes intervals and was replaced by an equal volume of fresh dissolution medium to maintain sync conditions. Samples were analyzed UV-Visible spectrophotometer at 328 nm and the percentage drug release was calculated.

Standard calibration curve

A standard calibration curve for ciprofloxacin powder was esrablished by serially diluting 100 mg of ciprofloxacin powder in 100 ml of 0.1 M HCl, resulting in a stock solution of 1 mg/ml. A UV spectrophotometer was used to detect absorbance at 328 nm after further dilutions at a factor of 10.

CHAPTER THREE

RESULTS AND DISCUSSION

3.1 FLOW PROPERTIES OF GRANULES

The results for the micromeritic properties (flow properties) of the formed ciprofloxacin hydrochloride granules are as shown below;

Table 3.1: **Flow Properties of Ciprofloxacin Granules**

Formulation	Bulk Density (gm/cm3)	Tapped Density (gm/cm3	Carr's Index (%)	Hausner's Ratio	Flow rate	Angle of Repose
F1	0.51	0.60	15.12	1.22	3 .12	28.60
F2	0.43	0.48	17.20	1.21	3.90	23.42
F3	0.41	0.47	11.54	1.13	4.70	22.53
F4	0.44	0.52	12.84	1.12	5.12	26.21
F5	0.46	0.58	11.69	1.15	4.10	24.20
F6	0.52	0.53	12.22	1.18	4.23	24.20
F7	0.54	0.42	13.04	1.17	2.82	25.93

a). YIELD OF PECTIN

Pectin was extracted by hot acid extraction technique and 75.4% of pectin was obtained from 100gm of dried citrus fruit peel.

b) ANGLE OF REPOSE

From table 3.1 above, the angle of repose for the various batches was between the ranges of 22.53° to 28.60° for the batches. According to British Pharmacopoeia (B.P) specification, angle of repose within the range of 20°-30° indicates good flow properties. The flowability of all seven (7) batches of the granules fell within the specified range and therefore were good.

c) CARR'S INDEX (C.I)

As shown in table 3.1 above, the carr's index of the various batches of the ciprofloxacin tablets were found to be within the ranges of 11.69% and 17.20%. According to B.P specification, compressibility index values below 15% (i.e ≤15%) indicate excellent flow while values greater than 20% (≥20%) indicate poor flow. The compressibility index values for all seven (7) batches of the granules fell within the specified range and therefore were good.

d) HAUSNER'S RATIO

The Hausner's ratio of the various batches was between the ranges of 1.12 to 1.22 and according to B.P specification, Hausner's ratio of less than 1.25 (i.e <1.25) indicates good flow characteristic of granules. The values for all seven (7) batches fell within the specified range and therefore had good flow characteristic of granules.

e) BULK DENSITY AND TAPPED DENSITY

Both bulk density and tapped density results are shown in table 3.2, the bulk density and tapped density ranged from 0.41gm/cm3 to 0.54gm/cm3 and 0.42gm/cm3 to 0.60gm/cm3 respectively indicating that the tablets had good packaging capacity and were uniformly distributed as the bulk and tapped density were within the acceptable range for wet granulation tablets which is 0.4-0.6gm/cm3 for bulk density and 0.5-0.7gm/cm3 for tapped density and to guarantee good wetting and binding qualities, moderate bulk and tapped densities are preferred for granulation powders.

The results for the physical parameters of tablets formed are shown in table 3.2 below;

TABLE 3:2 PHYSICO-CHEMICAL PROPERTIES OF TABLETS

Formulations	Weight Uniformity	Friability (%)	Hardness (Kg/cm2)	Thickness (mm)	Disintegration Time

	(mg)				(mins)
F1	502±0.01	0.76	7.6	4.2±0.03	8.2
F2	503±0.01	0.60	7.2	4.20±.22	26.4
F3	498±0.01	0.98	10.0	4.2±0.14	21.2
F4	500±0.02	0.92	8.7	4.2±0.01	16.3
F5	499±0.02	0.75	9.0	4.2±0.05	15.3
F6	504±0.01	0.84	8.2	4.2±0.04	11.5
F7	501±0.01	0.65	8.0	4.2±0.02	13.5

a) WEIGHT UNIFORMITY

From table 3.2, the weight uniformity test was between 498±0.01 to 504±0.01 indicating that all the formed ciprofloxacin tablets in the various batches contains approximately the same amount of drug substance since the weight variation was less than ±5% of the B.P. limit. Tablet weights across batches were consistent and had low standard deviation values.

b) FRIABILITY

The friability of tablets in the various batches was within the range of 0.60 - 0.98%. Tablets of friability value <1% is considered acceptable. Hence, the entire seven (7) batches were within the acceptable range indicating that the physical strength of the tablet were within acceptable range.

c) HARDNESS

Hardness was maintained to be within 7.2 to 10.0 kg/cm2 which is within the acceptable hardness range for tablets and possess good mechanical strength with sufficient hardness. The hardness test has significant effect on dissolution and disintegration of the tablet as an increase in the hardness of the tablet may prevent the tablet from disintegrating in the required period of time. From the results on table 3.2 shown above, F6 showed the highest value for hardness and F2 showed the lowest value for hardness.

d) THICKNESS

The thickness of the tablets was measured by using Vernier caliper by picking the tablets randomly. The mean values are shown in table 3.2 shows that the values are almost uniform in all formulations. Thickness was found in the range from 4.2±0.01mm to 4.2±0.22mm

respectively and uniformity in the values indicates that formulations were compressed without sticking to the dies and punches.

e) DISINTEGRATION TIME

The disintegration time for the pectin formulation rangers between 11.5 to 26.4 min. Formulation F1 showed the shortest disintegration time of 8.2 while formulation F2 showed the highest disintegration time of 26.4min. From the result, disintegration time decreased from F2 to F6 indicating that an increase in the amount of pectin in the formulations led to a corresponding decrease in the disintegration time.

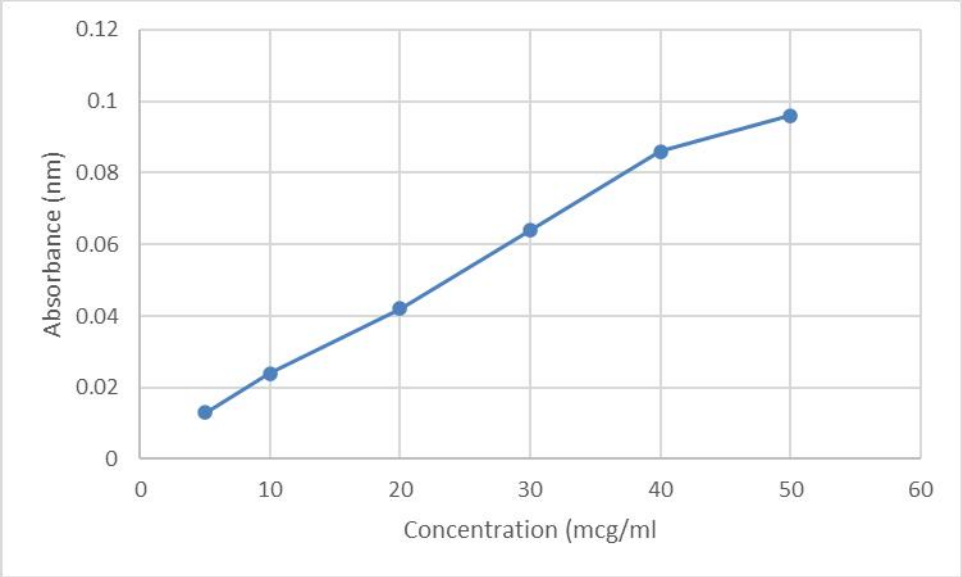

Figure 1: Standard calibration curve for ciprofloxacin

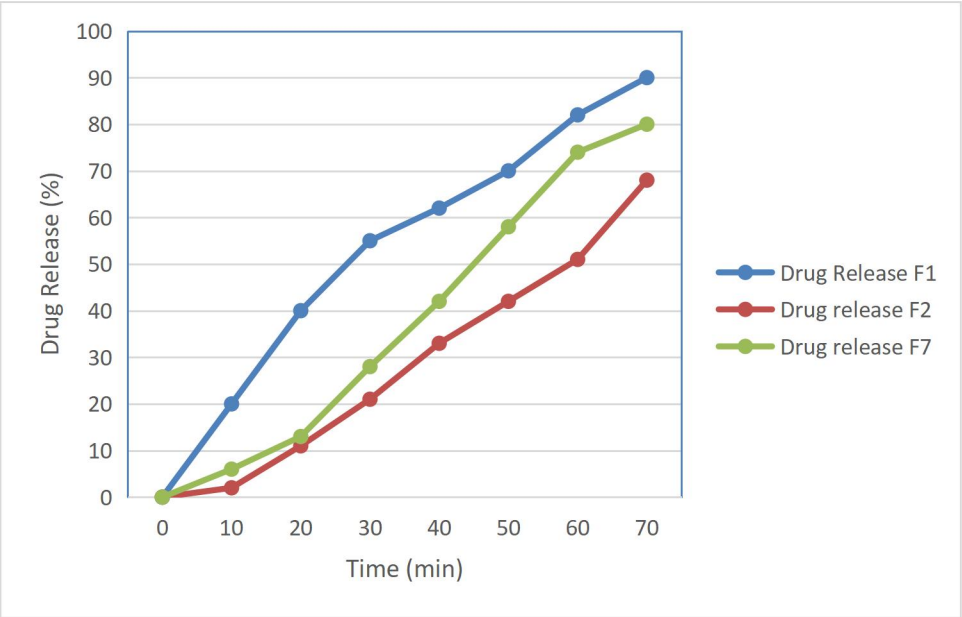

Figure 2: In-vitro Drug Release profile of batch F1, F2 and F7

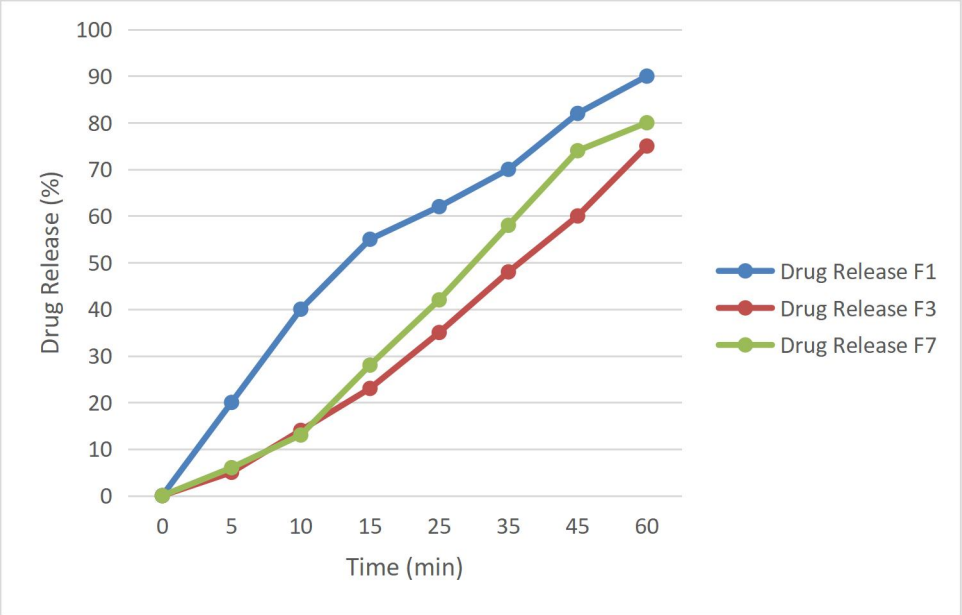

Figure 3: In-vitro Drug Release profile of batch F1, F3 and F7

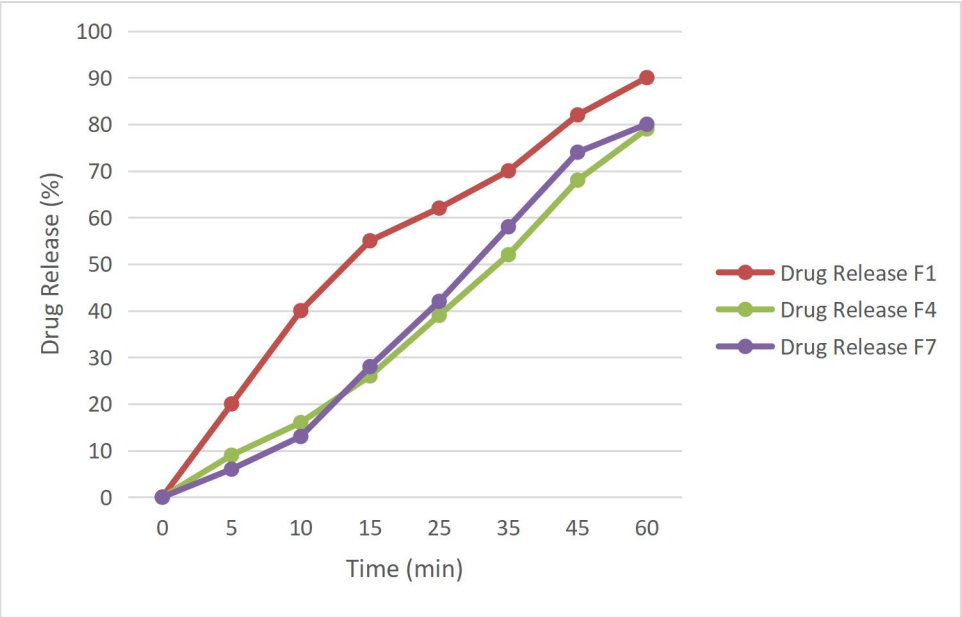

Figure 4: In-vitro Drug Release profile of batch F1, F4 and F7

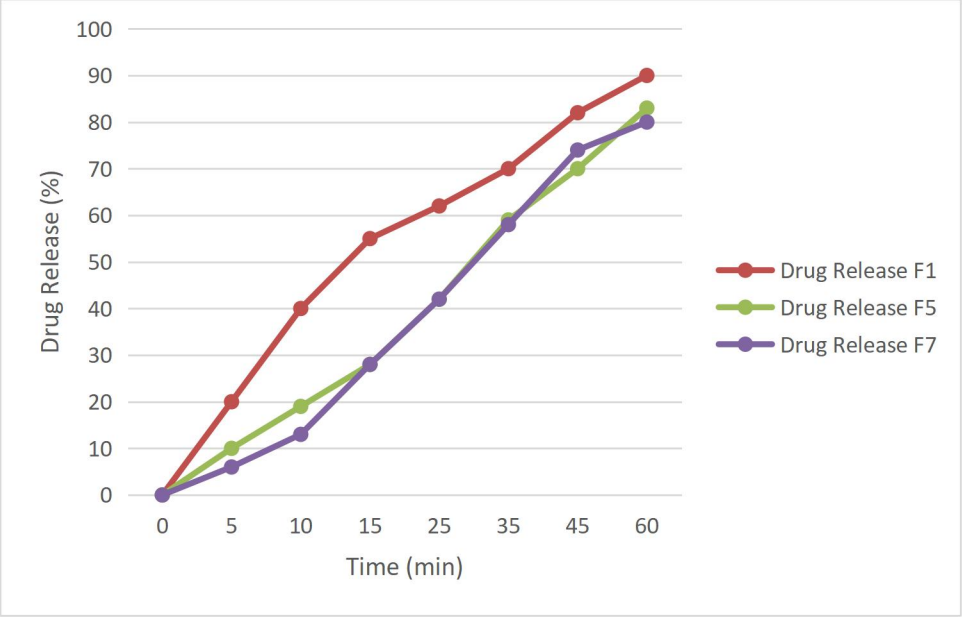

Figure 5: In-vitro Drug Release profile of batch F1, F5 and F7

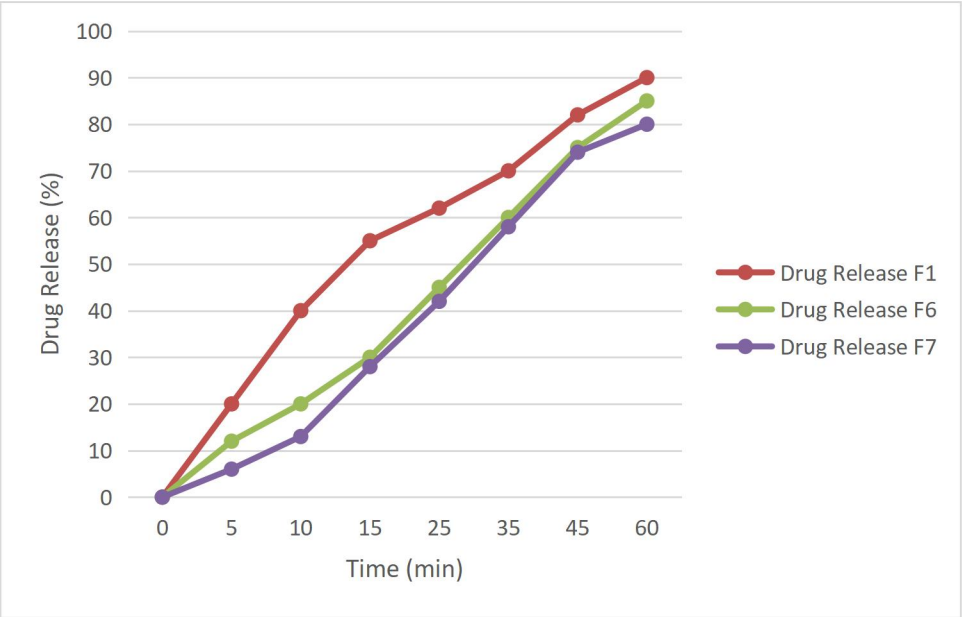

Figure 6: In-vitro Drug Release profile of batch F1, F6 and F7

From the in-vitro drug release study, the maximum drug release for pectin was found in formulation F6 which released about 85% of the drug after 60min. The data from F1 to F7 formulations were represented graphically showing F6 as having the greatest drug release profile among the formulation containing pectin as disintegrant. F1 containing sodium starch glycolate had a better in-vitro release of 90% after 60min followed by F6 which did a better than F7 (containing maize starch) by having an in-vitro release of 80% after 60min.

CHAPTER FOUR

4.0 CONCLUSION

The work showed that pectin was combined favorably with all the tablets as all the formulations from F2 to F6 which contained pectin showed good physico-chemical properties.

Pectin obtained from *Citrus sinensis* showed excellent disintegrating property and contributed favorably to the bioavailability of the drug as shown in the graph.

When compared with sodium starch glycolate and maize starch which are superdisintegrants and disintegrants respectively, 53.25% of pectin (F6) did better than maize starch while sodium starch glycolate had better disintegrating property as a super disintegrant.

CHALLENGES AND LIMITATIONS

Some of the possible challenges associated with carrying out the research included.

1. **AVAILABILITY AND COST OF RAW MATERIALS:** Orange peels are seasonal and may not be available throughout the year. Moreover, the quality and quantity of pectin in orange peels may vary depending on the variety, maturity, and storage conditions of the fruits. Therefore, researchers may face difficulties in obtaining sufficient and consistent amounts of orange peels for their experiments.

2. **SELECTION AND OPTIMIZATION OF EXTRACTION METHODS:** There are various methods for extracting pectin from orange peels, such as acid hydrolysis, enzymatic hydrolysis, microwave-assisted extraction, ultrasound-assisted extraction, and supercritical fluid extraction. Each method has its own advantages and disadvantages in terms of yield, purity, efficiency, environmental impact, and cost. Researchers need to select the most suitable method for their objectives and optimize the extraction parameters, such as temperature, time, pH, solvent type and concentration, enzyme type and dosage, microwave power and frequency, ultrasound intensity and frequency, and pressure.

3. **THE UNAVAILABILITY OF A FREEZE DRYER.**

The unavailability of a freeze dryer made it difficult to get the pectin extracted in powder form; rather, the extracted pectin was used in gel form to formulate the ciprofloxacin tablets, which impacted negatively on the hardness and disintegration time of the pectin batch compared to sodium starch glycolate and maize starch batch.

RECOMMENDATIONS

Some of my recommendations for the challenges and limitations includes,

1. To overcome the availability and cost of raw materials, researchers could collaborate with local farmers, fruit vendors, or juice industries to obtain orange peels as a by-product or waste material.

2. To select and optimize the extraction methods, researchers could conduct a literature review to compare the advantages and disadvantages of different methods and identify the best practices and parameters for extracting pectin from orange peels.

3. Adequate funding through government grants provided by both the federal and state governments is required to acquire the necessary equipment, materials, and resources for research activities and to maintain the standards and ethics of research practices.

REFERENCES

Anand N, Singh DRL, Sharma D. Emergence of natural superdisintegrants in oro-dispersible tablets: An overview. International Journal of Current Pharmaceutical Research. 2013 Apr 1;4:33–8.

Ansel, H. C., Allen, L. V., & Popovich, N. G. (2014). Pharmaceutical dosage forms and drug delivery systems. Lippincott Williams & Wilkins. p263

Aulton, M., & Wells, T. (2018). Pharmaceutics: The Science of Dosage Form Design. Churchill Livingstone.

Breitkreutz, J., Boos, J., Paepke, S., & Zimmer, A. (2013). Pharmaceutical technology of tablets: development, evaluation, and innovative strategies. In Tablets and Other Drug Forms (2nd ed., pp. 1-40). John Wiley & Sons.

Baldwin, E. A. (2019). Citrus. In A. C. Sims (Ed.), Handbook of Plant Breeding: Vegetables I (Vol. 11, pp. 9-36). Springer.

Bhavesh Patil1, Divesh Patel1, Jayesh Patil1 and Prof. R. L. (2022). Extraction of Pectin from Citrus Peels. International Journal of Advanced Research in Science, Communication and Technology (IJARSCT) Volume 2, Issue 1, p631

Chavhan, S. S., Pawar, H. A., & Chavhan, S. V. (2015). Natural disintegrants: An overview. International Journal of Pharmacy and Pharmaceutical Sciences, 7(3), 7-13.

Chen, L., Yin, L., Zhou, Q., Zhang, J., Gong, X., Yuan, Q., & Xie, J. (2019). Citrus fruits as a treasure trove of active natural metabolites that potentially provide benefits for human health. Chemistry Central Journal, 13(1), 1-19.

Chowdary, K. P. R., Rao, Y. M., & Vamshi Vishnu, Y. (2013). Tamarind seed polysaccharide as superdisintegrant in the design of fast dissolving tablets. Indian Journal of Pharmaceutical Education and Research, 47(2), 116-121.

Cui, S. W., Wang, Q., & Wang, M. (2016). Pectin: Structure and functions. In Y. Fang (Ed.), Food polysaccharides and their applications (2nd ed., pp. 175-196). CRC Press.

Dixit, R. B., Puthli, S. P., & Oral, M. V. (2012). Mouth dissolving tablets: A review. Journal of Controlled Release, 16(1), 10-21.

Dushyant Unde, Asst. Prof. Vikas Wamane (2023). A review on disintegrant tablet–Tablet Volume:05/Issue:05/May-2023

Ebringerová, A., & Hromádková, Z. (2010). Pectin: Structure, properties, and applications. In M. D. L. W. Roberts (Ed.), Encyclopedia of Biocolloid and Biointerface Science (2nd ed., pp. 1-13). CRC Press.

El-Menshawe, S. F., Soliman, G. M., & El-Kamel, A. H. (2019). Locust bean gum: A promising natural polysaccharide in drug delivery systems. Carbohydrate Polymers, 210, 148-158.

Gerhard Levy, Robert H. Gumtow. (2003). Effect of Certain Tablet Formulation Factors on Dissolution Rate of the Active Ingredient. Journal of Pharmaceutical Sciences
Volume 52, Issue 12, December 1963, Pages 1139-1144

Gerrit M. Westhoff, Ben F.M. Kuster, Michiel C. Heslinga, Hendrik Pluim, Marinus Verhage (2014). "Lactose and Derivatives". Ullmann's Encyclopedia of Industrial Chemistry. Wiley-VCH. pp. 1–9.

Gohel, M. C., Jogani, P. D., & Bariya, N. H. (2007). Pharmaceutical technology: Tablet manufacturing. Pharmaceutical Technology, 31(1), 50-60.

Gohel, M. C., Jogani, P. D., & Bariya, S. H. (2011). Pharmaceutical technologies: Tablets. Pharmaceutical Technology, 35(9), 48-60.

Goel H, Kaur G, Tiwary A, Rana V. Formulation Development of Stronger and Quick Disintegrating Tablets: A Crucial Effect of Chitin. Yakugaku zasshi : Journal of the Pharmaceutical Society of Japan. 2010 May 1;130:729–35.

Gupta, V. K., Beckert, T. E., & Prideaux, B. (2013). Orally disintegrating tablets: formulation, preparation, techniques, and evaluation. Drug Delivery, 20(2), 52-64.

Harshada Shinde, Anokhi Rathod, Pooja Karande,Prof Ashwini Thokal. (2014). Extraction Of Pectin From Orange Peels : A Review. Journal of Emerging Technologies and Innovative Research (pp.517)

Hosny KM, Mosli HA, Hassan AH. Soy polysaccharide as a novel superdisintegrant in sildenafil citrate sublingual tablets: preparation, characterization, and in vivo evaluation. Drug Des Devel Ther. 2015 Jan 12;9:465–72.

Hussain, Z., Thu, H. E., Shuid, A. N., & Katas, H. (2017). Overview of pectin: A versatile polysaccharide. In H. E. Thu, A. N. Shuid, & H. Katas (Eds.), Pectins - Extraction, Purification, Characterization and Applications (pp. 1-26). IntechOpen.

Jain, A. K., & Mehra, S. (2011). Chewable tablets: A review. Indian Journal of Pharmaceutical Sciences, 73(6), 131-141.

Javadzadeh, Y., & Siahi-Shadbad, M. R. (2011). A review on the manufacturing processes of tablets and compacts. Pharmaceutical Sciences, 17(3), 155-162.

Kertesz, Z. I., & Szabo, E. A. (2006). Pectin. In G. G. Birch (Ed.), Functional Food Ingredients and Nutraceuticals (pp. 111-129). CRC Press.

Kumar, L., Verma, R., & Yadav, S. K. (2013). Wet granulation: A review. International Journal of Pharmaceutical Sciences and Research, 4(12), 4424-4436.

Lachman, L., Lieberman, H. A., & Kanig, J. L. (2012). The theory and practice of industrial pharmacy. In L. Lachman, H. A.

Lieberman, & J. L. Kanig (Eds.), Pharmaceutical Dosage Forms: Tablets (pp. 201-285). CRC Press.

LeBel M: Ciprofloxacin: chemistry, mechanism of action, resistance, antimicrobial spectrum, pharmacokinetics, clinical trials, and adverse reactions. Pharmacotherapy. 1988;8(1):3-33.

Leon Lachman, Herbert A. Lieberman, Joseph L. Kanig (1996): The theory and Practice of Industrial Pharmacy, Varghese publication house, 3rd edition,, 293-373.

Kamble, P., Kuchekar, B., & Mahajan, H. (2018). Design and evaluation of directly compressed fast disintegrating tablets using natural polymers. International Journal of Pharmacy and Pharmaceutical Sciences, 10(4), 25-30.

Kumar, S., Singh, R., & Sharma, A. (2021). Aloe vera gel homogenate shows anti-inflammatory activity through lysosomal membrane stabilization and downregulation of TNF-α and Cox-2 gene expressions in inflammatory arthritic animals. Future Journal of Pharmaceutical Sciences, 7(1), 12. 3

Malik K, Arora G, Singh I. Locust bean Gum as Superdisintegrant- Formulation and Evaluation of Nimesulide Orodispersible Tablets. Polimery w medycynie. 2011 Jan 1;41:17–28.

Malviya R, Srivastava P, Bansal M, Sharma P. Mango peel pectin as superdisintegrating agent. Journal of Scientific & Industrial Research. 2010 Oct 1;69:688–90.

Nayak RK, Patil SR, Patil MB, Bhat M. Evaluation of disintegrating properties Of Mangifera indica gum. RGUHS Journal of Pharmaceutical Sciences. 2011;1:11–21

Nour, V., Trandafir, I., & Cosmulescu, S. (2018). A comprehensive study on the chemical composition of sweet orange essential oil. Industrial Crops and Products, 111, 11-16.

Parind Mahendrakumar Desai, Celine Valeria Liew, Paul Wan Sia Heng (2016). Review of Disintegrants and the Disintegration Phenomena Journal of Pharmaceutical Sciences,Volume 105, Issue 9,pp. 2545-2555

Patel, V. M., Prajapati, V. D., & Patel, N. M. (2016). Natural gums and modified natural gums as sustained-release carriers. Drug Development and Industrial Pharmacy, 42(3), 437-452.

Patel, H., Patel, K., & Patel, M. (2020). Preparation of biochar by mango peel and its adsorption characteristics of Cd(II) in solution. RSC Advances, 10(63), 35878–35888.

PharmIQ Glossary (2033). Dosage form; https://www.pharma-iq.com/glossary/dosage-form-df

Pietsch F, Bergman JM, Brandis G, Marcusson LL, Zorzet A, Huseby DL, Hughes D: Ciprofloxacin selects for RNA polymerase mutations with pleiotropic antibiotic resistance effects. J Antimicrob Chemother. 2017 Jan;72(1):75-84

Rajalakshmi, R., & Remya, K. (2018). Disintegrants in tablet formulation: A review. International Journal of Pharmaceutical Sciences and Research, 9(4), 1355-1363.

Rowe R, Sheskey PJ, Quinn ME. Handbook of pharmaceutical excipients. Sixth. RPS; 2009. 1–888 p.

Sharma, V., Sharma, R. R., Jain, A., & Jain, A. (2019). Role of superdisintegrants in drug dissolution: A comprehensive review. Journal of Pharmacy & Bioallied Sciences, 11(3), 194-203.

Shirwaikar A, Prabu SL, Kumar GA. Herbal Excipients in Novel Drug Delivery Systems. Indian J Pharm Sci. 2008;70(4):415–22.

Singh, A., Sharma, P., & Singh, S. (2022). Formulation and evaluation of novel functional snack bar with amaranth, rolled oat, and unripened banana peel powder. Journal of Food Science and Technology, 59(9), 3511–3521. 2

Sodhi, S., Bhatia, M., & Joshi, B. (2015). Natural superdisintegrants: An overview. International Journal of Pharmaceutical Sciences and Drug Research, 7(3), 225-231

Sudke, S. G., & Malshe, V. C. (2018). An overview on various types of tablets. International Journal of Pharmaceutical Sciences and Research, 9(10), 4026-4033.

Tejaswi Santosh Ubhe, Preeti Gedam (2020)A Brief Overview on Tablet and It's Types; Journal of Advancement in Pharmacology, Volume 1 (Issue 1), pp21-31

Uebbing, L.; Klumpp, L.; Webster, G. K.; Lo benberg, R.(2017) Justification of disintegration testing beyond current FDA criteria using in vitro and in silico models. Drug. Des. Devel. Ther. 11, 1163–1174.

Voragen, A. G. J., Coenen, G.-J., & Verhoef, R. P. (2009). Pectin, a versatile polysaccharide present in plant cell walls. Structural Chemistry, 20(2), 263-275.

Wang, J., Zhang, H., Zhang, Z., & Linhardt, R. J. (2017). Pectin extraction from apple pomace and citrus peel by-products. In G. Du, Z. Zhang, & G. Chen (Eds.), Food waste to valuable resources: Applications and management (pp. 277-289).

Wikipedia. (2023). Ciprofloxacin https://en.m.wikipedia.org/wiki/Ciprofloxacin

Appendix 1

Formulation Code	Disintegrants	Value (mg)

F1	Sodium starch glycolate	25.0
F2	Pectin	25.0
F3	Pectin	37.5
F4	Pectin	50.0
F5	Pectin	62.5
F6	Pectin	75.0
F7	Maize Starch	37.5

S/No	Concentration (mcg/ml)	Absorbance (nm)
1	5	0.096
2	10	0.086
3	20	0.064
4	30	0.042
5	40	0.024

6	50	0.013