PREPARATION AND CHARACTERIZATION OF A CO-PROCESSED EXCIPIENT FOR FAST TABLET DISINTEGRATION

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THE DISINTEGRANT EFFECT OF A CO-PROCESSED EXCIPIENT ON PARACETAMOL TABLET FORMULATIONS

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CERTIFICATION

This is to certify that this work was carried out by Favour Oritseweyinmi Fregene in the Department of Pharmaceutics and Pharmaceutical technology, Faculty of Pharmacy, University of Benin, Benin City in partial fulfillment of the award of the Pharm. D degree of the university

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DEDICATION

This work is dedicated to Almighty God, whose grace and infinite mercies have guided me throughout this journey of academic pursuit.

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ABSTRACT

Introduction: Excipients play a crucial role in pharmaceutical tablet formulation,influencing drug stability,bioavailabilty,and mechanical properties.Traditional excipients often present challenges such as poor flowability,inadequate compressibility and inconsistent drug release to address these limitations,co-processed excipients,which combine multiple excipients to enhance functionality,have gained attention.

Purpose: The primary aim of this study is to prepare and characterize a co-processed excipient for direct compression and fast tablet disintegration.

Method: The novel excipient was prepared through milling and co-processing of the selected excipient.The excipients physical and flow properties were characterized by measuring bulk density,tapped density,carr's index,hausner's ratio,moisture content,swelling index and hydration capacity.Paracetamol tablets were formulated using the excipient in different concentrations an evaluated for weight uniformity,hardness,friability,disintegration time and dissolution rate.

Results: The co-processed excipient exhibited improved physiochemical properties with hardness(6.6-7),Disintegration time(1.45secs) and drug release profile of above 80% within 50mins in two separate batches.It showed poor flow properties with carr's index of 60% and hydration capacity of 1.18

Conclusion: The result from the disintegration time of the different batches of tablet formulation with the co-processed excipient showed signs of a fast disintergratig tablet with a disintegration time of 1.45secs.

CHAPTER ONE

INTRODUCTION AND LITERATURE REVIEW

1.1. Background of the Study

In pharmaceutical formulations, excipients are the most substantial constituents (Gangurde et al. 2013) . In the late 1980s, the pharmaceutical industry began using co-processed excipients. Some of the earliest examples were co-processed glucomannan and galactomannan (1996), MEGGLE's co-processed cellulose and lactose (1990), and co-processed microcrystalline cellulose and calcium carbonate (1988) (Chaudhari et al. 2012) Up until now, the food industry has been a continuation of the excipients sector. Additionally, the food sector produces excipients, which has contributed to the good safety profile (Steinberg et al. 2001). In a completed pharmaceutical drug formulation, pharmaceutical excipients are substances that are not the active pharmaceutical ingredient (API). These often serve as coating, coloring, flavorings, lubricants, diluents, and binders for the formulation (Ren et al. 2008) . The International Pharmaceutical Excipients Council (IPEC) was established as a result of growing regulatory pressure on the excipients' safety, purity, and standardization (IPEC-America). Intentionally incorporated in a drug delivery system, excipients are defined by the International Pharmaceutical Excipient Council (IPEC) as "substances other than the API which have been appropriately evaluated for safety." Combining two or more compendial or non-compendial excipients with the intention of physically altering their qualities without changing their chemical properties is known as co-processing (Chaudhari et al. 2012) . Physical and chemical characteristics, stability and compatibility concerns, pharmacokinetic parameters, permeability characteristics, segmental absorption behavior, and drug delivery routes are all significant considerations when selecting an excipient for formulation

creation. This can help determine the necessary delivery platform and the problems with API absorption.

1.2. Overview of Excipients and Co-processed Excipients

Excipients can be classified into four categories generally: single entity excipient, a physical blend of multiple excipients, new chemical entity excipient and co-processed excipient (Chaudhari et al. 2012).

i. **Single Entity Excipients:** Single entity excipients are defined as excipients that contain a single component, the principal component (Chaudhari et al. 2012).

ii. **Physical Blend of Multiple Excipients:** For solid mixtures or blends, the individual excipients remain physically separate at a particulate level. For simple physical mixtures of two or compendial/non compendial excipients, the individual components are mixed together without undergoing significant chemical change using a low to medium shear process (Chaudhari et al. 2012).

iii. **New Chemical Entity Excipients:** Excipients that undergo chemical modification to create new or unique excipients are referred to as such. Typically, the FDA's inactive ingredient database does not include these. Any inactive substance purposefully added to medicinal and diagnostic products is referred to as a novel excipient (Desai et al. 2012).

iv. **Co-Processed Excipients:** Co-processed excipients are mixtures of two or more compendia or non-compendial excipients that are intended to physically alter their characteristics in a way that is not possible with straightforward physical blending and without appreciable chemical alteration .

1.2.1. Advantages of Co-Processed Excipients

The application of co-processed excipients in the pharmaceutical industry has increased due to significant improvements in their physicochemical characteristics. One of their key advantages is their suitability for direct compression, which results in tablets that are less likely to exhibit changes in their dissolution profiles after storage compared to those formed via granulation. Additionally, direct compression offers a major financial benefit over wet granulation as it requires fewer unit operations, thereby reducing production costs. Co-processed excipients also contribute to enhanced organoleptic properties, including improved palatability and a better tongue feel. Furthermore, they create a synergistic effect in the way individual components function, leading to improved overall performance. Given that official compendia now mandate dissolution criteria for most solid dosage forms, the use of co-processed excipients has become increasingly crucial. They also reduce the likelihood of punches and dies wearing out, thereby extending the lifespan of tablet manufacturing equipment. Moreover, they facilitate the delivery of highly potent substances in small doses that require minimal contaminants. By overcoming the limitations of existing excipients and improving flow properties, co-processed excipients provide a more efficient and effective approach to pharmaceutical formulation (Mamatha et al. 2017).

Limitations of Co-Processed Excipients

Despite their advantages, co-processed excipients have several disadvantages. Their processing often requires high temperatures and specialized filling equipment, making the production process more complex. Additionally, some lipidic excipients are not well tolerated by preclinical species, limiting their applicability in certain formulations. A significant drawback is the substantial material loss that occurs during various processing steps, which increases production costs. The overall process is expensive due to the need for skilled labor,

specialized equipment, additional space, and increased energy consumption. Furthermore, thermolabile and moisture-sensitive drugs are poor candidates for formulations involving co-processed excipients. The use of such excipients can also lead to reduced direct interactions between formulators and production personnel in the manufacturing area, potentially affecting quality control. The requirement for multiple pieces of specialized equipment further adds to the cost and complexity of the process. The high material loss remains a notable concern, impacting efficiency and cost- effectiveness (Mamatha et al. 2017).

1.2.2. Types of Excipients

1. Glidants

Glidants are pharmaceutical excipients that are added into the tablet powder blend to improve flowability into the die cavity of tablet presses. Glidants facilitate a smoother flow of tablet granulation by lowering friction between granules. The size and shape of the glidant particles and the granules dictate how glidants affect granule flow (Advankar et al. 2019). Examples of glidants are colloidal silicone dioxide, starch, talc and magnesium stearate (Panda et al. 2015).

2. Binders

In tablet formulation, Binders are used to provide plasticity and hence increase the bond strength between the particles in the tablet (Bin et al. 2022) . Granules are created when powders are joined together by binder, which acts as a "glue." Additionally, when compressed, they provide the cohesiveness required to bind the particles and create a tablet (Alanazi, 2010). Some examples of binders are acacia, starch paste, PVP, Hydroxypropyl Methylcellulose (HPMC), glucose and carboxymethyl cellulose.

3. Fillers/Diluents

Diluents, often known as fillers, are therapeutic substances that are necessary and helpful in pharmaceutical formulations but lack pharmacological activity. In order to facilitate

tablet handling during the production process and guarantee the desired content homogeneity, diluents—heterogeneous groups of ingredients—are employed to make up the necessary bulk of the tablet when the pharmaceutical dose is insufficient to create the quality. Diluents are frequently added to tablet formulations to enhance certain aspects of the tablet, such as enabling direct compression to enhance cohesiveness, boosting flow, and optimizing the weight of the tablet in relation to die capacity (Howerton et al. 2003). Examples of fillers are lactose, dextrose, sorbitol, MCC and dibasic calcium phosphate dihydrate.

4. Disintegrants and Super-Disintegrants

Chemicals known as disintegrants are added to tablets and some encapsulated medicines to aid in the disintegration of the tablet and capsule "slugs" into minuscule particles in an aqueous media. This increases the surface area that is accessible and speeds up drug release. They facilitate moisture absorption and dispersion in the tablet matrix. The disintegrants' primary function is to offset the effectiveness of the tablet binder and the physical forces that cause the tablet to compress (Howerton et al. 2003; Pahwa and Gupta, 2011). Examples of disintegrants are corn starch, clays such as Veegum HV, resins, clays and cellulose.

The superabsorbent material known as a super-disintegrant breaks down quickly as a result of the formulation's combined actions of water absorption and swelling. The swell of super-disintegrants increases the wetted surface of the carrier, which improves disintegration and dissolution by increasing the system's wettability and dispersibility. Good super-disintegrants improve compressibility and compatibility without compromising the mechanical strength of the preparation of high-dose drugs (Pahwa and Gupta, 2011). Examples of superdisintegrants are CCS, crospovidone, sodium starch glycolate.

5. Lubricant

Excipients called lubricants are employed to facilitate smooth operation. Lubricants are used in the formulation process to keep chemicals from clumping together. Lubricants prevent tablets from sticking to the punch's surface by lowering friction between the outer layer of the tablet and the die wall during the ejection process while maintaining formulation adherence. Lubricants can decrease inter-particle friction and increase powder flowability (Li et al. 2014; Poonam et al. 2018) . Examples of lubricants are talc, silica, stearic acid and magnesium stearate.

6. Thickening, Viscosity Imparting and Gelling Agents

Thickeners could be used in any composition that has a large amount of water. Polyose derivatives such as hydroxyethyl cellulose are commonly used in shampoo and body cleansers. Natural thickeners are polymers that expand and become more viscous as they absorb water. They also function as adhesives, stabilize foam, and impart various specialized qualities. Gelatin and gums such as Algarroba Bean Gum and Xanthan Gum are other examples of naturally derived thickener (Batra et al. 1994).

7. Coating Agents

Coating agents are used to coat or form a film around the dose form. Coating strategies improve drug protection and modify drug release. They maintain product safety from external conditions, hence increasing product effectiveness and appeal (Beneke et al. 2009; Gupta et al. 2013). Coating agents are utilized based on the specific site of drug release, such as avoiding the stomach and absorbing the drug through the intestines. Tablets, pills, capsules, and other dosage forms may contain coating agents. Natural coats have no hazardous effect on humans or the environment, and are easily biodegradable, digestible, and expelled from the body (Xie et al. 2010) . However, synthetic coating chemicals have a bitter taste, thus various

sweetening and flavoring compounds are utilized to mask their bitterness. Natural excipients utilized as natural coating agents include gelatin, xanthan gum, guar gum, and pectin (Rajinikanth et al. 2003; Fuchs-Koelwel et al. 2004).

1.2.3. Need for Developing New Excipients

It is widely acknowledged among formulation scientists that no one excipient satisfies all necessary requirements to enable the formulation of an active pharmacological ingredient into a particular dosage form (Chukwu, 2001) . To date, there has been little activity in the development of new excipients, as evidenced by the fact that not a single new chemical excipient has been introduced into the market for many years. This is because the development of new excipients has been market driven, meaning that they are developed in response to market demand, rather than marketing driven, meaning that excipients are developed first and market demand is created through marketing strategies. The expense of excipients is the main factor preventing the development of new chemical excipients exploration and advancement (Steinberg et al. 2001)).

As new pharmacological moieties emerge with diverse physicochemical and stability features, Formulators are under increasing pressure to find new excipients that can provide desired functionality. The following elements are influencing the hunt for novel excipients:

i. Modulation of medication solubility, permeability, and stability.
ii. The growing speed capabilities of tableting technology necessitate that excipients maintain low weight variation and high compressibility, especially during brief dwell durations.
iii. Existing excipients have drawbacks, including poor die filling due to agglomeration10, high moisture sensitivity, and loss of compaction of microcrystalline cellulose (MCC) upon wet granulation.

iv. There are also insufficient excipients that cater to the needs of particular patients, such as those with diabetes, hypertension, and lactose and sorbitol sensitivity.

v. The rising demands on excipient performance to handle problems including bioavailability, solubility, and disintegration (Li et al. 2014)

1.2.4. Sources of Co-Processed Excipients

1.2.4.1. Natural Sources

Natural excipients have attracted a lot of attention lately because of their wide range of medicinal uses. For instance, while developing and manufacturing medicinal dosage forms, natural polysaccharide polymers are utilized. Stability, bioavailability, and patient acceptance are all safeguarded, supported, or improved. Additionally, they aid in product identification and improve any other aspect of the drug's general safety, efficacy, and/or delivery throughout usage and storage (Alwossabi et al. 2021) . The pharmaceutical industry uses a number of plant-based pharmaceutical excipients, including cellulose, agar, starch, alginates, carrageenan, guar gum, xanthan gum, gelatin, pectin, acacia, tragacanth, and alginates, as binding agents, disintegrants, sustaining agents, protective, thickening/gelling agents, bases in suppositories, stabilizers, and/or coating materials (Wade and Weller, 1994) The demand for herbal materials as excipients has increased due to the fact that these excipients, which come from plants, are renewable and can be grown and harvested sustainably to ensure a steady supply of raw materials (Perepelkin, 2005).

However, compounds derived from plants present a number of possible difficulties, including the fact that they are often synthesized in small amounts and in structurally complex mixtures, which could lead to a time-consuming and costly isolation and purification process with yields

that differ depending on the species, region, climate, and time of year of collection. They may be exposed to the outside environment during manufacture, which increases the risk of heavy metal and microbial contamination (Shirwaikar et al. 2008; Jani et al. 2009) . Intellectual property rights are another issue that has grown in significance (Lam, 2007; McChesney et al. 2007).

1.2.4.2. Semi-Synthetic Sources

Semi-synthetic sources of excipients like Cellulose derivatives play an essential role as pharmaceutical excipients, with a wide range of applications in the pharmaceutical industry, including the production of current medicines, the creation of new dosage forms (DF), and modern pharmaceutical manufacturing techniques. Hydroxypropyl methylcellulose, also known as Hypromellose (HPMC), is a hydrophilic cellulose derivative that is widely employed in the pharmaceutical industry for the development of novel oral and oromucosal matrix DF with controlled drug release (Konno et al. 2008). Because of its capacity to swell and generate a gel layer that controls the rate of drug release on the surface of matrix systems, the polymer is commonly used in the creation of controlled release DF (Haque et al. 1993). HPMC's non-ionic nature assures a reduced risk of medication interactions and generally gives predictable drug release profiles, as the pH of the gastrointestinal (GI) fluids has no substantial influence on the HPMC-based matrix (Ford et al. 1985).

1.2.4.3. Synthetic Source: Limitations in Co-processing

Developing new chemical excipients, grades, and combinations of existing compounds can result in increased functionality (Shangraw 1993; Steinberg et al. 2001). Developing a new chemical excipient requires regulatory approval to address safety and toxicity concerns, which can be time-consuming and expensive. Additionally, the excipient must go through generic

development, shortening the market exclusivity time (Jacob et al. 2007) . The high risk and large cost are not warranted given the low returns from the novel excipients.

1.2.4.4. Principles Involved in Co-Processing Excipients

The development of co-processed excipients involves several critical steps to ensure optimal performance and functionality. First, suitable excipients are selected based on their material properties and functional specifications. The next step involves optimizing the ratio of different excipients to achieve the desired functionality.

Following this, the necessary particle size for co-processing is evaluated, which is particularly important when one of the components is handled in a dispersed phase. Once the particle size is determined, the most suitable co-processing technique is selected. Additionally, an appropriate drying method, such as flash drying or spray drying, is chosen to enhance stability and performance.

Finally, process optimization is carried out, as even minor variations in processing conditions can significantly impact the functionality of the excipients. Ensuring consistency at each stage is crucial for achieving high-quality co-processed excipients that meet pharmaceutical industry standards (Chowdary et al. 2012).

1.2.5. Methods of Co-Processing

1. **Spray Drying:** This process involves spraying feed into a hot drying medium to convert it from a fluid to a dry particle form. This is a continuous particle processing and drying procedure. The feed may be a solution, suspension, dispersion, or emulsion. Drying can produce powders, granules, or agglomerates based on the feed's physical and chemical qualities, dryer design, and desired powder properties (Chowdary et al. 2012; Chowdary and Ramya, 2013).

2.

3. **Solvent Evaporation:** Solvent evaporation requires the employment of a liquid production vehicle. The coating excipient is dissolved in a volatile solvent that is not miscible with the liquid manufacturing vehicle stage. Microencapsulation involves dissolving or dispersing a core excipient ingredient in a polymer coating solution. Using agitation, the core coating material combination is distributed in the liquid manufacturing vehicle phase to create the desired microcapsule size. Heat the mixture, if necessary, to evaporate the solvent. After evaporating the solvent, drop the liquid vehicle temperature to ambient (if necessary) and continue agitating. Microcapsules can be employed as a solution, coated on surfaces, or separated as powders. Core materials can be soluble or insoluble in water (Chowdary et al. 2012; Chowdary and Ramya, 2013).

4. **Crystallization:** Crystallization is the (natural or artificial) process of formation of solid crystals precipitating from a solution, melt or more rarely deposited directly from a gas. Crystallization is also a chemical solid– liquid separation technique, in which mass transfer of a solute from the liquid solution to a pure solid crystalline phase occurs (Rajinikanth et al. 2003).

5. **Melt Extrusion:** The technique of creating tiny beads or pellets from molten material that is extruded using an extruder is known as melt extrusion (Chowdary and Ramya, 2013).

6. Granulation/Agglomeration: Granulation refers to the formation and crystallization of grains. Granules vary in size from 0.2 to 4.0 mm. "Agglomeration" is a synonym. The agglomeration process, also known as particle size enlargement, is an effective way to adjust product attributes. Powder agglomeration enhances physical qualities like wettability, flowability, bulk density, and product appearance. The pharmaceutical business uses two types of granulation technologies: wet granulation and dry granulation. Wet

granulation is the recommended approach for co-processing (Chougule et al. 2012).

7. **Milling:** Milling involves the use of hammers, ball mills, and roller mills. The premixed excipients are ground using an incredibly fast milling machine. During milling, particles come into contact and form bonds, resulting in granules. One example provided is the synthesis of co-process cross-linked PVP and calcium silicate utilizing ball milling (Hussain et al. 2018).

8. **Roller drying:** This approach allows for the drying of a homogeneous solution or dispersion that includes previously mixed excipients. Co-processing lactose with lactitol and sorbitol can be done using the roller drying method (Garg et al. 2013).

1.2.6. Properties of Co-Processed Excipients

Co-processed excipients possess several advantageous properties that enhance their functionality in pharmaceutical formulations:

1. **Quick Disintegration** – These excipients improve compressibility, super-disintegration, and flow and wetting properties. They also help reduce production time and costs for orally disintegrating tablets (ODTs) by eliminating the need for supplementary excipients such as lubricants (Jain et al. 2023).

2. **Superior Compressibility** – Co-processed excipients are widely used in direct compression due to their enhanced flow characteristics and compressibility, making them ideal for tablet formulation (Bin et al. 2022).

3. **Enhanced Dilution Potential** – This refers to an excipient's ability to maintain compressibility even when mixed with other substances, ensuring consistent tablet strength and integrity (Pawar et al. 2019).

4. **Simplified Production Process** – Co-processed excipients streamline manufacturing by reducing the number of processing steps required.

5. **Better Flowability** – These excipients exhibit improved powder flow properties, which contribute to uniform weight distribution and consistent tablet production.

6. **Affordability and Cost-Effectiveness** – The use of co-processed excipients offers a cost- effective approach to pharmaceutical formulation by reducing the need for multiple excipients and minimizing processing complexities.

1.3. Tablet Formulation

The Indian Pharmacopoeia defines pharmaceutical tablets as solid, flat or biconvex plates with a unit dosage form. Compressed medications or mixtures can be manufactured with or without diluents. A tablet is a compacted solid dosage form that contains medications with or without excipients. They vary in shape, size, and weight based on the number of therapeutic compounds and route of administration (Lachman et al. 1976; Ubhe and Gedam, 2020).

Direct compression (DC) is a typical method for producing oral solid dosage forms like tablets. Advantages of this approach include eliminating the need for wet or dry granulation, achieving more consistent dissolving profiles, reducing punch wear and tear, improving API stability, and reducing microbiological contamination. Developing tablets utilizing Direct Compression can be challenging due to suboptimal compression and flow properties of active medicinal ingredients, especially with large drug loading. The feasibility of the DC method depends on the API's physicochemical properties, which affect the flow and compression behavior of the formulation, especially when they make up a significant portion of the tablet (Bhavana and Reddy 2023).

1.3.1. Properties Of Tablets

- The product should be stylish, unique, and free from faults like chips and cracks, discoloration and pollution.

- Products must be durable enough to survive shocks during production, packaging, transportation, and dispensing.
- Physical stability is essential for maintaining physical qualities throughout time.
- The medication agent(s) should release predictably and consistently in the body.
- The therapeutic agent(s) must be chemically stable over time.

1.3.2. Preparation of Tablets

Tablets are prepared by three methods including the wet granulation, dry granulation and direct compression method.

i. **Wet Granulation Method:** This is the most popular and extensively utilized strategy. This procedure includes several processes involving weighing components, mixing, granulating, screening, drying, lubricating, and compressing tablets. The active component, diluent, and disintegrant are combined and passed through a sieve (sifting).

ii. **Dry Granulation Method:** When making tablets, this technique is employed. Slugging may be employed to create the granules if they are moisture-sensitive or cannot withstand high drying temperatures. Double compression or dry granulation typically removes a number of processes that include slugging the powder mass. The slug is created by blending the lubricant, diluent, and active substance.

iii. **Direct Compression:** Direct compression involves direct compressing the powdered material into tablets (Tejaswi and Preeti, 2020).

1.4. Statement of the Problem

The quality and performance of pharmaceutical tablets are heavily reliant on the choice and properties of excipients used in their formulation. Despite significant advancements in excipient development, current excipients still present limitations such as poor flow properties,

inadequate compressibility, and inconsistent drug release profiles. Furthermore, excipient interactions can lead to variations in tablet hardness, dissolution rates, and overall stability, affecting the efficacy of the final product. A potential solution to these issues is the use of co-processed excipients, which combine two or more excipients to enhance desirable properties like improved flow, compressibility, and stability. However, the development of novel co-processed excipients tailored for specific formulations remains underexplored. There is a need for innovative, efficient, and cost-effective excipients that can address the shortcomings of traditional excipient systems in tablet formulation.

1.5. Justification of the Study

The pharmaceutical industry continuously seeks ways to improve the quality, stability, and efficacy of drug products. One of the key factors influencing these aspects is the choice of excipients used in tablet formulation. While the use of single excipients has been standard practice, the combination of multiple excipients through co-processing offers the potential for superior performance characteristics. This study is justified by the growing need for enhanced excipient systems that can provide better flowability, improved compressibility, and controlled release profiles, which are crucial for the development of high-quality tablets.

Furthermore, with the rise of complex drug formulations and the increasing demand for tailored drug delivery systems, co-processed excipients present an exciting opportunity to optimize pharmaceutical tablet formulations. The novel co-processed excipient developed in this study could provide a solution to longstanding challenges in tablet formulation, such as poor tablet strength and dissolution inconsistencies, while also being cost-effective and scalable. By developing and characterizing a novel co-processed excipient, this study contributes to the advancement of pharmaceutical excipient science, offering new possibilities for the efficient and reliable production of oral solid dosage forms.

Aim and Objectives of the Study

The primary aim of this study is to prepare and characterize a novel co-processed excipient for direct compression and fast tablet disintegration.

Specific Objectives include:

1. To prepare the co-processed excipient and carryout characterization of the formulated tablet

2. To prepare different batches of tablets by direct compression using varying concentration of novel excipient.

3. To evaluate the tablet properties of the formulated paracetamol tablet

CHAPTER TWO

MATERIALS AND METHODS

2.1 Materials

1. Paracetamol (BDH Chemicals, London),
2. Modified cellulose gum (FMC Corporation, USA),
3. Pototo Potato starch
4. Hydroxypropyl Methylcellulose
5. Paracetamol powder

2.2 Methods

2.2.1 Preparation of the Novel Excipient

Fast disintegrating tablets of paracetamol were prepared by direct compression method using three excipients Hyroxyl methyl cellulose,potato starch and modified cellulose gum.Paracetamol 500mg tablets containing 125mg of the co-processesd excipient were prepared. For all the formulations,potato starch was used as the filler.The novel excipient was formulated using a ball miller.

2.2.2 Evaluation of physiochemical properties of co-processed excipient

The powders were characterized to evaluate their physiochemical properties

Bulk Density

A specific quantity of the co-processed excipient was measured and transferred into a 50ml glass cylinder where its bulk volume was recoreded . The bulk density was calculated using the formula;

Tapped Density

Tapped density was measured by subjecting the cylinder containing the pre-weighed co-processed excipient to100 taps.The resulting volume was then recorded.The bulk density was calculated using the formula;

Angle of Repose

The angle of repose is the maximum slope angle relative to a horizontal surfaceat which a material remains stable before sliding.A measured quantity of the co-processed excipient was passed through a funnel until a conical heap was formed.The diameter of the base and the maximum height of the cone were measured and used to compute the angle of repose using the equation;

Flow Rate

Flow rate refers to the mass of a substance that passes through a specified orifice with a diameter of 0.85cm under the influence of gravity and the time taken for complete passage was recorded.The flow rate was calculated using the equation;

Moisture content

The moisture content represents the amount of water present in the co-processed excipient.A pre-weighed sample was dried in a hot air oven at 105C for four hours.The initial and final weights were recorded and the moisture content was calculated using the formula;

Swelling Index

A pre-weighed portion of the co-processed excipient with a known tapped volumed was placed into a 50ml measurimg cylinder.The powder was first dispersed in 1ml of absolute ethanol followed by 25ml of distilled water and the volume was adjusted with additional water.The cylinder was tightly sealed and shaken at 10-minutes interval for one hour.The dispersion was then left undisturbed for three hours,after which the final sediment volume was

recorded.The swelling capacity was calculated using the formula;

Hydration Capacity

A 1g sample of the co-processed excipient was placed into a 15ml centrifuge tube.After adding 10ml of water,the tube was sealed and shaken for two minutes.Tge sample was then allowed to settle for ten minutes before being centrifuged at 1000rpm for ten minutes using a bench centrifuge.The supernatant was decanted and the remaining sediment was weighed.The hydration capacity was calculated using the formula;

Particle Density

A 25ml specific gravity bottle (pycnometer)was filled with liquid paraffin,excess liquid was wiped off and the weight was recorded as a.The bottle was then emptied,rinsed with acetone and dried.A 1g sample of the co-processed excipient was introduced into the pycnometer,which was then refilled with liquid paraffin.the total weight was recorded after cleaning any excess paraffin from the bottle.The particle density was clculated using the formula;

Tablet Formulation

The table below outlines the formulation of tablets in different batches(A,B,C,D,E) indicating the quantities of the active pharmaceutical ingredient (paracetamol) and excipients. This variation helps assess the impact of the co-processed excipient on tablet properties.Each batch was subjected to direct compresion using a single punch tableting machine with a compression power of 38 pounds per square inch(psi).

Table 2.1: Composition of the Formulated Paracetamol Tablets

Ingredient (mg)	Batch A	Batch B	Batch C	Batch D	Batch E
Paracetamol	500	500	500	500	500
Co-processed Excipient	125	100	75	50	25
Filler: Potato starch	0	25	50	75	100
TOTAL	**625**	**625**	**625**	**625**	**625**

2.2.3 Tablet Characterization

The tablets were characterized using the following parameters:

Hardness

Hardness refers to the force required to break a tablet *al*ong its diameter. It is a measure of mechanical strength.Five tablets were selected from each batch.Using a mosanto tablet hardness tester,the hardness was determined and the values were recorded in Newtons (N).

Friability

Measures the tablet's resistance to chipping or breaking during handling.Ten tablets were randomly picked from each batch and weighed accurately before being placed in the friabilator machine.The machine was operated at 25rpm for 4minutes.Thereafter,thevtablets were dusted and reweighed.

Weight Uniformity

This ensures that tablets within a batch have consistent weight.Twenty tablets were individually weighed, and the percentage deviation from the average weight was calculated.

Disintegration Time

This involves the time taken for a tablet to break into smaller particles.A disintegration apparatus was used, six tablets from each batch were placed into the tubes of the disintegration apparatus that was suspended in a beaker filled with distilled water.The apparatus was then subjected to oscillation until every fragment from each tablet passed through the mesh basket at the bottom of the beaker. The time for complete disintegration

was recorded.

Dissolution Rate

This involves the rate at which the active ingredient dissolves in a specific medium.The test was conducted using type II apparatus.A 750ml volume of 0.1N HCL wa aded to thress vessels within the eight-chanber dissolution apparatus with the temperature of the meium maintained at 37C.A single tablet was placed in the basket of the three vessels containing the dissolution medium.the apparatus was then activated andset to operate at speed of 50rpm.At pre-determined time intervals,a 10ml sample of the dissolution medium was withdrawn and the equal volumeof fresh 0.1N HCL was added to maintain the total volume.the absorbance of the collected samples was measured at 281nm using 0.1N HCL as blank.the test was performed thrice and the average value was recorded.

Thickness and Width

This ensures uniformity in tablet dimensions, critical for packaging and dosing.Twenty tablets from each batch was measured using a vernier caliper to record the dimensions of individual tablets (Aulton and Taylor, 2018).

CHAPTER THREE

RESULTS AND DISCUSSION

3.1 Results

3.1.1 Evaluation of the Novel Co-Processed Excipient and Powder Mix for Tablet Formulation

Table 3.1 shows the flow properties of the novel co-processed excipient, which was characterized by a bulk density of 0.389 g/cm³ and a tapped density of 0.493 g/cm³. The excipient exhibited a Carr's index of 21.09% and a Hausner ratio of 1.22, indicating good flowability. The moisture content of the excipient was 0.9%, but other parameters such as angle of repose, flow rate, swelling index, particle density, and hydration capacity were not provided.

Table 2 presents the flow characteristics of the powder mix containing the active pharmaceutical ingredient (API) for tablet formulation. Batch A displayed the highest Carr's index (59.99%) and Hausner ratio (3.5), suggesting poor flow properties. In contrast, batches B, C, D, and E exhibited better flow characteristics, with a consistent Carr's index and Hausner ratio of 60% and 2.5, respectively.

Table 3.1: Physiochemical properties of the co-processed excipients

Characteristics	**Novel Excipient**
Bulk density(g/cm^3)	0.389
Tapped density (g/cm^3)	0.493
Carr's index (%)	21.09
Hausner ratio	1.22
Angle of repose (°)	-
Flow rate (g/s)	-
Moisture content (%)	0.9g
Swelling index	-0.3
Particle density (g/cm^3)	1.94
Hydration capacity (g/g)	1.18

Table 3.2. Flow Characteristics of Powder Mix (Containing API) for Tablet formulation

Batch	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)	Carr's Index (%)	Hausner's Ratio
A	2.34	5.83	59.99	3.5
B	2.5	6.25	60	2.5
C	2.5	6.25	60	2.5
D	2.4	6	60	2.5
E	2.4	6	60	2.5

3.1.2 Characterization of Paracetamol Tablets

Table 3 shows the properties of paracetamol tablets prepared using the novel co-processed excipient. The batch weight for all tablets was approximately 0.8 g, with a uniform tablet dimension of 12.5 mm. The hardness of the tablets ranged from 6 to 7 kp, while friability was consistent across the batches, with values ranging from 4.32% to 4.43%. Disintegration times for batches D and E were faster (1.45 to 1.47 minutes) compared to the other batches, suggesting enhanced dissolution performance.

Figure 1 illustrates the dissolution profile of the different batches of paracetamol tablets, showing variations in drug release over 50 minutes. All batches exhibited rapid initial dissolution, with Batch E showing the highest release (87.45% at 50 mins). In contrast, Batch A demonstrated significantly slower dissolution, peaking at only 20.63%. These results indicate that formulation differences impact dissolution behavior, with Batch E achieving the fastest and most consistent release, while Batch A showed the slowest and least complete drug release.

Table 3.3: Properties of paracetamol tablets prepared using the co-processed excipients

Batch Batch	Weight (g)	Table Dimension (mm)	Hardness (kp)	Friability (%)	Disintegration Time (min)
A	0.8	12.5	6.6	4.38	2.48
B	0.79	12.5	7	4.43	2.47
C	0.8	12.5	6	4.32	2.45
D	0.8	12.5	6.8	4.41	1.47
E	0.8	12.5	6.4	4.4	1.45

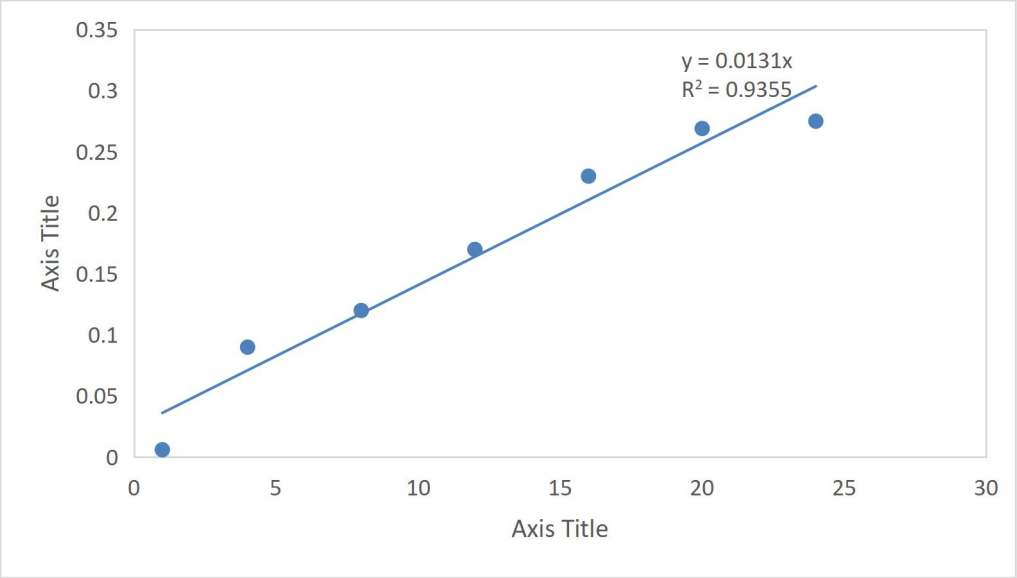

Figure 3.1 shows the Standard Calibration plot (Beer's plot) of Paracetamol.

The equation of the straight line obtained from linear regression o the data is given by:

$Y = MX + C$……..3.1

Where

Y = y-axis (Absorbance)

M = Slope

X = x-axis (concentration)

C = Intercept of curve on the y-axis

The data for the derivation of the standard curve for Paracetamol are listed in Table 5.1.

Analysis of the data yielded th following:

M (Slope) = 0.013

C (Intercept on y-axis) = 0

Such that the equation of the straight line (Y = MX + C) is

y = 0.013X + 0 or Y = 0.013X

The correlation coefficient (r^2) was 0.9355.

The percentage drug released per unit time was calculated using the formula:

$M_t/M_0 \times 100$……3.2

Where

M_0 = Amount of Drug

M_t = Amount of Drug released at time t.

M_t = Concentration of drug × Dissolution factor × Volume of diluent

The standard calibration curve of Paracetamol gave a straight line curve which confirms that Beer - Lambert's law was obeyed within the concentration range used. The law states that the intensity of beam of parallel monochromatic radiation decreases exponentially as it passes through a medium of homogeneous thickness.

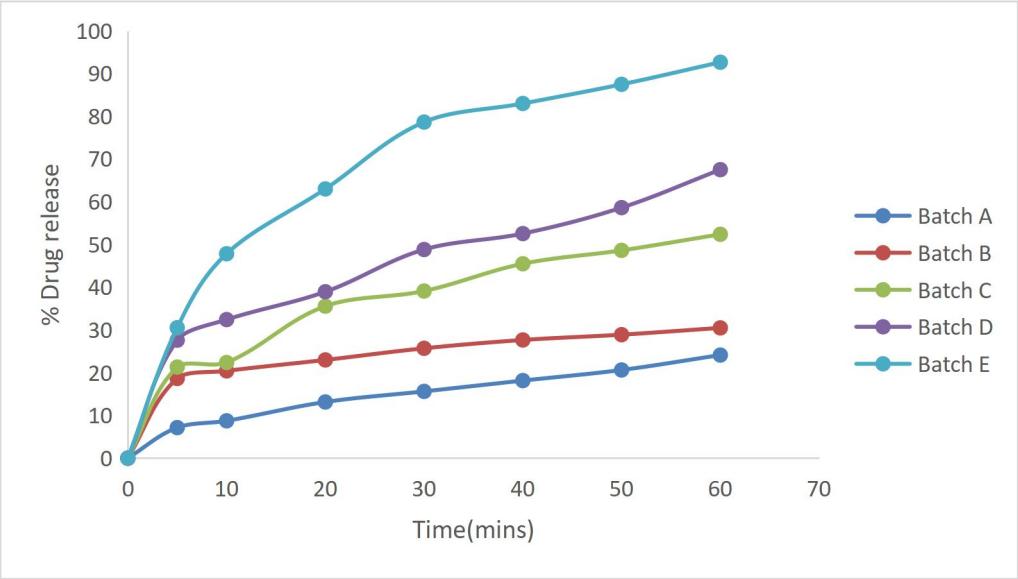

Figure 3.2: Dissolution profile of the different batches of paracetamol tablets prepared using the co-processed excipient.

3.2 Discussion

The novel co-processed excipient, comprising potato starch, modified cellulose gum, and hydroxypropyl methyl cellulose (HPMC), exhibited favorable flow properties. The Carr's index and Hausner ratio suggest good flowability, essential for uniform die filling and efficient tablet compression. Additionally, the low moisture content indicates minimal hygroscopicity, contributing to enhanced powder stability.

While these findings confirm acceptable flowability, further assessment of parameters such as angle of repose, swelling index, and hydration capacity could provide deeper insights into its functional performance. Nonetheless, its favorable Carr's index and Hausner ratio indicate efficient packing and compressibility, crucial for successful formulation.

In contrast, the powder mix containing the active pharmaceutical ingredient (API) exhibited significantly poorer flow properties. The high Carr's index and Hausner ratio indicate strong inter-particle cohesion, which could lead to challenges in tablet weight uniformity and compression efficiency. This disparity underscores the novel excipient's potential in improving powder handling and processing efficiency, essential for achieving consistent tablet properties.

Tablets formulated with the novel co-processed excipient demonstrated consistent weight and dimensions, meeting pharmacopeial standards for uniformity. Hardness values were within acceptable limits, balancing mechanical strength and friability to ensure stability during handling and storage.

Although friability values slightly exceeded pharmacopeial limits, formulation optimization could enhance tablet durability. Disintegration times varied, with certain batches exhibiting faster breakdown rates, likely due to the excipient's water uptake and swelling behavior. These findings suggest the excipient may possess superdisintegrant-like properties, improving

tablet disintegration and drug dissolution.

The dissolution profiles revealed batch-dependent variations, with the most favorable release rates observed in formulations demonstrating optimized excipient-API interactions. Differences in dissolution behavior may be attributed to excipient functionality, tablet porosity, and compression forces. The superior dissolution profile of select batches suggests enhanced drug wettability and solubility, while lower release rates in other batches indicate potential formulation inefficiencies requiring further optimization.

The findings of this study align with previous research on co-processed excipients, particularly regarding their impact on tablet flowability, compressibility, disintegration, and mechanical strength. For instance, Vodáčková et al. 2018 compared various co-processed excipients, highlighting their distinct physical and mechanical properties. Our results corroborate their observations, emphasizing that different co-processed excipients offer varying performance benefits. Similarly, Bowles et al. 2018 identified superior co-processed excipients for dispersible tablet formulations, reinforcing this study findings that co-processed excipients enhance functionality and mitigate traditional excipient limitations.

Mužíková et al. 2019 demonstrated the advantages of co-processed excipients over physical mixtures, particularly in terms of mechanical integrity and reduced lubricant sensitivity, findings that align with this study. IO and AO 2022 also reported improvements in flow properties and compatibility with co-processed excipients, supporting the observations of this study on enhanced performance in direct compression formulations.

Further research, such as Drašković et al. 2018, highlighted the critical role of co-processed excipients in ensuring adequate tablet ability and compatibility, aligning with our findings on improved mechanical resistance. Similarly, Borkhataria et al. 2019; Kothawade et al. 2019 demonstrated the benefits of precision-engineered excipients in improving compressibility, flowability, disintegration, and drug release, reinforcing the advantages observed in this study.

CHAPTER FOUR

CONCLUSION, LIMITATIONS AND IMPLICATION

3.2 Conclusion

This study successfully developed and characterized a co-processed excipient composed of potato starch, modified cellulose gum, and hydroxypropyl methyl cellulose (HPMC). The excipient demonstrated favorable flow properties, as indicated by its low Carr's index and Hausner ratio, which are crucial for efficient tablet compression and uniform die filling. Additionally, its low moisture content suggests minimal hygroscopicity, enhancing the powder's stability during handling and storage. When incorporated into tablet formulations, the co- processed excipient helped achieve consistent tablet weight, dimensions, and hardness values, all within pharmacopeial standards.

The excipient's potential to enhance tablet disintegration and dissolution was also observed through the different batches of tablets by direct compression using varying concentrations of the co-processed excipient, particularly in formulations where optimized excipient-API interactions were achieved. The study's results confirm that co-processed excipients can improve tablet functionality by addressing the flow, compressibility, and dissolution issues commonly encountered with traditional excipients. This aligns with previous research on co-processed excipients, demonstrating their ability to mitigate the limitations of individual excipients while enhancing the overall performance of pharmaceutical formulations.

3.3 Limitations

While the study demonstrated promising results, there are certain limitations that should be considered. One major limitation is the variability in dissolution profiles across different tablet batches. This batch-to-batch variation indicates that while some formulations exhibited enhanced dissolution, others did not perform as well. The discrepancy in dissolution rates

could be attributed to differences in excipient functionality, tablet porosity, and compression forces. Further optimization of the formulation parameters is required to ensure consistent dissolution behavior across all batches.

Another limitation is the slightly elevated friability values in some tablet formulations, which exceeded pharmacopeial limits. This suggests that while the novel excipient contributed to the overall mechanical strength of the tablets, further optimization in terms of excipient concentrations and compression parameters may be necessary to improve tablet durability.

Additionally, the study did not explore the long-term stability of the formulated tablets or the potential impact of storage conditions on tablet performance. Stability studies, particularly under accelerated conditions, would provide valuable insights into the shelf-life and real-world performance of the tablets containing the novel co-processed excipient.

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