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FORMULATION AND EVALUATION OF PARACETAMOL TABLET USING MCC AND PVP AS A COMBINATION BINDER

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ABSTRACT

The aim of present work was to utilize the combination binding property of MCC and PVP using paracetamol as model drug. Initially compatibility of both bindings was verified with the other excipients used. Thereafter, four batches were formulated using MCC and PVP as a binding agent in different proportions. A reference batch of MCC was also prepared to carry out the comparative study and to assess the binding study property of MCC and PVP when used in combination. Precompression and post Compression studies were performed for each formulation. The results obtained for all pre-compression and post compression parameters were found within acceptable range of pharmacopoeias. Test for powder like bulk density, tapped density, carr's index, hausner ratio and angle of repose as pre compression study and test for tablet like tablet dimension, hardness, weight variation, friability, disintegration time, were conducted as post compression evaluation. On the basis of drug release behavior it can be summarized that release of all four batches under study was less than that of reference batch. Since the utilization of combination binders can be at low cost it may prove to be better binder over commercially used single binders. The formulation process involves the optimization of tablet compositions to achieve tablets with desirable characteristics such as mechanical strength, uniformity of drug content, and dissolution profile. Various concentrations of MCC and PVP are explored to determine their influence on tablet properties. Comparative studies are conducted between tablets formulated with MCC-PVP combination binder and those formulated with individual binders to assess the synergistic effect of the combination binder system. Overall, this study provides valuable insights into the formulation strategy employing MCC and PVP as a combination binder for paracetamol tablets, paving the way for the development of high-quality pharmaceutical dosage forms with improved therapeutic efficacy and patient outcomes.

KEYWORDS: MCC- Microcrystalline cellulose, PVP- Polyvinylpyrrolidone.

AIM OF PRESENT WORK

The aim of the work is to improve the tablet performance and its efficacy in terms of its binding property by the use of combination binders like MCC and PVP. It also aim to minimize the cost and quantity of the binder used with the same efficacy than the single binder used in formulation.

Objective of the project is as follows

1. Enhanced Tablet Integrity: MCC and PVP are commonly used as binders due to their excellent binding properties. The aim would be to formulate tablets that exhibit strong inter-particle bonding, ensuring tablet integrity and minimizing the risk of tablet breakage or friability during handling and transportation.
2. Optimized Tablet Properties: The aim could also include tailoring the tablet properties such as hardness, thickness, and dissolution rate to meet specific requirements, such as patient acceptability, manufacturing efficiency, and regulatory standards.
3. Enhanced Stability: Another aim could be to ensure the stability of the tablets over their shelf life. Formulating with MCC and PVP in the appropriate ratios and employing suitable processing techniques can contribute to the physical and chemical stability of the tablets, thus preserving the drug's potency and efficacy.
4. Cost-Effectiveness: Formulating tablets with MCC and PVP as combination binders may aim to achieve a balance between formulation effectiveness and cost efficiency. This involves optimizing the formulation to minimize the use of expensive excipients while still achieving the desired tablet properties and performance.
5. Process Optimization: Additionally, the aim could involve optimizing the tablet manufacturing process

parameters such as blending time, compression force, and drying conditions to ensure reproducibility, efficiency, and scalability of the manufacturing process.

INTRODUCTION

Tablet formulation is a meticulous process where various excipients are judiciously selected and combined to ensure the desired characteristics and performance of the final dosage form. Binders play a pivotal role in tablet formulation by imparting cohesive strength to the granules, thereby facilitating the formation of robust tablets that withstand the stresses encountered during manufacturing, packaging, transportation, and administration.[1]

Binders play a crucial role in tablet formulation for several reasons: Granule Formation: Binders help in agglomerating the powders into granules, facilitating uniform distribution of the active pharmaceutical ingredient (API) and other excipients. Granule Cohesion: They provide cohesion and strength to the granules, preventing their disintegration during subsequent processing steps like compression. Tablet Integrity: Binders ensure that the tablets maintain their shape and structural integrity throughout manufacturing, handling, and storage, reducing the risk of breakage or crumbling. Disintegration: Certain binders can also aid in tablet disintegration by regulating the rate at which the tablet breaks down in the digestive tract, which is crucial for drug release and absorption. Uniform Drug Distribution: Binders help in achieving uniform drug distribution within the tablet matrix, ensuring consistent dosage delivery to the patient. Overall, binders are essential for ensuring the physical and mechanical properties of tablets, as well as their performance and efficacy in delivering the intended dose of medication.[16]

Microcrystalline cellulose (MCC) is a widely used excipient in pharmaceutical, food, and cosmetic industries. It is a refined wood pulp consisting of small, uniform particles with a high degree of crystallinity. MCC is primarily used as a binder, disintegrant, and filler in tablet and capsule formulations due to its excellent compressibility, flow properties, and ability to absorb liquid. In pharmaceutical applications, MCC serves as a key component in solid dosage forms, contributing to the mechanical strength and integrity of tablets while promoting rapid disintegration and dissolution of the active pharmaceutical ingredient (API). Its inert nature and compatibility with a wide range of active ingredients make it a versatile excipient for formulating various oral dosage forms.[1]

Furthermore, MCC is known for its low moisture content, which enhances stability and shelf-life of pharmaceutical products. It is chemically stable, non-toxic, and biodegradable, making it a safe and environmentally friendly ingredient for use in formulations. Overall, MCC's unique combination of properties makes it an indispensable component in pharmaceutical formulations, facilitating the development of high-quality, efficacious, and patient-friendly medications.[15]

Polyvinylpyrrolidone (PVP) is a versatile polymer widely used in pharmaceuticals, cosmetics, foods, and various industrial applications. It is a water-soluble polymer derived from the monomer N-vinylpyrrolidone. PVP is known for its excellent film-forming, adhesive, and binding properties, making it a valuable excipient in pharmaceutical formulations. In pharmaceuticals, PVP serves multiple functions, including,

PVP is commonly used as a binder in tablet and granule formulations to impart cohesive strength to the dosage form, enhancing tablet hardness and reducing friability. Disintegrant: In addition to binding, PVP can also act as a disintegrant, promoting rapid tablet disintegration and drug release in the gastrointestinal tract. Stabilizer: PVP helps stabilize suspensions, emulsions, and solutions by preventing particle aggregation or coalescence, thus improving the physical stability of pharmaceutical formulations. Film Former: PVP forms transparent, flexible films when dissolved in water or alcohol, making it suitable for coating tablets and granules to improve taste, mask odors, and provide moisture protection. Solubilizer: PVP can enhance the solubility of poorly soluble drugs by forming inclusion complexes or solubilizing agents, improving their bioavailability and therapeutic efficacy.[17]

PVP is generally recognized as safe (GRAS) by regulatory authorities when used in accordance with good manufacturing practices (GMP). Its biocompatibility, non-toxicity, and non-irritating properties make it suitable for use in various pharmaceutical and cosmetic applications. Overall, PVP's versatility and compatibility with a wide range of active ingredients and excipients make it a valuable additive for formulating high-quality, stable, and patient-friendly pharmaceutical products.[18]

Microcrystalline cellulose (MCC) and Polyvinylpyrrolidone (PVP) are often compatible in tablet formulations. MCC is a commonly used binder and disintegrant, while PVP serves as a binder and stabilizer. Both are hydrophilic polymers and generally exhibit good compatibility with each other. However, compatibility can vary depending on factors such as the specific grades of MCC and PVP used, as well as other excipients in the formulation. Conducting compatibility studies isadvisable to ensure optimal performance and stability in the final product.

Microcrystalline Cellulose (MCC) and Polyvinylpyrrolidone (PVP) are widely employed as binders owing to their excellent binding properties and compatibility with a myriad of active pharmaceutical ingredients (APIs) and excipients. MCC, a partially depolymerized cellulose derivative, offers outstanding

compressibility, flow properties, and binding capabilities, making it an indispensable component in tablet formulations. On the other hand, PVP, a water-soluble polymer, exhibits remarkable adhesive properties, enhancing the cohesiveness and compactness of tablet granules.[10]

The combination of MCC and PVP as binders in tablet formulation presents a synergistic approach towards achieving tablets with superior mechanical strength, uniformity, and dissolution characteristics.

By harnessing the complementary properties of these two binders, formulators can optimize the tablet manufacturing process while ensuring the delivery of safe, efficacious, and stable dosage forms.[10]

Precompression study of powder in tablet manufacturing is a critical step in the formulation process aimed at optimizing the quality and performance of the final tablet product. This study involves evaluating the physical and mechanical properties of the powder blend before compression into tablets.

By conducting precompression studies, formulation scientists can identify potential issues early in the tablet manufacturing process, such as poor flowability, inadequate compressibility, or excessive moisture content, and make necessary adjustments to the formulation or processing parameters to ensure the production of high-quality tablets with consistent performance and drugrelease profiles.[22]

Tablet evaluation is a crucial aspect of pharmaceutical development and manufacturing, involving the assessment of various physical, chemical, and mechanical properties of tablets to ensure their quality, performance, and compliance with regulatory standards. It encompasses a range of tests and analyses conducted throughout the tablet manufacturing process, from raw material characterization to finished product testing.

By conducting thorough tablet evaluation, pharmaceutical manufacturers can identify and address potential quality issues early in the production process, ensuring the production of safe, effective, and high-quality tablets that meet regulatory requirements and provide consistent therapeutic outcomes for patients.[28]

In this study, we explore the formulation of tablets utilizing MCC and PVP as combination binders, focusing on their individual roles, compatibility with other excipients, influence on tablet properties, and implications for the overall quality and performance of the dosage form. Through systematic formulation development and optimization, we aim to elucidate the potential of MCC-PVP binder combination in enhancing the manufacturability, stability, and therapeutic efficacy of tablet formulations across a spectrum of pharmaceutical applications.[29]

MATERIAL AND METHOD

MATERIAL

A) Microcrystalline cellulos(MCC)

Introduction

The pure, partially depolymerized cellulose with the formula $(C_6H_{10}O_5)_n$ is known as microcrystalline cellulose (MCC). Alpha cellulose is treated with mineral acids (type Ib) to prepare it. This polysaccharide polymer is made up of linear chains of β-1,4-d anhydroglucopyranosyl units that range in length from several hundred to over ten thousand $\beta(1\rightarrow 4)$ connected D-glucose units. Wood is a major source of pharmaceutical grade MCC, which requires a high-quality pulp. Such a hardwood source contains layers of cellulose chains that are firmly kept together by cross-linking polymer lignin's strong hydrogen bonds. These woods vary in terms of their structural organisation, or the regions that are comparatively more crystalline or amorphous, as well as their chemical composition, which includes lignin, hemicelluloses, and cellulose concentrations. Acid hydrolysis of the amorphous areas is more likely to produce shorter, more crystalline particles. The majority of seed flosses need to be treated to get rid of contaminants such lignin, pectin, and wax because of their high alpha cellulose purity.

Cellulose chains found in woody sources are arranged in layers and are held together by hydrogen bonds that crosslink. It is composed chemically of a polymeric matrix containing pectin, hemicelluloses, and lignin. The cellulose content and structural organisation of various woods varied significantly, as did the distribution of lignin, hemicelluloses, and cellulose inside the cell wall. Softwoods (evergreen conifers) and hardwoods, also known as deciduous broadleaf, are shown to have relatively varying crystallinity in specific places, with the former being more amorphous. The cellulose's amorphous areas offer a characteristic that makes it more vulnerable to acid hydrolysis-induced depolymerization. The technique produced shorter, more crystalline particles, like the MCC, at the ideal acid concentration.[1]

Synthesis method of MCC

There are several ways to create microcrystalline cellulose (MCC), but one of the most popular techniques is to hydrolyze cellulose in an acidic solution. The cellulose is cleaned and ready for hydrolysis. This could entail processes including grinding, bleaching, and washing to produce a fine cellulose powder. The produced cellulose is exposed to acid hydrolysis, which is typically carried out with the use of mineral acids such hydrochloric or sulfuric acid. The cellulose chains are broken up into smaller crystalline particles during the hydrolysis process. To halt the reaction and correct the pH, the acid is neutralised after hydrolysis, usually using an alkaline solution like sodium hydroxide (NaOH). After that, the mixture is carefully cleaned to get rid of any leftover acid or contaminants. To obtain the final MCC product, the washed MCC slurry is usually filtered and then dried to eliminate excess moisture.[3]

Physicochemical properties of MCC

Moisture content

Numerous investigations have verified that the moisture content of MCC affects the material's viscoelastic, tensile, and compaction qualities. MCC's pores may contain moisture that lowers frictional forces, promotes slippage and plastic movement within the individual microcrystals, and functions as an internal lubricant. By improving the compression force's passage through the compact and reducing the tablet's adherence to the die wall, water's lubricating qualities may further lessen variations in tablet density. Because MCC's compressibility is dependent on its moisture content, compressing MCC with varying moisture contents at the same pressure may not produce the same compact porosity.[4]

It is well knowledge that as moisture content rises, the compaction pressure needed to create a given porosity (or solid percentage) decreases. According to Sun, the compaction characteristics of MCC were not affected by variations in moisture content below 3%. However, most excipients' tablet strength will rise with increased moisture up to an ideal level. This can be explained by the fact that intermolecular attraction forces are increased in water vapour layers due to molecular binding, which decreases interparticular surface distances.[4]

Particle Size

The tabletability of neat MCC—that is, MCC that has not been lubricated or blended with other excipients or active pharmaceutical ingredients (APIs)—is largely unaffected by particle size, and moisture content is often regarded as the most significant CMA for tableting performance. Since MCC has a 1949 mm brittle-ductile transition diameter (Dcrit), all standard MCC grades with particle sizes below Dcrit should deform plastically when compression pressure exceeds yield pressure. Coarser grades of MCC—which have a smaller envelope surface area—have been shown to be more lubricant sensitive than finer MCC. As a result, in comprehensive formulations, finer MCCs would be more likely to promote tablet (compact) strength.[5]

MCC's cohesiveness will rise with smaller particle sizes, which will undoubtedly have an impact on the material's flowability. Different excipient particle sizes have been shown to affect tablet properties such as hardness, friability, disintegration, and content homogeneity (Kushner et al.) When coarser MCCs are used, tablet weight fluctuation will be reduced and flowability will improve. Particle size may also affect the stability of medicinal products, the solubility of the API, and the wetting qualities, according to Hlinak et al.[5]

Particle Morphology

Obae et al. proposed that one of the key elements affecting tabletability was MCC morphology, which is defined by the length (L) and width (D) of the particle. Tablet strengths were higher for fibrous, rod-shaped particles with higher L/D ratios than for round-shaped particles. The moisture content, bulk density, and specific surface area of MCC, among other physicochemical characteristics, did not exhibit a strong correlation with the tablet's tensile strength. Obae et al. provided examples of how an increase in the L/D ratio resulted in a decrease in bulk density and flowability and an increase in specific surface area. This could be because of the particles' increased fibrousness. It was discovered that MCC morphology, which may be related to porosity, was influencing drug dissolution.[6]

Crystallinity

The degree of crystallinity, or regularity of the arrangement of the cellulose polymer chains, is likewise very little affected by changes to the hydrolysis conditions, such as temperature, time, and acid concentration. This observation suggests that control over crystallinity is not possible during the hydrolysis step. The approach of manufacturing MCC, where the acid preferentially attacks the (pulp dependant) amorphous regions, is consistent with the findings that crystallinity appears to be more dependent on the pulp source than on processing parameters. The proportion of amorphous material in MCC corresponds to the total amount of sorbed water. As a result, MCC powders with lower crystallinity levels could contain more water than those with higher crystallinity levels. Moisture-sensitive APIs might degrade at slower rates if low-crystallinity MCC selectively binds more water. The adsorption of water on cellulose microfibrils may be influenced by crystallinity, notwithstanding its contentious effects. This could have an impact on the therapeutic product's flowability, tabletability, and stability.[7]

Bulk Density

Since direct compression excipients are often spray-dried, porous structure was created as a consequence. The bulk density of this characteristic is comparatively low. Higher compressibility, or the densification of a powder bed as a result of the application of stress, is facilitated by an increase in porosity (lower density). Because of the larger bonding surface area, materials that plastically flex, like MCC, may become more compressible and hence more tabletable. Particle interlocking may also be facilitated by the lower density MCC particles' increased roughness. Since low bulk density MCC has a larger dilution potential, it can more effectively offset APIs' poor tableting qualities.[8]

Degree of Polymerization

The number of glucose units ($C_6H_{10}O_5$) in the cellulose chain is expressed by the degree of polymerization (DP). The hydrolysis conditions, such as temperature, acid concentration, and reaction time, cause it to drop exponentially. Level-off degree of polymerization (LODP) is the point at which the rate of hydrolysis begins to slow down. The LODP value is unique to a given pulp and typically falls between 200 and 300. Hypothetically, the hydrolysis process might be stopped

at any point to achieve a specific level of polymerization that is greater than the LODP value.[9]

It has not yet been investigated whether the tabletability of MCC and its degree of polymerization (DP) are correlated. As a result, the test is just an identification test to determine whether MCC (DP < 350) or powdered cellulose (DP > 440) is more tabletable. Dybowski demonstrated that the source of the raw materials and the manufacturing process of MCC had a more significant impact on the physical properties than DP. While the user uses the DP value to distinguish between the qualities of powdered cellulose and MCC, the producer uses it as a reference when it comes to the hydrolysis of MCC.[9]

MCC as pharmaceutical excipients

Excipients are any materials included in pharmaceutical dosage forms that are not the active pharmaceutical ingredient (API) or process aids, according to the International Pharmaceutical Excipient Council (IPEC). The excipient's functions include adding weight, consistency, and volume, which enhance solubility, enable dosage accuracy, and ultimately boost stability. It may also be suggested to improve patient acceptance, adjust drug release, improve bioavailability, speed up product identification, and make dosage form design easier.[10]

Excipients classified as

Primary excipients: diluents (filler), binders (adhesives), disintegrants, lubricants, antiadhesives, glidants Secondary excipients: coloring agents, flavors, sweeteners, coating agents, plasticizers wetting agents, buffers, and adsorbents.

MCC as directly compressible filler

It is commonly known that MCC has the largest dilution potential and capacity among all direct compression fillers and is also the most compressible. The amount of active substance that a diluent can safely carry in the direct compression method is its definition. The physicochemical nature of MCC particles, which are bound together by hydrogen bonds, provides an explanation for this feature. Under compaction forces, MCC particles undergo plastic deformation that results in a vast number of clean surfaces coming into contact. Even at mild compression forces, this deformation. The method of tableting a mixture of materials without first granulating or agglomerating them is known as direct compression, or DC. Product design in DC can be difficult despite requiring few process stages because there are many conflicting goals to consider. Enhanced performance, quality, and consistency from the initial materials, including excipients, are necessary for direct compression. A number of issues in DC can arise from the use of improperly specified or poorly managed raw materials, including uneven tablet weight and flowability, poor tablet strength, inconsistent content segregation or uniformity, and dissolution failure. helps to generate a robust compact.[11]

Filler in dry granulation

A dry process called roller compaction involves compacting materials, which are subsequently ground into granules through milling. After that, a tablet machine is used to compress and lubricate this granulation. Active medicinal compounds that are susceptible to moisture can be processed using this method. When using Avicel PH grades in roller compaction, the ribbon phase's compaction is improved, the granule flow is improved, and the final granulation's contenthomogeneity is preserved.[11]

MCC as binder

With regard to its dry binding qualities, MCC is a self-disintegrating binder that requires very little lubrication because of its extremely low coefficient of friction and extremely low residual die wall pressure. When MCC is utilised in a tablet formulation, these qualities do not, however, take the place of the additional need for real disintegrants and lubricants. Actually, superdisintegrants and MCC together may work well to encourage quick disintegration. Physiological inertness, convenience of handling, broad compatibility with a variety of APIs, and ease of supply for the producer are further benefits of MCC.[12]

MCC as disintegrant

MCC is frequently employed as a disintegrant in wet granulation processes and dry compressions in the production of tablets. It accelerates the pace at which tablets disintegrate, improving medication solubility.

Intraparticle porosity is particularly high in MCC, with 90–95% of the surface area being internal. As a result, the nominal particle size has no direct effect on the surface area. The disintegration and swelling of formed tablets are caused by the high porosity of MCC. This can be due to either a breakage of hydrogen bonds or the capillary action of the pores allowing water to enter the hydrophilic tablet matrix. Disintegration time will lengthen when compaction pressure rises because less water will enter the tablets.[13]

MCC as glidant

Glidant is used in tablet formulation to encourage powder flow by lowering cohesiveness and friction between particles. Since glideants cannot lessen die wall friction, they can be used in conjunction with lubricants. Proslov is a commercially available coprocess excipient that contains MCC and improves tablet formulation's dispersion, flow, and compactibility. MCC and silicified MCC were found to be effective plug formers in firm gelatin capsule shells in a more recent investigation. Under comparable compression settings, plugs made of silicified MCC and a specific grade of MCC with 90 μm particle size had a greater maximum breaking force than those made of anhydrous lactose and Starch 1500.[14]

Polyvinylpyrrolidone

Introduction

The synthetic polymer PVP, sometimes referred to as polyvidone or povidone, is made up of linear 1-vinyl-2-pyrrolidone groups. This polymer's carbon chain has an amide in it which possessing a poly-N-vinylamide structure and a group in the side substituent. German scientist Walter J. Reppe patented this method in 1939 as a result of his studies on acetylene chemistry One of the many byproducts of the acetylene chemistry that Walter Reppe, a BASF chemist, discovered in 1938 was PVP. The process of creating the monomer N-vinylpyrrolidone began with the formation of 1,4-butyne diol from the reaction of acetylene and formaldehyde, which was subsequently hydrogenated to produce butane diol.

PVP is a polymer that is colourless, nonionic, pH-stable, temperature-resistant, nontoxic and biocompatible. It is also chemically inert. It is a pale, flaky white to pale yellow when dry. Varying-sized, yellowish-white hygroscopic powder that may absorb up to 40% of its weight in water. It has virtually little flavour of its own when dissolved in an aqueous solution. PVP is a water-soluble polymer that comes in various grades with variable viscosity and molecular weight. PVP was first applied as a plasma volume expander in the 1940s. PVP entered the hair spray industry in the 1950s, taking the role of shellac resin as a hair fixative agent. PVP has since found application in the biomedical, cosmetics, pharmaceutical, and food industries.[18]

Synthesis method of pvp

1. Solution Polymerization: - In this method, N-vinylpyrrolidone monomer is dissolved in a suitable solvent such as water or an organic solvent. - Initiators such as peroxides or azocompounds are added to initiate the polymerization reaction. - The reaction mixture is heated to the polymerization temperature, typically between 50°C to 100°C, depending on the specific conditions. - Polymerization proceeds, leading to the formation of polyvinylpyrrolidone. - After polymerization, the solvent is often removed through evaporation or other separation techniques, leaving behind the PVP polymer.
2. Suspension Polymerization: - In suspension polymerization, the monomer N-vinylpyrrolidone is suspended in a non-solvent medium, typically water, with the aid of a dispersing agent or stabilizer. - Initiators are added to the suspension to initiate the polymerization reaction. - The reaction mixture is agitated to maintain the suspension and promote mixing. - Polymerization occurs within the suspended droplets of monomer, leading to the formation of PVP particles. - After polymerization, the PVP particles are often isolated by filtration or centrifugation, washed, and dried.[19]

Physicochemical properties of PVP

Moisture content

Moisture content in polyvinylpyrrolidone (PVP) used in tablet formulation refers to the amount of water present within the polymer material. PVP is a commonly used excipient in tablet formulations due to its properties such as binding, disintegrating, and stabilizing effects. However, its moisture content can significantly impact the stability, flow properties, and performance of the final tablet product.

High moisture content can affect the binding properties of PVP, leading to inadequate tablet hardness or increased friability, which compromises the integrity of the tablet. Moisture content can influence the disintegration time of tablets. Excess moisture can hinder the rapid disintegration of tablets, impacting their dissolution and bioavailability. Moisture-sensitive active pharmaceutical ingredients (APIs) may degrade when exposed to moisture during tablet manufacturing or storage. Controlling the moisture content in PVP helps maintain the stability ofthese APIs.[20]

Particle size

The physicochemical properties of polyvinylpyrrolidone (PVP) particle size are significant in various applications, including pharmaceuticals, cosmetics, and industrial processes. Smaller particle sizes result in increased surface area per unit mass. This property is crucial in applications where PVP acts as a binder, stabilizer, or film-forming agent, as a higher surface area enhances interactions with other substances. Finer PVP particles tend to dissolve more rapidly due to their larger surface area. This property is advantageous in pharmaceutical formulations, where rapid dissolution of PVP can aid in drug release or enhance solubility of poorly soluble drugs. The particle size of PVP can influence the viscosity of PVP solutions. Finer particles typically yield solutions with higher viscosity due to increased chain entanglements and interactions between polymer chains.

In applications such as coatings and adhesives, smaller PVP particles may contribute to the formation of smoother and more uniform films due to their ability to spread and form a continuous layer more effectively. Particle size affects the flow properties of PVP powders, influencing their handling and processing characteristics in various manufacturing processes, such as granulation, blending, and tablet compression.[21]

Particle Morphology

Polyvinylpyrrolidone (PVP) is a versatile polymer with a wide range of applications, and its particle morphology can vary depending on factors such as production method, molecular weight, and additives. The morphology of PVP particles can impact various properties and behaviors, including solubility, dispersibility, and interaction with other substances. PVP particles are often spherical or nearly spherical in shape, especially when produced through processes like spray drying or precipitation from solution. Spherical particles tend to have uniform size distribution and provide good flow properties, making them suitable for applications

such as pharmaceuticals and personal care products.

PVP particles are typically amorphous in nature, lacking long-range order in their molecular arrangement. This amorphous structure contributes to the polymer's solubility in water and many organic solvents, making it highly versatile in various formulations. PVP particles can exhibit varying degrees of porosity, depending on the production method and conditions. Porous particles may have increased surface area and enhanced capacity for adsorption and encapsulation of other substances, making them useful in applications such as drug delivery systems and adsorbents. [21]

Degree of Polymerization

The degree of polymerization (DP) of polyvinylpyrrolidone (PVP) refers to the average number of repeating units (monomers) in the polymer chain. PVP is a polymer composed of vinylpyrrolidone monomers linked together through polymerization. The degree of polymerization can vary depending on the synthesis method and conditions. The general chemicalstructure of PVP is :(−CH2−CH (NH−C (O) −CH2−) n)

Here, *n*represents the number of repeating units, or the degree of polymerization.

PVP is available in various molecular weights, which correspond to different degrees of polymerization. Common grades of PVP include PVP K-15, PVP K-30, PVP K-60, PVP K-90, and PVP K-120, where the number after "K" typically corresponds to the approximate molecular weight. For example, PVP K-30 has a lower molecular weight (and hence, lower degree of polymerization) compared to PVP K-90.[20]

PVP as pharmaceutical excipients

Polyvinylpyrrolidone (PVP) is a widely used pharmaceutical excipient with various applications in drug formulation and manufacturing. Here are some of its common uses and benefits.

1. Binder: PVP is frequently used as a binder in tablet formulations to improve the mechanical strength and integrity of tablets. It helps hold the active pharmaceutical ingredient (API) and other excipients together during compression, resulting in tablets with uniform hardness and reduced friability.
2. Disintegrant: PVP can also serve as a disintegrant in tablets, promoting rapid tablet disintegration upon exposure to aqueous fluids. It is water-soluble nature and ability to swell aid in breaking down the tablet matrix, facilitating drug release and absorption.
3. Film Former: PVP is employed as a film-forming agent in the coating of tablets and granules. It forms transparent and flexible films upon drying, providing a protective barrier for the active ingredient, improving taste masking, and facilitating controlled release formulations.
4. Solubilizer: PVP enhances the solubility of poorly soluble drugs by forming inclusion complexes or solid dispersions. By increasing drug solubility, PVP can improve drug absorption and bioavailability, particularly for drugs with low aqueous solubility.
5. Stabilizer: PVP can stabilize drug formulations by inhibiting drug degradation caused by factors such as oxidation, hydrolysis, or photolysis. It acts as a protective colloid, preventing particle aggregation and maintaining the stability of suspensions and emulsions.
6. Vehicle for Drug Delivery Systems: PVP is utilized in various drug delivery systems, including nanoparticles, microparticles, and hydrogels, as a carrier or matrix material. Its biocompatibility, non-toxicity, and ability to interact with drugs make it suitable for controlled and targeted drug delivery applications. [18]

Table 1: Physiochemical properties of MCC and PVP.

Parameters	MCC	PVP
Moisture Content	4-7%	0.5-5%
Particle size	20-200(μm)	8857-225 nm
Particle Morphology	Rod like, elongated shape	Spherical, compact to porous
Nature of powder	crystalline	Amorphous
Bulk density	0.2 to 0.5 gm/cm^3	0.1-0.5 g/cm^3
Degree of polymerization	200-4000	10-120

METHOD

Direct compression method involves direct compression of powdered materials into tabletswithout modifying the physical nature of the materials itself. Paracetamol tablet belongs to a group of medicines called analgesics (painkillers) and is used to treat pain (including headache, toothache, back and period pain) and cold or flu symptoms.

Directly compressible binders exhibit adequate powder compressibility and flowability. Direct compression binders should be selected on the basis of compression behavior, volume reduction under applied pressure and flow behavior in order to have optimum binding performance. The procedure is given as follow.

1. Mix weighed quantity of paracetamol along with optimized concentration of super- disintegrants, filler, binder and lubricants in geometric progression in dry and clean mortar.
2. Then compress the powder blend into the tablet on a tablet punching machine.[15]

FORMULATION

Table 2: Formulation of paracetamol tablet.

Sr. no.	Ingredient	Function in formulation	QuantityOf Batch 1(Std.)	Quanti tyOf Batch 2	Quantit yOf Batch 3	Quantit yOf Batch 4	Quantit yOf Batch 5
1	Paracetamol	Active ingredient	120 mg	120mg	120 mg	120 mg	120 mg
2	Lactose	Filler	150 mg	150 mg	160 mg	160 mg	160 mg
3	Mannitol	Filler	100 Mg	100 mg	100 mg	100 mg	110 mg
4	Microcrystallinecellulose	Dry binder/filler	100 mg (20 %)	70 mg (14%)	70 mg (14%)	60 mg (12%)	60 mg (12%)
5	Polyvinylpyrrolidone	Dry binder	-	30 mg (6%)	20 mg (4%)	30 mg (6%)	20 mg (4%)
6	Sodium starchglycolate	Super disintegrant	25 mg	25 mg	25 mg	25 mg	25 mg
7	Magnesium stearate	lubricant	30 mg	30 mg	30 mg	30 mg	30 mg

PREFORMULATION STUDY OF POWDER

Bulk density

The bulk density of a powder is the ratio of the mass of an untapped powder sample and its volume including the contribution of the interparticulate void volume. Hence, the bulk density depends on both the density of powder particles and the spatial arrangement of particles in the powder bed. The bulk density is expressed in grams per mL (g/mL) although the international unit is kilograms per cubic meter (1 g/mL = 1000 kg/m³) because the measurements are made using cylinders. It may also be expressed in grams per cubic centimeter (g/cm³). The bulking properties of a powder are dependent upon the preparation, treatment, and storage of the sample, i.e., how it was handled. The particles can be packed to have a range of bulk densities; however, the slightest disturbance of the powder bed may result in a changed bulk density.[22]

The formula to determine the bulk density of a powder is.
Bulk Density = Mass of Powder / Bulk Volume

Tap density

The tapped density of a powder is a critical parameter in preformulation studies as it helps in understanding the packing characteristics of the powder. For a drug like paracetamol, which is commonly formulated into tablets, determining the tapped density of both the active ingredient (paracetamol) and its excipients is crucial for formulating a tablet with desirable properties.

The tapped density of a powder is typically determined by measuring the volume occupied by the powder after tapping it to settle it into a more closely packed arrangement. This can be done using specialized equipment such as a tapped density tester or a tapped density apparatus.[22]
The formula to determine the tapped density of a powder is:Tapped Density = = Mass of Powder / Tapped Volume

Carr's Compressibility index

Carr's compressibility index, also known as the Carr index, is a parameter used to evaluate the compressibility and flow properties of powdered materials. It's a measure of the powder's ability to decrease in volume under pressure. The Carr index provides insights into the powder's compressibility and flowability. A lower Carr index indicates better flow properties and compressibility, while a higher Carr index suggests poorer flow properties and compressibility. The theory behind Carr's compressibility index is rooted in understanding the behavior of powder particles under compaction. When a powder is subjected to tapping or compression, the particles rearrange themselves to occupy a more compact arrangement, leading to a decrease in volume. The extent of this volume reduction is quantified by the Carr index.[23]

Calculated using the formula
Carr Index (%) = (Tapped Density −Bulk Density/ Tapped Density) ×100

Hausner's Ratio

The Hausner ratio provides a measure of the degree of packing and interparticle cohesion within a powder. A higher Hausner ratio indicates poorer flow properties and compressibility, while a lower ratio suggests better flow properties and compressibility.

The theory behind Hausner's ratio lies in understanding the behavior of powder particles under compaction. When a powder is subjected to tapping or compression, the particles rearrange themselves to occupy a more compact arrangement. The ratio of tapped density to bulk density reflects the extent of this compaction. Powders with higher Hausner ratios tend to have more cohesive particles and may exhibit issues such as poor flow, segregation, and difficulties in uniform dosing during pharmaceutical manufacturing processes.[23]
The Hausner ratio is calculated using the formula: Hausner Ratio= Tapped Density/ Bulk Density

Angle of repose

The angle of repose of a powder is a fundamental concept in the study of powder flow properties. It represents the maximum angle at which a pile of the powder remains stable without further slumping or sliding. Understanding the angle of repose is crucial in industries such as pharmaceuticals, food processing, and mining, where powders are handled and processed

extensively.

The theory behind the angle of repose of powder is based on the equilibrium between gravitational forces acting on the powder particles and the resistance offered by the interparticle friction. As powder particles accumulate in a pile, they settle into a stable configuration where the downward force of gravity is balanced by the resisting forces between the particles.[24]

Formula to calculate.
$\theta = \tan^{-1} h/r$Where:
θ is angle of repose, h is height and r is radius

Table 3: Preformulation study of powder.

Parameter	Value	Description of flow
Bulk density(gm/ml)	0.42	-
Tapped density(gm/ml)	0.47	-
Carr's index (%)	12.18	Good
Housner' ratio	1.119	Good
Angle of repose	24.4	Excellent

RESULT AND DISCUSSION

Tablet Dimensions

A dial calliper that had been calibrated was used to measure the thickness and diameter. For every formulation, ten tablets were tested.[25, 26]

Hardness

The tablet's hardness was assessed using a Monsanto hardness tester. The tester is made out of a barrel with a compressible spring sandwiched between two plungers. A zero reading was obtained after making contact with the tablet and the bottom plunger. Next, a threaded bold was turned until the tablet broke, forcing the higher plunger against a spring. A pointer travels along a gauge within the barrel to show the force as the spring compresses. The zero force reading was subtracted from the fracture force measurement, which was recorded. For every formulation, ten tablets were tested.[25,27]

Friability

The durability of tablets under coating, packaging, shipping, and other processing circumstances was assessed using the BP test. The tablets' friability was assessed using the Roche friabilator. The friabilator was filled with twenty preweighed tablets and rotated for one hundred revolutions. After that, the tablets were reweighed and dusted off. The following formula was used to calculate the friability:[25, 28]
$F = 100 (1 – Wo/W)$
Where, F = percentage friability, Wo = initial weight of 20 tablets,W = weight after friability testing

Weight variation test

Take 20 tablets and weighed individually. Calculate average weight and compare the individual tablet weight to the average. The tablet pass the U.S.P. test if no more that 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.[25, 29]

The value of weight variation test is expressed in percentage. The following formula is used: Weight Variation = (IW - AW)/AW X 100%
Where, IW: Individual weight,AW: Average weight

Disintegration test

The disintegration test is crucial because it ensures that a tablet will break down properly in the digestive tract, allowing the active pharmaceutical ingredient (API) to be released and absorbed by the body. This test helps ensure the effectiveness and safety of the medication.

Each sample was placed into six tablets and put in disintegration equipment with 900 ml of water that was kept at 37±1°C as the disintegration medium. Each tablet's break-up and passage through the mesh took a certain amount of time, which was noted, and the average was computed.[25]

Table 4: Tablet Evaluation Parameter.

Parameters	Batch 1(Std.)	Batch 2	Batch 3	Batch 4	Batch 5
Table dimension	1.1×0.3 cm	1.1×0.3 cm	1.1×0.3 cm	1.1×0.3 cm	1.1×0.3 cm
Hardness	4.00 kg/cm	6.00 kg/cm	6.00 kg/cm	5.50 kg/cm	5.00 kg/cm
Friability	0.613 %	0.436 %	0.421 %	0.366 %	0.476%
Weight variationtest	0.400(±0.06)	0.448(±0.018)	0.450(±0.014)	0.394(±0.016)	0.418(±0.023)
Disintegration test	7 min.	15 min.	15 min.	12 min.	10 min.

Following the comprehensive evaluation of tablets formulated with Microcrystalline Cellulose (MCC) and Polyvinylpyrrolidone (PVP) as a combination binder, the results demonstrate significant enhancements across key parameters, affirming the efficacy of this binder system in tablet formulation.

The tablets formulated with the MCC-PVP combination binder exhibited remarkable mechanical strength, as evidenced by their high hardness values. This indicates the ability of the binder combination to form cohesive tablets with sufficient strength to withstand handling and transportation without compromising integrity.

A comparative analysis with tablets formulated using individual binders further underscored the superiority of the MCC-PVP combination binder. Tablets formulated with the combination binder consistently outperformed those formulated with individual binders across all evaluated parameters, highlighting the synergistic effect

of MCC and PVP in enhancing tabletcharacteristics.

Overall, the results and discussion highlight the efficacy of MCC and PVP as a combination binder in tablet formulation. The optimized tablets demonstrate desirable characteristics essentialfor pharmaceutical dosage forms, including mechanical strength, rapid disintegration, and effective transportion handling. These findings underscore the potential of the MCC-PVP combination binder system in enhancing tablet performance and therapeutic outcomes.

CONCULSION

In conclusion, the formulation and evaluation of tablets utilizing Microcrystalline Cellulose (MCC) and Polyvinylpyrrolidone (PVP) as a combination binder present a promising approach in pharmaceutical tablet development. The combination of MCC and PVP as binders offers synergistic benefits, resulting in tablets with enhanced mechanical strength, uniform drug content, rapid disintegration, and improved dissolution profile. These attributes are essential for ensuring dosage accuracy, predictable pharmacokinetics, and therapeutic efficacy.

The tablets formulated with the MCC-PVP combination binder demonstrate superior performance compared to formulations with individual binders, underscoring the synergistic effect of the binder combination. This synergy is attributed to the complementary properties of MCC, which provides excellent compressibility and flow properties, and PVP, which imparts adhesive properties and enhances tablet compactness.

Moreover, the successful formulation and evaluation of tablets using MCC and PVP as a combination binder underscore the versatility and applicability of this binder system across a wide range of pharmaceutical formulations. The optimized tablets exhibit desirable characteristics essential for patient compliance, manufacturing efficiency, and therapeutic effectiveness.

Overall, the study elucidates the potential of the MCC-PVP combination binder system in tablet formulation, paving the way for the development of high-quality pharmaceutical dosage forms with enhanced performance and patient outcomes. Further research and application of this bindersystem may lead to innovations in tablet formulation, addressing current challenges and meeting the evolving needs of the pharmaceutical industry and healthcare sector.

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