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Pharmaceutical Powders: Properties, Evaluation, Manufacturing and Quality Control: Principles, Techniques and Applications

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Abstract

Pharmaceutical powders are solid dosage forms made of finely divided particles of one or more active ingredients, with or without excipients. They are used directly as medicines and also serve as the starting material for tablets, capsules, granules, solutions and suspensions. The quality of a powder depends largely on its physical and mechanical properties: particle size and size distribution, shape, density, porosity, moisture content, cohesiveness and flowability. These properties govern mixing, segregation, filling accuracy, stability and the uniformity of dose between batches. This article reviews the classification of pharmaceutical powders, their key properties, size reduction, mixing and segregation, and the common methods of evaluation, including particle-size analysis, bulk and tapped density, angle of repose, Carr's index and Hausner ratio. It then describes the preparation, packaging, storage and quality control of powders and their main applications. Oral Rehydration Salts (ORS) are used as a case study to show how these principles are applied in practice. The review concludes that no single test describes a powder adequately; a combination of controlled processing, suitable evaluation, protective packaging and systematic quality control is needed to deliver a safe and consistent product.

Keywords: pharmaceutical powders, particle size, flowability, segregation, Carr's index, Hausner ratio, quality control, oral rehydration salts

1. Introduction

Pharmaceutical powders are preparations in which one or more active pharmaceutical ingredients (APIs) are present in a finely divided state, with or without suitable excipients. They are among the oldest and simplest dosage forms and remain widely used, both as finished products and as intermediates in the manufacture of other dosage forms [4–6]. Their simple composition, ease of preparation and flexibility make them valuable in formulation and manufacturing.

The behaviour of a powder is controlled by its physical properties. Each particle has a size, a shape and a density; the bulk powder has a size distribution, a degree of porosity, a moisture content, a tendency to stick together and a capacity to flow. These characteristics affect every manufacturing step, including weighing, mixing, transfer, filling and packaging. Flow is particularly important. A powder that flows poorly causes uneven die or container filling, slows production lines and makes the final product less uniform [1,2,4,5].

Manufacture of powders generally involves size reduction, sieving, weighing, mixing and filling. Each operation must be controlled to obtain a uniform mixture and a consistent product. Differences in particle size, density or other characteristics between components can cause segregation during processing and handling, so an understanding of powder behaviour is essential for maintaining product quality [3–5].

Powders can be classified by method of administration, degree of subdivision, composition and intended use. Evaluation relies on a set of physical tests rather than one parameter, because powder behaviour is complex. Packaging and storage also matter, since moisture, temperature, air, light and contamination can all change a powder's properties during its shelf life [4–6].

This article reviews pharmaceutical powders in a systematic way: their definition and significance, classification, properties, size reduction, mixing and segregation, evaluation methods, manufacture, packaging, storage, quality control and applications. An ORS case study illustrates how the principles combine in a real product.

1.1 Objectives

The aims of this review are to summarise the role of powders in pharmacy; to describe their classification and physical properties; to explain size reduction, mixing, segregation and flow; to outline the methods used to evaluate powders; to describe manufacture, packaging, storage and quality control; and to demonstrate these principles through the example of ORS [4–6,8,9].

2. Literature Review

Standard pharmaceutical textbooks explain that powder behaviour results from interconnected factors: particle size and distribution, shape, density, surface characteristics, moisture content and the interparticle forces that hold particles together [4–6]. Because these factors interact, the choice of measurement method influences which manufacturing process is judged most suitable.

Particle size and particle-size distribution are widely regarded as the defining attributes of a powder. Changes in size affect mixing, segregation, flowability, dissolution rate and the uniformity of a blend. Sieves or specialised instruments can be used for analysis depending on the sample, and USP General Chapter <811> describes the testing of powder fineness [3].

Flowability has also been studied extensively because of its role in mixing, processing and dispensing. USP General Chapter <1174> stresses that flowability cannot be fully described by a single test; angle of repose, flow rate through an orifice and compressibility are typically used together [1]. Shear-cell methods are described in USP <1063> [2]. Bulk density, tapped density, Carr's index and Hausner ratio are routinely used to describe packing and compressibility, but their results should be interpreted alongside other properties, since materials respond differently to environmental conditions and test details [1,2].

Blending and segregation are critical for even distribution of the active ingredient, particularly for low-dose or potent drugs. Segregation arises from differences in particle size, density, shape or surface features, and is controlled by selecting suitable equipment and setting up the blending operation properly [4,5]. Moisture is

equally influential: it changes cohesion and flow and promotes caking, while an excessively dry powder may also be problematic, so moisture and storage conditions must be controlled [4–6].

Textbooks such as Aulton's *Pharmaceutics* and Remington describe powder technology as a core part of pharmaceutical manufacturing, covering milling, blending, granulation and handling [4,5]. From a regulatory standpoint, the WHO Good Manufacturing Practice guidelines require controls over materials and processes so that products consistently meet their standards [7]. Taken together, the literature shows that powder quality depends on particle properties, on processing, and on packaging and storage, and that each must be controlled.

3. Pharmaceutical Powders

3.1 Definition

Pharmaceutical powders are dosage forms consisting of a mass of finely divided particles of pharmaceutical ingredients and excipients. They may be used as such or as intermediates in making other dosage forms. Depending on preparation and intended use, they can be given orally, applied topically or used by other routes, either directly or after dissolving or suspending in a suitable liquid [4–6,10].

Powders may contain a single ingredient or several, with excipients in varying proportions according to the dosage form, route of administration and stability needs. Common excipients include fillers or diluents, flow promoters, surfactants, binders and sweeteners. Because a powder is a multicomponent particulate system, its physicochemical properties must be managed carefully throughout processing [8,9].

3.2 Characteristics

Several physical and mechanical characteristics define how a powder is processed and used [4–6]:

Particle size and distribution influence surface area, content uniformity, flow, mixing and dissolution rate.

Particle shape (spherical, irregular, fibrous, elongated) affects packing, interlocking, flow and mixing.

Bulk and tapped density, and porosity indicate how well the powder packs under different conditions.

Flowability depends on cohesion, surface texture, size, shape and moisture; poor flow leads to poor mixing and dose variation.

Moisture content affects processing, cohesion and caking, and is a critical quality attribute for hygroscopic powders.

Cohesiveness causes caking and resistance to flow.

Homogeneity ensures even distribution of the API, which is especially important for potent drugs.

3.3 Significance

Powders are important both as dosage forms and as materials in manufacturing. They are used in granulation, milling, sieving, blending and filling, and controlling their properties helps achieve good mixing, tablet quality and filling uniformity. They can be administered by oral and topical routes and, in sterile form, after reconstitution for parenteral use. Oral Rehydration Salts, which are dissolved in water before use, show how important powder properties and quality assessment are in pharmacy practice [8,9].



Figure 1. Sieving of pharmaceutical powder in a controlled manufacturing environment.

Figure 1. Sieving of pharmaceutical powder in a controlled manufacturing environment.

4. Classification of Powders

Pharmaceutical powders can be classified according to route of administration, physical properties and intended application. Each category has its own requirements for production, packaging, labelling and storage [4–6].

Bulk powders. Bulk powders are supplied in a container from which the patient or pharmacist dispenses the required quantity. They are generally intended for use with a diluent where exact dosing is not critical, and may be for internal or external use. Packaging must protect against moisture and microbial contamination.

Divided powders. Divided powders are presented as individual doses, each wrapped in paper, a sachet or a folding carton. They permit accurate dosing because each unit is one dose, so proper mixing of the powder before division is essential.

Dusting powders. These are applied to the skin and must be fine enough to form a uniform film. Depending on the formulation they protect the skin, absorb moisture or deliver a drug. Fineness and microbial quality are especially important.

Effervescent powders. These contain an effervescent mixture, typically an acid and a carbonate, which reacts when water is added. The powder is dissolved in water and allowed to effervesce before use. Exposure to moisture during manufacture or storage can destroy the mixture, so tight control of humidity is required.

Powders for reconstitution. These are supplied dry and mixed with a defined volume of diluent before use. Many active ingredients are unstable in solution, so dry powders generally have a longer shelf life. The correct volume of diluent, as stated on the label, must be used.

Other categories. Powders are also used for filling tablets and capsules, for inhalation, and for incorporation into suspensions or other liquids. The technical and quality requirements depend on the intended use and route.

Classification therefore guides the choice of manufacturing method, packaging material and quality-control tests [4–6].

5. Properties of Powders

The physical properties of a powder influence handling, mixing, processing, packaging and performance. Understanding them allows appropriate manufacturing and quality-control procedures to be selected [4–6].

5.1 Particle size

Particle size affects surface area, mixing, flow, dissolution and handling. The distribution of sizes matters too, because a wide distribution can promote segregation. Size can be assessed by sieving and other particle-size analysis techniques [3–5].

5.2 Density

Density describes mass per unit volume. Bulk density refers to the powder in its loosely packed state, while tapped density is measured after controlled tapping. Together they describe how the powder packs and help in evaluating flow and compressibility [4–6].

5.3 Porosity

Porosity is the proportion of void space between and within particles. It relates to packing and influences air or liquid movement through the powder bed, as well as compression, dissolution and interaction with moisture [4–6].

5.4 Moisture content

Moisture increases adhesion between particles and so raises cohesiveness, which can impair flow and stability. Some powders are very sensitive to humidity, making moisture control and suitable packaging important [3–5].

5.5 Cohesiveness

Cohesiveness is the tendency of particles to adhere to one another through interparticle forces. Cohesive powders flow poorly and may form lumps or agglomerates. Size, surface properties, moisture and environmental conditions all influence it [4–6].

5.6 Flowability

Flowability describes how easily powder moves when forces act on it, and is critical during transport, mixing, hopper discharge and filling. It changes with particle size, shape, density, moisture and cohesiveness. Because so many factors are involved, flow is measured with several parameters rather than one test. Together these properties determine how a powder behaves in processing, how uniform and stable it remains and how well it performs [8,9].

6. Particle Size and Size Reduction

Particle size influences surface area, flow, mixing, dissolution and behaviour during processing. Smaller particles provide greater surface area, which can speed up reaction or dissolution in liquids. Differences in particle size between ingredients can cause separation during mixing and handling, so controlling size and size distribution is vital for consistent and reliable products [3–5].

Size reduction (comminution) is the process of making large particles smaller by impact, compression, cutting and attrition. Common industrial equipment includes hammer mills, ball mills, roller mills and cutter mills. The choice depends on the behaviour of the material, its moisture content, its hardness and the particle size required in the final product.

Particle-size analysis determines the size and distribution of particles. Sieving is a convenient method for suitable size ranges, while other methods are used for finer particles. The data confirm whether a powder meets specifications and provide information for process control [3].

Size must be chosen to suit the purpose of the product. Appropriate particle size makes handling and processing easier, but if particles are too small they may become cohesive and difficult to move [3–5].

Figure 2. Size-reduction equipment used in pharmaceutical powder processing (before and after milling).

7. Powder Mixing, Segregation and Flow

7.1 Mixing mechanisms

Mixing is the even distribution of two or more ingredients throughout a mixture. The main mechanisms are convective mixing (movement of groups of particles), shear mixing (slip planes within the powder bed) and diffusive mixing (movement of individual particles). Good mixing ensures that the active ingredient and excipients are spread uniformly. Particle size, shape, density and moisture content all affect how well mixing proceeds [4–6].

7.2 Causes of segregation

Segregation is the separation of components of a powder mixture, during or after mixing. It is caused by differences in particle size, density, shape or surface properties. Handling, vibration and transfer can also trigger it. Segregation is reduced by controlling particle characteristics and by using suitable mixing and handling methods [4–6].

7.3 Flow behaviour

Flow behaviour describes how readily particles move under applied force. Good flow is needed for transport, hopper discharge, mixing and container filling. It depends on particle size, shape, density, moisture, stickiness and interparticle forces, and is therefore usually tested by more than one method [1,2,4,5].

7.4 Angle of repose

The angle of repose is the steepest angle at which a pile of powder remains stable before sliding. It is an indicator of flow: a lower angle indicates better flow, whereas a higher angle shows that particles resist moving past one another. As a general guide, angles of about 25–30° indicate excellent flow, 31–35° good flow, 36–40° fair flow, 41–45° passable flow, and values above this poor to very poor flow [1].

7.5 Carr's index and Hausner ratio

Carr's index (compressibility index) and the Hausner ratio are calculated from bulk density and tapped density [1,2,4,5]:

$$\text{Carr's index (\%)} = [(\text{Tapped density} - \text{Bulk density}) / \text{Tapped density}] \times 100$$

$$\text{Hausner ratio} = \text{Tapped density} / \text{Bulk density}$$

Lower values indicate better flow. A Carr's index of up to 10% is generally described as excellent flow, 11–15% good, 16–20% fair, 21–25% passable and above 25% poor, while Hausner ratios of 1.00–1.11, 1.12–1.18, 1.19–1.25 and 1.26–1.34 correspond to excellent, good, fair and passable flow respectively [1]. These values

indicate compressibility and flow tendency, but they should not be treated as the only measure of flowability and should be considered together with other powder properties.

Figure 3. Industrial equipment used for pharmaceutical powder mixing (V-blender).

8. Evaluation of Powder Properties

Evaluation of powder properties involves examining physical and flow characteristics to understand how a powder behaves during processing and how consistent it is. A combination of tests is used to decide whether a powder is suitable for its intended pharmaceutical use [4–6,10].

8.1 Bulk and tapped density

Bulk density is the mass of powder occupying a given volume before tapping. Tapped density is measured after mechanical tapping under specified conditions. The difference reveals packing efficiency and compressibility, and the two values are needed to calculate Carr's index and the Hausner ratio [1,2,4,5].

8.2 Particle-size distribution

This test determines the range and proportion of particle sizes in a sample. It is important for mixing, segregation, flow, solubility and overall performance. Sieve analysis is commonly used for powders with a wide size range, and other analytical techniques are applied where finer particles or special requirements demand them [3–5].

8.3 Flow tests

Flow tests estimate how easily a powder moves during processing. Common tests include angle of repose, flow-rate measurement, and Carr's index and Hausner ratio. Results help predict behaviour during mixing, transfer and filling, and support formulation design. Since flow involves many factors, several tests are normally used together [1,2,4,5].

8.4 Moisture determination

Moisture determination estimates the water content of a powder. Excess moisture increases cohesiveness, impairs flow, promotes agglomeration and affects stability. Monitoring and controlling moisture during manufacture and storage is therefore often required for moisture-sensitive powders [4–6].

8.5 Uniformity evaluation

Uniformity evaluation provides information on the distribution of the active ingredient and other components, and so on the quality of the mixture. Achieving adequate mixing while avoiding segregation is central to formulation development and requires suitable analytical procedures and sampling techniques [4–6].

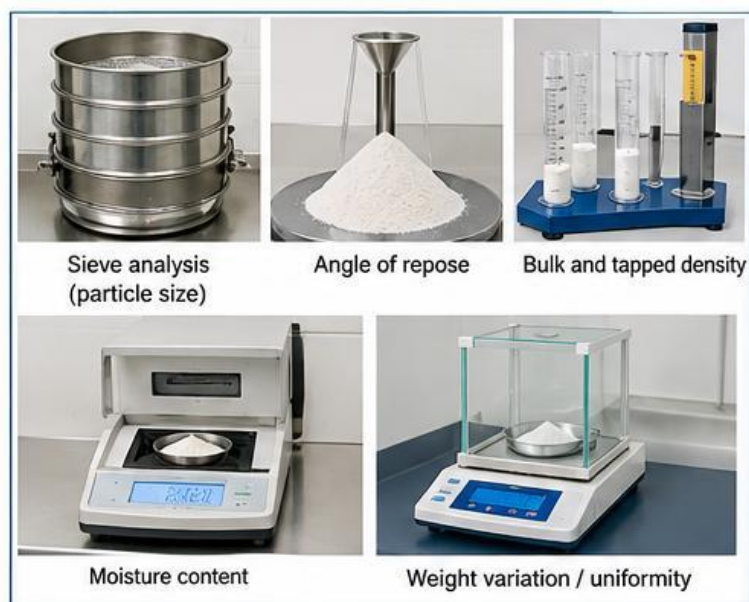


Figure 4. Laboratory evaluation of pharmaceutical powder properties.

Figure 4. Laboratory evaluation of pharmaceutical powder properties: sieve analysis, angle of repose, bulk and tapped density, moisture content and weight variation.

9. Preparation and Manufacturing of Pharmaceutical Powders

Preparation of pharmaceutical powders consists of carefully controlled steps that lead to a uniform product [4–6,10].

Weighing. Ingredients and excipients are weighed accurately. Correct weighing is essential for the right composition and dose [4–6].

Size reduction. Large particles are reduced to the required size using equipment such as hammer mills or roller mills, which also facilitates mixing [3–5].

Sieving. Sieving separates material by particle size, removing coarse particles and lumps and giving a more uniform powder [3–5].

Mixing. Ingredients are blended to distribute the active ingredient and excipients uniformly. Proper mixing is particularly important when an ingredient is present in a small proportion [4–6].

Filling. The finished powder is filled into containers, sachets or unit-dose capsules. Filling must deliver the required amount of drug while minimising powder loss and segregation [8,9].

Manufacturing controls. Controls include verifying material quantities, particle size, uniformity of the blend, moisture, equipment cleanliness and documentation. Proper control of every step is necessary to produce powders of uniform composition and high quality [4–6].

Figure 5. Pharmaceutical powder processing in a controlled manufacturing area.

10. Packaging and Storage

Correct packaging and storage are essential to maintain the quality, stability and safety of powders [4–6].

Packaging requirements. Containers must protect the product from environmental influences while preventing loss or contamination. The packaging material must be compatible with the powder and suitable for its use [1,2,4,5].

Protection from moisture and contamination. Moisture can make powders sticky, cause lumps and alter flow. Moisture-resistant packaging and correct handling protect against humidity, dust, microorganisms and other contaminants [1,2,4,5].

Labelling. The label should state the product name, strength or quantity, batch number, manufacturing and expiry dates, storage conditions and directions for use [4–6].

Storage conditions. Powders should be stored under the conditions specified for the product, with protection from moisture, heat, light and sources of contamination where applicable.

Correct packaging, clear labelling and suitable storage together maintain the quality and stability of pharmaceutical powders.

11. Quality Control of Powders

Quality control ensures that materials and finished products meet requirements for identity, purity, uniformity and performance [4–6].

11.1 Raw-material control

Raw materials are examined for identity, quality, purity, particle size and other relevant properties before use, so that unsuitable materials do not enter the process [3–5].

11.2 In-process controls

During manufacture, parameters such as particle size, mixing uniformity, moisture content and flow properties are monitored. This identifies variations early and helps maintain consistency [1,2,4,5].

11.3 Finished-product testing

The final powder is tested for particle size, moisture, density, flow properties and uniformity. The tests chosen depend on the nature and intended use of the powder [1,2,4,5].

11.4 GMP considerations

Good Manufacturing Practice requires controlled manufacturing, suitable equipment, hygienic environments, trained personnel and appropriate quality-control measures, which together reduce the risk of contamination and error [7].

11.5 Documentation and batch consistency

Manufacturing and testing steps must be documented. Batch records, test results and deviations are retained so that products are traceable and batches are consistent, and so that the cause of a problem can be identified [7].

A systematic approach to quality control, from raw materials to finished product, is what assures safe, consistent and high-quality powders [4–6].

12. Applications of Pharmaceutical Powders

Oral preparations. Powders may be taken by mouth directly or after mixing with a liquid, and can carry active ingredients and useful fillers [4–6,10].

External preparations. Dusting powders are used on the skin to protect, absorb moisture or deliver medication, depending on the formulation [4–6].

Powders for reconstitution. Dry powders mixed with a specified liquid before use often remain stable in storage better than ready-made liquids [4–6].

Manufacturing applications. Powders are starting materials and intermediates in making tablets, capsules, granules and other forms, where particle size, mixing and flow are decisive [3–5].

Healthcare applications. Powder preparations such as oral rehydration mixes are valued in health care for easy handling, transport and storage [8,9].

13. Case Study: Oral Rehydration Salts (ORS)

13.1 Background

ORS is supplied as a powder, usually in sachets, to be dissolved in a defined volume of clean water. It contains glucose and electrolytes in proportions that allow proper absorption and dissolution. The standard WHO-recommended formulation contains sodium chloride, anhydrous glucose, potassium chloride and trisodium citrate dihydrate [8,9]. This case study illustrates how general powder manufacturing and quality-control principles apply to ORS; it is not a manufacturing instruction for any batch.

13.2 Step 1: Raw-material checking and weighing

Each incoming ingredient (sodium chloride, glucose, potassium chloride and trisodium citrate) is checked for identity and quality. Each is then weighed according to the approved formulation. Deviations from the specified quantity of any component can alter the properties of the finished ORS, including its osmolarity [8,9].

13.3 Step 2: Sieving and particle-size control

Ingredients are sieved to remove coarse particles and brought to a suitable particle-size distribution. Similar particle sizes across ingredients reduce the risk of segregation during mixing, which matters because the components differ in density and crystal form [4–6].

13.4 Step 3: Mixing

The weighed ingredients are loaded into the mixer and blended for a defined time until a homogeneous mixture is obtained. Homogeneity is critical because it determines the glucose and electrolyte content of every sachet [8,9].

13.5 Step 4: Quality evaluation

The blend is evaluated for uniformity, moisture content and particle-size distribution, together with other physicochemical properties. The content of individual ingredients is also determined to confirm conformity with specifications [4–6].

13.6 Step 5: Filling and packaging

The blend is filled into sachets containing the defined quantity of powder. Sachets are sealed tightly to keep out moisture and contaminants, since ORS components are prone to absorbing water [8,9].

13.7 Step 6: Final quality decision

Results from raw-material testing, in-process control, powder evaluation and packaging checks are reviewed against the quality-control specifications. If the sachets conform, the batch can be released. If there is a deviation, production is halted and the cause is investigated.

Process flow: Raw materials → Weighing → Sieving → Mixing → Powder evaluation → Filling → Packaging → Final quality review [3–5].

13.8 Practical lessons

The ORS example shows that powder quality is affected by many factors, each needing attention at the relevant stage. Accurate weighing, suitable particle-size distribution, thorough mixing, protection from moisture and correct filling together ensure that powder batches conform to specification [8,9].

Figure 6. Oral Rehydration Salts (ORS) powder sachet.

14. Conclusion

Pharmaceutical powders are important both as dosage forms and as materials for making tablets, capsules, granules and other medicines. Their quality depends on particle size, density, moisture content, cohesiveness, flowability and the ability to mix uniformly. Accurate weighing, size reduction, sieving, mixing, testing, filling, packaging and storage are all needed to keep quality high. Quality-control tests and good manufacturing practice reduce problems such as segregation, moisture-related changes, contamination and batch-to-batch variation, and the ORS case study shows the importance of controlling both ingredients and process steps [4–9].

Future progress in powder technology is likely to come from better analytical methods, automated process control, improved tools for measuring particle size and flow, real-time process monitoring, data-driven quality checks and more advanced packaging solutions. Continued improvement in these areas should give greater consistency, longer shelf life, higher safety and better performance for medicines made from powders [3–5].

Declaration of Conflicting Interests

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