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Review Article

Compression Vehicle: A Technical Review

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Abstract

The compressed dosage forms such as tablets are the most preferred and widely accepted due to their dosing accuracy, compactness, manufacturing efficiency, stability and better patient compliance. Pharmaceutical Diluents or filler binders, usually referred to as Compression vehicles, contribute significantly to the formulation blend, especially in compressed solid dosage forms containing potent active pharmaceutical ingredients. The functionality of these filler binders mainly depends on their physicochemical and mechanical properties. They provide performance characteristics and quality attributes of the compressed solid dosage forms. Understanding the effect of compression vehicles' bulk and particle level properties is of prime importance in optimising various process parameters and unit operations. The mechanical properties of a compression blend viz plasticity, elasticity, viscoelasticity, brittleness, and bonding index play an essential role in the effective compaction of compressed solid dosage forms. In addition to this, the porosity, volume, density or void-volume ratio of compact with applied pressure is required to understand the compaction behaviour of solid to form a compact with well-defined geometry.

Keywords: compression vehicle, filler binder, pharmaceutical diluent, compaction, consolidation, excipient functionality

Introduction

It is a well-known fact that therapeutic agents can never be administered alone in their original or crude form; instead, they are generally administered as part of pharmaceutical dosage forms, which are prepared by admixing and processing them with suitable pharmaceutical excipients [1,2]. Despite vibrant and rapid growth in pharmacy and the development of novel dosage forms, compressed dosage forms such as tablets remain the most widely used and accepted dosage form due to their dose accuracy, compactness, manufacturing efficiency, stability and better patient compliance [3]. Tablets are manufactured either by granulation compression or by direct compression. Granulation methods (dry and wet) for tablet manufacture are multi-step and involve various complex processes, whereas direct compression involves compressing dry blends of formulation powders [4]. The direct compression technique is usually preferred over other tabletting techniques due to its simplicity, cost-effectiveness, and processing time with fewer manufacturing steps. Direct compression is also advantageous as it is suitable for thermolabile and moisture-sensitive active pharmaceutical ingredients [5,6]. However, due to poor compatibility and poor flowability, most of the active pharmaceutical ingredients available today are not suitable for direct compression [7,8]. Direct compression involves mixing Active Pharmaceutical Ingredients with various pharmaceutical excipients to impart desired tabletting properties [9]. Depending on the functionality, the pharmaceutical excipients can be categorised as excipients for processing, which impart additional physical properties and excipients that help alter the drug release. The selection of excipient for tablet manufacturing depends on the active pharmaceutical

ingredient's physicochemical characteristics and mechanical properties, the type of tablet dosage form required, the desired pharmaceutical properties of the tablet, and the manufacturing method to be used [10].

Pharmaceutical diluents or filler binders are usually referred to as compression vehicles and contribute a major portion of the formulation blend, especially in the case of compressed solid dosage forms containing potent medicaments. Hence the role of diluent is being shifted from just being a "Bulking agent" toward "Functional Ingredients" in the formulation of compressed solid dosage forms. They significantly impact the performance, processability and stability of the dosage form. Any modification, alteration, or substitution of diluent with different physicochemical properties remarkably affects the properties of a dosage form [11-14]. The present review highlights technical aspects and their impact on the performance of compression vehicles and compressed dosage forms.

Classification of Compression vehicle

It is always expected that, the formulation blend for direct compression shall have a perfect blend of materials with sufficient flowability and disintegrating property. Hence compression vehicles used for direct compression are usually classified based on their disintegrating property and flow behaviour. Diluents such as Micro crystalline cellulose, microfine cellulose, Starch DC are categorised as Disintegrating agents with poor flow properties. Dibasic Calcium Phosphate is a diluent categorised as Free flowing material does not disintegrate. Diluents such as Lactose SD, Anhydrous Lactose, Sucrose, Mannitol are Free flowing powders that disintegrate by dissolution [15,16]. Compression vehicles can also be classified on the bases of their chemical nature and solubility in aqueous media (Figure 1).

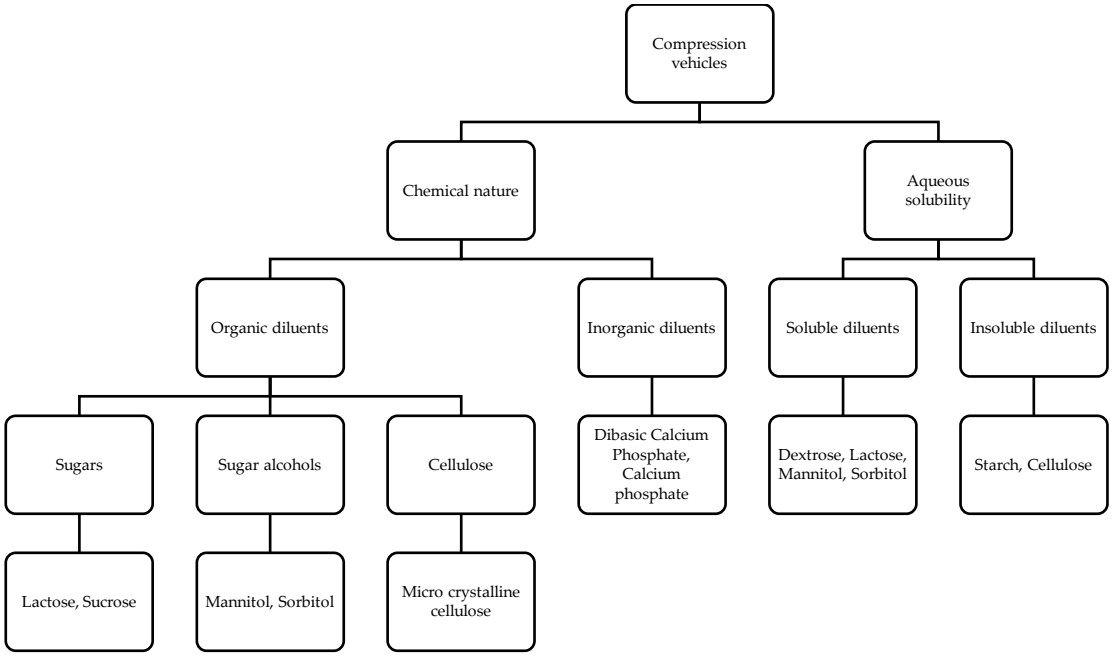

Figure 1. Classification of compression vehicles.

Source of compression vehicles

Pharmaceutical diluents from herbal sources have created significant interest for formulation scientists due to their safety, biocompatibility, inert property, better patient tolerance, and availability. Several plant-based polymeric materials, such as starch and cellulose, are commonly used to develop compressed solid dosage forms [17-22]. In addition to the excipients of natural origin, synthetic excipients as filler binders gain a tremendous interest in formulation scientists due to their purity and unique physicochemical properties [23,24]. Over the last three decades, modification of existing excipients from natural and synthetic origins for their physical and chemical characteristics has resulted

in the development of newer excipients [25]. Modifying a single entity excipient is referred to as particle engineering, while the modification of a combination of two or more excipients in an appropriate ratio is referred to as coprocessing. In the case of particle engineering, the size, shape and texture of excipient particles can be altered by suitable physical treatments such as freezing, drying, case hardening or solidification [27-28]. Coprocessing of excipients involves the treatment of two or more excipients in a suitable proportion to develop an excipient with improved functionality [28,29].

Compression and Compaction

Tablet is a solid unit dosage form consisting of one or more active pharmaceutical ingredients, admixed and processed with suitable pharmaceutical excipients to impart the desired mechanical and pharmaceutical properties [30,31]. Tablets are prepared by applying compression pressure on the formulation blend to form a solid compact. The word "Tabletability" could be used to explain the ability to blend powder that can be compressed into a solid compact [32]. Compaction is forming a solid specimen of defined geometry by reducing the bulk volume of the powder bed and creating interparticle bonds. A process of shrinkage in the bulk volume of a powder bed is called Compression, whereas an increased mechanical strength of the compact results in the formation of inter-particulate binding is a process of Consolidation. The tablet compression involves three stages viz filling of the die with tabletting blend, Compression of tabletting blend and ejection of the compressed tablet (Figure 2) [32,33].

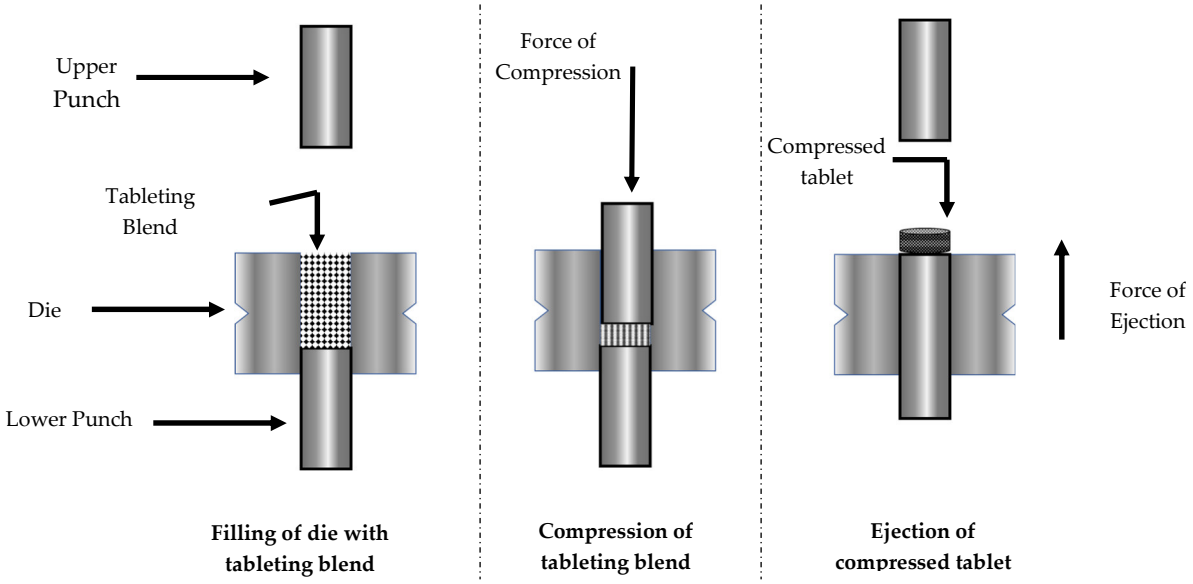

Figure 2. Stages of tablet compression

According to Klevan I, Powder could be considered a disperse system, whereas solid particles are dispersed in a gaseous phase. When compressional force compresses a powder mass, the powder particles will be brought closer. This results in the formation of inter-particulate bonds and the transformation of Powder into a coherent mass [32]. During compression, materials experience various stresses of complex nature, which results in a change in the structure of the powder bed, followed by consolidation of Powder. This process involves rearrangement, plastic deformation, and fragmentation of the powder particles [33].

At the initial compression stage, powder particles slide one over the another and get rearranged. This results in a reduction in inter-particular space and the formation of a compact structure. At a later stage of compression, the powder particles will be fragmented into smaller particles and/or undergo deformation based upon their mechanical behaviour under stress (Figure 3) [34].

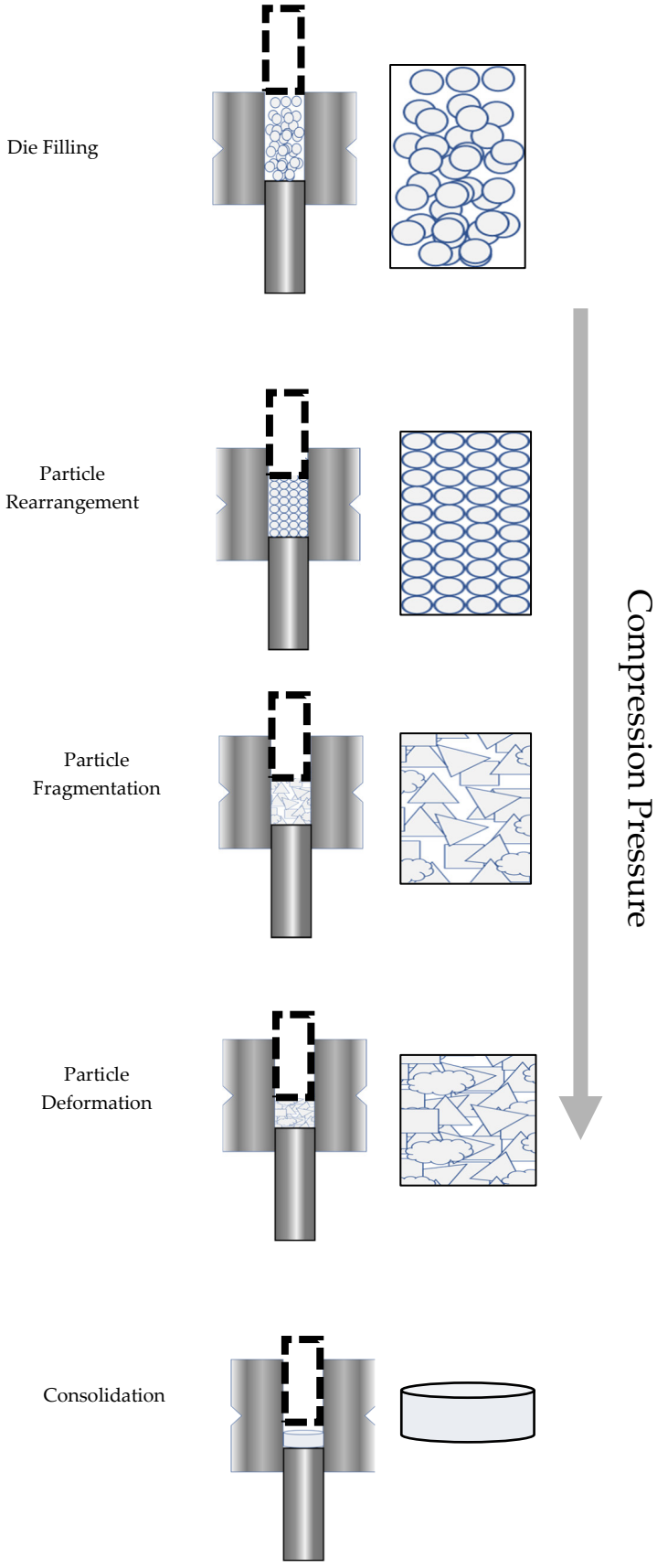

Figure 3. Process of powder consolidation.

Brittle materials get fragmented while plastic and elastic materials undergo deformation with applying pressure. The deformation may be elastic or plastic [35-37]. Though the material under compaction is not entirely elastic, plastic or brittle, it shows all types of behaviour, with only one type exhibiting a predominant response [37]. On application of compression pressure, elastic material will undergo deformation and reassume its original shape after removing the stress. On the other hand, plastic materials undergo permanent deformation. When exposed to compression pressure, Brittle materials undergo extensive fragmentation and breakdown into smaller particles as shown in Figure 4 [26,35].

To obtain tablets with desirable properties, the powder needs to undergo plastic deformation during compression and has a desired elastic recovery upon decompression [38,49]. These characteristics are rarely observed in a single excipient, and thus, generally, a combination of materials having brittle and plastic properties in the appropriate proportion is preferred, rather than using a single material [10]. Materials with plastic and/or viscoelastic properties produce tablets with better mechanical strength at reduced speeds, whereas materials with brittle fragmenting characteristics remain unaffected by the speed of compression due to rapid fragmentation [39].

Excipient Functionality

The functionality of an excipient is its ability to impart performance characteristics, and quality attributes to the drug product. The excipients' physicochemical and mechanical properties affect the excipient functionality (Figure 5) [40]. As stated earlier, a compression vehicle constitutes a significant portion of the formulation blend. Thus, the functionalities of the compression vehicle are the parameters of critical consideration for the development of robust compressed solid dosage forms. The physicochemical properties of diluents may be described at the Molecular level, particle level and bulk level. Crystalline organisations of independent molecules viz polymorphism, pseudo-polymorphism, and the amorphous state, are considered molecular-level properties of the diluents. Particle characteristics such as shape, size, surface area, and porosity are considered particle level properties and flowability, and densities are the bulk level properties of diluents [10,41].

The mechanical properties involved in compaction behaviour and binding properties of the material under compression include Tabletability, Compressibility and Compactability [42]. Tabletability is the ability of a powder mass to be compressed as a tablet with desirable mechanical strength as an effect of applied compaction pressure. Compressibility in the case of a powder mass is a reduction in volume that occurs due to applied compression pressure. Compactability is the potential of a powder to attain the form of a tablet with desirable mechanical strength. These properties describe the interrelationship between tensile strength, solid fraction and compression pressure [33,43].

Crushing strength, friability, disintegration and dissolution are the technological properties of compressed solid dosage forms, which gets affected by the functionalities of the filler binder. Hence a comprehensive characterization of excipient functionalities becomes mandatory [40].

Physicochemical characterization of Compression Vehicles

Powder comprises a large number of discrete particles, and thus, challenging to predict bulk characteristics based on the factors of individual particles. It is essential to study the impact of different properties of powder on a solid compact and helps to optimize process parameters, unit operations, and conditions to be maintained during manufacturing, packaging, and logistics [44].

Particle size and particle size distribution

During compression, the size and distribution of powder particles significantly affect the mechanical properties of tabletting blend and technical properties of compressed dosage forms [35,45,46]. Particle size affects the fragmentation propensity of material under pressure. The fragmentation propensity of material will increase within the particle size. Thus, the tablets compressed using a powder with larger particles will exhibit greater crushing strength, lower friability, and can resist elastic recovery [47]. Filler-binders with a broad particle size distribution range are always

preferred for tabletting. The smaller particles get embedded in the voids of larger particles, resulting in dense packing formation. This helps to enhance surface interactions between the particles [44,46]. The smaller particles also act as roller bearing for larger particles and help to improve flowability. However, in some instances, obstruction of flow may also observe with an excess of fines, which could be due to an increase in packing density [40].

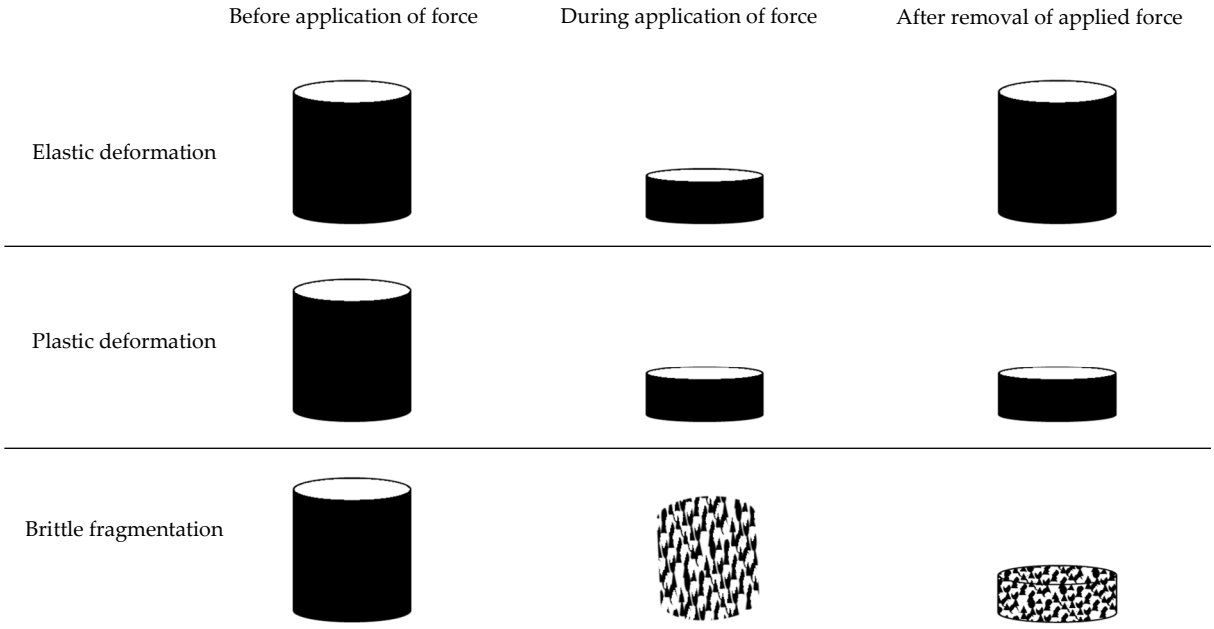

Figure 4. Mechanism of deformation.

Crystal Morphology

Crystal Morphology is another important characteristic of particle powder under compression. It affects the compactability as well as flowability of the powders. Powder with more than 50% of crystallinity exhibits better compressibility than that with less crystallinity [44,48]. Morphology of Crystal also affects the density of powder. Usually, needle-shaped crystals showed significantly lower bulk density than cigar-shaped crystals. Scanning Electron Microscopy and Light Microscopy are the techniques used to determine crystal morphology [44].

Porosity

Porosity is the ratio of the total pore volume to the apparent volume of the powder, excluding inter particular voids. Voids in powder include both inter-particular and intra-particular voids [40]. The porosity influences various physical properties of powders, such as thermal conductance, wetting behaviour, mechanical strength and densities [44]. Powder volume and related porosities may be measured either during compression ("in die" or "at pressure" method) or after ejection ("ejected tablet" or "at zero pressure" method) of the tablet. In the "in die" or "at pressure" method height of the powder, the column is monitored continuously during volume reduction. While in the case of the "ejected tablet" or "at zero pressure" method, the dimensions of a compact are measured [40].

Bulk density

It is the density of a powder with loose packaging. It can be regarded as the ability of a powder column to form a compact mass [40,44]. A powder's bulk volume is a volume of powder inclusive of inter-particular void volumes and depends on the particle shape, size, distribution, inter particulate friction, and cohesion (Figure 6). Irregularly shaped particulates in the powder form a highly porous structure. This results in a decrease in bulk density and may exhibit a high tendency of densification

[57]. The bulk density of a powder mass can be determined by noting the volume of untapped powder mass or aerated powder column [44].

Tapped Density

Tapped density is a ratio of powder mass to the tapped volume. Tapped volume is the volume occupied by the powder after tapping the powder column a specified number of times, representing the random dense packing (Figure 6). Tapped density can be measured by allowing the column of powder filled in a graduated cylinder to raise and drop for a fixed distance at a formal drop rate. Powders containing spherical shaped particles show higher tapped density when compared to that powders with irregularly shaped particles [40,44].

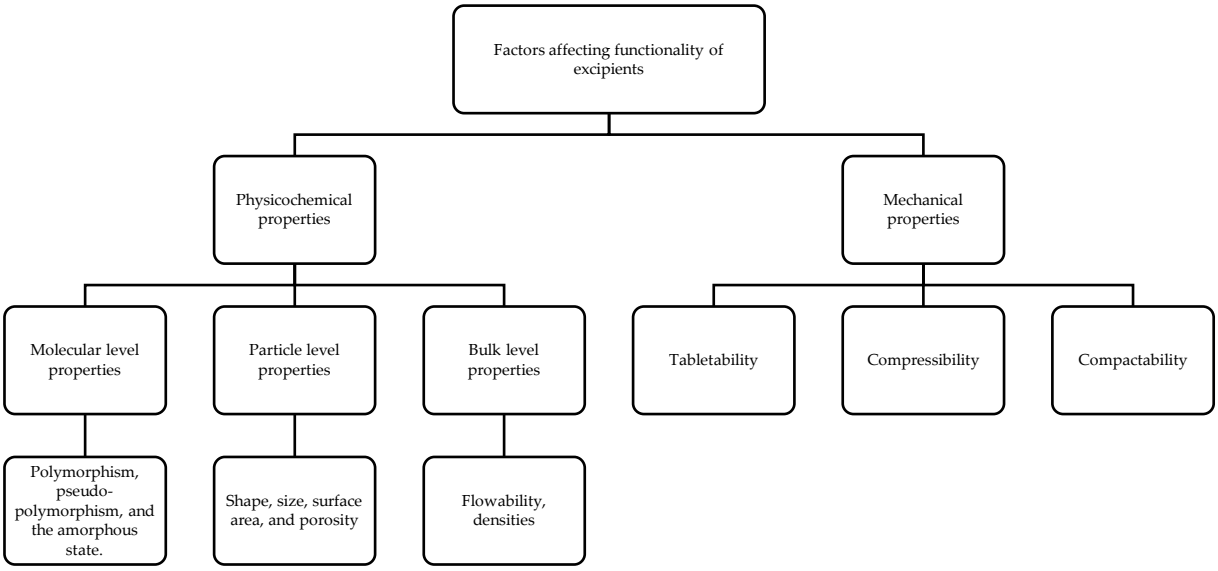

Figure 5. Various factors affecting excipient functionality.

True density

The true density of a material is a ratio of solid mass to the true volume of solid. True volume is the actual volume of powder, excluding the volume of void spaces but is inclusive of hallow spaces that represent the molecular packing arrangement of solids (Figure 6). The true density of a solid can be determined by using the liquid or gas displacement method. True density is indicative of the extent of powder compression [40,44].

Flowability of powders

Dynamic powder behaviour, i.e., flowability, represents the ability of powder particles to change their position with respect to each other within the bulk of powder [40,46]. Flowability of drugs, excipients and formulation blends affect the manufacturability of the solid dosage forms. Flowability depends upon the particle shape, size, moisture content and force of inter-particulate attraction [40]. Flowability can be determined by measuring the angle of repose and the extent of compressibility. Lower values in the case of both parameters indicate better flowability [46].

Angle of repose

The angle of repose also referred to as the critical angle of repose, is the steepest angle of descent or dip made by the heap of a powder to the horizontal plane when allowed to fall from a specified height. The angle of repose is a measure of inter-particulate friction or resistance offered to the inter particulate movement between particles [40].

Compressibility index

The compressibility index is a direct measure of the tendency of powder to consolidate. It represents interparticle forces and bulk packing of powder. Higher compressibility indicates higher interparticle forces with a denser packing of powder particles. The powders consisting of particles with greater inter particulate interactions forms bridges with each other, and thus such powders exhibit poor flow behaviour. Since powder flow and compressibility index are inversely proportional to each other, flow behaviour can be determined [40,46].

Assessment of Mechanical properties of Compression Vehicle

The mechanical properties of a compression blend viz plasticity, elasticity, viscoelasticity, brittleness and bonding index play a significant role in the successful compaction of solid dosage forms [33,43]. During the pre-compression phase of tablet compaction, the upper punch moves in the die cavity filled with the formulation blend. Particles of powder blend will undergo rearrangement resulting in reduced contact distance between each particle. Energy E1 is consumed during the precompression phase to overcome the frictional forces. After the rearrangement of the particles, the further applied stress will be utilised as Energy E2 for the deformation of the particles. The energy required for binding the particle (Wuse) is a fraction of the energy *E*2 that remains after the friction work (*FW*), i.e. *W*use = *E*2 −*FW*. The force applied by the upper punch during compression will be imparted radially to the lower punch and laterally to the die wall. The relay of the applied force from the upper punch to the lower punch depends upon the frictional force present between the die wall and powder blend under compression.
Similarly, during the phase of tablet ejection, the friction between the compressed tablet and die wall also consumes energy (Figure 7). When friction work is high, there is a need to add a suitable lubricating agent in the formulation blend to reduce friction. During the decompression phase, tablet expansion occurs even after ejection due to elastic recovery. This indicates that the plastic behaviour of powder during compression and elastic recovery during decompression plays a vital role during compaction [56,59]. Along with plastic and elastic deformation of powder bed during compression, the compressibility of powder will also be affected by fragmentation and brittle fracture of the particle [42].

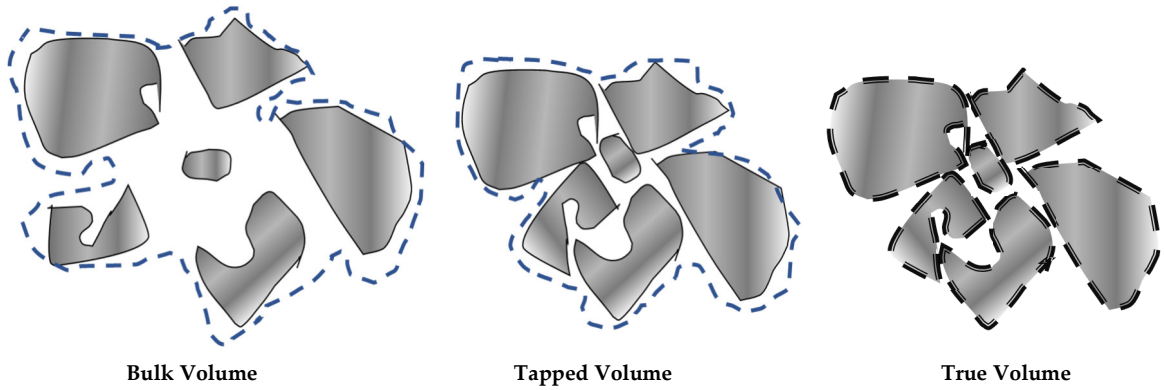

Figure 6. Particulate positioning or arrangements with different densities.

The term “Fracture” refers to separating a body into two or more parts. A brittle fracture is characterised by the rapid propagation of a crack throughout the material, whereas, in the case of ductile fracture, the material undergoes plastic deformation and then fractures (Figure 8) [33,43]. Change in the physical structure of the specimen when subjected to stress is often referred to as “Deformation”. Deformation may be elastic or plastic. When a change in the structure of a specimen is reversible, and the specimen regains its original shape on withdrawal of stress, such deformation is referred to as “Elastic Deformation”, while the permanent change in the structure due to applied stress is referred to as “Plastic Deformation” [40].

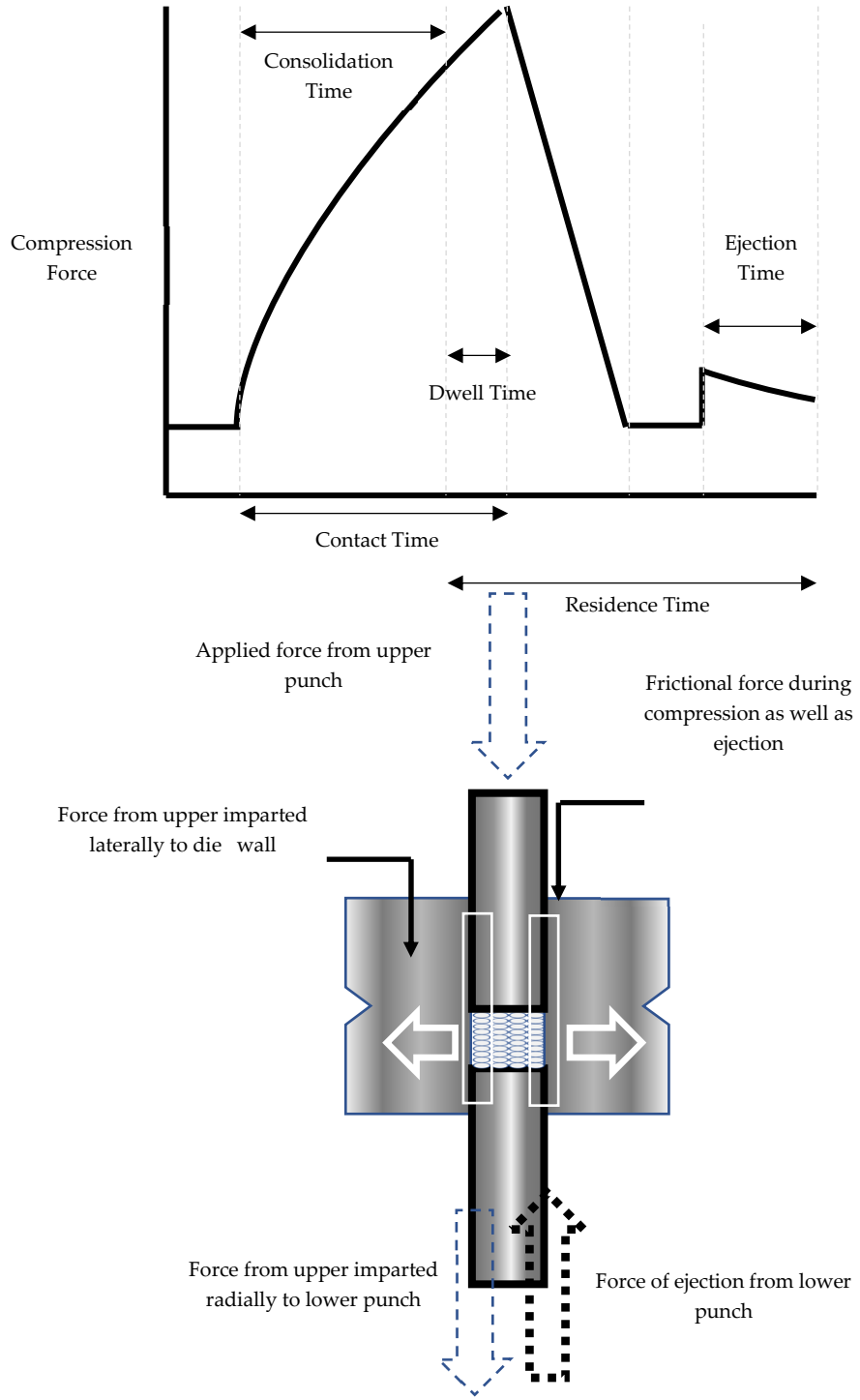

Figure 7. Sequence of events during compression and transmission of force.

The pharmaceutical materials exhibit time-dependent deformation, which may be related to the mechanism and dynamics of the consolidation process. Brittle materials consolidate mainly by fragmentation, whereas plastic materials get deformed by plastic flow. The time dependency of deformation is usually experienced in plastic materials compared to that of brittle materials. The brittle materials are often less influenced by the speed of compaction, which could be due to rapid fragmentation. It also showed a limited effect of prolonged exposure to compression force on the properties of tablets [33,43]. The formation of a large number of bonding points due to extensive

fragmentation of brittle material results in the formation of tablets with high porosity. On the other hand, the plastic deformation of ductile material enables the particles to move very close and form tablets with low porosity [35]. Plastic and/or viscoelastic materials generally produce tablets with better mechanical strength at reduced speeds, whereas brittle materials remain unaffected by compaction speed due to rapid fragmentation. Formulations containing materials that exhibit elastic or time-dependence deformation are highly prone to lamination and capping. They also experience reduced mechanical strength with an increase in punch velocity. The effect of punch velocity is prominently observed in the case of scaling up formulation from laboratory to large scale production [50]. Therefore, the blend for tabletting should consist of an optimum proportion of elastic and plastic materials. This will help avoid the formation of low- and high-pressure zones, usually due to uneven distribution of applied pressure. The low-pressure zones developed during compression lead to weak contact points and may result in capping or lamination [44,51].

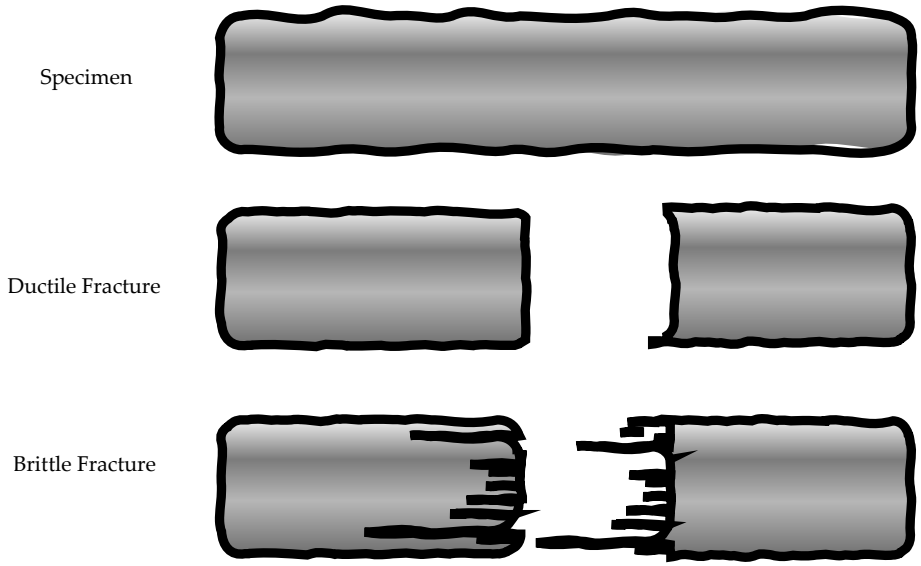

Figure 8. Different types of compression fractures on application of stress.

Various researchers reported that deformational properties as one of the causative factors for capping and lamination. In the viscoelastic material, compact strength increases with a decrease in tabletting speed. However, it has little or no effect on brittle materials [6]. On application of compression force, brittle materials will be fragmented immediately into smaller particles and create boning points. In contrast, plastic deformation is dependent on the time of force application. Thus, an increase in the speed of tabletting for a powder mixture containing a higher proportion of plastically deforming materials leads to a decrease in the hardness of the tablet. However, if the formulation blend consists of a suitable proportion of brittle material, the mechanical strength of the tablet remains unaffected [52].

The compressibility of powder will also be affected by the size of powder particles and applied compression pressure. At lesser compression pressure, larger particles of powder blend will be compressed more rapidly than smaller particles. Smaller particles produce stronger tablets than larger particles. The materials having greater fragmentability, the original particle size is less important as the reduction of volume of the powder bed and tablet strength are usually independent of particle size [47].

Compressibility

The measurement of the powder bed volume reduction due to applied compression pressure is a commonly used method for assessing the deformation mechanism. Volume reduction of powder bed

due to consolidation is usually expressed in reducing the height of cylindrical compact. The density pressure profile is generally measured by either the "in die" or "out die" method (Figure 9) [53].

The "Out-die" method involves the measurement of dimensions of ejected compact, whereas, in the case of the "in-die" method, the dimensions will be measured from punch displacement(s) values. The "In-die" method is usually preferred over the "out die" method since the "in die" method is quicker and requires lesser less material. Whereas separate compact is required for measurement in the case of the "out die" method for each compression pressure of interest [53].

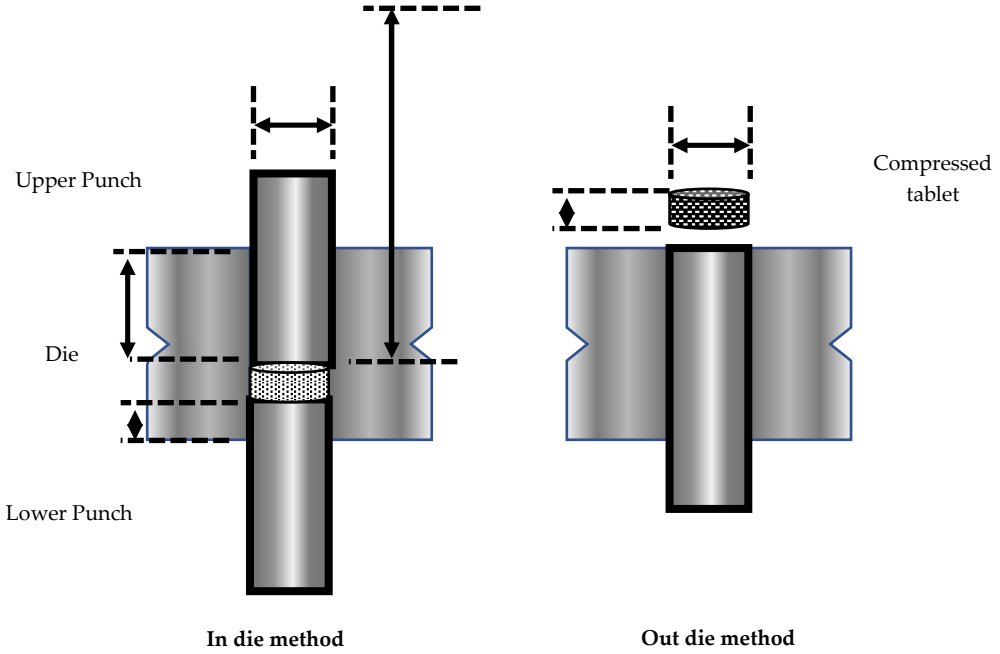

Figure 9. Different methods to assess compressibility.

Tensile Strength of Tablet

Diametrical crushing strength is the easiest and the most preferred method for determining the mechanical strength of tablets. However, it also depends upon the dimensions of the tablet. Thus, to avoid confusion in the terminology used to express mechanical strength such as force, strength and hardness, the term "Specific Crushing Strength" (SCS) can be used. Mathematically it can be expressed as:

$$SCS = \frac{F}{Dh}$$

Where F is the force required for crushing, h is compact height, and D is the diameter of the flat-faced cylindrical tablet. The SCS is expressed in the unit of pressure (Pa). The tensile strength (TS) of the tablet can be expressed as:

$$TS = \frac{2F}{\pi Dh}$$

The SCS deviates mathematically from TS only by the factor $2/\pi$ and thus has similar power in discriminative analysis [54].

Lubricant Sensitivity

Lubricating agents are essential for the smooth ejection of the tablet from the die cavity. When lubricating agents are blended with other excipients in the formulation, they coat powder particles with a thin and slippery layer. During compression, this layer combines with the cohesion between the particles of the powder blend, resulting in a decreased hardness of the tablet [52]. The nature and

concentration of the lubricating agent, mixing time and specific surface area are the factors that affect sensitivity to the lubricating agent. It is also affected by the deformation mechanism of material under compaction [55]. Materials with elastic or plastic nature are susceptible to the lubricating agent. Brittle materials prove very beneficial in case of lubricant sensitivity. During compression, brittle material will undergo fragmentation into many smaller particles and produce a large number of new surfaces. These newly formed surfaces are not coated with the lubricating agent and thus exhibit better hardness, even when a high concentration of lubricating agent is used [52]. Among the various lubricating agents, magnesium stearate is the most commonly used. It acts by reducing die wall friction during ejection of the tablet, helps to improve flowability, and minimises the powder's adhesion to surfaces of metal. However, due to its hydrophobic nature, it forms a hydrophobic layer on the surface of powder particles. This leads to a reduction in surface wettability, decreased dissolution rate, and a prolonged time of disintegration. Magnesium stearate also creates a hydrophobic interface on the powder particle surface and thus weakens the bonding of the powder mixture. These effects aggravate in case of high concentration of magnesium stearate, increased time of mixing and use of a higher proportion of plastic-deforming materials in the formulation. Therefore, the test for lubricant sensitivity is usually performed using magnesium stearate as a model lubricating agent. Lubricant sensitivity can be determined by compressing a blend of compression vehicles with an increasing proportion of magnesium stearate, and the compressed tablets are evaluated for the time of disintegration and % friability [28,56]. Fragmenting materials show less sensitivity to metal stearate due to "lubricant Free Surfaces" during compression. Plastic deforming materials will be affected as a lubricant layer on particles remains intact during consolidation [57].

Compactibility

It is an ability of a material under compressional force to form a coherent agglomerate. It can be assessed by evaluating the effect of compression pressure on tablet tensile strength. Tablets should exhibit good tensile strength to resist breaking or crumbling during logistics, handling, process or storage. The tensile strength is a measure of the bonding potential of the material and serves as one of the important “functionality parameters” for the selection of excipients [40].

Dilution Potential

A minimum amount of filler binder in the formulation blend is required to form tablets with adequate compactability and acceptable friability (<1%). The dilution potential may vary with the physicochemical properties of active pharmaceutical ingredients (API) and thus can be used as one of the important functionality parameters for selecting a suitable combination of API and filler binder. Dilution potential can be assessed by comparing the tensile strength of the tablets prepared by using varying ratios of drug and compression vehicles (Figure 10). Usually, paracetamol is used as a model for poorly compressible drugs to determine dilution potential [58,59]. The selection of appropriate filler binders with low dilution potential has generated significant interest [57].

Elastic Recovery

Elasticity is another essential property of the powder under compaction assessed to measure the increase in tablet thickness due to elastic recovery during ejection. Usually, axial elastic recovery (ER) is used as an assessment parameter to determine the elasticity of the compact particles. A higher value of elastic recovery indicates a reduction in bonding surface area, which may decrease the strength of the tablet. A Compact formulation blend containing materials with weak inter particulate attraction exhibits high elastic relaxation compared to a stronger inter particulate attraction. The ability of a tablet to withstand elastic recovery due to the release of stored elastic energy is one of the significant factors determining the compaction process's success [57].

Bonding index

The bonding index is an ability of a material to maintain a high fraction of the bond created during the compression. It reflects the tendency of a material to remain intact after compression. A higher value

of the bonding index indicates that the large portion of cohesive strength remains intact even after decompression, whereas a lower value represents a smaller cohesive strength. The bonding index of the compression vehicle can be determined by measuring the tensile strength and permanent deformation pressure of the tablet [40,51,59]. A material with a good bonding index gives a tablet with good mechanical strength. An ideal bonding index should be in the range of 0.001 to 0.06 [40].

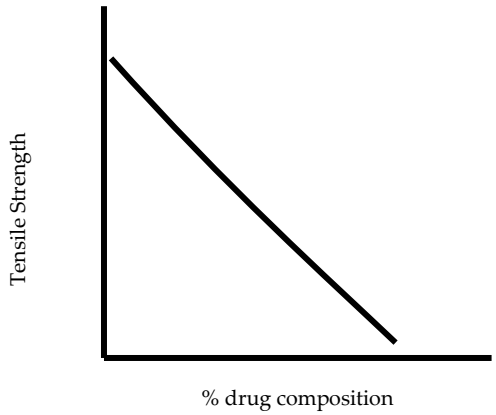

Figure 10. Graphical representation for determination of dilution potential.

Mathematical description of Compaction behaviour of solids

The compaction behaviour of solids can be studied by relating porosity, volume, density or void ratio with applied pressure. Such studies help predict the force required to formulate a compact of definite density. In 1923, Walker studied the relation of relative volume against applied axial pressure and proposed the equation as:

$$V_r = a_1 - K_1 InP$$

Where Vr is relative volume and P is applied axial pressure. Later, various researchers proposed several other mathematical descriptions of compaction by correlating applied pressure against density, porosity, void ratio and volume. Among these, equations proposed by Heckel and Kawakita are widely used [32,60,61]. According to the equation proposed by Heckel, the powder compression process follow first-order kinetics. If densification of powder is assumed as a product and powder porosity as a reactant, then the degree of densification of compact with increasing compression pressure is directly proportional to the porosity of the powder. Mathematically it can be represented as:

$$\frac{d\rho_r}{dp} = k\varepsilon$$

Where ρ_r is a relative density at pressure (P) and porosity (Ɛ) [32,60,61]. The ratio of a density of the compact at pressure (P) to compact density with zero porosity (i.e., true density) is referred to as relative density. Mathematically the porosity (Ɛ) can be represented as:

$$\varepsilon = \frac{V_p - V_0}{V_p} = 1 - \rho_r$$

Where V_P is the volume at any applied pressure and V_0 is the volume at theoretical zero porosity (i.e., true volume) [32,60,61]. Heckel plots are mainly used to identify deformation characteristics and mechanisms of consolidation. Past scientific literature shows that the materials that exhibit low mean yield pressures are deformed predominantly by plastic mechanisms, whereas the materials with higher mean yield pressure tend to be brittle and consolidated via fragmentation. Yield pressure can be calculated by using the formula (Py=1/k).

Where k is a slope of the linear portion of the graph of compression pressures versus reciprocal of relative porosities. Based on Heckel plots and compaction behaviour of materials, they can be categorized as type A, type B and type C (Figure 11) [32,60,61].

Materials under category type A are comparatively soft and can readily undergo plastic deformation with different degrees of porosity depending on their initial packing in the die. Type B materials are comparatively harder and exhibit higher yield pressures. They usually undergo compression by fragmentation to increase packing density. In the case of type C materials, it does not indicate a rearrangement stage, and densification occurs due to plastic deformation and asperity melting. The rate and duration of compression are the most common variables that affect Heckel analysis. In addition, results are also affected by the degree of lubrication, size and shape of tablet tooling. Thus, these variables need he consider during analysis [32,60,61].

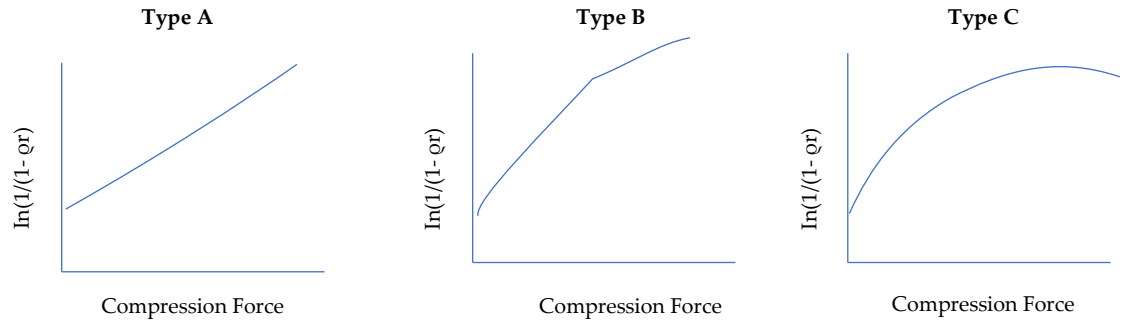

Figure 11. Heckel plots depicting compaction behaviour of materials.

The Kawakita equation is based on assessing the degree of volume reduction to investigate powder densification. Mathematically it can be expressed as:

$$C = \frac{V_0 - V_p}{V_0} = \frac{abP}{1 + bP}$$

or

$$\frac{P}{C} = \frac{P}{a} + \frac{1}{ab}$$

where V_0 is the initial volume of the powder bed and V_P is the volume of powder after application of pressure (P), a and b are constants that can be determined from the slope and intercept of the plot of P/C versus P, respectively (Figure 12) [32,60,61].

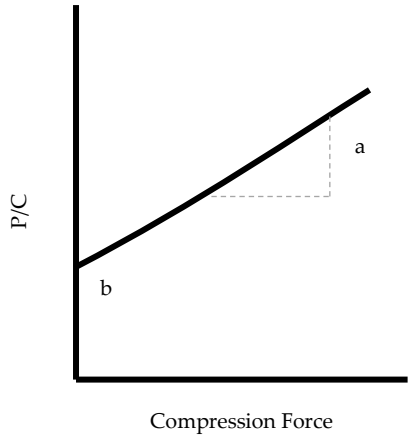

Figure 12. Kawatika plot representing degree of volume reduction against applied compression force.

The constant "a" is equal to the minimum porosity of the powder system before compression, while "b" (i.e., coefficient of compression) is related to the plasticity of the material [32,60,61].

Conclusion

Flowability, compressibility, bonding index and dilution potential are the parameters of critical consideration for compression vehicles to develop compressed solid dosage forms with good mechanical strength with ideal technical properties. These parameters may get affected due to changes in the particle level, bulk level and molecular level properties. The larger particles of the compression vehicle are responsible for high crushing strength, low friability, and low elastic recovery of the compressed solid dosage forms. In comparison, the desired proportion of smaller particles helps to improve flowability. The shape and size of particles of a compression vehicle significantly affect the bulk and tapped volume. Compression vehicles containing spherical shaped particles show higher tapped density than those with irregularly shaped particles. The extent of inter-particular void volume is dependent on the particle shape, particle size distribution and force of inter-particulate attraction. In addition to the parameters as mentioned earlier, the flowability of the formulation blend will also be affected by the acting inter-particular forces and the packing structure.

Crushing strength, friability, disintegration, and dissolution are the technological properties of compressed dosage form that may be affected by the filler binder's functionalities. The compressibility of powder is affected by the pattern of particle fragmentation and fracture. Consolidation of brittle materials occurs predominantly due to fragmentation, whereas plastic flow could be the reason for the deformation of plastic materials. Plastic and/or viscoelastic deforming materials usually produce tablets with higher mechanical strength at low speeds, whereas brittle materials remain unaffected by compaction speed. The compressibility of a powder will also be affected by the size of powder particles and applied compression pressure. The variation in compression ability between particle-size fractions decreased as compaction pressure increased. The ability of the tablet to withstand elastic recovery due to the release of potential elastic energy is one of the significant factors that determine the success of the compaction process. A high bonding index indicates a more significant portion of the mechanical strength remains intact after the removal of compression pressure, whereas a low bonding index indicates less of the mechanical strength remains.

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Authors Contribution

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Conflict of interest

The authors declare no conflict of interest.

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