A Review: Roller Compaction for Tablet Dosage Form Development

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ABSTRACT

Roller compaction is a dry granulation process device procedure in which the powders containing active ingredients and excipients are agglomerated between the compactor rollers. The dry powders of the active ingredients and excipients are combined in a blender during roller compaction, and further rollers are compacted and milled to form granulesThe resulting granules are then blended within in a blender and used for compression into tablets or for capsule filling. Compaction of powder is the term used to describe the situation in which these materials are subjected to some level of mechanical force. In pharmaceutical industries, the effects of such forces are very important in manufacturing of granule and tableting Particulate matter is compressed and densified in a roller compactor by rotating the material between two high pressure rollers. From a roller compactor, the densified material is then reduced by Frying to a uniform granule size. Roll compaction / dry granulation is a method of choice for the treatment of drugs sensitive to physical or chemical moisture, as no liquid binder is required in th. This analysis of the literature shows the development and use of RCDG in directly compressible excipient processing, drug compaction, and drug formulations. Avoiding deterioration caused by wet granulation, improving product quality, preventing segregation, reducing bulk volume, thereby decreasing storage volume and thus increasing transport efficiency and reducing possible environmental hazards. Dis-advantages of roller compaction are densification of the powder or particle which can adversely affects the dissolution of product and the powder to be compacted must be compressible or have to add compressible excipients or additives to the formulation. Sophistications available with roller compaction system are roller cooling or heating, vacuum de aeration, Separate feed funnel for small qua

Key words: Tablets, granulation, roll compaction, direct compression, wet granulation.

INTRODUCTION

For decades, oral pharmaceutical solid dosage types have been commonly used mainly because of their ease of administration and suitability to deliver drugs for systemic effects. Today the most widely used types of solid pharmaceutical dosage include granules, pellets, tablets, and capsules. Such dosage forms are either intended to enhance the physical and mechanical properties of materials during manufacturing and/or to provide a desired drug delivery mechanism. The tablets and capsules may be manufactured directly from powders, granules and pellets, or from several units coated with films. Tablets are now the most common method of dosage, accounting for about 70 per cent [1,2,3] .

The main purpose of roller compaction is to[32]:

- Improve powder flow properties.
- To avoid wet granulation induced degradation.
- To improve product stability.

- To prevent segregation.
- To reduce bulk volume hence minimizes storage volume and hence improves transport efficiencies.
- To reduce potential environmental hazards and ensures safety.

Recently roller compaction drawn attention of Pharma industry because of some advantages of dry granulation over other granulation techniques[32]:

- It is suitable for heat labile and moisture sensitive products.
- It improves flow properties of powders.
- It is economical process as it requires low personnel cost.
- It reproduces constant particle density.
- It is environment friendly.
- It prevents particle segregation.

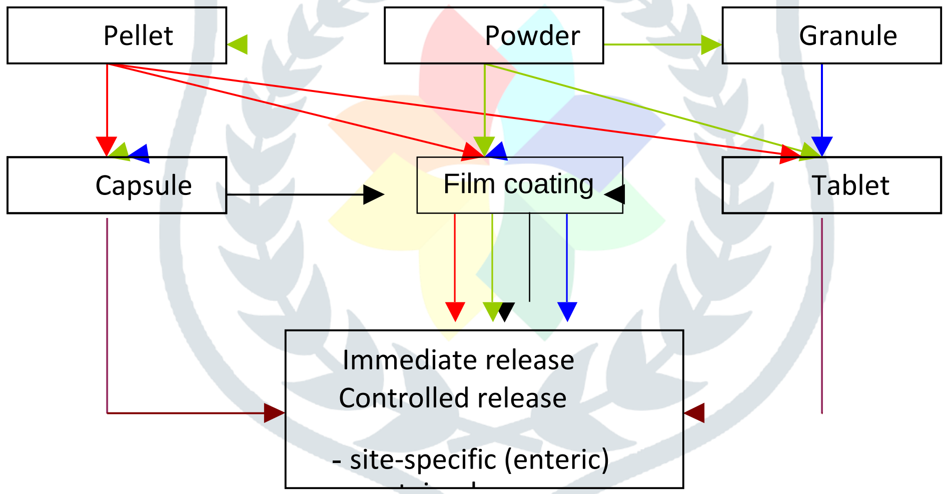


Figure 1 Relationship of pharmaceutical solid dosage forms

Tablets can be characterized as solid pharmaceutical dosing forms containing drug substances with or without acceptable diluents and prepared using either compression or molding methods. Tablets provide advantages for patients and manufacturers alike. Tablets are the most common dosage type thanks to their manufacturing simplicity and economy, relative stability and convenience in packaging, shipping.

Granulation

Granulation in the pharmaceutical industry refers to the act or procedure in which primary particles of powder are made to bind to form larger, multi-particle entities called granules. It is the mechanism whereby particles are brought together by forming bonds between them. Bonds are created by compression or the use of a binding agent. Granulation is used widely for tablet and capsule manufacture. The granulation process combines one or more powders and forms a granule that allows for predictability of the tableting process and will produce quality tablets within the appropriate tablet-press speed range. The key reasons for granulating powder for the manufacture of pharmaceutical dosage forms include avoidance of isolation of the powder mix constituents, improvement of the mix's flow properties and improvement of the mix's compaction properties. Hazardous material granulation may reduce the danger associated with producing hazardous dust which may occur when handling powders.[1] include prevention of segregation of the constituents of the powder mix, improve the flow properties of the mix and improve the compaction characteristics of the mix. The granulation of toxic materials will reduce the hazard associated with the generation of toxic dust that may arise when handling powders.

Effect of granule properties on tablet

The granule properties play a pivotal role in the final performance of a tablet; for example, granule size can affect the flow ability and hence, the average tablet weight and weight variation[4]. Having consistent flow of a granulation provides the needed avenues to control tablet weights. Consistent tablet weight will result in repeatable tablet hardness. Improved and homogeneous granulation will improve mixture, its flow ability, compressibility and therefore, improved disintegration with acceptable dissolution rate.

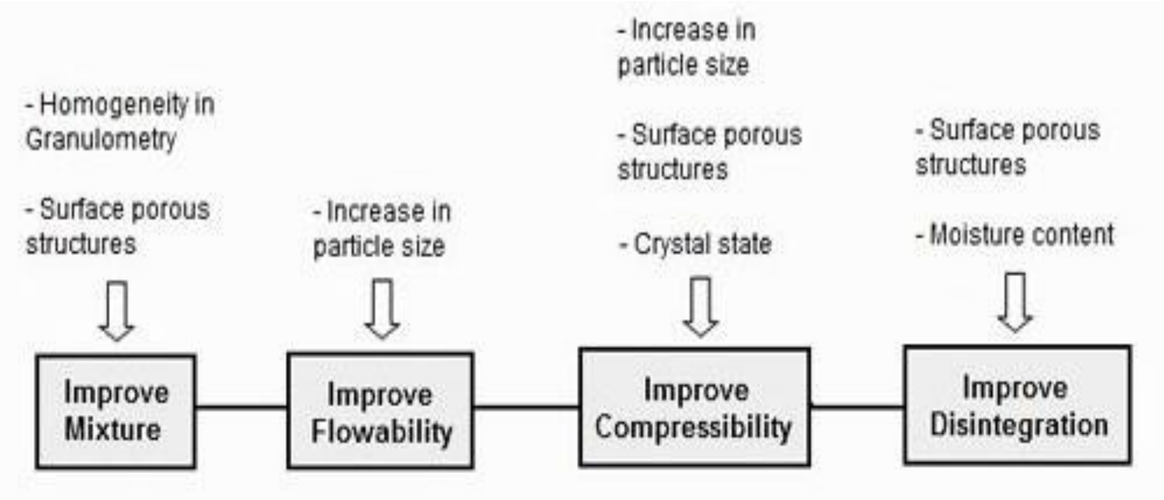


Figure 2 Effect of granules on physico-chemical properties of tablet

Methods of Granulation

The basic art of tableting comprises direct compression, wet granulation and dry granulation by three well-known methods. The numerous steps involved in the granulation process have a major impact on the particulate characteristics of the granulation resulting [7]

Direct Compression

The term "direct compression" is characterized as the method by which tablets are directly compressed from the API powder mixture and suitable excipients. Powder blend pretreatment by wet or dry granulation procedure is not required. Merits between the wet granulation process and the dry granulation process include a more effective process compared to other methods, as it requires only dry mixing and compaction of APIs and essential excipients, reduced processing time, reduced labor costs, less production steps, less equipment needed, less process testing, less power consumption. the stability but also the suitability for thermo labile and moisture sensitive API's particle size uniformity.[7]

Wet Granulation

A liquid binder solution in wet-granulation is combined with a bed of mixed powders to grind the particles into granules together. Then the damp mass is screened, dried, and milled to the desired dimensions. The mass may also be dry screened, lubricated and compressed or extruded through a perforated screen and then dried. During drying, a residual amount of humidity during. is also desirable.Wet granulation is facing a variety of inconveniences. A major downside is the number of separate steps involved, as well as the time and effort needed to complete the process. Further, the use of aqueous solvents is limited by the stability of the product to be granulated. Explosion concerns and environmental regulations may limit the use of certain organic solvents.[7]

Dry Granulation

Dry granulation can be used if there are sufficiently inherent binding or cohesive properties of the materials to form granules. Dry granulation refers to the granulation process, without the use of liquids. There are two dry granulation methods used in the pharma industry: slugging and roll compaction.[7]

Slugging method

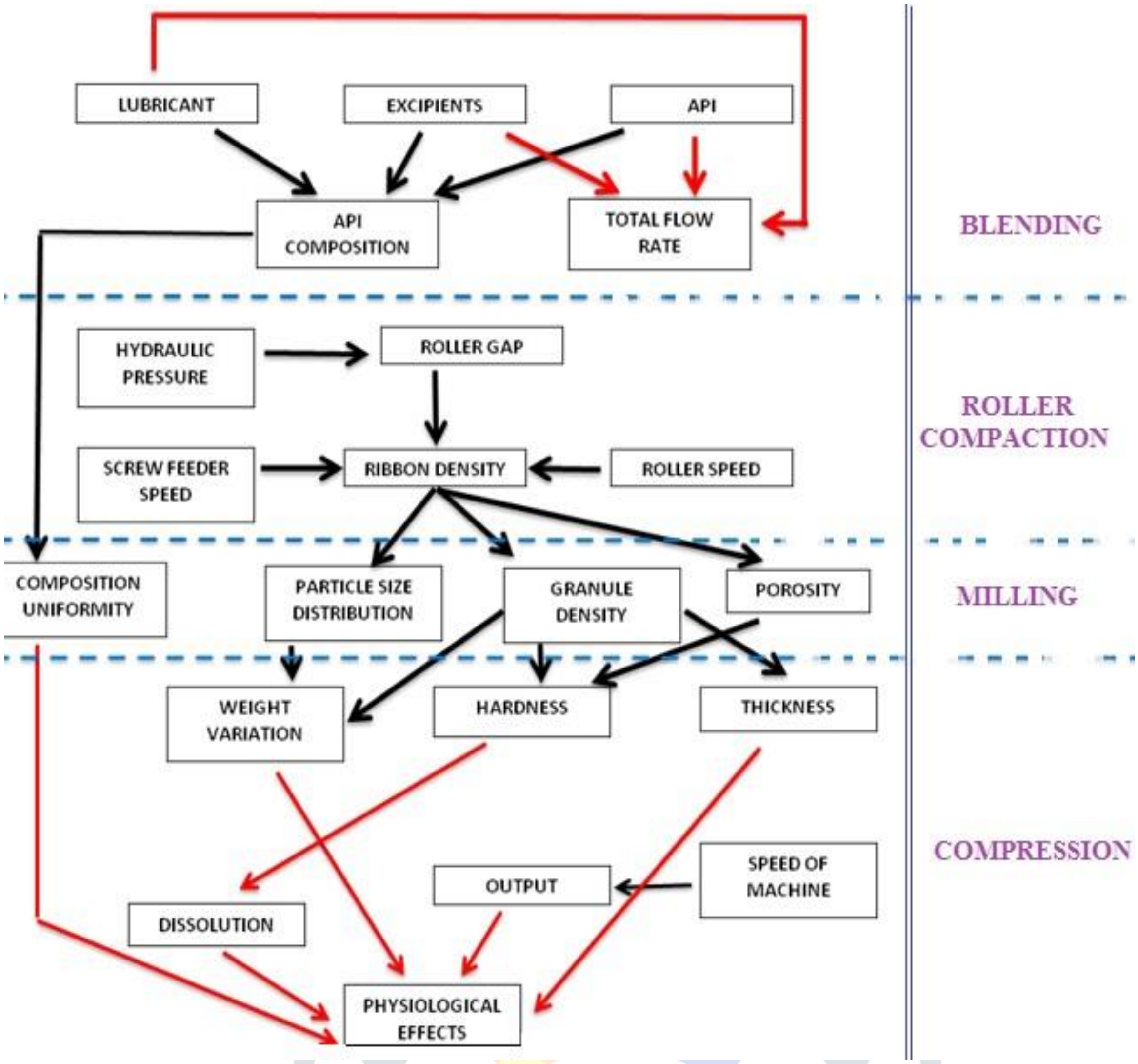
In "slugging" the material to be granulated is first made into a large compressed mass or "slug" usually using large flat-faced tooling by means of a tablet press. A fairly dense slug may be formed by allowing sufficient time for the air to escape from the material to be compacted. Compressed slugs are then comminuting through a desired mesh screen manually or automatically as for example by way Formation of granules by "slugging" is also known as precompression. When tablets are made from the granulated slugged material, the process is referred to as the double compression method.
Various disadvantages of slugging includes single batch processing, frequent maintenance changeover, poor process control, poor economies of scale, low manufacturing throughput per hour, excessive air, sound pollution, increased use of storage containers, more energy and time required to produce 1 Kg of slugs than 1 Kg of roller compact

Roller compactor method

Dry granulation may also be performed using a "roller compactor”. In a roller compactor material particles are consolidated and densified by passing the material between two high-pressure rollers. The densified material from a roller compactor is then reduced to a uniform granule size by milling.[9] Dry granulation roller compaction method is capable of handling a large quantity of material in a short time. Briquetting as a special subtype uses specially designed compaction rolls which divide the compacted powder into pieces (briquettes). For dry granulation the compaction force in extend and uniformity of distribution is essential in regard to uniformity of granules porosity Roll compaction is increasingly being used as a granulation technique because of its benefits, but it is not a easy process and can involve several variables such as roll strength, roll speed, horizontal / vertical feed screw speed, roller gap and screen size. Such parameters must be adjusted according to the materials and the type of equipment used to obtain desirable goods. Another granulation method now a day’s coming into importance is melt granulation. Melt granulation is a process by which powders are agglomerated with the aid of a binder, in either a molten state or a solid state that melts during the process. The apparatus of choice is a high-shear mixer, where the temperature of a powder can be raised above the melting point of a meltable binder by either a heating jacket or frictional forces generated by the impeller blades. Determination of the granulation end-point regarding temperature is crucial for the melt granulation. Therefore the process is difficult to control. Furthermore, often the granulation mass adheres to the walls of the granulator bowl generating a not uniform mass regarding distribution of the components, content uniformity of the API and particle size distribution[9]

Advantages of Roll Compaction/Dry Granulation Process

Roll compaction is a method of choice for processing drugs that are prone to physical or chemical moisture, because no liquid binder is needed in the granulation. This is suitable for compounds that have either a low melting point or rapidly degrade during heating, since the method does not involve any drying step.[10] RCDG is a useful processing method for drugs with low and inconsistent bulk and tap densities, with very small and inconsistent particle sizes and/or weak flow properties and poor performance. RCDG leads to reduced batch to batch variability due to online monitoring and automation of processing settings with improved product qualityThe method is theoretically more easily scalable, and due to continuous production with high efficiency and lower energy usage will minimize development times. Roll compaction can handle high drug loads enhancing flow and material uniformity as well as preventing segregation when compared with direct compression that can cause problems with high dose drugs, particularly for low bulk drugs RCDG results in granules that form porous tablets thus allowing water to penetrate more easily into the tablet. This leads to improved disintegration behaviour of tablets. There is reduction in a material loss during processing and capping tendency of tablets. The selection of the granulation method should be done on the basis of the physico- chemical properties of the active pharmaceutical ingredient and required excipients used for its formulation[9,10,11,12,13,14,15]



Basic Process of Roll Compaction/Dry Granulation (RCDG)

Functional principle of roll compaction

Roll compaction is an agglomeration process in which powder is fed through two equal diameter counter-current rotating rollers either by gravity or by means of a screw feeder. The friction between the material being processed and the roller surface brings the powder to the narrow space between the roll (nip region), where the powder is subjected to high stress that results in the formation of compact If the rolls are smooth or fluted or knurled, the material is compacted into dense ribbons (flakes, sheets, strips), whereas pocket rolls will form briquettes.[11,16] If in-line granulator/mill system is available with the system, it will mill ribbons or briquettes into granules otherwise densified sheets (ribbons) can be dry-sized by an oscillating mill, cone mill or impact mill The production of either briquets or granules depends on the application.[13,17,18] Usually, briquets are produced when large, dense agglomerates are required. Granules are produced when smaller, uniform particles are required for further processing. The granules formed are typically an intermediate type of the substance and are subsequently fed to a compression machine to ensure a more effective feedingstuff filled into capsules.[19,20]

The main bonding mechanism involved in compact formation includes strongest solid bridges between particles, weaker intermolecular / long-distance attraction forces (van der Waals forces, electrostatic forces, hydrogen bonding) or mechanical interlocking that indicates the hooking and twisting of irregularly formed particles.[21] The most dominant bonding for pharmaceuticals is long distance forces, especially van der

Waals forces and hydrogen bonds in some cases whereas; relatively simple molecular structure and plastic deformation e.g. sodium chloride are the prerequisite for solid bridges.[15] During roll compaction, the powder blends are fed into the gap between two rollers (compaction zone) which is divided into three regions namely slip or entry region, nip region and release region. The regions' boundaries are defined by their angular positions. In the slip or entry area, powder starts to travel, but at a speed that is lower than the speed of the roll, thus suggesting that slips are called "slips." Particle rearrangement and de-aeration may occur, but the pressure exerted on the powder is relatively small. Entry angle, θh defines the start of this region and correspond The area of the nip ends at a roll angle α, (nip angle), when the powder's wall velocity is equal to the rolls. The powder is 'nipped' and due to the decrease in the distance, densification occurs. This results in a noticeable increase in roll pressure. The release area starts when the roll gap starts to increase again and its size depends on the elastic stresses contained in the roll gap[20,22]

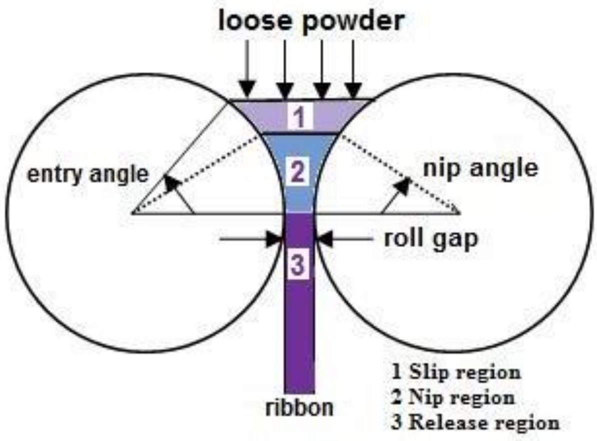


Figure 4 Schematic of the main regions during roll compaction

Requirements for roll compaction

For successful granulation by RCDG technique following conditions should be satisfied : adequate supply of the powder to the nip region and entire conveying of powder entering from nip region into the narrowest part of the roll gap. Uniform distribution of the compaction pressure over the whole roll-gripped mass. Adequate, effective and uniform de-aeration of powder mass via vacuum before it reaches the nip region. Material to be processed should be compressible, should have consistent increase in density with force, suitable for milling operation and recompression, if required[8,14].

Design of Roll Compactors

The roll press/compactor basically consists of a feed system which conveys powder to rolls, a roller compaction system which densifies/compacts loose powder into ribbons or briquettes and/or in-line granulator/mill system which mill ribbons or briquettes into granules and optional accessories to improve process control and automation.

Feed system designs

Feed systems play a critical role in effectively creating compact process parameters and monitoring them. Non-uniform filling / conveying can lead to poor compact quality, excess fining generation, and more uncompacted materials. Two types of feed system are used to distribute powder viz. Gravity feeding using hopper or force feeding with feed and screw feeder. The use of gravity feeding by a simple hopper, with a simple flap hopper and gravity feeder with flap distribution box, can be recorded when the powder is dense and free flowing. For fine and flaccid powders with poor flow capacity and inconsistent bulk density, a feeder is needed to provide the powder with pre-compression force as it enters the roller press. This force increases the friction between the powder and the roll surfaces to improve compaction. Two basic types of screw feeders can apply this force: single screw feeder. [23,24 (Hosokawa Bepex GmbH) and double screw feeder (Gerteis Maschinen + Process engineering AG, the Fitzpatrick Company) For larger roll widths double screw feeder system is convenient to feed powder uniformly across the entire roll**.** The horizontal screw fixed in the powder reservoir[26] conveys powder from the feed hopper to the vertical screw (temping screw) and each vertical screw partially de-aerates, pre-compresses and force-feeds the powder down into the nip region[26].Technological developments in feed systems have culminated in the implementation of a proprietary combi vent feeder consisting of an integrated whole package with the feed hopper with an inside stirrer, the screw feeder and the vacuum system. The stirrer inside the hopper ensures even flow of powder into the feeder for the screw. The vacuum system facilitates complicated transport, high volume and fluidizing transport...[26]

Roller unit

The roller unit includes two equal diameter counter rotating rollers. Two different types of roll compactors are commercially available: fixed gap systems and those which allow variable gap size due to moveable rolls (Gerteis Maschinen Process engineeringThe gap width between rollers is pre-defined and fixed when roll compactor with fixed rollers is used. In these systems material flow is controlled by screw feeder speed only to get a constant densification of the material between two rollers. In latter system even compaction force is achieved by control of both the gap width and the screw feeder speed. Additionally, movable gap systems have less bypass propensity. By changing roll gap, density profile of the compacts can also be changed with changed robustness of the granules which subsequently effect mechanical properties of the tablets.[28,29]. In fixed gap systems ribbons of same geometrical dimensions are produced but non- homogenous powder feed between the rollers is observed which leads to a change in porosity of the produced ribbons and variation in compaction pressure is also observed. This may lead to non desirable changes in product quality. In variable gap systems, at a given compaction pressure, actual gap size mainly results from screw feeder speed, roll speed and density of the fed powder. Thus, transportation of non-free-flowing powder and resulting changes in powder density may only lead to gap size variations which causes non-uniform ribbon thickness, with negligible effects on porosity due to maintenance of constant compaction pressure[28]. Bypass is un-granulated material that circumvents the rolls completely, or passes between the rolls without being adequately compacted and is major cause of segregation of blend and consequently content uniformity. Three major factors affecting bypass include roller surface roughness / design

Roll surface roughness/design

In maintaining a back pressure on the powder flow, the roll surface is important so that the powder does not pass through the nip region faster than the rolls turn. Bypass can be minimized by using rolls with greater roll rughness or by using (knurled) textured surfaces. There are three different types of continuous ribbon rolls with different surface designs for the maintenance. [30]

Roller orientation

Three types of roll orientation are commercially available as shown in figure 5

- Horizontal orientation: available from Hosokawa Bepex GmbH, The Fitzpatrick company, Freund Industrial Co.
- Vertical orientation: available from Alexanderwerk AG
- In-cline orientation (position between horizontal and vertical): available from Gerteis Maschinen + Processengineering AG

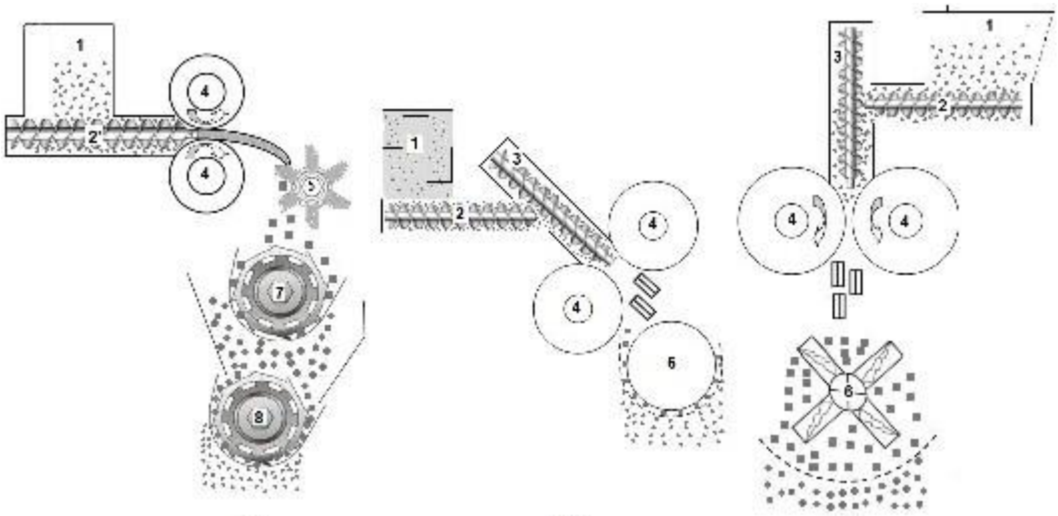


Figure 5 Sketch of a roll compaction process using three different roll orientations

(A) Vertical, (B) Inclined, (C) Horizontal

1: Filling hopper, 2: Feeding auger/screw feeder, 2': Screw feeder, 3: Tamping auger, 4: Rolls, 5: Flake crusher, 6: Granulator, 7 and 8: Two stage diagonal granulation system using coarse and fine granulator, respectively.

The roll orientation plays significant role in generation and minimization of bypass. In horizontal roll orientation the loss of material due to bypass is high as compared to other designs. Loss of un-compacted material is minimal in vertical orientation due to independence of feed to gravitational forces. The use of inclined roll orientation decreases bypass from 15-20% to 7%[27]. In horizontal orientation material may remain in nip region for certain, uncontrolled time period which may negatively affect ribbon uniformity. Incorporation of side seals (sealing strips) in compactor design reduces material bypass but this does not have significant effect to reduce material passing through the rolls without being sufficiently compacted.[28,31]

Vacuum de-aeration

This is an optional feature and usually applied during feeding to remove excess air from a fine powder with low bulk density. The application of vacuum eliminates entrained air that can cause the powder to resist the pre-compression force applied by the screw feeder. This technique is particularly useful for process with no screening or recycling steps or for greatly increasing the compaction efficiency of roll compactor. Vacuum de-aeration requires a vacuum pump system which is linked to the feeder and removes the powder's entrained air through a filter before the powder enters the roller press[19].

Granulator/mill system

Granulation/milling of ribbons or biquerette obtained from compaction can be done using an in-line oscillating rotor-granulator or separate granulation in an oscillating mill, a cone mill or impact mill. In most of the equipments in-line granulator can be used in two ways viz. use of coarse and fine (two stage) granulator (WP120 Pharma, Alexanderwerk AG, Germany) to get desired sized granules or use of fine (single stage) granulator (WP150 Pharma, Alexanderwerk AG, Germany) in which fines and oversize are separated using sifter and recycled via vacuum conveying system. An in-line rotor granulator system consists of a rotor that runs in a conventional U-shaped or diagonal positioned screen. The rotor pulls the material into the working gap and crushes it allowing the material to pass through the desired mesh size. By the use of diagonal oriented screen output is increased due to more mass holding of the material against the screen as compared to conventional U-shaped screen.[1]

Accessories

In some roll compactor systems a pre-breaker/flake crusher is located between rolls and granulator for coarse crushing of compacted ribbons/flakes. While in others gravity feeder or screw feeder does not provide enough flow of the powder material therefore use of feeder vibrator can be worthy. Feeder vibrator breaks stagnant powder bed and assists their flow toward rollers and help in densification and de-aeration of the powder[9]. Increase in temperature during compaction may harm product quality especially in case of temperature sensitive drugs. Roll cooling system can be used to cool the system.

Conclusion

This analysis shows the effect of several roll compactor variables, e.g. hydraulic strength, roller speed, roller distance, roller size, granulator speed and screw feeder speed on the product's deliverable granule properties. Flowability, bulk and tapped densities, particle size distribution are the deliverable properties studied in the granules.

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