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REVIEW ARTICLE

Roller Compaction for Solid Dosage Form Development and its Application – A Review

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ABSTRACT

Roller compaction is a dry granulation innovation in which powder is densified between two counter pivoting moves by the utilization of mechanical weight as powder goes through the rolls. Dry granulation process powders comprise of the active pharmaceutical ingredient and excipients, e.g., diluents, disintegrants, and ointments, are blended in appropriate blender. The powder blends are then roller compacted and estimate diminished to shape granules. Roller compaction is generally want to overcome unfavorable physical properties of powders and APIs, for example, poor stream, low mass thickness, mix consistency, isolation of powder mixes by upgrading process parameter and choice of excipients. Roller compaction process has noteworthy impact on particles size appropriation, flowability, homogeneity, compressibility, compactability of dynamic pharmaceutical fixings and excipients and therefore can influence thusly disintegration profile, breaking down time, hardness and other post pressure parameter of tablet. Roller compaction process offers favorable as contrasted and wet granulation process, for example, basic assembling technique, less demanding scale up, high volume generation yield, and generally low operational expenses. Roller compaction process prohibits fluid dissolvable or binder solution. This procedure is additionally vitality effective and reasonable for preparing pharmaceutical agents that are sensitive to moisture and heat. Great quality granules can be gotten by upgrading roller compaction process parameter, for example, pressure power, roller speed, screw feeder speed, roll gap and milling.

KEYWORDS

Roller Compaction, Dry Granulation, Pharmaceutical Technology, Solid Dosage Form

INTRODUCTION

Many oral solid dosages form including active pharmaceutical substances excipients and are passed through multiple processes of manufacturing and end with final product i.e. Tablets or capsule filling. The pharmaceutical industry uses various granulation methods to

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density small powder particles and enlarges into larger ones that improve flow properties of powder without segregation so that the material can be processed effectively and efficiently into oral solid dosage forms. Two pharmaceutical methods of granulations are wet Granulation and dry granulation[1,2].

Roller compaction process is a unit operation in dry granulation in which the powders containing active pharmaceutical ingredients and excipients are agglomerated within the rollers of compactor to form granules which have good flow

properties and stability[3]. During the dry granulation by roller compaction process the dry powders of the active pharmaceutical ingredients and excipients, e.g., diluents, dry binders, lubricants and disintegrants are mixed in a blender. These powder mixtures are roller compacted and size reduced to form granules[4,5]. The resulting granules are then blended with lubricant and either compressed into a tablet or encapsulated. During the roller compaction process, API and all the excipients are uniformly mixed to form powder blends and are passed through the gap between a pair of rotating compression rolls continuously to form solid ribbons or sheets. Such ribbons or sheets are passed through a mill or granulator equipped with screen of suitable mesh size to form uniform dry granules[6].

Roller compaction is usually composed of screw feeder or gravity feeder, feed hopper, flake crusher, two counter rotating rollers of equal diameter, and screens for milling process[7].

Main Purpose of Roller Compaction

- Roll Compaction improve powder flow properties.
- To avoid wet granulation this may induced degradation.
- To improve final product stability.
- To prevent segregation.
- To reduce bulk volume of final blend hence minimizes storage volume and hence improves transportation efficiencies.
- To reduce environmental potential hazards and ensures safety.

Advantages of Dry Granulation by Roller Compaction

- Simplicity of manufacturing procedure.
- It prevents particle segregation.
- It improves flow properties of powders.
- It reproduces constant particle density.
- Easier scale up and large production output.
- It is suitable for heat labile and moisture sensitive products.
- As compared to direct compression, roller compaction process can run more efficiently with high drug loading, improve flowability, and content uniformity without material segregation.
- It is economical process as it requires low personnel cost.

It has some disadvantages as well

- Roller compaction densifies the powder which can adversely affects the dissolution of product.
- The powder to be compacted must be compressible or have to add additives or compressible excipients to the formulation[8,9,10].

Roller Compaction Theory

Roll compaction is a granulation process in which powder is densified by passing through two equally diametric counter rotating rollers. Powder mixture which is to be compacted reaches to roller from screw feeder with different mechanisms. Powder passes through three different regions as the power get compacted. The Boundaries between the regions are defined by their angular positions.

Slip Region (Feeding Zone)

The slip region is the region close to the feeding of the powders. The slip region is effectively related to wall friction and interparticle friction of the feed. Material starts to move downward at a rate less than the surface speed causing the formulation “slips”. In this region particle rearrangement and de-aeration may occur, but the pressure exerted on the powder is relatively small in this region as compared to nip region[10].

Nip Region (Compaction Zone)

In the nip region, the material is subjected to maximum stresses between two rolls leading to the formation of solid compact or sheet. In this region powder moves at the same speed as that of roll surface. To achieve acceptable compaction, the nip angle must be sufficiently large.

Densification occurs due to the decrease in the gap and results in a significant increase in the roll pressure[11].

Extrusion Region (The Release Region)

In release region there is great decrease in pressure as roll gap starts to increase again as the compact is ejected and can expand due to elasticity. The compacted ribbon exhibits relaxation as pressure is released from the rolls. The beginning of the ejection region is sometimes referred to as a neutral point because it sets the boundary between the region where the material moves at the same speed as wall surface it comes in contact with and the region where the material moves faster than the roll[12].

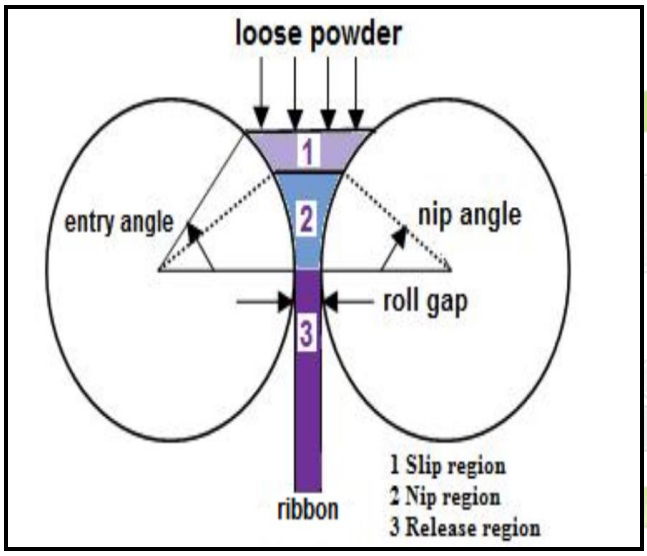

Figure 1: Schematic of the main regions during roll compaction

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[13].

Feed System Designs

Feed systems play a vital role in successful formation of compact and control of process parameters. Non-uniform filling/conveying may possibly lead to poor compact quality, generation of excess fines and more un-compacted materials[14]. Two type of feed system are used for powder conveying viz. gravity feeding by use of hopper or force feeding using feed hopper and screw feeder. When the powder is dense and free flowing, gravity feed system can be used reported the use of gravity feeding by a simple hopper, with a simple flap hopper and gravity feeder with flap distribution box[15]. For fine and fluffy powders having poor flow ability and inconsistent bulk density, a feeder is required to provide pre-compression force to the powder 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 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[16]. The horizontal screw fixed in the powder reservoir 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[17].

Technological advances in feed system have led to the introduction of patented combivent feeder which consist integrated whole unit having the feed hopper with a stirrer inside, the screw feeder and the vacuum system. The stirrer inside the hopper ensures even powder flow towards screw feeder. The vacuum system assists transport of difficult transportable, high voluminous and fluidizing materials. Further, fines/over sizes or additional additives can be uniformly re circulated into the process due to the availability of additional feed hopper chamber[18].

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 the 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[19].

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 nonfreeflowing powder and resulting changes in powder density may only lead to gap size variations which causes nonuniform ribbon thickness, with negligible effects on porosity due to maintenance of constant compaction pressure[20].

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 which influence bypass includes roller surface roughness/ design, roll orientation and vacuum de-aeration[21].

Roller unit consist of two equal diameter counter rotating roller through which powder is passed and get compacted. Rollers create pressure on powder material and converts into compacted ribbon. Two types of roller compactors are available according the nature of the gap between two rollers, those two types are roller compactor with a fixed gap system and roller compactor with variable gap system. In fixed gap system powder feed is controlled by screw feeder and in variable gap system powder feed is controlled by width between rolls and screw feeder[22]. Rollers are oriented on the machines in different ways and they varies from manufacturer to manufacturer.

A) Roller Orientation

Three types of roller orientation are commercially available.

a) Horizontal Orientation

This is most commonly used orientation design. In these design rollers are arranged horizontally. Also it should be noted that the roller orientation defines feeder orientation as well[23]. Usually in Horizontal orientation of rolls material loss is high from bypass. Bypass occurs because material may remain in nip region for certain, uncontrolled time period. This also negatively affects ribbon density as well. Incorporation of side seal in compacter design reduce material bypass. Vertical or inclined feeders are used for horizontally aligned rolls. E.g. Hosokawa Bepex GmbH, The Fitzpatrick Company, Freund Industrial Co.[24].

b) Vertical Orientation

In vertical orientation direct bypass through rolls is minimised because material movement is not governed by gravity feeding system. Due to the advantage of less bypass of material, this vertical design is preferred for low dose product[25].

c) In-Cline Orientation

In In-cline orientation (position between horizontal and vertical) Such type of design reduces bypass of material up to 10- 15 %. E.g. Gerteis Maschinen[26].

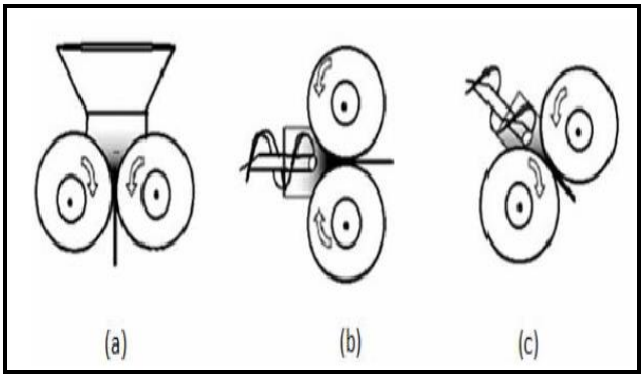

Figure 2: Roller orientation

B) Roll Surface

Roll surface is also important in maintaining flow of powder material through nip region. When the roll speed is fast, back pressure is created on the powder leading to the improper flow of material through nip region. Rough roller surface reduce the by-pass material. Types of roll surfaces are smooth, corrugated and fluted rolls. Corrugated and smooth rolls are the most commonly used in pharmaceutical industry. Smooth rolls can minimize sticking problems. Corrugated rolls are therefore particularly suitable for increasing bulk density of fluffy, light, aerated materials[27].

Flake Crusher

Flake crusher is located between granulator and roll. Flake or Compacted Ribbon which comes out from roller is crushed by flake crusher and converts in to smaller size pieces. Flake crusher improves material flow by crushing of flakes or compacted ribbon. The Flake Crusher is mainly designed for dust free processing[28].

Milling or Size Reduction

Milling is process in which the ribbons formed during compaction which is crushed by flake crusher to form different size compacted pieces[29,30]. These different size pieces is required make uniform particle size by using appropriate size screen[31]. Different mill screen orifice size used may be varying with blend to blend for size reduction. Milling improves flowability, particle size distribution, content uniformity and reduce segregation[32]. Screen located directly under the blade or scraper, prevents particles to leave the chamber which are larger than screen orifice size. Size reduction equipment is classify based on according to the way in which forces are applied, impact, shear, attrition and compression[33].

Table 1: Type of mills

Force	Type of Mill
Shear	Cut mill
Impact	Cut mill, Hammer mill, and Screen mill
Attrition	Ball mill
Compression	Jaw crusher and conical screen mill

Vacuum De-aeration[32]

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 precompression 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 deaeration 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.

Feeder Vibrator[33]

To maintain proper uniform continuous flow of feed material powder especially in case of a poor flow powder, a simple gravity feeder and force feeder may not work to be good enough. Installation of a feeder vibrator can be an easy and effective way to improve the flow. By providing a constant driving force, feeder vibrators can break the stagnant powder bed, drive the powder toward the rolls, and help densification and deaeration.

Temperature Control[33]

When powder bed is in rotation condition, the screw flight can generate a lot of heat. Excessive heat may elevate the local temperature, in a highly packed powder bed, and cause the powder to be partially melted and stuck to the flight. This may cause batch failure. In such case, special flight with a cooling jacket can be used to improve processibility[34].

Functional Principle of Roll Compaction

Roll compaction is an agglomeration/granulation process in which powder is fed by either by means of a screw feeder through two equal diameter counter currently rotating rollers or gravity[35]. The friction between the material being processed and roller surface brings the powder towards the narrow space between the roll (nip region), where the powder is subjected to high stresses which leading to the formation of compact[36]. If the rolls are fluted, smooth or knurled, the material is compacted into dense

ribbons (sheets, flakes, strips), whereas pocket rolls will form briquettes. If in-line granulator or milling system is available with the system, it will mill briquettes or ribbon into granules; otherwise densified sheets i.e. ribbons can be dry sized by a cone mill, impact mill or oscillating mill. The production of either granules or briquettes depends on the application. Usually, Granules are produced when smaller, uniform particles are required for further processing. Briquettes are produced when large, dense agglomerates are required[37,38]. The produced granules are usually an intermediate product form and subsequently will be fed to a compression machine to ensure more efficient filled into capsules or feeding.

The main bonding mechanism involved in compact formation i.e. compaction includes weaker attraction intermolecular/long distance forces (van-der Waals forces, hydrogen bonding, electrostatic forces) or strongest solid bridges between particles, or mechanical interlocking which denotes twisting and hooking of irregularly shaped particles or granules. The most dominant bonding for pharmaceuticals is long distance forces, especially hydrogen bonds and van der Waals forces, whereas; plastic deformation and relatively simple molecular structure e.g. sodium chloride are the prerequisite for solid bridges[39,40].

During roller compaction, the powder blends are fed or poured into the gap between two rollers (compaction zone) which is divided into three regions namely entry or slip region, nip region and release region. The boundaries between the regions are defined by their angular positions[41]. In the entry region or slip region powder starts moving but at a speed slower than the roll speed, thus indicating that slips occur therefore termed as "slips". Particle rearrangement and de-aeration can occur, but the pressure applied on the powder is relatively very small. Entry angle, **θh** define as the start of this region and corresponds to the angular position at which there is presence of a finite roll pressure. The nip region starts at a roll angle α, i.e. (nip angle), when the wall velocity of the powder becomes equal to that of the rolls. The powder is 'nipped' and further densification occurs due to the decrease in the gap between them. This may results in a significant increase in the roll pressure. The release region starts when the roller gap starts to increase again and its size depends on the release rate of compact, the roll speed and stored elastic strains in the compact[42].

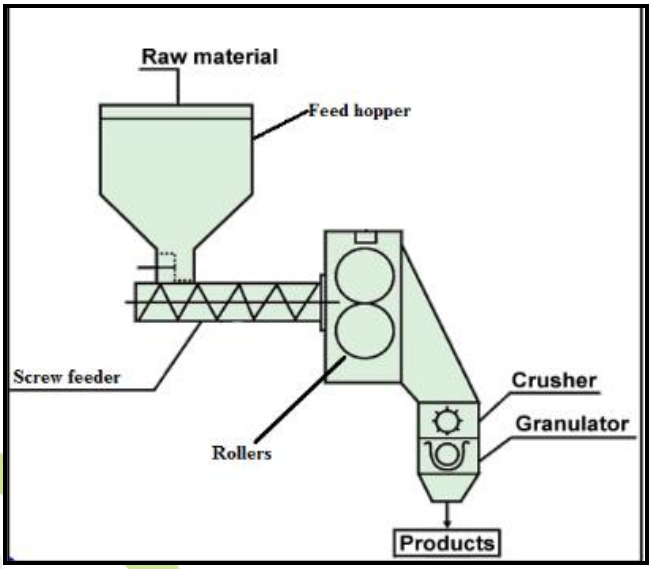

Figure 3: General diagram of roller compactor

Factors Affecting Efficient Granulation by Roll Compaction

Three types of variables such as equipment variables, process variables and formulation variable control the successful granulation by roll compaction as given in fig. No. 4[43].

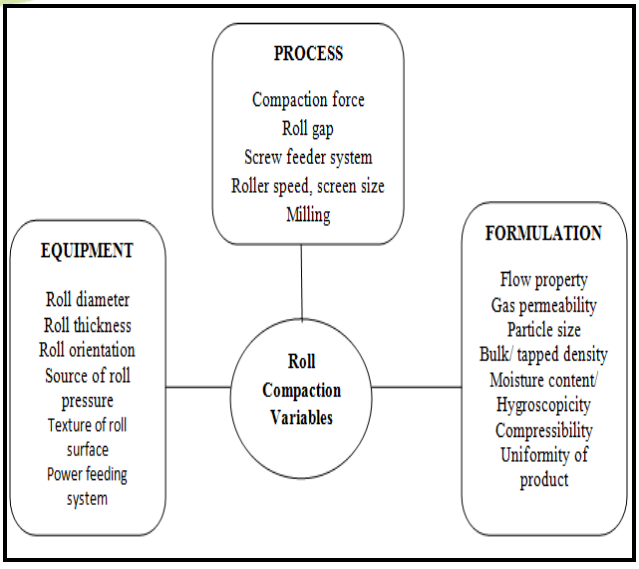

Figure 4: Summary of factors play vital role in efficient granulation by roll compaction

Impact on Process Parameters

Roller compaction process parameters have significant effects on the ribbon quality, granule flowability, and process feasibility and blend uniformity. Roller speed, compaction force, feeder screw speed, screen size, and roll gap are the critical parameters needed to be optimized to improve product quality.

a. Screw Feed

Screw speed is one of the critical process parameter in the roller compaction. Optimum range of screw speed depends upon roller speed, powder material flow and roller gap. At low screw speed, material reaches in nip region in insufficient quantity resulting in the formation of ribbons with low strength. At High screw speed it may cause a highly densified zone in the nip region, and cause caking or melting of particles on the flight. High screw speed is usually not solution for poor flow materials. Generally the feed rate should be equal to or near to the rate of discharge[44].

b. Roller Gap

Roller gap is the distance between two rolls at their nearest point. This is also one of the critical parameter of compaction and one that needs to be stabilized by the process parameters mentioned above. It is in a function of pressure applied to the rolls and the amount of material that is passed between them. Roller gap exhibited a significant impact on granule flowability, ribbon density, granules content uniformity and ribbon hardness. When decrease of roller gap; roller compaction force increases[45].

c. Compaction Force

For compact the loose powder, sufficient Compaction force is required. Powder gets densified under pressure and bonded to form Ribbon. Ribbon density increases, at increasing roller pressure at certain limit, granules mean particle size, granule flowability. Optimum compaction force which gives best quality granule may vary with mixture of material. Over compaction force may break the ribbon which results in poor quality granule that may create tablet compression problem such as capping, low hardness and high friability[46].

d. Roller Speed

Roller speed is inversely related to dwell time for particle compaction which affect mainly ribbon density. Roll speed needs to be adjusted in accordance to flow of powder and feeder screw speed. Material passing through rollers is being inadequately compacted; when roller speed is high, ultimately results in blend segregation and consequently loss of content uniformity[47].

e. Milling

Desired sized granules are required for uniform particle size distribution, good flowability, compressibility. Ribbons size gets reduced by applying force which results in desired size granules. The mill screen orifice size directly impacts particle size distribution which can potentially impact flowability and granule uniformity. If excessive fines are produced during milling process, it densifies the blend and may affects flowability. Excessive generation of fines subsequently affect on tablet hardness, content uniformity in tablet compression[48].

Impact on Equipment Parameters

Selection of variables associated with equipment like roller diameter and thickness, its orientation (horizontal, vertical or inclined) and texture is important to maintain consistency in drug formulation. Similarly increase in automation level of the system like availability of automatic powder feeding system, cooling of the rollers and machine to prevent excessive heat up is required with increase in batch size. For efficient granulation by roll compactor; roll compactor having roll width 4.4 and 1.9 cm, and roll diameter 15 cm and 20 cm, respectively. At constant linear roll force speed and constant compaction force/unit length no change in granulation quality was observed in terms of mean particle size (d50) and bulk density at low to medium range roll speed while these decreased at high roll speed mainly due to a decrease in dwell time which allowed less time for formation of bonds between particles[49].

Impact on Formulation Parameters

Formulation and development of product by Roller compaction is initiated with studying physical and chemical properties of drug Substance and excipients. Afterword's challenges involved in the formulation development are identified. Challenges would be high drug loading, poor flow, poor compactibility, high compressibility, low density etc.

Proper selection of formulation composition and excipients level can balance the poor physical properties of drug substance, thus greatly improve the processiblity of the powder mixture.

Size enlargement of fine particle by binding of particles is the important factor in roller compaction[50]. For roller compaction process selection of powder material is very critical.

Table 2: Major Challenges in roller compaction and their suggested solutions

Sr no	Problem	Possible Cause	Possible solution (Remedies)
1	Large fine particle fraction/ leakage of un-compacted materials between two roller seals (Bypass)	Air, occupying the voids between the particles i.e. air entrapment. Granules formation is strictly related to compressibility of the material (under high compression force as-contrary to wet granulation-capillary forces do not contribute to the binding mechanism therefore high fines fraction. High roller speed. Improper granulator speed and compaction force.	Recycling of fines. Use of vacuum screw feeder system which have de-aeration effects. Instead of flat rolls Use of concavo-convex rimmed shaped rollers to obtain less dust production. To reduce leakage of un-compacted powder, Use of side sealing plates. Controlled addition of water to formulation before roller compaction to reduce dust. Multiple compactions. Use of inclined roller orientation. Optimize roller, granulator speed and compaction pressure.
2	Poor tensile strength of tablet processed by Roll compaction (Loss in Tabletability/ Compactibility)	Work hardening phenomenon. Particle size enlargement. Limited binding potential of process material which is partially consumed in first compression step.	Addition of brittle excipients in formulation. Decrease the particle size of raw material. Formulation of small granules. Limiting the compaction pressure only to a degree necessary to get desire granules characteristics.
3	Sticking/ adhesion of materials on to the rolls of Roller compactor	Cohesive/hygroscopic nature of raw material. Improper roll configuration. Improper scraper adjustment. Melting of products due to heat generation.	Addition of lubricants, multiple compactions. Decrease clearance between scrapers and rolls. Use grooved rolls or smooth rolls. Roller cooling to decrease temperature.
4	Difference in density distribution of compacts.(Non-homogeneity of the compact)	Design of the screw feeder and its proximity to the roll. Larger roller gap.	Increase distance between screw feeder and rolls. Use of movable roller system instead of two fixed rolls. The problem can be improved by using rim roll system. Lubrication of powders.

Selection of powder material is based on particle size and morphological form. These two attributes of power material affects on flowability of granules and mechanical strength of tablets. Roller compaction may be unsuitable if the material is strongly adhesive to metal surfaces or non-compressible in nature. The robustness of roller compaction is also dependent on the variability of mechanical properties of API. The drug compaction capacity can vary, depending on the dose and API bulk properties. Other factors may affects efficient granulation by roll compaction are moisture content/hygroscopic nature of API and excipients, bulk and tapped density of powder, gas permeability and particle size of powder[51].

Challenges in Roll Compaction Technology

Roll compaction process has its own issues like poor tensile strength of tablets (loss of tabletability), larger fine particle fraction, non-homogeneity of compacts and sticking to the roll orientation these are challenges in Roll compaction Technology. Some of the systematic approaches of process and formulation variables can be used to overcome these challenges resulting in improving quality product. The major challenges in roller compaction process along with their possible solutions are tabulated in Table 2[52,53].

CONCLUSION

With mechanical advances in medication improvement, dry granulation by roller compaction is more invaluable than wet granulation process with basic assembling process, low operational cost, no utilization of fluid dissolvable, huge scale creation and appropriateness for heat and moisture sensitive drug. Choice of medication and excipient for roller compaction depends on their physical and synthetic attributes. Selection of definition plan and process parameter assume crucial part in roller compaction. Optimization of procedure parameters, for example, pressure power, move speed, move crevice, screw speed, processing speed, and processing screen opening size is vital and basic in roller compaction. Roller pressure influences particles size appropriation, flowability, homogeneity, compressibility, compactability of dynamic pharmaceutical fixings, and such parameters can in turn influence disintegration profile, breaking down time, hardness and other post pressure parameter of tablets.

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