ADVANCES IN ROLLER COMPACTOR BY INFLUENCE OF AUGER SPEED ON THE FLAKES, GRANULES AND TABLETS PROPERTIES DURING DRUG GRANULATION

GIRISH KUMAR VYAS[1]

Faculty of Health Sciences, Dr. K. N. Modi University, Rajasthan, India

ABSTRACT

This is attempting work for focus on the effects of roller compaction and granulation process at dry state. This continuous and very useful process which reduces the expenses for tablet manufacturing. This presented work is very effective because this uses recycling and reworking on the waste granular material. Most literatures are having poor awareness and knowledge about the availabity and necessity about advance methodologies. Here used some different types of machines to prepare and conventional and novel process.

KEYWORDS: Dry Granulation, Roller Compaction (RC), Methods, Condition, Angle, Pressure, Slugging

Granulation is a skill of molecule extension by lump, is one of the most important unit operations in the manufacturing of pharmaceutical dosage form, primarily tablets (1). Dry granulation is most preferable granulation process. This is very liable and suitable to moisture containing and being less compressing to wet granulation. Dry granulation is method which only uses pressure without adding heat and solvent. Some ways are given hereunder to achieve the dry granulation. (2-5).

1. Conventional method –

a) Slugging – It means Pre-compression

b) Flaking – It known as roller compaction

2. Novel Method - These methods are also known as patented methods.

a) Pneumatic evaporated (dry) granulation

b) Moisture triggered dry granulation

c) RC (Roller compactors) type Roller compactors

d) Gerteis® technology (Premium roller compactors and Dry granulation).

e) As conventional method, slugging method granules whose properties cann't be control well either. However, RC is beneficial to its benefits and preferring with increasing value [2, 6].

f) The compaction nature of powders in RC process is affecting by several elements, as follows [7-11].

- conditions related factors to method
- Nip angle and press of compound
- Vacuum deareate,
- Factors according to different powder properties.
- Process conditions related causes include roll speed, roll gap, mechanisms and speed of feeding, throughput, and roll-surface character. Difference is bicupsid volume of rolls adjustment nip angle and pressure. Application of vacuum decreases normal stress with subsequent increase in gap and ribbon thickness. Factors relating powder properties are particle size, shape, moisture content, and so on [9].
- Consequence of data and for announce lean, cost-effectivel, and continuous method a Swiss producer, Gerteis®, developed and patented roller compaction system, 'Gerteis®' [13-18]. While Powtec Maschinen und Engineering Gmbh, Germany advanced and popularized matter of RC type Roller compactors [19], 'Pneumatic dry granulation' by Atacama Labs [20, 21], and advanced copy of Chilsonator® RC by Fitzpatrick [22, 23].

Advance in wet granulation RC type roller compactors

- Roller compactors are advanced by Powtec Maschinen und Engineering Gmbh. These are high-performance RC developed for press-aglomerating powder and dust. For meeting demands from laboratory to production scale these offering a wide range of various roller compactors (Table-1). Laboratory machine is being processing a few hundred grams while production machine throughout more than 4,000 kg/h. Area of their application covering pharmaceuticals to chemical materials or metal powders right up to impression for food production [19].

[1]**Corresponding author**

Table 1: Features of model range of RC type roller-compactor machines [19].

Machine-Model	**Typical throughput** (kg/h)	**Press-Force absolute** (kN)	**Electrical power** (kW)	**Weight** (kg)
RC 100	15	49	2	300
RC 120	60	60	4	600
RC 150	120	76	6	900
RC 170	200	116	8	1.100
RC 210	350	186	12	1.700
RC 250	600	269	20	2.400
RC 290	900	402	25	3.300
RC 370	1.600	637	40	5.400
RC 500	4.500	1.127	80	9.900

Table 2: Options and features of Pactor® and Polygran® model range

Options and Features	**Mini-Pactor® [12]**	**Macro-Pactor® [13]**	**Ultra-Pactor® [14]**	**Polygran® [15]**	**Mini-Polygran® [16]**	**Mini-Polygran® Plus [17]**
Fully instrumentation	Available	Available	---	----	---	----
Full machine calibration	Available	Available	---	Available	---	----
Occupational exposure limit level	< 3µg/m³	< 3µg/m³	< 0.1µg/m³	---	----	< 5µg/m³
Gap between rollers (in mm)	1 – 6	1 – 6	2 – 6	2 – 5	1 – 4	1 – 4
Press force (in N/cm)	1 – 20	1 – 20	1 – 20	1 – 15	1 – 15	1 – 15
Roller speed (in rpm)	1 – 30	1 – 30	1 – 30	2 – 15	0.5 – 5	0.5 – 5
Throughput (in kg to kg/h)	0.1 to 400	0.1 to 400	0.1 to 400	0.5 to 300	10 to 20	10 to 40
Suitable for Research and Development Bench and small-scale Development and pilot scale Mobile frame Quick and fast maintenance Inter-batch changeover	Yes Yes Yes No No No	Yes Yes Yes No No No	Yes Yes Yes No No No	Yes Yes Yes No Yes Yes	Yes Yes No Yes Yes Yes	Yes Yes No Yes Yes Yes
Gross weight (in kg)	1200	1700	2500	1200	400	500

Table 3: Specifications of Chilsonator® machine with model range [23]**.**

Model	**Roller width X Diameter** (inches)	**Roll pressure** (lbs/ linear inches)	**Roll speed** (rpm)	**Throughout** (lbs/h)
IR220	0.75 X 8.0	0 - 15,000	4.0 - 14.0	0.1 - 22
IR520	2.0 X 8.0	0 - 15,000	6.0 - 24.0	22 - 220
IR4LX10D	4.0 X 10.0	0 - 10,000	6.0 - 24.0	220 - 2,200
4B4LX10D	4.0 X 10.0	0 - 19,650	6.0 - 24.0	220 - 2,200
7LX10D	7.0 X 10.0	0 - 11,900	6.0 - 24.0	440 - 4,400
12LX12D	12.0 X 12.0	0 - 10,300	6.0 - 24.0	770 - 7,260
12LX16D	12.0 X 16.0	0 - 16,800	6.0 - 24.0	990 - 9,680
12LX20D	12.0 X 20.0	0 - 19,625	6.0 - 24.0	1210 - 12,100
16LX20D	16.0 X 20.0	0 - 19,625	6.0 - 24.0	1760 - 19,360

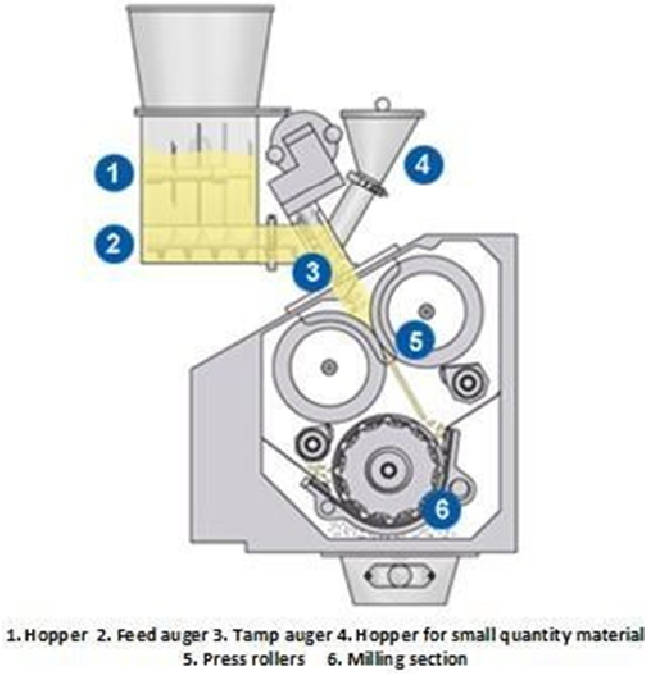

Figure 1: Basic design of roller compactors by Gerteis® [13-18].

These RC compactors suitable for powder that does not flow, cannot be dosing accurately, contain higher proportion of dust, segregates, or bulkier. Their advantages, standard options and special features are followings [18].

Advantages

Economical: Large assortment of models and exhaustive standard varieties is guaranteeing impressive decrease in expenses. Each machine customized to individual need and application.

Space sparing and high-grade: All machines are including reduced plan and developed from high-grade tempered steel.

Easy to clean: Featuring interesting protected move trade framework giving simple and fast cleaning of machine parts and machine. Moreover, machine segments are effectively available for investigations.

Variability and unwavering quality: Achieving wishing and movable granule properties like size, mass thickness, flowability and solvency. The models are

reasonable for bunch just as persistent procedure. Environment friendly: Minimize dust burden and product loss and avoid cross taints.

Special Features

- Innovative and latest state-of-the-art features assuring maximum throughput capacity, process stability, reproducibility and product quality.
- A specially manufactured pre-compression feeder tighten is enabling efficient processing, even of light, bulkier and fluidizing powders. In addition, feeder screw has de-aerating effect on the raw material.
- Improved accuracy of dosing assuring even product feed across entire roll width.
- Various shapes of roller surfaces improving the product feed behavior and maximize yield.
- Constant roll force distribution contributing for yielding flakes with consistent ribbon porosity and granules with consistent properties.
- Inbuilt novel roll-seal-system for optimizing compacting process, increases yield and reduces requirement for separation and recycling of fines.
- Drives with flexible speed and hydro chemical pressure are ensuring high process flexibility.
- The hydraulic unit keeps the set roll pressure constant for assuring homogeneous flake while scrapers keep the rolls clean.
- Compaction zone and mechanical drive area being enclosed individually and can be kept isolated from one another.
- The process results can be scaling up and down.
- Water-cooling of rolls feature is suiting thermo labile products.
- Pneumatically operated lifting device aids simple and fast cleaning of screw feeder.
- Rolls built from various materials with diverse surfaces featuring for wider usefulness.
- Gentle, high-performance, low dusting, and size reduction in one-stage or two- stage design is doable.
- Roll gap control is doable.
- Optional integrated sieving machine and pneumatic system (to re-feed under and over size particle).
- Special designs suit in handling abrasive products like metal or diamond powder.
- Designs suit for operation in hazardous and explosive areas complying ATEX guidelines.
- Complete turnkey DG systems.

Standard options

- Options for executing chemical, food, or pharmaceutical (in cGMP- design) is available.
- Feature with control system having touch-sensitive panel.
- Recipe administration is doable.
- Exhibition of Design Qualification/ Installation Qualification/ Operational Qualification/ Performance Qualification including Factory Acceptance Tests and Site Acceptance Tests, is optional feature.
- Various screw feeders and stirrers complying individual need and requirement.

Gertasis Roller Compactor System

Roller compaction is achieving either with floating/variable-gap rollers or with fixed-gap rollers. Maintaining comparable normal force applied by the rolls on ribbon for a given gap between rollers, is troublesome. Consequently, these contribute to large fluctuations in the properties of ribbon and granule [8.9, 12].

Gerteis® RC system is capable in averaging and controlling all product quality relevant parameters, on-line. Said system employs floating type roller minimises fluctuations in the properties of ribbon and granulates. Thus, allowing DG of wider ranges of formulation comparing fixed-gap roller compactor [13-18].

Gerteis® arrangement based machines from Gerteis® adjust and approve all the product quality relevant parameters and deliver a well-documented and assured manufacturing process. Managing inter-batch variations, said machines built with control systems allowing equal granule properties during manufacturing, according to ‘process analytical tool’. Option is available providing

solutions to Title 21 Code of Federal Regulations Part 11. Gerteis® system built with following unique features [13-18].

Unique features of Gerteis® roller compaction system

- It built in logical feeding system with torque control of screw feeder and tamp auger. This is ensuring precision dosing of powder to rollers.
- Reinforced angled compaction rollers with free-floating gap design and in process force control. These features allowing feed consistency, constant ribbon density and minimize temperature gain.
- Built larger diameter of rollers provides a longer dwell time in the nip area.
- Reinforcing superior punch and die roller design to provide a constant density over the ribbon width. Compaction system is employing interchangeable press roller with different surface like knurled, smooth, toothed or custom design. These features virtually eliminate fines minimizing demand for their recirculation or reworking.
- Built three-stage flake-milling process includes granulating oscillating mill and adjustable screen clearance. Granulator is open star rotor, closed pocket type integrated with bulk-breaking and pre-crushing featuring optimum results. Features ensuing consistent and controllable particle size distribution.
- Inbuilt perfect sealing system is reducing dusting of fines.
- High containment solution ensuing standard containment performance level < 3 $\mu g/m^3$.
- Complete harmonized designs makes scale-up simple, straightforward, and fast.

Roller compactor from Gertesis featuring RC system

- The head of Gerteis® had designed and engineered RC comprising a Gerteis® roller compaction system and a gentle milling (granulation) system. Inline co-existences of these two systems minimize generation of too many fines [13-18].
- The compactor deigns range comprises of two important classes, Pactor® with Polygran®. They comprise generally a feeding system, a compaction unit and a size reduction unit (Figure-1). Pactor® range include Mini-Pactor®, Macro-Pactor®, and Ultra-Pactor® while Polygran® range include Polygran®, Mini-Polygran®, and Mini-Polygran® Plus. However, model ranges are for meeting demands of development and pilot projects, and up to full- scale production batches (Table-2). Said model ranges differ by several options or features, add-on or optional (Table- 2). The add-on or optional options and or features are for assuring.

Pactor® and Polygran® range has full adjustable designs, being assuring with use of identical roller diameters. Complete harmonization makes scale-up simple, straightforward, and fast, avoiding common problems and risks. Said harmonization is breezing scale-up to full size production. In addition, is reducing cost of material and active and saving time by quickening market launching.

Advantages of Gerteis® roller compactors over current RC

- Gerteis® RC ensuing several benefits over current, as follows [13-18].
- No temperature issue, heating up of material throughout whole process is only 2-4°C.
- Roller cooling option is featuring handling of material with melting point < 30°C.
- Consistent material feeding system ensue consistent product characteristics and quality
- Reinforcing unique combinations of inclined roller arrangement, movable press roller with rims and gap control minimizing amount of un- compacted fines.
- Unique milling system ensue granules with optimal particle size distribution and minimise amount of fines.
- Featuring improved containment safety and ultra high containment options. Features are avoiding contamination of manufacturing areas and personal by high potent actives.
- Ranges of occupational exposure limit options with multiple cleaning options.
- Energy efficient, requiring no air conditioning, and low

running costs.

- Integrated air handling system, integrated nitrogen adding and oxygen monitoring option is available.
- Reproducible results are accomplishable along with real data calibration and calibration of the whole system is doable.
- Models can additionally be presenting with a pneumatic system.
- WiP option is for removing air borne dust during dismantling reducing cleaning cycle time. CiP option ensue complete automated cleaning without dismantling. Occupational exposure limit level designs of < 3 μg/m^3, < 1 μg/m^3, and < 0.1 μg/m^3. CiP feature and limits level design of < 0.1 μg/m^3eliminates contact of operator with potent and hazardous products.

Mini-Pactor®

The Mini-Pactor® arranged for laboratory advancement and small to medium scale, and for production runs but is ideal for laboratory development. Pilot projects and small- scale production batches be handling easily [13].

Macro-Pactor®

Macro-Pactor® is the premium roller compactor. It having throughout capacity up to 400 kg/h, however can handle amounts from as little of 100 g. Have suitability for development and pilot scale environments [14].

Ultra-Pactor®

The Ultra-Pactor® is the better technologically progressive one and progressive design of Macro-Pactor® being classing as 'high containment roller compactor'. It designed within an ergonomic containment isolator having throughput capacities from 100 g up to 400 kg/h. This feature allows processing of potent products where high containment is required. Compliance to high containment good practice Ultra-Pactor® is being designing with full CiP feature [15].

The Ultra-Pactor® is ensuing optimal protection of the operator from potent and hazardous substances. It is having ability to purge N_2 into the process area and designed with ATEX-compliancy. Said features truly push the boundaries in containment installations for DG applications [15].

Options of Mini-Pactor® and Macro-Pactor®

Available options with Mini-Pactor® and Macro-Pactor® are follows [13, 14].

- Options are of WiP / CiP cleaning.
- Featuring enhanced containment performance.
- Build in 'process analytical tool' control systems.
- Optional feature is of press roller cooling and or heating.
- Option is for vacuum de-aeration.
- Interchangeable different roller surface designs.
- Option is for separate feed funnel for small quantities.
- Build in industrial PC solutions.
- Novel features of Ultra-Pactor® comparing Mini-Pactor® and Macro-Pactor®
- Novel features Ultra-Pactor® over Mini-Pactor® and Macro-Pactor® are follows [13-15].
- Built ergonomically designed high containment isolator delivering highest safety to the operator.
- Inbuilt RTP ports for optimised operator handling.
- Filter designs are push-push.
- Online pressure monitoring of all seals and pressure zones is doing with inbuilt permanent online pressure monitoring system.
- Delivering containment performance < 0.1 μg/m^3.

Inbuilt feature completely automated cleaning, CiP and WiP and reassembly.

Maintenance and changeover from batch to batch can be doing in simple, quick and fast way, even from scale-up to production batch size achievable instantly and hassle-free.

Polygran® - setup based compactor for analysis and Development Said setup based compactor suiting lab scale is Mini-Polygran® and Mini- Polygran® Plus. These tabletop models are short system roller compactor suit Research & Development while Mini-Polygran® is

compact. They are striking perfect balance between performance and flexibility [17, 18].

Mini-Polygran®

Mini-Polygran® is most compact RC from Gerteis®, in their amount range. It belongs to Research and Development class however suiting for bench and small-scale with throughput capacity range of 10 g to 20 kg/h. Its wonderful design and engineering allowing give and take of the lower compression roller with the unique Gerteis® granulating mill, simply and quickly. Inbuilt offline granulation setup is achieving milling within the same housing. Followings are the features of Mini-Polygran® [17].

- Featuring optional small quantity feed system.
- Have longer dwell-times comparing other roller compactors, in same class or range.
- A range of different roller surfaces is available featuring for optimising process, in hand.
- basic no heat gain with the Gerteis® patented angled roller design.
- Reduced number of parts is featuring simple cleaning procedures and quick changeover.

Mini-Polygran® Plus

The Mini-Polygran® Plus is advanced design of Mini-Polygran®, with a fully integrated Gerteis® granulation-mill. This offering an outstanding opportunity for successful development of DG formulas with assured excellent results. Have throughput capacity between 10 g to 40 kg/h suiting DG development programme. Its add-on option for integrating assembly like Buck® Valve split butterfly valves or HicoflexÒ flexible containment. Said add-on option, an advanced sealing design, suits processing potent products without worry of operator exposure. Superior features of Mini-Polygran® Plus over Mini-Polygran® are follows [17, 18].

- Inbuilt is on-line and integrated two-step granulation system.
- Optional advanced sealing system suiting higher product containment.
- Featuring is optional WiP design.
- For facilitating flexible placement, it built with mobile frame with a fitting of four- wheels.

Pneumatic Dry Granulation

Pneumatic dry granulation, a technology from Atacama Labs traded as PDG Technology™. An contempory DG process built with increased pneumatic classification feature, for recycling excess fines. It is featuring with automatic or semi-automatic production of porous granules with excellent compressibility and flowability, and flexible high drug loading (70-95%). It is having several superiorities over conventional roller compaction process, as follows [20, 21].

- Process is economical, efficient and reliable, high throughput, and continuous production.
- This is a freedom of any person.
- Fast and simple development process (within weeks), even with difficult material.
- Suitable for lowering production costs, managing life cycle, and extending market, of new galenic forms.
- Can achieve high drug loading, even with materials known to be historically difficult to handle, taste masking, excellent stability, and so on.
- Enables soft modification of drug load, dissolution time and tablet hardness.
- Achieves good granulation results even at high drug loading,
- A locked system offering safety even with harmful materials,
- Little or no waste of material, and
- Scale-up is straightforward.

Followings are the important building components [20, 21].

Roller compactor (Mini-Pactor®): It is featuring with lowest possible compaction force to confer maximum binding capacity of the granules.

Classinator (Atacama): New gas-flow based fractionating device lowers level of fines ensuring excellent flowability.

Pneumatic recycling of fractionated fines improves process efficiency. Blend to be granulated recycled powder

feed hopper integrated mill PDG- 0260 in cGMP environment Closed-loop system minimizes leakage of dust.

Advanced model of Chilsonator®

Fitzpatrick designed leading model of Chilsonator® to provide the ultimate process flacidity for a wide variety of products (Table-3), model IR520 unique one. Its design features for quick dismantling and cleaning to meet sanitary and cGMP requirements, with accurate repeatable results suiting critical applications. Follows are the important features and options [22, 23].

- Versatile installation: Feature have self-contained freestanding or portable installation of machine. Feature is contributing from easy dismantling and reassembling characteristic for all operation units enclosing technical components.
- 'In-wall' design: The feature separates the product contact parts from the

  mechanical components.
- Easy to clean: Robust stainless steel parts quick disassembles for aggressive cleaning. In addition, components are designing with smooth accessible corners and without product catching ledges. These features are facilitating thorough inspection and easy reassembly. Optional WiP system is available.
- Feeding system: Alternative Fitzpatrick feeding system built in parallel feed screw for metering material, and a vertical pre-compression screw for pre-compression, de- aeration, and feeding material to compaction rolls. Additional de-aeration can be achievable with optional 'vacuum de- aeration system' assisting in drawing the entrained air of product.
- Low capacity feed system: This optional system is allowing processing as little as 50 g, and up to 2 kg, with minimal loss, suiting research and development requirements. This makes scale up to the standard IR520 or larger Chilsonator®(s), easy and convenient.
- Precise size reduction of compacted products: The granulating mill (FitzMill®) operating parameter be selecting and configuring to get the desired particle distribution. Selectable options of operating parameters include rotor type, screen type and operating speeds.
- Various roll surfaces: Its cantilever design allowing easy changing and installation of a variety of roll designs.
- Pneumatic feeding system: This charges material into the feed hopper of Chilsonator® from ground level utilizing pneumatic conveyor, manually with a wand, or automatically dumped from a bin into a pneumatic conveyor pick-up hopper. This confers simple and cleanable method of charging.
- Recycling system: Recycling system removes all fines and overs from the product. Recycling system typical includes compactor, granulator, screener, initial feeder, level sensors, and mechanical or pneumatic conveyor.
- Product check system and N_2 inert processing: Product check system, an add-on option of Chilsonator® system suits high check processing. This minimise product exposure to operator and environment, and prevents product contamination and product loss. For reducing product oxygen exposure and explosion risks, product containment system can be combining with system for N_2 inert processing.
- Bin-to-Bin processing - Typical Chilsonator® installation designs feeds material from an starting product bin, with the Chilsonator® and FitzMill®, and into a material recipient bin. This is featuring convenient and passed over processing with simple connection and betterment of product bins, totally in ring system.
- Chilsonator® automated control system: Optional feature, 'automated control system' providing optimum process control with excellent operator interface and data monitoring. Operator interface facilitates pictorial viewing of instrument measurements and machine status information. Controls system be designing for qualifying 'user requirement specifications' for meeting customer specified classifications and standards like execution of ATEX guidelines, special voltage requirements, and in-wall or portable electrical enclosure. Universal appearance of Chilsonator® automatic control system is following.
- On-line help and diagnostic functions,
- Restricted access of various functions,

- Maintenance and calibration procedures,
- Roll gap control,
- Historical trending,
- Report generation,
- Alarm management, and
- Title 21 Code of Federal Regulations Part 11 solutions.

Model IR520 Chilsonator® can be configuring with great features and options suiting variety of functions. These customized featuring components are easy to disassembling and installing, with hand fasteners. These convenient features make it amenable for laboratory and small production installations.

CONCLUSION

Novel and propelled machines will carry answers for dry-crush more extensive scope of plans. They will work inside guidelines, subject to utilization of proper machine and extra highlights. Basing on the exhibition and comfort utilization of Gertix.

RC will be astute choice, for medication and nourishment. The tale highlight is its blended structure, encouraging scale-up through basic, savvy, clear, and quick way. As an option RC roller compactors liking however requires various models from improvement to creation scale. Propelled model of Chilsonator® be utilizing for their versatility and helpful disassembling and reassembling highlight. These are appropriate for strong handling structure. Pneumatic dry granulator has least adaptability for all through component however uses protected granule fractionating gadget, helping effectiveness.

Mindfulness among experts relating utility of cutting edge roller compactor will upset DG process. In addition, on-line observing and controlling all item quality pertinent parameter and complete robotization will improve productivity and relevance. Exertion must permit dry-crush more extensive scope of definitions inside guidelines. Future will avow application by gifting huge item in field of pharmaceutical, nourishment and compound.

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