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DRY COATING OF PHARMACEUTICAL POWDERS

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ABSTRACT: This manuscript aims to figure out updated information on the dry coating of powder (DCP). In pharmaceutical processes, the inevitable is handling of fine and ultra-fine particles (FUFP). Their higher surface area associated surface and surface attributes contribute chiefly to exhibited complex phenomenon like bulk behaviors, physicochemical property, performances and functionalities of pharmaceutical importance, and many others. Nowadays particle engineering techniques are extensively exploited to modify surface and surface attributes of FUFP to find their worthy applications and new functionalities. Among available diverse techniques for particle engineering DCP is advocated as a worthy and efficient one. The DCP is considered to have multidisciplinary applications in drug development and drug delivery. Process basis of DCP calls for attaching and/or fixing the particles of coating material (PCM) or guest particle (GuP) onto the substrate/core particle (S/CP) or host particle (HoP). Fixing/ attaching the PCM onto HoPs mandates their interaction that may be mechanical, chemical, thermal, electro-chemical and many others. Scientific literature and patents are evidencing diverse processes and methods for interacting S/CPs or HoPs with PCM or GuPs. Amongst them, novel methods are Magnetically Assisted Impaction Coating (MAIC), Hybridizer®, Mechanofusion®, Theta Composer®, Electrostatic Dry Coating (EDC), Atomic/ Molecular Layer Deposition (ALMD), Chemical Vapor Deposition (CVD). Principle and method of working, applicability, limitations, and benefits of novel DCP process and methods are discussed and presented in this article. It's hope; that contained information will benefit pharmaceutical and allied field professionals.

INTRODUCTION: High surface area of FUFP is the reason for receiving interest in academia and many industrial sectors, nowadays [1-6]. Their bulk behaviors are highly complex phenomena [2-5, 7]. High surface area contributes to high surface energy, which is undoubtedly a robust parameter to characterize their interaction behavior [3-5, 7]. Pharmaceutical sectors are extensively working in finding applications and taking advantage of many worthy properties and new functionalities attributed to FUFP, such as drug delivery systems/ carriers [4, 7-9]. Accordingly, scientists and engineers are exploiting numerous elegant strategies of particle engineering methods to modify their surface and surface attributes [1-3, 9].

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Amongst them, coating the surfaces of FUFP with an appropriate additive is a widely exploited strategy [1-4]. Further, their coating achievable changes in visual properties, improved appearance, stabilization, enhanced mechanical properties, masking of odor and taste, and defined drug release profile in the biological system [1-4]. In addition, the coating is used frequently for imparting functional and/or protective (non-functional) attributes to the FUFP [1, 3, 7]. Application of coating for modifying surface and surface attributes of FUFP is a complex process [1, 3, 4]. Said modification is done either by wet coating method/ process or dry coating method/ process (DCM/P) [4, 10-13]. The basic mechanisms of the wet process may comprise sequential steps of droplet formation, wetting, spreading, evaporation and drying [1, 7, 10]. In this process, a suspension or solution of the coating material (CoMa) is sprayed onto the FUFP [1, 11-13]. After that, individual particles are wrapped by the liquid film of CoMa composition [3, 7, 10-13]. Upon evaporation of liquid from the liquid film, a new solid layer of CoMa is formed, thus resulting in a coating of FUFP at individual particle levels [1, 13].

Wet coating methods have become less preferable. They can reduce stability, cause particle agglomeration, leave residual organic solvents, and environmental concerns, arousing from unwanted waste streams and possible emissions of volatile organic solvents [1, 7, 10-12, 14]. Comparing the wet coating method, the DCM/P result in substantial energy savings, besides producing none of the organic gas or aqueous or liquid waste streams [3, 4, 7, 15, 16]. In a nutshell, DCM/P are cost effective and environmentally benign and enable producing fine particles with significantly different functionality [3, 4, 7, 15, 16].

Modifying particle surface and surface attributes by DCM/P have been recognized as a potentially cheaper, simpler, safer, faster, and environment-friendly approach comparing conventional and novel wet methods based on solvent [2-4, 15, 17]. Coating processes for FUFP based on the dry method are relatively new concerning wet one [3, 4, 7, 15]. DCM/P is still in the R&D stage of development and rarely finds commercial applicability [3, 4, 7]. Literature study evidence manuscript having better interpreting of method and principle of working, applicability, limitations, and benefits of DCM/P suiting FUFP are scarce, thus necessity this presentation [4, 15]. In this manuscript, applications and recent developments in techniques for DCP with applicability in the pharmaceutical sector are discussed and outlined. The presented information will increase the visibility of DCM/P suiting FUFP and inspire others to exploit this area, resulting in better interpreting of physico-chemical principles that influence the dry coating of FUFP side-by-side finding novel industrial applications of these.

Dry Coating: DCM/P directly attaches submicron-sized/ fine GuPs, onto relatively larger (micron-sized) S/CPs or HoPs without using any binders, solvents, or even aqua [3-15]. In contrast to wet methods, PCM interacts with substrate surface by applying the mechanical, thermal, electro-chemical, or electrostatic energy [3, 4, 15, 16]. As the sizes of the PCMs are very small, the van der Waals interactions are sufficiently strong enough to keep them firmly attached to S/CPs [3-16].

Thus the process makes achievable either a continuous or a discrete coating of S/CPs, depending on diverse operating conditions, including process time, the weight fraction of GuPs to S/CPs and particle properties [3-17]. Both continuous and discrete coating can consist of either a particle layer (monolayer or multilayer) or a continuous film [3, 4, 7, 15]. The continuous coating results in a continuous film that is generally non-porous and completely shields the surface of the underlying S/CPs; are thus generally preferred [3, 4, 7, 15]. In contrast to continuous coating, the film of discrete coating is porous and thus has some unique pros [3, 4, 7]. For instance, the application calls for the coating to change specific surface property, but a complete shielding of the underlying S/CPs is un-desirous [3, 4, 15, 17].

In some instances, the DCM/P may either deform the PCM or cause them to get embedded onto the surface of S/CP while bringing PCM in close vicinity to S/CP [3, 4, 15, 16]. Said deformation and/or embedding increases the contact area, thus causing the attraction between the particles to become even larger [3, 4, 15, 16]. By this, a much stronger coating is made obtainable vis-à-vis altering surface morphology, and reducing adhesive forces of PCM is made feasible [3, 4, 15, 16]. This process creates engineered particulates with tailored properties, *i.e.*, value-added composite particulate materials, and makes them possible with new & exciting applications [3, 4, 7, 15]. This means that apart from forming a barrier film, as in wet coating, the DCM/P can be used for having significant changes in functionality and/or properties of S/CPs [3, 4, 15, 16]. This approach for the past few years has been steadfastly established as a viable and worthy method in forming composite particles, which involves dry coating of them by mechanical, thermal, electro-chemical, or electrostatic means [3, 4, 15, 17].

Improving and/or modifying surface and surface attributes of FUFP of pharmaceutical importance are dispersibility, flowability [5, 7, 17], solubility, particle shape, sphericity, wet ability, hydrophobic and hydrophilic properties, electrostatic, magnetic, electric, optical, color, taste, flavor, solid-phase reactivity, sinterability, and many others [3, 4, 15, 17].

The DCM/P has reduced the use of high-priced or rare materials as highly expensive CoMa can be coated onto a cheaper substrate or carrier material [3, 4, 15, 16]. Comparing the wet coating method, the DCM/P does not call for a drying step, thus resulting in substantial energy savings, besides producing none of the organic gas or aqueous or liquid waste streams [3, 4, 7, 15]. Thus, to produce particulates with completely different functionality, the DCM/P is cost-effective and environmentally benign [3, 4, 15, 16]. In this regard DCM/P is a promising alternative to wet coating methods [3, 4, 15, 17, 18].

Basic Principle of Dry Coating Process: Dry coating comprises the application of PCMs onto the moving substrate bed with concurrent use of curing mechanism(s) facilitating the formation of even/ smooth/ continuous coat [2-18]. The process and equipment must provision for [2-4, 11, 12, 18]:

1. Application and distribution of CoMa: This is for layering and distribution of the PCMs over the whole of the available surface of S/CPs [4, 15],
2. Rotation of substrate: for continuous mixing of the substrate load and exposure of S/CP surface to adhere/ fix PCM [2-4, 11, 12, 15].
3. Curing: for coalescence & sintering of PCMs [4]. This is brought through the partial fusion of polymers [3, 4, 15] and
4. Leveling of CoMa: is for densification of layer by reducing empty spaces & smoothing surfaces [3, 4, 15].

In general, film formation in the DCM/Ps occurs by a sequential process involving PCM application, coalescence, and sintering [4, 15].

Classification of Dry Coating Process: Based on the methodology the DCM/P can be classified as follows [4, 6]:

- **a.** Heat dry coating
- **b.** Plasticizer dry coating
- **c.** Aerosolized dry particle coating
- **d.** Photocurable coating
- **e.** EDC
  - ✓ Plasticizer EDC
  - ✓ Electrostatic fluidized-bed coating
- **f.** Vapor phase deposition (coating) of powder
  - a) CVD
    - ✓ Plasma enhanced CVD
    - ✓ Initiated CVD
  - b) ALMD
  - c) Fluidized-bed chemical vapor coating
- **g.** Mechanical dry coating
  - ✓ MAIC
  - ✓ Hybridizer®
  - ✓ Mechanofusion®
  - ✓ Theta Composer®

Heat Dry Coating: Inclusion of plasticizer is common practice in DCM/P but is unsuitable for film-forming polymers with a lower glass transition temperature (Tg) [3, 4]. Further, high concentrations of plasticizers cause pre-plasticization [3, 6]. To combat said issues, heat dry coating is developed that abandons plasticizer in the coating process, which uses heat only as a binding force to realize coating [3, 4]. In this technology, PCMs were continuously spread onto the substrate contained in spheronizer using a screw powder feeder [3, 4]. An infrared lamp, as a heating source, is positioned on the top of the spheronizer [4, 6]. Spheronization coupled with heat results melting of PCM and its spreading on the surface of substrate [3, 6]. Then, the spread coating layer curing occurs due to the heat [6]. Eudragit® E PO is a suitable CoMa for this process [3, 4]. Major challenges to be overcome in heat dry coating technology are to get a uniform, smooth, and thick coating only with the help of the said heat-based adhesion [3, 6].

Plasticizer Dry Coating: DCM/P that makes usage of plasticizers is termed plasticizer dry coating [3, 4, 18]. Some coating process calls for the use of film-forming polymer with low *Tg*, as these are essential to protect actives from being damaged during processing at high temperature [3, 6, 18].

Powdered CoMa is spread onto the substrate surface and simultaneously plasticizer is sprayed from separate spraying nozzle [3, 4]. The sprayed liquid plasticizer wets PCMs and the substrate surface [3, 6, 18].

This promotes adhesion of the PCMs onto substrate surface [3, 4]. The coated substrates are cured for the predetermined time above *Tg* of the coating polymer to form a continuous film [3, 6]. The substrates can be tablets, particles, or FUFP [3, 4]. If the substrate is tablets, a pan coater can be used, but for particles and FUFP, a fluidized bed coater is required to avoid accumulation due to their smaller size and higher specific surface area, thus strong interactions [3, 6].

Aerosolized Dry Particle Coating: The technology for DCP following the aerosolized principle is firstly developed by Aston Particle Technologies [2-4, 14, 19]. Said technology is ambient temperature based on a one-step process [2, 3, 6, 19].

By controlling processing parameters, the process can deliver reproducible product performance using available commercial-grade excipients [4, 14, 19]. The underpinning science of said technology calls for a high G-force chamber with a curtain of nitrogen gas [2-4, 14, 19].

The gas curtain fluidizes the powder at the chamber wall to disperse any agglomerates of coarse or fine particles [2, 3, 6, 14, 19]. Co-aerosolization of particles results in coating the surfaces of the all and individual coarse particles with the fine particles [3, 4, 19].

The process can attribute designed functionalities to particles, even of highly sensitive active(s) [2, 6]. Attributed functionalities of particles enhance their inherent properties without their degradation in any way [2-4, 19]. No exposure to solvent/ heat/ mechanical attrition during processing is the significant advantage over other state-of-the-art technologies of dry coating [2, 6, 14, 19].

The superiority of said technology is, here, blending occurs thru particle-particle interaction in the aerosolized state as opposing solid-solid interactions involved in the high-shear blending of traditional technologies [2-4]. In an aerosolized state, clouds of individual particles result in intimate contact of individual particle clouds [2, 3, 6, 14, 19]. This facilitates attachment of all fine particles onto coarse particle surfaces without causing unwanted Physico-chemical modification to constituent particles [2, 4, 14, 19].

Mechanism/ Principle: Under normal mixing conditions, in a binary mixture of coarse particles and FUFP, the FUFP exhibits cohesivity of a higher degree [2-4, 14, 19]. This can lead to segregation or formation of agglomerates, thus producing non-homogeneous mixes in an interactive mix [2, 3, 6, 14, 19]. DCM/P for FUFP overcomes said high cohesivity associated with fine and ultra-fine GuPs, through uniformly bounding them onto surfaces of the coarse HoPs, by strong adhesive forces [2-4, 14, 19]. Said principle holds effective till the size difference between GuPs and HoPs is at least double [2, 3, 6]. Coating happens as the forces of attraction between fine and ultra-fine GuPs and HoPs are greater than the weight of the fine and ultra-fine GuPs themselves [2-4, 14, 19].

The principle of DCP with aerosol technology is penning from particle size difference between the HoPs and carrier GuPs [2, 6, 14, 19]. The principle/ mechanism of the DCP using aerosol technology can be presented in three primary steps/ stages [2, 3, 6, 14, 19], refer to Fig. 1. All these stages occur simultaneously.

Stage 1: Dispersal of all agglomerates of fine and ultra-fine GuPs and coarse HoPs by applying high G-force, which is generated by the revolving of the processing chamber at high speed and is balanced by the injection of nitrogen gas into the processing chamber [6, 14, 19].

Stage 2: Dispersal of fine and ultra-fine GuPs around coarse HoPs [6, 14, 19] and

Stage 3: Adhesion/ attachment of fine and ultra-fine GuPs onto the surface of HoPs, thereby reaching a uniform spatial distribution of fine and ultra-fine GuPs [6, 14, 19].

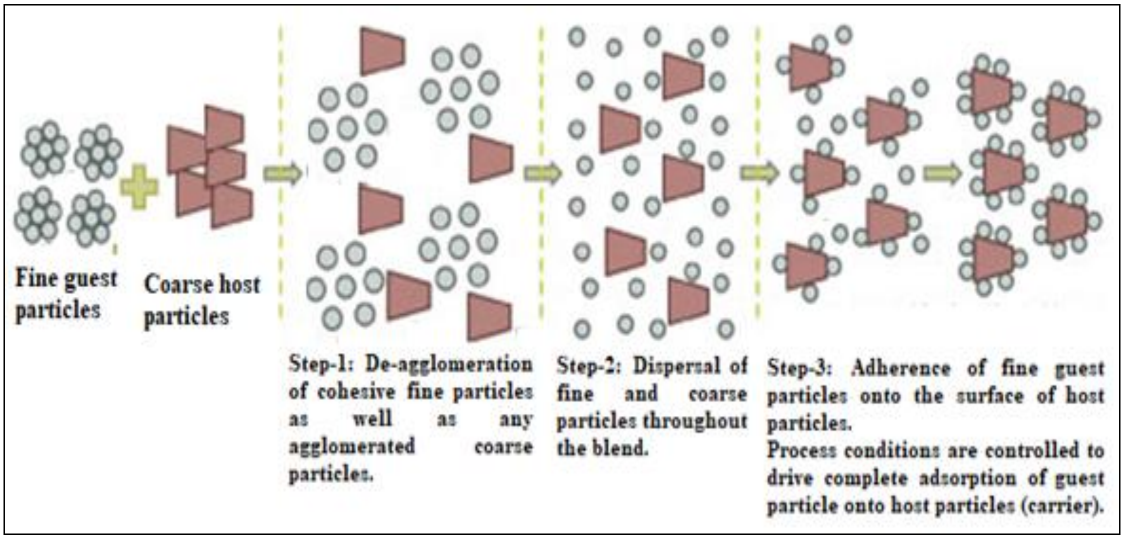

FIG. 1: MECHANISM/ PRINCIPLE OF AEROSOLIZED DRY PARTICLE COATING [6, 14, 19]

Photo Curable Coating: Photocurable coating or photocuring has wide commercial application in dental and medical fields [3, 4, 14, 20, 21]. It is used for coating of pharmaceuticals as a process of rapid conversion of specially formulated (usually liquid) solventless compositions into solid films by way of photocuring [3, 6, 20, 21]. Said curing involves irradiation with ultraviolet or visible light [4, 6]. The ultraviolet light curable coating is strong and photo-stable [3, 4, 14, 20, 21]. A chemical approach is proposed to coat substrates rapidly at or below room temperature with an extremely rapid rate of [3, 6, 14, 20, 21]. Said system generally consists of four major components [3, 4, 20, 21], as follows:

a) Pre-polymers or monomers.

b) Photoinitiators or catalysts.

c) Ultraviolet/visible light source for curing.

d) Pore-forming agents.

Most curing reactions are performed with light in the ultraviolet region [3, 4, 20, 21]. This bears the fact that ultraviolet light is more energetic and, therefore, more efficient in rupturing chemical bonds [3, 4, 18]. Contrary, visible light has many attractive features like safety and ease of handling, thus receiving attention as well [3, 6, 18, 20, 21]. In the photocuring process, curing can be done by a free-radical mechanism or an ionic mechanism like anionic and cationic (mostly) [3, 4, 20, 21]. Some compositions that result in curing are simultaneously mediated by [3, 6, 20, 21] changing pore-forming agent and proper choice of material desired number of coating layers with wished thickness can be reasonable for having immediate and sustained release profile [3, 4, 20, 21].

Pre-polymer or Monomer: Specially functionalized liquid pre-polymers or monomers having stability to ultraviolet light exposure during the entire coating process are suitable [3, 6, 20, 21]. But they should be polymerizing using an ultraviolet light curing process while keeping up acceptable film firmness, integrity, and stability [4, 6]. Since these are in a liquid state, thus can be easily spread on solid substrates like tablets and granules [4, 22, 23].

Photocurable siloxanes are widely used as photocuring material [3, 6, 20, 21]. These usually belong to two major classes, acrylic acid derivatives and enethiols [3, 4, 20, 21]. Important resins and reactive diluents from acrylates are epoxy acrylate, hexanediol diacrylate, polyurethane acrylate, polyester acrylate, tripropylene glycol diacrylate, trimethylolpropane triacrylate, unsaturated polyester, etc [3, 6, 22, 23].

Copolymerizable liquids with comparatively low viscosity preferred as reactive diluents [3, 4, 22, 23]. Polydimethylsiloxane is used widely as a photocuring material with good thermal stability and extraordinary flexibility [3, 6, 22, 23]. Acrylic siloxanes are prone to inhibition by atmospheric moisture and oxygen; thus system calls for purging with nitrogen [3, 4, 20-23]. While, since enethiol systems are unaffected by oxygen and moisture, thus allowing their use in open systems like pan coaters [3, 6].

Further, the curing process of enethiol system is faster and more complete comparing to that of acrylate siloxanes [3, 4, 20, 21].

Photo Initiators or Catalysts: Photoinitiator initiates the reaction that results in the formation of solid coating [3, 6]. Reaction products of them add to the unsaturated components accordingly become a part of the polymer layer [3, 4]. They are stable generally against rise in the temperature [3, 6]. Under normal room light conditions, their formulations were applied as layers [3, 4]. They cure only when exposed to intensive ultraviolet light [3, 6, 20, 21].

Most of the photoinitiators contain benzoyl groups [3, 4]. Said group is mainly responsible for the absorption of the radiation energy from the light, thereby generating free radical pair [3, 6, 20, 21]. During the ultraviolet light curing process, the absorption of radiation energy by the photoinitiators generates a free radical pair [3, 4].

The generated free radicals add to the double bonds of the unsaturated reaction partners [3, 6]. The photochemical generation of a radical pair can be bearing from a mono-molecular reaction or bimolecular reaction [3, 4, 20, 21]. Accordingly, photoinitiators are ether mono-molecular type or bi-molecular combinations [3, 6]. Mono-molecular photoinitiators are more effective comparing bi-molecular combinations [3, 4].

Examples of mono-molecular-type photoinitiators are amino ketones, benzoin ether, bis(acyl)phosphine oxides, diethoxyacetophenone, hydroxy ketones, and many others [3, 6, 20, 21]. The combination of benzophenone and amine is an example of bimolecular type [3, 4]. Nowadays, photoinitiators derived from phosphine oxides (mono- and bis(acyl)phosphine oxides) are receiving special interest [3, 6].

The photochemical curing process's mechanism can be described in three steps: initiation, propagation, and termination [3, 4, 20, 21].

Ultraviolet/Vis Light Source: The 80 W/cm medium-pressure mercury lamp is the often-using lamp type [3, 6]. Since this emits a broad spectrum in the short wavelength ranges between 200 and 320 nm; but also at discrete wavelength numbers of 360, 410, and 430 nm [3, 4, 18, 20, 21].

Pore Forming Agents: Ultraviolet light curing process used for derivatizing silicon polymer films results in a film that is a complete and almost perfect barrier for drug diffusion [3, 6]. In such instances, drug release depends on the presence of defects or weak points in the coating [3, 4]. Discussed fact is grounding for incorporation of the pore-forming agents [3, 6]. Therefore, pore-forming agents are needed to be incorporated in the polymeric film to confer functional and non-functional attributes (like immediate, sustained, or delayed-release) to the coatings [3, 4, 20, 21]. Examples of a pore-forming agents are Ac-Di-Sol, Explotab®, lactose, sodium chloride, polyethylene glycol 800, and many others [4, 6]. Pharmaceutical coatings, functional and non-functional, use powdered pore-forming agents [3, 6]. In these instances, the simple pore formers or superdisintegrants are added to an acrylate silicone matrix [3, 4].

Mechanism: Radiant energy of the light initiates a polymerization reaction that mediates through the generation of free radicals [3, 6]. Free radical generation involves cationic or anionic mechanisms, depending on the functional groups of monomers or pre-polymers and initiators or catalysts used [3, 4, 20, 21]. Generated free radical results chemical reaction of functionalized liquid monomers or pre-polymers leading to its polymerization thus its transition into solid film [3, 6, 22, 23].

The presence of oxygen and moisture slows down and/or reduces the extent of curing in some acrylate functionalized silicone systems [3, 4]. This complication comes from the quenching of excited states and the scavenging of free radicals from the initiator and growing polymer network [4, 6]. The said complication is usually overcome by purging the photocurable systems with nitrogen [3, 4, 20-23].

Electrostatic Dry Coating: EDC involves electrostatic deposition of charged coating particles onto the substrate surface. [4, 6, 15, 18, 24-29]. A flow chart of EDC is presented in **Fig. 2** [3, 4, 6]. An optimized process for coating substrate, even in pan coater, can result in a continuous film coat with excellent coating uniformity, smooth surface, and significantly similar drug release profile to that of substrate cores [6, 15, 18, 24-30].

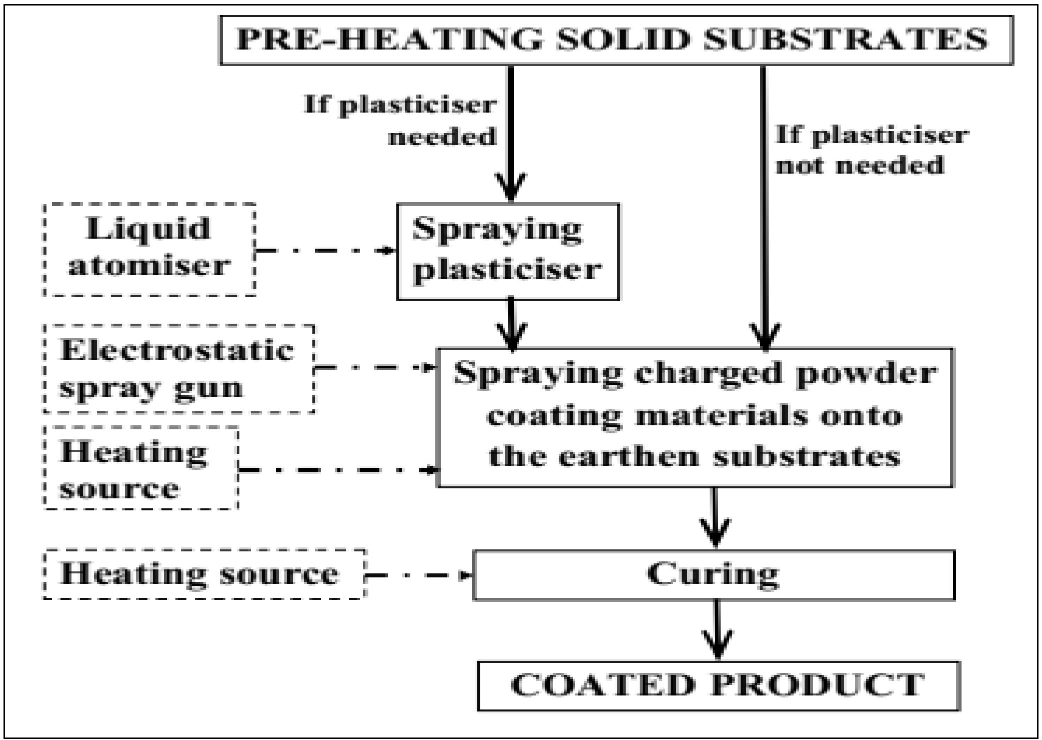

FIG. 2: FLOW CHART OF EDC PROCESS [3, 4]

Features and Advantages: EDC bears follow features and advantages [3, 4, 6, 29, 30]:

a) Requires applications of strong electrostatic charge for applying electrically conductive CoMa onto electrically conductive substrates [3, 4].

b) CoMa with oppositely charged electrically conductive ions is required to be sprayed on the charged substrates [6, 30].

c) The process can achieve complete and uniform coating even of edges and corners [4, 15, 30].

Limitations: Electrically non-conducting CoMa and/or substrate cores are problematic for EDC [6, 25, 29, 30]. Transmuting powdery organic CoMa into a smooth and even film coat with no damage of substrate cores is a difficult task [4, 25, 29, 30].

Process inherits reproducibility issue, as diverse factors contribute significantly to coating attributes like transfer efficiency, film thickness, adhesion, and appearance [6, 30]. Factors of importance are chemical composition of CoMa; particle shape, size, and size distribution; hygroscopicity; characteristics of charging (*i.e.,* corona charging or tribocharging, nozzle geometry and placement and distance of charging gun); electrical conductivity and resistivity and many more [4, 6, 25, 29, 30].

Principle: The principle of EDC involves spraying the mixture of CoMa (as fine powder) onto the substrate surface using a strong electrostatic charge [4, 6]. This is followed by heating the coated substrate in an oven for curing [15, 18].

Curing is done until the powder mixture fuses into film [4, 15, 18, 24, 25, 29, 30]. Accordingly, the process comprises of follow steps [6, 24, 29, 30]:

- Deposition step: is for depositing the PCM.
- Curing step: is for film formation.

The deposition step involves spraying the PCM onto the substrate surface using electrostatic spray guns [4, 6]. The deposition step is continued to adequate levels [4, 24, 31]. The curing step follows deposition steps [4, 6]. This step results coalesce together of lodged PCM to form a continuous coating film [6, 24].

Refer to **Fig. 2** for the principle of the EDC. Thus coating assembly must comprise an electrically earthen coating pan, electrostatic charging gun, and heating source [4, 24, 29]. A spray gun for charging the liquid plasticizer normally is also needed [6, 24, 29].

Charging Mechanisms: Available are two kinds of charging (spraying) units, basing on charging mechanisms [4, 29, 30]:

- Corona charging.
- Tribocharging.

Corona Charging: Charging gun of corona charging at its outlet has charging pins, a sharp-pointed needle-like electrodes [4, 6].

In this case, the charging mechanism involves the electrical breakdown of powdery CoMa particles followed by ionization of the air by imposing a high voltage on charging pins [4, 15, 29, 30].

Thus said particles pick up negative ions during their passage from the charging gun to the substrate surface [4, 25, 30]. The induced electrical field between spray gun's charging tip and earthen substrate, and repulsive forces amongst the charged particles of CoMa generates electrical forces [4, 18, 25, 30]. Ionization of the air generates a mechanical force [4, 6].

This force blows powder towards the substrate from charging gun [6, 15, 25, 30]. Combined mechano-electrical forces are resulting the movement of charged particles of CoMa between the substrate and spray gun [4, 25, 30].

Adjustment of the electrical field has to be done for direct powder flow and control flow pattern, density, size, and shape of powder upon its release from charging guns [6, 18, 25, 30].

Mechanism of Tribocharging: Friction charging is the principle of turbocharging mechanism [4]. Comparing corona charging here no electrical field, and free ions will be there [6, 29, 30].

The electrical forces with tribocharging guns are regarded only as repulsive forces amongst charged PCMs [4, 25, 29]. Upon spraying, the charged PCMs move into space adjacent to substrate [6, 30].

The attractive forces between charged PCMs and earthen substrate make the charged particles to deposit on the substrate surface [4, 18, 29, 30]. By joint effect of electrostatic attraction and mechanical forces, the charged PCMs get sprayed uniformly onto the surface of earthen substrate [6, 25, 29].

In tribocharging repulsive and attractive forces are important in determining coating efficiency and attributes [4, 29, 30]. The repulsive force exists between particles deposited on the substrate surface and approaching PCMs [6, 25, 30].

The attractive forces are from electrostatic attraction between the approaching PCMs and earthen substrate [4, 29]. Charged PCMs accumulate on the substrate surface until said repulsive force increases and exceeds electrostatic attraction [6, 29, 30].

Once equilibrium is reached between repulsive forces and attractive forces, there will be no further adherence of charged particles, thus, coating thickness will not increase anymore [18, 25, 29].

Plasticizer EDC: As the name indicates technology of this DCM/P is featured with a combined usage of heat, plasticizer, and electrostatic field [3, 4].

In this technique, plasticizer is used and is suitable for a process that calls for processing under lower curing temperatures [6, 30]. In said instances, incorporation of plasticizer promotes PCM adhesion and film formation [3, 4, 29].

This in turn, promotes EDC process and shortens processing time [6, 29, 32]. It can be done by charging a suitable quantity of suitable liquid plasticizer using separate charging guns [3, 4].

A liquid plasticizer capable of increasing the electrical conductivity of substrate and reducing *Tg* of coating polymer is suitable [24, 29, 32].

The technology of said coating process comprises of following steps [3, 4, 6]:

- Placing pre-heated powder substrates in the rotating coating pan electrically earthen [3, 4].
- Charging (i.e., spraying) of plasticizer and powdered CoMa onto the moving powder substrate in the coating pan [3, 6].
- A separate electrostatic spray gun is needed to charge powdered CoMa and plasticizer [3, 4].
- Charging is done for a preset time period [3, 6].

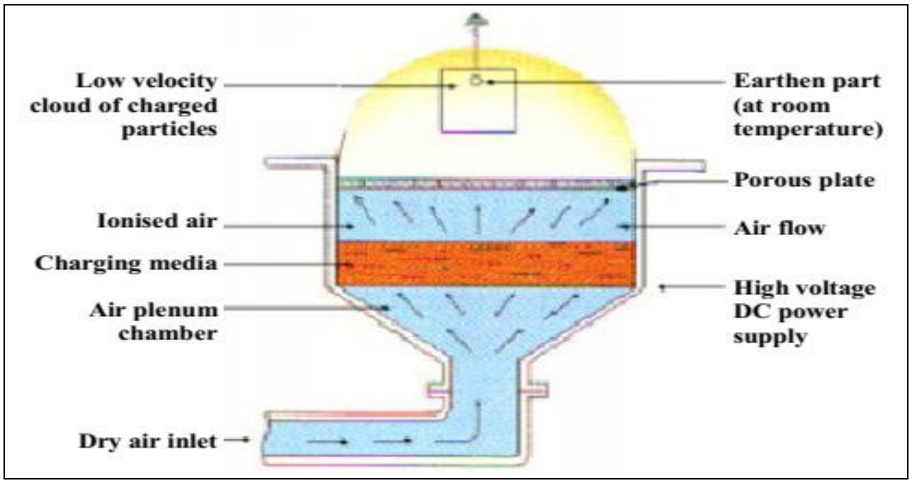

FIG. 3: FIGURE OF ELECTROSTATIC FLUIDIZED-BED COATER [6, 18]

Electrostatic Fluidized-Bed Coating: As the name refers, the process involves electrostatic costing with a fluidized-bed processor [6, 18, 33]. The fluidized-bed processor is for fluidizing the particle [4, 33]. In the fluidized state the particles of powder (GuPs and HoPs) are subjected for the electrostatic field by either of two ways [3, 4]. One involves placing an electrode beneath fluidizing powder [3, 18]. The second is thru charge transfer from pre-ionized fluidizing air [18, 33] refer **Fig. 3.** In combination with the repulsive effect of charged powder particles, the fluidizing effect results in their upward motion [18, 29]. These effects thereby generate or form a cloud of charged particles above the powder bed [32, 33]. Generated cloud is much more similar to that of conventional electrostatic gun [32, 33]. Through the said cloud, heated or unheated particle makes several pass [18, 31]. The electrostatic fluidized-bed coating process never dips the particles into powder bed [18, 29]. This process generally results thin coat to that resulting from coating processes using conventional fluidized-bed coater [18, 31]. The process is unsuitable for elongated substrates or other objects passing vertically or axially across through powder-bed and through powder cloud gets, as they gets deposited as layer of powder material [18].

Vapor Phase Deposition (Coating) of Powders: Vapor phase deposition (electro-deposition) is the underlying principle in vapor coating of powder [3, 6, 34]. The electro-deposition process is applicable in creating uniform, durable, and slow-dissolving coatings of controlled thickness on particles at individual levels [3, 4, 15]. Furthermore, it enables synthesizing polymeric coating films with satisfactory coating uniformity [3, 6]. Resulted film coat has an orchestrated surface, topography, and functionalities [4, 35-39]. Electro-dispersion is a novel approach for dispensing liquid or powder by application of electrostatic field [3, 6, 15, 18]. Said approach uses an intense electric field to disperse a part of a static-bed of powder or liquid into a stable cloud of fast-moving particles (dispersed phase) and maintain dynamic equilibrium within the phases (i.e., static and dispersed phase) [3, 6].

The coating is achieved by generating vapor of desired CoMa and allowing generated vapor to permeate dispersed particles [6, 15, 18]. The cloud density of the dispersed phase particles depends on legion factors, including the field strength and the nature of powders [15, 18]. Applied electric field is also ensuring that only uncoated particles are coated [6]. Further, it prevents the agglomeration of coated dispersed particles, as they possess the same charge and thus repel each other [15, 18].

Follows are major vapor phase deposition methods finds applicability to pharmaceuticals [3, 6, 15, 18].

a. CVD [3, 6]
  - ✓ Plasma enhanced CVD [3, 6]
  - ✓ Initiated CVD [3, 6, 34]

b. ALMD [3, 6, 39, 40]

c. Fluidized-bed chemical vapor coating [3, 6]

Vapor phase deposition reactions are similar for CVD and ALMD, as these utilize gaseous reagents for nurturing a film [6, 38-41]. CVD is a single-step process while ALMD is two-step one [39, 41].

In ALMD process, involved reaction is split-up into two surfaces half [18-41]. The ALMD process is designed to expose the substrate surface to one reagent only at a time [18, 39, 40]. Splitting the reaction into two steps to achieve that surface will react sequentially with each reactant/ reagent until the complete surface is coated by a new atomic-layer [18, 40]. For elucidation, when the process starts, suppose reactant A is reacting with the surface functional groups present on particle [6, 18], refer **Fig. 4**. As the said half-reaction completes, a new surface functional groups are in place [3, 6], refer intermediate product as in **Fig. 4**. In the subsequent step, this surface (*i.e.*, surface of intermediate product) exposes to reactant B [6]. Then, reactant B reacts with new functional groups, second half-reaction [18]. As the second half-reaction completes, all surface site totals transform back to original surface species [1, 3]. At this stage, the reaction stops; thus, the reaction is self-limiting [18, 40]. Then the process can be repeated sequentially till the film thickness of wished dimension is achieved [18, 39]. The ALMD process can result in a monolayer of the film (one complete cycle of A & B) with a thickness of 1 angstrom (0.1 nano-meters) [6, 18, 40]. Said process can achieve an effective film coating with a thickness of a few atomic layers only [6, 42]. Presently, the ALMD process is relatively expensive and often requires toxic precursors [6, 42].

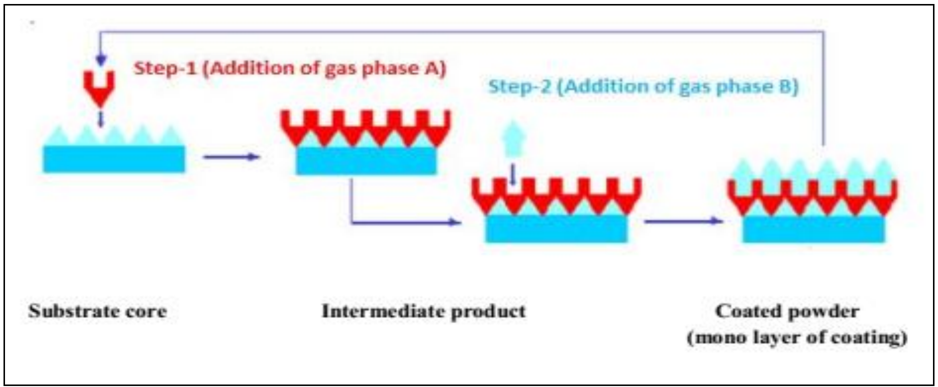

FIG. 4: SCHEMATIC PRESENTATION ON STEPS OF ALMD PROCESS [6, 18]

Mechanical Dry Coating: Techniques of mechanical dry coating processes involve high-energy and high-shear interactions between particle-particle or particle-device walls [3, 6, 17, 18]. Said generated interactions are directed to coat the surface of HoPs with PCM or GuPs [3, 4, 43]. The true mechanisms of dry mechanical coating have to be fully understood, yet [44, 45]. The reason is the process involves complex interactions between host-guest particles, guest-guest particles, device wall-HoPs, and device wall-GuPs [6, 18]. Further, the binding mechanisms between GuPs and HoPs can be dependent on the material and process [3, 4]. Also, physical and/or chemical binding might also contribute to the adhesion of GuPs onto HoPs [3, 18]. An example is a mechano-chemical reaction amongst the corn starch, the HoPs, and silicon dioxide, the GuPs [6, 18]. However, a generalized mechanism of DCM/P is attempted to present in **Fig. 5** [3, 4].

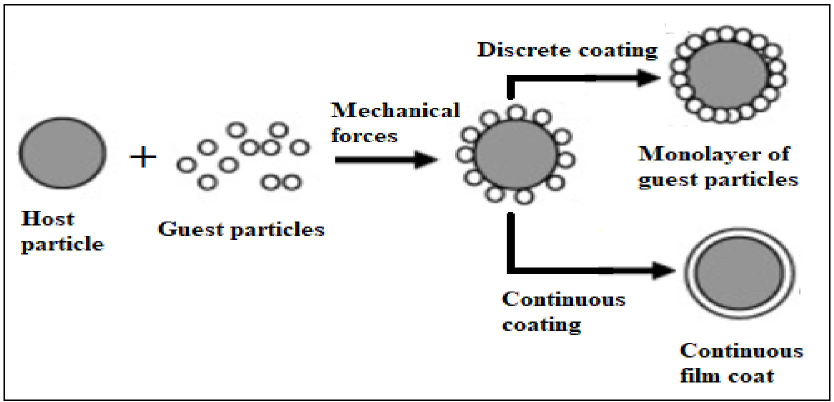

FIG. 5: MECHANISM OF MECHANICAL DRY COATING [1]

Devices based on the mechanical dry coating technique were pioneered by Japanese scientists from 1970 to 1980 [3, 6, 18, 44, 45]. They configured different devices with various configurations but with similar principles of operation [3, 4, 18]. This development is foundational for the commercially availability of a number of specialized devices, nowadays [3, 6, 18]. These include Magnetically Assisted Impaction Coater®, Hybridizer®, Mechanofusion®, Theta Composer®, Cyclomix®, Quadro Comil®, and many others [3, 4, 18, 44, 45]. However, Cyclomix® and Quadro Comil® are high shear mixers not specifically designed for coating purposes but have also been employed in coating cohesive powders [3, 18]. These dry coaters are considered a special type of high-shear mixers [6, 18]. They provide maximum surface interaction with minimized attrition effect [3, 4].

The operation of equipment for dry mechanical coating of the particle is mostly a one-step straightforward process [6, 18]. This means load the powder mixture (GuPs and HoPs) into the processing vessel of machines [3, 4]. Then turn on the machine for a set time and/or speed [4, 6]. Turn off the machine and then unload coated powders [3, 18]. The processes have the ability to be designed for continuous processing [3, 6]. Upon optimization and validation of the process, the manufacturing process will become a robust one with minimal concern of process deviation linked to the skills of operators [3, 4]. Further, most DCM/P possesses apparent potentiality to be scaled up [3, 6]. However, scalability of the DCM/P for larger manufacturing scale batches with pharmaceutical applications calls more robust investigation [3, 4].

Mechanofusion®: Of the available mechanical dry coating techniques, Mechanofusion® has arguably grabbed the most attention in the pharmaceutical field [4, 6]. The underlying principle of the process is bringing forth a mechano-chemical reaction among two or more powder materials to produce new material having differing properties [5, 7, 43-48]. Mechano-fusion® merges/ fixes HoPs on GuPs particles by inputting high mechanical energy through mechano-chemical reaction [3, 5-7, 48]. The mechano-chemical reaction occurs in the contact area of the GuPs and HoPs, thus resulting in a new composite [3, 4, 7, 48]. Furthermore, during processing, the sample in the mechanofusion reactor gets subjected to compression and simultaneous stress by intense shear [3, 6, 48]. Both of the strategies are dependent on processing time and rotor speed [5, 48]. The process employs a batch-operated, specifically designed device for fusing particle-to-particle at high compressive and shear forces, thus resulting in controlled particle shape and size [18, 44].

The device can be water-jacketed to cool the processing chamber wall if process-induced heat is a concern [3, 4]. An early version of the Mechanofusion® device was designed with a four-bladed propeller processor [3, 6]; refer to **Fig. 6 A**. The design approach comprises of outer processing vessel (rotating), inner piece (a round stationary processor), scraper (stationary), powder inlet channel, and powder outlet channel [5, 6, 43, 46-48], refer to **Fig. 6 (a)**. Driven by a motor, the outer vessel rotates at a controlled speed between 200 – 10,000 rpm [3, 4]. The round stationary processor (inner-piece) acts as a press head or arm head [4]. Scraper is for eliminating any caking and agglomeration [3, 6, 48]. The later version has a simplified design, based on rounded processors [3, 4]; refer **Fig. 6 B**. In the said design approach, the scraper and the processor are replaced by an exchangeable processor module [3, 6]; refer to **Fig. 6B**. Here the deviation is the vessel is stationary while the processor rotates at speed up to 6000 rpm [3, 4].

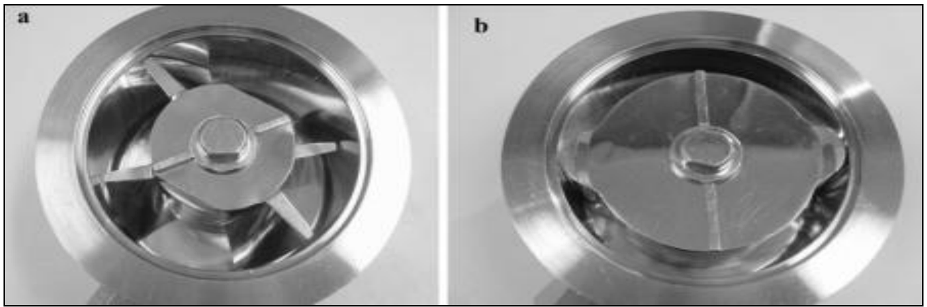

FIG. 6: MECHANOFUSION® WITH THE EXCHANGEABLE PROCESSOR [3, 6]

The coating performance of said two design modules is significantly equivalent [6, 18]. However, the earlier design allows higher powder load as is higher void space [3, 4]. The coating process involves placing of an aliquot quantity of HoPs and GuPs into the rotating vessel [15, 44]. When vessel rotates at a controlled speed between 200-1600 rpm, powders are pushed outwardly towards vessel walls [5, 43, 46, 47]. Gap between the rotating vessel and the inner stationary piece is controlled [3, 6].

As a result, powder particles passing through the gap are subjected for intense forces of compression and shearing [5, 43, 46, 47]. Intense shearing force may physically and chemically alter properties of materials which are associated with size reduction to some extent [3, 4]. A combination of compression and shearing forces acting on particles builds up localized temperature [3, 6]. The generated heat is sufficient to fuse the GuPs onto the surface of HoPs [4, 5, 43, 46, 47]. The gap between the inner piece and the vessel wall plays a crucial role in controlling the coating thickness [5, 6, 43, 46, 47]. Also, the gap between the scraper and the vessel wall requires controlling [4, 15, 18, 44].

Features and Advantages: Mechanofusion® process bears follow features and advantages [5, 43, 46, 47].

- Process results in composite particles having controlled particle shapes [6, 18].
- The process eliminates the requirement for pre-mixing of powder particles throughout particle performance improvement processes [4, 44].
- Process temperature can be controlled by jacketing the processing vessel [6, 18].
- The design of devices is compact, thus easing the coating process and increasing performance [4, 44].

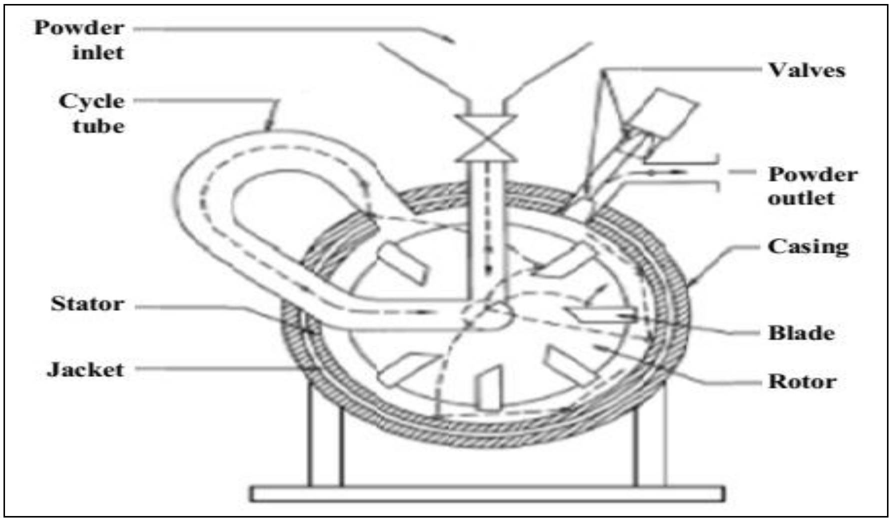

FIG. 7: SCHEMATIC DIAGRAM OF HYBRIDIZER® [4, 6, 18]

Hybridizer®: The design approach of Hybridizer® is similar to that of Mechanofusion® [3, 6, 44]. The design of the Hybridizer® machine basically comprises a processing vessel with six-bladed rotor assemblies, a stator, a re-circulation device for powder is made up of stainless steel or ceramic, units for powder inlet and outlet [4, 44, 45], refer **Fig. 7**. During operation, the rotating blade assembly rotates at very high speeds up to 16,000 rpm [3, 6, 45]. The processing vessel is jacketed for heating/ cooling so as to control local temperature [4, 44]. The re-circulation unit/ device moves the particles continuously in & out of the processing chamber and against the rotor blades [15, 18]. The processing comprises two steps, namely pre-mixing and hybridization [3, 6]. Pre-mixing steps involve feeding of GuPs and HoPs into a high shear mixer (like Ordered Mixture dizer) [3, 4]. In this step GuPs and HoPs are mixed and dispersed to form an ordered mixture [3, 6]. In the hybridization step, the powder mixture of HoPs and GuPs is placed in the processing portion of the hybridizer vessels [3, 6]. This is for subjecting powder blend to high shear impaction and dispersion [3, 4].

High rotational speed of hybridizer's rotating blade assembly disperses HoPs and GuPs and imparts them thermo-mechanical energy [6, 18]. High impaction forces build up the temperature and induce the particles to undergo numerous collisions [15, 18]. Said collisions result in breaking-up of fine agglomerates and powder coating due to embedding or filming of the GuPs onto the surface of HoPs [3, 6]. The built-up temperature aids in embedding or filming [4, 18]. The batch-operated device embeds or coats the GuPs onto the HoPs within a very short period, *i.e.*, 1-5 minutes [3, 6].

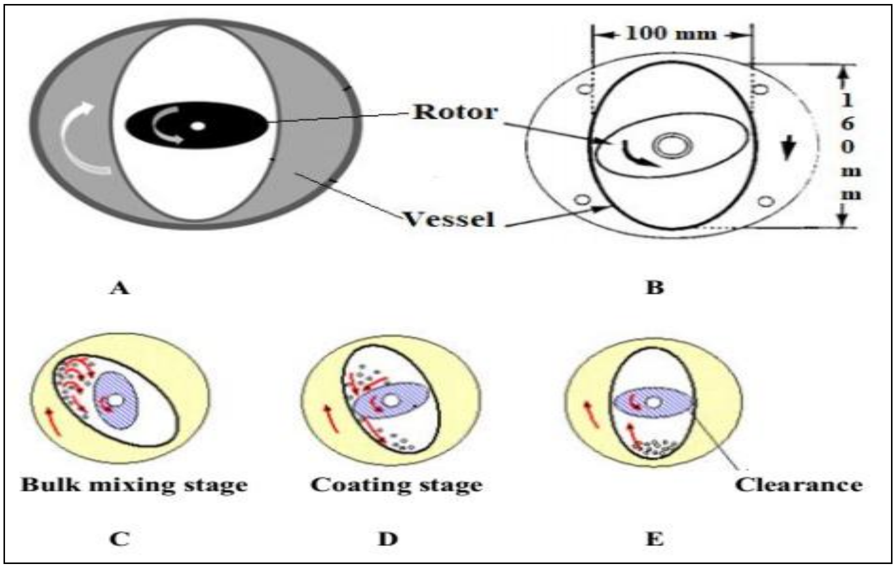

FIG. 8: SCHEMATIC DIAGRAM ON DESIGN AND OPERATION OF THETA COMPOSER® [4, 6, 18]

Theta Composer®: The design of Theta Composer® comprises of outer elliptical-vessel and inner elliptical rotor [3, 6], refer to **Fig. 8A**. The vessel rotates slowly (rotating at speed between 30-40 rpm) while the rotor rotates very fast (rotating at speed between 900-1200 rpm) and opposite vessels [4, 44, 45] **Fig. 8A**, **8B**, & **8C.** The rotor rotates anticlockwise inside the clockwise rotating vessel; as a result, the clearance width cycles between smallest to largest to smallest [3, 6], refer **Fig. 8C, 8D** & **8E**.

Due to this, the particles are lifted by the vessel with mixing in one stage, and the particles receive strong compaction forces and shear stress in the other stage, when they pass thru a very narrow clearance between the vessel wall and the rotor [3, 46], refer Fig. 8(d). Simultaneous application of strong shear stress and compaction force results in strong coating and formation of composite particles [3, 6].

Due to said peculiar rotation of rotor and vessel, in one stage, forces powder mixture of HoPs and GuPs through small clearance between the rotor and the vessel [3, 4], refer **Fig. 8D** & **8E**. Subject HoPs and GuPs for shearing and compressive stresses 44, refer to **Fig. 8D**.

As rotor and vessel continue to move, in another stage, the clearance between rotor and vessel wall becomes large [3, 6], refer **Fig. 8C**. There will be bulk mixing of HoPs and GuPs [18, 44], refer to **Fig. 8C**. The blending of HoPs and GuPs is to be done at a condition comprising container speed at low and rotor speed at high [18, 44].

At the same time, the application of strong shearing and compression forces accelerates precise blending & composite fabrication [18, 44].

The particles' critical revolution speed (Nc) can be obtained by following mathematical relations [4, 6, 49].

$$N_C = 60 / \Pi\sqrt{G} / 2D$$

Where, '*D*' is the inner diameter of the vessel and '*g*' is the acceleration due to gravity.

Practical Hint: The revolution of the outer vessel must be much smaller than the critical speed [4]. Otherwise, particles will adhere to vessel walls due to the centrifugal force [6].

Features and Advantages: Follows are the advantages and features of process use Theta Composer® [4, 6, 45]:

a. Its simple structure makes its operation and maintenance easier [6, 44].

b. The outside vessel rotates slowly, thus promoting and favoring bulk mixing [4, 18].

c. Inside rotor rotates at high speed [6]. This confers the high shear stress required for coating [18].

d. Elliptical shape of the inside rotor and outside vessel contributes stress and relaxation [4, 44].

e. As the vessel rotates, this assists for getting highly homogenous powder composite and prevents thermal deterioration [18, 44].

f. Instant compression and shearing of particles minimize rise in the temperature of materials [6, 44].

g. Processing time is very short [4, 44].

h. Optimum rotational conditions can be set, that suits the material(s) [6, 18].

i. Improves handling of the product, suppresses hygroscopicity, and increases flowability [4].

Fluid Energy Mill: The fluid energy mill is primarily used for size reduction of micron and sub-micron-sized particles and finds applicability in coating with some modifications [6, 50]. The modified version of the unit is presented in **Fig. 9**, which includes three air inlets [3, 6].

Amongst them, two are grinding air inlets, and one is feed air inlet [6]. The particles are fed into the feed funnel [3, 6]. The feed is then sucked into the milling chamber thru the venturi region made by the feed air [6]. In some instances, a volumetric feeder controls the feed rate [50].

The operational parameters that control the machine operation are the grinding pressure, the solid feed rate, and the feeding pressure [3, 6]. The use of a fluid energy mill for simultaneous micronization and dry coating of FUFP was pioneered by several research groups [6, 50].

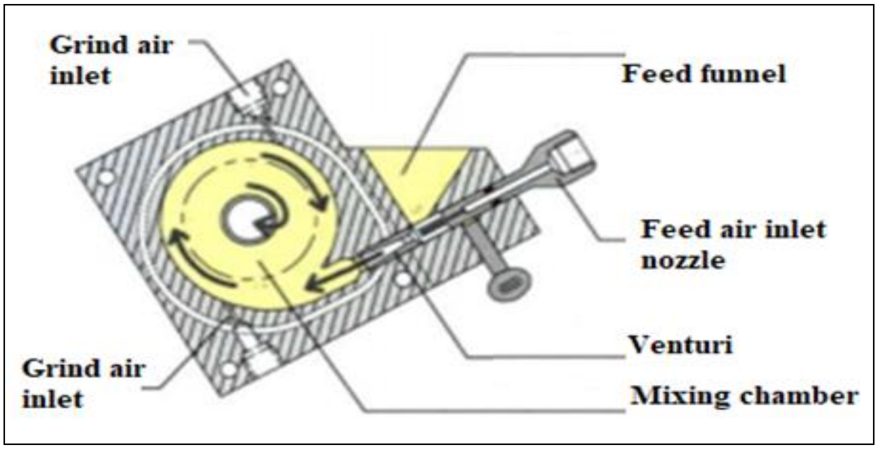

FIG. 9: CROSS-SECTION OF THE MILLING CHAMBER OF THE FLUID ENERGY MILL [6, 50]

Conical Screen Mills: Quadro Comil® and Cyclomix® are conical screen mills is commonly used for de-agglomeration/ de-lumping and fine control of granule sizes [3, 6, 16, 51]. This feature is exploited to find its applicability in coating dry powders [3, 4, 50]. Quadro Comil® and Cyclomix® have similar working & operational principles [6]. Thus schematic diagram of the Quadro Comil® is shown in **Fig. 10** [6, 50]. The key components of Quadro Comil® are screen and impeller [3, 4, 50]. The mills are available in a diverse designs to combine sieving and milling into a single operation [3, 6, 51]. Available design diversity is with ranges of screen sizes, screen types (like a round hole, rasping), and impeller types (like square-edged, round edge) [3, 4, 50]. The impeller is typically operated with a variable speed motor [4, 6]. This allows a range of tip speeds to be made achievable [3, 50]. A spacer is there to adjust the distance between the impeller and screens [4, 6]. Further refinements of said basic configuration may also be adopted [6, 50]. The capability of conventional Quadro Comil® for de-agglomeration with intensified mixing is exploited to find its applicability in DCP [3, 4, 50]. Upon charging the powder (mixture of GuPs and HoPs), into the mill, it is retained and blended in the middle of conical vessel [3, 6, 51]. The vessel's conical design and centrifugal force of the impeller propel the particle mixture outward and up towards the impeller tip and screen [3, 4, 50]. As particles get trapped between screen and impeller edge, imparted shear stress de-agglomerates the GuPs [3, 51]. It is postulated that during this residence phase, larger agglomerates of nano-sized GuPs break down into smaller sub-agglomerates [3, 6, 50]. These then preferentially attach to substantially larger HoPs thru van der Waals attractions [3, 4, 51]. Subsequent further residence state is expected to encourage repeated collisions between larger HoPs attached with some sub-agglomerates and sub-agglomerated GuPs [3, 6, 50]. This would lead to redistribution/ transfer of nano-sized GuPs, ultimately resulting in a uniform coating [3, 50]. After shearing, under-sized coated particles pass through the screen while the oversized particles are moved back into central mixing zones [3, 6, 50]. Likewise, particles pass through the screen until the entire charged volume is emptied [4, 51]. The design of Quadro Comil® makes it amenable for batch or continuous operations [3, 6, 50]. The ability for the largest selection of impellers and screens and the widest impeller speed range of any Quadro Comil® enables targeted particle size distributions and improves milling capacity without changing base model [4, 51]. The process calls for proper selection of Quadro Comil® design (screens and impeller) and operating conditions (powder feeding rate and operating speed) specific to candidate powder to maximize dispersion and enable high throughput without blinding of screens [3, 6, 51].

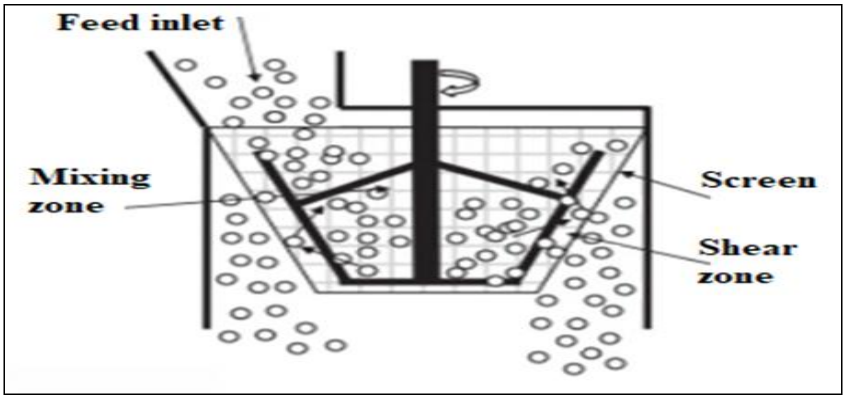

FIG. 10: SCHEMATIC DIAGRAM OF QUADRO COMIL® [6, 51]

Resodyn Acoustic Mixer: It is a sophisticated benchtop mixer where mixing operation is based on "*resonant acoustic technology*" [6, 52, 53]. The employed mixing technology creates a low frequency, a high-intensity shear field that helps in thorough and uniform mixing of material within a very short time [4, 52]. Intense vibration of the process disperses GuPs and adheres them to the surface of HoPs, thereby creating a uniform coating layer [6, 52, 53]. An external digital control system is there to vary and control intensity of vibration and mixing time [4, 52, 53]. The frequency of vibration is generally between 50-65 Hz [52, 53]. The primary parameter promoting mixing is acceleration [52, 53]. In the form of intense vibrations, the use of acoustic energy is to create high shearing zones within the mixing vessel of the device [52]. This state and increased energy create a virtually fluidized state for powder particles [52, 53]. In this fluidization process submicron-sized GuPs collide with HoPs, thereby resulting in dry-coated HoPs [53]. The schematic diagram presenting resonant acoustic mixing is with **Fig. 11.**

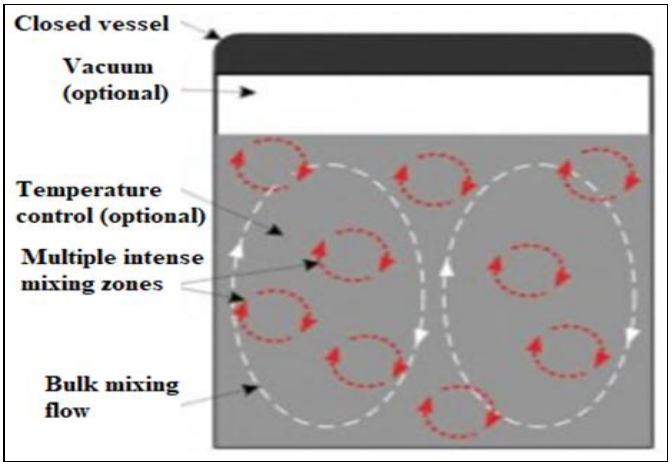

FIG. 11: SCHEMATIC DIAGRAM PRESENTING RESONANT ACOUSTIC MIXING [6, 52, 53]

MAIC: The design and operational mechanism of MAIC device are different to that of other devices used in mechanical dry coating [3, 6]. In these devices, magnetic beads are placed in a processing vessel along with powders of HoPs and GuPs [3, 4]. The surrounding vessel generates the oscillating magnetic field to agitate magnetic particles [3, 6]. This results in collisions between magnetic particles and the GuPs or HoPs, and between GuPs and HoPs, in fluidized states [3, 4]. The collision occurring among particles is crucial and important for impinging GuPs onto surface of HoPs and thus the formation of a semi-permanent coating on the surface of HoPs [25, 54].

Some instances call for coating the magnetic particles appropriately to overcome the shedding of contaminants [1, 3]. Magnetic particles usually are of barium ferrite with a polyurethane coating to prevent contamination of coated particles [1, 25]. It is a batch and continuously operates an able soft coating process with a shorter processing time that calls for less energy [6, 18, 44]. The process can handle core particles as fine as 0.25 microns and coat dry FUFP GuPs onto large dry HoPs [6, 18, 30]. This technique can fix GuPs onto HoPs that are soft with minimal degradation of components and deformation of their particle shape & size [15, 18, 25].

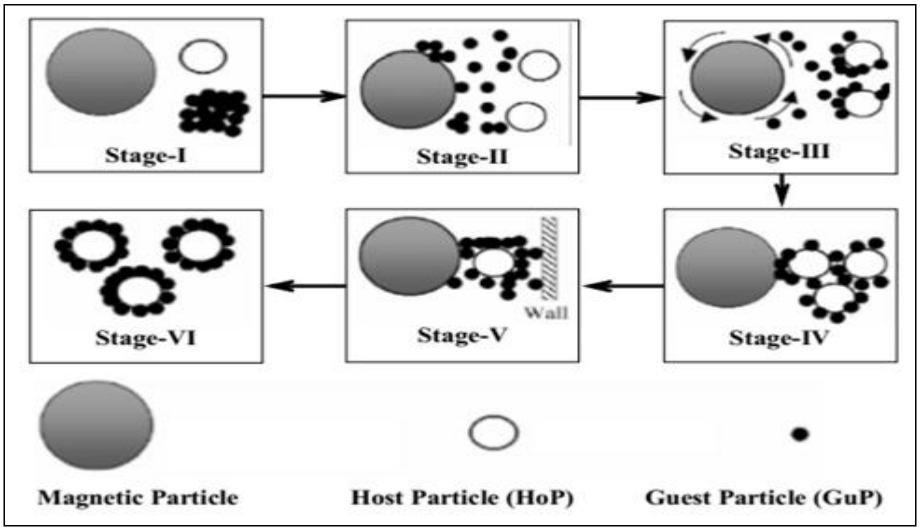

FIG. 12: SCHEMATIC DIAGRAM ON STAGES OF MAIC PROCESS [4, 51]

Mechanism and Stages of Coating in MAIC: The mechanism of coating involving MAIC processes can be conveniently described as comprising of the following stages [1, 4, 6, 15, 18, 25]; refer to **Fig. 12.**

Stage I: Excitation of the magnetic particles [15, 25],

Stage II: De-agglomeration of the CoMa, *i.e.*, GuPs [1, 25],

Stage III: Spreading and shearing of GuPs onto surface of the HoPs [6, 18],

Stage IV: HoP-magnetic particle and HoP-HoP interaction [15, 25],

Stage V: Magnetic particle-HoP-vessel wall interaction [4, 25], and

Stage VI: Formation of products, *i.e.*, coated particles [18, 25].

MAIC Apparatus and Process: MAIC apparatus comprises a processing vessel that is surrounded by a series of electromagnets [4, 6]. The electromagnets are connected to alternating current [1, 15, 18, 25, 44]; refer to **Fig. 13**. The powder of GuPs and HoPs along with the aliquot mass of magnetic particles, are poured into the processing vessels [6, 15, 25].

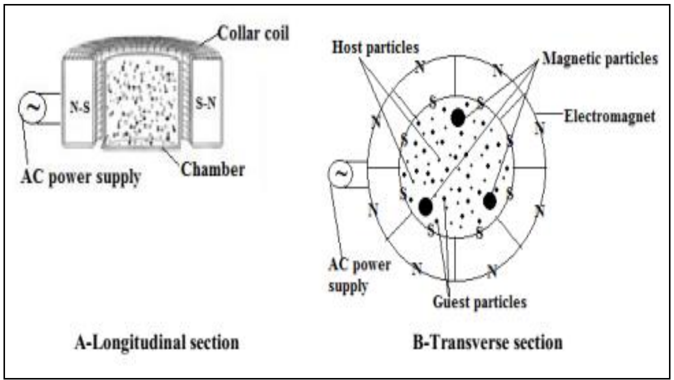

FIG. 13: FIGURE OF MAIC APPARATUS [1, 6, 15, 18, 25]

Application of alternating current generates oscillating magnetic field [18, 25]. Generated magnetic field agitates magnetic particles that oscillate/spin (move frequently) inside the vessel, thus fluidizing the particle as in a fluidized-bed system [4, 25, 54]. Agitation of magnetic particles imparts energy to GuPs and HoPs and thus causes their collisions (HoPs-GuPs, host-host particles, HoPs-GuPs-vessel wall) [15, 25]. Resulted in collisions allowing coating through impaction and/or penning of GuPs onto HoPs [25]. Spinning the magnetic particles promotes the de-agglomeration of GuPs vis-a-vis spreading and shearing of GuPs onto the surface of HoPs [1, 25, 54]. Further, translational speed allows the impaction of one particle onto some other and has significant effects in promoting coating [6, 18, 25].

Performance of MAIC process depends on parameters like particle size of GuPs and HoPs, ratio of powder mass-to-magnetic particles, particle size ratio of GuP-to-HoP and magnetic particle-to-HoP, processing time, voltage or current and frequency of the alternating current, speed of the magnetic particle, and many others [4, 25, 44, 54]. Further, the coating time depends on several parameters: number density of HoPs, diameter ratio of HoPs-to-GuPs, initial & final bed height of fluidized particle bed, and material properties of GuPs and HoPs [23, 44, 54]. There an optimal value of bed-height for which coating time is minimal [25, 54]. Coating time sharply increases with an increase or decrease in bed height from optimal value, and/or increase in diameter of the HoPs and/or increase in the ratio of diameter for host-to-guest particle [1, 6, 25]. These parameters must be looked at during the MAIC process [15, 18, 25].

CONCLUSION: Handling of FUFP is a generic industrial problem as these often tend to agglomerate and are very cohesive in bulk flow. Said problems are associated primarily with their particle size, but particle shape, density, and surface properties are also contributors. These issues call for engineering and/or modifying their surface and surface attributes. Nowadays, among the available diverse techniques and/or methodologies, the DCP received high attention. The sequential steps of DCP (application of PCM and their coalescence and sintering) are influenced by coating formulation and DCM/P. Herein appropriate particle size of materials (GuPs and HoPs) is essential for ensuring coating and reproducing coating uniformity. A general recommendation is, that the diameter of GuPs is less than 1 percent that of the S/CPs. This permits the application of CoMa onto the substrate surface to an acceptable degree of uniformity. In addition, it improves film adhesion and appearance and decreases processing time. DCM/P relying on mechanical compaction facilitates adhesion and coalescence of CoMa. With these methods, the stresses on the coating layer lead to the consolidation of the substrate bed. Here spreading of the coating layer across the interface is driven by deformation. This creates issues in the case of elastic CoMa, as deformation of these materials is reversible, resulting in poor contact across the surface.

But in the case of CoMa exhibiting plastic behavior, the deformation is irreversible. Here mechanical compaction contributes to greater adhesion on the surface layer. This improved adhesion is due to the possible mechanical interlocking of HoPs and GuPs and a larger surface area for contact between the HoPs and GuPs. EDC process inherits problematic issues from electrically non-conducting CoMa and/or substrate cores and powdery organic CoMa. The process bears issues of transfer efficiency, reproducible film thickness, adhesion and appearance, reproducibility and many others. Gas-phase methods like physical vapor deposition, CVD, and sputtering involve vacuum generation. This gas-phase method typically requires huge capital investments & large overhead costs in the process equipment. Strategies based on plasma-enhanced CVD and aerosol flow reactors are relatively expensive, complex, and challenging to scale up also issues. DCM/P possesses enormous pros but redressing the inferior uniformity of coating film is the biggest challenge. Their requirement for capital investments in addition to large overhead costs, hinders their application and commercialization; the main goal requires addressing.

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