Dry-Coating of Powder Particles is Current Trend in Pharmaceutical Field

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INTRODUCTION

Aqueous dispersions based coating process are energy and time consuming reasoning from the low level of the film former (i.e., coating polymer) and large quantity of aqua that calls for evaporation 1-7. Issues like cost and regulatory restrictions on use of volatile organic solvents, and energy and time requirement of aqua-solvent based coating process had lead to developing specialised dry-coating techniques, over few decades 4-12. These processes/techniques find applicability in the coating of the dry powder particles 2, 4, 8, 9.

Rational for coating of the dry powder particle are 4, 11, 12:

- To have functional coating that is to modify drug release profile (enteric coating, delayed/ sustained/ extended release coating) 4,8.
- For improving aesthetic property (like improvement in appearance, improve product appeal by masking obnoxious taste and odour, facilitate identification and swallowing, and many others) 4,9.
- To protect degradation of the product and the core from atmospheric degradants like oxygen, light, humidity, etc 4, 10.
- For facilitating product handling and production, by reducing friction and making them amenable to high-speed packaging equipment 4,11.
- To separate incompatible components by coating them individually and separately 4,12.

DRI Y COATING OF POWDER PARTICLES

Coating of powder particle following dry coating technique, a solventless coating process, is followed to have new-generation materials, as the method enables combining powders with different chemical and physical properties to get composites that bears new functionality or improves characteristics of the component materials 2,4. DPC technologies involves mechanically fixing the CoM herein termed guest particle (GP), in fine submicron state, onto surface of the substrate herein termed host particles (HP), relatively larger particles with size 1 to 200 µm 2,4. Here in these coating processes HPs termed cores that are mechanically coated with GPs using no liquid in any forms like binders, solvents, even water 3,4.

Advantages

DPC processes/techniques have follow advantages:

- Aqua and non-aqua solvent is not needed for coating the powder particles 2,4.

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Comparing solvent based coating, the dry coating method is less time consuming, environmental friendly, safe and cost-effective. A suitable coating methodology for coating drugs and foods those are sensitive to aqua and non-aqua solvents does not call for solvent recovery, as required with process based on volatile organic solvent, as are environmental pollutants.

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Said coating processes is rapid that to based on aqueous dispersions, as the later are energy and time consuming arousing out from the lower concentration of film former and large quantity of water that needs evaporation.

In nutshell, film formation occurs by a sequential process involving powder application, coalescence, and sintering.

CLASSIFICATION OF DPC PROCESS/TECHNOLOGIES

Follows are the classes of DPC process/technologies.

A. Electrostatic coating
   a. Corona charging
   b. Tribocharging
   c. Electrostatic fluidised-bed coating
   B. MAIC process/technology
   C. HMC processes/technologies
      a) HMC using tablet coating pan
      b) Spray congealing
      c) HMC using fluid-bed processor
      d) Solid dispersion hot-melt fluid bed coating or tumbling HMC
      e) Turbo jet coating process (modified)
   f) Theta-composer
   g) Mechanofusion
   h) HMC using spherizerizer
   i) Spheroidization
   j) Hybridizer

D. Vapour coating
   a. Chemical vapour deposition (CVD).
      i. Plasma enhanced chemical vapour deposition.
      ii. Initiated chemical vapour deposition.
   b. Atomic/molecular layer deposition (ALMD).
   c. Fluidised-bed chemical vapour coating
   E. SCF based coating
      a) RESF method
      b) GAS process
      c) SCF anti-solvent method
      d) GSS method

Mechanism

From a mechanistic perspective, DPC processes comprises of sequential steps similar to that of conventional solvent-based coatings. The process begins with pretreatment of CoM followed by application of CoM onto powdery substrate, and relying on adhesive nature of formulation for maintaining coating uniformity during process of film formation. Follows are summary on mechanisms of film formation in DPC process, while Figure-1 is schematic presentation of the same.

a. Layering is of coating powder onto the surface of powder substrate.
b. Coalescence & sintering of CoM’s particles is bearing through partial fusion of polymer.
c. Levelling of CoM includes densification of layer by reduction of empty spaces & smoothing of surfaces.
d. Cooling of applied coating layer followed by curing of the coating film.

In nutshell, film formation occurs by a sequential process involving powder application, coalescence, and sintering.

ELECTROSTATIC COATING

Electrostatic dry coating, a novel technique, as an alternate to coating processes based on aqueous and non-aqueous solvents finds applicability in pharmaceutical field, besides food and paint technology, metal coatings, and many others. In pharmaceutical field it is useful technology for coating of powders, tablets, capsules, and living cells. The method is devised by Yang et al. results electrostatic deposition of charged coating particles onto substrate surface, which in turn dramatically enhances uniformity of film coating. An optimised electrostatic coating process for substrates coating in pan coater can produce coated substrate with excellent coating uniformity, continuous film coat with smooth surface, and drug release significantly similar to that of substrate cores.

Advantages

Electrostatic dry coating finds advantages as follows:

a. The method is efficient for applying coating solution onto conductive substrates.
b. Involves applying strong electrostatic charge onto the substrate.
c. CoM comprising oppositely charged conductive ions are sprayed on charged substrates.
d. The process makes achievable the uniform and complete coating even of edges and corners.
Principle

Principle of electrostatic coating comprises spraying the mixture of finely grounded polymers and particles onto substrate surface using no any solvent followed by heating of substrate in an oven for curing until powder mixture fuses into film. Accordingly, the process consists of follow two steps: 3\(^8\), 15:

- Deposition of coating particle, and
- Film formation.

The deposition of coating particle step involves spraying of coating powder, onto substrate surface using electrostatic spray gun, till adequate deposition of coating powder is achieved. Following coating particle deposition step, there is film formation (curing) step that results coalesce of the lodged coating particles to form continuous film of coating. Refer Figure-2 for principle of the electrostatic coating.

Thus the coating assembly comprises of an electrically earthen coating pan, charging gun, and heating source. Liquid plasticiser spray gun normally is also needed to apply plasticisers. 8\(^9\), 15.

The coating process can be promoting by spraying suitable quantity of liquid plasticiser, that is capable of increasing electrical conductivity of substrate and reducing glass transition temperature (T\textsubscript{g}) of coating polymer. 8\(^9\), 15, 17, 19. Incorporation of plasticiser promotes adhesion of coating particles and film formation, under lower curing temperature, thereby shortens processing time. 15\(^2\), 20.

Charging Mechanisms

Basing on charging mechanism, there are two kinds of charging (spraying) units: 9\(^3\), 15:

- Corona charging.
- Tribocharging.

Mechanism of corona charging

Said charging mechanism involves electrical breakdown followed by ionising the air by imposing high voltage on charging pins, comprises sharp pointed needle like electrodes, at outlet of gun. 2\(^9\), 15. The powdery particles of CoMs pick up negative ions on their passage from gun to substrate. 2\(^9\), 10.

Electrical field between earthen substrate and spray gun’s charging tip, and repulsive forces amongst charged coating particles generates electrical forces. 4\(^9\), 10. Ionisation of the air generates a mechanical force that blows powder towards substrate from charging gun. 2\(^9\), 10. Combination of mechanical and electrical forces is resulting movement of particles between substrate and spray gun. 3\(^9\), 10. Adjustment of electrical field is done to direct powder flow and control flow pattern, shape, size, and density of powder as it gets released from charging gun. 4\(^9\), 10.

Mechanism of tribocharging

Tribocharging mechanism follows principle of friction charging, as of corona charging guns, linked to dielectric properties of solid materials, thus no electrical field and free ions will be there between spray gun and earthen substrates. 2\(^9\), 15. With tribocharging guns, the electrical forces are regarded only from repulsive forces amongst charged particles. 3\(^9\), 10, 15. Upon spraying charged particles moves into space adjacent to substrate, and attractive forces between charged particles & earthen substrate make charged particles to deposit on substrate surface. 4\(^9\), 10, 15. By virtue of electrostatic attraction and mechanical forces charged particles gets sprayed uniformly onto earthen substrate. 2\(^9\), 10, 15.

Charged particles accumulates on substrate surface till repulsive force between particles deposited on substrate surface and approaching particles increases and exceeds electrostatic attraction between the approaching particles and earthen substrate. 3\(^9\), 15. Once said repulsive forces gets equivalent to said attractive forces, charged particles no more adheres to substrate surface, thus coating thickness will increase no anymore. 4\(^9\), 10, 15.

Limitations

It is more difficult to have electrostatic coating of the electrically non-conducting substrate cores. 10\(^9\), 15. For secure smooth and even coating of tablet, powdery organic CoMs must be transmuted into a film with no damage of substrate cores, a difficult task. 10\(^9\), 15. Diverse factors like chemical composition of coating solution; hygroscopicity; particle shape, size, and size distribution; corona charging and tribocharging characteristics (i.e., distance and nozzle geometry); electrical resistivity; and many others contributes significantly to coating attributes like adhesion, film thickness, transfer efficiency, and appearance. 10\(^9\), 15.

Important patents on coating compositions and apparatus design used for having electrostatic coating of powdery particles onto pharmaceutical dosage forms presented with Table-1.

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**Figure 2:** Schematic diagram on principle of electrostatic dry coating. 2\(^4\).
Table 1: Important patents on electrostatic coating 10, 15.

| Patent number | Publication date | Title of patent | Assignee |
|---------------|-----------------|-----------------|----------|
| GB 2333474 A  | 28-07-1999      | Method and apparatus for the coating of substrates for pharmaceutical use. | Phoqus Pharmaceuticals Limited, USA. |
| WO 1998020861 | 22-05-1998      | Method and Apparatus for the Application of Powder Material to Substrates. | Phoqus Pharmaceuticals Limited, USA. |
| US 2002019738B | 26-12-2006     | Powder coating composition for electrostatic coating of pharmaceutical substrates. | Phoqus Pharmaceuticals Limited, USA. |
| US 20080020147 | 24-01-2008     | Powder material for electrostatic application to a substrate and electrostatic application of the powder material to a substrate. | Phoqus Pharmaceuticals Limited, USA. |
| US 20070028790 | 08-02-2007      | Electrostatic powder coating of electrically non-conducting substrates. | Raytheon Company, CA, USA |
| US 20070240976 | 18-10-2007     | Electrostatic application of powder material to solid dosage forms in an electric field. | Phoqus Pharmaceuticals Limited, USA. |
| US 7008668B2  | 07-03-2006      | Electrostatic application of powder material to solid dosage forms. | Phoqus Pharmaceuticals Limited, USA. |
| CA 2 220506A1 | 08-01-2008      | Electrostatic application of powder material to solid dosage forms. | Phoqus Pharmaceuticals Limited, USA. |
| US 20030113445 | 23-10-2007     | Electrostatic application of powder material to solid dosage forms. | Phoqus Pharmaceuticals Limited, USA. |
| WO 1998058748A1 | 30-12-1998  | Electrostatic application of powder material to solid dosage forms. | Phoqus Pharmaceuticals Limited, USA. |
| US 20040052938 | 10-01-2008     | Electrostatic application of powder material to solid dosage forms. | Phoqus Pharmaceuticals Limited, USA. |
| WO 2005105317A2 | 10-11-2005      | Electrostatic application of powder material to solid dosage forms. | Phoqus Pharmaceuticals Limited, USA. |
| WO 2005105317A3 | 16-02-2006     | Electrostatic application of powder material to solid dosage forms. | Phoqus Pharmaceuticals Limited, USA. |

**Electrostatic Fluidised-Bed Coating**

In this process powder material kept fluidised in fluidised-bed processor by passing dry air through porous base plate 4, 21. The particles of fluidised powder are subjected for electrical field by either of two ways. One is by of placing an electrode beneath surface of fluidising powder and second is through charge transfer from pre-ionised fluidising air 4, 15, 21. Fluidising effect in addition to repulsive effect of charged powder particles results upward motion of particles; thereby forming cloud of charged particles above the bed 20, 21. Generated cloud is much alike that from conventional electrostatic gun 19, 21. Through the said cloud heated or unheated particle makes several pass 4, 16. Fluidised-bed coating process assisted with electrostatic field never dips the particles into powder bed and generally results thin coat comparing to that from conventional fluidised-bed coating processes 4, 16. Elongated substrates or other objects passing vertically or axially across through powder-bed and through powder cloud gets deposited as layer of powder material, are unsuitable 4.

**MAIC PROCESS/ TECHNOLOGY**

Available diverse DPC process (like compression coating, electrostatic coating, plasticiser dry coating, and heat dry coating); generally involve application of higher impaction force, higher temperature, or high shearing stress to achieve coating 9, 22, 24. Strong mechanical force accompanied with generated heat is causes layering and embedding of the GPs (i.e., CoM) onto surface of HPs (substrate cores) 10, 22, 23. Many pharmaceutical and food ingredients are very heat-sensitive, thermolabile, relatively soft, and easily deformable by intense mechanical and thermal stress 5, 10, 24. These call for soft coating processes/methods which can attach GPs on HPs with a minimal deformation of particle shape & size, degradation of components by generated heat 5, 10. The MAIC process is developed to solve said issue 2-4.

Coating of particles onto particles by MAIC involves peening process 2-4. The process involves pouring small coating particle herein termed GPs and large core particle herein termed HPs into an assembly containing small oscillating magnets 2-4. Due to oscillation of magnets the small HPs readily gets coated onto GPs 2-4, 24. The process has ability to coat core particle as fine as 0.25 microns. A batch process with shorter processing time demands lower energy 4, 24. For overcoming batch processing limitation of earlier design, continuous type MAIC device is patented that enables separation of coated substrates from magnetic elements for continuous operation 2, 3. Said technique, a soft coating process, developed by Aveka, a US based company, accordingly patented MAIC continuous process to coat small dry particles onto large dry particles 3, 4, 9.

MAIC devices can conveniently handle soft organic GPs and HPs, while coating without deformation in their particle size and shape 2, 10, 24. This technique can fix GPs onto HPs that are soft with minimal degradation of components and deformation of their particle shape & size 2, 4, 10. Although due to collision of the particles heat is generated, on a micro-scale, during MAIC process is negligible 3, 9, 10. This could be an added advantage while handling thermolabile powders 2, 9, 10.

The process can improve effectiveness of powder’s mixing with particles of nano size without aid of heat or solvent 3, 25. Generally, uniform mixing of materials with nano size is more difficult comparing mixing of materials with larger sized particles 3, 4, 10. Still MAIC technology is in development that will be aiding manufacturing applications to produce products with higher quality 2, 10.

**Mechanism and Stages of Coating in MAIC Process**

During MAIC process, mixture of particles (magnetic particles, GPs, and HPs) stays in fluidised state; where distribution of velocities are Maxwell–Boltzmann type 10, 24.
25. The collision occurring among particles is important to impinge GPs onto surface of HPs and thus formation of semi-permanent coating on surface of substrate, i.e., HPs [10, 25]. For convenience, the coating mechanism of MAIC processes can be presented as comprising of follow stages, refer Figure-3 2-4, 10.

Stage-1: Excitation of the magnetic particles 2, 10,
Stage-2: De-agglomeration of the CoM, i.e., GPs 3, 10,
Stage-3: Spreading and shearing of GPs onto surface of the substrate particles (i.e., particles to be coated or HPs) 4, 10,
Stage-4: HP-magnetic particle and HP-HP interaction 2, 10,
Stage-5: Magnetic particle-HP-wall interaction 3, 10, and
Stage-VI: Formation of products, i.e., coated particles 4, 10.

MAIC Apparatus

MAIC apparatus comprises processing vessel that surrounded with series of electromagnets which are connected to alternating current, refer Figure-3 2-4, 10, 24. The GPs and HPs are poured into the vessel followed by adding measured mass of magnetic particles 2, 10. Magnetic particles usually are of barium ferrite that is with polyurethane coating for preventing contamination of coated particles 3, 10. Presence of magnetic field, agitates magnetic particles that move frequently (oscillates) inside vessel thus fluidises the particle as in fluidised-bed system 4, 10, 25. Agitated magnetic particle imparts energy to GPs and HPs thus causing their collisions (host-guest particles, host-host particles, host-GPs-vessel wall) 2, 10. Said collisions allow occurring of coating by way of impaction and/or peening of GPs onto HPs 10. Due to magnetic field the primary motion is spinning of the magnetic particles, which promotes de-agglomeration of GPs via-a-vis shearing and spreading of GPs onto surface of HPs 3, 10, 25. However translational speed allows impaction of one particle onto some other, is also has significant effect in promoting coating 1, 10.

Performance of MAIC process depends on parameters like particle size of GPs and HPs, particle size ratio of guest-to-host and magnetic particle-to-HP, ratio of powder mass-to-magnetic particles, processing time, voltage or current and frequency of alternating current, speed of magnetic particle, and many others 10, 24-26. These parameters must be considered during the MAIC process 2-4, 10.

However, the coating time depends on several parameters that include number density of HPs, diameter ratio of host-to-guest particles, initial & final bed height of fluidised particle bed, and material properties of GPs and HPs 23-26. There an optimum value of bed-height for which time of coating is minimal 10, 25. Coating time sharply increases as bed-height is lower or higher than optimal value, and/or as diameter of the HPs increases and/or ratio of diameter for host-to-guest particle is increased 10, 26.

Upon coating of particles by MAIC process, the process can modify surface property of HPs while their original size and shape is maintained almost, thus modifies their flowability 10, 22, 26. However, number of GPs present on surface of the HPs has only a minor effect on flowability of the HPs, once cohesion force is reduced by presence of one or more GPs 10, 24. Furthermore even with very discrete coating on surface of HPs, their flowability improves to significant level 10, 25.

When primary GPs are in sub-micron range, the attraction forces (electrostatic, Van der Waals, etc) among them are relatively very high thus requires larger forces for their separation 10, 22. HPs that are smaller can achieve higher velocities comparing to larger one from their collision with magnetic particles. This results in higher impact force; which is sufficient to break structure of agglomerated GPs 10, 24. Researcher found that reduction in cohesion force for the coated particles is inversely proportional to particle size ratio of guest-to-host particles 10, 25. This indicates smaller GPs provisioning larger reduction in their cohesive force 10.

HMC PROCESSES/TECHNOLOGIES

Situations calls for HMC are elimination for use of aqua or non-aqua solvents, enhancing solubility and dissolution rate of poorly aqua-soluble drug, enhancing chemical stability of moisture sensitive drugs, and many more 27-29. An absence of solvent evaporation phase results strong and nonporous particles 2, 3, 27, 30. In this process, as the name implies, melttable CoM, in the molten state, is applied onto substrate particle that solidifies upon cooling. The process uses melttable CoMs with low melting point, usually lipid or waxes 30-33. The process requirement is the melttable CoMs had to be heated to molten state for having their solution that then air-atomised and sprayed onto surface of moving solid substrate followed by
coating of the product. Upon cooling, a continuous film forms on substrate that acts as moisture protection barrier coating or rate-controlling membrane for drug release. Fan coater, spheronizer, spouted or fluid bed processors are required for HMC processes.

As a process requirement, during application the coating fluid is required to be maintained at a constant temperature that cannot exceed 150 °C. Thus meltable materials having molten viscosity below 300 centipoises and melting points below 80 °C are generally suitable, as prior to spraying the molten CoMs to be maintained at 40-60 °C above their melting point. Ideally, meltable materials must have defined melting point or narrow range of melting point.

Meltable materials are hydrophilic or water-soluble and hydrophobic or water-insoluble. Change in consistency of molten droplets is achievable by inclusion of viscosity modifier into melt matrix. Viscosity modifier may be meltable or non-meltable at processing temperature. Typical melting range of various water-soluble and water-insoluble binders being used in pharmaceutical formulation are provided with Table-2.

Dry particles (like powders, pellets, granules) with mean particle size ranging between 100-2000 µm can be subjected for HMC process using fluidised bed process where molten droplet size, temperature of outlet and inlet air, and fluidization air volume are well controlled.

Lipidic meltable CoMs are highly compatible with ingredients like artificial sweeteners, flavouring agents, surfactants and many others. These processes are suitable for herbal and hygroscopic products. Coated particles can be used in sachets, capsules, suspensions, and tablets. In flash melt and chewable tablet forms, plasticity along with resistance to fracture under pressure properties of the lipid coatings imparts interesting aspect of is these products.

Table 2: Most commonly used CoMs and their melting point.

| Hydrophobic meltable materials | Melting point | Hydrophilic meltable materials | Melting point |
|--------------------------------|--------------|--------------------------------|--------------|
| Beeswax                        | 62-65 °C     | Gelucire® 50/13                | 44 - 50      |
| Carnauba wax                   | 47-50        | Poloxamer 188                  | 50.9         |
| Cetyl palmitate                | 67-75        | Polyethylene glycols (PEGs)    | 42-53        |
| Cottonseed oil                 | 61-65        | PEG 2000                       | 48-63        |
| Glyceryl behenate              | 47-63        | PEG 3000                       | 49-63        |
| Glyceryl monostearate          | 48-57        | PEG 6000                       | 54-63        |
| Glyceryl palmitostearate       | 54-63        | PEG 8000                       | 57-64        |
| Glyceryl stearate              | 62-86        | PEG 10000                      | 53-66        |
| Hydrogenated castor oil        | 58-72        | PEG 20000                      | 49-69        |
| Microcrystalline wax           | 47-65        |                               |              |
| Paraffin wax                   | 46-69        |                               |              |
| Partially hydrogenated palm oil| 56-60        |                               |              |
| Stearic acid                   | 54-60        |                               |              |
| Stearyl alcohol                | 57-61        |                               |              |

HMC Using Tablet Coating Pan

It is termed also as direct blending coating. The process involves application of CoM, in molten state, onto moving substrate, in a tablet coating pan that is continuously heated.

Said technique is simple and does not call for sophisticated and complicated equipment. The process can be useful for wider range of substrates with diverse size and for coating in multiple layers. The method comprises of follow steps:

(i) Melting of CoM.
(ii) Dissolving or dispersing drug in molten coating agent.
(iii) Applying molten solution or dispersion of CoM onto the moving substrate bed in a hot coating pan.
(iv) Through mixing of the molten coating agent and substrate particle.
(v) Cooling of product with continued stirring of blend, and
(vi) Congealing of coated substrate particles.

Spray Congealing

A highly versatile technique of HMC process produces particles having diameter within range of 10-3000 µm. The process involves spraying a hot-melt of wax, fatty acid, or glycerides into an air chamber below melting point of meltable materials or at cryogenic temperature. Granular particles are obtained upon cooling.

HMC using Fluid-Bed Processor

Interest for using fluid-bed processor in HMC has grown to significant level since 2001. Powdered mixture of the meltable and the non-meltable materials are added onto the seeds (powder particle cores) in a fluid-bed processor. The meltable materials can be added to the starting powder mixture can be in the form of either solid particles or molten liquid. Accordingly the procedure of the process basically...
is either melt-in procedure or spray-on procedure 38. Solid meltable binder melts during the process termed as melt-in procedure 2, 24. Process where molten liquid, optionally containing the dispersed drug, sprayed on is termed as spray-on procedure 3, 35. The melt-in procedure eliminates flow of molten liquid renders the procedure simpler for production comparing spray-on. Thus from industrial point of view, the melt-in procedure is favoured over the spray-on 34, 36.

The particle size and the viscosity of meltable materials and the temperatures of the inlet-air and the product endpoint significantly influence performance of HMC process 24, 38. Increased meltable material content increases coating thickness decreases dissolution rate of active 38, 39. The temperatures of the inlet-air and the product endpoint have more pronounced effect on parameters of coatings 2, 3, 36, 39.

In case of melt-in procedure, small meltable particles with sufficient viscous binding forces are obligatory for production of smooth and reproducible coat, thus should be keeping at an optimum value 39, 40. The particle size of meltable materials should be 1/6 th or lower comparing the diameter of seeds and viscosity should be low 39. High viscosity materials should be excluding for avoiding rough surface and non-uniform coating 2, 3, 35, 40.

Use of meltable materials of controlled properties makes the HMC process well controllable 41. The melt pelletization and melt granulation processes desires meltable materials having a high viscosity and a reduced particle size 42, 43. High viscosity materials are desirable to improve mechanical strength of the coating but reduced particle size desirous to prevent rough surface of coating 2, 3, 41.

Solid Dispersion Hot-Melt Fluid-Bed Coating

A newer modified version of the HMC following fluid-bed process is solid dispersion based one, is often termed Tumbling HMC 2, 24, 35, 44. This process eliminates the spraying step thus does not calls for steam jackets, nozzles, and/or heating assembly 3. Powder particles (termed non-pareils) and powder of PEG (as divided solid particle with size 1.41–3.36 mm) were fluidised together 35, 36, 44. The inlet air temperature is increased to melt the PEG thereby transferring them onto the non-pareils 4, 44. Then typical steps (like cooling and congealing) of HMC are followed 4, 44. Multiple coatings, as multiple layers, can be applied following this process 4, 44. For this, CoMs with diminishing rank order of their melting point is to be used to produce additive coating layers thus result multiple layered coatings 4, 35.

Turbo Jet Coating Process (Modified)

As an adaption to coat solid particles the process of Turbo Jet coating process is modified. The modified process involves suspending the solid particles in a spiral of ascending air 2, 3, 24. Said air provides homogenous distribution of individual particles 2–4. The molten lipidic CoM is dispersed from bottom of tank and tangentially to particle flow 2–4. The lipid crystallisation within nozzle expansion is however prevented using micro-environment surrounding nozzle outlet 2–4. Said technique has ability to coat very fine particles, an advantage, as enable to suspend the particles within ascending air stream 2–4.

Theta-composer

Theta-composer comprises of slowly rotating elliptical-vessel and fast rotating) elliptical rotor, that are rotating in opposite directions 24, 45–49. Rotor rotates anticlockwise (rotating between 900-1200 rpm) inside a clockwise rotating vessel (rotating between 30-40 rpm) 4, 24. Anticlockwise rotation of rotor inside the clockwise rotating vessel forces powder mixture of HPs and GPs through small clearance between the rotor and the vessel thus subjects them for shearing and compressive stresses 24, 45–48. As rotor continue to move, clearance between rotor and vessel wall becomes large, there will be bulk mixing of HPs and GPs 4, 24. Through blending of HPs and GPs is to be done at a condition comprising of container speed at low and rotor speed at high 4, 24. At same time, application of strong shearing and compression forces accelerates precise blending & composite fabrication 4, 24.

Features and pros

Follows are the features and pros of theta-composer process 45-48;

a. Simple structure thus operation and maintenance is easier 4, 24.

b. Slow rotational speed of the outside vessel promotes and favours bulk mixing 4, 24.

c. High rotational speed of inside rotor confers high shear stress that is required for coating 4, 24.

d. Elliptical shape of outside vessel and inside rotor is for stress and relaxation 4, 24.

e. Rotation of vessel assists for getting fully homogenous powder composite without thermal deterioration 4, 24.

f. Instant shearing and compression of particles minimises rise in temperature of materials 4, 24.

g. Processing time is short 4, 24.

h. Required rotational conditions can be selected that suits the material(s) 4, 24.

i. Improves handling and increases flowability 4, 24.

j. Suppress hygroscopicity 4, 24.

Mechanofusion

Underlying principle of the process is bringing forth a chemical-mechanical-reaction among two or more powder materials, to produce new material having differing properties 24, 49-53. The process employs a batch operated specifically designed device for fusing particle-to-particle at high compressive and shear forces thus resulting controlled particle shape 4, 24. The device comprises of outer vessel (rotating), inner piece (stationary), and scraper (stationary) as its key parts 50-53.

Processing involves placing of aliquot amount of HPs and GPs into rotating vessel 2-4, 24. As vessel rotates at speed between 200 to 1600 rpm, powders are forced outwardly towards vessel 50-53. Gap between inner stationary piece and rotating vessel is controlled, result is the powder particles passing thru gap are subjecting for intense compressive and shearing forces 50-53. Combination of these forces acting on particles builds-up local temperature. The generated thermal energy is sufficient to fuse GPs onto surface of HPs 50-53.

The size of gap between vessel wall and inner piece plays very important role as it controls thickness of the coating 50-53. Gap between vessel wall and scraper also requires controlling 2, 4, 24.

Features and Pros

Features and pros of Mechanofusion process are as follows 50-53:

• Produce composite particles with controlled particle shapes 4.
• Eliminates need for pre-mixing of powder particles during processes of improving particle performance 24.
• Control of process temperature can be done using water cooled jacketed vessel 4.
• The compact design of devices eases coating process and enhances performance 24.

**HMC using spheronizer**

The process involves use of laboratory scale spheronizer with slight modifications 5, 4, 55. The process basis is feeding of dry CoMs along with substrate into spheronizer with smooth disk made up of stainless-steel 2-4. Edges of disk are keen at an angle of 45°, this facilitates tumbling movement of substrate and prevents loss of CoM 2-4. An infrared lamp is used as source of heating, so for maintaining processing temperatures above the melting point of coating polymer 3, 4. Power supply of infrared lamp should be regulated and can be varied suitably to monitor and maintain process temperature 2-3. Pipeline insulation is doing for preventing solidification of the molten CoMs, before occurrence of their final cooling on surface of substrate cores 3, 4. The process is advantageous as can use micronized polymers like Eudragit® E PO, an acrylic polymer, as CoM. Said coating process may be an alternate to aqueous or non-aqueous film coating process 4, 8.

The process calls for maintaining temperature of spheronizer disc below melting temperature of substrate but above Tg of meltable polymer, used. The Tg of meltable coating polymers are provided with Table-3 4, 8.

**Table 3: Some common meltable coating polymers and their Tg 4, 8.**

| Trade name | Polymer | Tg |
|------------|---------|----|
| Polyox WSR | Poly(ethylene oxide) | -67 |
| Carbowax | Polyethylene glycol | -20 |
| Kollidon | Poly vinyl pyrrolidone | 168 |
| PLGA | Poly (lactide-co-glycolide) | 40-60 |
| Elvanol | Polyvinyl alcohol | 85 |
| Ethocel | Ethyl cellulose | 133 |
| Klucel | Hydroxypropyl cellulose | 130 |
| Methocel | Hydroxypropyl methylcellulose | 175 |
| Eudragit® RS | Amino methacrylate copolymer | ~ 65 |
| Eudragit® RL | Amino methacrylate copolymer | 58-68 |
| Eudragit® E | Poly[(dimethylamino)ethyl methacrylate-co-methacrylic ester] | 40-50 |
| Eudragit® S | Poly(methyl methacrylate-co-methacrylic acid) | > 130 |

**VAPOUR COATING OF POWDERS**

It is a recently up-roused coating technology for solid dosage forms. It enables synthesising polymeric coating films with an orchestrated surface, topography, and functionalities with satisfactory coating uniformity. Vapour phase deposition is the principle used in methods for achieving vapour coating of powder 57, 61.

A powder or liquid can be dispersed by applying electrostatic field, a process referred as ‘electro-dispersion’ 2, 4. Electro-dispersion uses intense electric field to disperse a part of static-bed of powder or liquid into a stable cloud of fast moving particles (dispersed phase), and maintaining dynamic equilibrium in between the static phase and the dispersed phase 3, 4. Cloud density of the dispersed phase particles is dependent on numerous factors, including field strength and nature of powders 2, 3. Applied electric field also ensures that only uncoated particles are coated and avoids agglomeration of coated dispersed particles, as these repel each other due to possession of same charge 2, 4. Electro-deposition effect finds applicability in producing uniform, durable, and slow dissolving coatings of controlled thickness on individual particles 2, 3. This is achieved by generating a vapour of desired coating, typically semiconductor material
or a metal, and allowing vapour to permeate dispersed particles.

Basing on synthesis mechanisms follows major vapour phase deposition methods have applicability to pharmaceuticals:

a. CVD

i. Plasma enhanced chemical vapour deposition.

ii. Initiated chemical vapour deposition.

b. ALMD

Vapour phase deposition reactions of CVD and ALMD are similar to as both utilise gaseous reagents for nurturing a film. CVD is a single step process. While in ALMD, there is split-up of reactions into two surfaces half, it means a two-step reaction. This intends, it exposes substrate surface to one reagent at a time. As a result of splitting the reaction into two steps, surface will be reacting sequentially with each reagent until complete surface is gets coated by a new atomic-layer. In simple words as the process starts, suppose reactant A is reacting with the surface functional groups present on particle. Now, new surface functional groups are in place, and when this surface exposes to reactant B, the reactant B reacts with new functional groups. The reaction is self-limiting thus reaction gets stopped when all totals of surface sites had been transformed back to original surface species. At this point, process can be repeating sequentially until wished film thickness is made achievable. The process results a monolayer (one complete cycle of A & B) with a film thickness of an order of 1 angstrom (0.1 nano-meters).

Fluidised-bed chemical vapour coating: CVD on fluidised-bed of powder is one of most efficient technique to functionalise and to deposit or coat individual powder particles from gaseous species by combining two processes. One process is deposition itself while other process aims to suspend particles in deposition zone, i.e., most often by upwardly flowing the gas through the powders. In general the method is transport limited. The process is followed for coating of titania.

SCF based coating methods

SCFs are the highly compressed gasses. These possess several advantageous attributes of both gases and liquids. Supercritical carbon dioxide (CO₂), nitrous oxide (N₂O), and alkanes (C₂ - C₆) are used as SCF, most widely. However, for the pharmaceutical purposes, CO₂ is considered as an ideal SCF medium due to its comparatively low critical pressure of 72 bars and critical temperature of 311 °C, and follow advantages:

- Low critical pressure and temperature value.
- Readily available.
- Cost-effective.
- Nontoxic, non-flammable.
- Highly pure.

Process basis

A minor change in pressure and/or temperature causes significant change in SCF density and rapid change in their solvent power, near their critical point. Rapid expansion vis-à-vis rapid supersaturation translates into a rapid change in the density and solvent power of the SCF and therefore into rapid crystallization rates which result in precipitation of solute. Alternately rapid reduction in the solvent power of the SCF without any substantial change in pressure consists of contacting the SCF solution with an inert gas like nitrogen or helium in which the CoM is insoluble. Rapid mixing is of inert gas with the SCF decreases solvent power of SCF and CoM to precipitate.

SCFs based particle coating methods that used most widely are follows:

a. RESF method

b. GAS process

c. SCF anti-solvent method

d. GSS method

RESF method

Rapid expansion of the supercritical solution is the underlying principle for having particle coating by polymer encapsulation. The rapid expansion vis-à-vis rapid supersaturation translates into rapid change in the density and solvent power of the fluid and therefore into rapid crystallization rates result coating. The process basis is using SCF for preparing solution of CoMs followed by its release at atmospheric pressure thru small nozzle(s).

Limitations

- Poor solubility of most CoMs in SCF.
- Active core to be insoluble is the basic requirement.
- Calls for necessary investment for having high-pressure processing equipments.

In this process CoM is solubilised in SCF under high pressure in a vessel. A dispersion of active(s) in resulting solution is prepared by dispersing the active(s). The resultant suspension is maintained at high pressure which upon release thru a small nozzle, at atmospheric pressure, rapidly expands, thus reduces solvent power of the SCF. The sudden pressure drop causes desolvation of CoM thus gets precipitated onto particles of dispersed drug(s) in medium of SCF and forms a layer of coating on the dispersed drug particles.

CoMs having applicability were fatty acids, fatty alcohols, and lipids; lipids (viz. mono-, di-, & tri-glycerides of fatty acids) are used mainly, while combination of these CoMs with other lipids may be used.

Most of CoMs, including polymers, possesses very low solubility in SCFs (<1 % w/w) except for polymers with low cohesive force densities and fractions with low molecular weight. In these instances, co-solvents (acetone and/or methanol) are used for increasing their solubility in the SCFs. Further, in some instances non-solvents can be using, this increases solubility of CoMs in SCFs while don’t dissolve them at the atmospheric pressure.

For having successful coating, ideally the SCF should dissolve the CoM only while leaving core completely undissolved.

GAS process

Here rapid reduction in the solvent power of the SCF without any substantial change in pressure is achieved by interacting solution of solutes (drug and CoM) in SCF with an inert gas like nitrogen or helium in which the solutes are insoluble. The inert gas, which acts as an antisolvent for solutes, may be kept at pressure par to that of solute solution in SCF. Design of the process is for dealing solutes (active and CoMs) that are soluble in SCF but are insoluble in inert gas. Rapid mixing is of inert gas with
SCF decreases solvent power of SCF and causes solute to precipitate.  

Here the solution of CoM and active(s) in SCF maintained at high pressure, in a vessel. Then the inert gas, an antisolvent for solutes, is poured into the vessel. This results extraction of SCF from the solution causing super saturation to such extent that precipitation of solute occurs.  

**SCF anti-solvent method**  
Process has synonym in literature as ‘Aerosol solvent extraction systems’ while variation thereof has been disclosed as ‘Solution-enhanced dispersion by supercritical fluids’ (scf). A process designed for the solutes (active and CoMs) that are soluble in organic solvent but are insoluble in SCF and solution of SCF and volatile organic solvent whilst organic solvent be miscible with SCF. It is suitable for processing material that has little solubility in SCF of choice and thermolabile substances. Submicron particles can be coated with this method but unable to coat aqueous solvable materials. A batch process is limited in its ability to process large quantities of material.  

Here the SCF is used as an antisolvent to process a SCF-insoluble solute, from a pre-mixed batch of an organic solution of the solute, involving addition of SCF into the organic solution. Addition of the SCF causes its concentration in organic solution to increase and solution to expand. Solute precipitation takes place as the solution becomes supersaturated.  

Said process involves continuously adding the solution of solute in volatile organic solvent to continuously flowing SCF (antisolvent for the solute). Organic solution rapidly mixes and dissolves in SCF forming a homogeneous high-pressure fluid mixture. Since solute is considerably insoluble in SCF, and volatile organic solvent and SCF are miscible, this results in precipitation of solutes in the high pressure vessel. The SCF-organic solvent mixture is passed through a micro-filter and then expanded into a low pressure vessel where the SCF separates from the volatile organic solvent.  

**GSS method**  
Here mixing of core particles and CoMs in SCF is done, at high pressure. SCF penetrates CoM causing their swelling. Resultant mixture is then heated above the $T_g$ of polymer to liquefy coating polymer. Then, when pressure is released, the CoM gets deposited onto active cores. The process does not requires that the active core and the CoMs soluble in SCF.  

**CONCLUSION**  
The sequential steps of DPC (powder application, coalescence, and sintering) are influenced by coating formulation and process. In DPC processes, appropriate particle size of materials is essential for ensuring and reproducing uniformity of coating. A general recommendation is CoM’s diameter be less than 1% that of the substrate. This permits application of CoM onto substrate surface to an acceptable degree of uniformity, improve film adhesion and appearance, and decrease processing time. During coating process, heating of substrates are often doing above the $T_g$ of the CoMs for causing softening of layering materials to aid its adherence to substrate.  

Some of DPC process relies on mechanical compaction occurring naturally during the process. Said mechanical compaction facilitates adhesion and coalescence. Under this circumstances, the stresses on coating layer results consolidation of substrate bed and spreading of coating layer across interface driven by deformation. In case of elastic materials, deformation of material is reversible being bearing for poor contact across the surface. While in case of coatings exhibiting plastic behaviour, deformation is permanent (irreversible) and mechanical compaction contributes to greater adhesion of surface layer. This improved adhesion is due to larger surface area for contact between substrate and coating, as well as possible mechanical interlocking of the materials.  

Modification in the spreading and adhesion behaviour can also achievable through application of sub-coat to substrate. Sub-coating involves layering of new material, corresponding to 2-3 % w/w weight of substrate core, which can facilitate adhesion/adherence of the powder coat by changing interfacial energy.  

Literature reports on extensive use of low melting point hydrophilic polymers like PEG 3350 are there while available also report on use of other materials having amphiphilic and hydrophobic properties.  

Intentional selection of sub-coat material that can remain in molten (partially) state at the processing temperatures promotes further adhesion with the coating layer. Here molten priming layer promote adhesion of powdery coating particles forming through liquid bridge with the substrate surface. Interfacial interactions amongst the polymer particles (to be layered) and substrate surface are rather complex which depends on adhesion, interfacial tension, and wetting.  

Dry coating technologies possess enormous advantages but inferior uniformity of coating film is biggest challenge that hinders their application and commercialisation, the main goal requires addressing.  

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