International Journal of ChemTech Research
CODEN(USA): IJCRGG ISSN : 0974-4290
Vol.2, No.1, pp 733-737, Jan-Mar 2010

Advances in Pharmaceutical Coatings

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ABSTRACT: Recent trends in pharmaceutical technologies are towards the development of coating methods which overcomes the various disadvantages associated with solvent based coatings. In these newer technologies coating materials are directly coated onto solid dosage forms without using any solvent and then cured by various methods to form a coat, hence these methods sometimes called as solventless coatings. Various solventless coatings are available such as photocurable coating, magnetically assisted impaction coating, compression coating, hot melt coating, powder coating, electrostatic dry coating, supercritical fluid coating, herein only magnetically assisted impaction coating and electrostatic dry coating are discussed. This review summarizes the fundamental principles and coating processes of various dry coating technologies.

KEYWORDS: Magnetically assisted impaction coating, Electrostatic dry coating, corona charging, tribo charging.

INTRODUCTION

Pharmaceutical solid dosage forms include tablets, pellets, pills, beads, spherules and so on, thus are often coated for various reasons.

1- Protection of the drug from the surrounding (environment, air, light and moisture) and thus improve stability.
2- Modifying drug release, as in enteric coating and extended-release formulation.
3- Masking unpleasant taste or odour of the drug.
4- Improving product appearance and helping in brand identification.
5- Facilitating rapid identification by the manufacturer, the pharmacist and the patient (mostly colored).
6- Increasing the mechanical strength of the product.
7- Masking batch differences in the appearance of raw materials.
8- Prevention from destruction by gastric acid or gastric enzymes.
9- Making it easier for the patient to swallow the product.[1]

Currently, the most common technology for coating solid dosage forms is the liquid coating technology (aqueous based organic based polymer solutions). In liquid coating, a mixture of polymers, pigments and excipients is dissolved in an organic solvent (for water insoluble polymers) or water (for water soluble polymers) to form a solution, or dispersed in water to form a dispersion, and then sprayed onto the dosage forms in a pan coater (for tablets) and dried by continuously providing heat, typically using hot air, until a dry coating film is formed.[2, 3]

Organic solvent based coating provides a variety of useful polymer alternatives, as most of the polymers are soluble in the wide range of organic solvents. But there are several disadvantages associated with its use.[2, 4]

1. They are flammable and toxic
2. Their vapor causes hazards to coating equipment operator
3. High cost of solvent
4. Solvent residue in formulation.
5. Strict environmental regulations by US Food and Drug Administration (USFDA), Environmental

Protection Agency (EPA) and Occupational Safety and Health Administration (OSHA).[5,6]

All above problems with organic solvents resulted in shift to use of water as the preferred coating solvent. Aqueous-based coatings have been increasingly used compared with organic-based coatings. However water-based coatings also suffered from following problems.

1. Heat and water involved in coating process can degrade the drug.
2. Validation of coating dispersion for controlling microbial presence.
3. Solvent removal process is time consuming and extremely energy consumptive.[4]

In order to overcome above mentioned limitations of liquid coating technology, new efforts have been made in recent years to develop a solventless coating technology. Solventless coating technologies can overcome many of the disadvantages associated with the use of solvents (e.g., solvent exposure, solvent disposal, and residual solvent in product) in pharmaceutical coating. Solventless processing reduces the overall cost by eliminating the tedious and expensive processes of solvent disposal/treatment. In addition, it can significantly reduce the processing time because there is no drying/evaporation step.[4] Here we are going to discuss two solventless coating methods one is Magnetically assisted impaction coating (MAIC) and another is electrostatic dry coating.

I. MAGNETICALLY ASSISTED IMPACTION COATING (MAIC):

Several dry coating methods have been developed such as compression coating, plasticizer dry coating, heat dry coating and electrostatic dry coating.[7, 8, 9] These methods generally allow for the application of high shearing stresses or high impaction forces or exposure to higher temperature to achieve coating. The strong mechanical forces and the accompanying heat generated can cause layering and even embedding of the guest particles onto the surface of the host particles. Many food and pharmaceutical ingredients, being organic and relatively soft, are very sensitive to heat and can quite easily be deformed by severe mechanical forces. Hence, soft coating methods that can attach the guest (coating material) particles onto the host (material to be coated) particles with a minimum degradation of particle size, shape and composition caused by the build up of heat are the better candidates for such applications. The magnetically assisted impaction coating (MAIC) devices can coat soft organic host and guest particles without causing major changes in the material shape and size. Although there is some heat generated on a microscale due to the collisions of particles during MAIC, it is negligible. This is an added advantage when dealing with temperature sensitive powders such as pharmaceuticals.[10]

Mechanism of coating in the MAIC process:

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Stage-I: Excitation of magnetic particle.
Stage-II: De-agglomeration of guest particles.
Stage-III: Shearing and spreading of guest particles on the surface of the host particles.
Stage-IV: Magnetic-host-host particle interaction.
Stage-V: Magnetic–host–wall interaction. and
Stage-VI: Formation of coated products.[10]

Apparatus for MAIC:

Apparatus for MAIC consist of processing vessel surrounded by the series of electromagnets connected to the alternating current (Figure-1). The host and guest materials are placed in the vessel along with the measured mass of the magnetic particles. The magnetic particles are made of barium ferrite and coated with polyurethane to prevent contamination of the coated particles. When a magnetic field is present, the magnetic particles are agitated and move furiously inside the vessel, resembling a fluidized bed system. These agitated magnetic particles then impart energy to the host and guest particles, causing collisions and allowing coating to be achieved by means of impaction or peening of the guest particles onto the host particles. The magnetic particle motion studies suggests that the primary motion due to the magnetic field is the spinning of the magnetic particles, promoting de-agglomeration of the guest particles as well as the spreading and shearing of the guest particles onto the surface of the host particles. However, the effect of the translational speed is also significant as it allows for the impaction of one particle onto another, promoting coating.[10]

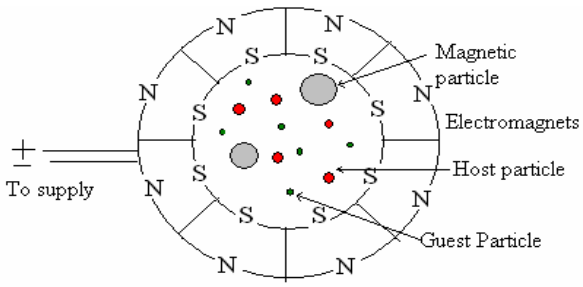

Figure-1: Schematic diagram of MAIC.

The parameters have to be considered during MAIC are particle size of guest particles and host particles, guest to host size ratio, magnetic to host size ratio, processing time, current or voltage and frequency, magnet to powder mass ratio, current and frequency, magnetic particle speed etc..[11, 12]

Ramlakhan M. et al. (2000) conducted an experiment to evaluate the effectiveness of the MAIC device in

modifying the surface properties of cornstarch and cellulose (host particles) when they are coated with silica (host particles). It was observed that very large agglomerates of silica were broken up into smaller primary sizes (de-agglomeration) during the MAIC process and soft organic materials (cornstarch and cellulose) get coated maintaining almost their original shape and size. The number of guest particles on the surface of the host particles has only a minor effect on the flowability once the cohesion force is reduced by one or more coating particles and hence even with a very discrete coating on the surface of the host particle there is a significant improvement in the flowability of the material.[11] Similar study was done by Raizza R (2006) where the coating of ibuprofen with two different Silica, R 972 and EH-5 is done to increase its flowability.[13] When the primary guest particles are in the sub-micron range, the attraction forces Van der Waals, electrostatic etc. among the primary particles are relatively strong and require larger forces to separate them. Smaller host particles can obtain larger velocities than larger host particles from collisions with the magnetic particles, resulting in higher forces of impaction, sufficient to break the agglomerated guest particle structure. Yang J. et al. (2005) observed that the reduction in the cohesion force for the coated particles is inversely proportional to the size ratio of the guest and the host particles, indicating that smaller guest particles provide a larger reduction in the cohesive force.[14]

According to Singh P. et al (2001) model, the coating time in the MAIC device depends on the number density of host particles, the diameters of the host and guest particles, the initial and final bed heights, and the material properties of the host and guest particles. Also there is an optimal value of the bed height for which the coating time is a minimum. The coating time increases sharply when the bed height is smaller or larger than the optimal value, and also when the diameter of host particles is increased. The model also suggests that the coating time decreases when the initial bed height is increased and also when the ratio of host and guest particle diameters is reduced.[12]

II. ELECTROSTATIC DRY COATING:

The electrostatic coating process is very useful in paint technology, food technology, metal coatings, finishing industry and coating of living cells.[15-19] It is also useful in the coating of tablets as well as capsules.[20] The principle of electrostatic powder coating involves spraying of a mixture of finely grounded particles and polymers onto a substrate surface without using any solvent and then heating the substrate for curing on oven until the powder mixture is fused into film. There are two types of spraying units, according to the charging mechanism a) corona charging and b) tribo charging.[21, 22]

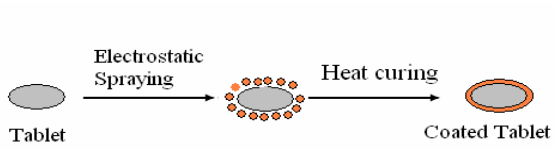

Figure-2: schematic diagram of electrostatic dry coating.

Mechanism of Corona charging:

This is done Characterized by the electrical breakdown and then ionization of air by imposing high voltage on a sharp pointed needle like electrode (i.e. charging pin) at the outlet of the gun. The powder particles picks up the negative ions on their way from the gun to the substrate. The movement of particles between the charging gun and the substrate is mainly governed by the combination of electrical and mechanical forces. The mechanical forces produced by the air blows the powder towards the substrate from the spray gun. For the corona charging, the electrical forces are derived from the electrical field between the charging tip of the spray gun and the earthen substance, and from the repulsive forces between the charged particles. The electrical field can be adjusted to direct the powder's flow, control pattern size, shape, and powder density as it is released from the gun.[21, 22, 33]

Mechanism of tribo charging:

Unlike corona charging guns, the tribo charging makes the use of the principle of friction charging associated with the dielectric properties of solid materials and therefore no free ions and electrical field will be present between the spray gun the grounded substance. For tribo charging guns, the electrical forces are only regarded to the repulsive forces between the charged particles.[22]

After spraying when charged particles move into the space adjacent to the substrate, the attraction forces between the charged particles and the grounded substrate makes the particle to deposit on the substrate. Charged particles are uniformly sprayed onto the earthen substrate in virtue of mechanical forces and electrostatic attraction. Particles accumulate on the substrate before the repulsion force of the deposited particles against the coming particles increase and exceeds the electrostatic attraction. Finally once the said repulsion becomes equivalent to the said attraction, particles cannot adhere to the substrate any more, and the coating thickness does not increase any more.[23]

Electrostatic coating of electrically non-conducting substrates and pharmaceutical tablet cores is more difficult. In order to secure the coating to the core, the powder must be transformed into a film without damaging the tablet core, which usually will include organic materials. Furthermore an even coating is required and it is difficult to obtain an even coating of powder on a tablet core.[24] Phoqus is a leading-edge

drug delivery company providing a range of innovative and patented drug delivery systems based on electrostatic dry powder deposition technology.[25] There are several patents on the design of apparatus for electrostatic coating of powders onto the pharmaceutical dosage forms.[24-27] Most of these apparatus are parented by Phoqus pharmaceuticals limited. There are also several patents which gives the various coating compositions for the electrostatic coating.[28-30]

Properties of powder such as particle size distribution, chemical composition, tribo and corona charging characteristics, electrical resistivity, hygroscopicity, fluidity and shape distribution play significant role on the performance of powder coating such as transfer efficiency, film thickness, adhesion and appearance.[31-33] Also deposition temperature, nozzle-to-substrate distance, nozzle geometry, and composition of the precursor solution plays an important role in the electrostatic coating process.[34] Puntarika R, et al. (2007) coated ten powders, differing in protein, carbohydrate and salt contents and ranging from 19 to 165 mm by nonelectrostatic and electrostatic coating and found that nonelectrostatic transfer efficiency (TE) increased to a maximum before levelling off with increasing particle size.

Measurement of the electrostatic powder coating properties can be done by using the Electrostatic Powder Coating Diagnostic Instrument (EPCDI). EPCDI analyses the electrostatic powder coating deposition efficiency by measuring the powder adhesion properties in the pre-cured state and it also measures the uniformity of the powder coating by moving the powder sample and measuring the infrared light transmission through it.[35] Another methods of adhesion measurements are drop test rig and virtual oscilloscope.[36]

Qtrol™

Qtrol™ is the core technology platform of Phoqus pharmaceuticals, which is derived from electrostatic deposition, the well-proven technology behind photocopying. Qtrol™ enables solid oral dosage forms such as tablets to be coated in a controlled and precise manner that can then be used to modify the way that a drug is released into the body. Qtrol™ technology enables the production of oral drugs with a broad range of release profiles. The way the drug(s) is packed and/or layered within the tablet coating and the manner in which the coating is applied can yield different release profiles, including delayed sustained release, rapid release, gradual release and delayed release. It also allows combination tablets to be made, supporting the release of one drug, then a quiescent period followed by the release of a second drug.

The application of Qtrol™ to Chronocort®

Hydrocortisone steroid (the synthetic analogue of the natural hormone cortisol) is specially formulated dosage form invented by Phoqus pharmaceuticals to enable sustained release and is then housed in a coating 'bucket', topped by an inactive, eroding layer. Only after the latter has been digested is the drug released. This design secures a 3-4 hour delay in drug release in order to parallel the normal pattern of circulating cortisol release, wherein levels are very low on going to bed and gradually increase during the night, peaking at around 7am. It means patients can take their tablet before bed and be woken by a natural cortisol 'high'. [37]

Conclusion

Magnetically assisted impaction coating and electrostatic dry coating avoids major disadvantages of solvents based coating. Both methods produce uniform coating but needs specialized instrumentation. Electrostatic dry coating requires special type of powder coating composition. Electrostatic dry coating enables coating of tablet with different colors on either side, it also enables printing on tablet on pharmaceutical dosage form. But safety aspects of these coatings in humans is in infancy, so further research in health and safety aspects of theses technologies will enable the commercialization of these technologies in pharmaceutical industry and will provide better alternatives to conventional coatings.

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