A Review on Solid Oral Pharmaceuticals Dosage Stabilizing Techniques

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The coating is a common pharmaceutical procedure used to development oral dosage. In this process a skinny polymer-based film applying to a drug containing granules and tablets. The products are processed by Pharmaceutical coating so that organoleptic properties could be developed. Thus the Pharmaceutical coating is considered an important step during drug development. The development of pharmaceutical doses in solid form is divided into different steps. Studies of last decades on coating technologies coating suggested the application of aqueous film coating is additionally increasing for pharmaceutical product development. Additionally, the physiochemical properties and stability of dosage forms could be improved and most significantly it controls the discharge profile of the drug. Typically horizontally rotated pans with a sparge of coating solution are utilized to cover the tablet's free surface. There is a number of coating techniques used to coat tablets i.e. enteric coating, sugar coating, film coating, and press coating. In this review paper, we tried to explore and discuss different tablet coating techniques in detail.

Key words: Coating, Development and techniques, recent trends, Polymer.

Introduction:

The most convenient dose forms in the pharmacy are solid oral dosage (Helliwell and Taylor, 1993). These doges forms offer many advantages, including a simple and convenient manufacturing process and good patient compliance (Alkilani et al., 2015). The physical attributes and chemical natures of drug molecules are diverse and each drug has its own hygroscopicity, taste, odour and light sensitivity (Bernards and Hill, 1992). In the early days during the consumption of drugs people feels Dysphagia (Khanna et al., 2010). Which is a disorder in which older people have difficulty swallowing solid oral dosage forms (Stegemann et al., 2012). To overcome Dysphagia the tablets were coated with sugar solution in the early days (Forough et al., 2018). Sugarcoating was eventually replaced by film coating due to its least time-consuming processing mechanism (Forough et al., 2018; Seo et al., 2020). The technique of putting edible paint on the surface of a pharmacological doses in order to obtain certain advantages is known as tablet coating (Shaikh et al., 2018). Thus coating is a technique in which a thin continuous layer of solid is deposited to the surface of a dosage form or its intermediary in the modern pharmaceutical business. This is an extra step in tablet processing that raises the price of the finished product (Shaikh et al., 2018). The coating is applied on tablets, particles, crystals, powders, granules, and pellets, to prepare the conventional form of oral doses (Muley et al., 2016). The oral doses are coated to improve product appearance, stability, ease of swallowing, mask the bitter taste and unpleasant odour (Jones. 2009). Side by side also reduces the chances to interact with other materials, stabilize volatile ingredients, moderate the release profile of the drug substances, etc (Jones. 2009; Muley et al., 2016).

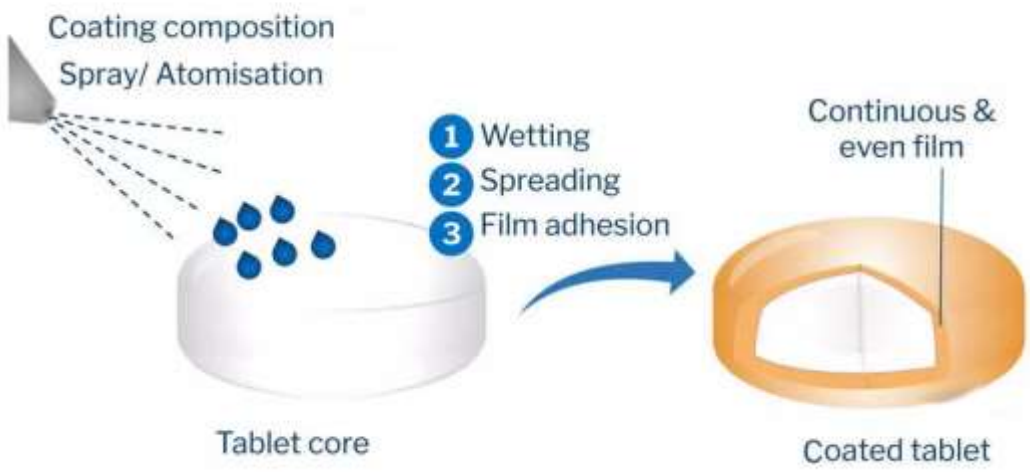


Figure 1: General Representation of Coating

The coating is a primary technique for stabilizing pharmaceuticals which are susceptible to hydrolysis (Singh et al., 2010). Tablet coating is the process of applying a coating substance on a revolving mattress of pellets while also using hot air to evaporate the liquid (Randall. 1998). Moisture protective barriers stabilize a moisture-sensitive API while simultaneously minimizing the risk of interaction with a secondary API in fixed-dose combination (FDC) formulations (Parmar et al., 2012). Deep concave punches and die sets are typically used to compress drug formulations (Parmar et al., 2012). This permits the applied coating substance to easily cover the tablet. So that they must tolerate the additional manufacturing steps, core dosage forms should be compacted harder than uncoated tablets. To guarantee a uniformly smooth coating, tablets must be dust-free (Saigal et al., 2009). For the pharmaceutical researcher working on the dosage form's coating, tablets that do not meet these standards generate a plethora of problems (Saigal et al., 2009; Singh et al., 2010; Parmar et al., 2012). Depending on the coating phase, many types of pharmaceutical coating materials are employed on tablets. Various seal coatings and moisture barriers were applied to a medication stacked pellet containing a moisture-sensitive inhibitor.

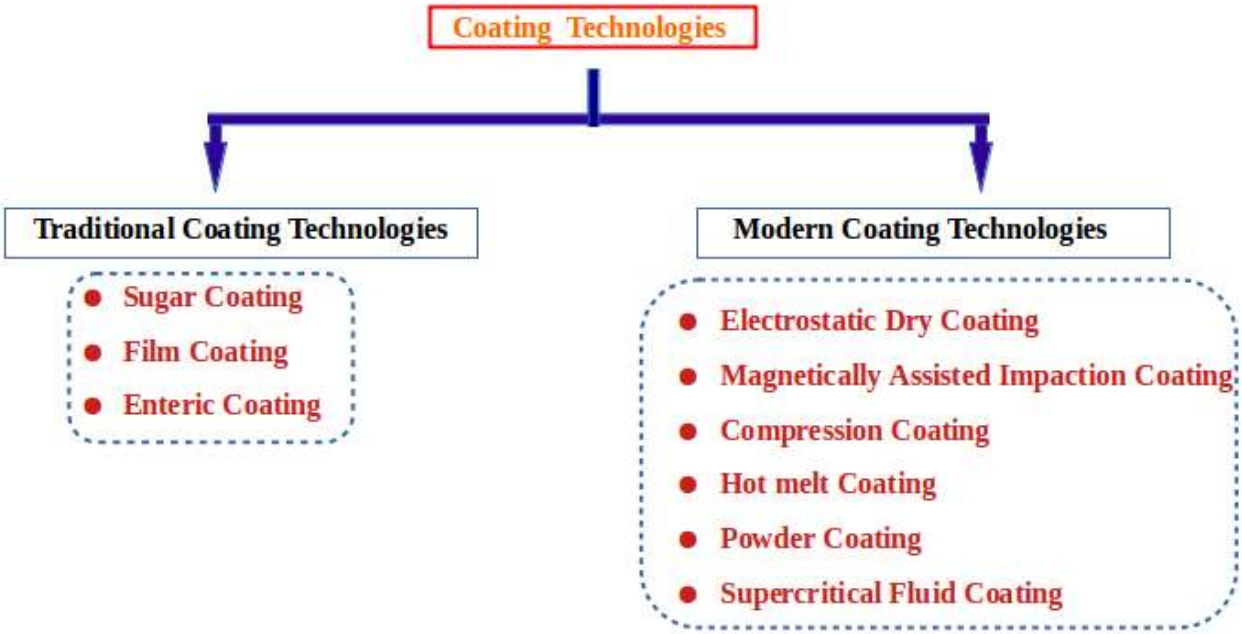


Figure 2: Classification of Coating Technologies

The tablet coating can be accomplished using a variety of methods. These methods are categorized into traditional and modern coating technologies. Traditional coating technologies comprise Sugarcoating, Film coating, Intrinsic coating. However modern coating technologies comprise Electrostatic dry coating, Magnetically assisted impaction coating, Compression coating, Hot melt coating, Powder coating, and Supercritical fluid coating.

A. Traditional Coating Techniques

1. Sugar Coating:

The typical method of covering medicinal active ingredients seems to have been sugar coating. Sugar coating, which has its roots in the confectionery business, is possibly one of the oldest medicinal techniques still in use (Ando et al., 2007; Porter. 2007). That's used to obscure the flavor and aroma of some medications or to improve the product's visual attributes (Krause et al., 1968). To meet USP tablet disintegration, dissolving criteria, and formulation challenges. Sustain release of active drug molecules from sugar-coated product sometimes become extremely difficult (Ceschel et al., 1980). Therefore these applications, the choice of core tablet and coating materials becomes more critical, demands thorough testing to ensure chemical and physical durability over time (Ohmori et al., 2004).

In Sugar coating process aqueous sugar solutions are deposited on the surface of the core tablet throughout the procedure (Krause et al., 1968; Ceschel et al., 1980). Sugar coating entails a number of procedures, therefore it needs knowledge and, in some cases demands specialized types of equipment (Ceschel et al., 1980). Though the number of phases depends on the manufacturer. A typical sugar-coating process includes the following steps:

- **Seal Coating:** The core of the tablet should be free from moisture and residual solvent therefore they must be sealed and fully dried before adding any sweetener (Porter. 2007). It's also known as waterproofing and includes the application of many numbers of coats of a waterproofing chemical by alcoholic spray styles (Reddy et al., 2013). During sugar coating technology carbohydrates are applied as aqueous formulations that allow moisture to infiltrate straight into tablet core, which potentially impact on product firmness and triggering tablet dissolution prematurely (Ohmori et al., 2004). Therefore a seal coat is placed to medical formulations. Previously, shellac was employed as a sealant. However, due to polymerization issues, zein was substituted.

- **Sub Coating:** The procedure is performed to provide round shape to thecorners of tablet or to mold to the desired look (Reddy et al., 2013). This step makes drug doses 5 - 10 % heavier. The tablet is smoothed out at this point, and color may be applied (Krause et al., 1968).

In this process the tablet is coated with a gum-based solution or syrup, then an appropriate powder filler is applied (Nieto. 2009). After that, the pill is dried. The method is continued until the tablet form required is obtained. The gum/sucrose solution is applied after the dry powder. The surplus water in the gum/solution is drained away by drying to harden the surface again (Thombare et al., 2016). As a result, sub coating entails alternate application of powder and gum solution until the proper form and consistency are reached. After each syrup application, excess water is removed (Ohmori et al., 2004).

- **Smoothing / Syrup Coating:** Filling in and smoothing uneven edges or sections of the tablets is the smoothing process. The tablet is smoothed after every filling stage by polishing and refinishing to obtain a smooth and complete appearance (Ohmori et al., 2004). The tablet's size is progressively increased to the desired dimensions during this procedure (Ohmori et al., 2005). If the tablet has a lot of anomalies a grossing syrup could be used. The solid suspended particles present in grossing syrup can fill the spaces of tablet's better than a sugar solution. During the smoothing process, the pill covering with around 60-70 percent sugar solids is usually sufficient (Shaikh et al., 2018). However, sometimes Starch, colors, acacia, gelatine and, if necessary, an opacifier is commonly included in the solution (Shaikh et al., 2018).

- **Color Coating / Colouring :** This stage of color coating is the most important since various sugar solutions are applied to guarantee that the desired color is produced. Soluble dyes have traditionally been employed to get the required color (Porter. 2021). Pharmaceutical industries, on the other hand, now prefer to utilize insoluble approved aluminum lake colouring material. These are compounds that disperse to color the tablet (Ohmori et al., 2007). The oil dispersible quality of lakes allows them to be blended with oils and fats. Sometimes glycerin, propylene glycol, and sucrose can be used to disperse or suspend lakes on tablets (Tomida and Saeki. 1999).

- **Polishing / Printing:** The stage of color coating is completed to give the tablet a glittering, unique appearance. The tablets are polished in a polishing pan using waxes such as carnauba wax, beeswax, candelilla wax, and hard paraffin. Sometimes the waxes were used as a heated solution in a suitable volatile solvent.

2. Film Coating:

As with sugar coating, film coating begins by wrapping the tablet's core in a layer of protective polymer (Entwistle and Rowe. 1979). The film coating can be done using traditional pans, but newer inventions employ more modern equipment that is more automated. Fluidized bed machines and rotating perforated drum machines are two examples. The polymer that will be used for the tablet coating should be dissolve able in a suitable solvent, with colors and plasticizes (Seo et al., 2020). The homogeneous solution of these components obtained to spray over the tablets. The tablets are dried to removes the excess solvent. After this process a thin coating of color and plasticizes remains around the tablet's core (Seo et al., 2020).

Independent of the particular equipment utilized, the basic criteria for film coating must be addressed. These include the best method for atomization of liquid during application, optimum mixing and agitation of tablet on bed, with enough hot air so that the solvent should be evaporate (Sohi et al., 2004). Exhaust performance is too critical for removing preservative air and dust.

The tablet's size, color, and even form are essential to promote the end product and influences the company's marketing strategy (Seo et al., 2004). Coating formulas that have been proved successful in the past may be considered by an expert formulator. When a new coating solution used to create film, first off all a trial film should cast onto a flat surface of Teflon or on glass by spreading the coating solution with the help of spreading bar to obtain the desired thickness (Wang et al., 2012). A spraying machine with a trial surface installed in the coating drum may also be used to make trial films.

The alterations in polymer to plasticizer ratio and the inclusion of other polymers offer desirable qualities to the coating. Every coating's basic formula is normally created by changing a previous formula to strengthen the coating's binding ability with the tablet's core by increase the coating's hardness and so on (Wang et al., 2012). The appropriate concentration of coloring material or opaquant is established at this step to assure the product's intended color and tone.

3. Enteric Coating

In the production of oral medicinal dosage forms, enteric coating is used for the pH dependent release of active integrates from tablets. The multi-layer formulation of enteric coating regulate the drug release in the stomach in a pH-dependent manner. Thus this methodology used to reduce variability in medicinal dosage concentration in stomach (Liu et al., 2009). The main advantage of enteric coating is that it protects the drug from stomach acidity and enzymatic degradation, as well as different pharmacological adverse effects (Maderuelo et al., 2019). The medication content in enteric-coated tablets is designed to pass through the stomach intact, dissolve and be released for absorption in the intestines and distribute the medicine to the circulating blood over a prolonged period (Maderuelo et al., 2019). The enteric coating, also known as a gastro-resistant coating, is a barrier that is added to oral medications to regulate where they are absorbed in the digestive tract. Because the name "enteric" refers to the small intestine, enteric coatings prevent a medicine from being broken down before it reaches the small intestine and prevents it from irritating the stomach (Hussan et al., 2012). Thus enteric coating is a technique for the modified release of pharmaceuticals integrated with orally administered dosage forms, with the conventional goal of ensuring the drug's stability in harsh stomach conditions and ensuring (Hasegawa et al., 1986). In entric coating generally, either a fluid-bed drier or air suspension coating technique is used to coat tablets.

The enteric coated tablets can be used for sustain release or controlled release of active drug integrates, with a longer duration of action (Patil et al., 2012). The polymers employed in enteric coatings include carboxylic groups, and their solubility is determined by the number of carboxylic groups present (Obara et al., 1999; Hussan et al., 2012; Maderuelo et al., 2019). Some of the potential polymers used in entric coating are dextrins, Polymethacrylates, cellulose acetate phtalate (CAP), hydroxypropyl methylcellulose acetate succinate (HPMCAS), PVAP, CAT, amylose starch, CAS, shellac , zein and starch derivatives (Obara et al., 1999; Liu et al., 2009; Hussan et al., 2012; Maderuelo et al., 2019).

B. Mordern Coacting Techniques

1. Electrostatic Dry Coating:

In electrostatic coating a coat is applied on conductive substance. A pan coater gadget was used to develop this technique (Qiao et al., 2013). The improved dry powder coating procedure used to produce smooth surface capsules with a homogeneous coating, and release profile that matches the tablet cores. This unique electrostatic dry powder coating approach for pharmaceutical items offers an alternative to aqueous or solvent-based coating techniques (Yang et al., 2015). The substrate receives a significant electrostatic charge (Qiao et al., 2010).

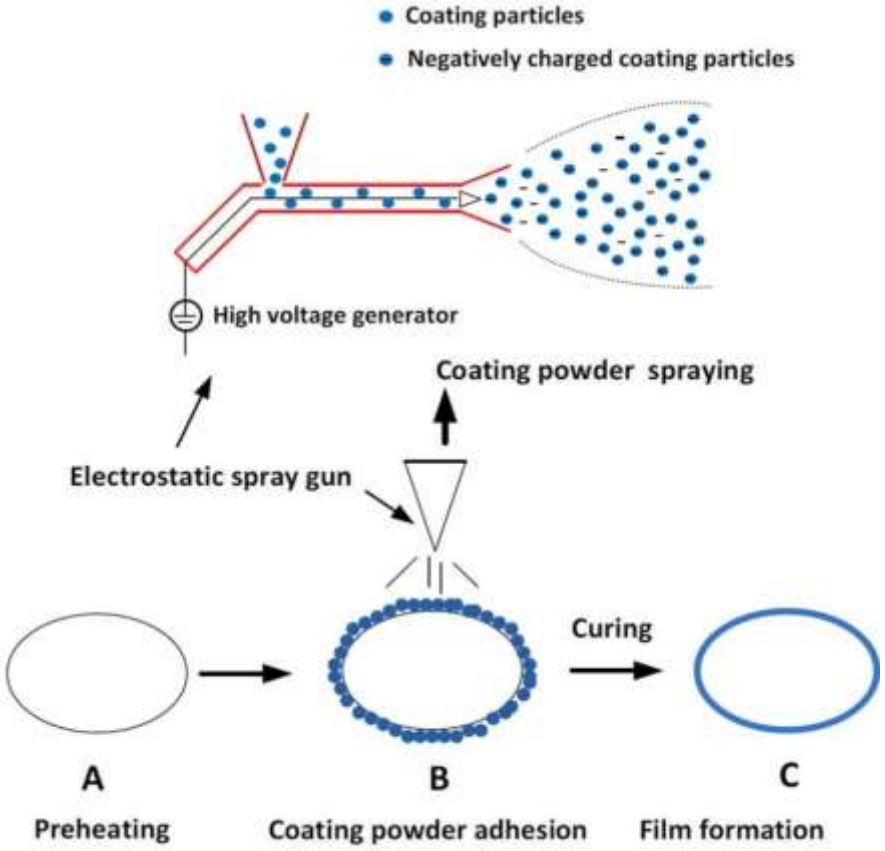


Figure 3: Method of electrostatic powder coating

In addition to pharmaceuticals, this method also used in paint, food and metal industry. This technology also used to develop the capsules. The electrostatic powder coating principle claims that a combination of finely ground particles and charged polymers sprayed on opposite charged substrate floor without using any solvent and that the substrate is then heated in an oven for curing until the sprayed powder fused to the tablet surface to form film (Qiao et al., 2010; Prasad et al., 2016). On the bases of charging process the spraying units are of two types

(a). Corona Charging Mechanism:

The ionization of the air is achieved via this process by applying high voltage on a needle electrode at the gun's hole (Giacometti et al., 1992; Prasad et al., 2016). On its way when the particles of powder travels from the gun to the substrate they obtain negative charge (Lean. 1994). Particle movement between the charging gun and substrate is accomplished using a combination of electrical and mechanical forces (Qiao et al., 2010). The mechanical force developed near the substrate when the mixture of air and powder propelled from spray gun to the substrate (Lean. 1994). The electrical forces developed due to the movement of charged subject between the earthen material and the spray gun's charging tip, as well as the repulsive forces also developed between the charged particles (Feng et al., 2001). As the control sample is released from the gun, the electrical discipline may be modified to guide the powder density, drift, shape, and size.

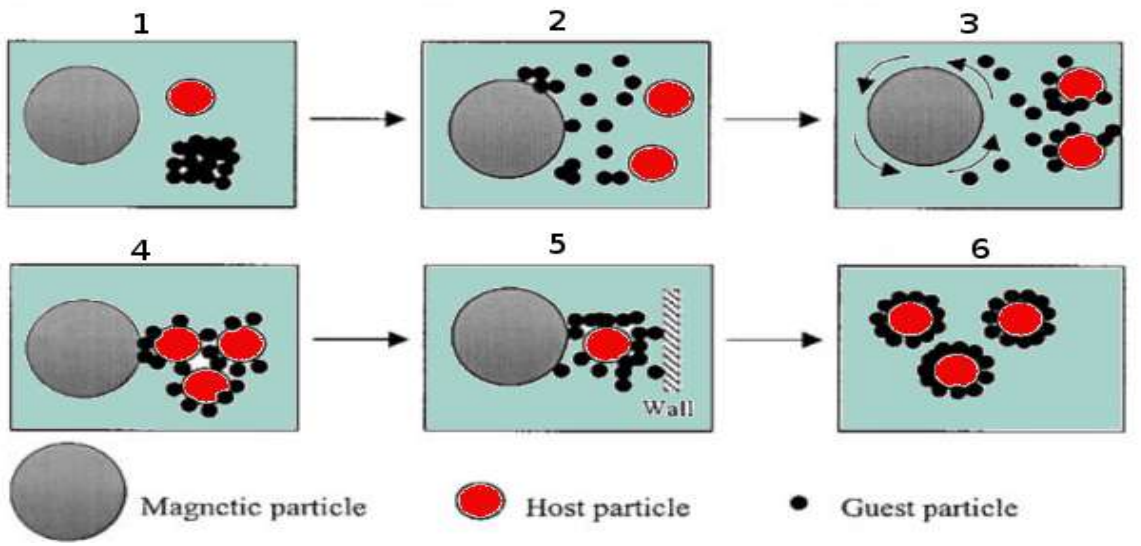
(b). Tribo Charging Mechanism

Tribo charging employs the friction charging concept, which is linked to the dielectric characteristics of solid substances, to ensure that no free ions or electric area exist between the spray gun and the level-headed material (Naik et al., 2016; Beretta et al., 2020). Electric forces are exclusively considered repulsive forces among charged particles in tribo charging gun (Taghavivand et al., 2017). Following the spraying, charged particles approach to the substrate, and due to attraction interactions between the charged particles and ground substrate, the particle are deposited on the substrate in a form of layer (Basu et al., 2013; Beretta et al., 2020).

2. Magnetically Assisted Impaction Coating (MAIC):

The electrostatics dry coating, heat dry coating, compression coating, and electrostatic dry coating are just a few of the dry coating processes that have been developed (Alli. 2021). To accomplish coating, these technologies often utilizes the high impaction and strong shearing stress, as well as an exposure to high temperature. In all of these above discussed process layering and even embedding of guest particles on the host particles might occur as a result of the intense mechanical forces and heat (Pundir and Parashar. 2019; Alli. 2021). Many food and pharmaceutical components are heat sensitive and easily distorted by intense mechanical pressures since they are organic and relatively soft (Jaimini et al., 2014). So the magnetically assisted impaction coating technology developed which is independent from heating and mechanical pressure.

To develop magnetically assisted impaction coating tools there is a extreme requirement to calculate coating time. The guest, host, and magnetic particles combination is expected to remain in a fluidized state with a Maxwell-Boltzmann-like velocity distribution (Gundgal. 2013). The collisions between the particles are thought to be crucial for impinging the guest and host debris, which produces a semi-permanent coating on the host surface (Jallo et al., 2012). The coating period is determined by a number of factors i.e. density of host substances, diameter ratio of guest and host particle., fluidized particle bed size, and qualities of host



and guest particles material (Pundir and Parashar. 2019).

Figure -3 : Mechanism of action of Magnetically Assisted Impaction Coating (MAIC) (1) Magnetic particle's excitation, (2) Guest particle's de agglomeration , (3) Guest particles are sheared and dispersed across the surface of host particles., (4) Interaction of magnetic, guest and host particles , (5) Interaction of magnetic,host and wall (6) product of Coating process.

3. Compression Coating:

Compression coating was first used to create conflicting medications in the 1950s and 1960s (Windheuser and Cooper. 1956). Because the procedure does not need the use of solvents, it involves a relatively quick production process, and allows for more weight gain to the core tablet, compression coating is becoming more popular, and formulation scientists are expressing interest in producing modified-release products (Porter. 2007; Qi et al., 2015) . The compression coating method entails compressing coating material around a prefabricated core tablet with a regular or particularly specialized tablet compression machine, and it does not necessitate the use of a special solvent for coating (Gunsel et al., 1998). As a result, it's also referred to as press coating, solvent-free coating, or dry coating. Compression-coated tablets are made up of two parts: an internal core and a surrounding coat. One turret prepares the core tablet, which is a tiny porous tablet, while another turret with a larger die cavity prepares the compression coating of the core tablet (Blubaugh et al., 1958; Gunsel et al., 1998). Compression-coated tablets are made by placing half of the coating material in the die cavity, then filling it with the remaining coating material to surround the core tablet and compress the powder that contains the core tablet (Beckert et al., 1996; Porter. 2007). The main drawback of this technology is obtaining a reproducible center arrangement of the core within the compression-coated tablet.

4. Hot Melt Coating:

In this process the coating material is applied to the substrate in a semi solid state and subsequently solidified by cooling (Achanta et al., 1997). The coating constituents are chosen largely for their purpose in the dosage form (e.g., delaying medication release,

limiting environmental degradation, and concealing disagreeable taste). Coating ingredients are often lipids and waxes (Jannin et al., 2003). The equipment used in fluidized-bed coating often be modified to meet the requirements of hot melt coating (Repka et al., 2007). Coatings must be thick and free of cracks and mechanical damage. The application of molten materials to protect and alter particle's characteristics is particularly successful with hot melt coating (Jannin and Cuppok. 2013; Stanković et al., 2015). The uniform dispersion is ensured by small droplets and a low viscosity. Fluid Bed Coating (Top Spray Coating, Bottom Spray Coating, and Rotor Coating) is a technological solution that offered by Glatt for coating various particles and tablets. Coating fluid is sprayed onto solid things that are placed in front of it. The film coating solidifies when process air is introduced. The uniform dispersion is ensured by small droplets and a low viscosity (Simões et al., 2019). The use of molten materials as coating solutions can eliminate the time and energy spent evaporating solvents. As the name indicates, a hot-melt coating material is applied to the substrate while still molten and then solidifies after cooling (Stanković et al., 2015; Simões et al., 2019).

Recent researches shows that the use of hot-melt coating to increase stability, conceal flavour, and produce prolonged release (Simões et al., 2019). Drug release from hot melt coatings is dependent on the coating material and can be a result of moisture, pH, heat, shear, or interaction with digestive enzymes, with diffusion and dialysis, pH-dependent dissolution, and enzymatic breakdown being the release mechanisms (Butreddy et al., 2021).

5. Powder Coating:

In this method dry powder is applied followed by heating to form a film (Bose and Bogner. 2007). It is applied with the help of a pigment and firm binder. During the heating process, the solid binder melts and mixed with the pigment the mixture cools down to form a pigment coat (Sauer et al., 2013; Yang et al., 2017). Now a days people are becoming more eco conscious so the coating business have to follow the health, safety, and environmental standards. As a result, there is a critical need to significantly cut on the usage of volatile organic compounds (VOCs) (Luo et al., 2008). The traditional organic coating, on the other hand, contained a wide range of VOCs, including hydrocarbons (hexane, toluene, xylene), ketones (acetone, MEK, MIBK), alcohol (methanol, ethanol, cyclohexanol), and esters (methanol, ethanol, cyclohexanol) (ethyl acetate, butyl acetate) (Dahmash and Mohammed. 2015; 2016). The REACH (Registration, Evaluation, Authorization, and Restriction of Chemicals), which seek to remove dangerous goods and minimise VOC's, have a significant influence on coating applications (Gaur et al., 2014; Dahmash and Mohammed. 2015; 2016).

6. Supercritical Fluid Coating:

A compound that is above its critical temperature and pressure remains in liqiud state is known as a supercritical fluid (SCF) (Tylor. 2009). SCFs have a low viscosity and a high diffusivity, and their density and solvent power may be adjusted easily by adjusting the temperature or pressure (Herrero et al, 2010). Because of its low critical conditions and wide availability, CO_2 is the most often utilised SCF (Weibel and Ober. 2003). Because CO_2 is gathered from other industrial processes and may be recycled in use, the usage of this fluid is also carbon neutral (Peters et al., 2011). SCFs' intriguing features have led to their use in a variety of fields, including extraction and chromatography.

The solvent characteristics of supercritical fluids (SCF) are used to explain a revolutionary solvent-free particle coating technique (Bose and Bogner. 2007; Dhuppe et al., 2012). It entails dissolving one or more coating materials in supercritical CO_2 and then modifying T/P parameters in the autoclave to render the coating substance insoluble in the CO_2.(Jung and Perrut. 2001) A coating forms on the surface of suspended particles as a result of this insolubilization phase (Karanth et al., 2006; Bose and Bogner. 2007). In this method bovine serum albumin and sugar granules were used to coat the drug doges. The coating is efficient, although the morphologies achieved varied depending on the coating substance utilized (Soh et al., 2019). Trimyristin, which precipitates as micro-needles, was used to create a discontinuous covering. In contrast, using a commercially available combination of glycerides and glyceride ester of PEG (Gelucire 50/02) as a film-forming agent, a smooth, regular coating was achieved (Yeo and Kiran. 2005; Keshari et al., 2016).

Conclusion:

Tablets, the most significant member of oral solid dosage forms, have been enhanced in recent decades by the introduction of tablet coating (Zaid. 2020). In the pharmaceutical sector, the coating is widely employed to solve various universal difficulties, such as poor palatability, dysphagia, and brand image employing (Walsh et al., 2014). Water-sensitive APIs' stability may typically be enhanced by using a coat with lower moisture permeability, whereas photosensitive medicines can be preserved by using a coat formulation that contains opacifying chemicals (Zaid. 2020). The pH-sensitive coatings are frequently employed to delay or change medication release to enhance patient outcomes. However, in order to put patient safety at the forefront, coating technologies need complex procedures. In reality, medications must be delivered at precise intervals and at precise locations inside the GIT (Ponchel and Irache. 1998). Various formulation strategies based on coating with other approaches to increase the bioavailability, of orally delivered medications have been investigated in recent years (Alkilani et al., 2015). As Electrostatic dry coating and magnetically assisted impaction coating avoid the hazard of solvents,which is used in primarily based coating. Electrostatic dry coating calls for a special type of powder coating composition. As a result, these criteria force the pharmaceutical coating sector to develop innovative and unique technologies. Pharmaceutical companies are always working to enhance their processes and products. This isn't limited to sugar and film coating but also includes other excipients. This would have a significant beneficial influence on the quality and ultimate cost of the coated brand manufactured. In the last four decades, the coating technique has seen significant progress and improvement in terms of energy usage, film distribution, and drying efficiency (Sastry et al., 2000; Arshad et al., 2021). However, coating processes still have a lot of room for improvement in the future.

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