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TABLET IN TABLET TECHNOLOGY

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Abstract
The tablet is the most often used dosage form among all of those available because of its robustness and patient acceptability. The coating is an essential component of the tablet's composition because film and sugar coatings were required for enhanced aesthetic attributes such color, texture, tongue feel, and taste masking. Providing a comprehensive examination of the formulation, characterization, and challenges faced in the manufacturing of tablets in tablet dosage form is the aim of the current work. Aesthetic attributes such as color, mouthfeel, texture, and taste masking are determined by coating techniques. Although this coating technology has several limitations or drawbacks, one of the best alternatives is the tablet in tablet. Examining in detail the formulation, characterization, and challenges faced in the production of tablets in tablet dosage form is the aim of the current work.• Cutting down on or eliminating toxicity. Raising the level of precision., Medication directed towards particular organs or cells, Improving the administration of vaccination adjuvants. creating innovative nanostructures for usage in particular fields, such as neurology, orthopedics, cancer treatment, and ophthalmology. Successful introduction of nanoscale items has the potential to occur in the fields of gene delivery, repair, and replacement of faulty genes.
Keywords: Tablets, formulations, dosage forms, color, Coating technology, texture.

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Introduction

Among all the dosage forms that are currently accessible, tablets are the most commonly utilized due to their ease of administration, affordability, and elegance [1]. The visual characteristics, such as color, texture, mouthfeel, and coating procedures affect flavor masking. There are various limitations or downsides to this coating technology that need to be addressed. One of the greatest substitutes is the tablet in Tablet. The goal of the current work is to provide a thorough analysis of the formulation, characterisation, and difficulties encountered during the production of tablets in tablet dosage form. The patent on the tablet containing cyclophosphamide and capecitabine is one of the very few that have been filed or awarded thus far; in this case, we concentrated on the reasoning for the creation of this dosage form. In this review, we aim to draw attention to the advancements in tablet manufacturing and discuss the advantages for the pharmaceutical business. Decreased in the layer of film. The patent on the tablet containing cyclophosphamide and capecitabine is one of the very few that have been filed or awarded thus far; in this case, we concentrated on the reasoning for the creation of this dosage form. In this evaluation, we aim to emphasize the progress made in the production method of tablets will also be discussed, along with its advantages and how it will alter the drug's release characteristics [2, 3]. In the 1800s, contemporary medications, or sugar coatings, were used to cover up the bitter taste. Certain limits or drawbacks of sugar coating include the need for multistep operations (sealing, sub-coating, smoothing, coloring, polishing, etc.) and lengthy processing times of up to seven days for skilled operators. The pharmaceutical business accounted for the majority of the processing time needed for sugar coating. Decreased in the layer of film [4].

1. Tablets

A tablet is a solid dosage form that has been compacted and may contain medication or excipients. Pharmaceutical tablets are defined as solid, flat or biconvex dishes that are made by
compressing a drug or combination of pharmaceuticals, with or without diluents [5]. This is in accordance with the Indian Pharmacopoeia.

Fig; 1 Types of tablets

2. Importance's of tablet in pharmacy

A tablet that is taken orally might be designed to provide a precise dosage to a particular location within the body; [6]. It can be given sublingually, buccally, rectally, or intravaginally. An oral medication can be taken in a variety of formats, including tablets, syrups, elixirs, and more.

3. Administration of tablets tablet in sublingual route:

If you are planning to exercise or anticipate a stressful situation, the sublingual tablets, sublingual powder, and oral spray can be taken to prevent angina attacks or to fast halt angina attacks that have already begun [8].

4. Administration of tablets vaginal routes

Historically, the vaginal method has been used to treat localized genital problems such infections, vaginitis, and to induce or avoid childbirth [9].

n general, a Tablet in Tablet or compression-coated tablet consists two parts; one is an internal drug core, and another is an outside coating shell. The outer layer surrounds the inner core, and it mainly controls the strength of the film coating, the release of the drug, and the stability.

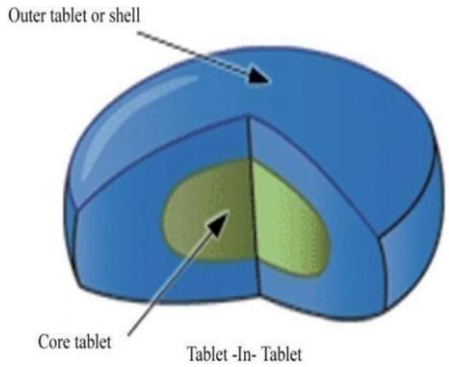


Fig 2; Over view of tablet in tablet technology

Types of tablets in tablets technology generally, it consists of two types

2.1. Inlay tablet technology

2.2. Tablet in tablet technology

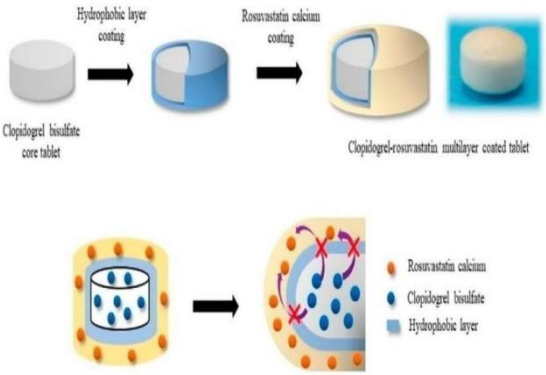
2.1 Inlay tablet technology:

A kind of multilayer tablet where the top surface is fully exposed and the core tablet is not entirely encased in coating. During the manufacturing process, the coating material (cup) is only filled to the bottom of the die cavity, and the core is positioned on top of it [10]. When compression force is applied, the coating material is moved, compressing the entire tablet.

2 2. Tablet in tablet technology:

The external outer coat entirely encloses the interior core tablet in this kind of tableting technology. This tablet is composed of two parts: an exterior coating and an inside core. From the outside, it appears to be a single tablet, but inside that tablet is another tablet. A few years ago, this technique attracted more attention for products that were updated and distributed. Granular material is compressed around an inner core tablet, or core tablet [11]. The hygroscopic, oxidative, photosensitive, and acid labile medications are protected by the tablet in tablet formulation. Compression coating is reasonably simple and affordable. While compressing tablets is simple in a lab setting, specialized equipment is required for large-scale production. The industry is more receptive to it because this technique makes use of traditional manufacturing.

Figure3: Common Tablet Defects



3. Tablet in tablet of manufacturing process

As far as solid oral dose forms go, tablets are the most widely used and practical option. There are many different kinds of tablets. One sort of tablet is called a modified release dosage form, and because it has so many benefits, it is more significant in drug therapy. The tablet in tablet technology is currently the best substitute for the bilayer tablet formulation for the incompatible drug when developing modified released products. Using specially made tableting machinery, granular materials are compressed around a prefabricated tablet core. Another name for the tablet in Tablet is solvent-free coating process or compression coating.

The two components of the tablet in tablet dosage form are the inner core and the outer layer. A somewhat smaller tool than that used to prepare the exterior coat was used to prepare the internal core, which is a little tablet. Following the production of the internal tablet core, it is positioned in the centre of another die that is somewhat filled with coating powder and larger than the core tablet [11]. The remaining coating powder is then added to the top of the core tablet and compressed, creating a tablet inside a tablet. This procedure

causes an issue where the core tablet may tilt when being transferred onto a different die.

Generally speaking, the coat is water soluble and readily disintegrates following oral administration to produce an immediate release product. The tablet in tablet can be used to create repeat action tablets by releasing the drug's initial dose first via the outer layer and then through the inner core later [12]. The risk of overdose toxicity is indicated by the repeat action tablet in tablet dosage form, as the drug is rapidly released from the core tablet and reaches radically different blood levels. a list of medications that are made as tablets or compacted coated tables. Hariharan and Gupta have also documented an additional technique for producing compressed coated tablets or tablets made from tablets. The core does not need to form independently when using this strategy. The core and coated tablets are produced simultaneously by the redesigned three-layer tablet machine [14]. One side of the press is used to make the core tablet, and it is subsequently moved to the other side for coating. This coating technique forms an exterior layer of a coating mix in the shape of a cup first, followed by the trapping of core material and the formation of an additional outer coating layer on top.

Beads, granules, microspheres, pure drug crystals, or drug-excipient mixtures can make up the core. The use of an IR spectrophotometric hydraulic press in tablet manufacture was documented [14]. Production of tablets on a big scale is not a good fit for this press. The manual process needed to create a dry coated tablet is described by the author. First, fill the die with coating powder. Next, place the core tablet in the middle. Finally, apply compression force. The coating powder's thickness and particle size have an impact on the dissolving lag time, which can last anywhere from one to twenty hours. Smaller particles can provide a longer lag period].

4. Ingredients

❖ Diluents / Bulking agents

Diluents are substances added to tablet or capsule dosage forms in order to increase the weight or volume of the dosage form, according to USP. Rockville and associates (1979). When the drug dosage is insufficient to create the necessary bulk for the tablet, diluents are fillers made to make up the difference Diluents are sometimes referred to as fillers or bulking agents [15]. Additional justifications for improving tablet characteristics include enhancing cohesiveness, facilitating flow, enabling direct compression manufacturing, and modifying tablet weight or thickness. The most crucial thing to remember is that, after calculating potency, only the diluent is changed to reflect the entire amount of active medication. Diluents are essential excipients for small-weight tablets.

❖ Binders

In order to create granules or encourage cohesive compacts for tablets that are directly compressed, materials known as tablet binders or binding agents are added during wet granulation, either in liquid or dry form. Binders, also known as granulators, are substances that give powdered material cohesive properties [16]. By incorporating granules with the appropriate size and hardness, they improve the tablet's free-flowing properties and provide the formulation the cohesiveness it needs to stay intact even after compression.

❖ Disintegrants

A disintegrant is a material or combination of materials that is added to a tablet to help it break up or disintegrate into small pieces or fragments and speed up the dissolving of a pharmacological component. Disintegrants, as defined by USP, are functional ingredientsadded to formulations to encourage quick disintegration into smaller units and speed up the dissolution of a medicinal material. Rockville and associates (1979) [17, 18].

Disintegrants absorb liquids and begin to expand, disintegrate, or form gels when they come into touch with water or stomach or intestinal secretions. This results in the tablet's structure rupturing and disintegrating, increasing the surfaces available for the drug's better breakdown. Essential excipients for tablets are disintegrants. Several disintegrants that are often and extensively utilized include L-HPC (Low-Substituted Hydroxypropyl Cellulose), Micro crystalline cellulose, starch pregelatinized modified etc.

❖ Lubricants

Lubricant is a non-toxic, pharmacologically inert substance that is added to the formulation to reduce interparticle friction, prevent adhesion of the tablet material to the surface of the dies and punches, make it easier to eject the tablets from the die cavity, and possibly even increase the rate at which the tablet granulation flows [12]. According to USP, lubricants are compounds that are generally used to lessen the forces that cause particles to rub against one another and against the metal surfaces of manufacturing tools like tablet punches and dies that are used to create solid dosage forms. Liquid lubricants may be incorporated into the tablet granule matrix prior to compaction. Essential excipients for tablets are lubricants. The most commonly used are calcium stearate, magnesium stearate, and sodium laurate sulphate.

❖ Glidant/ Anticaking agents

By reducing interparticle friction and cohesion, glidant—a non-toxic, pharmacologically inert material—improves the flow characteristics of tablet granulation or powder materials. Prior to compression, they are always added in a dry condition during the lubrication step. Glidants and anti-caking chemicals, according to USP, are used to encourage powder flow and lessen the possibility of caking or clumping when powders are stored in large quantities [8]. Moreover,glidants and anticaking agents lessen the likelihood of bridging during processing and emptying powder hoppers. The most often used glidant is colloidal silicon dioxide, which is

typically employed at low concentrations of 1% or less. Another usage for asbestos-free talc is as a glidant. Essential excipients for tablets are glidants.

❖ **Coloring agents**

Excipients used in a formulation to improve patient compliance are known as coloring agents, colorants, or color additives (British spelling) or coloring agents, colorants, or color additives (American spelling). From a regulatory perspective, pigment is a sensation found solely in the brain and is used in food, medicine, and cosmetics. The combination of seven lights that become visible through a prism is called color [9]. Actually, the three primary colors—red, green, and blue—combine to form all of the colors.

❖ **Flavouring agents / fragrance**

As defined by USP, a flavor is any single chemical or combination of synthetic or natural compounds that, when ingested or sniffed, can elicit a taste or olfactory reaction, also known as a fragrance. While perfumes are solely intended for external application and are only detectable through smell, flavouring compounds are ingested orally and are enjoyed by both taste and smell [4]. In chewable, oral disintegrating, dispersible, oral solutions, and oral suspensions, tastes are typically essential excipients because they cover up the taste and smell of the undesirable ingredients and improve the product's palatability, which increases patient compliance.

❖ **Sweeting agents**

Sweeteners are chemicals that are used to cover up disagreeable flavors and disguise unpleasant tastes in oral dose forms. It attaches itself to the tongue's receptors that give off the sweet taste [5]. Sucrose represents sweetness. For chewable tablets, lozenges, oral disintegrating tablets,dispersible tablets, oral solutions, emulsions, and oral suspensions, sweeteners are essential excipients.

❖ **Surfactants**

Surfactants are substances that possess distinct polar and non-polar areas, which enable them to group together in a solution to create micelles. Non-polar medications can then enter these micelles and become soluble [6]. They could lessen the interfacial tension, also known as the surface tension, between two liquids or between a gas and a liquid. As an illustration, sodium lauryl sulphate dissolves aspirins as a surfactant. Despite the extended disintegration, polysorbate 80 in tablet formulations including starch has produced faster medication dissolving rates.

❖ **Releasing - modifying agents**

Release-modifying agents are substances used as an excipient to control drug release in a modified-release dosage form such as in prolonged-release or controlled-release tablets. They are vital excipients for modified-release tablets.

❖ **Coating materials**

The substance used to coat tablets or particles. Any film-coating formulation consists mostly of a polymer, colorant, plasticizer, and solvent (or vehicle). Coating materials are vital excipients for tablets but not for all tablets.

5. Advantages of tablet in tablet of technology

- Separation of in compatible material can be achieved in the core and outer shell.
- If will use to develop a modified release product [e.g.; delayed release product.
- The tablet in tablet of two different drugs can be targeted in two different areas of the gastrointestinal tract.
- The need for a separate coating process of the tablet can be avoided in the press coating of the core and coating layer.
- It is a solventless coating, so it is not hazardous to the environment.
- The pharmacokinetics interactions [drug drug] between concomitantly administered medications can be avoided in tablet in tablet dosage form by creating the time interval in their release.
- The tablet in tablet dosage form gives protection to the hygroscopic orthro- liable drug.

6. Disadvantages of tablet in tablet of technology

- Cross contamination possibility between the layers.
- Between the d j a c e n t layers, the elastic modulus is a mismatch.
- There are an inadequate layer attachment and relatively low interfacial strength because of the high elastic modulus ratio between neighboring layers.
- Face challenges for long-term retaining and chemical integrity of t h e device during its storage.
- Due to the large tablet size, it creates a swallowing problem.
- The difference in coating performance when the core tablet is not located in the centre of the system.

7. Equipment used

7.1 Weighing and Dispensing

Weighing and dispensing transfer the calculated amount of raw material from bulk quantity
Storage(9). These estimated quantities are then used to manufacture pharma products of specific amounts and properties. weighing and dispensing is a dedicated facility or area for these processes.

7.2 Weighing scale

Weighing scales are used to determine the necessary raw material quantities. They have to be sufficiently precise and accurate to weigh the real number of raw materials. substance. To ensure that the output measurement is accurate, the weigh scale needs to be calibrated [10]. They need to be calibrated and checked every day, as well as validated against a standard weight and recorded.

7.3 Sizing equipment

Particles are produced with sizing equipment at consistent, authorized sizes. If size doesn't improve total yield, waste will rise [11]. Milling equipment is frequently utilized in the size process. Greater particles are broken up into finer, uniformly sized particles using mechanical energy. Wet mills and dry mills are the two types of mills that are employed.

7.4 Blender

It is used to blend excipients, API, and various compounds uniformly in powdered form. The powder is held within a sizable metallic structure that makes up the blender. Depending on the kind of blender and the needs of the product.

7.5 Fixing shell blender

This kind uses a metallic component known as an impeller or mixer to mix the powder while a metallic container stays stationary.

In order to blend chemicals, this blender can generate a comparatively larger force.

7.6 Rotating shell blender

This kind has a rotating shell that holds the substance. Gravity causes the materials inside the shell to mix. When compared to a fixed shell blender, the mixing force is lower.

7.7 Granulator

Granules are created from the powder using a granulator. When powders of tiny particles are mixed, granules—which are comparatively larger—are created. Granulators come in two varieties: wet and dry.

Water or any other organic solvent sprayed inside the granulator onto the mixing powder is used in a wet granulator. The process is terminated when the powdered form takes on the appropriate granular size and shape.

Neither water nor organic solvent are used in the dry granulator. Rather, a roller compactor is used to force the powder as it yields. The output that's left over is the sheet shape, divided into the appropriately sized particles.

7.8 Dryer

The dryer is used in the granulation stage to eliminate the liquid solvent or water content from the grains that are taken out of the granulator. The granulator's material output is sent straight into the drier, which eliminates the granules' water content.

7.9 Tablet press mechanie

The granulates are formed into tablets using a tablet press machine. Granules are pushed into a die in the tablet press machine using upper and lower punches. The powder is forced into the die by compression force applied at the upper punch.

Tablets are expelled from the die using the ejection system following compression. The hardness of the tablet is among the crucial factors. It is exactly proportionate to the punches' compression force. Hardness increases with increasing force and vice versa. The tablet press machine is the last piece of manufacturing equipment for certain product kinds.

7.10 Tablet coating machine

If the product needs to be coated, the tablet coating machine is the final piece of manufacturing equipment. Tablets are coated with the suitable solvent in a tablet coating machine. The machine is made out of a big pan that spins nonstop. Additionally, hot air from the input and output pipes travels through the pan(15). The necessary solvent is sprayed into the tablet pan using a spray gun.The liquid spray adheres to the surface, creating a layer of coating as it does so. The coating process is terminated when a certain amount of time has passed or the necessary parameters are met. After being taken out of the coating, the completed tablets are delivered to the packaging division for ultimate packaging.

Conclusion

The use of film and sugar coatings in tablet formulation is crucial for achieving aesthetically pleasing qualities such as color, texture, mouthfeel, and taste masking. There are a number of drawbacks to film and sugar coatings, but the primary one is that the use of organic or aqueous solvents can be hazardous. The best workaround for the aforementioned issue is to use the Tablet in Tablet approach. By using a tablet in tablet technology, it is possible to develop a modified release mechanism for a drug that is similar to one or distinct from the same category, or to achieve drug release at a different site of absorption.

Author contributions

All authors are contributed equally.

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Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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