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A concise review on tablet in tablet

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Abstract
History: Because of its durability and patient acceptance, tablets are the most often utilized dosage form among all current alternatives. Because the increased aesthetic features of color, structure, mouth sensation, and disguising the flavor relied by cat with sugar or film; this coat is a significant component of tablet formulation.
Introduction: One of the most serious disadvantages of film and sugar coating is the use of water or organic solvents that induce toxicity. Researchers have given close attention to the advancement of Tablet in Tablet dosage form, and various study papers and patent filings can be found in the literature.
Conclusion: The current study collected information on the most recent patent, formulation, kinds, benefits, and drawbacks of Tablet in Tablet or compression coating. The study also discusses the importance of Tablet in Tablet techniques in the creation of a modified release mechanism in greater depth.

Keywords: Tablet in tablet, inlay tablet, layered tablet, evaluation, osdrcs

1. Introduction
The coating also protects the pharmaceutical physically and chemically, as well as altering the drug's release behavior. In the 19th century, in other words sugar coating, was utilized to cover up the harsh flavour. Coating with sugar had certain disadvantages or constraints; it was necessary a lengthy processing a time of up to 6-7 days; it needed a multistep operation (sealing, sub coating, smoothing, coloring, polishing, and so on) that required a qualified operator. It also has difficulties such as a non-automated coating process, weight gain, and sugar solutions that is susceptible to bacterial growth, that prompted the development of other coating techniques. Film coating considerably reduced the time required for sugar coating manufacture. Abbott Laboratories released in 1954 the first ever tablet with film coating to the market [1]. Film coating is the most recent advancement in coating technology; it provides batch-to-batch consistency in production of formulations; it may be utilized for numerous dosage forms; & it allows for simple process management and automation.
Polymeric solutions based on both aqueous and organic bases were easily employed in the film coating process, but both of these polymeric solutions had limitation. Organic solutions that are employed in film coating have certain downsides such as flammability and toxic effects, organic solvent expenditure, and residual solvents in film. In the case of hydrophilic film coating, heat needs and longer drying periods greatly enhance total production costs and are a massive drawback [1].
Noyes initially described the compression coating process in an 1896 patent [2]. Compression coating, a unique coating technology, is one of the greatest possibilities in the creation of a new drug delivery system. It has been employed in the pharmaceutical industry for a variety of purposes, including the creation of revised release, colon-specific release, pulsatile release, and controlled release. According to the existing literature, press coating technology is employed for the production of tablet-like as tablet in tablet, such as the invention of zero-order release glipizide tablets [3].
Compressed coating is an alternative coat method for dealing with the problem of film or sugar coating. It is also called as a dry coating or press coating and was one of the first solvent-free coating procedures. A compression-coated tablet is composed of two parts: an inside pharmaceutical core and an outside coating shell. The surface layer, which surrounds the inner core, is principally important for the film coating's strength, release of drugs, and durability [4].

History

Because of its simplicity of administration, low production cost, and elegance, the tablets are the most frequently employed dose form within all known dosage forms. Color, structure, mouth feel, and taste masking are all affected by coating processes. Tablet in Tablet is among the best options for circumventing the constraints of this coating process. The goal of this study is to give a thorough examination of the formulations, identification and difficulties encountered during the production of Tablet in Tablet dosage form. There are presently only a few patents on this issue, such as the claim on the Tablet in Tablet containing cyclophosphamide and capecitabine, thus we focused on the rationale for establishing such a dosage form here. This research seek to highlight developments in the Tablet manufacturing process as well as illustrate how they assist the pharmaceutical industry.

1.1 Benefits of Tablet in Tablet technology

1. In both the internal part and the outer shell, incompatible materials can be isolated.
2. It will be used to build revised release goods.
3. Two distinct medications can be addressed in two different sections of the gastrointestinal system using the Tablet in Tablet [5].
4. The requirement for a separate tablet coating procedure may be removed by the inner center and exterior coating layer are pressed coated.
5. Because it is a coating without solvent technique, it is not harmful to the nature.
6. By creating a periodic interval in their release, pharmacokinetic interactions (drug-drug interactions) concurrently given drugs in Tablet dose type might be avoided.
7. The hygroscopic or thermo-liable medication is protected by the Tablet in Tablet dose form.
8. The instant & sustained release effects of a comparable or different medication combination can be obtained in a single Tablet in Tablet dose form.
9. Optimal dosage at the appropriate time and in the correct place [6].

1.2 Problems associated with Tablet in Tablet technique

1. Contamination from other sources across strata is a possibility.
2. The elastic modulus represents a mismatch between adjacent layers. There is insufficient layer adherence and relatively low interface fortitude because to the considerable ratio of elastic modulus between adjacent layers [5].
3. Face obstacles in preserving the Stability, both physical and chemical of the equipment throughout storage.
4. Because of the big tablet size, it is difficult to swallow.
5. The variation in the coat effectiveness so the inner core tablet is not in the system's center [7].

2. Types of tablet in tablet

1. Tablet in tablet
2. Inlay tablet
3. Layered tablet

2.1 Tablet in Tablet

2.1.1 Manufacturing procedure of tablet in tablet

The dose form in tablet form is the least frequent and efficient oral solid dosage form available. Tablets are categorized in to the several categories; preparations are one type of tablet that has acquired relevance in medication therapy since it offers a number of advantages. Nowadays, the Tablet in Tablet innovation (Fig.1) is the ideal solution for bilayer tablet production for incompatible drugs when developing changed released goods. Using specifically specialized tableting machinery, granular materials are compressed around a prepared tablet core. Compressed coating is another name of the tablet in tablet.

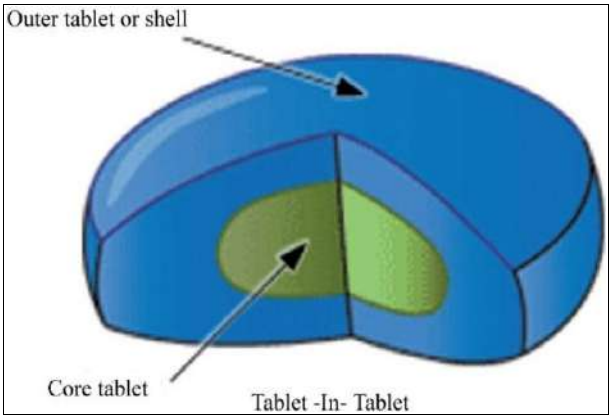

Fig 1: Tablet in Tablet

In tablet shape, the two portions are the central core and the external layer. The inner core is a tiny tablet that is created utilizing tooling that is relatively smaller in size than the equipment used to manufacture the top layer. Following the creation of the inner tablet core, it is situated (centrally) in another die that is affordably priced inhabited with coating particles and greater than the core tablet, and also the residual coating particle has been positioned on external part of the centered placed tablet and pressurized, as a result of development of tablet in tablet [3]. This procedure causes an issue in that the core tablet may be slanted during the transfer to another die. The coat should be soluble in water and dissolve easily after oral administration to generate a fast release material. The Tablet in Tablet can be used to make repeat action tablets, in which the outer layer gives the first dose of medicine and the inner core releases it later. Because the center placed tablet has quickly released the medicine that has totally acquired varied blood concentration, the repeated activity in these types of dosage form illustrates the danger of toxic effects from over dosage [8]. Table 1 contains a list of medications that are manufactured in Tablet in Tablet.

Hariharan and Gupta [9] revealed one more technique for producing Tablet in Tablet. Here no requirement to separate the core formation in this procedure. The updated three-layer tablet machine was intended to make core and coated tablet at the same time. The core tablet is formed on one side of the press and then moved to the opposite side for coating. This coating process begins with the formation of a cup-shaped outside layer of a coating mix, followed by the trapping of core material and, lastly, the development of an additional outer coatings layer on top. Pure drug crystals, drug-excipient mixtures, granules, microspheres, or beads [1] may be used as the core.

Lin *et al.* [10]. described using an IR spectrophotometric hydraulic press to make tablet in tablet. This machine is not

designed for mass tablet manufacture. The author outlines the laborious process of creating a dried coated tablet. Filling the die first with coating powder, then putting the inner core tablet in the middle, and then applying compression force. The dissolution lag time varies from 1 - 20 hours based on the thickness & diameter of the coated powder particles. A greater delay period can be provided by minuscule particles [10].

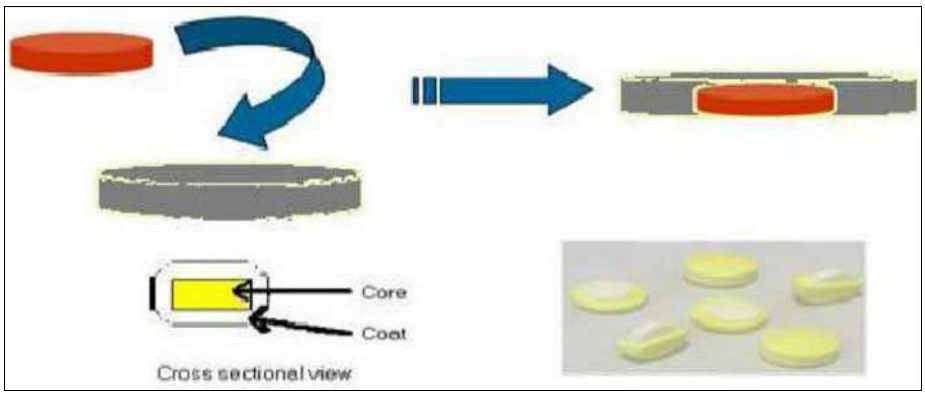

Fig 2: Tablet in Tablet

2.1.2 Recent advancement

In the standard dried-coating or Tablet in Tablet production procedures mentioned above, the core tablet transfer might cause issues such as non-core, twofold, off-center, and inlay. As a result, regular tablets are more popular than dry coat or Tablet in Tablet. Because the above-mentioned strategy (illustrated in section 2.4) requires the compression of the center placed tablet in progress, the overall cost of production of the dosage form would rise.

To solve concerns with conventional dried-coating techniques of tablet fabrication, novel one-step dry-coating (OSDrC®) apparatus was built, ushering in a tablet manufacturing revolution. Sanwa Kagaku Kenkyusho Co., Ltd., Japan, owns the OSDrC® trademark. Using this method, researchers were able to control drug delivery by altering the depth of the outermost coat layer composition [11].

The outermost coat layer powder is put in the space generated by the lower center punch & lower outer punch before being precompressed by the upper center punch.

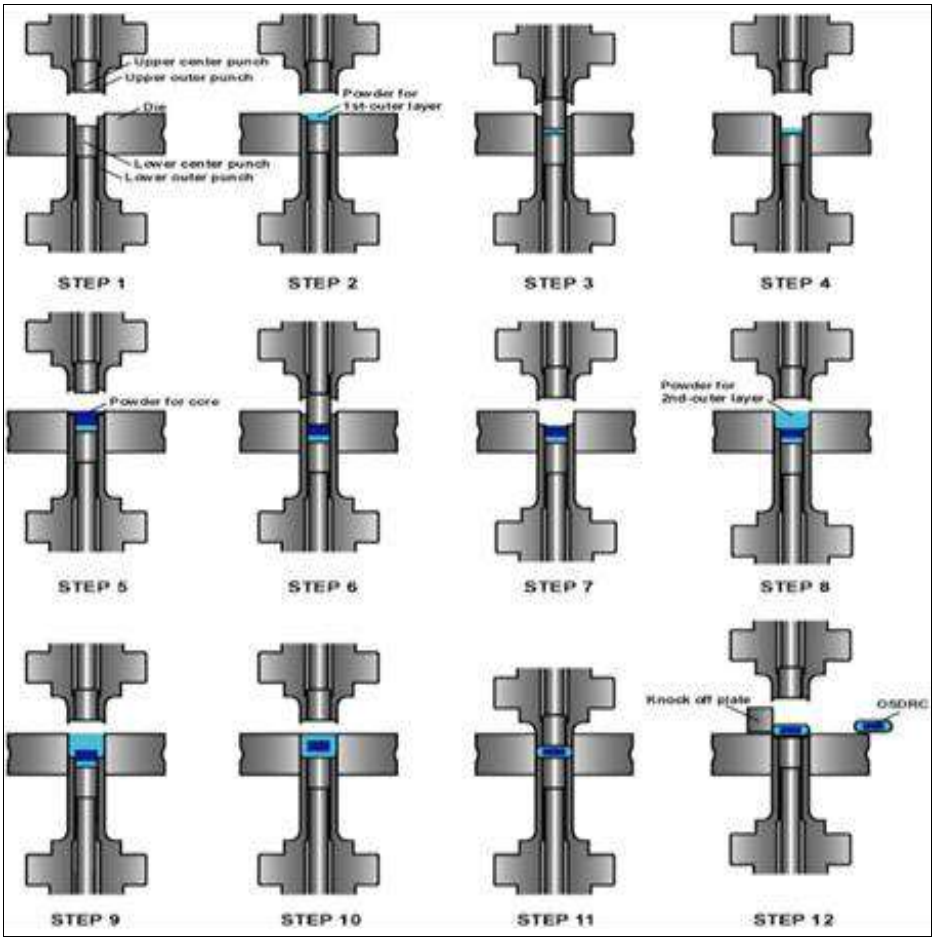

Fig 3: Steps of OSDrC® manufacturing method

The lower-center punch is then moved down as the upper-center punch presses the first outer layer that has already been compressed. After removing the upper-center impact, the inner core powder is deposited in the resulting space. The upper-center punch then compresses this.

At last, the punch at the bottom is lowered, & outer layer powder fills & covers the pre - compressed core / first-outer layer. The upper and lower punches crush the core / first - outer layer combination and the second - outer layer complex, in which the center punches are linked with the outside punches, respectively [12]. The mechanics of the OSDrC® generation system is depicted in Fig.3.

2.1.3 Benefits of OSDrC®

1. Because it functions in a single phase, this indicates that the tablet and core are generated in one spin of the punch on the turntable, this technology will manage the load of the various layers of the tablet.
2. It uses an innovative cam movement mechanism and a customizable twin punch arrangement to generate accurate coatings of any thicknesses and tablet form [5].
3. Creating a core tablet does not need a separate procedure. It is a solvent less, one-step coat technique [11].
4. Because of the separately moving movable double punch design, it produces precise quality tablet.
5. The modified release formulation or drug delivery can be developed by utilizing this OSDrC® technology.

2.1.4 Example

Tablet in Tablet of cyclophosphamide and capecitabine

Cyclophosphamide is a chemotherapeutic agent that is converted into its activated state in the liver; the active component is solely responsible for suppressing the multiplication of cancer cells. Cyclophosphamide is used to treat diseases such as cancer treatment, ovarian, whether single or even in combo. Capecitabine is a drug which is also used to treat advanced breast cancer. Furthermore, capecitabine's combination partner is essential for activating the thymidine phosphorylase (TP) enzyme, which converts capecitabine to active 5-FU (fluorouracil).

Many doctors believe that using cyclophosphamide and capecitabine orally may be more effective in treating metastatic breast cancer. When these two drug molecules were used together, the total impurity level increased considerably; it is only owing to the mismatch of two pharmaceuticals that the synthesis of steady oral the formulation of these medications proved fairly complex. Cyclophosphamide hydrolyzes and is quickly destroyed in the presence of water lights and solutions. It can also withstand extreme temperatures [13].

The foregoing challenge may be solved in this case study by developing a Tablet in Tablet (US 20190142755) single-unit oral stable dosage form.

Table 1: List of drugs formulated in Tablet-in-Tablet or compressed-coated tablet

Active ingredient	Category / We	Excipients	References
Paliperidone	Antipsychotic	HIC-H, Euragit RL-PO, Glyceryl behenate, MCC, HPMC-K100 M	[4]
Orlistat and venlafaxine	Anti-obesity and antidepressant	For core tablet-I3CD, SD Mannitol, Ludiflash, Kollidon CLF, Kollidon-30, SLS, Sucrose, Talc, Mg-Stearate, Cherry Flavour, Methyl Paraben For outer coating-BCD, Eudragit EPO, Ludimess LCE, Maltodexuin, Xanthan Gum, Kollidon-30, Citric Acid, Sucralose, Peppermint flavor, Propyl Paraben, Talc, Mg. Sterate	[5]
Amoxicillin and Potassium clavulanate	Antibacterial and p lactamase inhibitors	Static acid and a• ieel layer	[14]
Acetaminophen	Analgesic and antipyretic	HPMC, Mg. Sterate, Lactose-crystal cellulose	[12]
Glipizide	Anti - diabetic	pCD, WPC-L, HPC-M, MCC, Eudragit RL PO, Mg. Sterate	
Noledipme	Anti hypenensive, calcium channel blockers	HPC-L, HPC-, Eudragit RSPO, Mg. Sterate	[31]
Prednisolone	Immuno-suppressant	Carboxymethyl neaten gum, Sodium alginate, Calcium	[15]
		Chloride, MCC, Polyplasdone XL, Tri-Sodium (Citrate, Trisodium orthophosphate dodecahydrate, Mg. Stenue.	
Carvedilol	Antihypertensive or non-selective beta - adrenergic receptor blocker	Polyoxy Ethylene Oxide WSR 205, HPMC K4M, MCC, Sodium starch glycollate, Mg. Sterate.	[15]

2.2 Inlay tablets

A multilayer tablet in which the top surface is entirely exposed rather than the core tablet being completely contained by coating. The tablet was compressed using core rod tooling, with just one surface of the core exposed to the exterior and the other medication integrated in the cup part. [8] During manufacturing, just the bottom of the die chamber is coated with material, and the core is put on top of it. The main body component might be uncoated granulation compacted around an enteric coated inlay piece. The main body section of the tablet is initially released and absorbed in the gastrointestinal system in this modification, while the enteric coating shields the inlay portion for a specified amount of time, allowing for time delayed or sustained medicine. Inlay tablets with unique combinations like Metformin 500mg sustained release (outside coat) and Pioglitazone 15 mg are available from A to Z. (core tablet).

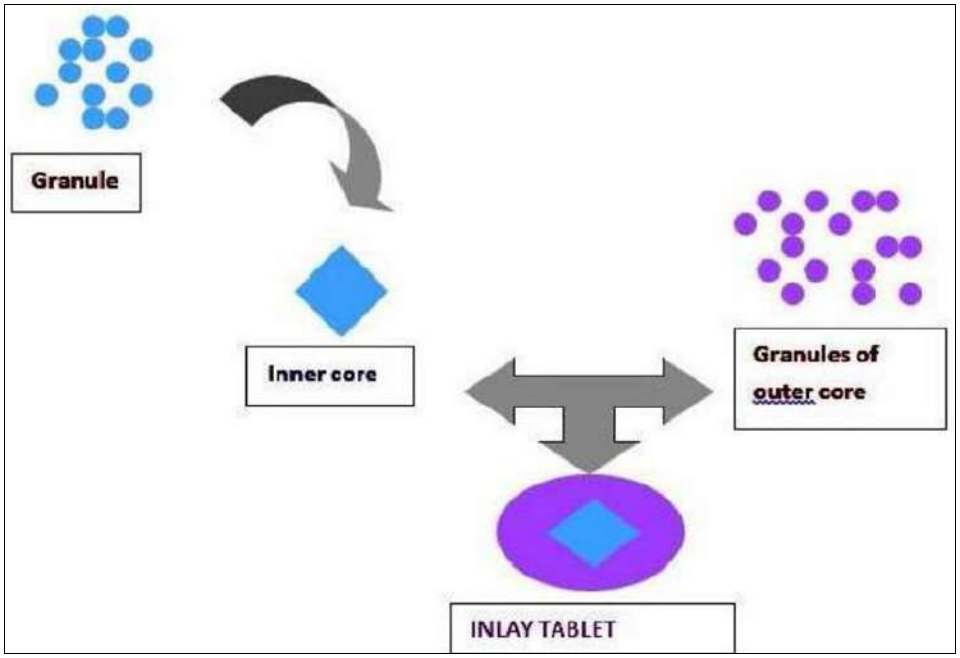

Fig 4: Preparation of inlay tablets.

2.2.1 Benefits of inlay tablets

1. It is possible to create a dosage form combining a modified release active ingredient and a fast release active ingredient.
2. Has the capability to release insoluble and soluble medicines in dissolving solutions at a zero-order rate.
3. The frequency with which highly water-soluble drugs are administered can be lowered while maintaining the same efficacy.
4. Various forms of tablets.
5. The adverse consequences of low plasma level can be ignored.
6. Throughout therapy, plasma concentration can be kept steady & considering therapeutic parameters.
7. The bursting effect, defined as the rapid release of a large amount of drug, is frequent in drugs that are extremely soluble & should be avoided since it can lead to an excessive level of active ingredients in the circulation.

2.2.2 Preparation Of inlay tablet

To manufacture a cup-shaped tablet, a carefully weighed amount of powder mix (coating blend) was placed in the die and squeezed at a known force using a Carver Pressing (Wabash, IN) with the tooling shown in Figure 7. (cup) [8]. The cup was left in the die, and a measured amount of either a model drug or a drug-containing mixture was put into it before being lightly tamped with the punches in an extended position. To make the final pressure coated tablets, a weighed quantity the cup was crushed a second attempt at a known force after a layer of the coating blend was applied on over of the die contents with the punch in a retracted position.

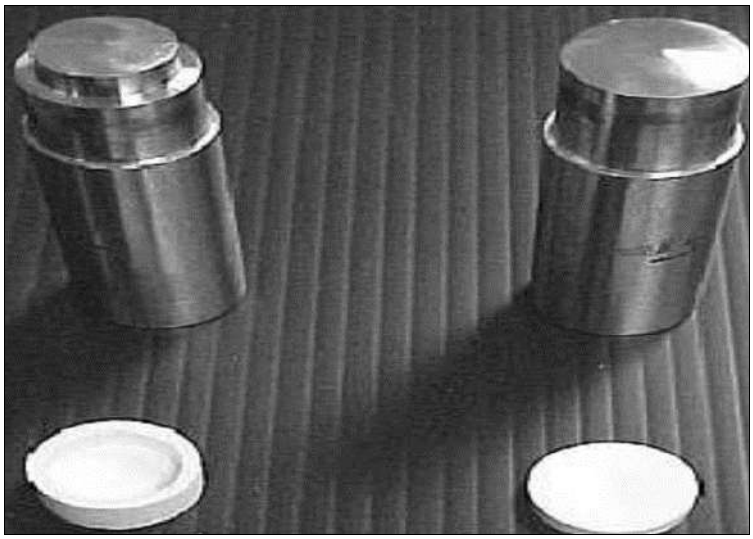

Fig 5: A photo showing the tooling used to illustrate Proof-of-Concept, as well as a cup and a completed dose form

2.2.3 Patented formulations of inlay tablets

1. Pravastatin Sodium (10 mg) + Niacin (500mg)
2. Pravastatin Sodium (10 mg) + Niacin(1000mg)
3. Lamotrigine (25 mg) + Sodium Valproate(500 mg)
4. Lamotrigine (25 mg) + Sodium Valproate(1000 mg)

5. Rosiglitazone Maleate (2 mg) + Metformin Hydrochloride (500 mg)
6. Rosiglitazone Maleate (2 mg) + Metformin Hydrochloride (1000 mg)
7. Rosiglitazone Maleate (4 mg) + Metformin Hydrochloride (500 mg)
8. Rosiglitazone Maleate (4 mg) + Metformin Hydrochloride (1000 mg)
9. Glimipride (1 mg) + Metformin Hydrochloride (500 mg)
10. Glimipride (2 mg) + Metformin Hydrochloride (500 mg) [7]

2.3 Layered tablet

Layered tablets are made up of two or three layers of granulation that have been compacted together. Because the edges of each layer are visible, they have the appearance of a sandwich [17]. When two or more active pharmaceutical components must be supplied concurrently and they are incompatible, the formulation pharmacist's best choice is to create a multilayered tablet. A single tablet made up of two or more layers, each of which is generally a different color to form a unique appearing tablet Equipment-Versa press [18].

2.3.1 Types of layered tablet

a) Bi Layer
b) Triple Layer
c) Multilayer

2.3.1.1 Bi Layer

Bilayer tablet technology is used to stabilize two incompatible medications, hide the taste of pharmaceuticals, administer two drugs with synergistic effects, or provide a drug with a biphasic drug release profile, and to extend patents [19]. When compared to traditional monolayer tablets, bilayer tablets have several significant benefits. For example, such tablets are frequently employed to eliminate chemical incompatibilities of formulation components by physical separation. Furthermore, by combining layers with different release patterns or by mixing slow-release and immediate-release layers, bilayer tablets have enabled the creation of controlled distribution of active medicinal components with pre-determined release profiles [20]. And also a broad variety of polymers were successfully used to create bilayer tablets [21]. Unlike regular tablets, bi-layer tablets need three weight controls: separate layers, as well as the final tablet weight control [22].

Fig 6: Bi layered tablet

2.1.3.2 Triple Layer tablet

The first layer of a triple layer tablet is for quick release of the medicine, and the second layer is for continuous release. The intermediate barrier layer separates the two layers. This is better suited for the administration of two medications that interact with one another. Figure 7 depicts triple layer tablets.

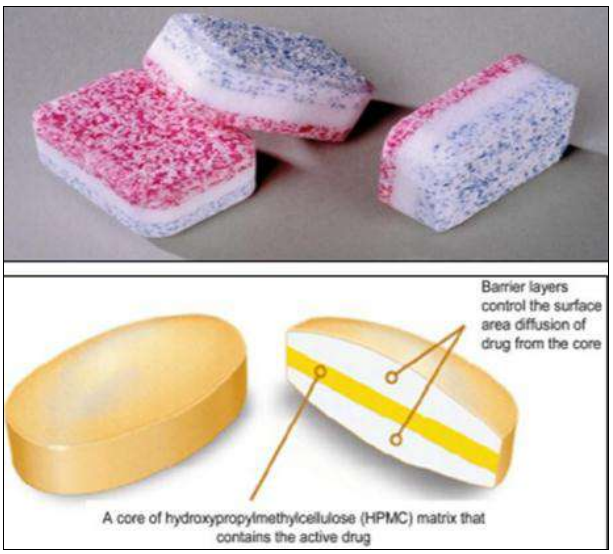

Fig 7: Triple layer tablet

2.3.1.3 Multilayer tablet

The multilayer tablet represents a new era in the successful creation of controlled release formulations, as well as other characteristics to produce a successful drug delivery system. Conventional dose forms provide a broad range of fluctuations in drug concentrations in the bloodstream and tissues, resulting in undesired toxicity and inefficiency. As a result of variables such as repeated dosage and unpredictable absorption, the notion of controlled drug delivery systems was born.

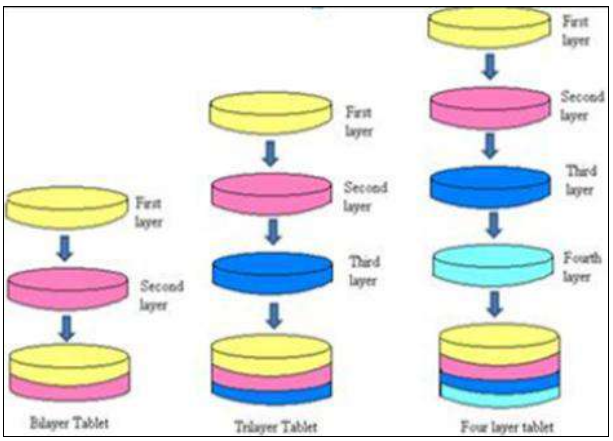

Fig 8: Multilayer tablet

2.3.2 Advantages & Disadvantages of layer tablet Advantages

1. They are unit dosage form and have the most capabilities of any oral dosage form in terms of dose accuracy and content flexibility [20].
2. The price is reduced when compared to the other oral dose forms.
3. Lighter and more compact.
4. The simplest and cheapest method of packaging and stripping.

5. Probably easier to swallow with little potential to hang up.
6. The coating process can disguise objectionable odours and harsh tastes.
7. Suitable for large-scale manufacturing.
8. Has the highest chemical and microbiological stability of any oral dose form.
9. When using an embossed or monogrammed punch face, product identification is simple and quick, needing no additional processes.
10. Concept that is adaptable [23].

Disadvantages

1. Children and the unconscious may have difficulty swallowing.
2. Several drugs resist compressing into dense compacts due to their amorphous structure and low density [18].
3. Drugs with poor solubility, slow dissolving properties, and optimal absorption high in Gastrointestinal may be difficult to package or manufacture as a tablet while still giving adequate or total drug bioavailability.
4. Bitter testing medications, pharmaceuticals with an undesirable odour, and drugs that are oxygen sensitive may necessitate encapsulation or coating.
5. Hardness & may also contain capping problem [24].

2.3.3 Manufacturing of layer tablet

Understanding the fundamental elements affecting compression and tablet breaking force becomes more challenging as manufacturing procedures like as wet granulation/roller compaction and the addition of binders are used. [25] As a result, the tablet breaking force and proclivity for delamination/capping during manufacture and storage must be closely monitored. Aside from the crucial material properties of individual components and the final mix, the tablet press has a significant impact on the production of multilayer tablets.

Understanding the fundamental elements affecting compression and tablet breaking force becomes more challenging as manufacturing procedures like as wet granulation / roller compaction and the addition of binders are used. As a result, the tablet breaking force and proclivity for delamination / capping during manufacture and storage must be closely monitored. Aside from the crucial material properties of individual components and the final mix, the tablet press has a significant impact on the production of multilayer tablets.

Compaction pressure and punch velocity have an effect on compact densification and compressibility within the die cavity. It was shown that increasing the punch velocity between 50 and 500mm/s reduced porosity reduction on particular layers [26].

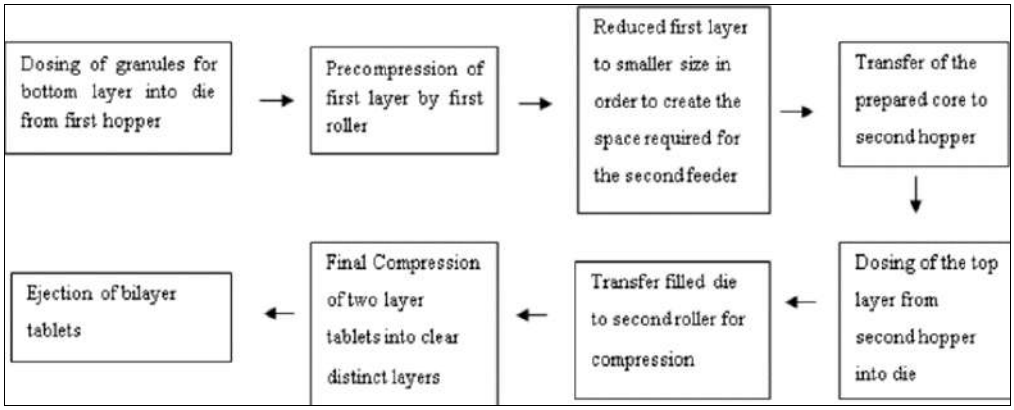

Fig 9: Steps involved in manufacturing of bi layer

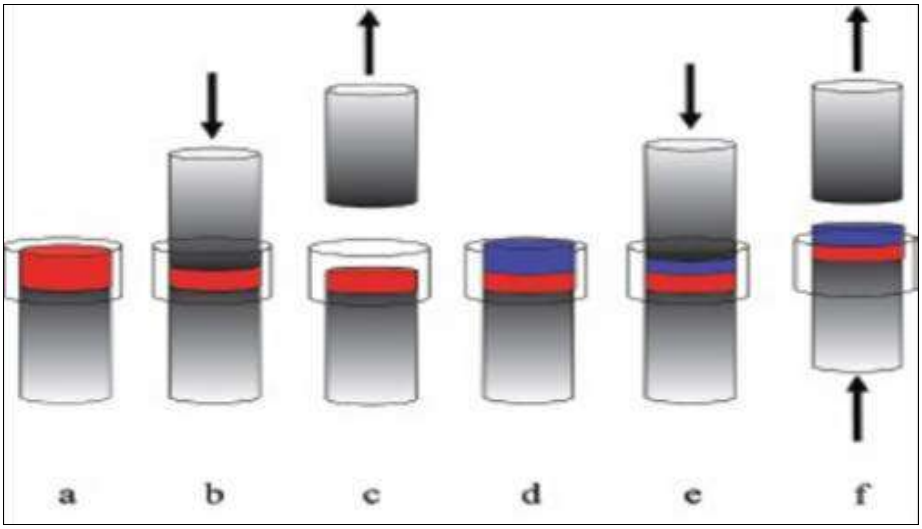

Fig 10: Bi layer manufacturing, a) First layer fill, b) First- layer tamping, c) Upper pinch withdrawal, d) Second layer fill, e) Main compression, f) Ejection

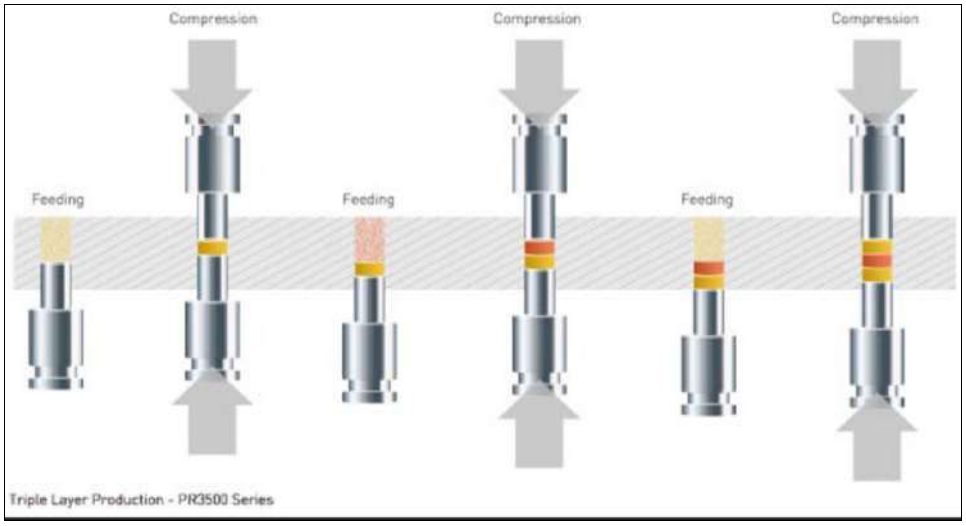

Fig 11: Tri layer manufacturing

Table 1: Example of layered tablet

Sr.no	Drug	Immediate release / sustain release	Treatment	Year	Reference
1	Nebivolol and Nateglinide	Immediate release - Nebivolol Extended release - Nateglinide	Diabetes and hypertension	2015	[27,28]
2	Pioglitazone HCI and Gliclazide	Pioglitazone HCI –as immediate release Gliclazide- as controlled release	Type-2 diabetes mellitus	2014	[29]
3	Metoprolol and Amlodipine	Metoprolol- as sustained release Amlodipine- as immediate release	Hypertension	2014	[30]
4	Pioglitazone hydrochloride And Metformin hydrochloride	Pioglitazone HCI -as immediate release Metformin HCI- as controlled release	Type-2 diabetes mellitus	2013	[31,32]
5	Levofloxacin and Ambroxol hydrochloride	Levofloxacin- as immediate release Amoxol HCI- as sustained release	Respiratory tract infections	2013	[33]
6	Metformin HCI and Atorvastatin Calcium	Metformin HCl- sustained release Atorvastatin calcium- immediate release	Hyperlipidemia	2011	[34]
7	Piracetam and Vinpocetin	Piracetam-immediate release Vinpocetin-sustained release	Alzheimer's disease	2011	+
8	Atorvastatin and Nicotinic acid	Immediate release-Atormtstatin Extended release- Nicotinic acid	Hyperlipidemia and prevention of cardiovascular disease.	2008	[26]

3. Characterization of tablet in tablet

The tablets were tested for physical and chemical characteristics in accordance with the Indian Pharmacopoeia's general tablet standards [36].

3.1 Radial tensile strength measurement

Tensile strength (Kg / cm 2) is the measurement of tablet strength [37]. A tablet hardness tester may be used to measure the radial tensile strength of unevenly distributed picked tablets (Toyama Kagaku; TH-203). Prior to usage, tablets are put in a desiccator for 24 hours. With the plunger, apply a force on the tablet and afterwards measurement the load capacity H when the tablet cracks. Radial tensile (T) strength is calculated using the following equation: [38].

$$T = \frac{2H}{\pi dL}$$

Where,
D represents the diameter of the tablet, & L is the thickness of the tablet.

3.2 Friability evaluation

Friability is a characteristic of a tablet's resistance to abrasion [39]. This is the accepted method for assessing tablet mechanical strength. Weigh the randomly chosen tablet samples in accordance with USP [40] and insert them in a plastic drum friabilator (Electroblot; EF-1 W) containing 20 polystyrene beads (Wako Pure Chemical; 6 mm diameter) [31]. The drum is then spun at 25 revolutions per minute for four minutes before even being weighed again to determine the amount of pill weight lost. The formula [41] is used to compute the percentage friability.

$$F = \frac{1-W}{W_0} \times 100$$

Where
W0 = Tablet weight before friability.
W = Tablet weight after friability

3.3 Internal intensity measurement

The internal potency of the pill was measured using a continuous load-bearing intensity tester. The amount of drill point penetration that occurs during tablet boring was measured. The drill has a weight of 150 g and a rotating speed of 200 rpm. The boring speed was used to calculate the relative intensity of the tablet's inside [39].

3.4 *In vitro* release testing

According to the model drug's official monograph, the *in vitro* dissolution investigation was conducted using a USP

type-I or type-II equipment. The dissolving solvent or medium used in the evaluation of a model drug was 900 ml of the appropriate pH indicated in the experiment. Maintaining a temperature of 37 0.5 °C, the rotatory speeds of the paddles should be as specified in the official monograph. At regular intervals, samples were evacuated and reconstituted with the equal amount of fresh solvent. All sample were then filtered through a 0.45-m filter membrane and examined using UV (Ultra Violet) spectrophotometric ally at the relevant wavelength for the model medication. For each formulation tested, the drug release studies were repeated 6 times in parallel, and standard deviations were computed [3]. This is an overall ailment, but you should consult the pharmacopoeia or the product's instructions for each drug. The percentage rate release is measured [42].

3.5 Mechanism of Release

Three distinct stages occurred during the drug's release from Tablet in Tablet dosage form, as indicated by Fig.11. The initial process involves the entry of the dissolving media into the tablet, which causes thickening of the covering layer. The outer coating barrier is eroded in another stage due to fast penetration of the dissolving liquid through the outer layer. The pressure causes the covering layer to break due to expansion of the internal core tablet. The dissolving correlating to a fast medication release of the core tablet occurs in the last stage after an elapsed time.

3.6 Erosion and absorption studies

Absorption and time erosion tests are conducted with gravimetric examination using the USP type-II dissolving equipment in the creation of a modified release formulations in the form of Tablet in Tablet. The tablets were arranged in a basket and submerged in a 900-ml buffer solution at 37 0.5 °C. At various time intervals, tablets were carefully taken from the dissolving liquid and weighed after carefully removing excess surface water with filter paper. The tablets were then dry in a hot-air oven set at 60 °C until they reached an uniform weight, with six distinct tablets checked at each stage. A fresh or new pill was utilized at each time point. Erosion is used to calculate the remaining mass (RM). The swelling ratio described the process of water intake and expansion (SR). The following formula was used to compute the RM and SR.

$$\mathrm{RM}(\%) = \frac{W_r}{W_0} \times 100$$

$$\mathrm{SR}(\%) = \frac{W_t - W_r}{W_r} \times 100$$

Where,
W0 is the dry tablet's starting weight;
At time t, Wr is the wg of the leftover dried tablet after penetrating the medium;
Wt is the wg of the tablet excluding water on the surface.

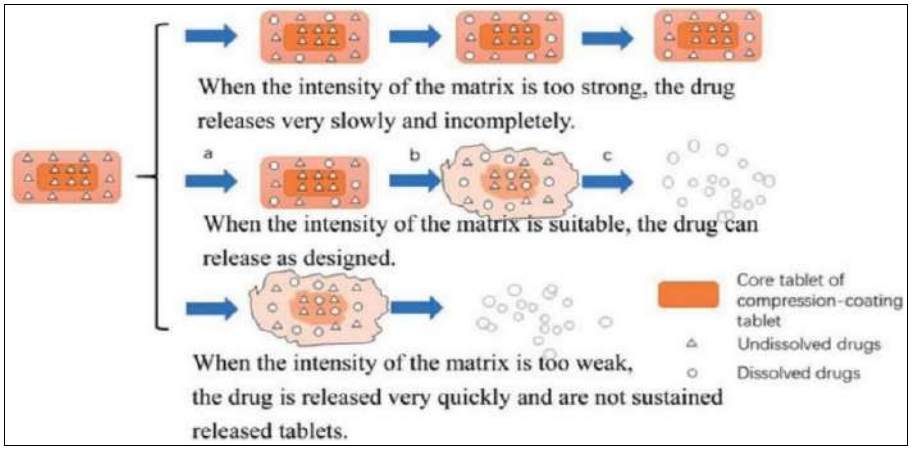

Fig 11: Mechanism of release

4. Application of tablet in tablet technique in pharmaceutical formulation:

Compression coating was first used to create incompatible medications between 1950 and 1960. Because the approach does not need the use solvents, involves a relatively short production, and provides for more weight gain to the inner tablet, this coating has become more popular in the last two decades. Currently, the pharmacological aspects of pressure tablets in dosage form study are:

1. To safeguard pharmaceuticals that are hygroscopic, light-sensitive, oxygen-labile, or acid-labile;
2. To keep incompatible medicines apart and achieve continuous release;
3. To alter the rhythm of medication release.

5. Conclusion: Sugar and film coatings are a key aspect of the tablet formulation to create better attractive qualities such as color, texture, mouth feel, and flavor masking. The use of aqueous or organic solvents in film and sugar coatings causes toxicity, which is the most serious drawback. The Tablet in Tablet approach is the greatest option for dealing with the aforementioned issue. The creation of a modified release method for a comparable medicine or other pharmaceuticals from a different category, Tablet in Tablet approach can be used to achieve medication release at diverse sites of absorption.

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