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A Review of Tablet in Tablet Vitamin D3 Formulation Techniques

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ABSTRACT

The studies is to review formulated core tablets (tablet in tablet) and difficulty in the formulation and evaluation. Numerous techniques are used overcome the problem of stability. The tablet coating have number of advantages like masking odor, taste, color of the drug, providing physical and chemical protection to drug, Protecting drug from the gastric environment. Most of the tablets are instable in gastro industrial tract. Coated, encapsulation, capsules instructed tablet, gel coated tablet. Vitamin D3 containing **cholecalciferol** (made from 7-dehydrocholesterol in the skin). Several forms (vitamins) of vitamin D exist. The two major forms are vitamin D_2 or **ergocalciferol**, and vitamin D_3 or **cholecalciferol**; vitamin D without a subscript refers to either D_2 or D_3 or both. Vitamin D3 contain natural foods like Fatty fish, like tuna, mackerel, and salmon Foods fortified with vitamin D, like some dairy products, orange juice, soy milk, and cereals, Beef liver, Cheese, Egg yolks. Industrial production encovndred several evaluation error like weight variation, hardness, friability, thickness, solubility, disintegration test. Here dissolution test not necessary because vitD3 was a supplementary USP not recognized. Nutrients do not work alone, and when it comes to taking vitamin D, its important that you take any compound and vitamin D together and not JUST vitamin d alone in large doses as this can lead to what people BELIEVE are vitamin d side effects.

Keywords: Vitamin D3, cholecalciferol , coated tablet

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INTRODUCTION

Vitamin D3(cholecalciferol) is derived from 7-dehyrocholesterol and involved in bone health. Scientists have recognized that, depression, back pain, cancer, both insulin resistance and pre-eclampsia during pregnancy, impaired immunity and macular degeneration are directly linked to the Vitamin D3 deficiency[1]. Inadequate Vitamin D3 may cause secondary hyperparathyroidism that increases the risk of osteoporosis and fractures and change the regulatory mechanisms of parathyroid hormone (PTH)[2,3] . Other types of condition such as high blood pressure, fibromyalgia, diabetes, multiple sclerosis, rheumatoid arthritis has been linked to the low levels of Vitamin D3[4,5] . Vitamin D3 deficiency is responsible psychiatric and neurologic disorders and associated with low mood [6] .

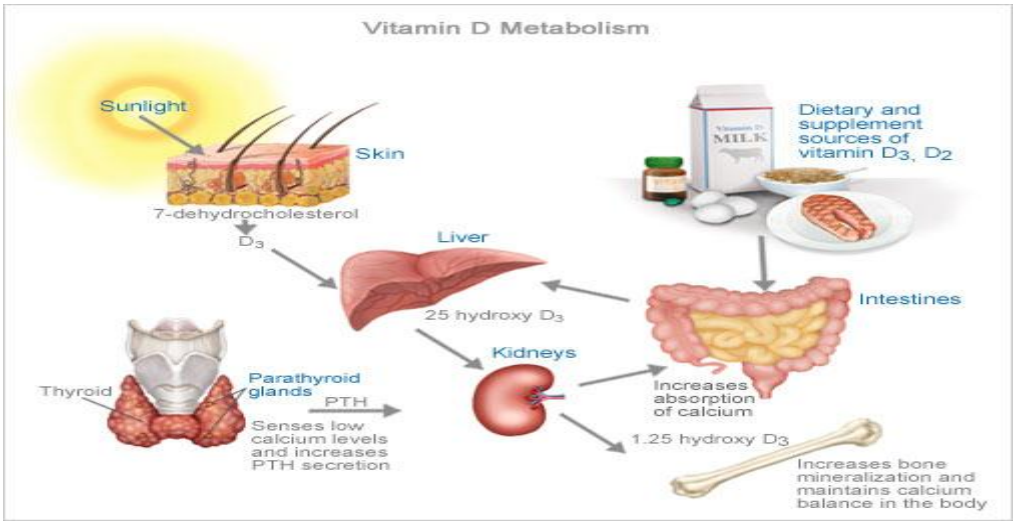

Figure 1: Vitamin D metabolism

ORAL TABLETS:

Standard compressed tablets e.g. Paracetamol tablet′ Multiple compressed tablets′ I. Compression coated tablet- sugar coated tablet, Film coated tablet, Gelatin coated tablet, Enteric coated tablet II. Layered tablet III. Inlay tablet Targeted table [7,8,9] .

Figure: 2 vitamin D Deficiency

Floating tablet′ II. Colon targeting tablet

Different types of Tablets:

Tablets ingested orally: 1. Compressed tablet, e.g. Paracetamol tablet 2. Multiple compressed tablet 3. Repeat action tablet 4. Delayed release tablet, e.g. Enteric coated Bisacodyl tablet 5. Sugar coated tablet, e.g. Multivitamin tablet 6. Film coated tablet, e.g. Metronidazole tablet 7. Chewable tablet, e.g. Antacid tablet[10,11,12] . Tablets used in oral cavity: 1. Buccal tablet, e.g. Vitamin-c tablet 2. Sublingual tablet, e.g. Vicks Menthol tablet 3. Troches or lozenges 4. Dental cone[13,14] . Tablets administered by other route: 1. Implantation tablet 2. Vaginal tablet, e.g. Clotrimazole tablet (D) [15,16] . Tablets used to prepare solution: Effervescent tablet, e.g. Dispirin tablet (Aspirin) 2. Dispensing tablet, e.g. Enzyme tablet (Digiplex) 3. Hypodermic tablet 4. Tablet triturates e.g. Enzyme tablet (Digiplex) [17,18] .

Tablet-in-tablet technology:

Tablets are indeed the most popular solid dosage form for oral administration. One category of tablet formulations that has gained remarkable importance in drug therapeutics owing to various benefits it offers is controlled or modified release formulations[19,20,21] . Although less popular, tablet-in a tablet technology (see Fig 1) gained increased interest in the recent years for creating modified released products[22,23] . It involves the compaction of granular materials around a preformed tablet core using specially designed tableting equipment. Compression coating is a dry process[24,25,26] . This type of tablet (compression coated tablet) has two parts, internal core and surrounding coat[27,28] . The core is small porous tablet and prepared on one turret. After tablet core manufacture it is transferred (centrally positioned) to another slightly larger die that is partially filled with coating powder. More coating powder is filled on the top of the core and compressed again resulting in tablet with in tablet. Mechanically, it is a complex process, as the tablet may be tilted when transferred to the second die cavity. Mostly, the coat is water soluble and disintegrates easily after swallowing, in order to achieve immediate release product. This tablet readily lend itself in to a repeat action tablet as the outer layer provides the initial dose while the inner core release the drug later on. But, when the core quickly releases the drug, entirely different blood level is achieved with the risk of over dose toxicity. To avoid immediate release of both the layers, the core tablet is coated with enteric polymer so that it will not release the drug in stomach while, the first dose is added in outer sugar coating. Even so, coating operation requires interpretation while manufacturing and dawdling the manufacturing process. Sometimes, inner core may be of liquid formulation to provide immediate release of core after the coat gets dissolved[29,30] . Tablet coating is the key step involved in the manufacturing of

tablets having controlled release, delayed release profiles. The tablet coating have number of advantages like masking odor, taste, color of the drug, providing physical and chemical protection to drug, Protecting drug from the gastric environment. Tablets are usually coated in horizontal rotating pan with coating solution is either directly poured or sprayed on to them. The amount of coating on the surface of a tablet is critical to the effectiveness of the oral dosage form. Recent trends in tablet coating focuses on overcoming disadvantage of solvent based coating. This review concerns with the coating process, equipment's involved, coated tablets evaluation and specialized coating techniques. Tablets are usually coated in horizontal rotating pans with the coating sprayed onto the free surface of the tablet bed. Tablets must have a coating mass that lies within a prescribed range with very little inter-and intra-tablet coating variability. Using the Discrete Element Method (DEM) tablet coating can be simulated on the computer [31,32,33].

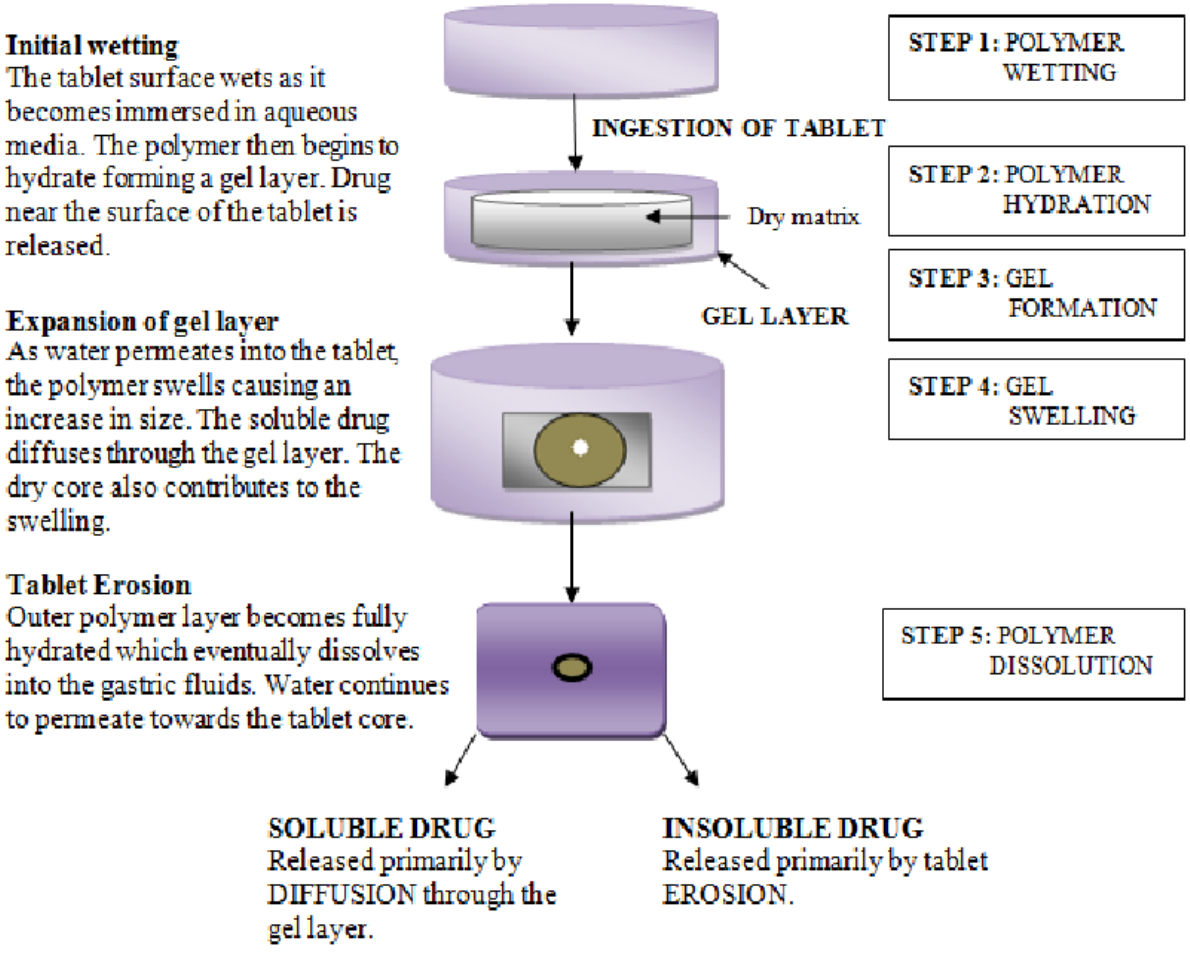

Figure 3: Formulation Tablet in Tablet

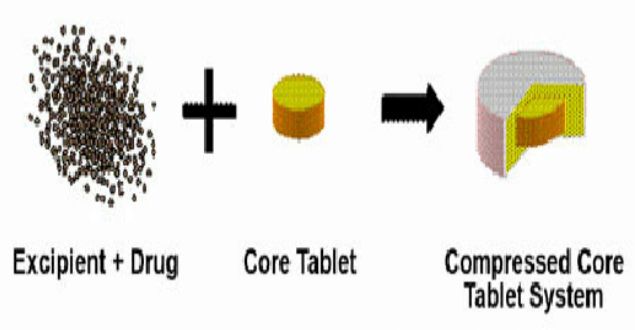

Figure :4 Compressed Core Tablet System

Simulation data provide the position, velocity and orientation of each tablet within the coater allowing accurate measurements of the time and orientation that each tablet spends exposed to the coating spray. The blend was compressed on a single punch machine, tablets were subjected to various tests (weight variation, diameter and thickness, hardness, disintegration and assay of the drug) and the results were also in compliance with the official specifications [34, 35].

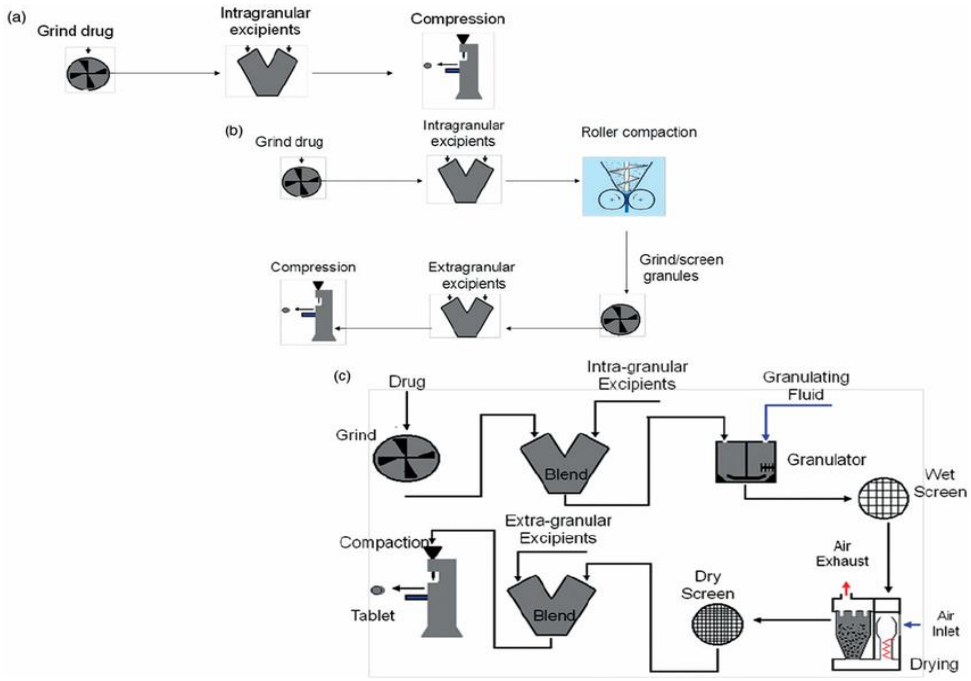

Figure: 5 Tablets Various Compression

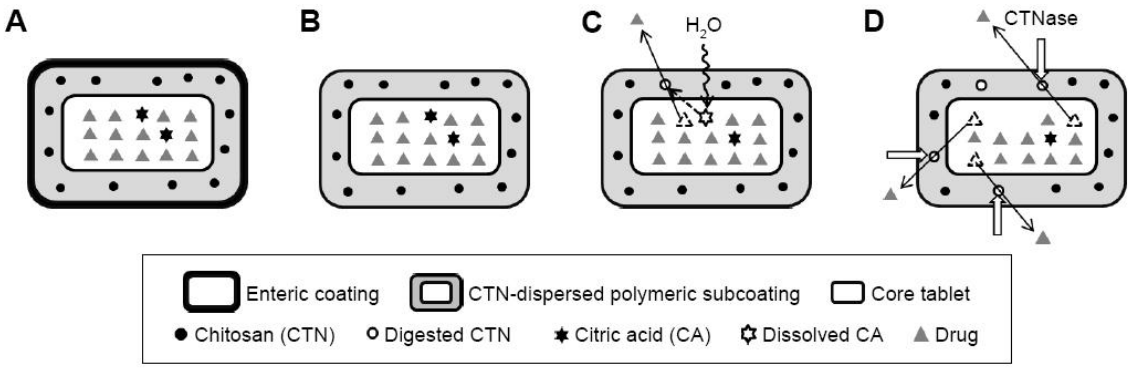

Figure 1 Stepwise illustration of DL-CDDS as a platform for colon targeting.
Notes: (**A**) In the stomach, the outermost enteric coating layer inhibits drug release; (**B**) in the small intestine, the inner CTN-dispersed polymeric subcoating layer impedes drug release; (**C**) in the colon, water infiltrates the core tablet and dissolves CA, resulting in microclimate acidification and pore generation to some extent; (**D**) in the latter part of the colon, under the influence of microflora, such as CTNase, a number of microporous channels are formed by enzymatic CTN digestion, thus facilitating drug release.
Abbreviations: DL-CDDS, double layer-coated colon-specific drug delivery system; CTN, chitosan; CTNase, chitosanase.

Figure : 6 Core Tablet Designed

All the physical properties studied indicated that all excipients are good pharmaceutical excipients in tablets. The objective of this work was to present Vitamin D3 in granular and tablet form with improved dispersability, to minimize the complexity of formulations and to make cost effective product[36,37].

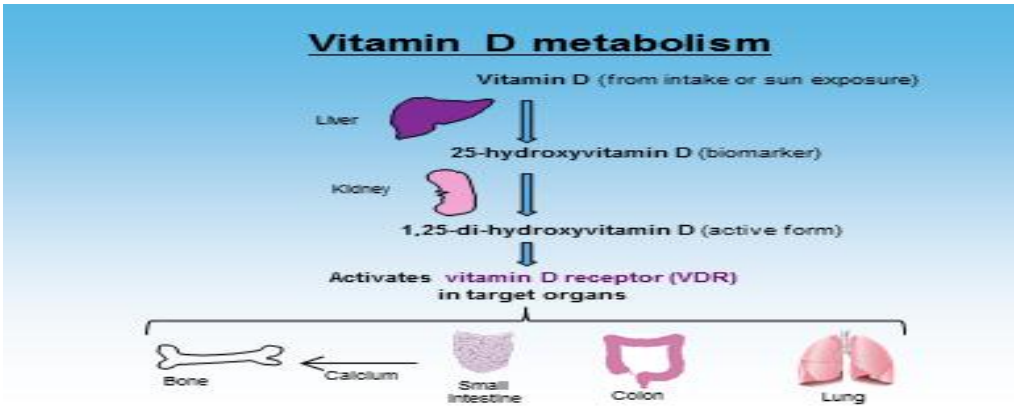

Figure :7 Vitamin D Metabolism

Coating techniques: - Generally three methods are used for tablet coating A) Sugar coating. B) Film coating. C) Enteric coating.

A) Sugar coating:

Sealing/Water proofing: provides a moisture barrier and harden the tablet surface. Sub coating causes a rapid buildup to round off the tablet edges. Grossing/Smoothing: smoothes out the sub coated surface and increases the tablet size to Predetermine dimension. Coloring gives the tablet its color and finished size. Polishing produces the characteristics gloss[38,39].

B) Film coating:

Film coating and the sugar coating share same equipment and the process parameters. There are basically 2 methods of film coating they are Pan pour methods: Tablets coated by pan pour method subjected to alternate solution application, mixing and drying steps are similar to pan pour sugar coating. This method is relatively slow and relies heavily on the skill of operator. Pan-spray methods: The introduction of spraying equipment was the next evolution in improving the film coating process allows for automated control of liquid application. Broad flat spray patterns are usually chosen by appropriate nozzle systems[40,41] .

Spray dryer: Spray drying is a method of producing a dry powder from a liquid or slurry by rapidly drying with a hot gas[42,43] . This is the preferred method of drying of many thermally-sensitive materials such as foods and pharmaceuticals. A consistent particle size distribution is a reason for spray drying some industrial products such as catalysts. Air is the heated drying medium; however, if the liquid is a flammable solvent such as ethanol or the product is oxygen-sensitive then nitrogen is used. All spray dryers use some type of atomizer or spray nozzle to disperse the liquid or slurry into a controlled drop size spray. The most common of these are rotary disk and single-fluid high pressure swirl nozzles. Atomizer wheels are known to provide broader particle size distribution, but both methods allow for consistent distribution of particle size. Alternatively, for some applications two-fluid or ultrasonic nozzles are used. Depending on the process needs, drop sizes from 10 to 500 µm can be achieved with the appropriate choices. The most common applications are in the 100 to 200 µm diameter range. The dry powder is often free-flowing. The most common type of spray dryers are called single effect. There is a single source of drying air at the top of the chamber (see n°4 on the diagram). In most cases the air is blown in the same direction as the sprayed liquid (co-current). A fine powder is produced, but it can have poor flow and produce a lot of dust. To overcome the dust and poor flow of the powder, a new generation of spray dryers called multiple effect spray dryers have been produced [44] .

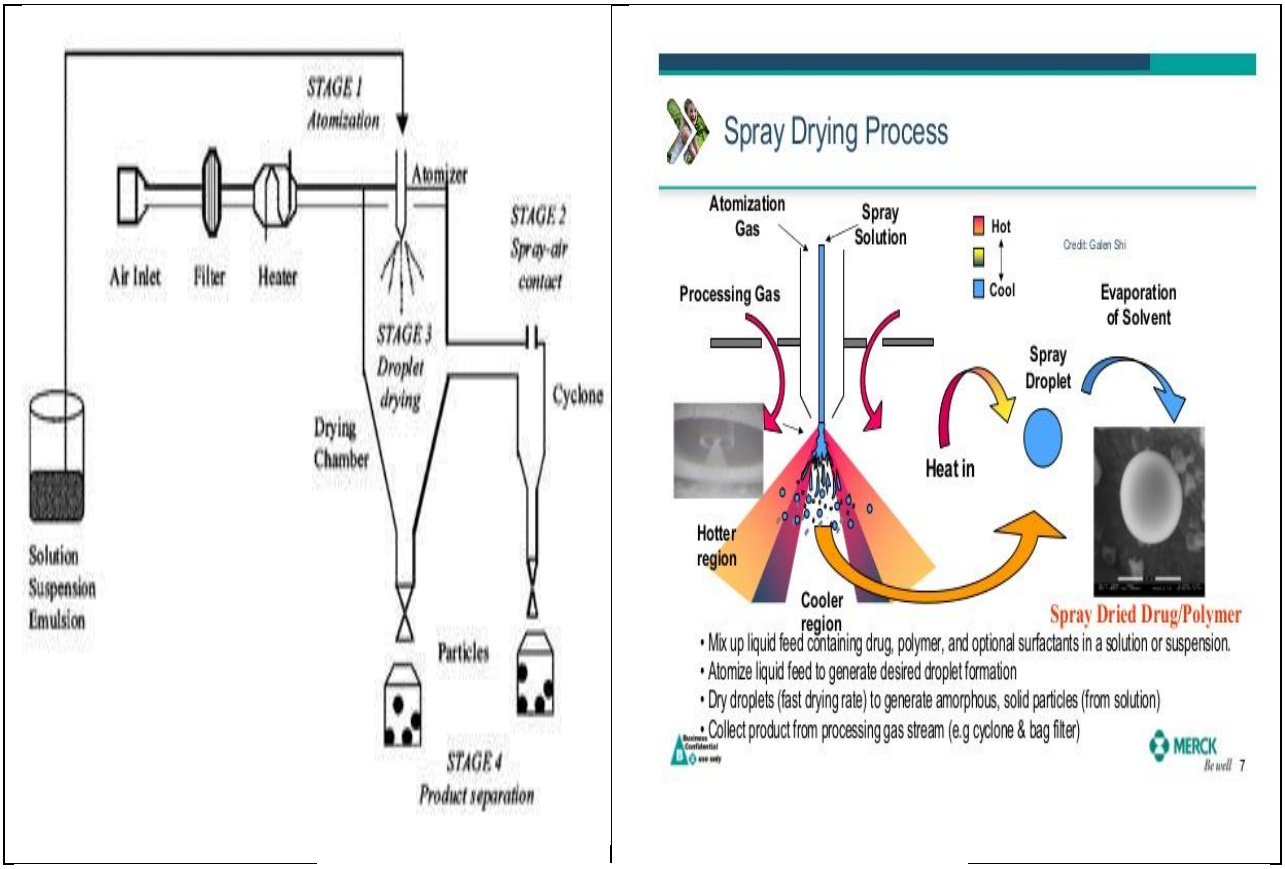

Figure :8 Tablet Compression and Formulation

Encapsulation method:

Encapsulation relates to technologies which enable to formulate one active compound (or more), inside individualized particles with a specific geometry and properties. Encapsulation defines no size notion • Microencapsulation usually refers to sizes ranging from 1 µm to 1 mm • Nanoencapsulation is used for nanometric sizes but sometimes refers to sizes ranging up to 1 µm or few micrometers. Methods: droplet extrusion (single or multi nozzle device, simple gravity, spinning disk, jet breakage systems, co-extrusion) of a (bio)polymer solution in a gelation bath or in ambient/cold air[45,46,47] . Particles properties (standard): Size range: from 50 µm to 7-8 mm, Final state: wet (can be dried or lyophilized), Active type: liquid, solid; hydrophilic or lipophilic, Active content: up to 400 mg/g (wet), 900 mg/g (dry), Structure: matrix, core / shell (s), (matrix core) / shell[48] .

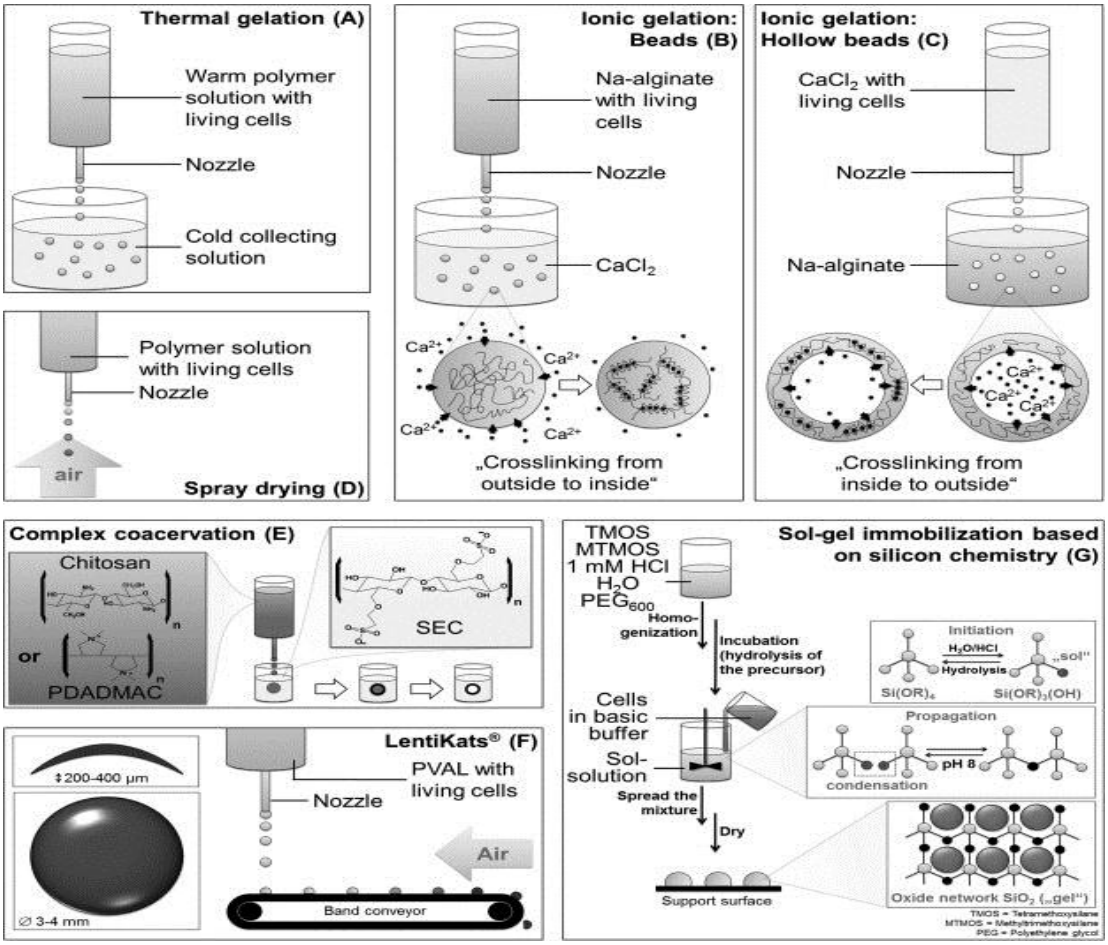

Figure :9 Hydrogenation Method

Hydrogenation – to treat with hydrogen – is a chemical reaction between molecular hydrogen (H_2) and another compound or element, usually in the presence of a catalyst such as nickel, palladium or platinum. The process is commonly employed to reduce or saturate organic compounds. Catalytic hydrogenation has evolved into a key process technology for the manufacture of pharmaceutical and fine chemicals, replacing chemical reduction methods that generate large quantities of waste. According to Roessler [1•], 10 to 20% of chemical reactions in fine chemical synthesis at Roche are catalytic hydrogenations. Catalytic hydrogenations strike a balance among reaction kinetics, reactor design, catalyst activity and selectivity, process control, mass transfer and mixing. Each of these factors contribute to the performance of hydrogenation processes and their products[49,50,51,52] .

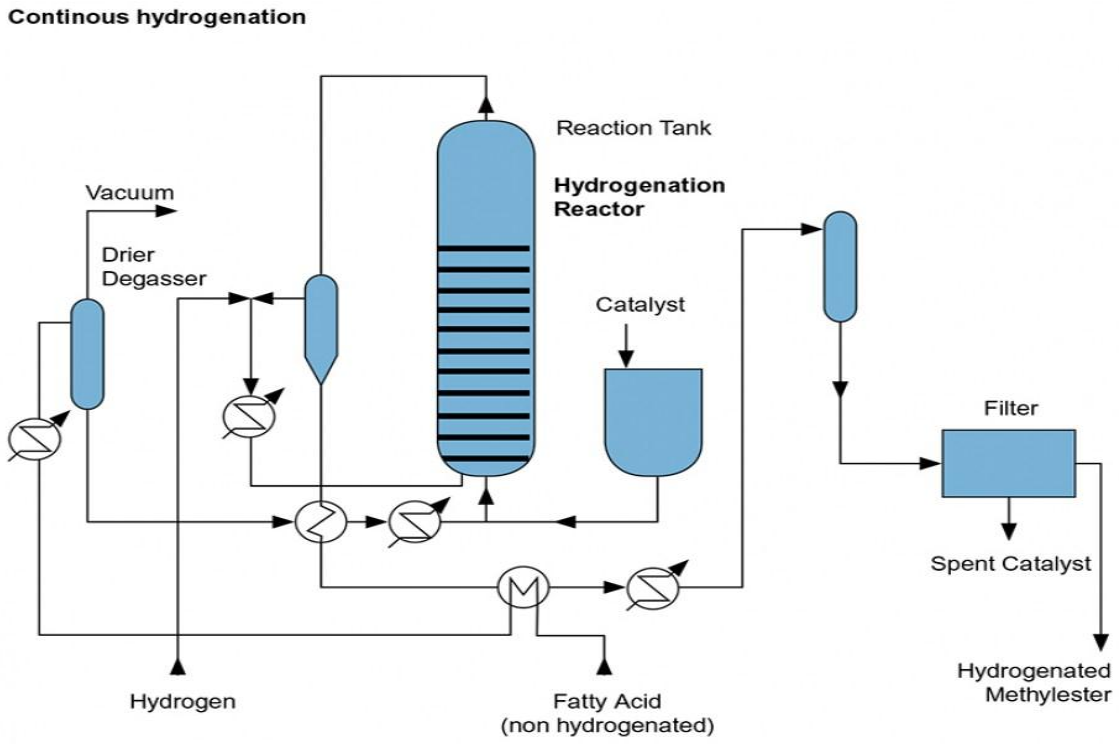

Figure :10 Continuous Hydrogenation

CONCLUSION:

Tablet in tablet is improved beneficial technology to overcome the limitation of the single layered tablet. Bi-layer tablet is suitable for sequential release of two drugs in combination of vitamin D3, separate two incompatible substances and also for sustained release tablet in which one layer is immediate release as initial dose and second layer is maintenance dose. The preparation of tablets in the form of multi layers is used to provide systems for the administration of drugs, which are incompatible and to provide controlled release tablet preparations by providing surrounding or multiple swelling layers. To developed techniques promote the new formulation overcome the supplementary like vitamin D3 tablets. Finally explains why many different types of presses are being used to produce tablet in tablets, ranging from simple single-sided presses to highly sophisticated machines.

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