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Review

Evolution of Oral Solid Dosage Forms (Tablets): A Comprehensive Review of Advanced Manufacturing Technologies and Delivery Systems

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Abstract

The pharmaceutical landscape is shifting from conventional single-unit tablets toward sophisticated, patient- centric delivery systems that balance therapeutic efficacy with manufacturing efficiency. This review provides a comprehensive overview of five pivotal advancements in oral drug delivery: Bi-layer tablets, Orally Disintegrating Tablets (ODTs), Multi-Unit Pellet Systems (MUPS), Hot Melt Extrusion (HME), and 3D Printing. Bi-layer and MUPS technologies are analyzed for their ability to manage incompatible active pharmaceutical ingredients (APIs) and provide programmed release profiles, such as combined immediate and sustained release. To address the challenge of patient compliance, particularly in pediatric and geriatric populations, the formulation of ODTs using super-disintegrants is explored. Furthermore, the review examines the transition from batch to continuous manufacturing through HME, a solvent-free process critical for enhancing the bio-availability of poorly soluble drugs. Finally, the trans-formative potential of 3D printing is discussed as the ultimate tool for personalized medicine and complex "poly-pill" architectures. By integrating these technologies, the pharmaceutical industry can achieve precise control over drug release kinetics, reduce side effects, and transition toward individualized therapy.

Keywords: ODTS, MUPS, Bi-layer tablets, Hot Melt Extrusion, 3D Printing.

INTRODUCTION

Oral solid dosage forms remain the most widely used drug delivery systems due to their convenience, stability, accurate dosing, and cost-effectiveness. Among them, tablets dominate global pharmaceutical markets. However, conventional tablets often fail to meet complex therapeutic requirements such as modified drug release, poor solubility enhancement, combination therapy, and patient-centric dosing. These challenges have stimulated the development of advanced tablet formulation technologies that integrate material science, process engineering, and digital manufacturing.

Recent advances include bilayer and multilayer tablets for dual-release profiles, multi-unit pellet systems to minimize dose dumping, hot melt extrusion for solid dispersions and continuous manufacturing, 3D printing for personalized dosage forms, and orally disintegrating tablets for improved patient compliance. This review integrates these technologies into a single scientific narrative, highlighting their principles, advantages, limitations, and industrial relevance.

EVOLUTION OF TABLET FORMULATION TECHNOLOGIES

Historically, tablet manufacturing relied on wet granulation, dry granulation, and direct compression. While effective, these methods offer limited flexibility in controlling drug release and formulation complexity. The evolution toward advanced systems was driven by:

- Increasing prevalence of poorly water-soluble drugs
- Need for fixed-dose combinations
- Demand for patient-centric dosage forms
- Regulatory emphasis on quality by design (QbD) and continuous manufacturing

Advanced techniques now enable precise modulation of drug release kinetics, improved bioavailability, and scalable production.

BILAYER AND MULTILAYER TABLET FORMULATIONS

Concept and Rationale

Bilayer tablets consist of two distinct layers, each containing different drugs or release characteristics. They are designed to achieve immediate–sustained release profiles, drug separation to avoid incompatibility, or combination therapy. The main objective of sustained-release drug delivery systems is to ensure safety, improve drug efficacy, and enhance patient compliance. Bilayer tablets are particularly suitable for the sequential release of two drugs in combination, for separating incompatible substances, and for sustained-release formulations in which one layer provides immediate release. The oral route is the most important method for systemic drug administration, with tablets and capsules being the most commonly used oral dosage forms, as they accurately contain a single dose of the drug.

Manufacturing Approaches

Bilayer tablets are commonly produced using specialized tablet presses capable of sequential compression. Critical factors include layer weight control, interfacial bonding strength, and prevention of layer separation.

Tablet in Tablet: The Tablet in Tablet is also known as compression coating or solvent-free coating technique. The coating technology having certain limitation or drawbacks to overcome this limitation Tablet in Tablet is one of the best alternatives. The present work aims to comprehensively review the formulation, characterization and challenges in the development of Tablet in Tablet dosage form. Currently a very less number of patents are filed or granted on this topic; it includes the patent on the Tablet in Tablet of cyclophosphamide and capecitabine and here we focused on the rationable behind the development of such dosage form. The coating also gives physical and chemical protection to the drug; apart from this, it will also modify the release behavior of the drug. In the nineteenth century, to mask the bitter taste, modern pharmaceutical coating i.e. sugar coating was applied.

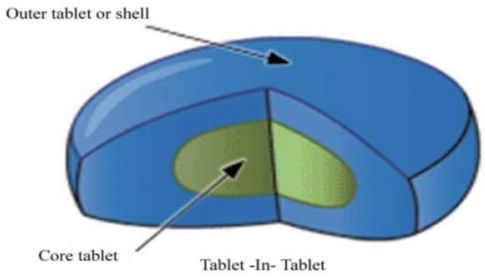


Figure 1

Advantages of Tablet in Tablet technology

➢ Separation of incompatible material can be achieved in the core and outer shell.
➢ It 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 tablets can be avoided in the press

3.3 Novel Bilayer Technologies

OROS® push–pull systems
L-OROS™ and DUROS® technologies
Programmable oral drug absorption systems (PRODAS)

Challenges

Major challenges include delamination, cross-contamination, and scale-up difficulties, which require careful optimization of formulation and compression parameters.

MULTI-UNIT PELLET SYSTEMS (MUPS)

Overview

MUPS consist of multiple discrete pellets compressed into a single tablet or filled into capsules. Each pellet acts as an individual drug delivery unit.

Pelletization Techniques

Extrusion–spheronization, Powder layering, Solution/suspension layering, Spray congealing.

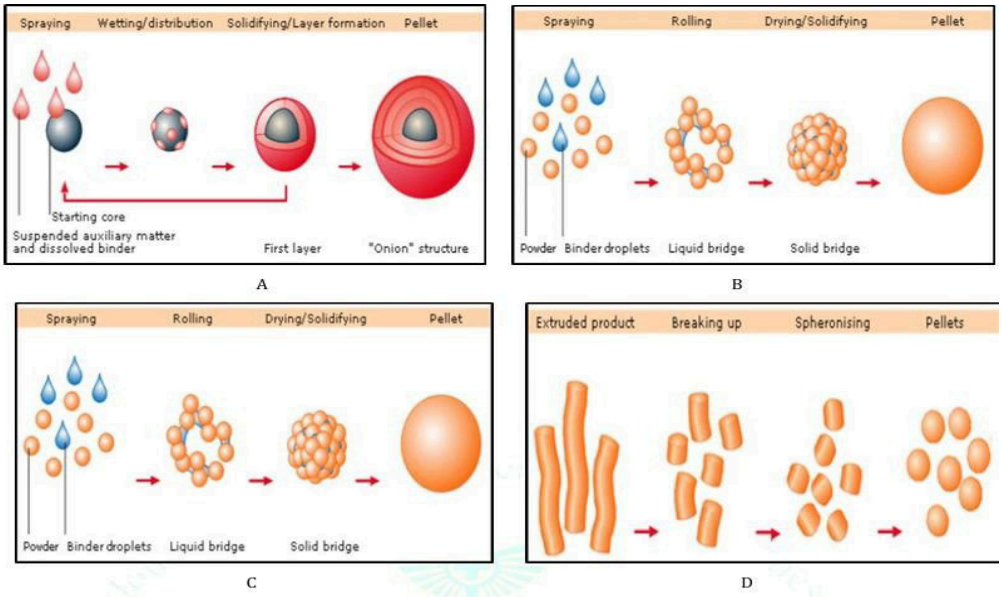


Figure (2): Different principles of pelletization techniques. (A) Solution/suspension layering, (B) Powder layering (C) Direct pelletization, (D) Extrusion-spheronisation

Advantages

Reduced risk of dose dumping
Uniform drug distribution in the GI tract
Improved safety and efficacy

Evaluation and Quality Control

Pellet size distribution, friability, drug release profiles, and content uniformity are critical quality attributes.

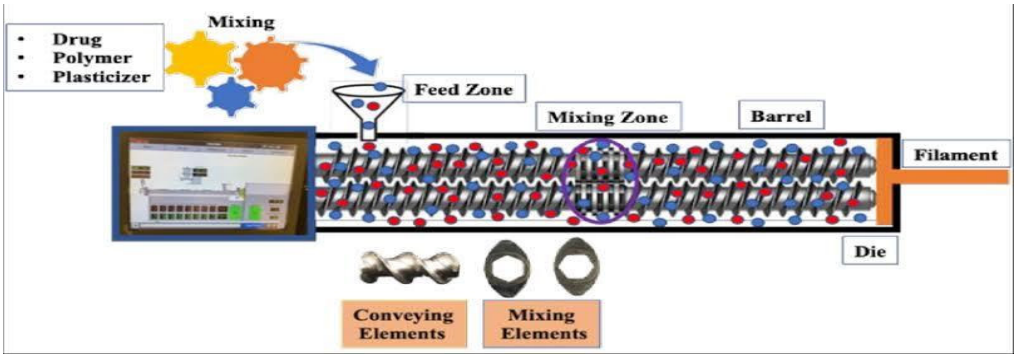
HOT MELT EXTRUSION (HME) TECHNOLOGY

Principle of HME

Hot melt extrusion involves the application of heat and mechanical shear to process drug–polymer mixtures into homogeneous products without the use of solvents. In today's world, improving solubility is the major challenge faced by the pharmaceutical industry. Approximately 50%- 60% of the new chemical entities within the developmental pipeline are said to be poorly soluble, limiting the oral bio-availability of the drug substances. Improving solubility is the primary prerequisite for developmental scientists. For any drug substance designed to be administered in the form of intravenous (IV) dosage, improving bio-availability is not the primary concern since the drug will be directly administered in solution form. Various manufacturing strategies, such as hot melt extrusion, spray drying, fluid bed granulation, electrospinning, and kinetisol, have been investigated for developing ASDs. HME was most widely employed among the various manufacturing strategies due to its simple manufacturing and solvent-free process.

Equipment and Process Parameters

Single-screw and twin-screw extruders are employed, with critical parameters including barrel temperature, screw speed, and feed rate. The process of HME is also called as "green technique" since it requires no solvent for developing formulations. The other competing technology for HME is spray drying. However, the spray drying process requires a tremendous amount of solvent and remains a significant concern to the pharmaceutical industry. Hot melt extrusion can be employed for a single-step continuous manufacturing process by mounting suitable process analytical technology (PAT) tools.



Figure; 3

Pharmaceutical Applications

Amorphous solid dispersions, Sustained and controlled release systems, Taste masking, Pellet and filament production. HME is a novel and robust technology in the pharmaceutical industry used for manufacturing various drug delivery systems like sustained-release (SR) and delayed-release (DR) drug delivery systems. It is also used for processes like taste masking, bioavailability enhancement, and production of films for transmucosal and transdermal drug delivery systems and also for developing amorphous materials.

Coupling HME with 3D Printing

Integration of HME with fused deposition modeling (FDM) enables continuous production of drug-loaded filaments for personalized 3D-printed tablets.

THREE-DIMENSIONAL (3D) PRINTING OF TABLETS

Overview

3D printing, or additive manufacturing, constructs dosage forms layer by layer from digital designs, enabling unprecedented control over tablet geometry and drug distribution. Three-dimensional(3D) printing, also known as additive manufacturing, is gaining interest, due toits versatility, ease of use and its huge variety of applications among different fields. Nowadays, three-dimensional(3D) printing is one of the fastest developing branches of technology, art and science, and still broadens the applications. International Standard Organization (ISO) defined 3D technology as: “Fabrication of objects through the deposition of a material using a print head, nozzle, or another printer technology”. In this technique 3D model are used for preparing the parts in the process of joining materials layer by layer. 3D printing refers to a various processes used to synthesize a three-dimensional object. In 3D printing successive layers of material are formed under computer control to create an object. 3D printing is a layer-by-layer process having capability to produce 3D drug products from digital file. The 3D printing technology is unparalleled, flexible, rapid and with exceptional manufacturing capability of pharmaceutical drug products of desired quality. At the first, Charles Hull invented 3D printing, which he called as Stereolithography, in the early 1980s. Later he founded the company 3D systems, which developed the first 3D printer, called as Stereolithography apparatus (SLA). [23] Then in 1989, Scott Crump, filed a patent on another 3D printing technology i.e.,Fused depositionmodeling (FDM), where extruded polymer filaments heated into a semi- liquid state and were extruded through a heated nozzle and deposited onto a build platform layer by layer to harden. Since there are many other methods have been developed for 3D printing techniques. [24,25] In 2015, The US Food and Drug Administration (FDA) approved the first 3D printed drug product Spritam®, developed by Aprecia Pharmaceuticals as the first 3D printed orodispersible tablet Levetiracetam for seizure treatment. Seizures (tonic-clonic and partial-onset) in adults and in children can be treated from this drug.

3D Printing Techniques

Fused deposition modeling (FDM)
Selective laser sintering (SLS)
Stereolithography (SLA)
Inkjet and binder jet printing
Semi-solid extrusion

Advantages

Personalized dosing
Complex release profiles
Polypill development

Challenges and Regulatory Aspects

Material selection, mechanical strength, scalability, and regulatory acceptance remain key challenges for widespread adoption.

ORALLY DISINTEGRATING TABLETS (ODTS)

Concept

ODTs rapidly disintegrate in the oral cavity without the need for water, improving compliance in pediatric, geriatric, and dysphagic patients. In contrast to other traditional oral solid dosage forms, oral disintegrating tablets (ODTs) are a unique oral solid dosage form that quickly dissolves in the mouth (within seconds to minutes of oral administration) without chewing and without the need for water.[7]Orally disintegrating tablets offer benefits of easy swallowing, not requiring water, stability, accurate dosing, suitability to paediatrics and geriatrics, bedridden, mentally retarded,as well as bio-pharmaceutical advantages such as pre-gastric absorption. During the passage of saliva carrying the drug down to the stomach, some drugs are absorbed in the tract before the stomach leading to greater bio-availability than ordinary dosage forms. Compared to conventional disintegrants, super disintegrants are effective at lower concentrations and provide rapid tablet disintegration without compromising tablet hardness or stability. The
development of orally disintegrating tablets using super disintegrants offers advantages such as rapid onset of action, improved bioavailability, ease of administration, and better patient acceptability. Therefore, the present project focuses on the formulation and evaluation of orally disintegrating tablets using super disintegrants to achieve fast disintegration and optimal drug release. Commonly used super disintegrants include croscarmellose sodium, sodium starch glycolate, and crospovidone.

Formulation Strategies

Use of superdisintegrants such as croscarmellose sodium, crospovidone, and sodium starch glycolate is central to ODT design.

Mechanism of action of super disintegrants

1. Capillary action
2. Swelling
3. Chemical reaction
4. Particle repulsive force
5. Deformation recovery
6. Enzymatic reaction
7. Combination reaction.

Evaluation Parameters

Disintegration time, wetting time, hardness, friability, and dissolution behavior are essential quality metrics.

METHODOLOGY

BILAYER AND MULTILAYER TABLET FORMULATIONS

Bilayer tablets are prepared with one layer of drug for immediate release while the second layer designed to release drug later, either as a second dose or in an extended release form. The bilayer tablets with two incompatible drugs can also be prepared by compressing separate layers of each drug so as to minimize the area of contact between two layers.

Method of preparation:

Tablets are generally prepared by some techniques i.e. Wet granulation method, Dry granulation method and direct compression method.

Wet Granulation Method.

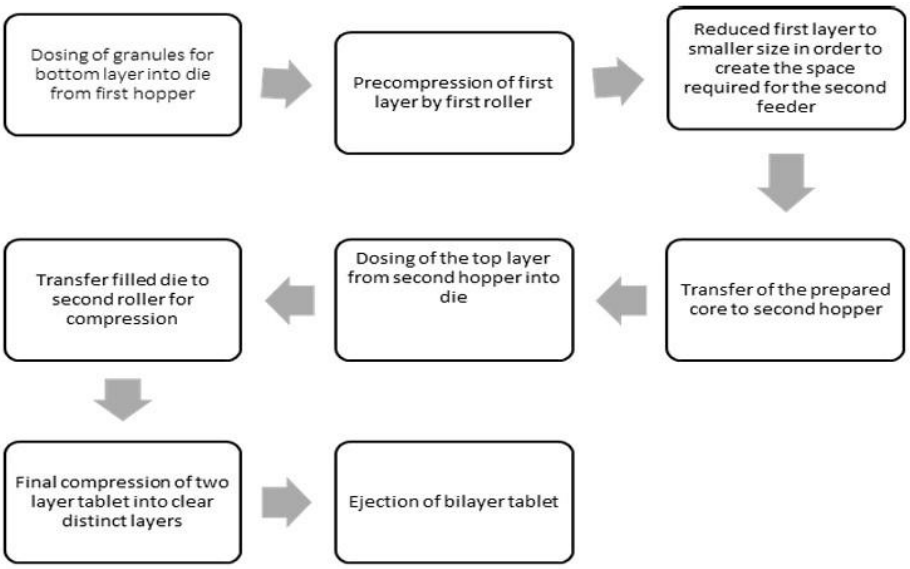
Wet granulation is a process of using a liquid binder to lightly agglomerate the powder mixture. This method involves steps like weighing of ingredients, mixing, granulation, and screening of damp mass, drying, lubrication and compression of tablets. The amount of liquid has to be properly controlled, as over-wetting will cause the granules to be too hard and under-wetting will cause them to be too soft and friable. The main active ingredient, diluent, disintegrant are blended together and then it is allowed to pass through the sieve (sifting). Tray drying is most common method of drying the tablet granules.

Dry Granulation Method.

Dry granulation processes create granules by light compaction of the powder blend under low pressures. This method is used for tablet preparation, in case of tablet ingredients are highly sensitive to moisture or unable to withstand elevated temperatures during drying, slugging may be used to form the granules.

The compacts so-formed are broken up gently to produce granules (agglomerates). This process is often used when the product to be granulated is sensitive to moisture and heat.

Direct Compression Method.
Direct compression involves direct compressing the powdered material into tablets. Direct compression is adopted, if drug constitutes major portion of tablet [86–90] total weight. Tablets containing 25% or less of drug substance can be formulated, with a suitable diluent which acts as a carrier or vehicle for the drug. Tablets prepared by above method are subjected to compression machine which may be single station or multiple stations. The technology involved in this method assumes great importance in the tablet formulations, because it is often the cheapest means, particularly in the production of generics that the active substance permits.



Steps involved in preparation of tablets

Preparation of immediate release layer (IR).
All the ingredients were accurately weighed and passed through mesh 60#.In order to mix the ingredients thoroughly drug, super disintegrant, microcrystalline cellulose, magnesium stearate and talc were mixed in a mortar and pestle. The powder was passed through 60# sieve and compressed on rotary tablet punching machine. (Made- Krishna Engineering).

Preparation of sustained release layer (SR).
It was performed by wet granulation method. The required amount of sustained release polymer were blended with baclofen and passed through 80 mesh sieve. Binding solution was prepared by dissolving required amount of PVP k 30 in iso propyl alcohol (IPA).Blended powders were granulated with IPAsolution and sieved using 40 mesh sieves. The granules were dried at 45˚c for 30 min in tray dryer to evaporate the IPA and then lubricated with required amount of talc, magnesium stearate, store the lubricated granules with suitable label till it's further used.

Final compression of bilayer tablets
Bilayer tablets were prepared by feeding 200 mg of SR granules manually into punch and compressed them with pre compression force. Then 100 mg of IR granules were manually fed into same die cavity SR granules and applied final compression force into rotary tablet punching machine.

MULTI-UNIT PELLET SYSTEMS (MUPS)

Processing of MUPS
Compaction factors that can influence preparation of MUPS include –
1. *Compression force exerted*
Opitz reports the effect of the compression force on the drug release from the MUPS. Increasing the compression force from the minimum required to have a compact till a certain value, which differs for each formulation, film ruptures are enhanced and the dissolution rate is increased.21 Beyond this value, both disintegration and dissolution are delayed, which testifies the formation of undesired matrix tablets.
2. ***Compression velocity***
is more related to dwell time (time period for which the punch head is in contact with the compression roller) during the compression cycle. MUPS are more prone to capping during compression. An increase in dwell time favours formation of strong bonds between

particles being compressed and thus prevents capping and lamination.

Tabletting Equipment for Processing of MUPS

Any tablet compression machine with little modification can be used for preparing MUPS. Modifications are often required in the feed frame and forced feeders. The former designed to ensure uniform clearance from the turret throughout the compression process to prevent attrition and crushing of coated pellets. Design of forced feeders should also intend to prevent such eventualities as abrasion or grinding of pellets.

Future Directions

Evidently the challenges in developing a MUPS formulation are many. Albeit the number of MUPS formulations reaching the market is few, development of such formulations is being pursued actively by both industry and academia since the technology possesses the potential of providing certain distinctness in the designed formulation. A major edge that MUPS provides is a formulation which is difficult for potential competitors to replicate from a regulatory perspective and thus such a dosage form enjoys monopoly for a much longer duration.

Factors to be Considered in the Design of MUPS Tablets

Formulation Variables

Pellet core

Type – matrix or reservoir
Composition – hard brittle e.g. sucrose or plastic, e.g. MCC
Size
Shape
Porosity
Elasticity – is directly related to pellet composition
Thermoplastic layer on surface of drug pellet

Membrane coating

Type of polymer – cellulosic or acrylic, etc.
Coating thickness
Type and amount of placticizer
Presence of pigments
Additional outer coat on polymer surface – plastic layer or powder layer

Cushioning excipients

Nature – deformable (plastic) or fracturable (brittle)Size – powder or pellets
Amount – ideally 50 to 75%

Process variables

Compression force
Compression speed

Equipment variables

Design of tabletting machine, powder feeding mechanism, etc

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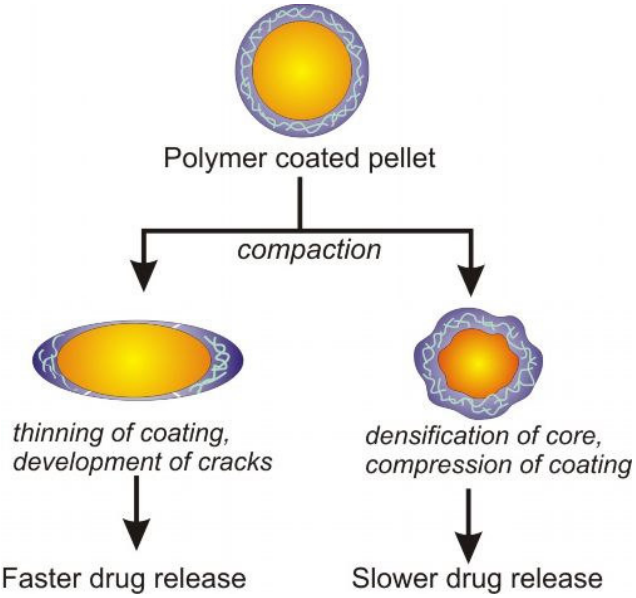


Figure 4. Impact of compaction on pellet deformation and drug release

HOT MELT EXTRUSION (HME) TECHNOLOGY

Hot-melt extrusion equipment consists of an extruder, auxiliary equipment for the extruder, downstream processing equipment, and other monitoring tools used for performance and product quality evaluation. The extruder is typically composed of a feeding hopper, barrels, single or twin screws, and the die and screw driving unit. The auxiliary equipment for the extruder mainly consists of a heating/cooling device

for the barrels, a conveyer belt to cool down the product and a solvent delivery pump. The monitoring devices on the equipment include temperature gauges, a screw-speed controller, an extrusion torque monitor and pressure gauges. The theoretical approach to understanding the melt extrusion process is therefore, generally presented by dividing the process of flow into four sections

1) Feeding of the extruder. Screw driving unit
2) Conveying of mass (mixing and reduction of particle size).
3) Flow through the die.
4) Exit from the die and down-stream processing.

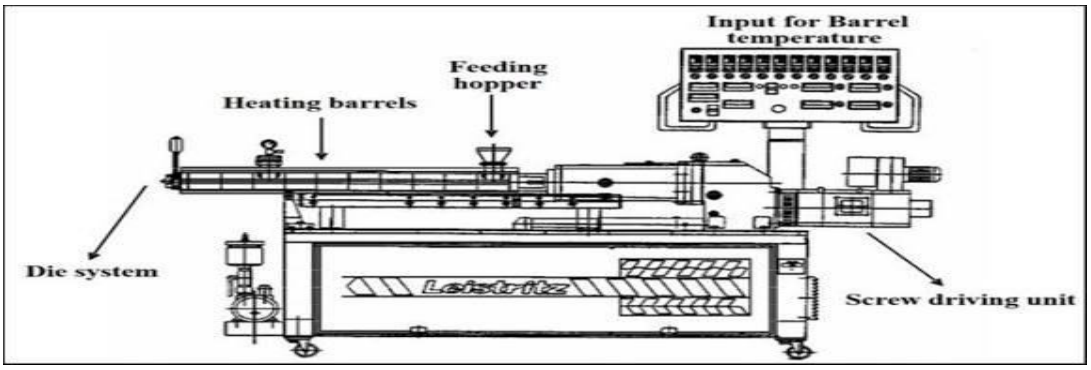


Figure 5

Micro-18 Twin screw co-rotating Leistritz extruder
Generally, the extruder consists of one or two rotating screws inside a stationary cylindrical barrel. The barrel is often manufactured in sections, which are bolted or clamped together.An end-plate die, connected to the end of the barrel, determines the shape of the extruded product.

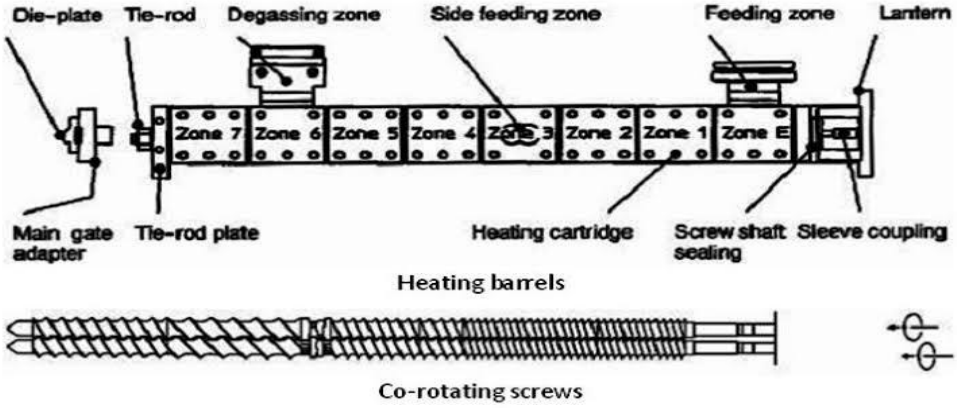


Figure 5. Heating barrels and co-rotating screws for hot-melt extruder.

The heat required to melt or fuse the material is supplied by the heat generated by friction as the material is sheared between the rotating screws and the wall of the barrel in combination with electric or liquid heaters mounted on the barrels. P harmaceutical manufacturers are using twin-screw extruders to mix molecules of active pharmaceutical ingredients (APIs) with appropriate polymers in situations where drug ingredients are poorly soluble or unstable during processing. Extruders are also useful in preparing enteric coated medication, developing sustained release dosages, in taste-masking, and in creating specific forms such as films. Hot-melt extrusion (HME) is the processing of polymeric materials above their glass transition temperature to effect molecular level mixing of thermoplastic binders and/or polymers with active compounds. However, the theoretical approach to understanding the melt extrusion process can be summarized by classifying the whole procedure of HME compaction into the following.
1. feeding of the extruder through a hopper, 2. mixing, grinding, reducing the particle size, venting, and kneading, 3. flow through the die, and 4. extrusion from the die and further downstream processing.

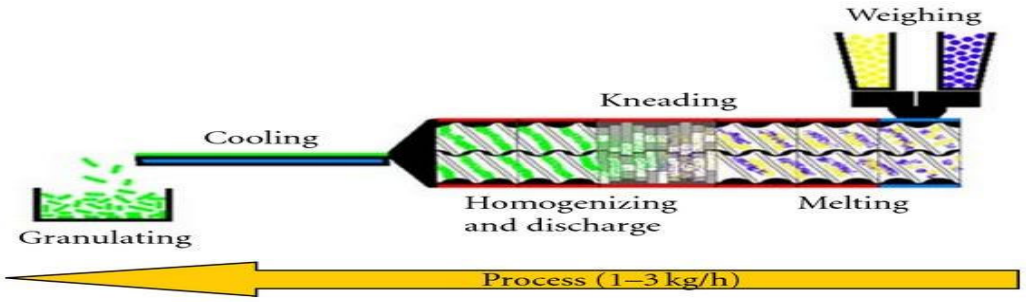


Figure 6. Schematic diagram of the HME process.

THREE-DIMENSIONAL (3D) PRINTING OF TABLETS METHODS /TYPES OF 3D PRINTING

Figure 7. 3D Printing Methods Applied For Drug Formulation

Selective Laser Sintering (SLS):

Introduction: Selective Laser Sintering (SLS) or Selective Laser Melting (SLM) is an additive and quick manufacturing process based on the use of powder coated metal additives and that uses a laser as the power source to sinter (melt) powdered material (typically nylon or polyamide), aiming the laser automatically at points in the space defined by a 3D model, binding the material together to create a solid structure, a process generally used for rapid prototyping. For e.g., Paracetamol as an orodispersible tablet.

Working: A continuous laser beam is used as heating source, for scanning and aligning particles in predetermined sizes and shapes of the layers. The geometry of the scanned layers corresponds to various sections of the models established by Computer-aided design or from files produced by stereo-lithography. After scanning the first layer, the scanning of second layer continues which is placed over the first, repeating the process from the bottom to the top until the product is complete. To fuse small particles of plastic, metal, ceramic or glass powders into a mass that has the desired three dimensional shapes, this technology uses high power laser. Scanning the cross section or layers generated by 3D modeling program on the surface of powder bed, laser selectively fused the powdered material so that the powder bed is lowered by one layer thickness. Then a new layer of material is applied on top and the process is repeated until the object is completed.

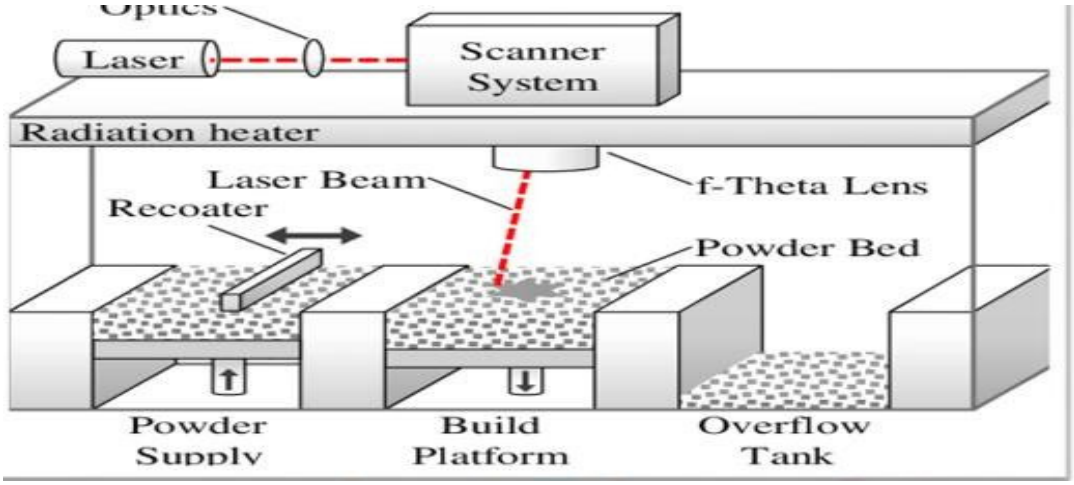


Figure 8. Schematic Diagram Slective Laser Sintering (SLS).

Stereolithography or Stereolithography Apparatus (SLA)

Introduction: In 1988, Charles Hull discovered this technique as a first method for 3D printing technology. It is rapid and popular prototyping technology which can produce highly accurate and detailed product. This method is also called Stereolithography apparatus (SLA) and photo-polymerization. The drug would be dissolved into a liquid pool of hydrogel or resin material. The material of choice must be photosensitive.

Working: Stereolithography (SLA) builds objects one layer at a time by tracing a laser beam on the surface of a vat of liquid photopolymer, inside of which is a movable stage to support the part being built. Stereolithography utilises a laser or projector to solidify material while in bulk setting. During the printing process, photopolymer material like resin or acrylate were used which can cure by UV laser. When the laser beam strikes onto the surface of the pool/bed of liquid photosensitive, drug-loaded material, the material cures and quickly solidifies. This method has extremely high resolution and considerably fast, but the nature of the pool of drug-loaded material has an inherent risk of cross-contamination between the fabrications of different drug products. A resultant layer is formed on top of the previously completed layers. Thus 3D object out of many layers formed completely due to the self- adhesive property of material causes each succeeding layer to bind to the earlier one. Once complete, the part is elevated above the vat and drained. Excess polymer is swabbed or rinsed away from the surfaces. In several cases, a final cure is given by placing the part in an UV oven. After the final cure, supports are cut off the part and surfaces are polished, sanded or otherwise finished.

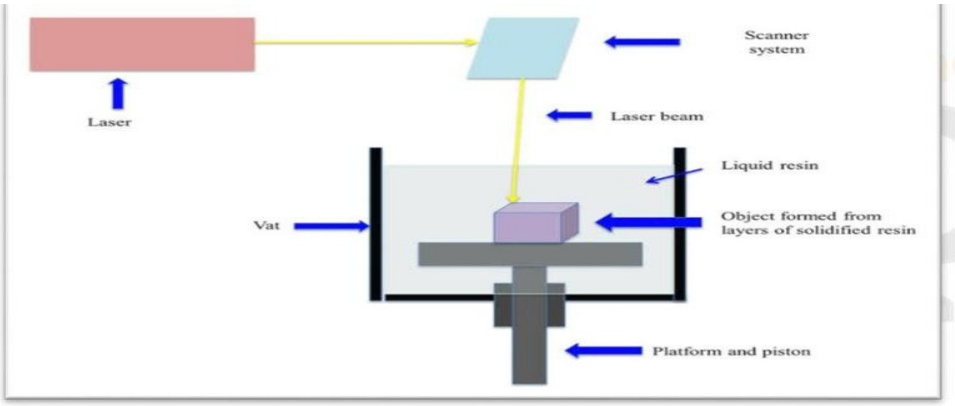
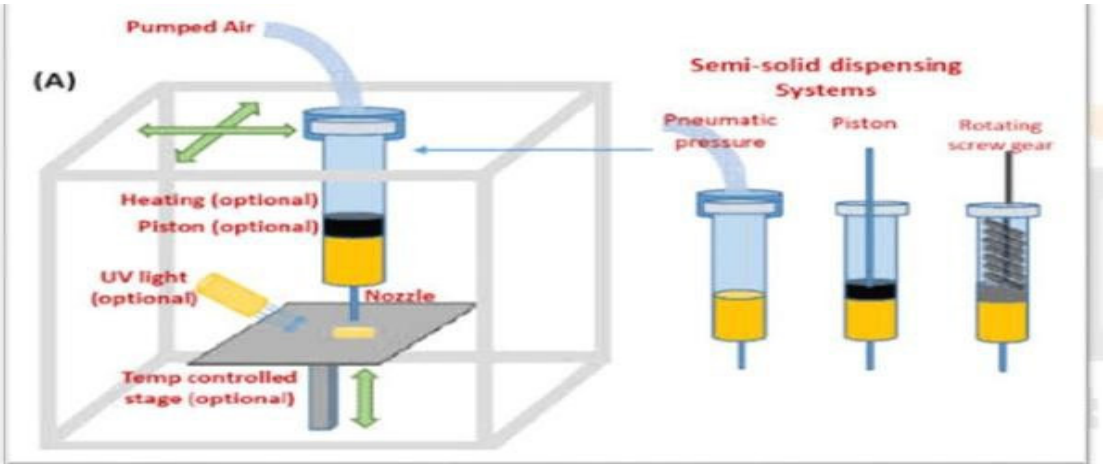


Figure 9. Schematic Diagram Stereolithography or Stereolithography Apparatus (SLA).



Semi-Solid Extrusion (SSE) / Pressure Assisted Syringe (PAS).

Introduction: Several studies have demonstrated the suitability of SSE for the production of thermo-sensitive drugs. The tablet was produced using a hybrid approach that uses an extrusion-based system delivered by a simple metal syringe. Likewise, semi-solid extrusion (SSE) was used to produce solid lipid tablets incorporating a poorly water-soluble drug, fenofibrate. The pharmaceutical ink was prepared using different IJNRD2406241 International Journal Of Novel Research And grades of polyvinyl alcohol (PVA) and polyvinylpyrrolidone (PVP), together with plasticiser and lubricants.

Working: A drug-loaded semi-solid material (e.g. Gel or Paste) is extruded using a syringe- based tool head. The printer head is moved along the x-y-z axis to release the extrudate, which solidifies at room temperature onto a build plate.

Semi-Solid Extrusion (SSE) / Pressure Assisted Syringe (PAS).

DESIGN OF ORALLY DISINTEGRATING TABLETS(ODT's)

CRITERIA FOR SELECTION OF EXCIPIENTS IN ODTs

Formulation approaches for ODTs begin with selecting excipients to shorten the disintegrating time and comply with the pharmacopeia specifications.

While selecting excipients, the following factors must be considered:

1. Rapid disintegration and dissolution
2. Good mouthfeel (no grittiness or bitterness)
3. Non-toxicity and GRAS status
4. Compatibility with drug
5. Adequate mechanical strength
6. Low hygroscopicity
7. Chemical and physical stability
8. Ease of processing (direct compression preferred)

PREPARATION OF POWDER BLEND FOR ORALLY DISINTEGRATING TABLETS

The performance of ODTs depends on the technology used in their manufacture. The orally disintegrating property of these tablets is attributable to the quick ingress of water into the tablet matrix, which creates porous structure and results in rapid disintegration. Hence, the basic approaches to develop ODTs include maximizing the porous structure of the tablet matrix, incorporating the appropriate disintegrating agent and using highly water-soluble excipients in the formulation.

The **powder blend preparation** is a critical step in ODT formulation because it directly affects **blend uniformity, flowability, compressibility, tablet hardness, and disintegration time**.

1. Objectives of Powder Blend Preparation

 Ensure **uniform distribution of API** (especially low-dose drugs)
 Achieve **good flow properties** for uniform die filling
 Maintain **rapid disintegration** (≤ 30 seconds ideally)
 Prevent **segregation and content variability.**

Component	Examples	Purpose
Active pharmaceutical ingredient (API)	Drug substance	Therapeutic effect
Diluent	Mannitol, lactose, MCC	Bulk, mouthfeel
Super disintegrant Binder (optional)	Croscarmellose sodium, PVP K30, MCC	Rapid tablet breakup Mechanical strength
Sweetener	Aspartame, sucralose	Taste masking
Flavor	Mint, orange	Patient acceptability
Glidant	Colloidal silicon dioxide	Improve flow
Lubricant	Magnesium stearate	Reduce friction

Typical Composition of Powder Blend for ODTs

2. Step-by-Step Preparation of Powder Blend (Direct Compression Method)

Step 1: Sifting of Ingredients

 Sift **API, diluent, super disintegrant, sweetener, and flavor** through **#40 or #60 mesh**

 Purpose:

o Break agglomerates21

o Achieve uniform particle size

o Improve homogeneity

Step 2: Primary Blending

 Transfer sifted powders (except lubricant & glidant) into a **polybag, double cone blender, or V-blender**

 Blend for **10–15 minutes**

 Low shear mixing preferred to avoid:

o Loss of super disintegrant efficiency

o Electrostatic charging

Note: For low-dose drugs, apply **geometric dilution**.

Step 3: Addition of Super disintegrant (Optional Split Addition)

 Super disintegrant may be added:

o **Intra-granular (50–70%)**

o **Extra-granular (30–50%)**

 Blend gently for **5 minutes**

 Improves **wicking and swelling action**

Step 4: Addition of Glidant

 Add **colloidal silicon dioxide**

 Blend for **2–3 minutes**

 Improves powder flow and prevents segregation

Step 5: Lubrication

 Add **magnesium stearate (0.25–1%)**

 Blend gently for **1–3 minutes only**

 Over-mixing may:

o Reduce tablet hardness

o Delay disintegration

Avoid high-shear mixing during lubrication.

IDEAL CHARACTERISTICS OF ODT'S

ODTs should depict some ideal characteristics to distinguish them from traditional conventional dosage forms. Important desirable characteristics of these dosage forms include.

 Rapid Disintegration: Disintegrates in the mouth within 5 to 30 seconds (maximum 60 seconds) upon contact with saliva.

 No Water/Chewing Required: Allows for administration without the need for additional fluids.

 Pleasant Mouthfeel & Taste: Masking of bitter tastes is essential; the tablet should feel smooth, creamy, and leave no residue.

 Adequate Mechanical Strength: While porous to allow fast disintegration, the tablet must be hard enough to withstand production, packaging, and shipping without breaking.

 High Porosity: Structure allows for rapid water (saliva) penetration.

 Low Sensitivity to Environment: Stable under varying humidity and temperature conditions.

 High Drug Loading: Ability to carry a reasonable amount of Active Pharmaceutical Ingredient (API).

 Compatibility with Conventional Manufacturing: Amenable to standard packaging (like blister packs) and production processes.

CONCLUSION

The integration of Bi-layer tablets, ODTs, MUPS, HME, and 3D printing signifies a paradigm shift in pharmaceutical science moving away from "one-size-fits-all" medication toward high-precision, patient-centric therapy. While technologies like HME and

MUPS have already optimized the bioavailability and safety of complex APIs, the emergence of 3D printing and advanced geometric configurations offers a future where dosages can be customized at the point of care. The successful industrial adoption of these platforms depends on overcoming current regulatory and scalability hurdles. Ultimately, these innovations do more than improve drug delivery; they enhance the quality of life by ensuring that complex treatment regimens are safer, more effective, and significantly easier for patients to follow.

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CONSENT AND ETHICAL APPROVAL

It is not applicable

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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