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REVIEW ARTICLE

A Review on Rotary Tablet Machines and Recent Advancements in Tableting Technologies and Tablet Design

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Abstract: Rotary tablet machines have been instrumental in the manufacturing of solid oral dosage forms, enabling accurate dosing, stability during storage, and convenient administration. This review comprehensively discusses the fundamental components, operating principles, and manufacturing methods associated with rotary tablet machines. Furthermore, it delves into recent groundbreaking advancements in tableting technologies, with a particular emphasis on three-dimensional (3D) printing technology for personalized drug manufacturing. 3D printing, also known as additive manufacturing, has emerged as a game-changer in the pharmaceutical industry, allowing for the production of personalized 3D-printed drugs through computer-aided model design. This technology offers significant advantages over traditional manufacturing processes, including the ability to create complex drug delivery systems, achieve intricate release profiles, and rapidly produce small batches of drugs tailored to individual patient needs. In addition to 3D printing, the review highlights recent innovations in tablet design, such as tablet-in-tablet, multilayer tablets, tablet-in-capsule, and microchip-embedded tablets. These advancements have the potential to enhance drug delivery, improve patient compliance, and optimize therapeutic outcomes.

Keywords: Rotary tablet machine; 3D printing; Personalized drug manufacturing; Tablet design innovations; Drug delivery systems.

1. Introduction

Oral drug delivery remains one of the most preferred and widely adopted routes of administration due to its non-invasive nature and exceptional convenience. Among the various oral solid dosage forms available, tablets have emerged as a formulation of choice, offering a multitude of advantages that contribute to their widespread use in the pharmaceutical industry. One of the primary benefits of tablets is their ability to provide accurate and consistent dosing. [1,2] The manufacturing process of tablets involves the precise weighing and blending of active pharmaceutical ingredients (APIs) and excipients, ensuring that each tablet contains the intended amount of drug. This accuracy in dosing is crucial for ensuring therapeutic efficacy and minimizing the risk of adverse effects associated with over- or under-dosing. Another advantage of tablets is their inherent stability during storage. The solid nature of tablets, combined with appropriate packaging and formulation strategies, can significantly extend the shelf life of the drug product. This stability not only enhances patient safety by reducing the risk of degradation but also contributes to the overall cost-effectiveness of the medication by minimizing wastage due to expiration. Tablets are also highly convenient for patients, as they can be easily administered without the need for specialized equipment or trained personnel. This ease of administration promotes better patient compliance, which is crucial for achieving desired therapeutic outcomes, particularly in the management of chronic conditions. [3]

Furthermore, tablets offer a tamper-proof nature, which is essential for maintaining the integrity and quality of the drug product. The compressed structure of tablets makes it difficult to alter or manipulate the formulation, ensuring that patients receive the intended medication and dosage. From a manufacturing perspective, the production of tablets is generally more economical compared to other dosage forms, such as liquids or parenteral formulations. The use of high-throughput rotary tablet machines and the ability to produce large batches contribute to the cost-effectiveness of tablet manufacturing. [4] Additionally, tablets are convenient for dispensing and packaging, as they can be easily counted, bottled, or packaged in blister packs, making them suitable for various distribution channels, including pharmacies, hospitals, and mail-order services.

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The production of tablets is achieved through the compression of granules or powders of drugs, with or without excipients, using a specialized instrument known as a rotary tablet machine or rotary tablet press. These machines are designed to apply precise and consistent compression forces, ensuring the formation of uniform tablets with the desired characteristics, such as hardness, friability, and disintegration properties. [5] Rotary tablet machines are highly efficient and capable of producing large quantities of tablets in a short period of time, making them essential for large-scale pharmaceutical manufacturing operations. These machines are also highly versatile, allowing for the production of various tablet shapes, sizes, and formulations, further contributing to their widespread adoption in the industry. In recent years, the demand for natural and organic lip care cosmetics has surged, driven by increasing consumer awareness and concerns about the potential impact of synthetic ingredients on human health and the environment. Manufacturers have responded by incorporating botanical extracts, vitamins, and antioxidants into their formulations, offering products that not only enhance the appearance of the lips but also provide additional benefits, such as anti-aging properties and protection against environmental stressors. Advancements in cosmetic science have led to the development of long-wearing formulations, innovative delivery systems, and the incorporation of active ingredients with specific benefits, such as skin-lightening, anti-aging, and sun protection. These innovations aim to meet the evolving needs and preferences of consumers while ensuring the safety and efficacy of lip care cosmetic products.[6].

2. Rotary tablet machine

2.1. Basics

Rotary tablet machines consist of several key components [7-10], including:

- Hopper: A container that holds the granular or powdered material to be compressed into tablets.
- Tooling: The punches and dies that are responsible for the compression and shaping of the tablets.
- Die cavity: The space within the die where the powder is compressed into a tablet.
- Feeder: Mechanisms that transfer the powder from the hopper to the die cavities. Two types of feeders are commonly used:
- Force feeder: Used for high-speed operations and rotary tablet machines with more than 45 stations. It consists of paddle wheels that force the powder into the die cavities.
- Gravity feeder: Used for slower operations and rotary tablet machines with fewer stations. The powder falls into the die cavities due to gravitational force.
- Compression rollers: Responsible for applying the compression force to the punches, thereby compressing the powder into tablets.
- Cam tracks: Precisely timed mechanisms that control the filling, metering, and ejection of the tablets from the die cavities.
- Control mechanisms: Ensure the accurate and consistent operation of the machine.

Figures 1 and 2 shows the illustrations of single-sided and double-sided rotary tablet machines.

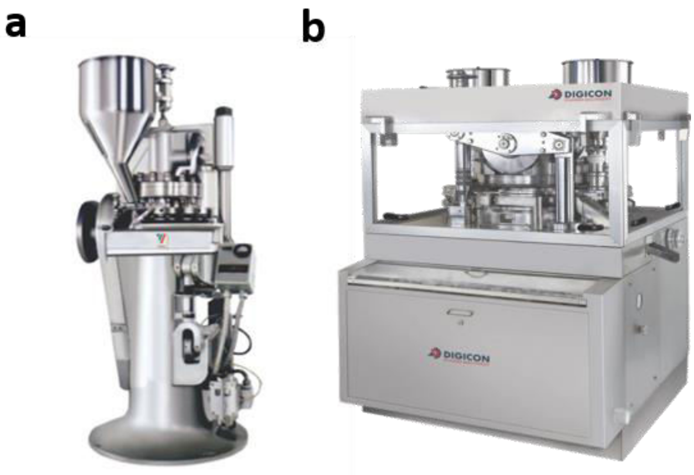

Figure 1. a. single-sided and b. double-sided rotary tablet machines

2.2. Manufacturing methods

Tablets are generally manufactured by two primary methods [1, 11-14]]: wet granulation and dry granulation.

2.2.1. Wet Granulation

This is the most widely used method for tablet and capsule preparation. In wet granulation, the powder mixture is wetted with a liquid binder, which is added by a suitable solvent before being mixed with the blended powders. The resulting wet granules are then dried and milled to the desired size. Although a multi-stage and time-consuming process, wet granulation meets all the requirements for tablet formation.

2.2.2. Dry Granulation

The dry granulation process is used to form granules without using a liquid solution. This method is recommended for products that are sensitive to moisture and heat. The main advantage of dry granulation is that it eliminates the addition of moisture and the application of heat, as found in the wet massing and drying steps of the wet granulation method.

2.3. Tablet compression operation

The tablet compression operation involves four main stages [1, 11-14]

2.3.1. Filling stage

The top punch is withdrawn upwards, and the bottom punch is withdrawn downwards, creating a cavity in the die. The bottom punch is directed by the filling cam track. (Figure 2a)

2.3.2. Metering stage

The bottom punch moves upwards to expel excess powder outside the die, as directed by the metering cam track. (Figure 2a)

2.3.3. Compression stage

The top punch is driven into the die by the upper cam, and the lower punch is driven upwards. The punches enter into pre-compression and main compression rollers, leading to the compression of the powder into a tablet. (Figure 2b)

2.3.4. Ejection stage

The top punch is withdrawn by the upper cam, and the lower punch is pushed up to eject the compressed tablet from the die surface (Figure 2c)

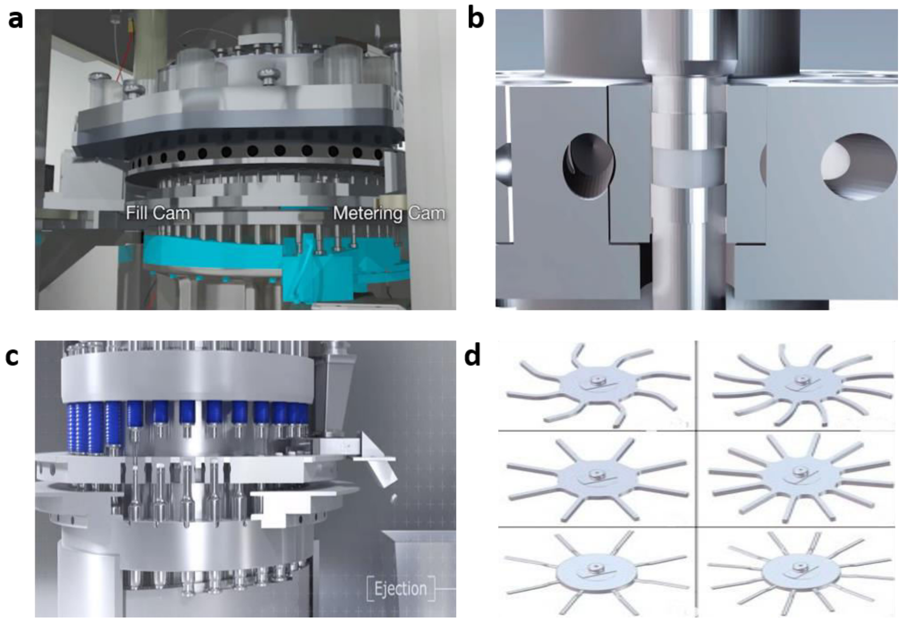

Figure 2. a. Filling and Metering b. Compression c. Ejection d. Force Feeders

2.4. Feed tooling

The feed tooling (Figure 2d) of a rotary tablet machine includes feed frames that transport, mix, and fill the powder into the die cavities. Two types of feed frames [15, 16] are commonly used:

2.4.1. Force feeder

Used for high-speed operations and rotary tablet machines with more than 45 stations. The force feeder can have two or three compartments, each with paddle wheels that facilitate the accurate and continuous supply of powder to the die cavities.

2.4.2. Gravity feeder

Used for slower operations and rotary tablet machines with fewer stations. The gravity feeder consists of a hopper, metering scrapers, excess powder collection scrapers, and an ejection scraper. The powder falls into the die cavities due to gravitational force.

2.5. Materials used in fabrication

The outer chamber of a rotary tablet machine is typically made of Type 304 stainless steel, which is corrosion-resistant and composed of 17.5-19.5% chromium, 8-10.5% nickel, and other alloying elements. The inner module, which has restricted parts, is often made of Type 316L stainless steel, which is highly corrosion-resistant and smooth, containing 16-18% chromium, 10-14% nickel, and 2-3% molybdenum

3. Applications and Advantages of Rotary Tablet Machines

Rotary tablet machines have become an indispensable part of various industries due to their versatility, efficiency, and ability to produce high-quality tablets on a large scale. Their applications extend beyond the pharmaceutical industry, making them valuable assets in diverse sectors. In the pharmaceutical industry, rotary tablet machines are widely utilized for the preparation of various tablet types, catering to a wide range of therapeutic areas and formulation requirements. One notable application is the production of ayurvedic tablets, which are an integral part of traditional Indian medicine. These tablets are formulated using a combination of herbal ingredients and are often designed to address specific health conditions or promote overall well-being [17, 18]. Rotary tablet machines ensure consistent and accurate dosing of these intricate formulations, maintaining the integrity and efficacy of the finished product.

Furthermore, rotary tablet machines play a crucial role in the manufacturing of cosmetic tablets, which are commonly used as supplements or skin care products. These tablets may contain active ingredients such as vitamins, minerals, antioxidants, or botanical extracts, and their production requires precise formulation and compression to maintain the desired release characteristics and stability. In the realm of fitness and wellness, rotary tablet machines are employed in the production of various supplements and dosages aimed at supporting healthy lifestyles [19, 20]. These tablets may contain a wide range of ingredients, including proteins, amino acids, herbs, and other natural compounds, and their manufacture necessitates careful control over the compression process to ensure optimal bioavailability and dissolution profiles. One of the significant advantages of rotary tablet machines is their ability to produce multilayer tablets. These complex dosage forms consist of multiple layers, each containing different active ingredients or formulations, allowing for the simultaneous delivery of multiple therapeutic agents or tailored release profiles. Multilayer tablets offer numerous benefits, such as improved patient compliance by reducing the number of tablets to be taken, as well as the potential for synergistic or complementary therapeutic effects.

In addition to their extensive applications in the pharmaceutical industry, rotary tablet machines are also employed in the food industry for the preparation of regular and irregular-shaped candies [21, 22]. These machines can precisely control the compression forces and tablet dimensions, enabling the production of uniquely shaped and visually appealing confectionery products. The advantages of rotary tablet machines extend beyond their versatility and wide range of applications. One of their key benefits is the low space requirement, particularly for machines with more than 35 die stations. These compact machines can be easily integrated into existing manufacturing facilities, optimizing the use of available space and reducing the need for extensive infrastructure modifications.

Another significant advantage is the potential for reduced labor costs, especially for rotary tablet machines with a high number of die stations. These machines are highly automated, minimizing the need for manual intervention and allowing for efficient and continuous production with fewer personnel required. Moreover, rotary tablet machines are designed to deliver uniform compression, ensuring consistent tablet quality and physical characteristics throughout the production run. This uniformity is essential for maintaining the desired therapeutic effect, as well as meeting regulatory requirements for product quality and reproducibility. The powder filling mechanisms employed in rotary tablet machines are engineered to be easy and efficient, facilitating a smooth and continuous flow of granules or powders into the die cavities. This not only enhances production efficiency but also minimizes material wastage, contributing to cost savings and environmental sustainability. Despite these numerous advantages, rotary tablet machines also have certain drawbacks that must be considered. One of the primary challenges is the high initial cost associated with acquiring and installing these specialized machines. The complexity of their design and the requirement for precise engineering often result in substantial capital investments, which may be a barrier for smaller pharmaceutical companies or those with limited financial resources. Furthermore, rotary tablet machines require a reliable and consistent power supply to operate effectively. Fluctuations or interruptions in power can disrupt the production process, leading to potential quality issues, material wastage, and costly downtime. As a result, manufacturing facilities utilizing these machines must ensure a stable and uninterrupted power source, which may involve additional investments in backup generators or power conditioning systems. The availability of sophisticated parts and components for rotary tablet machines can also be a challenge, particularly for older or specialized models. These machines often incorporate intricate mechanisms and high-precision components, which may require sourcing from specialized manufacturers or suppliers. Delays or shortages in obtaining replacement parts can lead to prolonged production downtime and potentially impact overall productivity. Finally, the cleaning and maintenance of dies and die cavities in rotary tablet machines can be a time-consuming and challenging task. These components are subjected to high compression forces and may accumulate residues or debris over time, potentially affecting tablet quality or causing cross-contamination issues. Thorough cleaning and inspection procedures must be implemented to ensure consistent product quality and compliance with regulatory requirements. Despite these drawbacks, the advantages offered by rotary tablet machines, such as their versatility, efficiency, and ability to produce high-quality tablets on a large scale, have solidified their position as essential equipment in various industries, including pharmaceuticals, cosmetics, and food production

4. Recent Advances in Tableting Technologies

4.1. 3D Printing of Pharmaceutical Dosage Forms

Three-dimensional (3D) printing technology, also known as additive manufacturing, has emerged as a promising advancement in the field of pharmaceutical manufacturing. This technology allows for the personalized production of 3D-printed drugs through computer-aided model design. In recent years, the use of 3D technology in the pharmaceutical field has become increasingly sophisticated. The successful commercialization of Spritam® (levetiracetam), an anti-epileptic drug, in 2015 marked a significant milestone as the first 3D-printed tablet approved by the U.S. Food and Drug Administration (FDA) [23]. Since then, there has been a succession of 3D-printed drug applications that have received investigational new drug (IND) approval from the FDA. Compared to traditional drug preparation processes, 3D printing technology offers significant advantages in personalized drug manufacturing, allowing for the easy production of preparations with complex structures or drug release behaviors and rapid manufacturing of small batches of drugs.

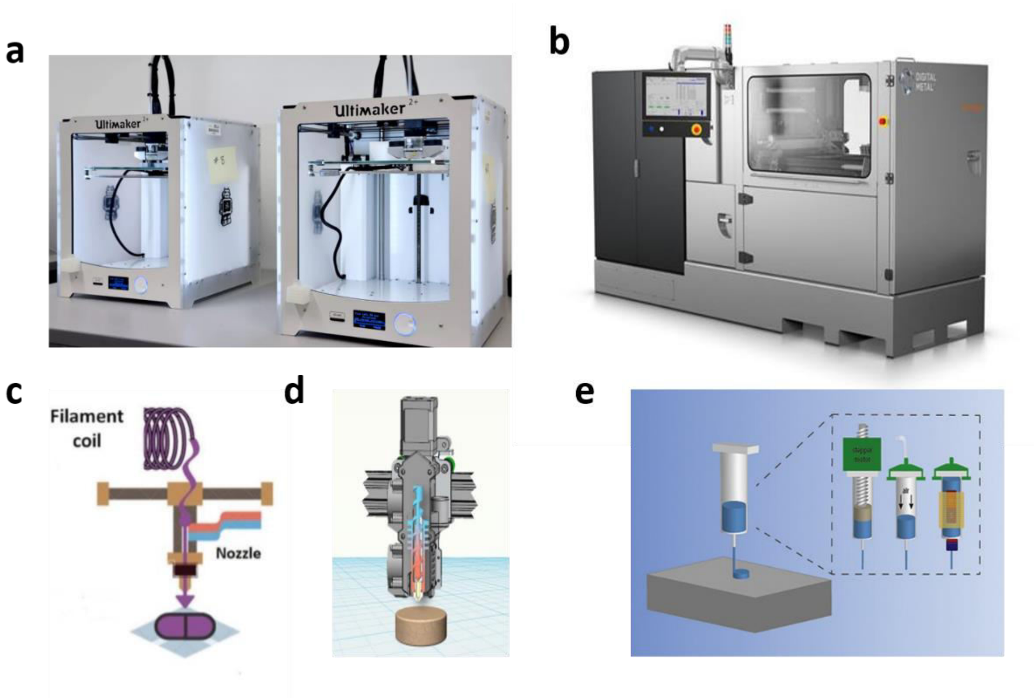

Figure 3. a.Ultimaker^{2+} 3D printer b. Binder jet printer c. Fused deposition modelling d. Printer head printing tablet e. Semi solid extrusion

4.2. Steps in 3D Printing and Drug Delivery:

The process of 3D printing and delivering drugs to patients typically involves the following steps [1, 24]:

- Diagnosis
- Examination of the electronic prescription
- Printlet design
- Designing the tablet shape
- Determining the tablet size
- Instructing the appropriate dosing of ingredients
- Printlet production
- Personalization or delivery to the patient

The average time taken by a 3D printer to produce tablets depends on factors such as the number of layers, printer type, material properties, layer thickness, post-processing requirements, batch size, complexity, and the trade-off between quality and speed.

4.3. Applications of 3D Printers in Pharmacy

3D printers have found numerous applications in the pharmaceutical field, including:

- Customization of implants according to patient requirements
- Achieving complex drug release profiles
- Unique designing of dosage forms other than tablets
- Preparation of veterinary medicines
- Drug development and research
- Automatic compounding
- Emergency care and disaster relief in hard-to-reach areas
- Providing personalized medication to astronauts during space missions

4.4. Advantages of 3D Printing in Pharmaceuticals

The use of 3D printing technology in the pharmaceutical industry offers several advantages [1, 25]:

- 3D printing allows for the production of personalized medications tailored to individual patient needs, accounting for factors such as age, weight, and disease state.
- 3D-printed dosage forms can be designed with intricate geometries and structures, enabling the achievement of complex drug release profiles, such as delayed, sustained, or pulsatile release.
- 3D printing is well-suited for the rapid manufacturing of small batches of drugs, reducing the need for large-scale production facilities and minimizing waste.
- 3D printing technology can produce dosage forms with unique shapes, colors, or flavors, potentially improving patient adherence and compliance.
- 3D printing enables on-demand manufacturing of pharmaceuticals, reducing the need for stockpiling and minimizing the risk of drug shortages.
- 3D-printed dosage forms can incorporate multiple drugs in a single unit, simplifying the administration of complex drug regimens.
- For small-scale manufacturing or orphan drugs, 3D printing can be more cost-effective compared to traditional manufacturing processes.

4.5. Recent Advances in Tablet Design

In addition to 3D printing technology, there have been several recent advances in tablet design, aiming to improve drug delivery, patient compliance, and therapeutic outcomes [1, 25]:

- Tablet-in-tablet design: This design (Figure 4a) involves incorporating a smaller tablet within a larger one, allowing for the simultaneous delivery of two different drugs or modified release profiles.
- Multi layer tablets: These tablets consist of multiple layers (Figure 4b), each containing different drugs or release rates, enabling combination therapy or tailored drug release profiles.

- Tablet in capsule design: In this design (Figure 4c), a tablet is enclosed within a capsule shell, providing an additional barrier for modified release or taste-masking purposes.
- Microchip-embedded tablets: These tablets (Figure 4d) incorporate microchips that can transmit information about the medication to a receiver, enabling real-time monitoring of drug delivery and patient compliance.
- Floating tablets: These tablets are designed to remain buoyant in the stomach for an extended period, allowing for prolonged gastric retention and improved bioavailability of drugs with an absorption window in the upper gastrointestinal tract.
- Orally disintegrating tablets (ODTs): ODTs are designed to rapidly disintegrate or dissolve in the oral cavity, without the need for water, improving patient compliance and convenience

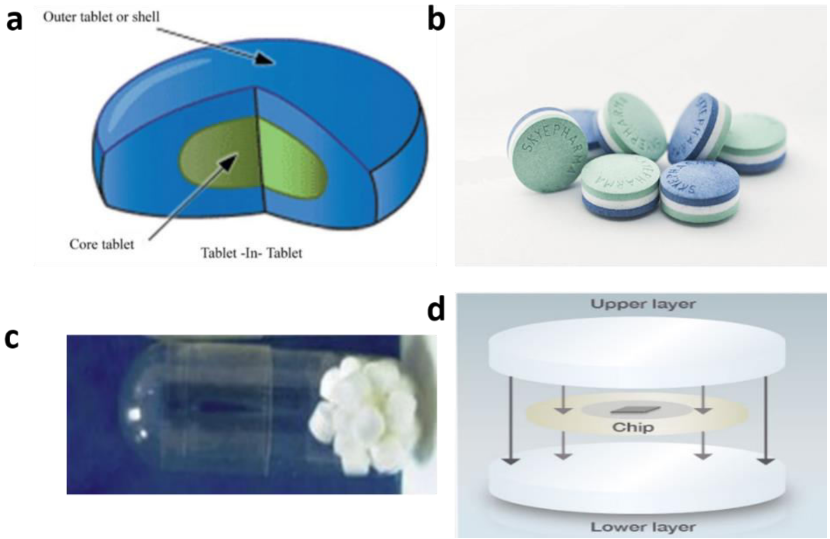

Figure 4. a. Tablet in Tablet design b. Multilayer tablet c. Tablet in capsule design d. Microchip-embedded tablets

5. Conclusion

Rotary tablet machines play a crucial role in the manufacturing of solid oral dosage forms, offering advantages such as accurate dosing, stability, and convenient administration. Recent advancements in tableting technologies, particularly 3D printing, have opened new avenues for personalized drug manufacturing, complex drug release profiles, and rapid small-batch production. Additionally, innovative tablet designs, including tablet-in-tablet, multilayer tablets, and microchip-embedded tablets, have the potential to improve drug delivery, patient compliance, and therapeutic outcomes. As research and development in this field continue, we can expect further advancements that will revolutionize the way pharmaceutical products are manufactured and administered.

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