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Influence of Surface Area on Dissolution of Additively Manufactured Polyvinyl Alcohol Tablets

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***Abstract*—**Additive manufacturing is revolutionizing production in different industries, including pharmaceuticals. This case study explores the influence of surface area on the dissolution of additively manufactured polyvinyl alcohol parts as a polymer candidate. Specimens of different geometries and constant mass were fabricated using a Fused Deposition Modeling (FDM) 3D printer. The dissolution behavior of these samples was compared with respect to their surface area. Improved and accelerated dissolution was observed for samples with a larger surface area. This study highlights the capabilities of additive manufacturing to produce samples of complex geometries that cannot be manufactured otherwise to control the dissolution behavior for pharmaceutical and biopharmaceutical applications.

***Keywords*—**Additive manufacturing, polymer dissolution, fused deposition modelling, geometry optimization.

I. Introduction

ADDITIVE Manufacturing (AM) is an advanced technique that constructs complicated structures by adding layers based on digital 3d models. This method enables quicker, more efficient, and cost-effective production in different industries. AM has revolutionized production processes in different industries, including food and pharmaceuticals [1]-[3]. In the pharmaceutical industry, most drugs are administered in the form of oral tablets. These are manufactured using rotary tablet presses whereby the powder formulation is compressed using punches in dies of fixed geometry. Here, the release profile of the tablets is often controlled via the compression stress applied during manufacturing [4]. Although rotary tablet presses enable the manufacturing of large numbers of tablets per unit of time, the shape of tablets that can be manufactured is limited to a few simple geometries some of which are shown in Fig. 1. The limited flexibility of tablet shapes offered by rotary tablet presses is one of its main drawbacks. Due to the mechanics of how they work, these presses are designed to produce tablets with simple and regular geometry efficiently. Their manufactured tablets frequently have uniform thickness, straight edges, and symmetrical shapes that facilitate the press's rotation.

The design potential of conventional tablet press technology is constrained to simple geometries, which prevents the investigation of complex designs. However, the transformative leap that AM offers enables pharmaceutical experts to use complicated geometries for medication formulation and release dynamics. With the help of this paradigm change, pharmaceutical researchers can construct tablets with particular features that go beyond traditional constraints. Because of this, the potential for creating complex and unique tablet designs using these traditional presses is still limited. A fascinating paradigm change in the field of tablet fabrication has been brought about by the development of AM approaches, such as the fused deposition modeling (FDM) methodology. In addition to releasing the manufacturing process from the limitations of conventional tooling, AM techniques enable researchers and manufacturers to design tablets with extremely complex and customized geometries that have the potential to revolutionize drug delivery strategies, dissolution behavior, and overall therapeutic efficacy.

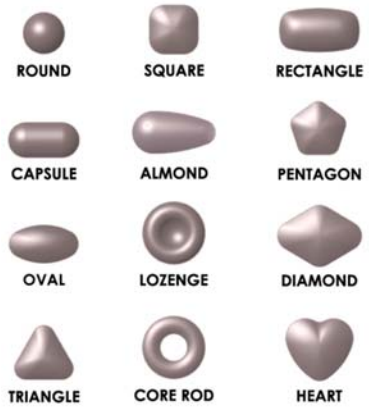

Fig. 1 Common pharmaceutical tablet geometries

The shape of the tablet and its size directly influence the dissolution behavior through the surface area contact between the tablet and the solvent. Optimizing the surface area can accelerate the pace at which a medicine dissolves [5], [6], since a larger surface area allows for more drug particle interaction with the fluid surrounding it, speeding up the diffusion process. Diffusion and dissolution are two interrelated processes that determine the rate and quantity of drug absorbed. Dissolution is a prerequisite for diffusion, and the rate of dissolution may impact the rate of diffusion, which can then impact the rate of drug absorption [7]. Molavi et al. [8] observed a more significant drug release rate for tablets of increased surface area. The findings of the study offer important new insights into the formulation and design of pharmaceutical tablets, highlighting the significance of taking surface area into account as a crucial element in managing drug release kinetics.

AM methods, including the FDM technique, can fabricate

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parts with complex geometries that are otherwise impossible to manufacture. For pharmaceuticals, AM offers a route to fabricating solid dosage forms of complex shapes and geometries for controlled dissolution behavior. By using AM to create complicated geometries that affect the surface area-to-volume ratio and therefore the drug release rate, this method has the potential to create pharmaceutical tablets with precise and controlled disintegration behaviors. The findings not only highlight the link between tablet surface area and drug release kinetics, but they also connect with the developing discipline of AM in pharmaceutical research and development.

Different researchers have examined the capabilities of FDM for manufacturing pharmaceutical products [9] and evaluated the influence of surface area on the dissolution behavior of additively manufactured products. Goyanes et al. [10] observed some correlations between the surface area, surface area to volume ratio and the dissolution behavior. In an earlier study, Goyanes et al. [11] used an extruded Polyvinyl alcohol (PVA) filament containing paracetamol or caffeine to fabricate caplets using FDM and evaluated the influence of internal structures, drug loading and composition on dissolution behavior. They found that the caplets' porosity could not be used to predict the release profile.

Jamróz et al. [12] used a PVA and Itraconazole filament to investigate the role of infill density of simple geometries on dissolution profiles. They found that lower infill density accelerates the pharmaceutical release rate from printed tablets whilst negatively affecting reproducibility. In another work, the FDM process was used to manufacture drug-loaded hydroxypropyl cellulose (HPC) hollowed tablets and observed improved bioavailability compared to commercially available alternatives [13].

This study highlights the importance of surface area on the dissolution behavior of polymer samples and demonstrates the potential of AM as a powerful method for fabricating pharmaceutical solid dosage forms with complex geometries and designated surface areas. Furthermore, AM is shown to be a promising technique for producing complicated solid dosage forms, offering more design and modification possibilities for medication delivery. By adopting the drug release profiles to specific demands and medical circumstances, the pace of recovery and adverse effects of medication can be controlled.

II. Material and Method

In this study, the selection of PVA as the polymer candidate to represent pharmaceutical materials was underpinned by its exceptional properties. PVA, renowned for its biocompatibility and lack of toxicity, stands as a prime choice in the realm of controlled drug delivery systems. Its versatility and seamless processing have made it a staple in the pharmaceutical industry, enabling the formulation of innovative drug delivery solutions. Notably, the utilization of a commercially available PVA filament, supplied by Ultimaker, Netherlands, with a filament diameter of 2.85 mm, exemplifies the practicality of this research. Employing an Ultimaker3 FDM 3D printer further attests to the convergence of cutting-edge technology with pharmaceutical applications, exemplifying the intersection of material science and advanced manufacturing techniques.

The samples fabricated include a torus, a cube, and a custom cubic shape as shown in Fig. 2 from left to right.

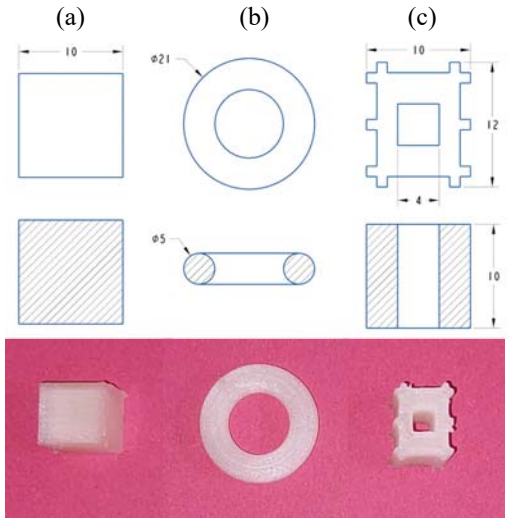

Fig. I Images and dimensions for (a) cube, (b) torus, and (c) custom cubic shape samples.

The samples' geometry was selected so that a constant designed mass of 1.25 g is achieved considering the PVA solid density of 1.23 g/cm^3. Three specimens were fabricated from each sample and the final mass of the specimens was measured using an accurate scale. The designed geometry of specimens and their mass after manufacturing are summarized in Table I. In the table, the surface area, and volume are determined using the CAD software used. This use of CAD software not only highlights the strictness of the research process but also exemplifies how advanced computational tools and conventional experimental approaches work in perfect balance to reveal complex insights in the field of pharmaceutical sciences.

TABLE I
The Design and Measured Properties for Manufactured Specimens of Three Sample Shapes Fabricated Using FDM

Geometry	Designed mass (g)	Surface area (mm^2)	Volume (mm^3)	Average measured mass (g)
Torus	1.25	904.77	986.9	1.21
Cube	1.25	789.50	1000.0	1.19
Custom cubic shape	1.25	1051.5	983.8	1.21

The manufacturing process involved precise control over parameters to achieve optimal results. The print speed was set at 70 mm/s, balancing efficiency, and accuracy in material deposition. A 250 mm/s travel speed was chosen for swift nozzle movement, minimizing smearing or distortion. The critical nozzle temperature remained constant at 200 °C, promoting uniform layer bonding and structural integrity. These settings exemplify the combination of technical finesse and scientific difficulty in producing pharmaceutical geometries of exceptional quality and consistency.

The dissolution profile of specimens was measured using a

PTWS 120D USP (IV) machine (Pharma Test, Germany). For each test the bath temperature was set to 37 °C to replicate the body temperature, the solvent volume (distilled water) was set to 500 ml and the stirring speed was adjusted to 50 rpm. At varying time intervals, 5 ml of solutions were separated and the absorbance of PVA was determined using an Evolution 60S UV-Visible Spectrophotometer (Thermo Scientific, US) at a peak wavelength of 206 nm. Using the calibration curve shown in Fig. 3, the concentration of PVA in water at different times was calculated. The tests were continued for more than seven hours. This analytical approach enabled the dynamic monitoring of PVA dissolution over an extended period, giving detailed insights into the dissolution kinetics.

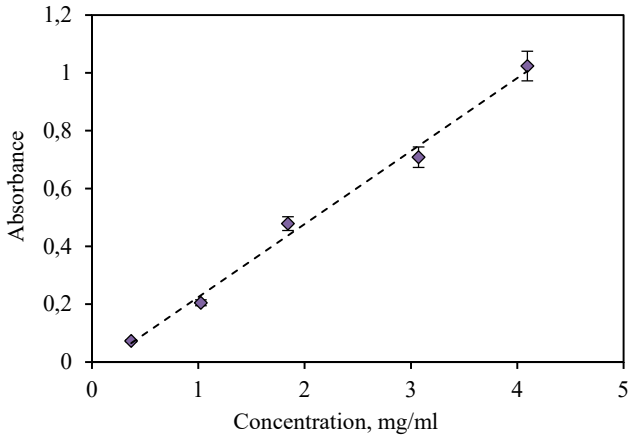

Fig. 3 The calibration curve for converting the absorbance to the concentration of PVA dissolved in water (R2 = 0.99)

III. Result and Discussion

Fig. 4 accurately records the concentration dynamics of PVA in the aqueous medium over the course of the measurement period and provides a visual representation of the changing dissolution profiles for the three different samples. The difference in dissolution kinetics between the cube, torus and custom cube shape is seen in this figure. The custom cube design stood out for displaying the most prominent disintegration rate, which is indicative of its ability to release drugs quickly and may have an instant therapeutic effect.

Conversely, the solid cube exhibited a more measured and deliberate release profile, presenting an intriguing contrast that underscores the potential of tailored shapes as instrumental in molding therapeutic outcomes and reinforcing patient adherence. What further accentuates these findings is the pronounced influence of surface area on dissolution kinetics, as observed across the sample geometries. The positive correlation between higher surface area and increased dissolution rate arises from the heightened contact interface between the solute and solvent, an effect well substantiated in the study conducted by Goyanes et al. [10], thereby corroborating the validity of the observed phenomena. These findings from the study not only improve our understanding of dissolution dynamics but also provide a solid basis for developing pharmaceutical design methods that will improve efficacy and focus on the needs of the patient.

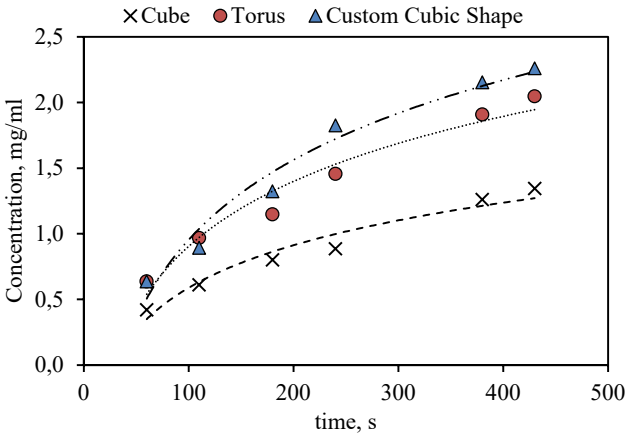

Fig. II Concentration per time for cube, torus, and custom cubic shapes with PVA

A more detailed comparison of the data for the torus and custom shape samples shows that despite having similar volume and mass, a larger rate of dissolution was recorded for the custom shape. This is solely due to the difference in the surface area of the samples. Therefore, by adjusting the sample surface area, the dissolution behavior can be manipulated for specific applications. The more surface area that is available for this contact, the more effectively the drug molecules may be carried from the tablet into the dissolution of a medium and released from it.

The study highlights a unique insight by making a significant comparison between the results produced from the solid cube—a representation of standard tablets—and the finely built custom-shaped structure. The disintegration rate can be significantly increased while still maintaining the same size restrictions by making minor changes to the geometry. Notably, in this case, it was discovered that the dissolution rate was two times greater for the custom-shaped structure, illustrative of the significant influence that specific geometric alterations can have on drug release kinetics.

These results highlight the potential of AM for manufacturing tablets of complex geometries with improved dissolution rates. This can be extended to applications where the polymer or the drug has reduced dissolution or diffusion capabilities. Here, by manufacturing a sample with a significantly larger surface area (a lattice structure for example), a larger contact surface between the solvent and solute will be available which will improve the release rate substantially.

It must be noted that when these structures are designed, the size of the openings and holes must be selected with respect to the surface tension of the solvent. The solvent must be able to penetrate and flow through (to avoid local saturation) these structures to ensure effective dissolution/diffusion from all external surfaces of the structure. Thus, for small cavities, there is no expected effect on dissolution behavior, as suggested by Jamróz et al. [12]. Also, AM is ideal for creating bespoke dosage forms due to its ease of shape and content

customization. However, the relationship between structural and functional characteristics of printed products has not been thoroughly examined in 3D printing research.

Tablets with complex shapes can be produced using AM, which improves dissolving rates. This is especially useful for medications or polymers with poor diffusion or dissolving properties. Researchers can achieve a larger contact area between the tablet and the dissolution medium, leading to increased drug release rates, by using complicated structures like lattice forms. This invention could improve therapeutic outcomes and advance pharmaceutical manufacturing. Since there is more surface area, the medicine dissolves more quickly, increasing the amount of drug that can be absorbed by the body.

IV. Conclusion

By improving dissolving rates and altering drug administration, AM revolutionizes the pharmaceutical industry. Controlled drug release mechanisms can be achieved by constructing complex internal structures within tablets, enabling longer therapeutic effects and decreased dose frequency. This method can also result in multi-layered tablets made of several medication ingredients, which can have synergistic effects and allow for customized treatment plans. It is possible to include extra features like real-time drug monitoring sensors and particular excipients. Standardizing manufacturing procedures, guaranteeing regulatory compliance, and increasing production all continue to be difficult tasks. By enhancing dissolving and altering the way we develop, design, and deliver medications, AM has the potential to change the pharmaceutical industry when these challenges are overcome. This would eventually improve patient outcomes.

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