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FEATURES OF 3D PRINTING OF ORAL FILMS

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ABSTRACT

The development of 3D printing technologies has led to significant changes in production across various sectors, particularly in the medical field. This technology is currently used to manufacture numerous medical products. However, the approach to utilizing this technology has significantly evolved, especially concerning the formulation of medications. The application of 3D printing in producing oral films is promising as it allows for the creation of medications that consider the individual characteristics of patients, ensuring accurate dosages and specific properties. 3D printing technology enables the precise adjustment of drug dosages and compositions to meet the unique needs of each patient, which is crucial in modern medicine where the focus is on maximizing effectiveness and minimizing side effects. This enhancement not only improves treatment outcomes but also increases patient comfort by reducing the frequency and severity of potential adverse reactions. Furthermore, 3D printing offers new research opportunities in pharmaceuticals by enabling the production of dosage forms with complex properties that are challenging or impossible to achieve with traditional methods. This approach could significantly expedite the development and clinical integration of new drugs, underscoring the importance of ongoing research and development in 3D printing within the pharmaceutical industry.

Keywords: 3D Printing, clinical integration of new drugs.

1. THE AIM OF THE STUDY

The study aims to comprehensively analyze the potential of 3D printing technology for creating oral films, with a particular emphasis on the technology's capacity for accurate dosing and uniform distribution of active pharmaceutical ingredients. The primary objective is to determine how various 3D printing methods can enhance the effectiveness and safety of medications while facilitating personalized treatment.

2. MATERIALS AND RESEARCH RESULTS

The research concentrated on analyzing scientific papers that describe the use of 3D printing technologies internationally for manufacturing medical devices. The findings indicate that 3D printing is an exceptionally effective method for creating various dosage forms, including oral films. By examining different 3D printing techniques—such as stereolithography, extrusion printing, photopolymerization, and selective laser sintering—the study identified their advantages and limitations within the context of medical mold manufacturing.

This method utilizes thermoplastics, which melt into a liquid state when heated to specific temperatures. This transformation allows the material to be easily extruded through the printer's nozzle. During the printing process, the material is dispensed in the form of thin filaments, layered successively on the printing platform. Each new layer solidifies and adheres to the previous one, creating a robust 3D structure. Extrusion printing is noted for its high precision in controlling the size and shape of objects, an essential feature for medical applications such as the production of oral films where precise dosage control is critical. A distinctive feature of this method is its compatibility with a broad range of thermoplastic materials, including ABS, PLA, and PEEK, each offering unique mechanical and thermal properties. Crucially for medical use, many of these materials are biocompatible, making them suitable for creating implants and other medical devices. By regulating the temperature and feed rate of the material, the printing process can be optimized to produce high-quality products free from defects like cracks or distortions. This precision ensures uniform distribution of active ingredients within the final medical product, which is vital for accurate medicinal dosing.Although extrusion 3D printing is widely used in producing various objects, including medical devices, it has several drawbacks that could impact the quality of the final product, particularly in terms of accuracy and safety[1]. A significant limitation is the method's limited resolution, which may not meet the requirements for complex medical devices that require high detail. This issue can be addressed by using smaller nozzles and implementing more precise temperature controls during printing, which enhances detail and form accuracy. Additionally, the porosity of materials produced through extrusion 3D printing poses

another challenge. This characteristic can affect the durability and hygiene of the final products, crucial factors in medical applications.The porosity of materials used in extrusion 3D printing can compromise the durability and hygiene of products, which are critical attributes for medical devices. Porosity can be mitigated through post-treatments such as acetone vapor treatment or epoxy coating, which fill the pores and create a smooth surface, thereby eliminating porosity and preventing surface contamination. Additionally, the utility of some thermoplastics in this method is constrained by their physical properties, such as high melting points, which may be incompatible with certain pharmaceutical applications. To address this, there is potential for developing and introducing new thermoplastic materials specifically optimized for extrusion 3D printing in the production of medical molds.

Stereolithography is one of the most precise 3D printing techniques available, utilizing ultraviolet light to solidify liquid photopolymers layer by layer. The process initiates by immersing a platform into a tank filled with photosensitive resin. An ultraviolet laser then precisely focuses light onto the surface of the resin, causing polymerization and forming a solid layer. After each layer is created, the platform is lowered, and the process repeats, layer by layer, culminating in a detailed three-dimensional object. The primary advantage of stereolithography lies in its ability to produce highly detailed products with smooth surfaces, making it ideal for creating prototypes, precision medical instruments, and other components essential in healthcare. This technology is renowned for its exceptional precision and capability to reproduce complex structures, often beyond the reach of other 3D printing methods. However, stereolithography comes with certain drawbacks, including the necessity for post-processing. Typically, objects produced using SLA require the removal of excess resin and subsequent polishing to refine their appearance. Additionally, these products often need further UV curing to attain full strength and stability, ensuring they meet the rigorous demands of their intended applications. Improvements to SLA-produced products may include the application of special protective coatings that increase their resistance to wear and chemical exposure. Despite its high accuracy, it is important to note that SLA technology utilizes expensive materials and requires high-precision equipment, leading to increased production costs. Nevertheless, its capability to fabricate high-quality, complex structures renders stereolithography indispensable for specialized applications, particularly in medicine and other fields requiring exacting precision.

Selective Laser Sintering (SLS) is an advanced 3D printing technology with significant potential in the manufacturing of medical devices, especially oral films. This technique employs a laser to sinter powdered materials, such as polymers, forming solid objects layer by layer. SLS is celebrated for its ability to create complex structures with enhanced strength and durability, offering extensive opportunities within the medical sector. However, SLS faces its own set of challenges, particularly concerning the precise dosage control of active ingredients. This issue is crucial in the production of dosage forms, where accurate control over the quantity and distribution of active substances is essential. Furthermore, the selection of the appropriate polymer for production is critical, as it directly influences the quality and efficacy of the final medical product.

The polymers used in this process must meet high requirements for physicochemical and pharmacological characteristics, as well as ensure compliance with the specific properties required for oral films. The main criteria to consider when selecting polymers for oral film production include palatability, which is crucial for improving patient interaction, especially in pediatric medicine, and moisture resistance, as oral films must retain their shape and structure in conditions of high oral humidity. Additionally, appropriate surface tension is necessary to preserve the shape of the film during movement in the mouth and to promote better adhesion to the mucous membrane. Effective dissolution of active ingredients in saliva is required for the rapid release of active substances. To achieve these characteristics, synthetic polymers with properties such as biocompatibility, thermoplasticity, chemical and mechanical resistance are primarily used. Such polymers include Polycaprolactone (PCL), chosen for its bio-soluble properties and flexibility [2]; Polylactide (PLA), popular in the medical field due to its biocompatibility and biodegradability [3]; Polyvinylpyrrolidone (PVP), which provides good solubility in water, making it ideal for oral films; and Polyvinyl alcohol (PVA) and Hydroxypropylmethylcellulose (HPMC), known for their film-forming properties and used to create comfortable and effective oral films [4, 5, 6, 7].

Three-dimensional inkjet printing is a pivotal technology in the field of 3D printing, capable of creating highly detailed medical and pharmaceutical products. This method employs specialized fluids that must adhere to strict viscosity and surface tension parameters to ensure proper droplet formation, placement, and adhesion to the print platform. For adequate droplet formation, the liquid should have a viscosity ranging from 10 to 20 mPa·s and a surface tension between $28–42\ mNm^{-1}$. These criteria restrict the choice of active substances and other materials,

as not all can conform to such specific requirements. Excessively high viscosity can hinder the droplet's exit from the nozzle, while too low viscosity may cause the liquid to spread uncontrollably on the surface, distorting the image and compromising the quality of the printed product. Additionally, the surface tension of the liquid influences the interaction of the droplet with the printed surface; thus, maintaining the optimal balance of these parameters is critically important. Another significant challenge is the chemical compatibility of active substances with the carrier liquid. Incompatibility can lead to precipitation or alter the physical properties of the fluid, adversely affecting both the printing process and the quality of the final product. It is crucial that active substances remain stable and effective throughout all stages of printing to ensure the drug's efficacy. Factors such as high temperatures, UV radiation, and other processing variables may compromise the stability of active components and require careful management. Ongoing research aims to develop new polymers and materials that not only meet the required viscosity and surface tension specifications but also provide enhanced chemical and mechanical stability. Moreover, the use of natural materials like cellulose, starch, and gelatin, which offer greater biocompatibility and lower toxicity, frequently encounters challenges related to insufficient mechanical strength and stability—issues that are currently being addressed through scientific advancements. In extrusion methods of creating films, variations in the viscosity of the carrier after component mixing pose further challenges. Such changes can significantly impact print quality and the final product; improper mixing before printing may clog the printer nozzle, while post-printing mixing might degrade product performance. The issue of viscosity is particularly critical when utilizing diverse types of polymeric materials, each with distinct solubility properties. These range from insoluble materials such as ethyl cellulose and Eudragit RL, to fast-dissolving substances like polyethylene oxide (Kollicoat IR), enteric soluble materials (Eudragit L, HPMC acetate succinate), and swelling agents (PVA, hydrophilic cellulose derivatives, Soluplus). Specialized filaments designed for 3D printers must conform to these characteristics to ensure both efficient printing processes and high-quality final products[9]. Furthermore, in the realm of light-based 3D printing technologies, particularly those employing LCD methods, the compatibility of polymer materials with lithographic processes is crucial. This compatibility ensures that the materials properly interact with the technology, maintaining quality and functionality throughout the printing process.

The polymers employed in these processes must be capable of hardening under the influence of LED light transmitted through liquid crystal displays. Materials such as Hydroxypropyl Methylcellulose (HPMC), Polyethylene Glycol Diacrylate (PEGDA), Tartrazine, Diphenyl (2,4,6-trimethylbenzoyl) Phosphine Oxide (TPO), and Polyethylene Glycol (PEG) are selected for their properties that render them effective under the specific conditions of these printing technologies. The task for developers extends beyond merely selecting appropriate materials; it also involves optimizing the mixing and printing processes to ensure high quality, efficiency, and reproducibility of dosage forms [10]. Developing new materials and technologies is crucial for addressing current challenges and enhancing the capabilities of 3D printing in the medical and pharmaceutical sectors.

CONCLUSIONS

The research conducted has established extrusion 3D printing as the most effective method for producing oral films within the pharmaceutical industry. This technology offers numerous advantages, making it exceptionally suitable for medical applications, particularly in the realm of personalized treatment. Primarily, extrusion 3D printing facilitates high-precision dosing of active ingredients, crucial for pharmaceuticals where each dose must adhere to stringent standards. The uniform distribution of these ingredients across the film ensures consistent effectiveness, vital for the therapeutic process. Moreover, the capabilities of this technology allow for the customization of dosage forms to meet individual patient needs, enabling the production of medicated films with varied dosages, shapes, sizes, and formulations tailored to specific medical requirements. This adaptability and precision, coupled with the potential for rapid prototyping and scalability of production, significantly enhance the prospects for advancing the efficacy and safety of medications. The deployment of extrusion 3D printing is set to drive progress in the pharmaceutical industry by introducing innovative manufacturing solutions and improving patient care through customized treatment approaches. Looking forward, this technology is poised to play a pivotal role in the development of more effective and safer medications, thereby expanding the capabilities of modern medicine substantially.

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