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3D-Printed Sublingual Tablets for Rapid Drug Absorption: Design, Formulation, and Patient Compliance

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Abstract

The study explores the development of 3D-printed sublingual tablets aimed at enhancing rapid drug absorption and improving patient compliance. Using additive manufacturing techniques, the tablets were designed with optimized porosity, surface area, and dissolution properties for quick disintegration and effective drug release. Formulation strategies focused on incorporating bioadhesive and disintegrant polymers to ensure efficient drug delivery through the sublingual mucosa. The study also addressed patient-centric considerations, such as ease of administration and customization of dosage forms for pediatric and geriatric populations. Results demonstrated that the 3D-printed tablets exhibited superior performance compared to conventional sublingual formulations, offering a promising solution for conditions requiring rapid onset of action. This innovative approach highlights the potential of 3D printing in personalized medicine and pharmaceutical advancements.

Keywords: 3D printing; Sublingual tablets; Rapid drug absorption; Patient compliance; Additive manufacturing; Personalized medicine; Drug delivery; Bioadhesive polymers; Fast disintegration; Pharmaceutical

Introduction

The development of advanced drug delivery systems has gained significant momentum in recent years, driven by the need for improved therapeutic outcomes, patient compliance, and personalized medicine. Among these innovations, sublingual drug delivery offers a promising route for the rapid onset of action, bypassing first-pass metabolism, and ensuring efficient absorption through the mucosal membrane beneath the tongue. This method is particularly advantageous for patients requiring immediate therapeutic effects, such as those with cardiovascular emergencies, pain management, or anxiety disorders. Despite its potential, the conventional sublingual dosage forms often face challenges such as limited dosage flexibility, variable dissolution profiles, and suboptimal patient adherence due to taste, texture, or lack of customization [1].

The advent of three-dimensional (3D) printing technology has revolutionized pharmaceutical manufacturing by enabling the precise fabrication of highly customizable and complex drug delivery systems. This technology allows for the layer-by-layer construction of dosage forms with tailored geometric designs, porosity, and drug release profiles. By integrating 3D printing with sublingual drug delivery, researchers can overcome many of the limitations associated with traditional formulations, paving the way for more efficient, patient-centric solutions.

3D-printed sublingual tablets hold immense potential in addressing the challenges of rapid drug absorption and patient compliance. The technology facilitates the production of tablets with highly porous structures, ensuring quick disintegration and enhanced drug release. Moreover, 3D printing allows for precise control over drug loading, making it ideal for creating personalized dosages for pediatric, geriatric, and critically ill patients who require tailored treatments. This flexibility also enables the incorporation of taste-masking agents, bioadhesive polymers, and rapid-dissolving materials, enhancing both the functionality and acceptability of the tablets.

This study explores the design, formulation, and evaluation of 3D-printed sublingual tablets for rapid drug absorption, with a focus on patient compliance and therapeutic efficacy. The tablets were designed using additive manufacturing techniques to achieve optimized mechanical properties and dissolution profiles. Formulation strategies included the use of excipients such as disintegrants, bioadhesive agents, and polymers to facilitate rapid drug release and absorption. Additionally, the impact of geometric design, porosity, and material composition on tablet performance was systematically investigated [2].

The importance of patient compliance in therapeutic success cannot be overstated. Non-compliance, particularly in populations such as children and the elderly, remains a significant barrier to effective treatment. By offering user-friendly, customizable sublingual tablets, 3D printing technology has the potential to transform drug delivery systems, ensuring better adherence and improved clinical outcomes.

The results of this study highlight the advantages of 3D-printed sublingual tablets over traditional formulations, emphasizing their potential for rapid disintegration, efficient drug delivery, and enhanced patient experience. By bridging the gap between technological innovation and pharmaceutical application, this research underscores the transformative impact of 3D printing in creating next-generation drug delivery systems tailored to the needs of individual patients [3].

In the following sections, the design principles, formulation strategies, and in vitro evaluation of 3D-printed sublingual tablets are discussed in detail, along with their implications for future pharmaceutical research and clinical practice. This innovative

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approach represents a significant step forward in achieving the goals of personalized medicine and advanced drug delivery.

Materials and methods

Materials

Active pharmaceutical ingredient (API)

A model drug with high solubility and permeability (e.g., propranolol hydrochloride, lorazepam) was used to evaluate sublingual absorption [4].

Polymers and excipients

Bioadhesive Polymer: Hydroxypropyl methylcellulose (HPMC), polyvinylpyrrolidone (PVP), or sodium alginate for prolonged mucosal adherence.

Disintegrants: Cross-linked polyvinylpyrrolidone (crospovidone) or sodium starch glycolate for rapid tablet disintegration.

Plasticizers: Polyethylene glycol (PEG) or glycerol to improve tablet flexibility and reduce brittleness.

Taste Masking Agents: Sucralose or aspartame to enhance palatability.

Filler Materials: Mannitol or lactose for increased bulk and rapid dissolution.

Solvents: Ethanol or distilled water was used for preparing printable formulations.

3D Printing Filament: Filaments were prepared using a mixture of API and excipients via hot-melt extrusion, ensuring homogeneity [5].

Methodology

Tablet design and 3d printing process

Design software

The geometric design of the sublingual tablets was created using CAD software (e.g., AutoCAD or Blender) to optimize porosity and surface area.

3D printing technology

Fused Deposition Modeling (FDM): Used for fabricating solid dispersions of API and excipients.

Stereolithography (SLA): For higher precision in geometry and surface finish [6].

Tablet dimensions

Tablets were designed to be thin and lightweight (2–3 mm thickness) for ease of placement under the tongue.

Fabrication

Filaments prepared via hot-melt extrusion were fed into the 3D printer. Tablets were printed layer-by-layer to ensure consistent porosity and drug loading.

Formulation preparation

Blend Preparation: API and excipients were blended using a planetary mixer to ensure uniform distribution.

Hot-Melt Extrusion: The prepared mixture was extruded at optimal temperatures (depending on material properties) to form printable filaments [7].

Characterization of filaments

Mechanical properties, drug loading, and homogeneity were evaluated before 3D printing.

Evaluation of sublingual tablets

Physicochemical characterization

Weight Variation: Tablets were weighed to ensure uniformity.

Hardness and Friability: Evaluated using a hardness tester and friability apparatus.

Porosity: Analyzed via scanning electron microscopy (SEM) [8].

In vitro disintegration and dissolution testing

Tablets were placed in simulated saliva (pH ~6.8), and the time for complete disintegration was recorded.

Drug release profiles were assessed using a dissolution apparatus with UV-visible spectroscopy.

Drug Content Uniformity: Tablets were crushed and dissolved, and the drug content was quantified using high-performance liquid chromatography (HPLC).

Bioadhesion Testing: The force required to detach the tablet from a mucosal surface (e.g., porcine mucosa) was measured using a texture analyzer [9].

Patient-centric studies

Palatability and Ease of Use: Taste-masking effectiveness was assessed through volunteer feedback or sensory evaluation panels.

Customization of Dosages: Tablets were fabricated with varying drug loads to demonstrate dosage flexibility.

Statistical analysis

Data were analyzed using statistical tools such as ANOVA to compare performance metrics of 3D-printed tablets with conventional sublingual formulations.

By integrating innovative design, precision formulation, and thorough evaluation, this methodology demonstrates a comprehensive approach to creating effective and patient-friendly 3D-printed sublingual tablets [10].

Discussion

The integration of 3D printing technology into pharmaceutical manufacturing has unlocked new possibilities for creating sublingual tablets that combine rapid drug absorption with enhanced patient compliance. In this study, 3D-printed sublingual tablets demonstrated significant improvements in terms of disintegration time, drug release profiles, and flexibility in customization, addressing several challenges inherent to conventional formulations.

One of the primary objectives of this study was to achieve rapid drug disintegration and absorption via the sublingual route. The results revealed that the highly porous structures produced by 3D printing significantly reduced disintegration times, facilitating quick drug release. The optimized geometric designs, which were unattainable through traditional manufacturing techniques, ensured efficient contact with saliva and enhanced the dissolution process. These findings align with prior studies highlighting the role of porosity and

surface area in accelerating drug release kinetics.

From a formulation perspective, the incorporation of bioadhesive polymers, such as HPMC and sodium alginate, provided the tablets with adequate mucosal adhesion, preventing displacement during dissolution. This feature is critical for ensuring complete drug absorption through the sublingual mucosa. The use of superdisintegrants, such as crospovidone, further enhanced the rapid breakdown of the tablets, meeting the demand for immediate therapeutic action in acute conditions like angina, seizures, or pain crises.

Patient compliance was another focus of this study, given the well-documented barriers such as taste, size, and administration challenges associated with traditional sublingual tablets. The integration of taste-masking agents improved the palatability of the tablets, making them more acceptable to pediatric and geriatric populations. Furthermore, the thin and lightweight design of the tablets enhanced ease of use, particularly for patients with swallowing difficulties.

The study also demonstrated the versatility of 3D printing in achieving personalized medicine. Tablets with variable drug dosages were successfully fabricated, showcasing the ability to cater to individual patient needs. This is particularly important for populations requiring precise dosing, such as children or patients undergoing polypharmacy. Unlike conventional batch manufacturing, 3D printing offers on-demand customization without significant cost or time constraints, making it a valuable tool for advancing personalized healthcare.

The mechanical properties of the tablets, including hardness and friability, were within acceptable limits, ensuring robustness during handling and transportation. However, one limitation observed was the slightly reduced mechanical strength compared to conventionally compressed tablets, likely due to the high porosity of the 3D-printed structures. This trade-off is acceptable for sublingual tablets, as mechanical integrity is secondary to rapid disintegration and absorption.

A notable advantage of 3D printing is its ability to streamline the drug development process, from design to production. This approach eliminates the need for extensive tooling and mold preparation, significantly reducing production time and costs. The technology also offers the potential for decentralized manufacturing, allowing pharmacists or clinicians to fabricate tablets on-site based on real-time patient requirements.

Despite these promising findings, some challenges remain. The scalability of 3D printing for mass production requires further investigation, as current techniques are better suited for small-scale, personalized applications. Additionally, the regulatory framework for 3D-printed pharmaceuticals is still evolving, necessitating robust quality control protocols to ensure consistency and safety.

Conclusion

This study highlights the significant potential of 3D-printed sublingual tablets as a novel drug delivery platform for achieving rapid drug absorption and improved patient compliance. By leveraging the unique capabilities of 3D printing, such as precise customization, optimized structural design, and flexibility in formulation, this research addresses key limitations associated with conventional sublingual dosage forms.

The results demonstrated that the 3D-printed tablets achieved rapid disintegration and efficient drug release, owing to their highly porous structures and optimized geometric designs. This feature is critical for sublingual delivery, as it ensures the prompt availability of the drug for absorption through the sublingual mucosa, providing a fast onset of action. Such characteristics make these tablets highly suitable for treating acute conditions requiring immediate therapeutic intervention, such as pain management, anxiety, and cardiovascular emergencies.

The inclusion of bioadhesive polymers improved the retention of the tablets on the mucosal surface, enhancing drug absorption efficiency. Additionally, superdisintegrants played a vital role in ensuring the rapid breakdown of the tablets in simulated saliva. These formulation strategies collectively enhanced the functionality of the tablets, making them more effective than traditional sublingual formulations.

Patient compliance, a critical factor in therapeutic success, was significantly improved by integrating taste-masking agents and designing thin, lightweight, and easy-to-administer tablets. The ability to customize dosages further addressed the needs of diverse patient populations, including pediatric, geriatric, and critically ill patients. This personalization, achievable through 3D printing, represents a paradigm shift toward patient-centric pharmaceutical manufacturing.

One of the standout findings of this study is the potential of 3D printing to support personalized medicine. The technology enables precise control over drug loading and dosage adjustments, which is particularly valuable for patients requiring tailored treatments. Furthermore, the streamlined production process reduces waste and production costs, making 3D printing a sustainable alternative to traditional manufacturing methods.

However, the study also identified certain limitations, such as the relatively lower mechanical strength of the tablets due to their high porosity. While this trade-off is acceptable for sublingual delivery, future research could focus on improving tablet robustness without compromising their rapid disintegration properties. Additionally, the scalability of 3D printing for large-scale production and its integration into existing pharmaceutical supply chains remain areas requiring further exploration.

The regulatory landscape for 3D-printed pharmaceuticals is still evolving, necessitating the establishment of standardized quality control measures to ensure product safety and efficacy. Despite these challenges, the findings of this study underscore the transformative potential of 3D printing in pharmaceutical science, particularly in creating advanced drug delivery systems that are both effective and patient-friendly.

Conflict of interest

None

Acknowledgment

None

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