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3D Printing for a Novel Ibuprofen Tablet with Gastroprotective Effect

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SUMMARY

3D printing has the potential to play a significant role in pharmaceutical research by optimizing medication usage and minimizing adverse effects. However, various obstacles hinder the full utilisation of this technology to optimise the efficacy of numerous medications such as the quality of tablets, speed of printing etc. Among the various 3D printing techniques, FDM printers combined with HME stand out as one of the most widely used due to their ability to produce high-quality products without the need for organic solvents, however, the elevated temperatures required during these processes raise concerns about the stability of the components within the dosage form. Therefore, it becomes crucial to manage various critical factors, particularly the selection of appropriate polymers and drug-release modifiers, to achieve the desired dosage form. To address this, the present study aims to develop a novel tablet of ibuprofen with an enteric coating-like effect using 3D printing technology coupled with hot melt extrusion (HME).

INTRODUCTION

3D printing is a technique that used a computer-aided design to fabricate a structure layer by layer. The utilization of 3D printing in the pharmaceutical industry has seen a significant rise in recent years due to its potential to decrease production time and costs (Ehtezazi et al., 2018). It enables the production of personalized medicines and can enhance the physiochemical properties of various drugs, such as improving the solubility and release rates of certain medications (Shi et al., 2021).

One of the primary technologies utilized in 3D printing for pharmaceutical manufacturing is Fused Deposition Modelling (FDM). FDM is a technique that uses a heated nozzle to extrude a thermoplastic filament to a building plate form. This technology is notable for its capability to create high-quality products without the need for organic solvents (Bandari et al., 2021). Moreover, coating ibuprofen plays a significant role in enhancing the drug's effectiveness and reducing adverse effects (Irvine et al., 2018). This research aims to develop an ibuprofen formulation with a gastroprotective effect through the utilisation of 3D printing technology. The goal is to enhance the therapeutic effectiveness of ibuprofen while simultaneously reducing its associated side effects.

MATERIALS AND METHODS

The sustained-release filament is created through hot melt extrusion (HME), which comprises ibuprofen, ethyl cellulose sourced from Sigma-Aldrich, and Eudragit L 100-55 sourced from Evonik.

The filament was formulated using 2g of ibuprofen, 6g of ethyl cellulose, and 2g of Eudragit L 100-55 (formula 1-F1) and a control filament was formulated by using ibuprofen 2g and Ethyl cellulose 8g (controlled formula-CF). F1 was extruded at 100°C and printed at 165 °C, while CF was extruded at 100°C and printed at 175°C. The bed temperature was 50°C. The drug and excipients were extruded using a single-screw Noztek Pro Filament Extruder (Noztek, LLC, UK) to create the filament. The printed tablets were produced using a MakerBot FDM 3D printer. The tablet design was accomplished using dedicated software known as TinkerCad. In vitro release testing

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was conducted using UV-spectroscopy at a wavelength of 220 nm and Two calibration graphs were used one with phosphate buffer at pH 7.2 and another with hydrochloric acid 0.1 M pH 1.2.

RESULTS AND DISCUSSION

The formulation was extruded to produce the filament with a thickness of 1.7 mm, which exhibited satisfactory mechanical properties that make it printable. Subsequently, this filament was utilized in printing the designed tablet with an infill of 30 %, and the printing temperature was lower than what was previously reported (Shi et al., 2021). The tablet's dimensions were set at 15 mm in length, 6 mm in width, and 3 mm in thickness, with an average weight of 0.2g (Fig. 1).

In F1, Eudragit L 100-55 acts as the release modifier, while ethyl cellulose serves as the main polymer in the formula. This innovative approach allows the production of an ibuprofen enteric-coated-like effect formulation in a one-step process without the use of solvents as in previous work (Hao et al., 2013).

Table 1. *Drug release after 24 hours*

	Average tablet weight (mg)	Drug release (mg/L) [a]	Percentage release (%)
F1 in HCl acid	204.4	1.52	3.40
F1 in buffer pH 7.2	209.23	5.82	15.19
CF in buffer Ph 7.2	215.5	1.99	4.56

[a] Drug release after 24 hours.

Consequently, in vitro analysis of the formulation demonstrated that ibuprofen was released in alkaline media more than its release in acidic media (Tab.1). This distinct drug release pattern was achieved by application of Eudragit L 100-55 in the enteric coating.

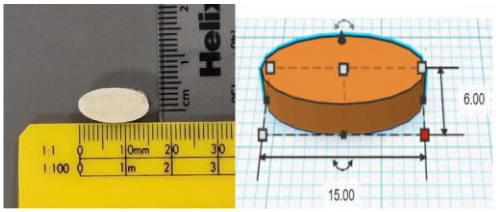

Fig. 1. *Tablet designed and tablet printed.*

CONCLUSIONS

In conclusion, 3D printing presents an excellent opportunity for manufacturing ibuprofen tablets with gastroprotective properties. The release modifier (Eudragit L 100-55) enhances the solubility and release of ibuprofen in alkaline compared to acidic environments and control, facilitating dissolution in the small intestine rather than the stomach which will give the desired protective effect.

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