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Original article

Sustained Release of Linalool from DLP 3D-Printed Films for Topical Antimicrobial Applications

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ABSTRACT

Background: Linalool is a naturally occurring antimicrobial agent with potential applications in dermatological treatments. Achieving sustained and controlled release of such volatile compounds remains a challenge in topical delivery systems. Digital Light Processing (DLP) 3D printing offers precise control over formulation parameters, enabling the fabrication of customised polymeric films with tailored release properties.

Aims: This study aimed to investigate the sustained-release characteristics of linalool from DLP-printed polymeric films, examining the influence of formulation and printing parameters on release kinetics and therapeutic performance.

Method: Photocurable resins were loaded with linalool at varying concentrations and processed into films using DLP 3D printing under different conditions, including variations in resin type and projector power. Linalool release was quantified using High-Performance Liquid Chromatography (HPLC). Structural and thermal properties were characterised via Fourier Transform Infrared Spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC). Antibacterial activity was assessed to determine therapeutic applicability.

Results: Resin composition and linalool concentration significantly influenced release kinetics, with higher loading levels resulting in increased release rates. Projector power variation did not produce notable changes in the release behaviour. Films containing 20% w/w linalool exhibited strong activity against *Staphylococcus aureus* demonstrating both efficacy and sustained-release properties.

Conclusion: DLP 3D printing enables the fabrication of customised polymeric films capable of sustained linalool release, with performance through formulation adjustments. These findings suggest a promising approach for the development of topical antimicrobial delivery systems, particularly for dermatological conditions such as acne.

KEYWORDS: 3D Printing; Dlp; Linalool; Skin Infections

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INTRODUCTION

Staphylococcus aureus commonly referred to as *S. aureus* is a Gram-positive bacterium that naturally colonizes human skin and nasal passages. While often harmless as a commensal organism, it can become pathogenic when skin integrity is compromised, or the immune system is weakened (Honeyman A. et al, 2002). *S. aureus* is notably implicated in various dermatological infections, including acne and folliculitis. Standard treatments for *S. aureus*-related infections include β -lactam antibiotics such as flucloxacillin (Moser et al, 2021) and cefazolin (Li et al, 2017). However, the emergence of antibiotic-resistant strains, including methicillin-resistant *S. aureus* (MRSA), has raised concerns regarding treatment efficacy and the need for alternative antimicrobial strategies. As a result, natural compounds, especially essential oils, have garnered interest for their antimicrobial properties. Studies have demonstrated that essential oils like thyme (Puskarova et al, 2017) and lavender (Shirkhani et al, 2015) possess antifungal property. Lavender oil, for example, is marketed in over-the-counter oral supplements, though its use can be limited by dosage form challenges such as difficulty swallowing large capsules.

Acne is a chronic and recurrent inflammatory condition of the skin, and short-term treatments often result in relapse. Therefore, there is growing demand for topical formulations that can retain active ingredients on the skin surface and deliver them in a controlled, sustained manner. Sustained-release (SR) patch-type formulations are particularly promising in this context. While microsphere- and liposome-based (Zambom et al, 2019) delivery systems have shown potential, their widespread application is hindered by complex manufacturing processes, high production costs, and limited physicochemical stability.

To overcome these limitations, three-dimensional printing (3DP) has emerged as a novel and versatile platform for fabricating sustained-release drug delivery systems (Rowe et al, 2000). Among the various 3DP techniques, Digital Light Processing (DLP) has attracted attention in the medical and cosmetic fields due to its precision, speed, and ability to fabricate finely structured objects via photopolymerization (Goyanes et al, 2015). In DLP printing, an entire layer of photosensitive resin is simultaneously cured using a projector, unlike stereolithography (Arcaute et al, 2010), which cures resin point by point using a laser. This allows for rapid fabrication of multilayered structures with high spatial resolution. Notably, DLP printing enables the incorporation of active pharmaceutical ingredients (APIs) directly into the resin prior to curing. Because DLP involves minimal thermal stress during fabrication, it is particularly suitable for formulating APIs that are sensitive to heat (Shi et al, 2023). Parameters such as light intensity, exposure time, layer thickness, and resin composition can all influence the drug release profile from the printed matrix (Ali et al, 2022).

Among potential active compounds, linalool has been recognized for its broad-spectrum antimicrobial and antifungal properties. Linalool is a naturally occurring monoterpene alcohol found in lavender and other essential oils. In medical applications, linalool has been shown to be effective against fluconazole-resistant strains of *Staphylococcus aureus*, with mechanisms involving interactions with ergosterol in fungal cell membranes, leading to disruption of membrane integrity. Other studies have also reported that linalool inhibits membrane biosynthesis, increasing ion permeability and exerting fungicidal effects (Li et al., 2022).

Linalool was selected as the model drug in this study due to its antimicrobial potential and relevance to skin infections such as acne. The primary aim of this study is to investigate the release and sustained-release characteristics of linalool from DLP-printed films using high-performance liquid chromatography (HPLC). Various formulation and printing conditions were tested to understand how these factors influence the drug release profile. Subsequently, optimal conditions were identified and applied in further evaluations including antibacterial testing, Fourier-transform infrared spectroscopy (FTIR), and differential scanning calorimetry (DSC). This study contributes to the growing field of personalized drug delivery systems by proposing a novel and tenable approach to topical acne treatment using DLP-based sustained-release films.

MATERIALS AND METHODS

MATERIALS

The API used in the formulation was Linalool (CAS number 78-70-6) purchased from Sigma Aldrich. The resin used in this formulation was Ultracur3D FL300 and Ultracur3D EL 60 purchased from FORWARD am based on Germany.

Methods

Preparation of films

The formulations are provided in Table 1. F1 was printed as a standard by adding 9 mL Ultracur FL300 and 1-mL Linalool following the user guide of company where resins were purchased into the centre of the petri dish. After printing, the printlet was soaked in 10 mL of water to wash off the uncured liquid resin on the surface of the film. In F2, the project power increased from 20% to 30%. In F3, the resin was changed from Ultracur FL300 to EL60. In F4, the linalool concentration in the pre-printing solution increased to 20 %. The differences in linalool release for each entry are observed using HPLC.

Formulation	Linalool %(v/v)	Resin	Power (%)
F1	10	FL300	20
F2	10	FL300	30
F3	10	EL60	20
F4	20	FL300	20

1. Table 1 compositions of different 3D printed linalool films by DLP.

3D printing of films

The films were printed using Digital light processing Cellink Lumen X supplied at UK office. The film was designed to be a small serpentine film with a length of 13.00 mm; a width of 9.00 mm and height of 3.00 mm. Body exposure time 4s, body exposure time factor 1X and project power level 20% for Entry 1.3.4, 30% for Entry 2. The height of each layer was 100µm. The printing time was 8 minutes.

Determination of linalool concentration in the film over time

The released amounts of linalool in each film were determined by applying a previously reported high performance chromatography (HPLC) method. Briefly, an Agilent 1200 series HPLC (Stockport, Cheshire, UK) was used with an RP C-18 column (4.6 mm × 150 mm, 5 µm; Waters®, USA) employing an acetonitrile and water (35/65 v/v) as the mobile phase with a flow rate of 1.0 mL/min. The column temperature was set to 25°C and the detection spectrophotometer was set at 210 nm, with a sample injection volume of 5 µL. Solutions of linalool (97 %) were used to prepare the calibration curve. It showed excellent results for linalool aqueous solution with R² of 0.9982. A single film was placed into a membrane tube and both ends were sealed. The tube was then immersed in a conical flask containing 50 mL of deionized water, maintained at 32 °C. A magnetic stir bar was used to stir the water in which the tube was immersed. Each experiment was performed in triplicate. The results are given as mean ± standard deviation (SD).

FTIR

FTIR spectra were obtained for films using an Agilent 4500a instrument. This is headquartered at California in USA. The system was connected to Micro lab PC software. The samples were analysed in the 4000–650 cm⁻¹ range under ambient conditions; a soft cleaning wipe and isopropanol was used to carefully clean the diamond in the FTIR stage which was then followed up with a background scan. Once a background scan had been taken, a printed film was placed on the FTIR stage in direct contact with the diamond, which was secured by releasing the lever and twisting it into place. Spectra were then taken and then exported to a USB pen drive. The same steps were repeated for three times.

Antibacterial Activity

Agar diffusion method was employed to evaluate antibacterial activities of linalool films. Briefly, Savoured dextrose plates (10g dextrose, 2.5g yeast, 28g of agar powder per litre) were inoculated with *Staphylococcus aureus*. Previous work has shown that the linalool antibacterial minimum inhibitory concentration was in the range of 256 µg/mL to 512 µg/mL. Then films comprising linalool each about 20 mg were placed on the agar plates and inoculated with 0.2 mL of *Staphylococcus aureus*. The plates were incubated at 25°C for three days and examined. Negative control plates did not contain film but did contain the microorganism. The experiments were repeated three times.

Differential scanning Calorimetry

DSC analysis (DSC 7; Perkin Elmer®, Waltham, MA, USA) was used to analyse the thermal characteristics of powder mixtures, filaments and FDFs. The process involved a nitrogen flow rate of 20 mL/min and a heating rate of 20°C/min. The samples were heated up to 220 °C. An indium standard was used to calibrate the system. The minimum and maximum values of the endothermic and exothermic peaks, respectively, were used to determine the melting (T_m) point.

Weight Uniformity

When collecting the weight uniformity of the films, 3 films each formulation when weighed individually using a weighing balance and the average, along with the standard deviation were calculated.

RESULTS AND DISCUSSION

Images of each formulation

Once cured, the resin did not dissolve in any solvent containing water. Its colour was white, and transparency increased as the concentration of linalool increased. Compared to the conventional square shape, this design was selected for its greater complexity and to increase the surface area. Although there are limitations in height, both the width and length can be realized with high precision. The thickness of each layer was set at 0.1 mm. Film with linalool were successfully printed with DLP printer. The printed film showed uniformity in size as well.

Figure 1 shows printed serpentine films respectively.

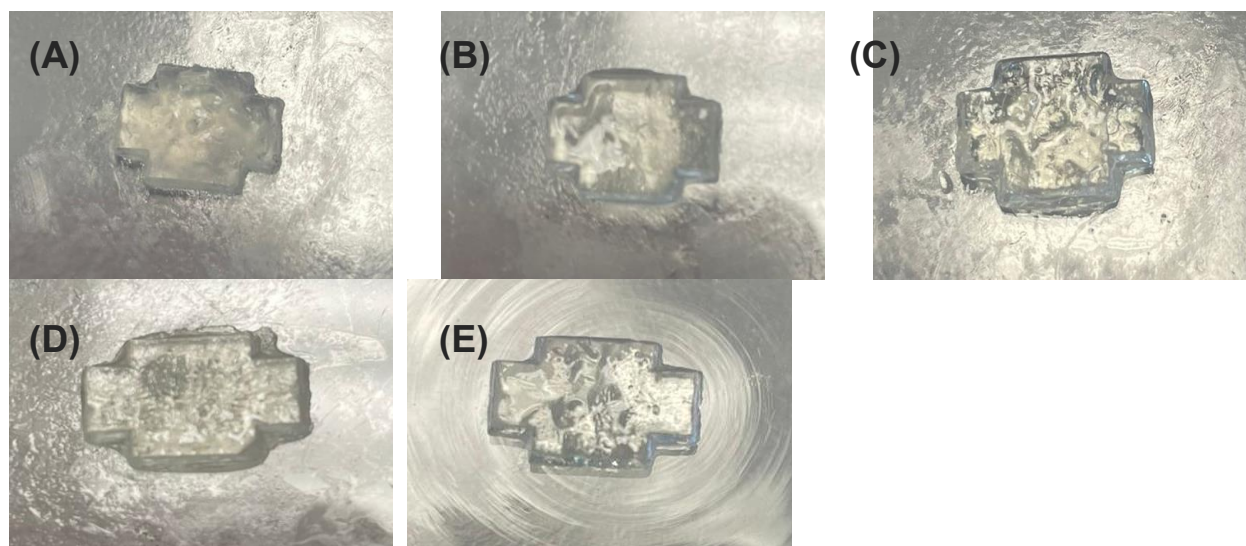


Figure 1 Images of 3DP film with (A) blank, (B) Formulation 1, (C) Formulation 2, (D) Formulation 3 and (E) Formulation 4.

Weight Uniformity

Figure 2 shows the weight uniformity and standard deviation of the weight uniformity of each formulation film respectively. Compared to the blank, Formulation F1 showed a decrease in weight and greater variability. In contrast, in F2 and F3, changes such as using a different type of resin or increasing the project's power resulted in increased weight and reduced variability. These outcomes suggest that higher-precision printing was achieved. Additionally, it was indicated that increasing the concentration of linalool may affect the durability of the films.

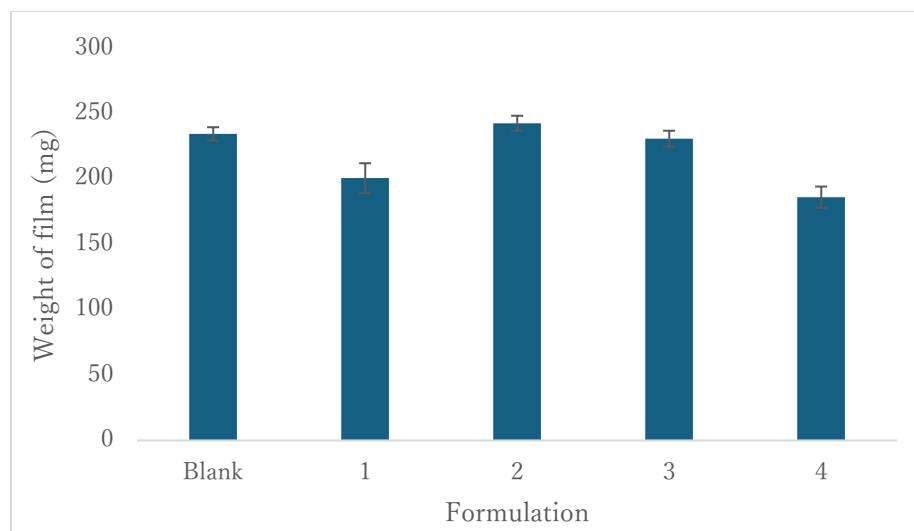


Figure 1 Weight of uniformity for each formulation. Error bars show SD (n=3)

Determination of linalool shown ration in the film over time

Figure 3 shows the amount of linalool released over time. To ensure reproducibility, each measurement was conducted three times. The concentrations were calculated using a calibration curve, and the release percentage relative to the theoretical value was determined. To avoid solubility issues with linalool, its content was limited to a maximum of 20%. Elution began immediately after immersion, and under all conditions, the release was completed within 24 hours. F1 condition was treated as the standard, and comparisons were made with the entries listed below. It showed how changes in a single parameter affected the amount and behaviour of release compared to the standard conditions.

Quantification by HPLC revealed that the projector power had no significant effect on the amount of linalool released. When the resin was changed from FL300 to EL60, no noticeable difference was observed in the initial release amounts (e.g., at 1 hour or 6 hours). However, in the samples collected after 24 hours, formulations F1, F2, F4 (containing FL300 resin) exhibited a higher release amount compared to formulation F3 (containing EL60 resin). When the linalool concentration was increased from 10% to 20%, the amount of release also nearly doubled.

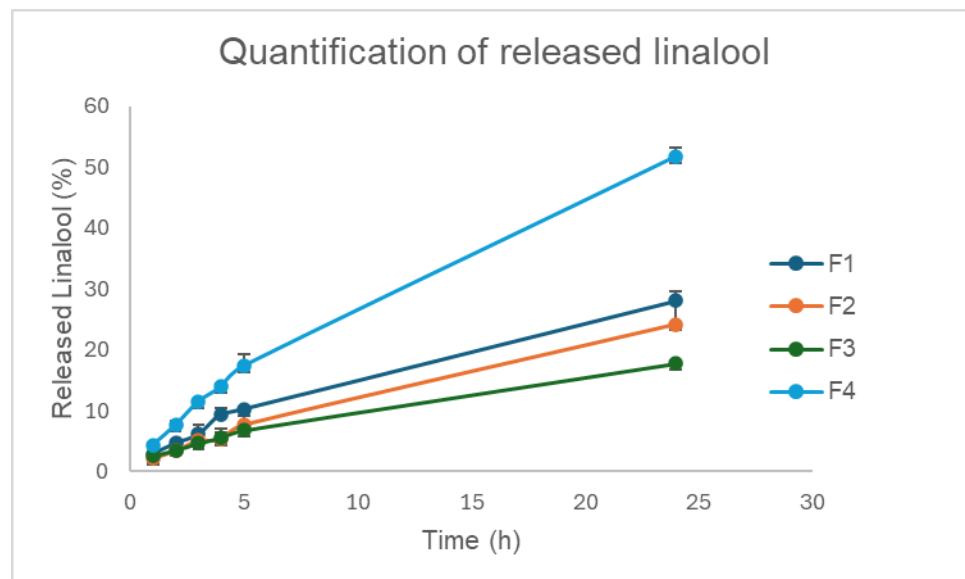


Figure 3 Linalool release profiles for different linalool films prepared by DLP 3D printing. Error bars indicate average SD (n=3).

FTIR

FTIR were comparable for the 20% Linalool formulation and film printed without linalool, suggesting that the linalool concentration is low, and its peaks are masked by the resin (Figure 4). Linalool constitutes only about 9% of the total formulation that is calculated from HPLC result, and with the detection sensitivity of FTIR (especially using the ATR method), its signals may be obscured.

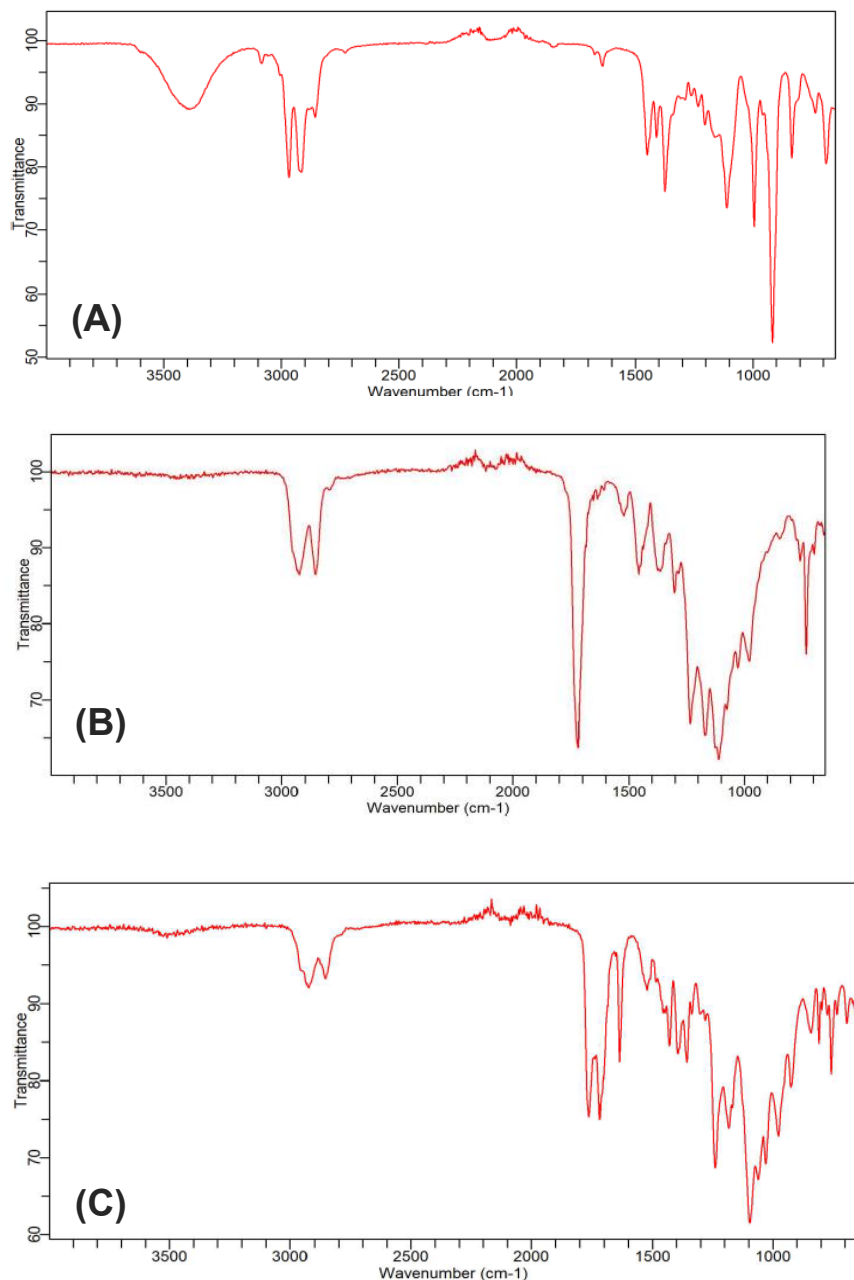


Figure 4 FTIR spectra; (A)Linalool only, (B)Resin only and (C)F4 (20%Linalool film).

Antibacterial Activity

Based on the HPLC results, formulation 4 was found to contain the highest amount of linalool; therefore, F4 was selected as the optimal formulation for testing in the following sections. Figure 5 illustrates the difference in antibacterial activity between a film without linalool and a film containing 20% linalool as a comparative experiment. No antibacterial activity was observed in the film without linalool, whereas the

20% linalool film showed clear inhibition around the film. These results indicate that the 20% linalool film contained enough linalool to exhibit antibacterial activity.

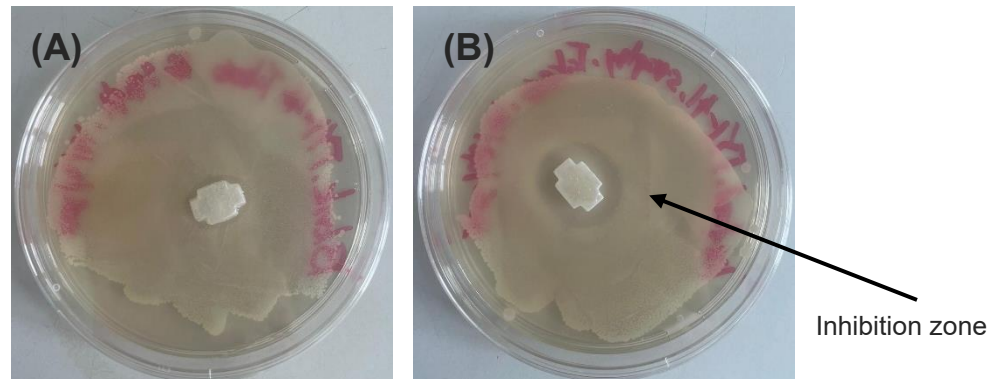


Figure 2 Antibacterial activity of (A) blank film and (B) F4 (20% linalool film).

DSC

DSC thermograms (Figure 6) presented only major melting points related to the polymers. However, the DSC thermograms (Figure 5) showed endothermic peaks at temperatures above 150°C for films (formulations 4) printed with 20% linalool. These observations suggested the evaporation of linalool from the film.

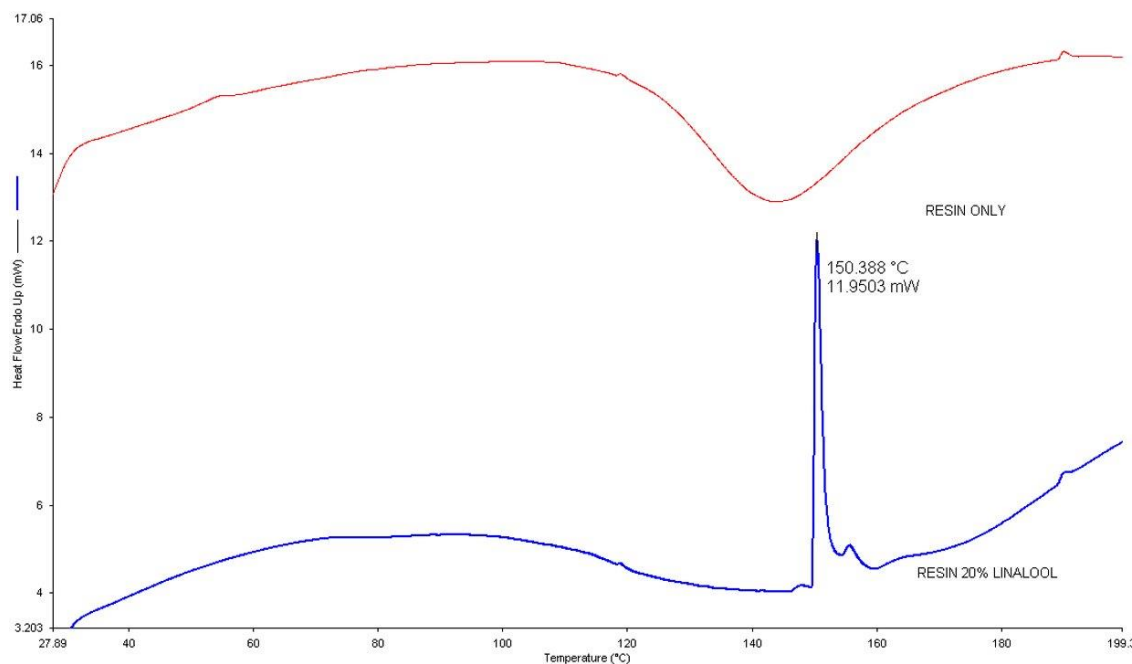


Figure 3 DSC thermograms of Blank and F4 (20% linalool film).

In this study, the release behavior of linalool from photopolymerized films fabricated by digital light processing (DLP) was quantitatively evaluated under various formulation and printing conditions. Linalool possesses volatility and hydrophobicity, making its controlled release highly dependent on its dispersion state and interactions within the polymer matrix. (Li et al, 1998). As shown in Figure 3, all formulations demonstrated sustained release over time, with elution beginning immediately after immersion and reaching completion within 24 hours. These findings suggest that the system exhibits not immediate burst release, but rather sustained-release properties suitable for prolonged delivery (Deng et al, 2025).

The percentage of linalool released increased in a time-dependent manner, with significant differences observed particularly between 6 and 24 hours. Under standard conditions (F1), a relatively consistent release profile was observed, whereas other conditions produced notable variations in both the amount and reproducibility of release. For instance, when the resin type was changed from FL300 (F1, F2, F4) to EL60 (F3), no significant differences in early-stage release (e.g., at 1 h or 6 h) were found. However, the cumulative release at 24 h was clearly higher in the FL300 containing formulations. This suggests that FL300 may possess superior long-term diffusivity or weaker interaction with linalool, allowing more complete release over time. These differences may be attributed to the resin's network density, polarity, or degree of cross-linking, all of which influence diffusion and retention behavior of small molecules (Wu et al, 2009).

In contrast, altering the projector power from 20% to 40% (F2) had little effect on release kinetics. This result indicates that increasing UV light intensity under the tested range did not significantly affect the degree of polymerization or network density to a level that would alter diffusion of linalool (Abedin et al, 2016). Therefore, under the specific DLP parameters used in this study, projector power can be considered a relatively minor factor in controlling release.

Notably, increasing the concentration of linalool from 10% to 20% (F4) led to an almost twofold increase in the amount of linalool released. This direct relationship between drug loading and elution supports the conclusion that the initial concentration gradient is a key driving force in the diffusion process. Higher concentrations may also lead to localized saturation within the matrix, thereby facilitating outward diffusion and increasing cumulative release. These results suggest that linalool concentration is a crucial modifiable factor in optimizing release performance.

From the perspective of pharmaceutical technology, sustained drug release offers multiple benefits, including reduced dosing frequency, improved patient compliance, and prolonged therapeutic efficacy (Sadosky et al, 2013). The DLP-based system explored in this study offers precise control over structural parameters such as the power of the light projector, the ratio of polymer and active ingredient, and the type of resin. This flexibility makes it well-suited for designing personalized drug delivery systems tailored to specific therapeutic requirements. The observed differences in release behavior highlight the importance of optimizing both resin composition and drug content to achieve desired release profiles.

Formulations containing FL300 resin exhibited numerous peaks corresponding to C–H, C=O, and C–O bonds. These overlap with key linalool signals, such as O–H stretching vibrations ($\sim 3400\text{ cm}^{-1}$) and C=C/C–O stretching ($1600\text{--}1100\text{ cm}^{-1}$), making it difficult to distinguish linalool from the resin background. The DSC thermograms clearly illustrate the differences in thermal behavior between the neat resin (red curve) and the resin containing 20% linalool (blue curve). A sharp endothermic peak was observed at approximately 150.4°C in the linalool-containing sample, with a peak intensity of 11.95 mW, indicating a significant thermal event attributable to linalool.

This endothermic peak is likely associated with the evaporation or volatilization of linalool from the polymer matrix. Although the boiling point of pure linalool is reported to be around 198°C , the onset of evaporation could have occurred at lower temperatures when linalool was physically entrapped or dispersed within a polymeric network (Shi et al, 2016). Factors such as polymer–linalool interactions, matrix permeability, and the open nature of the DSC measurement system could contribute to this shift. Therefore, the observed thermal peak near 150°C suggests that linalool begins to diffuse and vaporize from the matrix well before reaching its standard boiling point.

In contrast, the neat resin sample showed no such endothermic feature, confirming that this thermal event was uniquely associated with the presence of linalool. Additionally, in the linalool-containing film, a gradual

shift in the baseline can be observed between 100–180 °C, which may reflect progressive diffusion or partial evaporation of linalool over this temperature range.

These findings are consistent with the results of the release studies and support the hypothesis that the release behavior of linalool was governed not only by surface elusion but also by internal diffusion and temperature-dependent volatility. In the case of the 20% linalool-loaded film. The prominent endothermic peak further indicates that a substantial portion of linalool remained in a free or weakly bound state within the polymer matrix and was released rapidly upon heating.

From a formulation perspective, this thermal behavior highlights the importance of temperature control in both storage and application of such materials. The potential loss of active ingredients due to premature evaporation must be considered, especially for volatile compounds like linalool. To mitigate this, future designs may focus on modifying the resin system, increasing crosslinking density or selecting more hydrophobic matrices to better retain volatile actives and achieve more sustained release profiles.

CONCLUSIONS

Overall, this study showed possess inherent sustained-release capabilities and that the release performance is significantly influenced by the type of resin and the concentration of the active compound. In contrast, the effect of projector power appeared negligible under the conditions tested. These insights contribute to a deeper understanding of how formulation and processing parameters influence the diffusion of volatile actives such as linalool within 3D-printed polymer matrices.

Future work should focus on modeling the diffusion kinetics in more detail, as well as exploring microstructural analysis techniques such as SEM or AFM to elucidate the internal network structure of the films. In addition, expanding this approach to other active ingredients with different physicochemical properties could broaden the applicability of DLP-based drug delivery systems in both pharmaceutical and cosmetic fields.

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Conflict of interest

The authors have no conflict of interest regarding this article.

Authors contributions

TY: Conducted the experiments and prepared the draft manuscript.

SDS: Reviewed the manuscript and provided critical feedback.

TE: Designed the project and contributed to manuscript preparation.

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