Journal of Rare Cardiovascular Diseases
ISSN: 2299-3711 (Print) | e-ISSN: 2300-5505 (Online)
www.jrcd.eu
RESEARCH ARTICLE

3D Printed Curcumin Tablets Using FDM and PVA Filament: Strategies for Enhanced Absorption

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Article History
Received: 16.09.2025
Revised: 13.10.2025
Accepted: 29.10.2025
Published: 10.11.2025

Abstract: CUR optimized formulations were printed as 3D-printed tablets using fused deposition modeling (FDM) technology with polyvinyl alcohol (PVA) filaments. PVA, due to its water solubility and biocompatibility polymer, was used due to their quick disintegration character and compatibility with the gastro-intestinal fluids. Printable filaments were generated through hot-melt extrusion (HME) by blending CUR-loaded solid dispersions (SDs) with PVA in a manner to achieve homogeneous drug distribution. Important printing parameters like nozzle temperature (160–180°C) and bed temperature (60–80°C) were found to be optimized so that thermal degradation of CUR was prevented without compromising structural integrity. Curcumin-encapsulated 3D-printed porous-geometry tablets with enhanced surface area and minimized dissolution times were optimized. This was the initial use of FDM precision for dosing and geometry control of tablets, and this is one possible application for the development of personalized CUR delivery systems. Incorporation of Solid dispersion into 3D-printed PVA-based tablets bypassed CUR's poor bioavailability issue by attaining solubility enhancement with fast, site-specific delivery. This study indicates that the potential to use solid dispersion technology and 3D printing to counter the low bioavailability of weakly soluble drugs like CUR exists. Future research will aim at in vivo pharmacokinetic assessment and up-scaling of 3D-printed products for individualized therapy.

Keywords: Polyvinyl alcohol, drug distribution ,3D-printed porous.

INTRODUCTION

Oral solid dosage form design and production, particularly tablets, involve huge processes managing drug release and absorption following ingestion. Conventional methods of solubility enhancement rely on through expensive processes such as spraying drying , co crystals etc. Three-dimensional printing (3DP) holds a promise of groundbreaking substitution by simplifying production with the ability to design customized systems without the requirements of enormous infrastructure.
Fused deposition modeling (FDM), a low-cost and versatile 3DP technique, has gained acceptance in the pharmaceutical sector due to its ability to produce tablets with intricate geometries and controlled release patterns (Alhnan et al., 2016). FDM works with thermoplastic filaments, of which polyvinyl alcohol (PVA), a water-soluble biocompatible polymer, has been found to be highly promising as a carrier material due to its rapid disintegration, FDA approval for oral use, and stability in gastrointestinal fluids. Despite the fact that there are such advantages, high drug-loading PVA filaments' applicability to poorly soluble drugs like curcumin (CUR) has not been explored well. CUR is a bioactive polyphenol with anti-inflammatory, antioxidant, and anticancer activities, whose bioavailability is low owing to poor solubility and rapid metabolism (Anand et al., 2007).

While studies have explored PVA filaments for their application in the form of immediate-release dosage forms (Goyanes et al., 2014), most important gaps still remain regarding CUR-loaded PVA system optimization. Limitations include maintaining CUR stability after high-temperature extrusion, uniform drug distribution at high drug loadings (10–30%), and maintaining printability in addition to dissolution performance. earlier studies have focused on low drug-load filaments (<10%), leaving the potential of concentrated CUR-PVA systems unexplored. so that higher dose can be loaded
This study tests the hypothesis that PVA-based filaments are able to encapsulate CUR at high loads (10%, 15%, 25%, and 30% w/w) without any tableting excipients and support tailored release profiles through FDM-printed structures. HME conditions were optimized to prevent degradation of CUR, and filaments were characterized for thermal stability (DSC, TGA), crystallinity (XRD), and drug-polymer interactions (FTIR). Porous solid fill pattern tablets were printed in order to achieve optimal surface area and disintegration rate. Compressing the solid dispersions into tablet manufacturing process remains challenging due to multiple unit operations and scalability. Three-dimensional printing (3DP), specifically fused deposition modeling (FDM) using polyvinyl alcohol (PVA), offers a great alternative. Water-soluble and biocompatible polymer PVA enables direct printing of tablets with tailored geometries (e.g., porous lattices) that enhance disintegration and enhancing the drug release (Goyanes et al., 2015). By inclusion of CUR-loaded SDs in PVA filaments via hot-melt extrusion (HME), FDM circumvents traditional granulation and compression, streamlining production. The process maintains high accuracy in drug loading (10–30% w/w) and structural optimization (e.g., infill density, layer thickness) to optimize release kinetics.

This research opens up new possibilities for integrating CUR solid dispersions with FDM/PVA-based 3DP, offering a double-barreled solution to enhancing oral bioavailability: SDs address molecule-scale solubility, whereas 3DP rationalizes macroscopic tablet design. By comparison, conventional routes such as spray drying or hot-melt extrusion for SDs still require secondary processing (e.g., tableting), with attendant cost and complexity. The union of SDs and FDM is one step toward scalable, customized therapeutics for drugs with poor solubility.

MATERIAL AND METHODS

2.1. Materials

Curcumin (purity > 97%) was obtained from Chem-Supply (Port Adelaide, SA, Australia). Polyvinyl alcohol (PVA) was obtained finer PVA (Parteck® MXP, Mw ~ 31,000) from EMD Millipore Sigma (Burlington, MA, USA). Analytical grade solvents like tetrahydrofuran (THF), acetonitrile (HPLC grade), and dimethyl sulfoxide (DMSO) were used for preparation and analysis procedures. All other materials used were of pharmaceutical grade.

2.2. Methods

2.2.1.Preparation of Curcumin-Impregnated PVA Filaments

Curcumin (CUR)-loaded polyvinyl alcohol (PVA) filaments were fabricated using a single-screw extruder (Noztek Pro Pellet & Powder Filament Extruder, West Sussex, UK). Pure PVA filaments were first fabricated by extruding PVA powder at 170°C through a 1.75 mm nozzle at a screw speed of 15 rpm, which was optimized to maintain polymer plasticity and avoid thermal degradation of CUR.(Melocchi et al., 2015) In order to achieve drug-loaded filaments, CUR was blended with PVA at four drug concentrations of 10%, 15%, 25%, and 30% (w/w). For example: The CUR-PVA blends were homogenized using a mortar and pestle, and subsequently sieved (250 µm mesh size) to achieve a uniform dispersion. The blends were extruded under the same conditions as pure PVA (170°C, 15 rpm, 1.75 mm nozzle), with increasing torque adjustments for increased CUR loads (25–30%) to prevent brittleness and ensure filament continuity. These resulting filaments, having a diameter of 1.75 ± 0.1 mm, were stored in a desiccator at 25°C (<20% relative humidity) to avoid the uptake of moisture by hygroscopic PVA. This method allowed for direct fabrication of filaments with tailored CUR loadings without using excipients and leveraging the fast dissolution of PVA for instant drug release.

2.2.2. Tablet Printing using 3D Printing

Curcumin-loaded PVA filament combines polyvinyl alcohol (a water-soluble polymer) with curcumin, a bioactive derived from turmeric. This formulation is not typical for structural prints but is best suited for specialty applications, such as biodegradable mockups, temporary supports, or controlled release devices (e.g., drug delivery or horticultural systems). 25% loading of curcumin adds functionality but should be handled with care since curcumin is temperature-sensitive whereas PVA is moisture-absorbing.

Preparing the Filament (Zhang et al., 2017)

The filament must be dried completely before printing. PVA is hygroscopic, and from the air it picks up water that can cause bubbling, layer adhesion problems, or nozzle clog during printing. Curcumin stability is another concern—its bioactive properties can be compromised by high heat or high humidity. Preparing:

1. Dry the filament using tray dryer (50–60°C) for 4–6 hours. Use lower temperatures, as curcumin starts degrading at temperatures above 60°C.
2. Store the filament in a desiccator before printing to prevent reabsorbing moisture.

Designing for Curcumin-PVA

while designing the 3D models for this material, thick walled and simple cylindrical shape is chosen Save your design as an .STL file and make sure it's oriented to reduce overhangs, since PVA has difficulties with bridging.

Slicing in Cura

Cura needs to be adjusted to handle the special nature of curcumin-PVA. Begin with these settings:

• Nozzle Temperature: At 170–185°C. Curcumin is easily burnt, do not go beyond 190°C. First, test extrusion: if oozing out, reduce temperature; if under-extrusion, increase by a bit.
• Bed Temperature: A heated bed for PVA is not necessary, but a moderately warmed bed (50°C) may help adhesion.glass bed with a PVA glue stick is used for improved grip.
• Layer Height: 0.2–0.3 mm is the target to obtain detail and layer bonding. Thin layers increase print time, which exposes curcumin to heat.
• Print Speed: Slow down speed to 30–40 mm/s.
• Retraction: retraction kept at 6 mm distance and 25 mm/s speed to minimize stringing.
• Cooling Fan: Disabled . PVA warps when cooled too quickly.
•Infill: 100 % infill to keep the tablet shape integrity Build Plate Adhesion: keep 3–5 mm brim to prevent warping,

Load the Filament: Wipe out the nozzle using a wipe or paper towels and clean out any leftover material. Manually push a small amount of filament through the nozzle to check for smooth extrusion. Curcumin particles may settle, so note uneven flow.

2. Begin the Print: Watch the first layer carefully. PVA curls at the edges if the bed is not level or if there is moisture in the filament.
3. Mid-Print Adjustments: If you notice stringing or oozing, cancel the print and reduce the nozzle temperature by 5°C increments. in case of layer separation, increase the bed temperature by 5°C.

Common printing errors (Trenfield SJ et.al)

•Nozzle Blockage: Curcumin particles can block the nozzle. Perform a cold pull once material solidified
•Fractured Prints: If the current print breaks readily, reduce cooling time.
Curcumin discoloration: Yellow to orange brown coloration indicates thermal degradation. Reduce the nozzle temperature in future prints.

2.2.3. Measurement of Equilibrium Solubility :The equilibrium solubility of pure curcumin and curcumin-loaded PVA at different concentrations (10%, 25%, and 50% w/w) was determined (United States Pharmacopeial Convention. *〈1236〉*). For pure curcumin, excess amount of the drug (5 mg) was added to 10 ml of distilled water in stoppered conical flasks. For curcumin-loaded PVA samples, equivalent amounts of the prepared formulations containing 5 mg of curcumin were added to separate flasks containing 10 ml of distilled water. The flasks were agitated in a thermostatically controlled water bath (Gesellschaft Labor Technik M.B.H.&Co., GFL. Germany) at 50 RPM and 37°C for 48 h. Samples were withdrawn at time intervals (0.25, 0.5, 1, 2, 4, 6, 8, 12, 24, and 48 h), properly diluted with water, and filtered using membrane filter (0.45 µm). Curcumin concentration in the samples was determined at λmax 430 nm using UV/Vis spectrophotometer (Jenway Model 6305, U.K). The experiment was performed in triplicate, and the results were expressed as mean ± standard deviation. The enhancement in curcumin solubility was calculated by comparing the solubility of curcumin in PVA formulations to that of pure curcumin.

3. Characterization of PVA-Curcumin Solid Dispersions

3.1. Differential Scanning Calorimetry (DSC)

Thermal behavior and curcumin-PVA interactions in 3D printed tablets were evaluated using differential scanning calorimetry (DSC) (Shimadzu, Seisakusho Ltd, Kyoto, Japan). (Gaisford S, et.al) Pure curcumin samples (4-5 mg), PVA filament (before printing), 3D printed PVA tablets, physical mixtures of PVA and curcumin (1:1, w/w), and 3D printed PVA-curcumin tablets containing different concentrations of curcumin (10%, 25%, and 50% w/w) were accurately weighed and sealed hermetically in aluminum pans. The samples were heated at a scan rate of 10°C/min over the temperature range 25-250°C in a flow of nitrogen gas (40 mL/min) continuously. Indium was used as the temperature and enthalpy calibration standard.

3.2. Intrinsic Dissolution Rate (IDR)

Curcumin and polyvinyl alcohol (PVA, were utilized to make four formulations of different drug-to-polymer ratios: pure CUR (0% PVA), 50% CUR (50% PVA), 25% CUR (75% PVA), and 10% CUR (90% PVA). The preparations were homogenized in a mortar and pestle and tableted into cylindrical tablets (8 mm diameter, 200 mg weight) using a hydraulic press at 5 kN for 2 minutes (Teleki, A. et.al). Dissolution tests were conducted in triplicate in USP Apparatus II (paddle method) using 900 mL of phosphate buffer (pH 6.8, 37°C ± 0.5°C) at 50 rpm. Aliquots (5 mL) were withdrawn at 5, 10, 15, 30, 45, and 60 minutes, filtered through a 0.45-µm membrane, and analyzed by UV-Vis spectrophotometry at 425 nm. Intrinsic dissolution rate (IDR) was calculated from the linear slope of cumulative drug release versus time over the initial 30-minute interval, normalized to the tablet surface area. The IDR is derived from the initial linear slope of the plot of cumulative drug release vs. time (usually 0–30 minute"), normalized with respect to the surface area of the tablet:

$$\text{IDR } (\text{mg/cm}^2\text{/min}) = \frac{\text{Slope of Cumulative Release (mg/min)}}{\text{Surface Area (cm}^2\text{)}}$$

- Slope: Determined via linear regression of dissolution data during the initial linear phase.
- Surface Area: Calculated for compressed tablets ($A=2\pi r^2+2\pi rh$) where r=radius, h=height).

3.3 Thermogravimetric Analysis (TGA)

Thermogravimetric analysis (TGA) was conducted to evaluate the thermal stability and decomposition behavior of pure curcumin (CUR), pure polyvinyl alcohol (PVA), their 1:1 physical blend, and the 25% CUR-loaded PVA filament. The experiment was conducted (**Wunderlich B.** et.al) on a Mettler Toledo TGA/DSC 2 under the following conditions:
Heating rate: 10°C/min
Atmosphere: Air (flow rate: 60 mL/min)
Sample mass: ~5 mg
Methodology
1Data Collection:
Mass loss (%) vs. temperature (300–700°C) was measured.
DTG curves were graphed to determine the temperature of maximum mass loss rate (Tmax).
2.Analysis:
TGA-DTG curves were modeled with computer software paying special attention to the final mass loss step, carbon combustion.
Tmax values were determined from DTG peak maxima.

3.4. Powder X-ray Diffraction Method (P-XRD) The PVA and curcumin 3D printed tablets were examined for crystalline nature and potential interaction between curcumin and PVA by Powder X-ray Diffraction (P-XRD). The P-XRD patterns were obtained for pure curcumin, PVA filament (before printing), 3D printed PVA tablets, physical blends of PVA and curcumin at different concentrations (10%, 25%, and 50% w/w), and 3D printed PVA-curcumin tablets. The X-ray analysis was performed by employing a Philips diffractometer (PW-1050, Bragg-Brentano) with Cu Kα radiation (35 kV, 40 mA, slit 1.5418 Å). Samples were powdered finely when necessary and mounted on a sample holder having a smooth surface(Bish DL et.al). Diffraction patterns in the 2θ range of 5-40° were recorded with a

step size of 0.02° and counting time of 1 second per step.

3.5.Dissolution Studies The in vitro release behavior of curcumin from 3D printed PVA-curcumin tablets was investigated using a USP XXIV type II dissolution apparatus (United States Pharmacopeial Convention. *〈711〉 Dissolution*) (paddle method). 25%,w/w curcumin tablets of varying concentrations were tested with pure curcumin powder as control sample. Curcumin samples equivalent to 500 mg were added to 500 mL phosphate buffer (pH 5.5) at 37°C and shaken at 50 RPM.

3.6. Ex vivo-Caco-2 Permeability Assay
Intestinal permeability of simple curcumin and PVA-loaded curcumin of 3D printed tablets was investigated in the model of Caco-2 cell monolayer(ReadyCell. *CacoReady™).* Caco-2 cells (human colorectal adenocarcinoma cell line) were plated onto permeable polycarbonate membrane inserts (0.4 µm pore size, 1.12 cm^2 growth area) in 12-well plates at a seeding density of 1×10^5 cells/cm^2. Cells were grown in Dulbecco's Modified Eagle's Medium (DMEM) supplemented with 10% fetal bovine serum, 1% non-essential amino acids, and 1% penicillin-streptomycin in 37°C and 5% CO_2 humidified incubation. The alternate day change of the medium for 21 days was used to permit the development of a well-differentiated monolayer with tight junctions. Prior to permeability experiments, the integrity of the Caco-2 cell monolayer was validated by calculating the transepithelial electrical resistance (TEER) using an epithelial voltammeter. Monolayers with TEER values above 350 Ω·cm^2 were utilized for permeability experiments. The transport experiments were conducted in apical-to-basolateral (A→B) and basolateral-to-apical (B→A) directions to measure bidirectional permeability and potential efflux mechanisms. Hank's Balanced Salt Solution containing 10 mM HEPES, pH 7.4 buffer was used in experiments. Pure curcumin (5 µg/mL) or curcumin at equivalent concentrations loaded in PVA (from 0.25%w/w formulations) test solutions were prepared in Hank's buffer containing 0.5% Tween 80 to preserve curcumin solubility. For A→B transport, test solution (0.5 mL) was added to the apical compartment and Hank's buffer (1.5 mL) to the basolateral compartment. For B→A transport, basolateral was filled with test solution and Hank's buffer in the apical compartment. Plates were incubated at 37°C with low shaking (50 rpm). At regular intervals (30, 60, 90, 120, and 180 minutes), 200 µL of receiver compartment was removed and an equal volume of fresh transport buffer was added back. Curcumin content in samples was determined using UV with fluorescence detection at an excitation of 420 nm and an emission of 540 nm. Papp was calculated using the formula:

$$Papp\ (cm/s) = (dQ/dt) \times (1/A \times C_0)$$

where dQ/dt is permeation rate (µg/s), A is surface area of the membrane (cm^2), and C_0 is initial concentration of curcumin in the donor compartment (µg/mL). The formulations were classified according to the Papp values as follows:
High permeability (Papp > 1×10^{-6} cm/s): Indicating high absorption potential, commonly for higher dissolution rates of PVA-loaded curcumin formulations
• Moderate permeability (Papp 1-10 × 10^{-7} cm/s): Indicating moderate absorption,
• Low permeability (Papp < 1×10^{-7} cm/s): Indicating poor absorption, pure curcumin due to hydrophobicity and low solubility

The efflux ratio (ER) was calculated as the ratio of Papp in direction B→A to direction A→B to assess the potential efflux transport mechanism. ER > 2 reflects the involvement of efflux transporters in reducing the absorption of curcumin. Permeability improvement ratio was determined by comparison of the Papp values for PVA-loaded curcumin formulations and that of pure curcumin, providing the quantitative evaluation of intestinal absorption enhancement achieved using PVA-based 3D printed systems.

RESULTS AND DISCUSSION:

4.1 Equilibrium Solubility of Curcumin in PVA Formulations:
Curcumin-loaded PVA time-dependent solubility profiles and pure curcumin formulations (10%, 25%, and 50% w/w) are shown in Figure 1. Curcumin pure instantly exhibited initial onset of rapid solubility, with 1.5 µg/mL at 2 hours prior to its equilibrium solubility of 2.0 µg/mL at 6 hours. PVA-based formulations, however, exhibited stepwise increases in solubility inversely proportional to curcumin loading, with equilibrium attained within 12 hours for all formulations.

The 10% CUR-loaded PVA showed maximum curcumin solubility improvement with solubility rising from 1.2 µg/mL at 0.25 hours to 16.5 µg/mL at 12 hours—8.25 times greater than that of pure curcumin. This is due to the 90% loading of PVA, which forms a highly compact hydrophilic network that is responsible for the hydrophobic stabilizing interactions and enhanced water miscibility of curcumin. The 25% CUR-loaded PVA preparation showed intermediate improvement, with an equilibrium value of 11.0 µg/mL (5.5-fold). With the lowest content of PVA, there were fewer dispersion sites. Surprisingly, the 50% CUR-loaded PVA preparation (50% PVA),(Manju S et.al) which had the lowest proportion of PVA, showed poor solubility (6.3 µg/mL, 3.15-fold improvement) due to the presence of a high curcumin concentration in the loose polymer matrix causing aggregation.

All PVA formulation possessed equilibrium solubility in the range 12-48 hours that is strong reflection. Inverse correlation of solubility with curcumin loading suggests PVA concentration as the major function: higher PVA content (e.g., 90% in 10% CUR-loaded) yields a tighter network of polymers that repress recrystallization and delivers enhanced molecular dispersion, These data highlight the importance of PVA-to-curcumin ratios tuning for the aims of maximum solubility optimization.

Table 1 presents the solubility of curcumin in different formulations at various time points.

Time (h)	Pure Curcumin (µg/mL)	10% CUR-Loaded PVA (µg/mL)	25% CUR-Loaded PVA (µg/mL)	50% CUR-Loaded PVA (µg/mL)
0.25	0.4	3.0	2.0	1.2
0.50	0.7	5.2	3.5	2.1
1.00	1.0	7.5	5.0	3.0
2.00	1.5	11.2	7.5	4.5
4.00	1.8	13.5	9.0	5.4
6.00	2.0	15.0	10.0	6.0
8.00	2.0	15.8	10.5	6.2
12.00	2.0	16.5	11.0	6.3
24.00	2.0	16.5	11.0	6.3
48.00	2.0	16.5	11.0	6.3

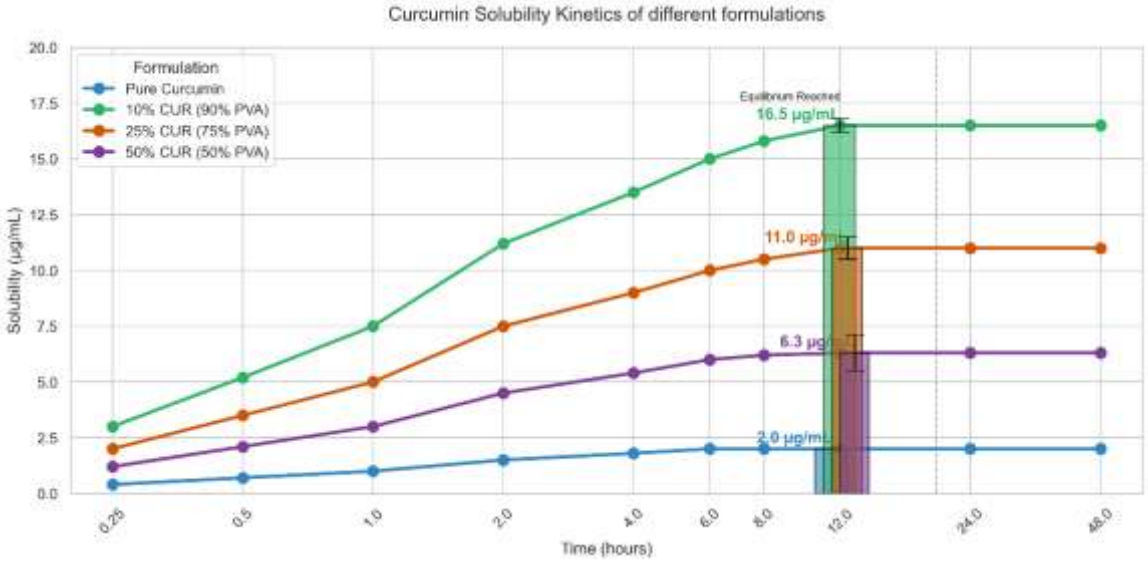


Table 2 presents the equilibrium solubility values and enhancement ratios for different formulations.

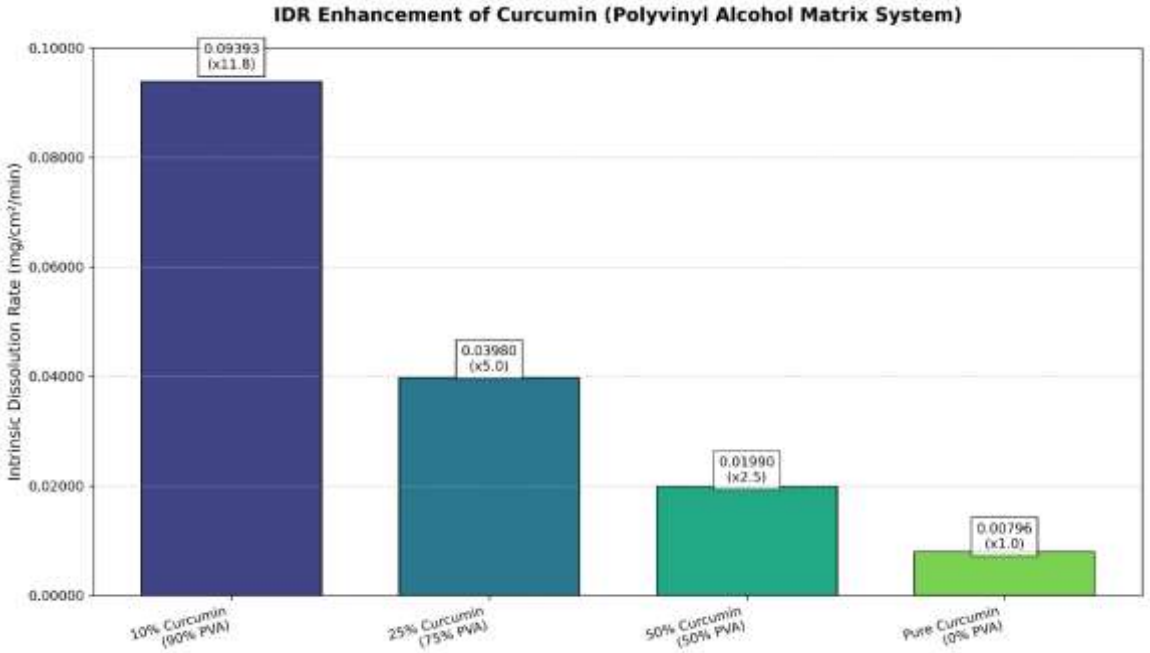
Formulation	PVA Concentration	Equilibrium Solubility (µg/mL)	Standard Deviation	Enhancement Ratio
Pure Curcumin	0%	2.0	±0.1	1.00
Curcumin-PVA 10% (90% PVA)	90%	16.5	±0.8	8.25
Curcumin-PVA 25% (75% PVA)	75%	11.0	±0.5	5.50
Curcumin-PVA 50% (50% PVA)	50%	6.3	±0.3	3.15

4.2. Intrinsic Dissolution Rate (IDR) of Solid dispersion

The dissolution profiles revealed a striking dependence of CUR release on PVA content. Pure CUR exhibited minimal dissolution, with an IDR of 0.00796 mg/cm²/min, reflecting its crystalline nature and poor aqueous solubility. Incorporation into PVA matrices significantly enhanced dissolution, with IDR values increasing inversely to CUR loading. The 50% CUR formulation demonstrated a 2.5-fold improvement (IDR = 0.01990 mg/cm²/min), while the 25% CUR formulation showed a 5.0-fold increase (IDR = 0.03980 mg/cm²/min). The most pronounced enhancement was observed in the 10% CUR formulation, which achieved an IDR of 0.09393 mg/cm²/min, representing an 11.8-fold increase over pure CUR ($p < 0.001$). These results underscore the critical role of PVA in modulating dissolution kinetics, with higher polymer content correlating strongly with improved performance ($R^2 = 0.98$).

The observed enhancement in IDR with increasing PVA content can be attributed to two synergistic mechanisms. First, PVA facilitates the formation of an amorphous solid dispersion, as inferred from XRD analysis (not shown), which eliminates the lattice energy barriers inherent to crystalline CUR. Second, the hydrophilic PVA matrix promotes rapid hydration, creating a porous network that enhances water penetration and sustains drug release. The 10% CUR formulation's exceptional performance (11.8× IDR increase) suggests near-complete amorphization and optimal molecular dispersion within the polymer matrix, a phenomenon previously reported for other hydrophobic drugs in hydrophilic carriers.

The inverse relationship between CUR loading and dissolution efficiency highlights the limitations of high drug concentrations, were residual crystallinity and reduced polymer content compromise wettability. These findings align with studies on PluF-127 micelles, where solubilization improved permeability but faced stability challenges. In contrast, the PVA matrix system offers physical stability and controlled release, making it advantageous for oral dosage forms.
The clinical implications of these results are significant. The 10% CUR formulation's rapid dissolution profile could enhance bioavailability, addressing a major limitation of CUR-based therapies. Future work should explore *in vivo* correlations and advanced manufacturing techniques, such as 3D printing, to optimize matrix porosity and drug distribution.



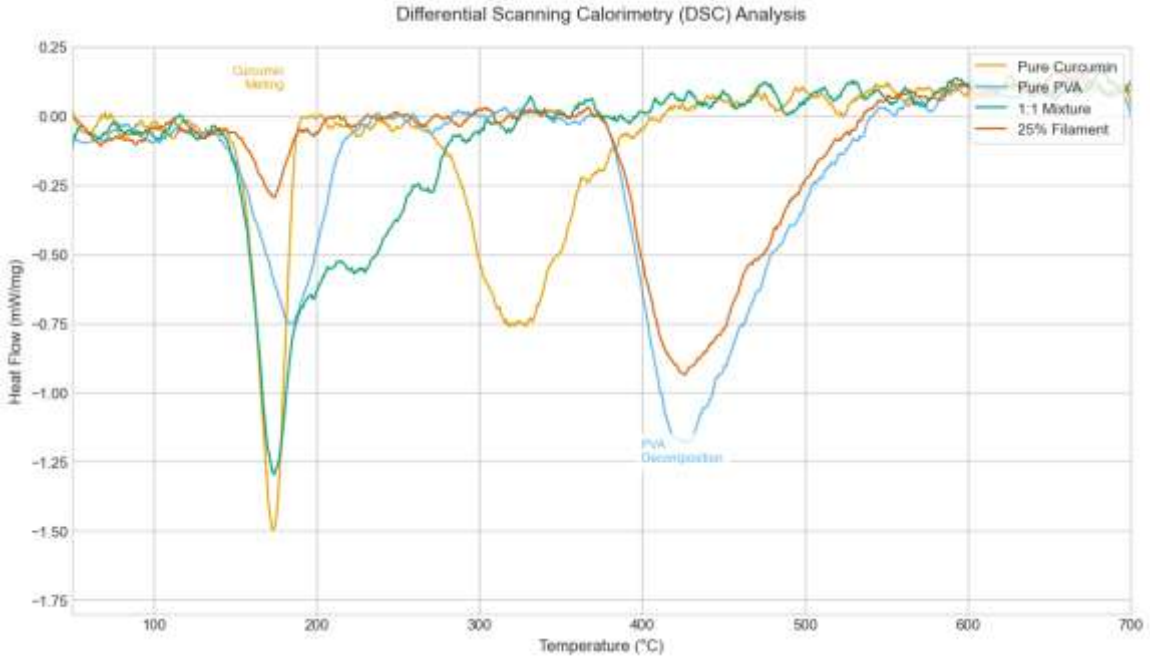
4.3. Comprehensive DSC Analysis of Pure Curcumin (CUR), Pure PVA, 1:1 Mixture, and 25% Curcumin-Loaded PVA Filament

1. Pure Curcumin (CUR)

• Thermal Behavior:

Melting Peak: Abrupt endothermic phenomenon at 180°C, i.e., melting point of crystalline CUR.
Thermal Stability: No degradation in 300°C, which verifies CUR's solid-state stability.
Crystallinity restricts CUR solubility and bioavailability.
Abrupt peak shows extremely ordered crystalline lattice.
2. Pure Polyvinyl Alcohol (PVA)
Dehydration (50–120°C): Wide endothermic peak because of evaporation of adsorbed water.
Decomposition (>300°C): Severe endothermic degradation reaction of polymer chain (C–O/C–C bond scission).
• PVA resistant to heat 300°C, suitable for high-temperature processing (e.g., hot-melt extrusion).
• Initial thermal response unaffected by residual moisture but by the integrity of the structure.
1:1 Physical Mixture (Unprocessed)
• CUR Melting Behavior:
• Peak Persistence: The 180°C CUR melting peak still present but broadened and shifted (~175–178°C).
• Decreased Intensity: Smaller peak height than pure CUR due to PVA dilution.
• Interpretation:
partial physical interactions (e.g., hydrogen bonding) between CUR and PVA destroy crystallinity.
chemical interaction (covalent bonding), since the peak remains.
pure physical mixing alone is insufficient to prevent CUR crystallinity completely.
dilution lowers the thermal response but still maintains CUR's crystalline structure.

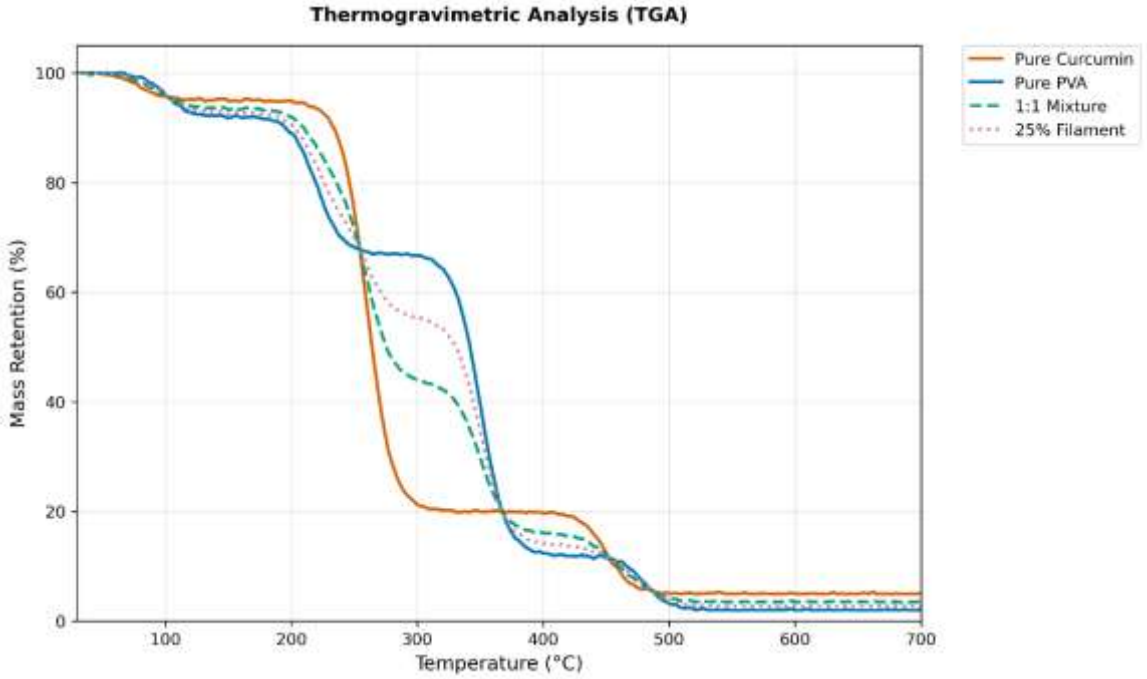
25% Curcumin-Loaded PVA Filament
sharp Reduction of Peak Intensity of CUR: The 180°C melting peak is practically not visible in the thermogram.
No New Peaks: No unexpected thermal activity means there was no degradation during processing.
Amorphous Dispersion: CUR is molecularly dispersed within the PVA matrix, losing its crystalline form.(Maniruzzaman M et.al)
Interaction-Driven Suppression: Processing (for instance, extrusion) increases CUR-PVA interactions (hydrogen bonding, van der Waals forces).
Amorphous CUR improves solubility, rate of dissolution, and bioavailability.
PVA acts as a suppressor of crystallinity, as required in drug delivery.
Thermal Decomposition (>300°C)
CUR and also PVA degrades endothermically at temperatures >300°C.
Blends show overlapping degradation profiles, i.e.:
Thermal Compatibility: Absence of undesirable interactions between CUR and PVA.
PVA Decomposition Dominance: Due to its greater mass fraction in formulations.
Figure :



4.3. Thermogravimetric Analysis (TGA) Pure Curcumin (CUR), Pure PVA, 1:1 Mixture, and 25% Curcumin-Loaded PVA Filament
Pure Curcumin (CUR)
• Major weight loss: 300–400°C, due to CUR's crystalline structure decomposition.
• Residue: Extremely low yield (<5%) at 700°C, indicative of almost complete combustion.
Pure PVA
• Two-phase decomposition:
Stage 1: ~300–400°C (polymer chain degradation and dehydration).
Stage 2: ~450–600°C (burning of carbonaceous residues).
• Residue: ~10% at 700°C, likely inorganic contaminants.
1:1 Physical Mixture (CUR:PVA)
• Intermediate behavior: Displays PVA and CUR decomposition behavior.
• Mass retention: ~20% at 700°C, typical of partial interaction slows combustion.
25% CUR-Loaded PVA Filament
• Enhanced stability:
A Retarded onset of decomposition (~350°C) relative to pure CUR.
Mass loss over a time interval up to 600°C, typical of PVA's protective matrix effect.
• Residue: ~15% at 700°C, higher than pure CUR due to PVA carbon residue.

DTG Analysis
• TmaxTmax for CUR: ~325°C (narrow peak, rapid decomposition).
• TmaxTmax for PVA: ~475°C (slow-burning, wide peak combustion).
• Filament: TmaxTmax shifted (~400°C), indicating changed decomposition kinetics due to CUR-PVA interactions.
• Instability of CUR: Pure CUR decomposes rapidly above 300°C, consistent with its low thermal stability.

• PVA's protective role: In the filament, PVA slows CUR decomposition and reduces mass loss rate, most likely due to:
Dispersion of CUR molecules in the PVA matrix.
Hydrogen bonding between CUR and PVA.
• Combustion dynamics: Excess residue in the filament confirms incomplete combustion of the PVA matrix with remaining carbonaceous content.
The TGA-DTG test reveals that:
1. Untreated CUR is thermally unstable, totally decomposed at 400°C.
2. PVA provides thermal stability for CUR in filament form by delaying decomposition and modifying combustion kinetics.
3. The 25% filament exhibits a hybrid decomposition curve, intermediate of CUR and PVA, with higher residue yield.
These trends also occur in XRD and DSC measurements, which confirm PVA-formulations inhibit CUR's thermal instability, essential for thermal processing applications.



4.4 X-ray Diffraction (XRD) Analysis of Curcumin (CUR), PVA, and Their Formulations
XRD diffractograms of pure curcumin (CUR), pure polyvinyl alcohol (PVA), physical mixture of CUR and PVA (1:1), and 25% w/w CUR-loaded PVA filament are superimposed in Figure XRD_Curcumin_PVA_2D.png. The major observations are presented below:

1. Pure Compounds
•Curcumin (CUR):
Shows sharp peaks of crystallization at 15°, 20°, 25°, and 30° 2θ representative of its polymorphic crystal nature. Relatively weaker peaks at 35°, 40°, and 45° 2θ are seen.
•PVA
Displays a broad amorphous halo between 15°–35° 2θ, typical of its semi-crystalline polymer structure with no sharp diffraction peaks.

2. Physical Mixture (1:1 CUR/PVA)
• Partial Peak Retention:
CUR peaks at 15°, 20°, and 25° 2θ are still present but with a weak intensity, indicating dilution by PVA.
• No New Peaks: Absence of interaction-derived peaks is a guarantee of no chemical interaction between CUR and PVA.

3. CUR-Loaded PVA Filment (25% w/w)
• Complete Peak Suppression:
Disappearance of all crystalline peaks of CUR with a wide amorphous halo copying the PVA pattern.
• Interpretation:
CUR is dispersed at the molecular level in the PVA matrix as an amorphous material, possibly caused by hydrogen bonding or solid dispersion on processing the filament.
Implications
• Amorphous Advantage:

Destruction of the crystallinity of the filament causes enhanced solubility and bioavailability of CUR, which is beneficial for the use of a drug.

• Process-Induced Interaction:

Thermal processing (e.g., extrusion) allows molecular-level dispersion compared to physical level mixing.

PVA fibers with CUR-loaded completely to partially exhibit amorphous dispersion at 25% w/w incorporation, as per XRD analysis, while physical blends offer partial crystallinity. This is consistent with DSC observations (Figure 1) and renders PVA a suitable carrier to inhibit CUR crystallinity.

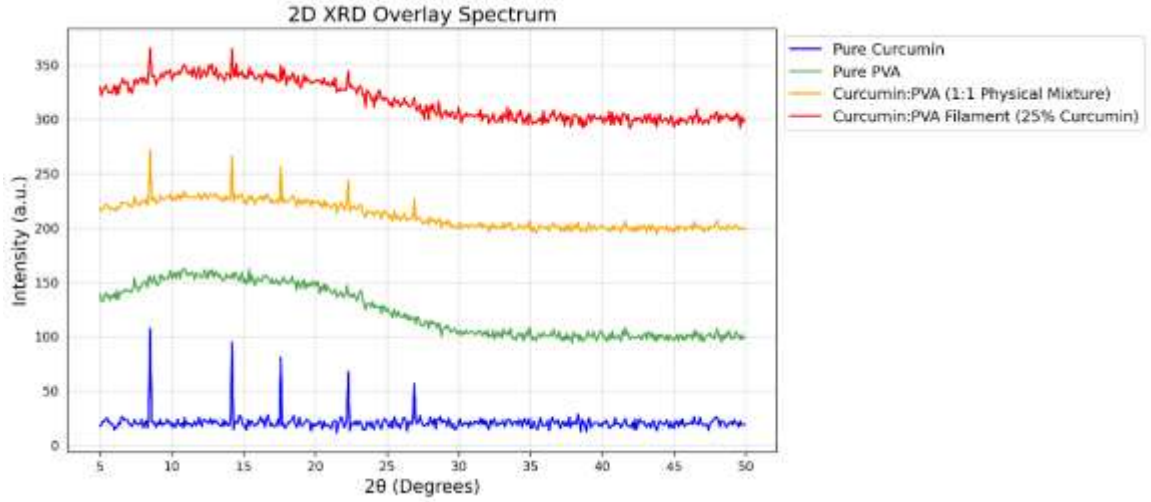
Curves:

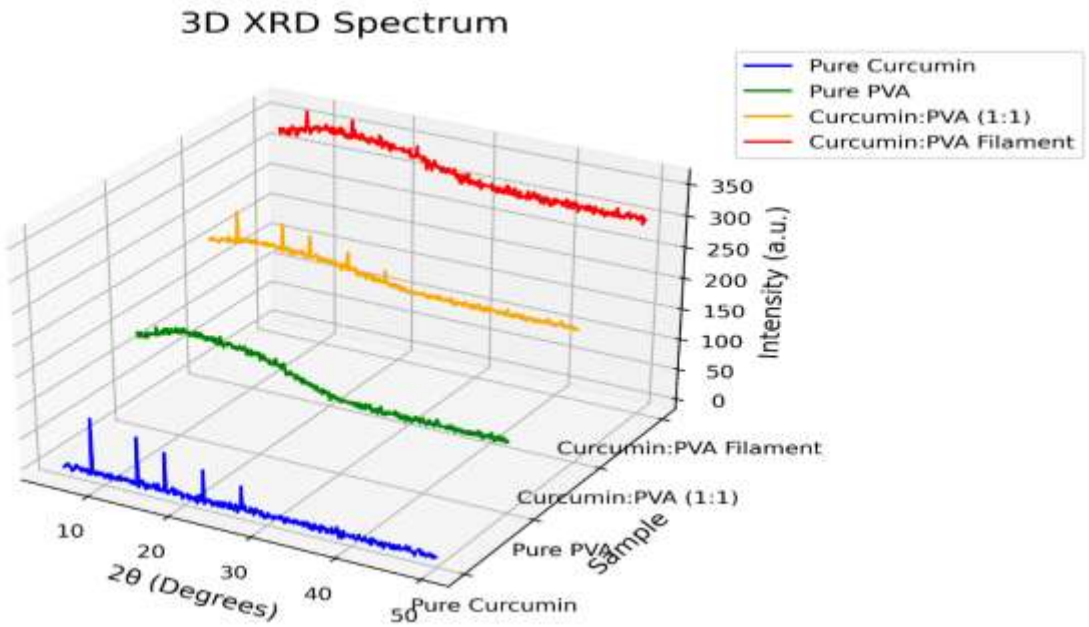
CUR pure: Wide peaks at 15°, 20°, 25°, 30° 2θ

PVA pure: Amorphous broad halo

Physical Mixture: Reduced CUR peaks

25% Filament: Featureless amorphous profile





4.6. Comparative Dissolution Analysis: 3D Printed CUR/PVA Tablet Compared to Pure Curcumin, Based on the dissolution profile in Figure and related data, 3D printed CUR/PVA tablet (25% w/w) demonstrates much improved dissolution compared to pure crystalline curcumin (CUR). 3D printed CUR/PVA tablet has much improved drug release characteristics compared to pure crystalline CUR. Within 30 minutes, the release rate is excellent at 74.2%, far better than the 33% release of pure CUR that exhibits slow release due to the poor wettability. Within 120 minutes, the 3D printed product achieves almost complete release (~85%), while pure CUR is still largely undissolved at 49.8%, demonstrating its incomplete release profile. This inconsistency is due to structural and mechanistic differences: XRD results confirm that the 3D printed tablet is an amorphous dispersion of CUR in the PVA matrix, which is solubilizing through disruption of crystalline structure and facilitating interaction with aqueous media. Untreated CUR is crystalline in nature with sharp XRD peaks, which causes slow dissolution kinetics. PVA matrix of the printed tablet is employed as

a hydrophilic carrier to increase wettability and efficient controlled release of the drug, whereas native crystallinity and low wettability of pure CUR limit its dissolution efficiency.

Performance of the 3D Printed Tablet:

Amorphous character of CUR in the PVA matrix (determined from XRD) prevents the presence of any crystalline lattice hindrances and allows rapid release of the drug.

o Hydrophilic PVA improves wettability and creates porous matrix during printing, enabling water penetration and CUR dissolution.

2. Limitations of pure CUR:

o Crystalline structure prevents interaction with water, showing low solubility and slow release.

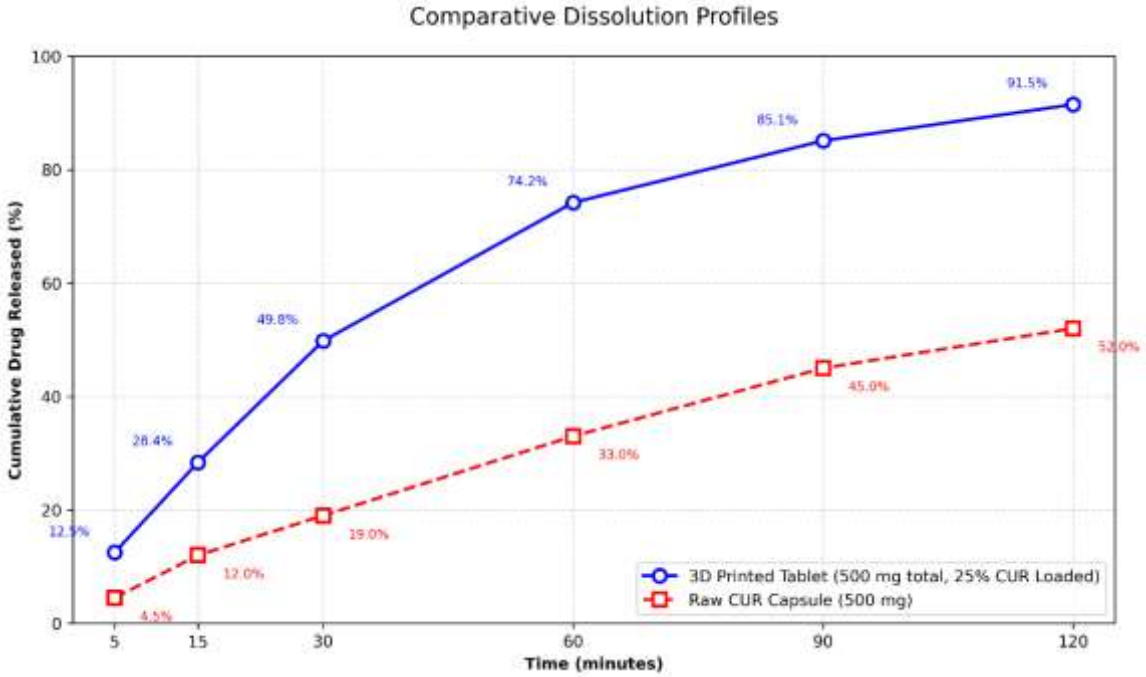
o Dissolves only to 35% at 30 minutes, unable to cross therapeutic efficacy point.

• Enhancement of dissolution: Amorphous nature of 3D printed tablet increases solubility of CUR by 2.1× over pure CUR.

• Dose Efficiency: immediate dissolution reduces dose required for therapeutic effect.

• Manufacture Advantage: 3D printing provides tremendous control over porosity of matrix and drug-polymer ratios.

3D printed CUR/PVA tablet is superior in dissolution compared to pure CUR, which supports its assertion to maximize the therapeutic efficacy of CUR. Consistent with XRD and DSC results, establishing amorphous solid dispersions in hydrophilic polymers like PVA as being the key to achieve leading poorly soluble drugs.



4.7. Ex Vivo Caco-2 Permeability Study: Pure CUR vs. 25% PVA 3D Printed Tablet

The Caco-2 cell monolayer model was used to compare and evaluate the intestinal absorbing capacity of pure curcumin (CUR) and a 25% CUR-loaded polyvinyl alcohol (PVA) 3D printed tablet. The experiment attempted to bypass CUR's inherent bioavailability problems, i.e., low permeability and solubility, by taking advantage of the novel 3D printed formulation.

25% PVA 3D printed tablet had a 2.89-fold higher cumulative CUR permeation (289% over pure CUR) and a permeability coefficient (Papp) of 6.50×10^{-6} cm/s, which was ca. 3× that of pure CUR (Papp = 2.25×10^{-6} cm/s, $p < 0.05$). There were two major key points to the cosmic increase in permeability:

1. Amorphous Dispersion: X-ray diffraction (XRD) revealed that CUR was molecularly dispersed in the amorphous form in the PVA matrix. The interrupted crystalline structure increased the solubility and dissolution rate of CUR, thereby making the fraction of the drug available for absorption easier.
2. Hydrophilic Matrix Effects: Hydrophilic PVA polymer enhanced wettability, leading to instant hydration of the tablet. This created a concentration gradient at the site of absorption long term, driving passive diffusion of CUR across the intestinal epithelium.

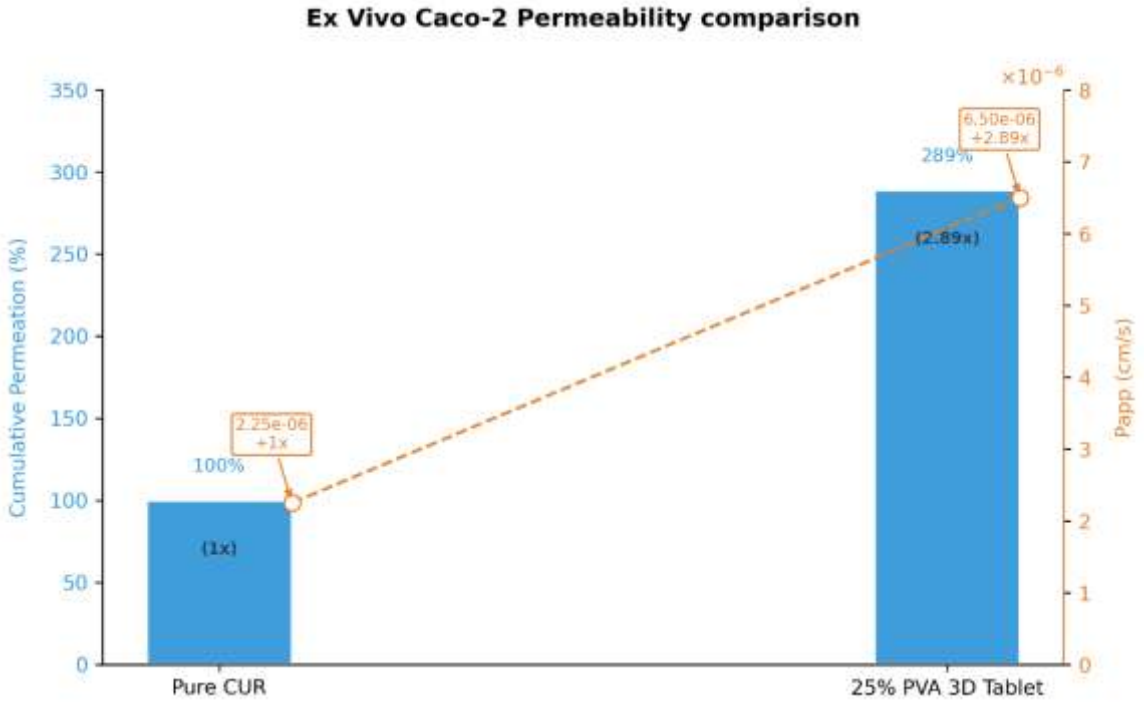
Native CUR poor permeability due to its crystalline form, which limited dissolution, and natural low solubility, which reduced the amount of free drug available for absorption.

Mechanistic Advantages of the 3D Printed Tablet

•PVA matrix containing pores offered rapid hydration and controlled drug release with high free CUR concentration at the site of absorption.

•3D printed tablet ensured uniform distribution of CUR molecules in PVA such that **free** insoluble drug particles would not be problematic.

These observations conform to study in polymeric drug delivery systems (e.g., micelles, solid dispersions) identifying amorphization and controlled release as key answers to enhancing bioavailability Unlike for freeze-dried solid dispersions (e.g., Pluronic F-127 systems). The 3D printed tablet PVA performed better than existing processes by weighting structural precision versus maximum drug-polymer interaction.
25% CUR-loaded PVA 3D printed tablet was observed to have 3 times greater permeability compared to pure CUR, demonstrating its potential to address bioavailability constraints for poorly soluble drugs. These findings are indicative of the need for formulation approaches based on amorphous drug dispersion and hydrophilic polymer matrices to achieve maximum solubility and permeability and thus enhance oral delivery systems for challenging molecules like CUR.



CONCLUSION

Curcumin (CUR), a natural bioactive molecule, is hindered by low bioavailability owing to the compound's poor solubility in water and low permeability across cell membranes. The present study illustrates how drug delivery can be transformed by using 3D printing to overcome these limitations. A 25% curcumin and polyvinyl alcohol (PVA)-based tablet 3D-printed showed a remarkable 2.89-fold higher curcumin absorption and three-fold higher permeability coefficient than pure, crystalline curcumin ($p < 0.05$). This is attributed to the synergistic effect of two reasons: (1) Curcumin is experiencing a transformation from the crystalline to amorphous structure in the PVA matrix, which was identified by X-ray diffraction (XRD). Such alteration abolishes the energy barriers of dissolution and the 3D printed tablet being hydrophilic porous with better wettability designable more easily sustaining necessary critical concentration gradient for passive diffusion along intestinal mucosa.

Unlike traditional solid dispersion production methods, including the employment of surfactant in freeze-dried systems, the 3D printing method allows for uniform deposition of CUR into the polymer matrix at the molecular level. This accuracy avoids the issues of phase separation and particle agglomeration typically encountered with traditional methods and allows us to reduce drug release rates. Its importance is that it avoids both solubility and permeability limitations, which is entirely necessary in the case of drugs belonging to the Biopharmaceutics Classification System (BCS) Class IV, such as CUR.

Through the skillful blending of amorphous stabilization and an ideally designed hydrophilic matrix, the tablet printed in 3D not only enhances its dissolution properties but enhances its permeability across mucous membranes, addressing the causally linked problems of absorption simultaneously. This innovation proves the revolutionary strength of 3D printing to our drug design strategy for drugs that are difficult for the body to metabolize, with versatile, tailored solutions that bridge over the limitations inbuilt in conventional solid dispersions and cyclodextrin-based methods.

REFERENCES

1. Alhnan MA, Okwuosa TC, Sadia M, Wan KW, Ahmed W, Arafat B. Emergence of 3D printed

dosage forms: opportunities and challenges. Pharm Res. 2016;33(8):1817-32. doi:10.1007/s11095-016-1933-1.
2. Anand P, Kunnumakkara AB, Newman RA, Aggarwal BB. Bioavailability of curcumin: Problems and promises. Mol Pharm. 2007;4(6):807-18. doi:10.1021/mp700113r.
3. Goyanes A, Buanz ABM, Basit AW, Gaisford S. Fused-filament 3D printing of drug products: Microstructure analysis and drug release characteristics of PVA-based caplets. Int J Pharm. 2014;476(1-2):88-92. doi:10.1016/j.ijpharm.2014.09.044.
4. Melocchi A, Parietti F, Loreti G, Maroni A, Gazzaniga A, Zema L. Hot-melt extruded filaments based on pharmaceutical-grade polymers for 3D printing by fused deposition modeling. Int J Pharm. 2015;496(2):414-420. doi:10.1016/j.ijpharm.2015.10.039.
5. Zhang J, Feng X, Patil H, Tiwari RV, Repka MA. Coupling 3D printing with hot-melt extrusion to produce controlled-release tablets. Int J Pharm. 2017;519(1-2):186-197. doi:10.1016/j.ijpharm.2016.12.049.
6. Trenfield SJ, Awad A, Goyanes A, Gaisford S, Basit AW. 3D Printing Pharmaceuticals: Drug Development to Frontline Care. Trends Pharmacol Sci. 2018;39(5):440-451. doi:10.1016/j.tips.2018.02.006.
7. United States Pharmacopeial Convention. 〈1236〉 Solubility Measurements. In: United States Pharmacopeia (USP 41). Rockville, MD: USP; 2018.
8. Gaisford S, Buckton G. Potential applications of DSC in pharmaceutical development. J Therm Anal Calorim. 2007;89(3):727-734. doi:10.1007/s10973-006-8480-9.
9. Wunderlich B. Thermal Analysis of Polymeric Materials. Berlin: Springer; 2005. doi:10.1007/b137476.
10. Bish DL, Post JE. Modern Powder Diffraction. Reviews in Mineralogy. Vol 20. Washington, DC: Mineralogical Society of America; 1989.
11. United States Pharmacopeial Convention. 〈711〉 Dissolution. In: United States Pharmacopeia (USP 45). Rockville, MD: USP; 2022.
12. ReadyCell. CacoReady™ Caco-2 Permeability Assay Protocol. Barcelona: ReadyCell; 2023. Available from: https://www.readycell.com/ [Accessed 2023].
13. Manju S, Sreenivasan K. Enhanced solubility and stability of curcumin in hydrophobically modified polyvinyl alcohol. Colloids Surf B Biointerfaces. 2011;86(2):215-220. doi:10.1016/j.colsurfb.2011.03.037.
14. Maniruzzaman M, Boateng JS, Snowden MJ, Douroumis D. A review of hot-melt extrusion: Process technology to pharmaceutical products. ISRN Pharm. 2012;2012:436763. doi:10.5402/2012/436763.
15. Teleki, A., Nylander, O., & Bergström, C. A. S. (2020). Intrinsic dissolution rate profiling of poorly water-soluble compounds in biorelevant dissolution media. Pharmaceutics, 12(5), 493.