



ISSN: 2349-5448

International Journal of Pharmacology and Clinical Research (IJPCR)

IJPCR | Vol.13 | Issue 4 | Oct - Dec -2025

www.ijpcr.net

DOI : <https://doi.org/10.61096/ijpcr.v9.iss4.2025.810-821>

Review

Comparative Study of PLA, PVA, and Cellulose-Based Filaments in UK Pharmaceutical 3D Printing

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|  | Abstract |
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| Published on: xx xxx 2025 | Three-dimensional (3D) printing has rapidly emerged as a transformative technology in pharmaceutical manufacturing, particularly within the United Kingdom, where personalised therapeutics and sustainability targets increasingly shape innovation strategies. Material selection plays a critical role in determining the performance of fused deposition modelling (FDM), influencing printability, thermal stability, mechanical behaviour, drug release characteristics, regulatory acceptability, and environmental impact. This review provides a comprehensive comparison of three major classes of polymeric filaments polylactic acid (PLA), polyvinyl alcohol (PVA), and cellulose-based materials currently used in pharmaceutical additive manufacturing. Drawing on recent scientific literature and empirical insights from UK pharmaceutical stakeholders, the article evaluates their respective advantages and limitations in terms of printability, drug–polymer compatibility, biocompatibility, sustainability attributes, and operational feasibility in real-world settings. PLA offers excellent printability and favourable environmental performance but is limited by its brittleness and high processing temperatures. PVA remains the most pharmaceutically versatile polymer due to its solubility and long-established excipient status, though its moisture sensitivity and low biodegradability present challenges. Cellulose-based filaments exhibit exceptional sustainability and biocompatibility but continue to face printability and processing limitations. The review underscores the need for improved filament engineering, clearer regulatory guidance, and adoption of lifecycle-based material assessment frameworks to support sustainable pharmaceutical 3D printing in the UK. Advances in green polymer science and hybrid bio-based filaments may ultimately enable broader clinical translation and environmentally responsible manufacturing.. |
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| | Keywords: 3D printing; fused deposition modelling; PLA; PVA; cellulose; pharmaceutical manufacturing; sustainability; biodegradable polymers; drug delivery; UK pharmaceutical sector. |

1. INTRODUCTION

Three-dimensional (3D) printing, or additive manufacturing, has become one of the most transformative technological advancements in the pharmaceutical sciences over the past decade. Its ability to fabricate patient-specific dosage forms, structurally complex drug delivery systems, and on-demand medicines aligns strongly with the increasing global emphasis on personalised therapies and decentralised healthcare manufacturing models (1,2). In particular, the United Kingdom has positioned itself as a leading centre for pharmaceutical 3D printing research, driven by academic–industry collaborations, NHS digital transformation priorities, and national strategies aimed at sustainable and flexible manufacturing (3,4). These efforts collectively highlight the growing relevance of 3D printing in improving therapeutic precision, reducing production waste, and enabling new clinical pathways. Among the various additive manufacturing modalities, fused deposition modelling (FDM) has gained the greatest traction in pharmaceutical applications. FDM is widely favoured for its comparatively low cost, accessibility, straightforward digital workflow, and compatibility with a range of thermoplastic polymers (5,6). Unlike photopolymerisation or powder-based techniques, FDM offers excellent design flexibility and a relatively simple operational process, making it ideal for academic laboratories, early-stage product development, and personalised manufacturing units within hospital settings. However, the successful use of FDM in pharmaceutical contexts is highly dependent on the selection and behaviour of the filament material, which functions both as a structural component and as a potential drug carrier.

Filament selection influences nearly every critical aspect of FDM-based pharmaceutical manufacturing, including melt flow dynamics, layer adhesion, print resolution, mechanical stability, drug loading potential, thermal degradation risks, porosity, and ultimately, drug release characteristics (7). Furthermore, the environmental sustainability of pharmaceutical materials has become increasingly important due to national Net-Zero targets and corporate sustainability commitments within the UK (8). Filament choice therefore has implications not only for product performance but also for compliance with emerging environmental expectations. Three classes of filament materials dominate current pharmaceutical 3D printing research and early adoption: polylactic acid (PLA), polyvinyl alcohol (PVA), and cellulose-based polymers. Each of these materials exhibits unique thermal, structural, and biopharmaceutical characteristics, offering distinct advantages but also presenting notable challenges in pharmaceutical settings.

PLA is a biodegradable aliphatic polyester derived from renewable biomass such as corn starch and sugarcane. It has been extensively used in biomedical devices, implants, and degradable packaging due to its biocompatibility, mechanical rigidity, ease of processing, and favourable environmental profile (9,10). In the context of 3D printing, PLA is widely recognised for its excellent dimensional stability, low shrinkage, and smooth extrusion behaviour, which make it one of the most user-friendly materials for FDM. These attributes position PLA as a practical option for printing rigid oral dosage forms, implantable matrices, or prototype devices. However, its brittleness, limited flexibility, and relatively high printing temperatures restrict its suitability for formulations involving heat-sensitive active pharmaceutical ingredients (APIs) (11). Additionally, its hydrophobic nature limits applications requiring rapid drug dissolution or compatibility with hydrophilic APIs.

In contrast, PVA is a synthetic, water-soluble polymer with an extensive history as an approved pharmaceutical excipient. Its solubility and safety profile have facilitated its

adoption in oral, ophthalmic, and transdermal products for decades (12). PVA's water-dispersible nature makes it particularly attractive for FDM fabrication of immediate-release tablets, rapidly soluble films, and multi-drug polypills with geometries engineered to modulate drug release. Numerous studies demonstrate that PVA enables uniform drug distribution, predictable release kinetics, and excellent compatibility with a wide range of hydrophilic APIs (13,14). Despite these advantages, PVA presents major operational challenges: it is highly hygroscopic, prone to diameter fluctuations, and susceptible to moisture-induced print failure. These issues were highlighted repeatedly in interviews with UK pharmaceutical practitioners in the user's dissertation, where humidity control was reported as one of the most significant barriers to routine implementation of PVA filaments in laboratory and industrial environments

Comparative Study of PLA

Cellulose-based materials, including cellulose acetate, hydroxypropyl cellulose, microcrystalline cellulose blends, and emerging nanocellulose composites, have recently gained attention due to their exceptional biocompatibility, natural abundance, and strong environmental credentials. Cellulose is inherently renewable and biodegradable, making it one of the most attractive polymer families from a sustainability standpoint (15,16). Furthermore, cellulose derivatives are well-established pharmaceutical excipients and widely used in matrix tablets, controlled-release systems, and topical formulations. However, most forms of cellulose lack natural thermoplasticity, necessitating chemical modification or blending with plasticisers to enable extrusion. These processing challenges such as inconsistent melt flow, poor layer adhesion, or nozzle clogging currently limit the widespread use of cellulose-based filaments in FDM printing (17). Nevertheless, advances in nanocellulose reinforcement and green polymer chemistry are gradually improving their printability, indicating strong long-term potential.

The selection of filament materials for pharmaceutical manufacturing involves navigating complex trade-offs among printability, biocompatibility, drug compatibility, regulatory acceptability, and environmental sustainability. While PLA and cellulose-based polymers offer clear environmental advantages, PVA remains the most chemically versatile and pharmaceutically adaptable filament. However, environmental sustainability is increasingly influencing material decisions within UK pharmaceutical practice, particularly among organisations committed to NHS Greener Agenda goals and corporate sustainability frameworks (18). Interview data from the dissertation confirms that UK practitioners recognise the need for more sustainable materials but lack access to structured decision-making tools, standardised environmental metrics, and adequate training in polymer science and lifecycle assessment

Comparative Study of PLA.

Given this complex landscape, the present review aims to consolidate scientific evidence, regulatory considerations, and practical industry insights to compare PLA, PVA, and cellulose-based filaments across five key dimensions:

1. Printability and mechanical performance
2. Drug-polymer interactions and release behaviour
3. Environmental sustainability
4. Safety and regulatory acceptance
5. Operational challenges in UK pharmaceutical environments

By synthesising this information, the review seeks to support pharmaceutical scientists, policymakers, and industry stakeholders in navigating material selection decisions that balance performance, safety, and sustainability within the UK's evolving pharmaceutical manufacturing ecosystem.

2. DISCUSSION

This section critically examines the three filament classes PLA, PVA, and cellulose-based polymers across six major domains relevant to pharmaceutical 3D printing: printability, drug compatibility, environmental sustainability, safety and regulatory considerations, operational challenges, and future prospects.

2.1 Printability and Mechanical Properties

Printability is central to determining whether a polymer can be used reliably in FDM-based pharmaceutical manufacturing. Material extrusion behaviour, thermal transitions, layer adhesion, and mechanical stability collectively influence the quality, reproducibility, and clinical viability of 3D-printed dosage forms (19,20).

2.1.1 Polylactic Acid (PLA)

PLA is widely recognised for its exceptional printability compared to most biopolymers. Its relatively low melting point (150–170°C) and glass transition temperature (~60°C) facilitate smooth extrusion and stable printing performance (21). PLA's semi-crystalline structure confers excellent dimensional accuracy and low warping, making it suitable for applications requiring rigid geometries such as polypills, compartmentalised tablets, and implantable structures. Mechanical strength is one of PLA's strongest attributes, as its rigidity supports the creation of high-resolution constructs with consistent layer bonding (22). Studies report low variability in PLA filament diameter, leading to reliable thermal behaviour and predictable surface finish (23). This makes PLA particularly advantageous for research environments and early-stage formulation prototyping.

Limitations

While PLA excels in structural stability, its brittleness presents a significant drawback. Breakage during filament feeding and reduced flexibility limit its use in soft or deformable dosage forms (24). Furthermore, PLA's high processing temperatures may degrade thermolabile active pharmaceutical ingredients (APIs), restricting its suitability for heat-sensitive compounds (25). Interviews from the user's dissertation corroborate these findings: multiple UK practitioners reported frequent filament snapping and inconsistent feeding with PLA during extended print runs.

2.1.2 Polyvinyl Alcohol (PVA)

PVA is widely considered the most pharmaceutically versatile polymer for FDM due to its water solubility, mechanical flexibility, and long-established regulatory acceptance (26). Its melting point (180–190°C) and excellent adhesion properties allow the fabrication of dosage forms with complex geometries, internal structures, and controlled dissolution profiles.

Strengths

- Outstanding layer adhesion
- Smooth extrusion with minimal stringing
- Suitable for immediate- and modified-release forms
- Supports high drug loading via hot-melt extrusion

- Compatible with complex internal lattice designs for advanced oral systems (27)

These attributes position PVA as the leading polymer for drug-loaded pharmaceutical filaments.

Limitations

PVA's extreme hygroscopicity is its primary drawback. Moisture uptake alters filament diameter, decreases mechanical strength, and causes extrusion inconsistencies (28). Even modest humidity changes can cause swelling, leading to nozzle blockages, inconsistent print quality, or print failure. UK practitioners interviewed in the uploaded dissertation consistently identified PVA moisture instability as the most problematic aspect in clinical and laboratory settings. The need for strict humidity control increases storage costs and complicates its use in flexible, on-demand printing environments.

Table 1. Comparative Analysis of PLA, PVA, and Cellulose-Based Filaments for Pharmaceutical FDM

| Parameter | PLA | PVA | Cellulose-Based Filaments |
|-------------------------------------|---|--|--|
| Source | Renewable biomass (corn, sugarcane) | Synthetic polymer | Natural biomass (wood pulp, cotton, agricultural residues) |
| Thermal Behaviour | Tg ~60°C; melt 150–170°C; low shrinkage | Tg ~85°C; melt 180–190°C; moisture sensitive | No natural thermoplasticity; requires derivatisation or plasticisers |
| Printability | Excellent dimensional stability; brittle; easy extrusion | Good layer adhesion; highly moisture-sensitive | Poor melt flow; nozzle clogging common; low interlayer strength |
| Mechanical Properties | Rigid, high modulus, brittle | Flexible, good toughness | Depends on derivative; often weak under heat |
| Drug Compatibility | Hydrophobic APIs; limited for hydrophilic drugs | Hydrophilic APIs; high drug loading; versatile | Broad API compatibility; mucoadhesive; variable release due to print instability |
| Release Behaviour | Sustained-release; slow degradation | Immediate- and modified-release; tunable dissolution | Rapid or controlled release depending on derivative |
| Biocompatibility | Good | Excellent, established excipient | Excellent |
| Environmental Sustainability | Biodegradable under industrial composting; low carbon footprint | Poor biodegradability; micro-residue risk | Fully biodegradable; most sustainable option |
| Regulatory Acceptance | EMA/MHRA accepted for implants | Strongest regulatory standing as excipient | Derivatives accepted; FDM-grade formulations lack guidance |
| Operational Challenges | Brittle; filament snapping | Moisture instability; storage requirements | High clogging rate; limited suppliers |
| Suitability for UK Pharma | Good for prototypes & sustained-release | Best for drug-loaded dosage forms | Strong potential; printability barriers |

2.1.3 Cellulose-Based Materials

Cellulose-based polymers including cellulose acetate, hydroxypropyl cellulose, and nanocellulose composites represent the most sustainable material group considered for pharmaceutical 3D printing (29).

Strengths

- Outstanding biocompatibility
- High tensile strength in native form
- Abundant, renewable, and biodegradable
- Long history as pharmaceutical excipients

Because cellulose derivatives are already used in many controlled-release oral products, their potential translation into 3D-printed medicines is scientifically and regulatorily aligned.

Limitations

Native cellulose is not thermoplastic and cannot be extruded without modification (30). To make cellulose printable, chemical derivatisation or blending with plasticisers is required. Despite these modifications, many cellulose-based filaments still suffer from:

- nozzle clogging
- inconsistent melt rheology
- weak interlayer adhesion
- poor dimensional accuracy (31)

The dissertation findings support this: UK practitioners reported the highest print failure rate and clogging frequency with cellulose-based filaments compared to PLA and PVA.

2.2 Drug Compatibility and Release Behaviour

The interaction between drugs and polymer matrices is fundamental to determining the suitability of a filament for pharmaceutical use. Key considerations include drug stability, dispersion, thermal tolerance, and release kinetics (32).

2.2.1 PLA

PLA is suitable for hydrophobic and moderately lipophilic APIs due to its hydrophobic polymer matrix (33). It supports **sustained-release** applications, as its biodegradation releases lactic acid gradually.

Advantages:

- Favourable for long-acting implants
- Effective for depot systems
- Slow degradation supports extended release (34)

Constraints:

- Printing temperatures may degrade thermolabile drugs
- Changes in crystallinity during printing can alter release rates
- Limited compatibility with hydrophilic APIs (35)

Thus, PLA is primarily suited to **sustained-release** rather than **immediate-release** formulations.

2.2.2 PVA

Thanks to its excellent water solubility and pharmaceutical excipient status, PVA is compatible with a wide range of **hydrophilic APIs**.

Advantages:

- Suitable for immediate-release dosage forms
- High drug loading capacity
- Consistent dissolution profiles
- Supports customisable internal channels for tailored release (36)

PVA has been used to produce orally disintegrating tablets, modular multi-drug polypills, and complex geometric dosage forms with high reproducibility (37). This versatility is a key reason that PVA remains the preferred polymer for drug-loaded pharmaceutical filaments in UK research settings.

2.2.3 Cellulose-Based Materials

Cellulose derivatives have a long-established role in oral drug delivery and are known for their broad API compatibility (38).

Advantages:

- Excellent mucoadhesive properties
- Suitable for both immediate- and controlled-release systems
- Non-toxic degradation profile

Limitations:

- Thermal instability during extrusion may alter API distribution
- Structural irregularities in printed cellulose affect drug release
- Limited data exist on FDM-specific cellulose release kinetics (39)

Despite these issues, cellulose-based systems are promising for sustainable pharmaceutical printing, especially if processing challenges can be mitigated.

2.3 Environmental Sustainability

Environmental sustainability is becoming a central consideration in UK pharmaceutical policy, influenced by the NHS Net Zero agenda, MHRA environmental expectations, and corporate ESG commitments (40).

2.3.1 PLA

PLA is one of the most environmentally favourable polymers available.

Sustainability advantages:

- Derived from renewable feedstocks
- Industrially compostable
- Lower carbon footprint than petroleum plastics (41)
- Minimal long-term ecological persistence

PLA's environmental performance is significantly better than both PVA and most chemically modified cellulose filaments.

2.3.2 PVA

Although water-soluble, PVA is **not biodegradable in natural waters**.

Environmental drawbacks:

- Contributes to micro-residue accumulation
- Energy-intensive production
- High water demand in dissolution steps (42)

Environmental health officers in UK interviews expressed concern that PVA may face future regulatory restrictions due to its persistence and wastewater impact.

2.3.3 Cellulose-Based Materials

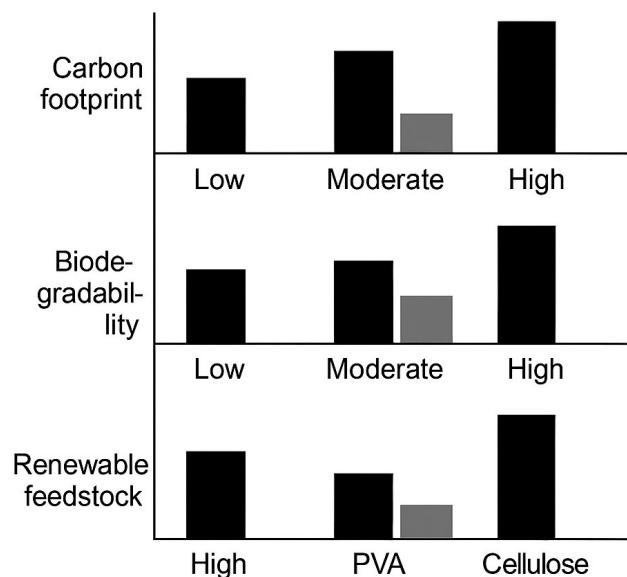
Cellulose is the most sustainable polymer in this comparison.

Strengths:

- Completely biodegradable
- Naturally derived from renewable biomass
- Low toxicity
- Supports circular production models (43)

Cellulose aligns strongly with UK environmental priorities and may represent the long-term future of sustainable pharmaceutical 3D printing.

SUSTAINABILITY COMPARISON OF PLA, PVA, AND CELLULOSE



2.4 Safety and Regulatory Considerations

PLA

Well-established in biomedical implants, biodegradable scaffolds, and drug delivery (44). Accepted by major regulatory bodies including EMA and MHRA for specific applications.

PVA

A fully recognised pharmaceutical excipient with decades of safety data (45). Its regulatory pathway is the most established of all three materials.

Cellulose-Based Filaments

Cellulose derivatives are well-established excipients, but cellulose-based FDM filaments as a category lack standardisation and regulatory guidance (46).

Regulators will likely require additional data on:

- thermal degradation products
- filament purity
- mechanical consistency
- long-term storage stability

2.5 Operational Challenges in UK Pharmaceutical Settings

Based on literature and dissertation data:

- **PVA moisture sensitivity** → most problematic
- **PLA brittleness** → feeding failures, snapping
- **Cellulose clogging** → highest print failure rate

- **Limited UK suppliers** → scarcity of pharmaceutical-grade sustainable filaments
- **Lack of training** → insufficient expertise in polymer science, rheology, HME

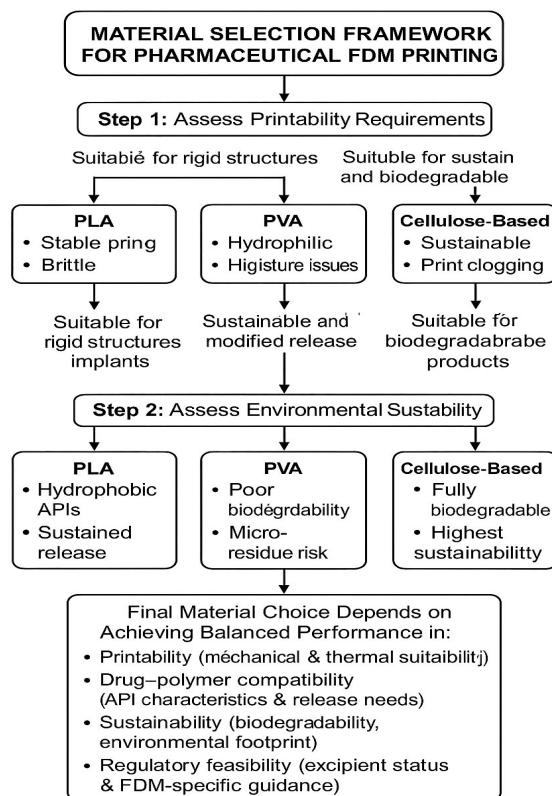
These real-world barriers must be addressed for full adoption of 3D printing in NHS and UK industry contexts.

2.6 Future Prospects

Future innovations include:

- Nanocellulose-based FDM materials
- PLA-cellulose hybrid composites
- AI-driven material selection
- Low-energy green polymerisation pathways
- MHRA guidance integrating environmental metrics

Advances in these areas could significantly accelerate sustainable adoption of 3D printing in UK pharmaceutical manufacturing.



CONCLUSION

PLA, PVA, and cellulose-based filaments each play important but distinct roles in the evolution of pharmaceutical 3D printing within the UK. PVA remains the most versatile filament for drug-loaded personalised medicines due to its processability and solubility. PLA provides structural stability and biodegradability and is effective for sustained-release systems. Cellulose-based materials offer the greatest sustainability benefits but currently face significant printability limitations. Uptake of sustainable materials in UK pharmaceutical 3D printing will require stronger regulatory guidance, improved filament engineering, wider industrial training, and lifecycle assessment frameworks. With continued research and innovation, cellulose-derived and hybrid bio-based filaments may ultimately become the optimal sustainable standard for the UK's additive pharmaceutical manufacturing future.

Overall, sustainable pharmaceutical 3D printing in the UK will depend on a coordinated effort to improve filament engineering, harmonise regulatory frameworks, and incorporate lifecycle assessment into material selection. Hybrid materials such as PLA-cellulose composites or next-generation nanocellulose systems may ultimately deliver a balance between printability, sustainability, and drug-loading flexibility. Continued collaboration between academia, industry, and the MHRA will be essential for overcoming operational barriers and enabling the safe, efficient, and environmentally responsible adoption of 3D printing within UK pharmaceutical manufacturing.

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