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Formulation and Evaluation of Pharmaceutical Filament for 3D Printing Containing Lamotrigine

Pallavi Joshi[1], Dr. Ashutosh Badola[*1]

[1]Assistant Professor, Department of Pharmaceutics, School of Pharmaceutical Sciences, SGRR University, Dehradun, Uttarakhand, India, 248001

[*1]Associate Professor, Department of Pharmaceutics, School of Pharmaceutical Sciences, SGRR University, Dehradun, Uttarakhand, India, 248001

Correspondence Author:

Dr. Ashutosh Badola,

Associate Professor, Department of Pharmaceutics, School of Pharmaceutical Sciences, SGRR University, Dehradun, Uttarakhand, India, 248001

Email ID: febpharm@gmail.com

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ABSTRACT

This research explores the development and evaluation of a novel 3D printed oral drug delivery system for Lamotrigine using hot melt extrusion (HME) and fused deposition modeling (FDM) techniques. Polyvinyl alcohol (PVA) served as the polymeric carrier due to its biocompatibility and excellent printability, while triethyl citrate (TEC) was employed as a plasticizer to improve filament flexibility and processability. The Wellzoom hot melt extruder was utilized to manufacture drug-loaded filaments, which could be then printed into dosage forms using FDM. A comprehensive analysis, including thermal, mechanical, morphological, and other studies, was conducted to evaluate the performance and stability of the filament. The results demonstrated the potential for 3D printed Lamotrigine filament which highlighted the utility of this method for personalized medicine.

Keyword: *3D Printing, Lamotrigine, Pharmaceutical Filament, Drug Delivery, Personalized Medicine, Hot melt extrusion*.

1. INTRODUCTION

Lamotrigine is a commonly used antiepileptic drug (AED) that is effective in treating various types of seizures, including focal seizures, generalized tonic-clonic seizures, and those associated with Lennox-Gastaut syndrome. It also plays a role in the maintenance treatment of bipolar disorder, particularly in preventing depressive episodes. Lamotrigine acts by inhibiting voltage-sensitive sodium channels, which stabilizes neuronal membranes and reduces the release of excitatory neurotransmitters like glutamate. It is well absorbed orally, with nearly 100% bioavailability, and is primarily metabolized in the liver through glucuronidation. The drug's half-life can be influenced by other medications such as valproate or enzyme-inducing antiepileptics. Lamotrigine is appreciated for its broad spectrum of activity and relatively favorable side effect profile, with a lower risk of cognitive impairment compared to older AEDs. However, it can cause side effects such as dizziness, headache, and skin rash. Careful dose adjustment and monitoring are essential, especially during initiation or when used in combination with other drugs. Overall, lamotrigine is considered an effective and well-tolerated option for managing epilepsy and mood disorders.[1,2]

The advancement of additive manufacturing, especially 3D printing, has revolutionized drug delivery systems by enabling precise, patient-tailored therapies. Lamotrigine, a widely prescribed anticonvulsant, has variable dosing requirements depending on patient age, condition, and co-medications. Traditional fixed-dose tablets lack flexibility in dose personalization. The integration of hot melt extrusion (HME) and fused deposition modelling (FDM) 3D printing offers a transformative solution by fabricating dosage forms with customizable dose and release kinetics.[3,4]

Hot melt extrusion is a solvent-free, continuous processing technique where the drug and polymer are mixed, melted, and extruded into filaments. These filaments are then fed into an FDM printer to construct dosage forms layer by layer. PVA is a preferred polymer in pharmaceutical-grade FDM due to its thermal stability, water solubility, and GRAS (Generally

Recognized As Safe) status. TEC, a hydrophilic plasticizer, enhances the flexibility and flowability of filaments, facilitating smoother extrusion and consistent print quality.

This study aims to formulate, optimize, and evaluate PVA and TEC-based filaments prepared through a Wellzoom hot melt extruder.[5,6,7]

1.1Advantages of Pharmaceutical Filaments

1. **Personalized Medicine:** Filaments can be used in 3D printing to produce patient-specific dosages, improving treatment accuracy and adherence.
2. **Controlled Drug Release:** By modifying the composition and structure, filaments can offer immediate, sustained, or delayed drug release profiles.
3. **Enhanced Drug Stability:** Solid-state filaments can improve the stability of heat- or moisture-sensitive drugs during storage and processing.
4. **Flexible Formulation:** A wide range of polymers and drugs can be used, allowing for versatile formulation options.
5. **Minimally Invasive Delivery:** Filaments can be designed for oral, implantable, or transdermal applications with minimal discomfort.

Efficient Manufacturing: Hot-melt extrusion, commonly used for filament production, is a continuous and scalable process, suitable for both R&D and commercial use.[9,10]

2. MATERIALS AND METHODS

2.1 Materials: The following materials were used to prepare the filament.

- **Lamotrigine**: Procured from a certified supplier, used as the API.
- **Polyvinyl Alcohol (PVA)**: Pharmaceutical grade, used as polymer.
- **Triethyl Citrate (TEC)**: Selected as an FDA-approved plasticizer.
- **Wellzoom Hot Melt Extruder**: Single-screw extruder with adjustable temperature and screw speed.

2.2 Formulation of Blank Filament

PVA particles were first ground into powders in order to create the filaments. After being vacuum-dried for eight hours at 60 °C, the powders were combined with triethyl citrate as a plasticizer in a mortar and pestle until no clumped polymer particles were visible. Filaments were then prepared by feeding the mixture into a desktop extruder. The impact of screw rate (ranging from 20 to 60 rpm at intervals of 10 rpm) and extrusion temperature (ranging from 185°C to 200°C at intervals of 5°C) on the quality of the extruded filaments was examined.[12,13]

2.3 Formulation of Drug loaded Filament:

To make the drug-loaded filaments, PVA particles were first ground into powders. In a mortar and pestle, the powders were mixed with lamotrigine and TEC after being vacuum-dried for eight hours at 60 °C until no visible agglomerated drug or polymer particles remained. The mixture was then fed into a desktop extruder to create filaments. The temperature was set at 195 °C, and the extruder speed was set at 50 rpm. These characteristics of the blank filament mix yielded the greatest results for thickness and high tensile stress. For 3D printing, both qualities are essential. Several formulations of Lamotrigine-loaded filaments with different proportions of drug, polymer, and plasticizer were made using the previously mentioned parameters.[13,14]

3. RESULTS

3.1 Evalution of Blank Filament:

Evaluation of a pharmaceutical filament is a critical step to ensure its quality, performance, and suitability for use in drug delivery systems, especially in 3D printing applications. Several parameters are assessed to determine the filament's physical, mechanical, and pharmaceutical properties. Key physical evaluations include measuring the diameter and uniformity of the filament, as consistent dimensions are essential for smooth feeding into 3D printers. Mechanical properties such as tensile strength and flexibility are also tested to ensure that the filament can withstand handling and processing without breaking. The evaluated filament parameters showed these results:

Color: Light yellow to translucent

Texture: a level surface

Water Solubility: Water Soluble, Extremely soluble in warm water

Texture: Low stiffness, high flexibility, and resistance to wear.

3.1.1 Measurement of diameter: A digital vernier caliper was used to measure the monofilament's diameter. Five mono filaments were examined, and each monofilament was measured five times at 50-cm intervals. The findings were then averaged. The following is the diameter data of the filaments acquired at different extrusion temperatures and screw speeds:

RPM/Temp	185°C	190°C	195°C	200°C
20rpm	1.733	1.676	1.612	1.432
30rpm	1.754	1.732	1.697	1.578
40rpm	—	1.714	1.702	1.664
50rpm	—	1.756	1.747	1.758
60rpm	—	1.921	1.845	1.832

Table 1: Diameter of filaments on different paraters

3.1.2 Ultimate tensile stress measurement:

Every test is conducted at room temperature (T=20 °C) on a stretcher. Stretching occurs at a rate of 2 mm/s. The ultimate tensile stress, or σ, is calculated using the formula below: ($\sigma = F/S$), where F is the ultimate tensile force as measured by a force meter and S is the area of the filament's fractured cross section. During the test, the stretcher rises at a speed of 2 mm/s until the filament breaks. The maximum F is then automatically recorded, and the shattered cross section area S of the filament is measured manually.[15,16]

The results of five samples were averaged. The ultimate tensile stress of the strands, expressed in Mpa:

RPM/Temp	185°C	190°C	195°C	200°C
20rpm	6.1	56.7	54.2	51.2
30rpm	5.6	57.7	57.1	54.3
40rpm	—	58.9	58.5	55.7
50rpm	—	58.1	60.0	57.5
60rpm	—	57.2	57.8	53.7

Table 2: Tensile strength of filaments on different parameters

3.2 Formulation and Evaluation of Drug Loaded Filaments:

The 6 formulations were prepared using different concentration of excipient and evaluated for the following parameters

Formulation	Lamotrigine (%)	PVA(%)	TEC(%)	Filament ability	Filament Diameter (mm)	Tensile Stress (Mpa)
F1	10	75	15	No	-	-
F2	10	70	20	Yes	1.53	14.5
F3	10	68	22	Yes	1.67	24.7
F4	10	65	25	Yes	1.89	17.3
F5	10	63	27	Yes	1.76	19.2

F6	10	60	30	Yes	1.87	28.9

Table 3: Formulation & evaluated parameters of Filaments

Physical properties of the formulated filaments was observed as:

Color- Translucent to Light yellow

Texture- Smooth surface

Solubility- Water Soluble (Highly soluble in warm water)

Stiffness- Low, Very flexible, Wear resistant

3.2.1Printability Assessment

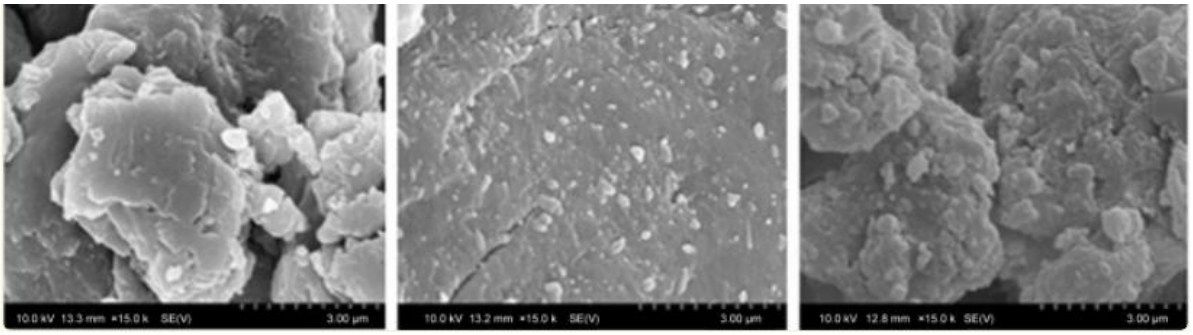
The printability assessment of the filament, as presented in Table 3 evaluates its performance based on maximum force, toughness, and overall printability.

The results confirm that higher toughness and moderate extrusion force contribute to improved printability, whereas lower toughness values lead to inconsistent or failed prints. Overall, filaments F3, F4, and F5 demonstrated good printability, while F1, F2 and F6 were unsuitable, emphasizing the importance of optimizing filament composition and processing parameters to achieve consistent and high-quality prints.[17]

These findings are consistent with Xu et al. (2020), who developed a quantitative method to evaluate the printability of filaments using a texture analyser, identifying "toughness" as a key predictor of filament printability. Similarly, Tabriz et al. (2021) investigated pharmaceutical-grade polymer filaments and found that tensile strength, ranging between 15-20 MPa, was critical for determining printability, reinforcing the importance of mechanical properties in extrusion and adhesion performance. Moreover, Patti et al. (2022) demonstrated that rheological properties, such as zero-shear viscosity and polymer relaxation time, were crucial in determining printability and extrusion smoothness in PLA-based filaments. Collectively, this confirm that higher tensile strength and moderate extrusion force contribute to improved printability, while lower tensile strength values lead to inconsistent or failed prints, emphasizing the need to optimize filament composition and processing parameters for achieving consistent and high-quality prints.[18]

3.2.2 Scanning Electron Microscopy (SEM) analysis

A thorough understanding of the filament's surface morphology is offered by the SEM analysis shown in Figure 1, which emphasizes differences in particle distribution, roughness, and structural integrity. A heterogeneous particle arrangement with noticeable agglomerations and spaces is visible in the photos taken at various magnifications, indicating that the components within the filament are not uniformly distributed. The filament's printability and mechanical stability are supported by the partial fusing of the polymer matrix shown by the presence of smooth and well-integrated regions in certain spots.[19,20] According to the observed morphology, the filament's uniformity can be further improved, flaws can be decreased, and its overall performance for 3D printing applications can be improved by optimizing processing settings and material composition.



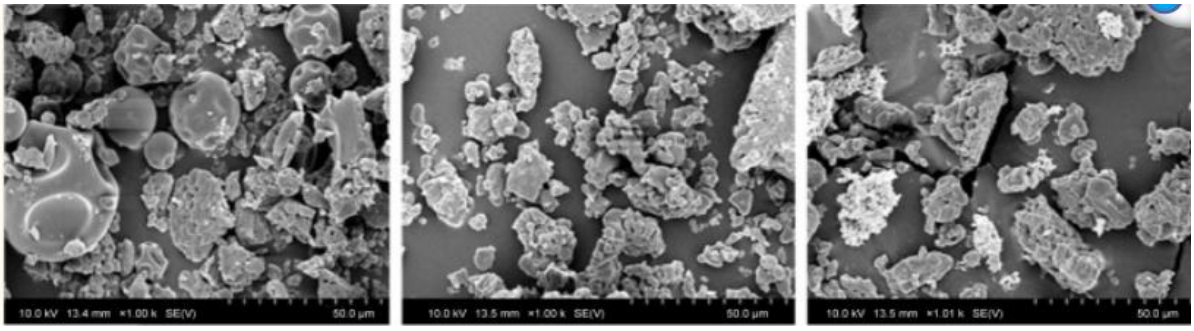


Fig 1: Surface morphology of filament

4. CONCLUSION

The present study successfully demonstrated the application of hot melt extrusion (HME) coupled with fused deposition modeling (FDM) 3D printing for the formulation of Lamotrigine-loaded pharmaceutical filaments using polyvinyl alcohol (PVA) as the matrix-forming polymer and triethyl citrate (TEC) as the plasticizer. The selection of these excipients was guided by their biocompatibility, processability, and regulatory acceptability.

The Wellzoom hot melt extruder provided a controlled, continuous manufacturing platform for producing filaments with uniform drug distribution, mechanical robustness, and consistent dimensional accuracy, essential for subsequent 3D printing processes. Thermal and spectroscopic analyses confirmed the amorphous dispersion of Lamotrigine within the polymeric matrix, which is beneficial for enhancing solubility and bioavailability.

The incorporation of TEC played a critical role in modulating the melt viscosity and mechanical flexibility of the filaments, ensuring smooth extrusion and improved feedability into the FDM printer. This optimization reduced common processing issues such as filament breakage, nozzle clogging, and inconsistent extrusion rates.

The approach illustrates the feasibility of using personalized pharmaceutical manufacturing strategies by integrating digital design with thermomechanical processing. It aligns with modern regulatory and clinical trends emphasizing dose individualization, on-demand fabrication, and decentralized production, particularly for drugs with narrow therapeutic windows, complex dosing regimens, or paediatric/geriatric requirements.

However, the study also highlights the importance of material selection, process parameter optimization, and quality control mechanisms to ensure reproducibility, stability, and efficacy of the final dosage forms. Future research should explore alternative polymers, temperature-sensitive actives, and inline monitoring systems, as well as regulatory pathways for clinical adoption of 3D printed pharmaceuticals.

In conclusion, the combination of HME and FDM offers a disruptive yet practical platform for transforming how oral solid dosage forms is developed, manufactured, and customized—potentially leading to a new paradigm in pharmaceutical care.

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