

Development of Linezolid-Graphene Composite-Loaded Nanoengineered Scaffolds for Healing of Burn Wound

Rajesh Kumar¹, Ajay Kumar¹, Anupriya Kapoor¹, Shashi Kiran Misra^{1*}

¹School of Pharmaceutical Sciences, CSJM University Kanpur, 208024

*Corresponding Author

Dr. Shashi Kiran Misra

Associate Professor

School of Pharmaceutical Sciences, CSJM University Kanpur, 208024

rajeshkumar25389@gmail.com, ajaykumar@csjmu.ac.in, anupriya321@gmail.com,

shashikmishra@csjmu.ac.in

Abstract

Linezolid-graphene nanocomposites have enormous potential as an intelligent medication system to efficiently treat burn injuries, resolving important issues such as the requirement for regulated drug release, a high risk of infection, and a prolonged healing period. Here, we created a novel nanoengineered electrospun scaffold for smart burn wound care using graphene composites loaded with Linezolid and embedded in a biocompatible polymeric matrix. Targeted antibacterial activity is provided by the inclusion of Linezolid, a potent broad-spectrum antibiotic, while mechanical strength, thermal stability, and a favorable environment for cell development are provided by the graphene additive. Nanofibers scaffolds with enormous surface area-to-volume ratios, resembling the extracellular matrix, and sustained drug administration were made possible by the electrospinning technique. Both in vitro and in vivo studies demonstrated enhanced fibroblast proliferation and improved re-epithelialization, along with exceptional antibacterial activity against multidrug-resistant infections. Graphene has superior optical, electrical, and thermal capabilities, high surface area of its planar structure, high loading potential, and mechanical and chemical stability; it has been known as a dominant carrier for a wide variety of medicinal compounds. In this work, Linezolid, an antifungal drug, was mingled with Graphene nanoplatelets to develop composite via the wet chemical method, embedded in a biocompatible polymeric blend of Polyvinyl Alcohol (Industrial grade) and subjected to electrospinning to obtain nanoengineered scaffolds (nanofibers) for enhanced antibacterial property. Pursuing a set of optimization experiments, 10% w/v Polyvinyl Alcohol (Industrial grade) was found to be adequate for formation of smooth, defect-free, and regular fibers. Conclusion declared the superior antifungal activity of Linezolid-Graphene entrapped nanofibers as compared to Linezolid entrapped nanofibers and recommended believable dressing materials for a dominant regimen of burn wound infections.

Keywords: Graphene, Linezolid, Composite, Burn Wounds, Dressing materials.

1. INTRODUCTION

Over the last decade, Graphene has been widely used in biomedicine and health services to control the delivery of bioactive agents for therapeutic purposes (Mousavi et al. 2022). A single sheet of densely packed carbon atoms, graphene has a huge surface area and several attachment sites. It also acts as a draft-fateful bandstand for unique chemical interactions with microorganisms (Akiyama et al., 2023). Graphene is found in simple organic structures and causes discontinuities in the cell activities of microorganisms because to its extremely high surface to volume gauge and small size in comparison to cells and cellular components. (Hosseinkazemi & Hessam, 2024). The enormous loading of the bioactive agent onto the surface of graphene sheets enclose with promising Nano platforms for designing antimicrobial dosage formulations (Ittoo et al. 2025). Improvement in the case of burn patients, inflammatory response syndrome, and severe sepsis syndrome are major causes of morbidity and mortality. As a result, further development of antimicrobials may hold some promise for future research (Clara et al. 2024). The burn wound caused by heat represents which until the development of effective topical antimicrobial chemotherapeutic agents was the most common site of infection which is caused morbidity and, when invasive, virtually died in the burn patients (Clayton et al. 2021). Even though there is an inventory of traditional antimicrobial drugs in the trade, they are dominant as prophylactic at prelim stage, but at the advanced state of infection, these measures prove nay unassisted due to some shortcomings concerned with the type of dosage formulations (ElMokadem et al. 2025). Also, their indiscriminating and long enormous doses generally cause infection return up to 20–40%, struggle and easygoing anxiety by producing opposing things (Gutiérrez-Brito et al. 2025). Moreover, the treatment also activates on host's

immune system and creates sensitive symptoms like burning or scorching sensations in the patients (Shahabudin et al. 2024).

Burn wounds infections and other bacterial infections are treated with linezolid. Linezolid is a member of the oxazolidinone class of antibacterial. It works by preventing bacteria from growing (Liu et al. 2025). Available as injectable solutions, oral suspensions, and tablets, linezolid has drawbacks such as poor effectiveness, and pain at the administration site, which lengthens the course of treatment (Rampedi et al. 2024).

Therefore, one of the goals of the current study is to reduce these faults by establishing an efficient linezolid dose formulation against burn wound treatment with adequate patient compliance and lowering the likelihood of recurrence (Sartelli et al. 2022). Through their unique surface area and sharp mechanical support, structure-oriented, therapeutically functional, and therapeutically active 3D nanofibers can replicate the original cell niche and demonstrate an infinite use in tissue engineering, cell development, and cell proliferation, according to a review of the field's literature (Kaka et al. 2025).

Electrospun scaffold nanofiber constructions are more capable for usage as scaffolds and matrices for topical dressings since it is possible to upload several bioactive composites into them. The localized effective arena of the medicine operating against the infection is another feature of such a preparation (Rajput et al. 2023). It firmly maintains a consistent confinement and prevents drug escalation into nearby regions, preventing medication interactions with healthy host tissue (Sahoo et al. 2025). For the production of nanofibrous scaffolds, polymers (10% w/v polyvinyl alcohol) have been used because to their intrinsic qualities, which include efficient adhesion, biocompatibility, and classiness over the skin surface (Öztürk et al. 2024). The current study investigates the use of a separate fraction of both polymers for regulated drug release from the nanofibrous scaffold because of the varied permeability nature (Abboud et al. 2025). By creating polyvinyl alcohol scaffolds loaded with a Linezolid–graphene composite, we investigated the topical antifungal properties of graphene and evaluated it's in vitro efficacy against burn wound treatments (Vijapur et al. 2025).

1.1 Electrospinning

Formhals (1934) patented a procedure in which an experimental set-up for the creation of polymer filaments employing electrostatic force was described. This technique is known as electrospinning when it is used to spin fibers. In other terms, electrospinning is a technique that uses an electrically charged jet of polymer melt or solution to spin nanofibers. When a polymer fluid is electrospun, a high voltage is used to induce charges inside the fluid. A fluid jet will erupt from the droplet at the needle's tip when the quantity of charges in the fluid reaches a critical level, creating a Taylor cone (Al-Abduljabbar et al. 2022). The electrospinning jet will move in the direction of the area with the lowest potential, which is typically a grounded collection. The morphology of the resulting electrospun fibers will depend on a variety of factors and may take the form of beaded fibers or fibers with surface pores (Yu et al. 2025).

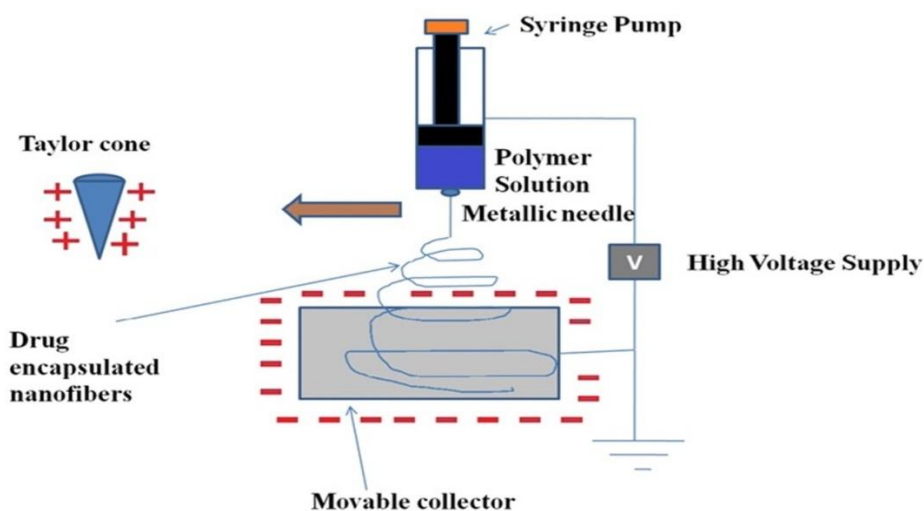


Fig.1. A simple electrospinning setup

1.2 Components of Electrospinning

A simple electrospinning setup for electrospinning polymer solutions consists of the following components:

- Syringe

- Pump
- Voltage generator
- Accumulator

The syringe's polymer solution is forced through the capillary by the pump. The drop is stretched into a cone (Taylor cone) by the generator's electrical charge of the solution. The accumulator or collector is where the nanofibers are collected (Zaarour et al. 2024).

1.3 Parameters

Numerous elements influence the electrospinning process. These are divided under three categories:

- environmental,
- solution, and
- The parameters of electrospinning.

Among the properties of the solution are its conductivity, viscosity, solvent concentration, and polymer concentration. Two examples of environmental parameters are temperature and relative humidity. The development of smooth, beadless electrospun fibers is directly impacted by each of these factors. The needle diameter, flow rate, needle-to-collector distance, and electric field strength are a few of the electrospinning parameters. To better understand the electrospinning process and the production of polymeric nanofibers, it is crucial to fully understand the significance of each of these regulating factors (Cho et al. 2025).

1.4 Characteristics of Solution

The following are important features of electrospinning: To dissolve the polymer, the right solvent must be present. It must have the right vapor pressure to evaporate quickly enough to preserve the fiber's integrity after it reaches the target, without solidifying before it reaches the nanoscale scale. Additionally, it needs to have the proper surface tension and viscosity such that the fiber cannot form in the polymer solution before it reaches the nanoscale level. To create and maintain the jet from the pipette, the energy source must be sufficient to cut through the viscosity and surface tension of the polymer solution (Tinsley et al. 2025).

1.5 Humidity and Temperature

Humidity causes variations in the diameter of the nanofiber by controlling the solidification of the charged jet. However, the chemical character of the polymer determines this impact. Temperature has two opposing impacts that change the average nanofiber diameter: (1) it increases the solvent's rate of evaporation, and (2) it decreases the viscosity of the solution. The average fiber diameter decreases as a result of both the increase in solvent evaporation and the decrease in solution viscosity, which work in opposing ways (Qosim et al. 2024).

1.6 Parameters of Electrospinning

- Voltage.
- Flow rate,
- Needle diameter.
- The distance between the needle tip and collector.

These parameters do affect fiber morphology and diameter specifically.

1.6.1 Voltage

Each polymer has a distinct critical applied voltage. When the applied voltage is increased, the polymer solution stretches in response to the charge repulsion inside the polymer jet, producing small-diameter nanofibers. Beads or beaded nanofibers will form if the applied voltage increases over this critical amount (Sharma et al. 2025).

1.6.2 Flow rate

The flow of the polymeric solution in the metallic needle tip determines the shape of electrospun nanofibers. It may be possible to create uniform, beaded, and electrospun nanofibers using a polymeric solution's critical flow rate. Bead formation could occur if the flow rate increases past the critical point. Changes in flow rate have an impact on the diameter and development of nanofibers; a minimal flow rate is preferred to balance the exiting polymeric solution and introduce a new solution to replace it during jet formation (Mathew et al. 2025).

1.6.3 Needle Diameter

There is a correlation between the electrospun nanofiber morphology and the needle's diameter. The average diameter of the nanofiber decreases together with the needle's internal diameter, becoming smooth and slim with no development of beads or cluster. Furthermore, compared to a large needle diameter, the porosity of the nanofibrous increases with a smaller needle diameter (Zhang et al. 2025).

1.6.4 Distance of Needle Tip and Collector

The distance between the metallic tip of the needle and the collector has a significant impact on the shape of an electrospun nanofiber. Important characteristics of nanofiber development that are readily influenced by distance include the deposition duration, the rate of evaporation, and the whipping or instability period. Therefore, there must be a crucial spacing in order to create smooth and uniform electrospun nanofibers; any variation from this distance will alter the nanofibers' morphology (Cho et al. 2025).

2. MATERIALS AND METHOD

Carbon allotrope graphene nanoplatelets was purchased from Reinste Pvt. Ltd. India. Drug linezolid was collected from Laborate Pharmaceuticals India Ltd. Biocompatible polyvinyl alcohol polymer was received from BAL-LABS, Kanpur, Uttar Pradesh, India. All the solvents and other excipients were from Merck Pharma Pvt. Ltd.

2.1 Preparation of linezolid-graphene (Lz-Gn) composite

Originally, drug linezolid was loaded efficiently on the graphene nanoplatelets through wet chemical route to get composite of linezolid-graphene nanoplatelets. To put it briefly, a uniform dispersion of graphene in acetone was mixed with Linezolid (1 mg/ml) and sonicated for a short while. The resultant dispersion was ultra-centrifuged for 30 minutes at 15,000 rpm after being agitated for the entire night at room temperature in the dark.

2.2 Fabrication of Lz-Gn composite loaded nanofibers

Furthermore, Lz and Lz-Gn were loaded into a polyvinyl alcohol polymer solution at concentrations of 1% w/v each. Taking into account the aforementioned process parameters, the produced dispersion was subjected to the electrospinning procedure. When the voltage was increased, the pendant drop was drawn into a conical shape called a Taylor Cone by the repulsive electric force. Once the electrical force overpowers the surface tension, a liquid jet forms from the syringe and travels in nanoseconds to the bra's collector as fine fibers (Gupta et al. 2025).

3. Characterization

3.1 Fourier Transform Infrared (FTIR) Spectroscopy

FTIR spectroscopic studies to evaluate the materials' local chemical and compositional characteristics. Wave numbers ranging from 4000 to 500 cm^{-1} were used to record measurements on the distinct physical mixture, Lz, Gn, formulation composite, Lz-loaded nanofibers, and Lz-Gn-loaded nanofibers.

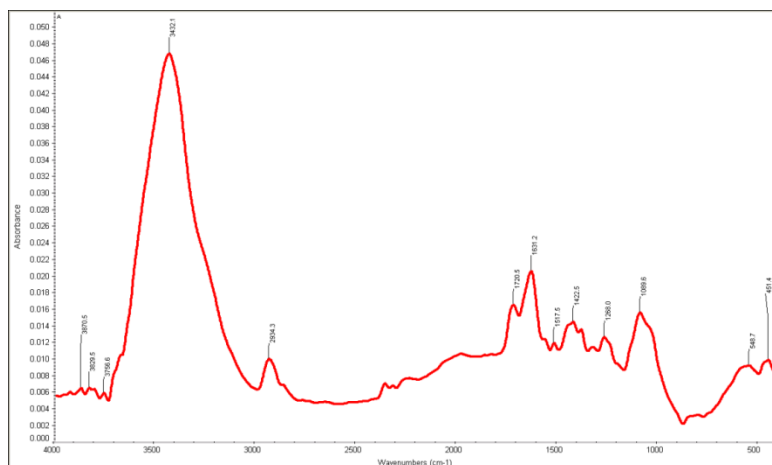


Fig.2 FTIR (Fourier Transform Infrared) spectrum

This spectrum is Fourier Transform Infrared (FTIR), with wavenumbers (cm^{-1}) on the X-axis and absorbance on the Y-axis. The spectrum's peaks are caused by different chemical bond vibrational modes in the sample.

3.2 Surface topography

The topography of the surface of the produced nonwoven electrospun nanofibers was examined using Field Emission Scanning Electron Microscopy. The samples were gold sputter-coated to enhance conductivity for imaging. Average diameter of fibers and distribution of fibers were determined.

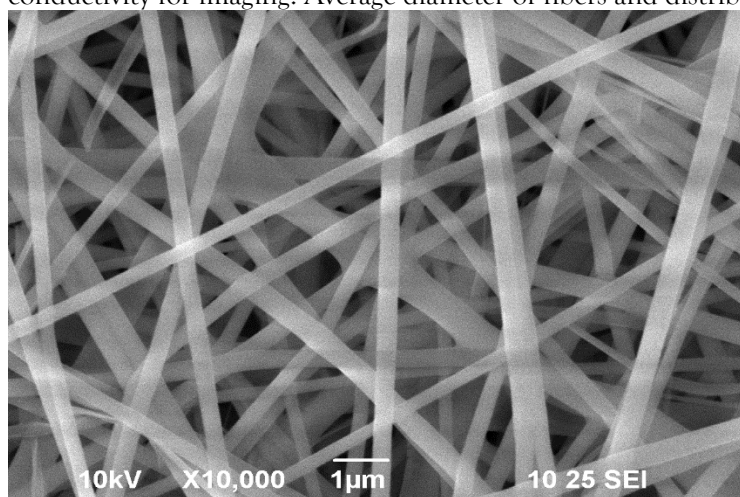


Fig.3 Scanning electron microscope (SEM), shows fibrous

This image, taken with a scanning electron microscope (SEM), shows a fibrous substance that may be electrospun polymer fibers or a nanofiber mesh. At 10,000x magnification, the image shows a complicated, interconnected network of thin filaments. Given that the scale bar shows a length of one micrometer (μm), the fibers' diameters are likely in the nanometer to sub-micrometer range. An accelerating voltage of 10 kV is required for SEM imaging. This kind of structure is typically found in nanotechnology and healthcare scaffolds.

Static water contact angle (WCA) was examined to explain the degree of hydrophilicity by sessile drop method with Kruss Drop Shape Analyzer DSP 25 contact angle goniometer under video capture at room temperature. Using a micro syringe, 30 μL of deionized water was pipetted onto a dried electrospun nanofiber (2 cm^2) in a saturated water vapor atmosphere (Siddiqui et al. 2024). To avoid any fluctuations, WCA was estimated after 60 s of incubation. To get a good value, the average of three different contact angles was calculated.

3.3 XRD

The main analytical use for X-ray diffraction (XRD) is the phase determination of crystalline materials. While XRD of scaffolds loaded with Gn was unable to alter the highly crystalline nature of Gn, the pattern

exposed shifted peak at 18° may be the result of the molecular dispersion of metastable polymers in Figure. In Figure, an intense sharp peak was obtained at 26° Gn, suggesting a neatly arranged microcrystalline nature.

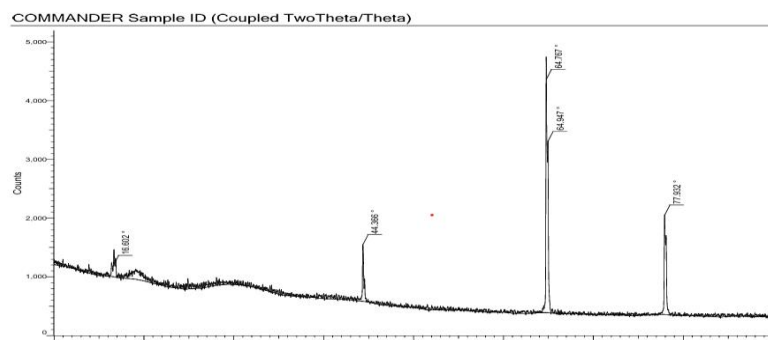


Fig.4 Phase determination of crystalline materials

Plotting data using the diffraction angle (2θ) in degrees on the X-axis and the relative intensity (counts), or the observed X-ray signal, on the Y-axis is known as X-ray diffraction (XRD). A characteristic of materials is the pattern's broad baseline with a few distinct peaks. At approximately 16.602°, 44.356°, 64.497°, 64.767°, and 77.932°, distinct diffraction peaks are observed, which correlate to the sample's distinctive crystallographic planes. They are crisp and provide crucial information regarding the phase constitution and atomic structure of the substance.

3.4 SWELLING INDEX

When using the gravimetric approach on skin with a pH of 7, the swelling index is considered a major tool for estimating the drug release behavior from the nanofibrous scaffold (Jung et al. 2025). Every nanofibrous scaffold (1 cm²) that had been constructed was put in a Petri plate with 10 ml of medium and cultured for 24 hours at 37 °C. After using filter paper to peel off the media that was stuck to the scaffold surface, the wet weight was measured until it was constant. Three successive measurements of each nanofiber were used to calculate the average level of the swelling index.

The experimental results for determining a material's swelling properties over time—that is how much liquid it absorbs and grows in weight—are shown in the graph. To ensure consistency, three duplicates are taken at various time intervals (measured in hours) for the results. Weight Wet (W2) is the sample's weight following soaking, while Weight Dry (W1) is the sample's initial dry weight. The liquid absorption is measured by the difference between W2 and W1, which is then utilized to calculate the Swelling Index using the formula.

$$\text{Swelling Index} = (W2 - W1) / W1$$

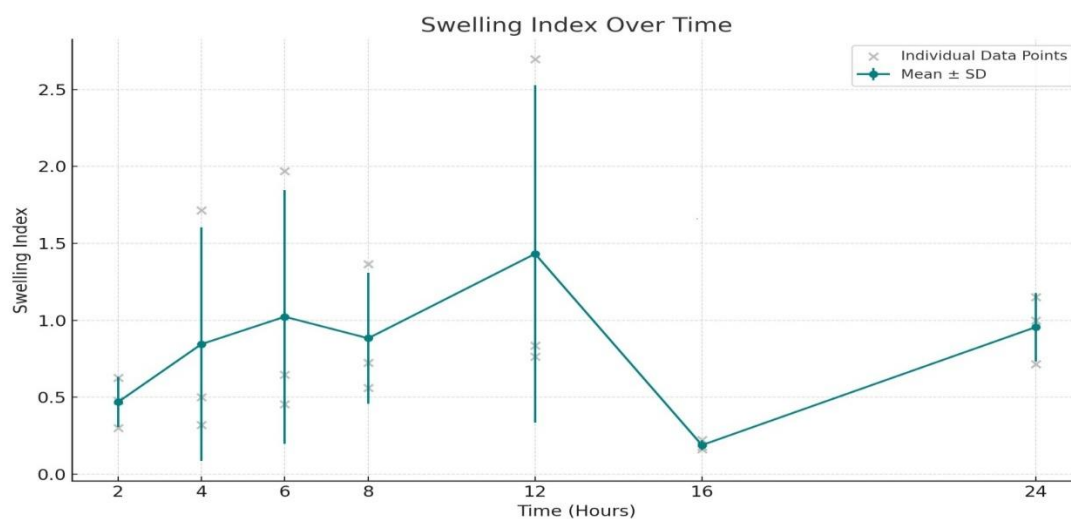


Fig.5. Swelling Index

This index shows the amount of swelling the material has experienced. The data generally shows that the swelling index rises with time, reaching a peak at 12 hours (the highest reading was 2.697), and then falling at later times, such as 16 hours. Although individual duplicates may vary, the general pattern is constant and illustrates the material's dynamic absorption activity. Applications like materials science, pharmaceuticals, and polymer engineering, where the swelling and liquid absorption properties are critical to material functionality and use, benefit greatly from such data.

4. RESULTS AND DISCUSSION

Creation of the Linezolid-Graphene Composite (Lz-Gn) Graphene nanoplatelets (Gn) facilitated direct physical adsorption and noncovalent interaction with the aromatic hydrophobic drug Lz. Hydrogen bonding between their functional groups may be the basis for the creation of a composite with Gn and Lz. It would modify macromolecules with biologically active modules to transport into target tissue/cells invaded by burn wounds. The enhanced loading capacity is explained by the decreased steric hindrance impact of the loaded molecule throughout the composite creation process. The composite created by creating Lz-Gn would not emit bioactive agent during its delivery route, preventing harmful effects on healthy tissue or cells, unlike liposomal drug carriers or micelles. Optimization of polyvinyl alcohol polymer concentration for the production of nanofibers following electrospinning, beaded, uneven, and nonuniform nanofibers appeared on the collector, accompanied by polymeric droplets of the polyvinyl alcohol polymer solution (8% w/v). In order to achieve regular beadles and a consistent nanofibrous scaffold, the concentration of polymers was increased to 10%w/v, which was thought to be polyvinyl alcohol polymer (Fig. 3).

5. CONCLUSION

In the present study, graphene (Gn) was inserted into nanofibrous scaffolds of the polyvinyl alcohol polymer with drug loading of Linezolid (Lz), and its graphene-based composite Lz-Gn was joyfully created. Produced from the polymer to the extracellular matrix, nanofibers demonstrated rapid hydrophilicity, high swelling properties, and drug release control. These properties were predicated on new uses for bandages or dressing materials to treat burn wounds.

At the first stage, the drug release profile from nanofibers was advantageous for treating burn wounds; thereafter, the restricted and regulated drug release enhanced the nanofibrous scaffold's antibacterial efficacy indefinitely. The synergistic action of Lz and Gn may be the reason for the greater antibacterial activity. Consequently, the Lz-Gn-loaded nanofibrous scaffold would offer a way to construct dressing materials for the management of severe burn injuries.

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