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FABRICATION AND CHARACTERIZATION OF CARBAMAZEPINE-LOADED FIBERS FOR CONTROLLED DRUG DELIVERY

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Carbamazepine (CBZ) is a widely prescribed antiepileptic and mood stabilizing drug. However, its limited water solubility and low bioavailability challenge its effective use. This study focused on the fabrication and characterization of CBZ-loaded polylactic acid (PLA) / polyethylene glycol (PEG) fibers for controlled drug delivery. The morphology and diameter of the fibers were characterized using scanning electron microscopy (SEM) and Fourier transforms infrared spectroscopy (FTIR) confirmed the successful encapsulation of CBZ within the fibers. Differential scanning calorimetry (DSC) analysis revealed the physical state of the drug in the fiber matrix. As a result of CBZ loading on fibers, the average fiber diameters were measured as ϕ = 1.177 ± 0.238 μm for 10 mg CBZ and ϕ = 1.119 ± 0.248 μm for 50 mg CBZ. It was observed that the increase in electrical conductivity due to an increasing drug concentration, caused a decrease in fiber diameter. When drug release results were analyzed, the fibers showed a controlled release profile extending up to 10 h. These results suggest that the fabricated CBZ-loaded PLA/PEG fibers hold promise as a controlled drug delivery system for CBZ, offering the potential for enhanced therapeutic efficacy, reduced side effects, and improved patient compliance.

Keywords: carbamazepine; electrospun fiber; epilepsy; drug delivery

ИЗРАБОТКА И КАРАКТЕРИЗАЦИЈА НА ВЛАКНА НАТОВАРЕНИ СО КАРБАМАЗЕПИН ЗА КОНТРОЛИРАНА ДОСТАВА НА ЛЕКОВИ

Карбамазепинот (CBZ) е широко препишуван антиепилептик и стабилизатор на расположение. Сепак, неговата ограничена растворливост во вода и ниската биорасположливост ја отежнуваат неговата ефикасна примена. Оваа студија се фокусира на изработка и карактеризација на влакна од полилактична киселина (PLA)/полиетилен гликол (PEG) натоварени со CBZ за контролирана достава на лекови. Морфологијата и дијаметарот на влакната беа карактеризирани со скенирачка електронска микроскопија (SEM), а Фуриеова трансформирачка инфрацрвена спектроскопија (FTIR) ја потврди успешна инкапсулација на CBZ во влакната. Анализата со диференцијална скенирачка калориметрија (DSC) ја откри физичката состојба на лекот во матрицата на влакната. Како резултат на внесувањето на CBZ во влакната, просечните дијаметри на влакната беа измерени како ϕ = 1.177 ± 0.238 μm за 10 mg CBZ и ϕ = 1.119 ± 0.248 μm за 50 mg CBZ. Се забележа дека зголемувањето на електричната спроводливост поради повисока концентрација на лекот предизвика намалување на дијаметарот на влакната. При анализа на резултатите од ослободувањето на лекот, влакната покажаа контролирано ослободување кој траеше до 10 часа. Овие резултати укажуваат дека влакната изработени од PLA/PEG натоварени со CBZ имаат потенцијал за контролирана достава на CBZ, нудејќи можност за зголемена терапевтска ефикасност, намалени несакани ефекти и подобрена приспособеност на пациентите.

Клучни зборови: карбамазепин; електроспинувани влакна; епилепсија; достава на лекови

1. INTRODUCTION

In recent years, the development of innovative drug delivery systems in pharmaceutical sciences, aimed at enhancing the therapeutic efficacy of various drugs, has gained momentum. Among these approaches, nanofiber-based drug delivery systems have garnered significant attention due to their potential to address challenges related to traditional drug formulations. One particular area of interest is the production and characterization of nanofibers loaded with antiepileptic drugs, which hold the potential to improve treatment outcomes for individuals with epilepsy.[1]

Epilepsy is defined as a chronic brain disorder characterized by unprovoked seizures, affecting over 70 million people worldwide.[2] Epilepsy is highly resistant to pharmacological treatment; more than a third of patients continue to experience seizures despite taking multiple antiepileptic drugs (AEDs), necessitating the urgent need for alternative therapies.[3] Approximately 70 % of these patients are adequately controlled with oral AEDs, while the remaining 30 % do not respond to oral treatment. In the latter group of patients, even though the plasma concentration of antiepileptic drugs is within normal therapeutic ranges, they considered pharmacoresistant. Studies have indicated that changes in the permeability of antiepileptic drugs across the blood-brain barrier (BBB) may be a significant factor contributing to pharmacoresistance.[4] Among the drugs used, carbamazepine (CBZ) continues to be the best option due to its effectiveness, safety, and cost-effectiveness.[2] CBZ is used clinically to treat seizure disorders, trigeminal neuralgia, and, more recently, bipolar disorder.[5] Due to its favorable therapeutic behavior, CBZ remains the best-selling anticonvulsant and widely used antiepileptic drug, and is classified as a Class II drug in the biopharmaceutical classification system.[6] After oral administration of CBZ in solid dosage form, its poor water solubility (0.17 mg/ml at 24 °C) leads to slow and erratic gastrointestinal absorption, resulting in incomplete bioavailability.[7] Since the absorption of CBZ is limited by its solubility, improving its dissolution characteristics could enhance the absorption rate and increase oral bioavailability.[8] Dissolution of CBZ in methanol, PEG 400, or 2-pyrrolidone, and the adsorption of these solutions onto high surface area carriers such as silica or cross-linked polyvinylpyrrolidone can improve its dissolution properties.[9] Other strategies to enhance the dissolution rate of Class II drugs involve formulating active pharmaceutical ingredients (APIs) using polymers,[10] surfactants,[11] liposomes, or lipids.[12] Various methods have been employed to increase the dissolution rate of CBZ, including co-crystallization,[13] solid dispersion,[14] self-micro emulsifying,[7,15] adsorption onto silica substrates,[16] nanodispersion,[17] nanofibers,[2,18,19] and nanoparticles.[5,20] CBZ is currently available as an oral suspension, immediate-release, controlled-release (Tegretol CR), and extended-release (Carbatrol) tablets.[20] However, there are limitations. Its lipophilic nature, particularly oral administration, complicates formulation design and delivery. Problems associated with commercially available formulations, such as irregular and slow absorption, lead to drug resistance that compromises therapeutic efficacy, resulting in uncontrolled seizures, a higher risk of brain damage, and higher mortality rates.[20] Significant efforts have been directed towards developing nanocarriers that aid in delivering drugs to the brain, assisting in systemic distribution.[21–23] Local administration of drugs directly to the site of action has significant potential to enhance the therapeutic efficacy of epilepsy drugs, potentially allowing for lower therapeutic doses and fewer adverse effects.[3,24] These improvements have driven research towards the development of localized drug delivery systems for epilepsy.[21,25] For instance, Williamson et al. developed an organic electronic ion pump consisting of poly(3,4-ethylenedioxythiophene) coated with polystyrene sulfonate, which enables on-demand, region-specific delivery of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) through polystyrene sulfonate electrodes.[26] Similarly, Halliday et al. used levetiracetam-loaded, biodegradable polymer implants in a genotoxic rat model with temporal lobe epilepsy, showing that drug delivery polymer implants represent a promising treatment option for refractory epilepsy.[27] Pritchard et al. have also developed silk fibroin coatings on solid reservoirs of the anticonvulsant adenosine[28]

Nanofiber-based drug delivery systems offer a promising solution to overcome the challenges associated with drug formulations. For the production of nanofibers, electrospinning is the preferred technique. This technique involves the injection of a polymer solution through a nozzle under a high electric field. At the nozzle tip, the polymer solution forms a droplet. When the electric force exceeds the surface tension of the droplet, one or more charged jets are ejected from the tip of the droplet. As the ejected solution moves toward the collector plate, the solvent evaporates, resulting in the formation of continuous ultrafine fibers on the collector plate.[2,30] Electrospinning is widely used to produce polymeric fibers of different diameters by adjusting solution properties and process control parameters. It is a versatile technique that can be used to produce a wide range of drug delivery systems, including fibers, mats, scaf-

folds, and nanoparticles.[29,30] This technique can be applied to produce nanofibers from a wide variety of polymer types, including natural polymers, synthetic polymers, and hybrid blends.[31]Natural polymers such as collagen, gelatin, chitosan, hydroxyapatite, and silk fibroin exhibit superior biocompatibility, low immunogenicity, and in some cases intrinsic antibacterial properties, making them favorable for clinical. However, these materials have disadvantages such as low mechanical strength, rapid degradation, immunogenicity, batch consistency, higher supply and production costs, and cross-contamination.[32] Synthetic polymers, on the other hand, offer durability, cost-effectiveness, controlled degradation time, and strong mechanical properties. Additionally, they provide advantages such as thermal stability and the ability to produce different shapes. However, these polymers lack cell affinity due to their low hydrophilicity and lack of surface cell recognition sites.[31,32] Biodegradable polyester polymers such as poly(lactide-co-glycolide) (PLGA), which is a copolymer of polylactic acid (PLA) and polyglycolic acid (PGA), is the most widely used biodegradable synthetic polymer.[31,32] PLA is notable for its biocompatibility, long-lasting immunity, good mechanical properties, non-toxicity, and non-carcinogenic effects on the human body, making it ideal for medical applications. Nanofibers can also be employed to mitigate the side effects of administered drugs,[33] such as by incorporating polyethylene glycol (PEG), an amphiphilic nanomaterial, that prolongs drug circulation time in the body.[34]

Various studies have been conducted on the use of PLA/PEG nanofibers loaded with different drugs, aiming to achieve a synergistic combination of the desired properties of both polymers.[35–37] These efforts have encouraged the development of local drug delivery systems for epilepsy treatment. For example, Bauquier et al. developed electrospun poly(D,L-lactic-co-glycolic acid) (PLGA) nanofibers loaded with lacosamide, aiming to impact seizure activity in a rat model, as evidenced by an absence of epilepsy for up to 7 weeks.[24] Chen et al. investigated levetiracetam-loaded PLGA-based microspheres, flattened microspheres (spheroids), and microfibers in order to study, their release behaviors.[25] In a study conducted by Ramos, controlled-release CBZ-loaded PLGA nanofibers for surgical implantation in selected epilepsy patients were produced using electrospinning.[2]

In other approaches, Ana et al. designed a formulation for the oral administration of CBZ based on chitosan-coated lipid nanoparticles to provide a consistent absorption model and eliminate resistance mechanisms.[20] Similarly, in a study conducted by Liu et al., carboxymethyl chitosan nanoparticles were produced for nasal drug administration of CBZ in order to penetrate the blood-brain barrier (BBB) and achieve better therapeutic efficacy for antiepileptic drugs.[5]

Research has revealed the potential of local drug delivery systems in treating epilepsy. However, it has become evident from these studies that there is a need for further development of systems with controllable and uniform morphologies, high drug-loading efficiencies, and predictable drug release profiles. Although controlled release systems for CBZ have been reported in the literature, there is no existing report on the use of CBZ-PLA/PEG nanofibers as a tool for extended drug release. This investigation intended to formulate and optimize non-cytotoxic PLA-PEG-based polymeric fibers to improve the therapeutic efficacy and pharmacokinetics of CBZ, a frequently administered antiepileptic medication. The morphology and structure of nanofibers were assessed using scanning electron microscopy (SEM). The thermal properties of the fibers were determined using Fourier transform infrared (FTIR) spectroscopy and differential scanning calorimetry (DSC). In addition, the successful loading of CBZ onto the fibers was demonstrated by evaluating the effect of drug concentration on the drug release behavior.

2. MATERIALS AND METHODS

2.1. *Materials*

The poly(L-lactic acid) (PLA; Mw: 110,000 g mol^{-1}) 2003D was purchased from Nature Works LLC, Minnetonka, MN. Acetic acid (CH_3COOH), chloroform, carbamazepine, polyethylene glycol 4000 (PEG 4000) with a molecular weight range between 3,500 and 4,500 g/mol, and Tween 80 (a viscous liquid) were purchased from Sigma-Aldrich. Additionally, phosphate-buffered saline (PBS) solution with a pH of 7.4 was also obtained from Sigma Aldrich.

2.2. *Preparation of electrospinning solutions*

Solutions for fiber production were prepared according to Table 1. PLA was dissolved in chloroform with magnetic stirring for about 2 h to obtain a concentration of 8% (w/v) at room temperature. After mixing for 15 minutes, 3% (w/w) Tween 80 was added to the solution. For additional 10 minutes, the solution was stirred with 1% (w/v) PEG.[35,38]

For the preparation of electrospinning solutions containing CBZ, CBZ solutions prepared in ethanol (70:30; v/v) at different concentrations (50

mg and 10 mg) were added to the PLA/PEG/Tween 80 mixture. The final solution was stirred for 20 min. Pure fibers (PLA/PEG) and PLA/PEG/CBZ with two different CBZ concentrations were electrospun under ambient conditions.

T a b l e 1

Contents of solutions used in fiber production

Solutions	PLA cont. (wt. %)	PEG cont. (wt. %)	Tween 80 (wt. %)	CBZ (mg)
PLA/PEG	8	1	3	–
PLA/PEG/CBZ10	8	1	3	10
PLA/PEG/CBZ50	8	1	3	50

2.3. *Fabrication of electrospun fibers*

Fibers were fabricated using the electrospinning method. The experiment was conducted with the following equipment: a syringe pump (NE-300, New Era Pump Systems, Inc., USA), a high-voltage power supply connected to the needle, a single brass needle (1.63 mm diameter), and a laboratory-scale electrospinning unit (NS24, Inovenso Co., Turkey). During the electrospinning process, a voltage of approximately 23 kV was applied. The solutions were administered continuously using a syringe pump at a flow rate of 2.5 ml/h. A distance of 150 mm was maintained between the needle tip and the circular collector that was coated in oily paper. The experiments were carried out under standard environmental conditions with a temperature of 25 °C and humidity levels ranging from 40 – 45 %.[39]

2.4. *Characterization of fibers*

A scanning electron microscope (SEM) (EVO LS 10, ZEISS) was used to examine the morphology of the fibers after gold-palladium coating for 120 seconds, operating at accelerating voltage of 10 kV. The diameter of the electrospun fiber was measured on 100 randomly selected fibers in each SEM image using image analysis software (Olympus AnalySIS, USA). For statistical analysis, SPSS software was used to analyze the collected data.

The functional groups of electrospun fibers were qualitatively characterized using Fourier transform infrared spectroscopy (FTIR) analysis (Jasco FT/ IR-4700). The spectra were recorded over the range of 400 and 4000 cm^{-1}, with each spectrum averaged over 32 scans at a resolution of 4 cm^{1}

Thermal properties, including primary heating curves and thermal transitions of the fibers, were analyzed using differential scanning calorimetry (DSC) (Shimadzu DSC-60 Plus). For all groups of electrospun nanofibers, the temperature range was set at a heating rate of 10 °C min^{-1} over a temperature range of 25 °C to 300 °C.

Before mechanical testing, the thickness of the different types of fiber meshes was measured using a digital micrometer (Mitutoyo MTI Corp., USA) on samples 5 cm long and 1 cm wide. A tensile tester (Shimadzu Corporation, EZ-LX, Kyoto, Japan) was used to analyze the mechanical properties. Three specimens were tested for each group.

2.5. *Drug release*

To study the release of the drug, the fibers loaded with CBZ were cut into small pieces (10 mg each), and 2 ml of PBS (pH 7.4) was added to each piece separately. The samples were then placed in a BIOSAN ES-20 orbital shaker-incubator at 37 °C and shaken at 200 rpm for 10 hours. The amount of CBZ released was monitored by measuring its absorbance at 283 nm using UV-Vis spectroscopy (Shimadzu UV-2250 spectrometer) (Fig 1a).[18,40]

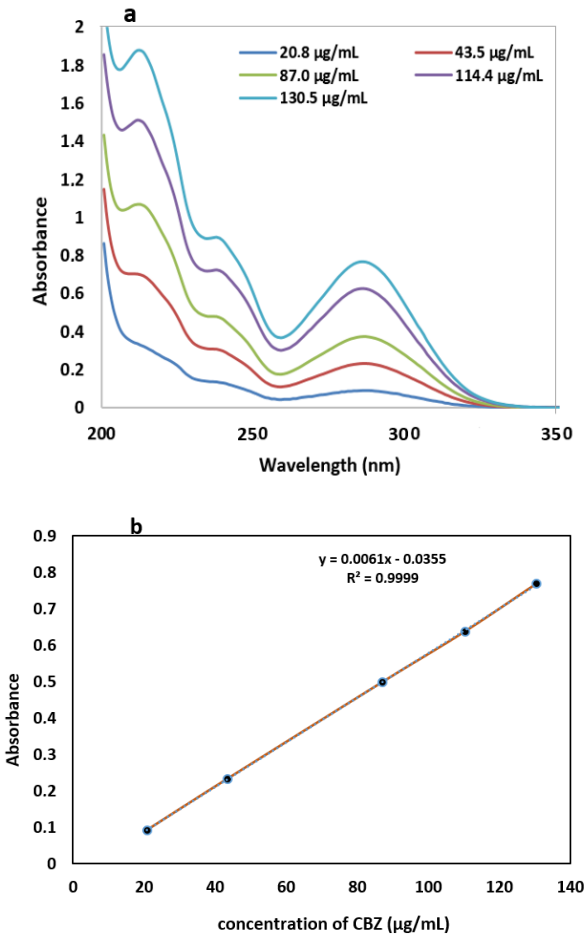

Fig. 1. a) Absorption spectra of CBZ at different concentrations, b) CBZ calibration curve

A standard drug calibration curve was used to evaluate the cumulative CBZ release (Fig 1b). The concentration range for CBZ was $0.0208 - 0.1305$ mg/ml, and the calibration equation was $y = 0.0061x - 0.0355$, with an $r^2 = 0.9999$ for 283 nm. Each test was repeated three times.[37]

2.6. *Statistical analysis*

A single-factor ANOVA analysis program was used to statistically analyze the data obtained from the measurements. The SPSS analysis program was used to measure the diameter of the fibers. All results are presented as mean ± standard deviation (SD). Statistical significance was defined as $p < 0.05$.

3. RESULTS AND DISCUSSION

In this study, the therapeutic performance and pharmacokinetics of CBZ, a widely utilized antiepileptic drug known for its favorable therapeutic action, were enhanced by encapsulating the drug in polymeric fibers. This approach aimed to reduce the dose-related side effects when used alone. PLA-PEG polymers have received great attention as drug carriers due to their numerous advantages.[41] A nanofiber structure based on PLA/PEG has been developed as a carrier for the delivery of CBZ, successfully achieving retention and controlled release of CBZ within the nanofiber matrix.

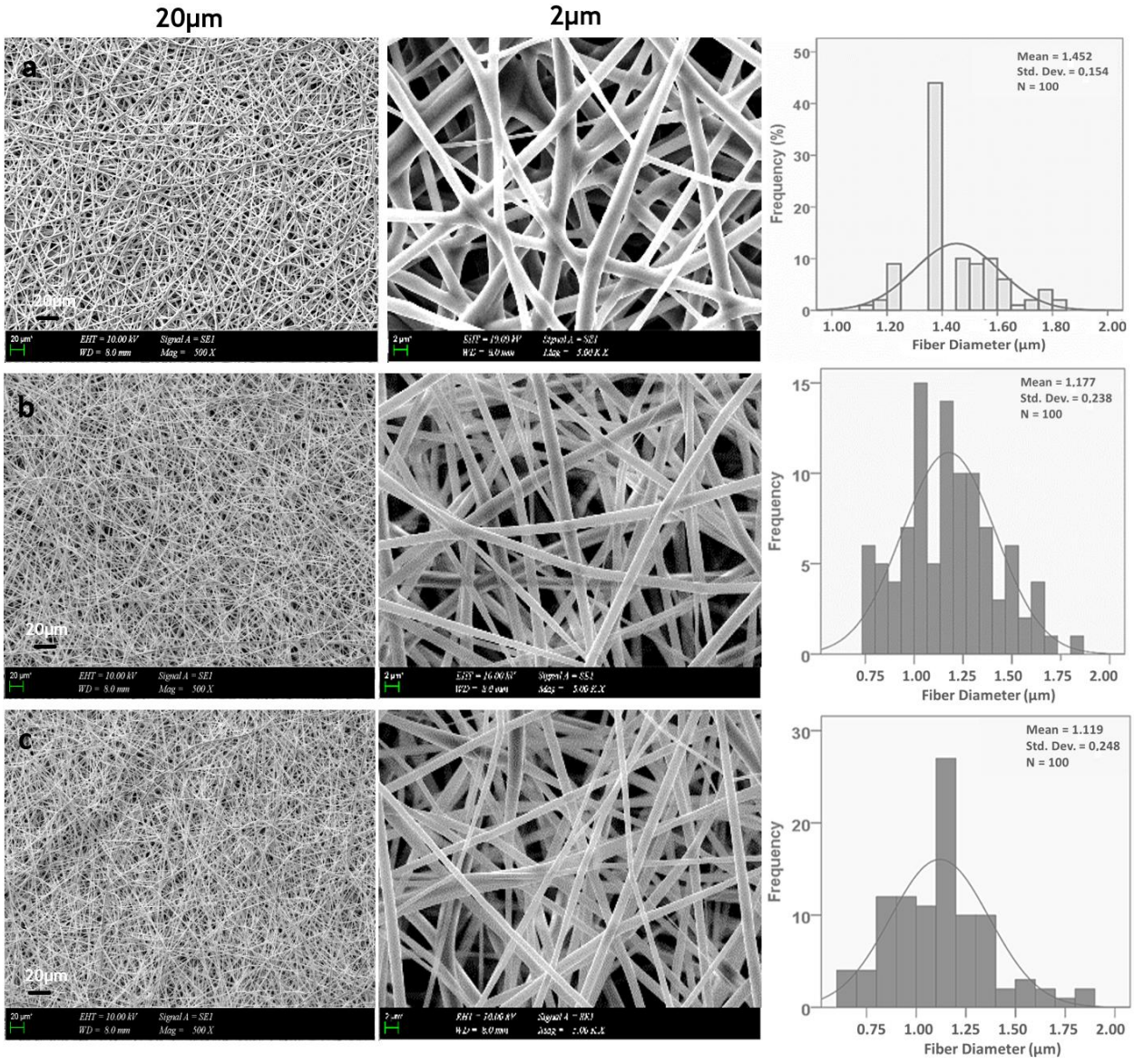

Fig. 2. Scanning electron microscopy images and fiber diameter distribution of fiber patches;
a) PLA/PEG, b) PLA/PEG/CBZ10, c) PLA/PEG/CBZ50

3.1. *Morphology of electrospun fibers*

SEM images in Figure 2 show that the average fiber diameter of the PLA-PEG sample is $\phi = 1.452 \pm 0.154$ μm. The average fiber diameters of the CBZ-loaded nanofiber mats were measured as $\phi = 1.177 \pm 0.238$ μm for the 10 mg CBZ sample and $\phi = 1.119 \pm 0.248$ μm for the 50 mg CBZ sample.

Wang et al. showed that nanofibers obtained from a homogeneous PLA-PEG polymer/hydrophobic drug solution contained the drug uniformly dispersed in the fiber.[41] After electrospinning, since CBZ was readily soluble in the electrospun PLA/PEG mixture, all fiber samples exhibited a thin, beadles fiber morphology, with no drug crystals detected in the fiber structure.

3.2. *Fourier transform infrared spectroscopy*

FTIR spectroscopy was used to investigate the chemical bonding structure of PLA/PEG and CBZ-loaded fiber mats. Figure 3 shows the results of the FTIR analysis. The characteristic absorption bands of PEG were observed: the stretching vibration of the –CH_2– group at 2884 cm^{-1} and the stretching vibration of the C–O–C group at 1248 cm^{-1}, 1113 cm^{-1}, and 963 cm^{-1}.[39] The main absorption bands for PLA observed were: The C–COO stretching peak at 867 cm^{-1}, C–CH_3 stretching at 1042 cm^{-1}, C–O, C–O–C stretching at 1080 cm^{-1}, CH_3 asymmetric scissoring at 1453 cm^{-1} and the C–O vibration peak at 1749 cm^{-1}.[35, 41]

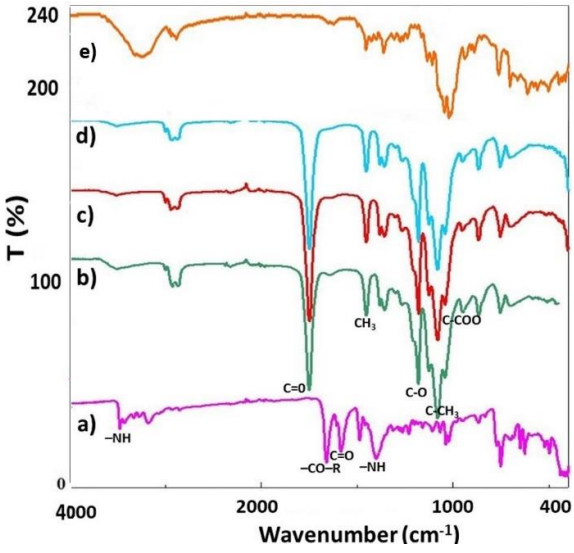

Fig. 3. FTIR spectra of a) pure CBZ, b) pure PLA, c) PLA/PEG/CBZ10, d) PLA/PEG/ CBZ50, and e) pure PLA/PEG fibers

In the FTIR spectrum of CBZ, the vibrational bands appear at 3463 cm^{-1} (aromatic N–H stretching), with aromatic C–H stretching vibrations occurring at 3150 cm^{-1}. A weak absorption band at 1240 cm^{-1} corresponds to C–N stretching vibrations, while the peak at 1372 cm^{-1} indicates N–H stretching. The C=C ring stretching vibration is observed at 1486 cm^{-1}, and a medium intensity band at 1672 cm^{-1} is due to the C=O bond of the amide group. In addition, the peak at 1372 cm^{-1} corresponds to NH_2 stretching vibrations. There is a slight difference in wavenumbers compared to the literature data.[6,7] However, all data confirm the presence of form III CBZ.[7] Since PLA is the main component in the PLA/PEG fiber blend and CBZ contains functional groups also found in PLA, such as carbonyl groups (C=O), hydroxyl groups (OH), and alkyl groups, the spectral properties of PLA dominated the overall spectrum obtained from the fibers. In the FTIR spectra of CBZ-loaded fibers, peaks of a similar type, but with different intensities, were obtained. These results indicate that the formulation was successful and the drug was effectively encapsulated.

3.3. *Differential scanning calorimetry analysis*

The thermal behaviors and phase transitions of PLA/PEG and CBZ-loaded fibers were analyzed using DSC during the heating process, and the resulting thermograms are shown in Figure 4. Melting temperature (T_m), glass transition temperature (T_g), and crystallization temperature (T_c) were investigated for all composite fibers. It was observed that the glass transition temperature (T_g) and crystallization temperature (T_c) of the PLA/PEG nanofiber gradually decreased with increasing CBZ content in the fiber. Carbamazepine, used as an anticonvulsant, is known to exist in two crystal forms (form I and form III). Previous studies have reported that CBZ typically exhibits a first endothermic peak corresponding to the melting of Form III (monoclinic) at 175.64 °C. Subsequently, CBZ crystallizes as Form I (triclinic), which is detectable through an exothermic peak at 177.19 °C. The second endothermic peak observed in the CBZ thermogram at 192.45 °C corresponds to the melting of Form I.[20,42,43] This single melting peak indicated the presence of only one polymorph; this study revealed that there were no polymorphic impurities within the sample and no conversion to other polymorphs. Upon examination of DSC thermograms of formulations containing CBZ, no melting transition peak corresponding to the drug

was evident. The absence of a melting peak for CBZ indicates its complete entrapment within the polymer. Similar results have also been reported by other researchers.[18,20] Considering all DSC data, it can be concluded that CBZ present in the fiber formulations may be molecularly dispersed within the fiber matrix.

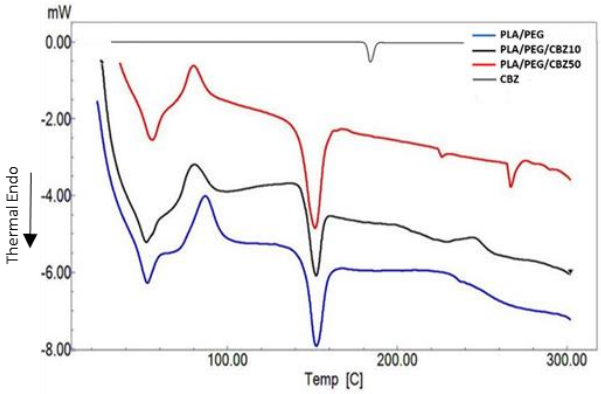

Fig. 4. DSC thermograms of the electrospun fibers

3.4. *Mechanical properties*

The tensile strength and strain at break for each of the fiber samples are given in Table 2. The results of the tensile strength and strain at break measurements indicate that the addition of CBZ to the PLA/PEG blend caused an increase in tensile stress values that is proportional to the concentration of CBZ. Specifically, it was observed that by adding different amounts of CBZ drug to the polymer matrix increased tensile strength to 0.20 and 0.25 MPa. Consequently, these findings suggest that the tensile strength increases as the diameter decreases.[34,38]

T a b l e 2

Tensile test measurements of electrospun fibers

Solutions	**Tensile strength (MPa)**	**Strain at break (%)**
PLA/PEG	0.19 ± 0.02	35.70 ± 6.50
PLA/PEG/CBZ10	0.20 ± 0.05	72.40 ± 9.20
PLA/PEG/CBZ50	0.25 ± 0.02	81.50 ± 2.30

3.5. *Drug release studies*

For the investigation of the release properties of CBZ from electrospun fibers, *in vitro* drug release tests were carried out in this study. As described in section 2.5, the amount of CBZ was determined by measuring it absorbance at 283 nm using a UV–Vis spectrophotometer[7,40,44] The amount of CBZ was calculated as mentioned in Section 2.5.

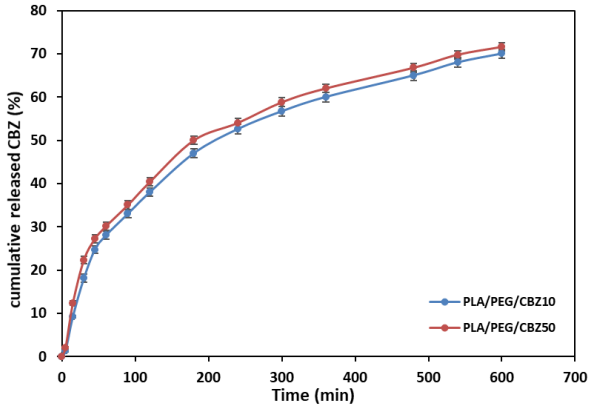

Fig. 5. In vitro drug release profiles of PLA/PEG/CBZ fibers. All the measurements were repeated three times, and the errors were less than 5%.

Figure 5 shows the cumulative release profiles of CBZ from electrospun fibers with varying CBZ concentrations. Drug release investigations were conducted in a PBS solution (pH 7.4) to simulate physiological conditions. The drug release percentage of CBZ at different time intervals was calculated in pH 7.4 medium and reported in tables 3 and 4. The results demonstrated a controlled and sustained release of CBZ for approximately 10 hours for all samples. From the cumulative release data, CBZ shows a characteristic two-step release pattern across all fibers. A burst release of CBZ was observed in the first 90 minutes, followed by a slow and sustained release. Increased drug loading, due to greater amounts of surface-bound drug and the large surface area of the fibers, often results in increased initial release.[45] Xie and Buschle-Diller[46] also studied the effect of fiber diameter on the release of 2 wt. % loaded chlortetracycline from poly(D, L-lactide) (PDLLA) electrospun fibers. The release studies showed that the larger diameter fibers resulted in a slower rate of release compared to smaller diameter fibers.[47]

The diameters of CBZ-loaded fibers are smaller than those of PLA/PEG nanofibers, with the diameter values of the drug-loaded nanofibers being close to each other. This was reflected in the release behavior and a slight difference was observed. The long-term release behavior of CBZ-loaded fibers is likely due to the homogeneous distribution of the drug in the fiber and the fiber diameter structure. In addition, the swelling behavior and the solubility of the drug in the different fiber formulations may be responsible for these differences in drug release as a function of fiber diameter.[35,41]

T a b l e 3

In vitro drug release parameters of PLA/PEG/CBZ10 fiber

Time (min)	Cumulative CBZ10 released (%) experiment 1	Cumulative CBZ10 released (%) experiment 2	Cumulative CBZ10 released (%) experiment 3	Mean ± SD
0	0	0	0	0
5	1.57	1.04	1.30	1.30 ± 0.27
15	9.37	9.21	9.02	9.20 ± 0.18
30	17.10	18.13	18.97	18.07 ± 0.94
45	25.68	24.41	24.01	24.70 ± 0.87
60	27.92	27.14	28.98	28.01 ± 0.92
90	32.11	33.92	32.94	32.99 ± 0.91
120	38.99	37.02	38.08	38.03 ± 0.99
180	46.74	46.14	48.15	47.01 ± 1.03
240	53.82	52.43	51.69	52.65 ± 1.08
300	56.64	55.62	57.84	56.70 ± 1.11
360	61.15	59.98	58.87	60.00 ± 1.14
480	63.92	66.13	64.97	65.01 ± 1.11
540	69.11	66.95	67.96	68.01 ± 1.08
600	69.01	70.02	71.04	70.02 ± 1.02

T a b l e 4

In vitro drug release parameters of PLA/PEG/CBZ50 fiber

Time (min)	Cumulative CBZ50 released (%) experiment 1	Cumulative CBZ50 released (%) experiment 2	Cumulative CBZ50 released (%) experiment 3	Mean ± SD
0	0	0	0	0
5	1.66	2.31	2.02	2.00 ± 0.33
15	11.82	12.86	12.23	12.30 ± 0.52
30	22.98	22.56	21.36	22.30 ± 0.84
45	26.21	27.37	28.01	27.20 ± 0.91
60	31.11	30.03	29.19	30.11 ± 0.96
90	36.03	35.01	34.02	35.02 ± 1.01
120	40.15	41.42	39.51	40.36 ± 0.97
180	49.03	50.01	51.03	50.02 ± 1.00
240	53.03	54.02	55.08	54.04 ± 1.03
300	59.78	58.92	57.71	58.80 ± 1.04
360	61.11	61.97	62.93	62.00 ± 0.91
480	66.98	65.98	67.71	66.79 ± 1.03
540	70.81	69.65	68.98	69.81 ± 0.93
600	72.36	71.82	70.64	71.61 ± 0.88

4. CONCLUSIONS

The fabrication and characterization of carbamazepine-loaded fibers for controlled drug delivery represents a significant advancement in pharmaceutical sciences and drug delivery technology. This study aimed to develop a novel drug delivery system that addresses the challenges asso-

ciated with carbamazepine (CBZ) therapy, such as poor solubility, variable bioavailability, and dose-related adverse effects. In this study, PLA/PEG/CBZ fibers for epilepsy treatment were successfully produced with the electrospinning technique.

The electrospinning technique proved to be a versatile and effective method for producing uniform PLA/PEG fibers loaded with CBZ. The successful encapsulation of CBZ within the fiber matrix was confirmed through various characterization techniques, including scanning electron microscopy (SEM), Fourier transform infrared spectroscopy (FTIR), and differential scanning calorimetry (DSC).

DSC measurements indicated that CBZ loading affects the mobility of the molecular chains within the PLA/PEG fibers, resulting in changes in the thermal behavior of the material. The FTIR spectra of the CBZ-loaded fibers exhibited similar peaks with varying intensities, as shown by the FTIR data. The SEM images revealed that all the fiber samples had a thin fiber morphology with no beads and that no drug crystals were detected in the fiber structure. Furthermore, the diameters of the PLA/PEG/CBZ10 and PLA/PEG/CBZ50 fibers were measured at ϕ =1.177 ± 0.238 μm and ϕ =1.119 ± 0.248 μm, respectively. These results are an indication of successful formulation and encapsulation. When drug release results were analyzed, the fibers showed a controlled release profile extending up to 10 h suggesting that CBZ-loaded fibers can provide sustained drug release at local sites. The controlled drug delivery system presented in this study holds promise in improving CBZ therapy by enhancing drug solubility, extending release duration, and potentially reducing side effects associated with conventional formulations. By providing a continuous and controlled release of CBZ, the developed fibers offer the potential to improve patient compliance and treatment outcomes.

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