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REVIEW PAPER

Poly (Lactic Acid) Nano-fibers as Drug-delivery Systems: Opportunities and Challenges

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ABSTRACT

Numerous Scientists have discovered the procedure of nano-technology, explicitly nano-fibers, as drug-delivery systems for trans-dermal uses. Nano-fibers can be used to deliver drugs and are capable of controlled-release for a continued period of time. Poly (Lactic Acid) (PLA) is the lastly interesting employed synthetic polymer in bio-medical usage owing to its well categorized biodegradable properties. PLA (–[CH(CH3)COO]n–)is linear biodegradable aliphatic polyester which can be derived from 100% re-newable bio-resources like rice and wheat through fermentation and polymerization. PLA has been accepted by FDA to be applied in bio-materials, for instance sutures, bone plates, abdominal mesh, and drug-delivery systems. PLA holds stereo-isomers, for instance Poly (L-Lactide) (PLLA), Poly(D-Lactide) (PDLA), and Poly(DL-Lactide) (PDLLA). PLGA is a co-polymer of PLA and Poly (Glycolic Acid) (PGA) that are most usually used biodegradable synthetic polymers for bio-medical uses for instance scaffolds and drug-delivery systems. The objective of this review paper is to highpoint the possibility of PLA nano-fibres as drug-delivery substances and to give full information about the new progresses about the PLA, PLLA and PLGA nano-fibers fabrication as novel drug-delivery systems.

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INTRODUCTION

Nano-fibers are unlike from other fibrous constructions with a diameter in the variety of nano-meters although the length in the collection of meters, and are therefore mentioned to as relation among nanotechnology and micron size world. Numerous synthetic, semisynthetic and natural polymers have been utilized to produce Nano-fibers. Electro-spun Nano-fibers offer several necessary structures as drug-delivery systems[1].

1) The electro-spinning procedure can be used to manufacture Nano-fibers from a wide variety of solutions of both natural Polymers.
2) Nano-fibers have high surface-layer area to volume ratios that provide efficient delivery of both hydrophilic and hydrophobic drugs.
3) The drug-release-profile can be tuned to meet the specific clinical usage by modulating a variety of parameters, for instance the drug to polymer ratio, fiber diameter, morphology, and-or porosity.

Fig. 1 signifies the standard electro-spinning method used to create drug-delivery systems.

Mechanism of Drug Loading and Drug-releasing from Nano-fibers

Loading of drug in polymer Nano-fibers has been reported by means of various techniques, for instance, coating, embedding, or encapsulating so as to attaining control in the drug-release kinetics[2-4]. If the drug and polymer are soluble in the same solvent, the drug can be dissolved directly in the polymer-solution or in the item [5] wherever the drug and polymer are not soluble in the same solvent, the drug can be solubilized in a small amount of an-other solvent before adding

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to the polymer-solution[6-8]. In a various method for drug and polymer insolubility in a public solvent, the drug can be dissolved in a solvent that is immiscible with that wherein the polymer is dissolved and the two solutions can be loaded in separate capillaries to be electro-spun coaxially, or the two solutions could be blended, resulting in an emulsion that can be electro-spun[9, 10]. This tactic leads to the encapsulation of the drug in the polymeric matrix[11, 12]. There is however an-other system for loading the drug after manufacturing the Nano-fibers[5, 13]. In this system drug is absorbed in the Nano-fibers through immersing the Nano-fibers in a drug-solution [14-16]. The releasing of the drug from Nano-fibers is principally via the mechanisms of: desorption from the Nano-fiber surface-layer, diffusion through the canals and pores of Nano-fibers or matrix degradation[17-19]. The drug-release kinetics can be modified by means of the selecting of polymer and controlling over the Nano-fiber diameter, porosity, geometry, and morphology with regulating the numerous processing variables during Nano-fibers production[3, 20, 21]. Fig. 2 illustrated the Scheme image of the various methods for drug loading in Nano-fibers.

Fig. 3 shows the scheme for physical and chemical interactions between drug-molecules and Nano-fibers.

Controlling the Drug-release from Nano-fibers

Nano-fibers can be used by way of release-rate controlling strategies[3, 22]. Drug-release from Nano-fibers could be because of desorption of drug from the surface-layer, diffusion from pores and-or matrix degradation[23, 24]. These all procedures of drug-release are possible to get affected by select of inactive (polymer or other material), porosity,

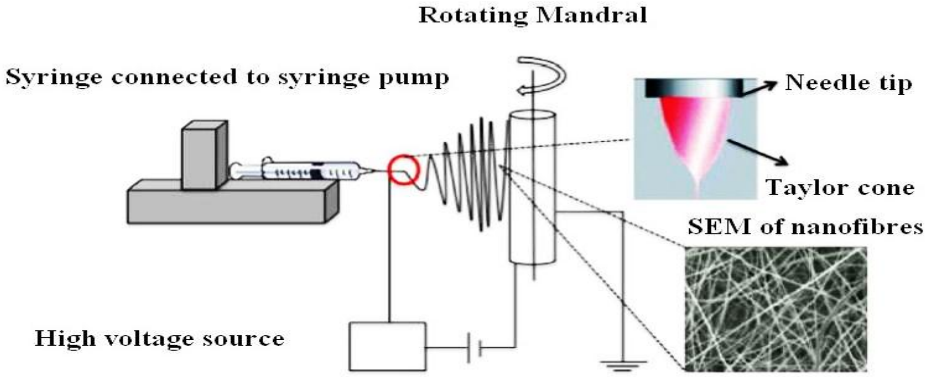


Fig. 1 . Scheme of a standard horizontal electro-spinning setup including at least one syringe pump, a polymer- with or without drug, a high voltage supply, a source electrode, and a collector electrode.

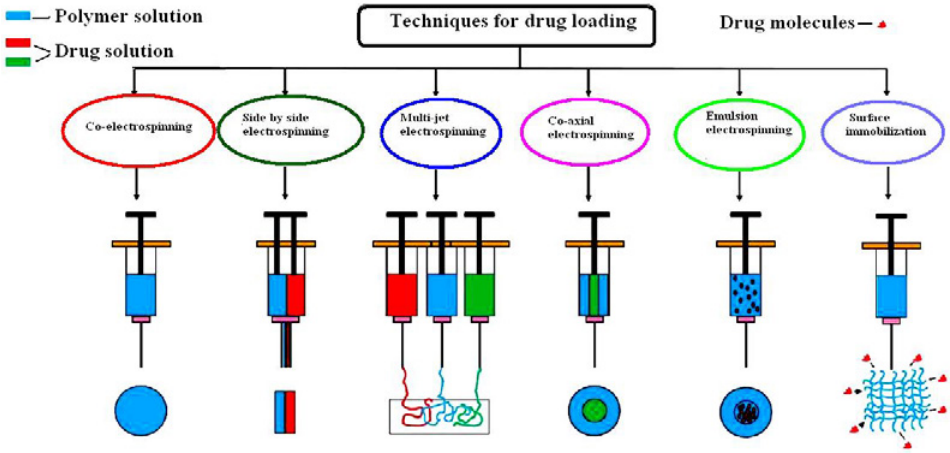


Fig. 2. Techniques for loading drug-molecules in Nano-fibers.

morphology, and geometry of Nano-fibers[22, 25, 26]. Usually smaller the diameter of Nano-fiber quicker the release-rate is reflected from it based on the statement that reduced diameter fiber has advanced surface-layer area and dissolution rate[6, 27, 28]. Advanced conclusions recommended that drug-release cannot be only run by means of diameter and simultaneously influence of porosity is to be considered [4, 24]. It is repeatedly revealed that thicker Nano-fibers with very high porosity releasing drug quicker as compared to thinner fibers with low porosity[26, 29]. Nano-fiber alignment is a various factor recognized to mark drug-release and generally randomized design is associated with quicker drug-release owing to improved affinity of water uptake[6, 10, 13].

Drug Related Factors Affecting Drug-release

Drug associated factors affecting its releasing form Nano-fibers are *drug loading*, *molecular weight*, *the physical state of drug*, *solubility*, and *drug-polymer interactions*[30]. Generally, higher drug loading is connected with the faster-release [31, 32]. The crystalline arrangement of the drug becomes deposited on Nano-fiber external and offers burst-release[9, 33]; whereas amorphous arrangement gets deposited deeper inside and get released in a sustained style. Low molecular weight drugs are recognized for their fast release-rate[2, 5, 34]. Fig. 4 offers glimpse of drug related factors affect drug-releasing.

Poly (Lactic Acid)(PLA)

PLA (–[CH(CH_3) COO]$_n$–) is a linear bio-based, bio-degradable and bio-absorbable aliphatic polyester (Fig. 5) [35, 36]which can be derived from 100% re-newable bio-resources like rice , wheat and sweet potato, through fermentation and polymerization [37, 38]. PLA has been accepted by FDA to be applied in bio-materials, for instance wound-dressings, sutures, bone plates and drug-delivery systems [34, 39-41].

Poly (L-Lactide) (PLLA)

PLA holds stereo-isomers, for instance Poly (L-Lactide) (PLLA), Poly(D-Lactide) (PDLA), and

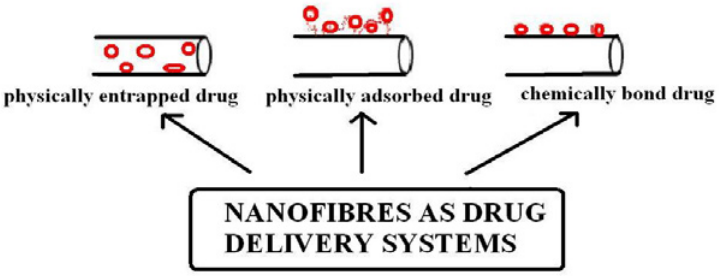


Fig. 3. Scheme of interactions between drug and Nano-fibers.

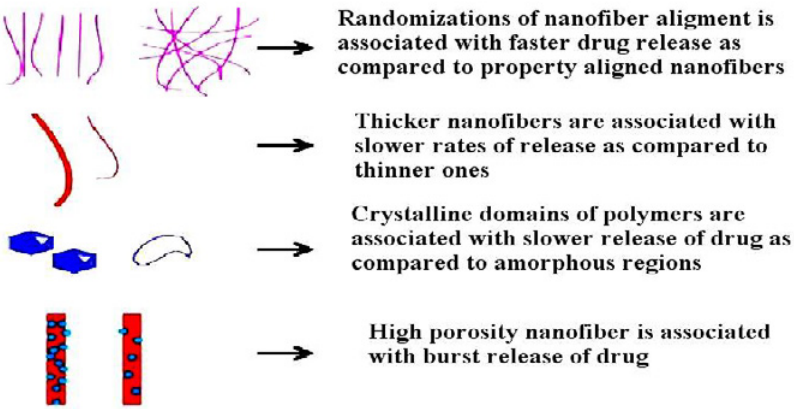


Fig. 4. Influence of Nano-fiber diameter, porosity, Nano-fiber alignment, polymer crystallinity , molecular weight on drug-releasing.

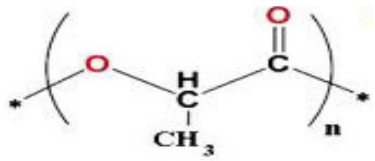


Fig. 5. A) Chemical structure of PLA.

Poly(DL-Lactide) (PDLLA). PLLA has attained enormous attention in medical uses owing to its exceptional biocompatibility and mechanical properties [34].

Poly(Lactic-co-Glycolide) PLGA

PLGA is a co-polymer of PLA and Poly(Glycolic Acid) (PGA) that are most usually used biodegradable synthetic polymers for bio-medical uses for instance scaffolds and drug-delivery systems [11, 42-44].

PLA, PLLA and PLGA Nano-fibers as Drug-delivery Systems

For drug-delivery usages, PLA, PLLA and PLGA Nano-fibers have been exploited in an enormous variety of systems like Nano-fibers incorporated with plants, Nano-fibers covered with other polymers, Nano-fibers containing chemical additives, porous Nano-fibers combined with growth factors which will be reported in detail in below [16, 31, 37, 40]. . In all cases various styles of drugs were incorporated in the Nano-fibers[23, 31, 45, 46]. Drug-release types were studied to estimate the behavior of the Nano-fibers as drug-delivery materials. Furthermore the studies of the Nano-fibers were done by SEM, AFM and Fluorescence Microscopy.The chemical structure of samples were characterized by FT-IR. Also the mechanical properties (Young's modulus, tensile-strength) of the Nano-fibers were examined. The outcomes of these valuations will also be defined briefly on the following pages.

The novel Dexamethasone releasing PLLA/ Pluronic P123 multilayer Nano-fibers constructed by Birhanu *et. al.* [47] are ideal for drug-delivery usage. The drug was loaded in the central layer. The scaffolds constructed have appropriate surface-layer properties, but with various mechanical strength and osteo-genic proliferation and differnetion. The drug-release-profiles of the scaffolds were entirely various: single layer scaffolds displayed burst-release in the first day, whereas multilayer scaffolds a controlled delivery of Dexamethasone with better osteo-genesis. Therefore, the existence of a layer covering the drug-loaded layer is necessary for controlled-release of drugs and-or bio-active molecules at the position of scaffold implantation[47]. Nano-fibrous samples of PLA and PEG with various PLA/PEG ratios were organized by means of solution-blow-spinning. Terpinen-4-ol, a main phyto-constituent from tea tree oil (Melaleuca alternifolia) was incorporated in the Nano-fibers. PEG performed as a plasticizer resulting in a decrease in PLA crystallinity. Adding PEG controlled to a quicker drug-release. Samples with terpinen-4-ol, exhibited an operative anti-microbial activity against *A. actinomycetemcomitans* [48]. Scaffaro *et. al.*[31] explored the possibility of incorporating CAR in PLA Nano-fibers. PLA Nano-fibers holding evenly dispersed CAR were effectively formulated. The outcomes showed that CAR has a good compatibility with PLA. The regular-release of CAR from PLA Nano-fibers permitted an important anti-microbial activity up to 144 h. The samples immersed in PBS kept at 37 °C released more than 60% of the total collective CAR released after 6 hours followed by a fast leveling off up after 24 h. At the end of the examination, the quantity of CAR released was about 90% of the loaded amount[31]. PLA Nano-fibers with a defined release with doxorubicin were constructed. The influences of technique factors, for example concentration, distance, applied voltage, temperature and flow rate on the mean diameter of PLA/DOX Nano-fibers were explored. DSC was employed to recognize the existence of DOX within Nano-fibers. DSC outcomes displayed that the DOX was loaded in the Nano-fibers effectively. *in-vitro* drug-release in phosphate buffered-solution and acetate buffer for the best and non-optimized samples proved that diffusion is the dominant drug-release mechanism for Nano-fibers. The initial burst-release was observed for non-best Nano-fibers compared to best Nano-fibers[49]. Dzikowski *et. al.* [50] assessed PDLLA(Poly D,L-(Lactic Acid))/PCL Poly (ε-Caprolactone) nano-Fibrillar matrices attained via jet spraying and having ciprofloxacin (CIF). The effect of CIF combination was evaluated in regard of matrices fiber diameter, mechanical properties and degradation whereas antibiotic release from the polymer blends of various PDLLA/ PCL ratios was quantified in buffers of various pH. The CIF crystals were dispersed in the Nano-fibers, without broad embedding. CIF release-profiles

were not controlled with the polymer blend ratios. Nevertheless, sustained-release was perceived over more than 23 days. Owing to the antibiotic pH dependent solubility, burst-release was more protuberant in acidic conditions[50]. PLA Nano-fibers holding Hydroxy-Propyl Methyl-Cellulose (HPMC) and Tetracycline-Hydrochloride (THC) were solution- blow-spun from two various solvents, chloroform-acetone (CA, 80:20 v/v) and 2,2,2-Tri-Flouro-Ethanol (TFE). FT-IR outcomes specified effective combination of HPMC and THC in the Nano-fibers. Furthermore, phase-separation happened between PLA and HPMC in the Nano-fibers. Nano-fibers having HPMC had superior inhibitory regions against *Escherichia Coli* and *Listeria monocytogenes* than those without HPMC. This was owing to HPMC being capable to swell and release more THC when in contact with water[51]. Jiang *et. al.* [51] assessed the Release-behavior of tetracycline hydrochloride-loaded PLA/Chitosan (PLA/CS/Tet) Nano-fibers constructed by means of electro-spinning method. The electro-spinning-solution was a blend of Tet, CS Formic-Acid-solution and PLA Chloroform/ Ethanol-solution. The interface between CS and PLA in PLA/CS Nano-fibers was approved to be Hydrogen-Bond. The combination of Tet produced a small reduction in the diameter of Nano-fibers with Tet quantity below30%. PLA/CS/Tet Nano-fibers displayed insignificant initial burst in the first 4 hours before a gradual- increase in cumulative release, and the release amount increased with increasing Tet quantities. Tet-release ($\frac{Mt}{M\infty} < 0.6$) from the antiseptic Nano-fibers could be pronounced by Fickian diffusion model and the release-profiles displayed two sequential phases (Fig. 3). PLA/CS/Tet Nano-fibers displayed an operative and supportable inhabitance on the growth of *Staphylococcus aureus*, and the anti-microbial activity improved fast with increasing Tet quantities below 20%[51]. Nano-fibrous PLA scaffolds holding 10, 20, or 30 wt % ibuprofen(IBP) were produced and IBP release-profiles calculated. Two styles were seen while studying the IBP release-profiles. First, as predictable, an increased temperature (37˚C) produced a greater release of IBP from the IBP-loaded PLA scaffolds as compared to room temperature. Second, the 30 wt % IBP-loaded PLA scaffolds at 37˚C manufactured the highest IBP-release, ~ 0.25 mg at 336 h. At both room temperature and 37 ˚C, the data recommended that a direct -correlation occurred between IBP concentration in the scaffolds and the amount of IBP-released. *in-vitro* cytotoxicity to human-epidermal keratinocytes (HEK) and human-dermal fibroblasts (HDF) of the scaffolds by changing IBP concentrations were assessed and compared to pure PLA nano-fibrous scaffolds. PLA Nano-fibers having 20 wt % IBP support human-skin-cell viability and proliferation *in-vitro*, decrease wound reduction *in-vivo*, and when seeded with skin-ccells, furthermore develop new blood vessel creation[52]. Poly (Ethylene Glycol) (PEG) is a hydrophilic polyether commercially accessible in various molecular weights with narrow distribution. To assess the effect of molecular size on the release-rate and the total-released quantity generally, PEGs with molecular-weights of 2000, 6000, 10000 and 20000 g/mol were choices as model molecules. The PEG has substantial influence on the drug-release. In a work, the PEGs were added to the solutions of polymers and were incorporated in PLA Nano-fibers through electro-spinning. The release-behavior of these molecules in the water medium was explored. The release experimentations exposed two styles – the release-rate relies on the molecular weight of model PEGs in addition to the type of nano-fibrous polymer. Larger molecules were rapidly released faster than smaller ones. The release-rate and the total-released quantity absolutely associated with molecular weight of the incorporated molecules[53]. Mefoxin (antibiotic drug)-loaded PDLLA Nano-fibers manufactured by means of enhancing the instrumental factors for instance electric field, concentration, salt addition and feeding rate. Nano-fibers were treated in a 20 mL buffer-solution for *in-vitro* drug-release examination. Comprehensive releasing of the drug at 48 hours was established from the release-profile[54]. Li *et. al.* [55] constructed blend Nano-fibers of PDEGMA (Poly(di(Ethylene Glycol) Methyl Ether Methacrylate) and P(LLA-CL) (Poly(L-Lactic Acid-co-ε-Caprolactone) holding the antibiotic ciprofloxacin (CIF) through electro-spinning. XRD (X Ray Diffraction) displayed the drug to be existent in the amorphous physical form post-electro-spinning. The Nano-fibers indicated distinct thermo-sensitive properties and provided sustained-release of CIF over more than 160 20 hours *in-vitro*. The Nano-fibers could support the proliferation of fibroblasts, and through varying the temperature cells could simply be attached to and detached from the fibers. Antibacterial examinations proved that Nano-fibers-loaded

with ciprofloxacin were active in inhibiting the growth of *E. coli* and *S. aureus*. *in-vivo* analyses on rats specified that the P(LLA-CL)/ PDEGMA Nano-fibers-loaded with CIF had much more effective wound-healing properties than a gauze and CIF-loaded Nano-fibers made only of P(LLA-CL)[55]. Co-polymerization with PEG (Poly ethylene Glycol) has been recommended by Javadian1 *et. al.* [56] for advancing the hydrophilicity, degradation rate and crystallization of PLA. Nanfibers of PEG-PLA co-polymers were constructed and described so as to be used as drug-delivery system. Triblock co-polymer of PLA/PEG was manufactured well. The Nano-fibers were manufactured via electro-spinning method by means of a solution of co-polymer in DCM (30%). SEM was used to explore the morphology and average diameter of the Nano-fibers. The composition of PLA-PEG-PLA co-polymer was checked through HNMR, and FT-IR(The existence of methane). SEM test checked the creation of Nano-fibers. GPC examination determined the average molecular weight of co-polymer. The diameter of Nano-fibers was exposed by SEM to be in range of 157 nm. Moreover, DSC was used to characterize Nano-fibers. The outcomes displayed that tamoxifen was well incorporated and dispersed evenly in PEG-PLA Nano-fibers[56]. Braided PLLA Nano-fiber sutures loaded with Cefotaxime Sodium (an antibiotic) produced, which acted better *in-vivo* than silk sutures[57]. PLA and Poly (Vinyl Pyrrolidone) (PVP) Nano-fibers loaded with Copaiba oil were created with solution-blow-spinning. This oil is extracted from Copaifera L., a tree natural to steamy areas of Latin America and West Africa. Some of the vigorous principals in this oil are β-bisabolol, an anti-inflammatory agent, and β- caryophyllene, a bactericidal and anti-inflammatory composite. The oil was described by means of GC (GC : Gas Chromatography). PLA and four PLA-PVP blends holding 20% (wt %) oil were spun. GC analysis proved that the chief component of the Copaiba oil was β-caryophyllene, a recognized anti-microbial agent. *in-vitro* release-examinations of Copaiba oil volatiles exhibited a higher release-rate in Nano-fibers having PVP. Nano-fibers prepared from blends holding higher quantities of PVP had superior anti-microbial act against *Staphylococcus aureus* [58]. Researchers stated the applicability of Nano-fiber samples as drug-delivery structures by PLA, Poly(Ethylene-co-Vinyl Acetate) (PEVA), and a 50 : 50 blend of the two polymers. The polymers were separately dissolved in chloroform and tetracycline HCl, which was used as a model drug, and then added to the polymer-solutions. The drug-release-rate as verified from individual polymeric Nano-fiber samples was maximum for PEVA, releasing nearly 65% of drug followed by 50 : 50 PLA-PEVA blended Nano-fiber samples that exhibited a releasing of 50% drug-quantity over a period of 5 days[4]. Nano-fibers of PLGA-Cefazolin were constructed via the electro-spinning procedure. Cefazolin(Cef) was dissolved in the polymer-solution to provide a homogeneous single-phase-solution of CEF and PLGA in the solvent mixture (THF + DMF). It was expected that the combination of CEF would reason an increase in average Nano-fiber diameter and that the CEF particles could probably jut out of the surface-layer of the Nano-fibers. The tests showed an increase in Nano-fiber diameter with ADDING CEF; but, the morphology of the Nano-fibers were objective as smooth as the Nano-fibers without any CEF incorporated in them. This designated that the existence of CEF was not interfering with the electro-spinning method[19]. Qi *et. al.* [43] formulated Tetracycline Hydrochloride (TCH)-loaded PLGA/Halloysite nano-tubes composite Nano-fibers (PLGA/HNTs/TCH) as drug-delivery system. The combination of TCH-loaded HNTs in the PLGA Nano-fibers is capable to develop the tensile-strength and preserve the three dimensional structure of the nano-fibrous samples. *in-vitro* viability-test and SEM observation of mouse-fibroblasts cultured on the samples prove that the PLGA-HNTs-TCH Nano-fibers are cyto-compatible. More significantly, the PLGA-HNTs-

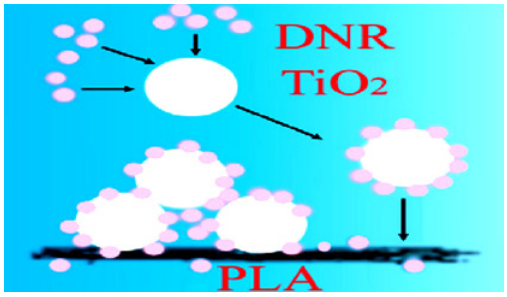


Fig 6. Scheme of the probable procedure for the self-assembly and accumulation of the DNR drug on the PLA/ TiO_2 Nano-fibers[59].

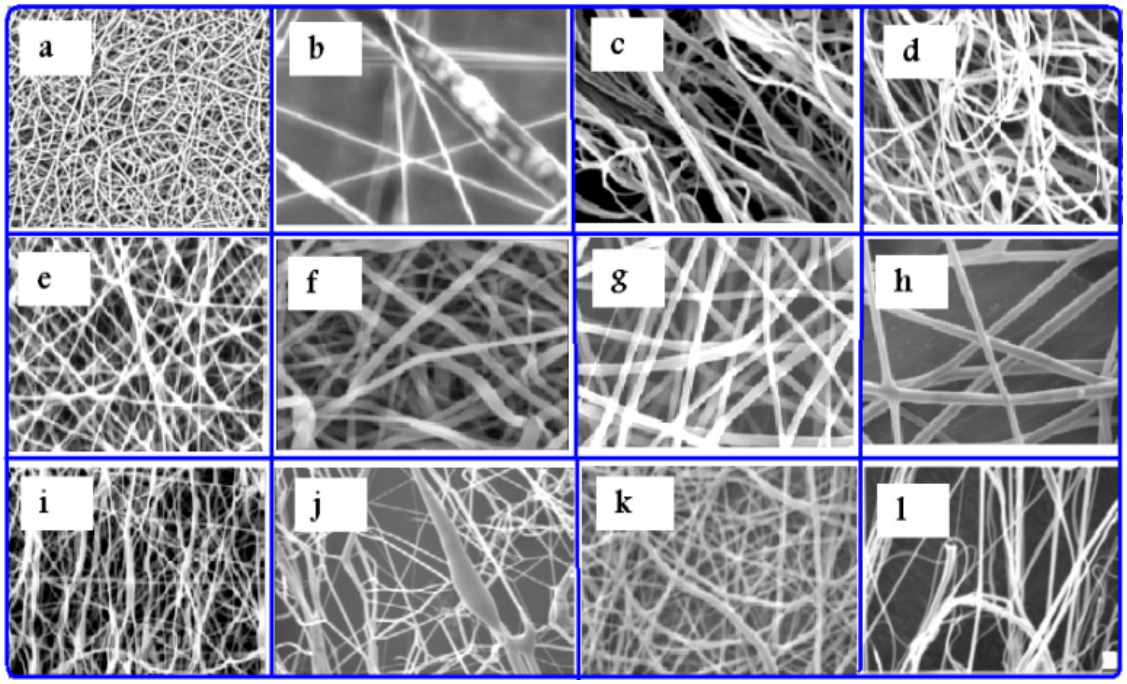


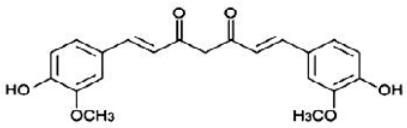
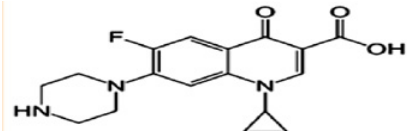
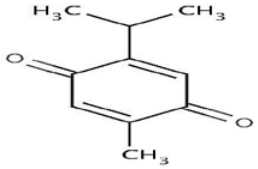
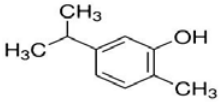
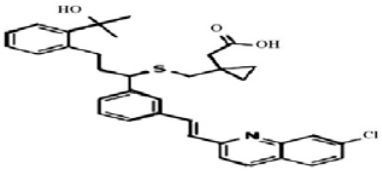
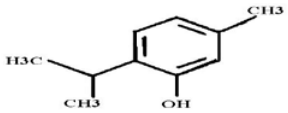
Fig. 7. a) PLA/CAR Nano-fibers; b) PLA/PEG20/terpinen-4-ol Nano-fibers; c) 60PLA/40HPMC/THC/CA Nano-fibers; d) PLA/THC/TFE Nano-fibers; e) PLGA/HNTs/TCH Nano-fibers; f) PLA/PEG 20 molecules Nano-fibers; g) PLA/IBP Nano-fibers; h) PLA/CS/Tet Nano-fibers; i) PLLA/P123/Dexa Nano-fibers; j) PCL/ PDLLA/ CIF Nano-fibers; k) P(LLA-CL)/ PDEGMA/CIF Nano-fibers; l) PLA/PVP/CO Nano-fibers [48, 49, 51, 53, 58].

Table 1. Drug-release Studies of PLA Drug loaded Nano-fibers

PLA Nano-fibers	Drug	Amount of Drug-releasing According to Number of Days							Ref.*
		1	3	5	10	15	20	25	[47]
PLLA/ Dexa/ Plasma Nano-fibers		-	-	55%	62%	75%	76%	78%	[47]
PLLA/P123/ Dexa Nano-fibers	Dexamethasone	-	-	70%	85%	85%	90%	91%	[47]
PLLA/(PLLA/ Dexa/ P123) Nano-fibers		-	-	42%	45%	45%	50%	59%	[47]
PLLA/(PLLA/ Dexa/ P123)/ PLLA/ P123 Nano-fibers		-	-	22%	38%	39%	42%	45%	[47]
PLLA/(PLLA/ Dexa/ P123)/ PLLA/ Plasma Nano-fibers		-	-	18%	25%	27%	35%	38%	[47]
PDLLA/PCL/CIF 90%/10% Nano-fibers	Ciprofloxacin	-	-	20%	29%	34%	40%	44%	[50]
PDLLA/PCL /CIF 75%/25% Nano-fibers		-	-	17%	19%	22%	40%	43%	[50]
PDLLA/PCL/CIF 50%/50% Nano-fibers		-	-	16%	19%	22%	25%	28%	[50]
PLA/DOX (pH=7.4) Nano-fibers	Doxorubicin	20%	-	24%	-	-	-	-	[49]
PLA/DOX (pH=4.8) Nano-fibers		50%	-	62%	-	-	-	-	[49]
P(LLA-CL)/ PDEGMA 1:1 loading CIF 0.9% W/V Nano-fibers	Ciprofloxacin	52%	-	81%	-	-	-	-	[55]
PLA/PVP 5-CO Nano-fibers	Copaiba Oil	1700 µg/24 h	-	3000 µg/24 h	-	-	-	-	[58]
PLA/PVP 10-CO Nano-fibers		1900 µg/24 h	-	1900 µg/24 h	-	-	-	-	[58]
PLA/PVP 15-CO Nano-fibers		2900 µg/24 h	-	3300 µg/24 h	-	-	-	-	[58]
PLA/PVP 20-CO Nano-fibers		1800 µg/24 h	-	2000 µg/24 h	-	-	-	-	[58]
PLA/CO Nano-fibers		50 µg/24 h	-	50 µg/24 h	-	-	-	-	[58]
PLA/IBP 30% wt at 37°	Ibuprofen	0.19 mg	-	0.23 mg	0.25 mg	-	-	-	[52]
PLA/CS/30% wt Tet Nano-fibers	Tetracycline Hydrochloride	35%	-	87%	-	-	-	-	[51]
PLGA/TCH Nano-fibers	Tetracycline Hydrochloride	5%	-	-	-	-	100%	-	[43]
PLA/PEG 2 molecules Nano-fibers	PEG	-	2%	-	-	-	-	-	[53]
PLA/PEG 6 molecules Nano-fibers	PEG	-	4%	-	-	-	-	-	[53]
PLA/PEG 10 molecules Nano-fibers	PEG	-	6%	-	-	-	-	-	[53]
PLA/PEG 20 molecules Nano-fibers	PEG	-	12%	-	-	-	-	-	[53]
PLA/CAR Nano-fibers	Carvacrol	-	0.25 mg	-	-	-	-	-	[31]

TCH Nano-fibers are able to releasing the drug TCH in a sustained style for 24 days and display anti-microbial activity only related with the encapsulated TCH drug[43]. In an-other work, PLA Nano-fibers have been made-up via electro-spinning and then PLA nano-composites have been prepared with accumulating Daunorubicin drug (DRC) on PLA Nano-fibers combined with TiO_2 nano-particles.

Table 2. Characteristics of molecule drugs used in PLA Nano-fiber drug-delivery systems.

Drug Molecule	Agent		Chemical Structure	Ref
	Aq. Sol. † (mg/mL)	Log P ‡		
Curcumin : :A famous extract of the root of Curcuma longa L., having anti oxidation, anti inflammatory, anti cancer and wound-healing properties. (Chemical formula: [1,7-bis(4-Hydroxy-3- Methoxyphenyl)-1,6-Heptadiene-3,5-Dione]).	0.006	3.62		[42]
Ciprofloxacin: A Fluoro-quinolone, Have a durable efficacy on a many bacteria.	1.35	-0.57		[55]
Thymoquinone: A phytochemical found in the volatile oil of *Nigella sativa* seeds, known as black seeds. Such seeds have been used as a traditional medicine for wide range of illness for decades.(2-isopropyl-5-methyl-1, 4-benzoquinone) have antibacterial, anti-cancer, anti-diabetic, and anti-inflammatory effects.				[1]
Carvacrol: An essential oil.				[31]
Montelukast : A cysteinyl leukotrienes,				[17]
Thymol:				[13]
Cefazolin: A broad-spectrum antibiotic.	0.487	-0.4		[60]
Ketoprofen	0.0213	3.29		[34]
1. Doxorubicin : Anticancer chemotherapy drug. An Anthracycline antibiotic for treatment of Leukemias and Hodgkin's lymphoma, in addition to cancers of the bladder, breast, stomach, lung, ovaries, thyroid, soft tissue sarcoma and multiple myeloma.				[49]
2. Dexamethasone: 3. One of the famous bio-logically active Osteo-genic differention agent with ß Glycero-phosphate and Ascorbic Acid.				[47]

Atomic force microscopy and (LSCM : laser scanning confocal microscope) analyses prove that the respective drug-molecules could be freely self assembled on the surface-layer of the PLA/TiO_2 nano-composites, which could more competently assistance the drug-permeation and accumulation on the leukemia K562 cells(Fig. 6) [59].

Drug-releasing behaviors of various PLA Nano-fibers will be described in Table 1 briefly, also the Characteristics of molecule drugs will be displayed in Table 2. *Release (%)* is calculated from the following formulae.

$$Release\,(\%) = \frac{Release\,drug}{Total\,loaded\,drug} \times 100(\%)$$

SEM images of various PLA Nano-fibers as drug-delivery systems will be display in Fig. 7.

CONCLUSIONS

In this review, drug-releasing behaviors and properties of various types of drug-loaded PLA Nano-fibers have been covered. PLA has been shown to be a potential bio-material to be used in drug-delivery uses owing to its biocompatibility and bio degradability nature. On the other hand Nano-fibers can be used to deliver drugs, so as PLA Nano-fibers are the novel materials that are capable as drug carriers in human- body for numerous usages, for instance wound-dressing and tissue engineering scaffolds.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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