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REVIEW PAPER

Hemocompatibility poly (lactic acid) nanostructures: A bird's eye view

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ABSTRACT

The usage of clinical devices in the cardiovascular treatment, hemodialyze system and other biomedical applications has improved recently. Direct contacts of biomaterials like poly(lactic acid) biopolymer with blood result in the activating of platelets, white blood cells , coagulation structure and complement cascades. Poly(lactic acid) is a sustainable, renewable, compostable, biobased, biodegradable, bioabsorbable , biocompatible polymer. This polymer has many applications in the synthesis of blood contacting mats like nanofibrous vascular scaffolds and hemodialyze nanosheets.

Mechanical interruption of the blood vessel wall throughout grafting of cardiovascular devices starts local hemostatic replies. Improving the safety of the blood contacting nanostructure grafts is a main necessity. The controlling of the interactions of proteins and platelets to the surface of a blood contacting biomaterial is a significant factor. So, the assessments of these material's influences on blood are necessary.

This article references more than 80 articles published in the last decade and reviews the latest hemocompatibility assays of poly(lactic acid) nanostructures used in the blood contacting field.

Key Words: *Biomedical, Hemolysis, Hemocompatibility, Nanostructures, Poly (lactic acid)*

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INTRODUCTION

Today several natural material (like cellulose and chitosan) and synthetic polymers (like polyvinyl chloride, polyethylene, poly(lactic acid)) and polysulfone have been applied in biomedical uses that involve contacting with blood stream[1]. Some of these applications will be stated in next sentences[2, 3].

*Artificial organs[4, 5].

Biodegradable medical devices like stents and artificial heart valves, braided vascular prosthesis[6-8].

*Surgical sutures.

*Disposable clinical apparatus (such as blood pumps, peace maker, dialyzers, plasma separators) [9-12].

The contacts of blood with a body external surface start a cataract of procedures which are described in next section.

1)Protein adsorption at the outer surface.

2)Adhesion of platelets to the body foreign surface through adherent proteins.

3)Activating of additional neighbored platelets.

4)The steadying of the thrombi with fibrin in a native net construction [13-15].

Hemocompatibility of materials

Hemocompatibility is one of the strategic biocompatibilities to blood communicating biomaterials. Hemocompatibility limited the medical applicability of blood contacting biomaterials [16-18].

The various processes which are important for analyzing of the hemocompatibility of biomaterials are shown in Fig 1.

These substances come in close interaction with blood, which is a multifaceted "structure," including 55% plasma, 44% erythrocytes, and 1% leukocytes and platelets[19-21].

Consequently, adversative communications among anew advanced materials and blood should be widely examined to avoid motivation and damage of blood components [22-24].

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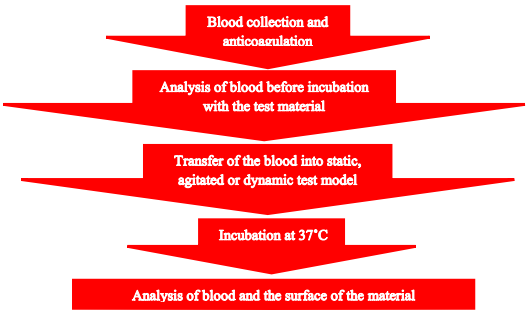

Fig 1. Scheme of the processes for assessment of the hemocompatibility of biomaterials

Hemocompatibility tests

The most important methods for evaluating the hemocompatibility of materials are illustrated in Fig 2[23, 25-27].

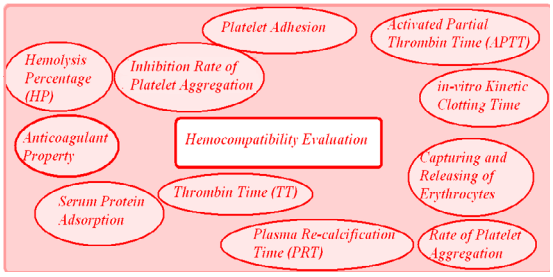

Fig 2. Important hemocompatibility tests

Poly (lactic acid) : A biobased polymer

PLA (poly(lactic acid) or polylactide) with chemical formulation of (C3H4O2)n is a sustainable, renewable, compostable, biobased, biodegradable, bioabsorbable , biocompatible linear aliphatic thermoplastic polyester(Fig 3) [28-32]. PLA manufactured from 100% renewable resources like corn, starch, sugar cane, wheat, sweet potato and rice [28, 33, 34].

The strategic advantages of PLA are the lower energy consumption required and lower greenhouse gas emission during production[35, 36]. PLA biodegrades to water and CO2 at the end of its life cycle [37].

The PLA market is estimated to spread 5.2 billion US dollars in 2020 for all of its industrial usages [38] . The chief uses are separated into areas for instance packaging, agriculture, electronics, textiles and biomedical such as tissue engineering, wound dressing, drug delivery systems, antibacterial mats, food packaging [39-41]. Poly (lactic acid) is a very important biopolymer for its usages in biomedical applications [29, 42-44]. PLA mats can be applied therapeutically or diagnostically [45-48].

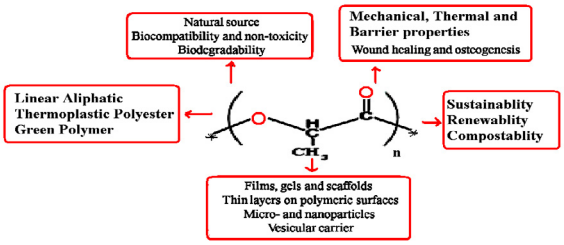

Fig 3. Poly (Lactic Acid) : A biobased polymer

PLA nanostructures (like nanofibers[49-52], nanoparticles [53, 54], nanosheets[55, 56], nanocomposites[57, 58] and nanospheres[59]) have been extensively used in the field of biotechnology procedures[60, 61].

These PLA nanostructures have been improved to bio-mimic heparin via chemical grafting, plasma deposition, radiation and self-assembly [62-64].

The natural blood vessel barrier has exceptional topography [65-67]. Geometrical statistics of the PLA nanostructures have been designed to bio-mimic the construction of blood vessels wall to catch respectable hemocompatibility[26, 68-70].

The subjects of this article chiefly focus on various blood compatibility evaluations of different types of PLA nanostructures materials like PLA nanosheets, nanofibers and nanocoatings in blood contacting systems and security assessments.

in vivo and in vitro analyzes of PLA nanostructures for the hemocompatibility assessment

In 2019, Da Silva *et al* [71], evaluated the hemocompatibility of two various dimension PLA nanoparticles (PLA/A and PLA/B), created via two approaches. After production, PLA/A nanoparticles mean diameter (187.9 ± 36.9 nm) was greater than PLA/B (109.1 ±10.4 nm). Irrespective of size variances, none of the PLA nanoparticles showed an inflammatory possible or a hemolytic activity in human blood.

Chen *et al* [72], fabricated PLA nanofibrous scaffolds for bone repair. The researchers use a new in situ polymerization thermal induced phase separation technique to construct PLA scaffolds with using polyaniline nanoparticles. The outcomes established that the corporation of polyaniline in PLA nanofibrous scaffold reduced the hemolytic activity compared to virgin PLA. Consequently, PLA nanofibrous scaffolds hold

exceptional hemocompatibility.

In a novel work in 2018[73], PLA nanofibrous scaffolds with various topographies (smooth, porous) fabricated for cardiovascular applications. PLA nanofibers of all three collections displayed acceptable hemolytic percentage (HP < 5%). In contrast, no morphological variations were detected in red blood cells cultured on smooth and porous PLA nanofibers. Porous nanofibers displayed outstanding anti thrombogenic property and adhered reduced platelets and preserved the morphology of native platelets. Though, smooth PLA nanofibers were originated to activate the platelets and distort the red blood cell membrane reliability. Therefore, the PLA nanofibers with porous constructions afford a perfect topography for time free hemocompatibility[73].

PLA membranes with nanoporous construction were advanced for hemodialysis via phase inversion by Gao *et al*[74]. Heparin was restrained to PLA membrane external by the durable adhesion capacity of dopamine. The *in vitro* outcomes revealed that surface heparinization enhanced the hemocompatibility of PLA membrane, repressed the adhesion of platelet, prolonged plasma recalcification time, and also reduced hemolysis ratio. In the other exploration in 2018[40], PLA nanosheets were produced for hemodialysis applications. For improving the hemocompatibility of PLA nanosheets, dopamine-g-carboxylated graphene oxide (DA-g-GOCOOH) was manufactured and then restrained on PLA sheets using a mussel inspired adhesion technique. The noteworthy enhancement of hydrophilicity and electronegativity of the PLA membranes efficiently improved the surface adhesion of platelets, elongated the decalcifications time and decreased the hemolysis ratio under 0.3%[40].

In a research in 2018[19], copolymer of PLA and poly(caprolactone) (PLCL) were electrospun to nanofibrous scaffolds for vascular regeneration. PLCL did not reason noticeable hemolysis. It was displayed that inherent coagulation pathway was continued after incubation with PLCL. Thrombogenicity valuation of testers exposed great thrombogenic possessions of materials that were similar to high amount of collagen thrombogenicity. The quantity of platelet activation was reliant on chemical composition and surface morphology of verified samples.

Li *et al*[75], advanced an innovative anticoagulant PLA nanoporous membrane via immobilizing hirudin via the hydrogen bonding communication.

The anti-clotting commotion of PLA membrane improved with the hirudin amount.

The improved hemocompatibility were definitely represented with the blood concretion four objects (APTT, PT, TT and FIB), mostly owing to the surface immobilization of hirudin.

In a different investigation in 2017[76], fluorescent nanoparticles were selected, which were attained using as initial material a pegylated PLA/polyaspartamide copolymer. The nanoparticles amounts near the blood wall increases with advancing pressure drop, individually of red blood cells concentration, and that the propensity for Fluorescent nanoparticles margination reduces with improved hematocrit**.**

Wang *et al*[77]*,* reported 1 stage immobilization of heparin nanocoating on PLA membranes by means of initiated chemical vapor deposition (iCVD) technique for improved hemocompatibility. The nanocoating presented on the PLA membrane surface using the cross linking of P(MAA-EGDA). The P(MAA-EGDA) covered PLA membranes indicated repressed platelet adhesion and long clotting time. The outcomes established that the nanocoating of P(MAA-EGDA) by the use of iCVD technique meaningfully improved the hemocompatibility of PLA membranes.

In another work by means of Lv *et al*.[78], carboxy methyl chitosan was crushed to nanopowder (NCMC). 400 mg NCMC was positively electrospun to nanofibers with the associate of 4 g PLA to formulate PLA/NCMC nanofibrous nets. The existence of NCMC improved the spinnability of PLA rendering to the electrospinning factors. Cross linked PLA/NCMC nets communicated respectable blood compatibility consistent with the outcomes of experiments.

Weijie *et al*[79], used coaxial electrospinning method for combining cistanche polysaccharide (CDPS) with PLA so as to prepare nanofibrous vascular scaffolds.

Compared to natural tissues, PLA/CDPS coaxial scaffolds displayed outstanding biomechanic possessions and hemocompatibility.

Shao *et al*[80], created nanofiber bone scaffolds via electrospinning technique from blending of poly(l-lactic-co-glycolic acid), tussah silk fibroin (TSF), and graphene oxide.

Hemocompatibility assays demonstrated that these scaffolds have admirable hemocompatibility.

Table 1. Blood coagulation assessments of various PLA nanostructures

PLA nanostructure	Blood Clotting Time (s)	Plasma Re-calcification Time (s)	Activated Partial Thrombin Time(s)	Thrombin Time(s)	Ref.
PLA nanoporous membrane	—	—	43	14.7	[77]
PLA/PVP nanoporous membrane	—	—	42	14.7	[77]
(PLA+PVP)/P(MAA:EGDA 8:1) nanocoating	—	—	52	16.1	[77]
(PLA+PVP)/P(MAA:EGDA 12:1) nanocoating	—	—	53	16.1	[77]
(PLA+PVP)/P(MAA:EGDA 16:1) nanocoating	—	—	54	16.5	[77]
PLA/P (MAA:EGDA 8:1) nanocoating	—	—	54	16.4	[77]
PLA/P (MAA:EGDA 12:1) nanocoating	—	—	57	17.5	[77]
PLA/P (MAA:EGDA 16:1) nanocoating	—	—	58	17.4	[77]
PLGA/PEG nanoparticles	3.9	150	37	14	[82]
PLGA/PEG/FA(Cisplatin : Paclitaxel = 2:1) nanoparticles	4.1	152	36	13	[82]
PLGA/PEG/FA(Cisplatin : Paclitaxel = 1:2) nanoparticles	4.2	148	36	15	[82]
PLA nanoporous membrane	—	223	—	—	[74]
Polysulfone nanoporous membrane	—	272	—	—	[74]
PLA/Polydopamine (2.0 g/L) nanoporous membrane	—	230	—	—	[74]
PLA/Polydopamine (1.0 g/L) nanoporous membrane	—	244	—	—	[74]
PLA/Polydopamine (0.5 g/L) nanoporous membrane	—	240	—	—	[74]
PLA/Polydopamine(2.0 g/L)/heparin nanoporous membrane	—	278	—	—	[74]
PLA/Polydopamine(1.0 g/L)/heparin nanoporous membrane	—	280	—	—	[74]
PLA/Polydopamine(0.5 g/L)/heparin nanoporous membrane	—	270	—	—	[74]
PLA nanocoating	—	120	—	—	[40]
PLA/(DA-g-GOCOOH) nanocoating	—	130	—	—	[40]
PLA/(DA-g-GOCOOH) (0.5 mg mL^{-1}) nanocoating	—	160	—	—	[40]
PLA/(DA-g-GOCOOH) (1 mg mL^{-1}) nanocoating	—	180	—	—	[40]
PLA/(DA-g-GOCOOH) (2 mg mL^{-1}) nanocoating	—	220	—	—	[40]
Smooth PLA nanofibers	—	230	—	—	[73]
Porous PLA nanofibers	—	270	—	—	[73]
PLA 3D nanofibers	—	—	28.6 ± 0.5	19.5 ± 0.2	[78]
PLA nanofibers	—	—	38.25	13.10	[83]
PLA/Curcumin(1%) nanofibers	—	—	36.91	12.94	[83]
PLA/Curcumin(3%) nanofibers	—	—	38.58	13.01	[83]
PLA/Curcumin(5%) nanofibers	—	—	42.60	13.86	[83]
PLA/Carboxymethyl chitosan (200-800 nm : 3D) nanofibers	—	—	31 ± 0.3	19.3 ± 0.3	[78]
PLA/Carboxymethyl chitosan (200-700nm : curve) nanofibers	—	—	33.3 ± 0.4	20.3 ± 0.4	[78]
PLA/Carboxymethyl chitosan (200-500 nm : curve) nanofibers	—	—	31.2 ± 0.6	19.4 ± 0.4	[78]
PLA/Carboxymethyl chitosan (violently distributed) nanofibers	—	—	32 ± 0.5	19.6 ± 0.4	[78]
PLCL nanofibers	—	—	28.2	11.8	[19]

In a different investigation, Shao *et al*[81], constructed a unique bone scaffold containing of multilayer nanofiber fabrics via weaving nanofiber yarns of PLA and TSF.

The results displayed that PLA, PLA/TSF woven scaffolds, and PLA/TSF nonwoven scaffolds represented exceptional hemocompatibility. He *et al* [82], applied folic acid modified poly(ethylene glycol)/poly(lactic-co-glycolic acid) to encapsulate cisplatin and paclitaxel drug molecules for lung cancer treatment. Blood compatibility examines and accompaniments examinations exposed that these nanoparticles did not prompt blood hemolysis, blood clotting, or complement activation[82]. Chen *et al.*[83] fabricated PLA/ curcumin nanofibrus membranes. Curcumin with various quantities (1, 3 and 5 wt%) was overloaded to the PLA nanofibers for exploring its anticoagulant possessions as a drug eluting stent. The *in vitro* blood compatibility investigations of stents exposed that the blood compatibility of PLA/curcumin mats is greater than the virgin PLA membrane, and the blood compatibility suggestively advances with curcumin amount.

Table 2. Blood anti-coagulation assessments of various PLA nanostructures

PLA nanostructure	Anti-coagulant Property (OD) (According to the time)									Ref.
	0 min	10 min	20 min	30 min	40 min	50 min	60 min	2 Hours	96 Hours	
PLA nanofibers	—	—	—	—	—	—	—	0.107±0.011	—	[79]
PLA/Cistanche polysaccharide (1%) nanofibers	—	—	—	—	—	—	—	0.093±0.005	—	[79]
PLA/Cistanche polysaccharide (3%) nanofibers	—	—	—	—	—	—	—	0.091±0.006	—	[79]
PLA/Cistanche polysaccharide (5%) nanofibers	—	—	—	—	—	—	—	0.104±0.004	—	[79]
PLA/Cistanche polysaccharide (7%) nanofibers	—	—	—	—	—	—	—	0.094±0.003	—	[79]
Smooth PLA nanofibers	0.085	0.075	0.06	0.055	0.05	0.047	0.045	—	—	[73]
Porous PLA nanofibers	0.0115	0.065	0.065	0.063	0.061	0.057	0.055	—	—	[73]
PLCL nanofibers	0.5	—	—	—	—	—		1.75	0.2	[19]

Table 3. Hematology and platelets assessments of various PLA nanostructures

PLA Nanostructure	Contact Angle	Hemolysis Ratio (%)	Platelets Adhesion Number	Rate of Platelet Aggregation (%)	Inhibition Rate of Platelet Aggregation (%)	Ref.
PLGA/Poly(methyl vinyl ether-co-maleic acid)/montelukast nanofibers	—	—	1×10^6 /mm^2	—	—	[87]
PLA/Polyaniline (5%) nanofibers	—	5	—	—	—	[72]
PLA/Polyaniline (10%) nanofibers	—	2.5	—	—	—	[72]
PLA/Polyaniline (15%) nanofibers	—	3.5	—	—	—	[72]
PLA nanofibers	—	7	—	—	—	[72]
PLGA/MWCNT(Vertically aligned) nanocomposite	—	—	22×10^{15}/mm^2	—	—	[85]
PLGA/MWCNT (Randomly dispersed pristine) nanocomposite	73	—	10×10^{15}/mm^2	—	—	[85]
PLGA./MWCNT (Randomly dispersed etched) nanocomposite	50	—	25×10^{15}/mm^2	—	—	[85]
PLGA	82	—	12×10^{15}/mm^2	—	—	[85]
PLA nanoporous membrane	93	—	—	—	—	[77]
PLA/PVP nanoporous membrane	87	—	—	—	—	[77]
(PLA+PVP)/P(MAA:EGDA 8:1) nanocoating	73	—	—	—	—	[77]
(PLA+PVP)/P(MAA:EGDA 12:1) nanocoating	72	—	—	—	—	[77]
(PLA+PVP)/P(MAA:EGDA 16:1) nanocoating	70	—	—	—	—	[77]
PLA/P(MAA:EGDA 8:1) nanocoating	75	—	—	—	—	[77]
PLA/P(MAA:EGDA 12:1) nanocoating	74					[77]
PLA/P(MAA:EGDA 16:1) nanocoating	72					[77]
PLGA nanofibers	108.3±6.9	0.9±0.3	—	—	—	[80]
PLGA/Tussah silk fibroin nanofibers	64.2 ± 4.5	1.3±0.2	—	—	—	[80]
PLGA/Tussah silk fibroin/Graphene oxide nanofibers	56.1 ± 4.2	1.8±0.4	—	—	—	[80]
PLA nanofibers	132.3±1.6	0.9 ±0.3	—	—	—	[81]
PLA/Tussah silk fibroin nanofibers (Fabric)	71.3 ± 2.7	1.3 ±0.2	—	—	—	[81]
PLA/Tussah silk fibroin nanofibers (Nonwoven)	72.1±1.1	1.8 ±0.4	—	—	—	[81]
PLA nanofibers	—	3.72±2.07	—	—	—	[79]
PLA/Cistanche/Polysaccharide (1%) nanofibers	—	1.83±1.18	—	—	—	[79]
PLA/Cistanche/Polysaccharide (3%) nanofibers	—	1.62±1.22	—	—	—	[79]
PLA/Cistanche/Polysaccharide (5%) nanofibers	—	3.27±1.17	—	—	—	[79]
PLA/Cistanche Polysaccharide (7%) nanofibers	—	1.98±0.84	—	—	—	[79]
PLGA/PEG nanoparticles	—	0.3	—	—	—	[82]
PLGA/PEG/FA (Cisplatin : Paclitaxel = 2:1) anoparticles	—	0.6	—	—	—	[82]
PLGA/PEG/FA (Cisplatin : Paclitaxel = 1:2) anoparticles	—	0.45	—	—	—	[82]
PLA nanoporous membrane	—	3.24	—	—	—	[74]
PLA/Polydopamine (2.0 g/L) nanoporous membrane	—	2.30	—	—	—	[74]
PLA/Polydopamine (1.0 g/L) nanoporous membrane	—	2.62	—	—	—	[74]
PLA/Polydopamine (0.5 g/L) nanoporous membrane	—	2.10	—	—	—	[74]
PLA/Polydopamine(2.0 g/L)/Heparin nanoporous membrane	—	1.46	—	—	—	[74]
PLA/Polydopamine(1.0 g/L)/Heparin nanoporous membrane	—	1.68	—	—	—	[74]
PLA/Polydopamine(0.5 g/L)/Heparin nanoporous membrane	—	1.36	—	—	—	[74]
PLA 38 µg/mL nanoparticle	—	0.05	—	—	—	*[71]*
PLA 50 µg/mL nanoparticle	—	0	—	—	—	*[71]*
PLA 200 µg/mL nanoparticle	—	0.3	—	—	—	*[71]*
PLA 250 µg/mL nanoparticle	—	0.25	—	—	—	*[71]*
PLA 75 µg/mL nanoparticle		0.1	—	—	—	*[71]*
PLA 100 µg/mL nanoparticle	—	0.05	—	—	—	*[71]*
PLA 300 µg/mL nanoparticle	—	0.2	—	—	—	*[71]*
PLA 400 µg/mL nanoparticle	—	0.25	—	—	—	*[71]*
PLA nanocoating	—	10.5	23 (10^5, cell per cm^2)	—	—	[40]
PLA/(DA-g-GOCOOH) nanocoating	—	6	28 (10^5, cell per cm^2)	—	—	[40]
PLA/(DA-g-GOCOOH) (0.5 mg mL^{-1}) nanocoating	—	0.2	15 (10^5, cell per cm^2)	—	—	[40]
PLA/(DA-g-GOCOOH) (1 mg mL^{-1}) nanocoating	—	0.1	11 (10^5, cell per cm^2)	—	—	[40]
PLA/(DA-g-GOCOOH) (2 mg mL^{-1}) nanocoating	—	0.05	3 (10^5, cell per cm^2)	—	—	[40]
Smooth PLA nanofibers	—	1.2	—	—	—	[73]
Porous PLA nanofibers	—	3.8	—	—	—	[73]
PLA 3D nanofibers	—	—	—	—	—	[78]
PLA nanofibers	—	—	—	28.42	9.43	[83]
PLA/Curcumin(1%) nanocomposite	—	—	—	15.80	49.65	[83]
PLA/Curcumin(3%) nanocomposite	—	—	—	14.60	53.47	[83]
PLA/Curcumin(5%) nanocomposite	—	—	—	11.68	62.78	[83]
PLA nanocoating	81 ± 0.8	—	119±5 (×10^3/mL)	—	—	[74]
PLA/heparin nanocoating	69 ± 0.3	—	142±3(×10^3/mL)	—	—	[74]
PLA/NH_2 nanocoating	79 ± 1.2	—	—	—	—	[74]
PLGA nanocomposite	93.43	—	—	—	—	[86]
PLGA/CNT nanocomposite	64.94	—	—	—	—	[86]

Furthermore, PLA/curcumin mat can efficiently elongate the blood coagulation time compared with the plasma, and the blood coagulation time of PLA/curcumin mats increases expressively as curcumin amount improving.

Sharkawi *et al*[84], defines a way for immobilizing heparin via covalent bonding to the surface of PLA film with the purpose of display enhanced hemocompatibility. Carboxyl groups existent in heparin molecules were motivated by means of reacting with N-hydroxy-succinimide and permitted for rejoining to free amino groups formed at the surface of poly(dl-lactic acid) films with controlling aminolysis. Platelets adhesion displayed fewer platelet adhesions on heparin modified PLA films besides to conserved morphology.

PLGA nanocomposites with multi walled carbon nanotubes (PLGA/MWCNT) were constructed with two various nanotube orientations**.** PLGA/MWCNT nanocomposite holding vertically aligned nanotubes displays very low stages of fibrinogen adsorption and platelet adhesion. Platelet adhesion demonstrates a respectable association with the existence of ACOOH groups and seems to be delicate to the topographic structures of the nanocomposites[85].

Poly(lactic-co-glycolic-acid)/carbon nanotube (PLGA/CNT) is investigated by Koh *et al*. [86] as a substance for fabricating artificial blood prostheses.

These nanocomposites were manufactured with an electrostatic layer by layer deposition method, wherein sheets of carbon nanotubes were adsorbed on a PLGA film. A noteworthy decrease of adhesion is detected on the PLGA/CNT composite, in addition to the lack of platelet activation. In contrast, both platelet adhesion and platelet activation are perceived on control testers.

Blood coagulation of PLA nanostructures

The blood coagulation of different PLA nanostructures is discussed in Table 1 and 2.

Hematology of PLA nanostructures

Hematology and platelets assessments of various PLA nanostructures are reported in Table 3.

Thrombosis assessment of PLA nanostructures using SEM technique

Fig 4 demonstrate the thrombosis assessment (SEM images of platelet adhesion) of various PLA structures by SEM technique.

Conclusions and future perspectives

Bioresource materials are considered as exceptional applicants for developing biomedical substances which would moreover decrease the fuel source materials in clinical uses. Among them, PLA has been predictable to play a main character for achieving such an objective especially in blood contacting devices for cardiovascular and hemodialyze applications. The review has widely offered consequences of assessing PLA nanomats which are in direct contact with blood structure for avoiding the toxic effects.

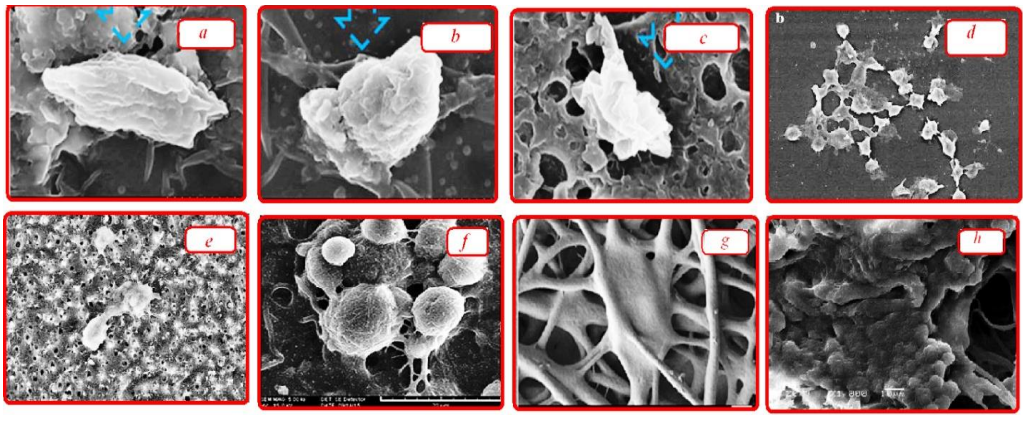

Fig 4 . Platelets adhesion on PLA nanostructures: a) PLA/P(MAA:EGDA 8:1) nanocoating, b) (PLA+PVP)/P(MAA:EGDA 8:1) nanocoating, c) PLA/P(MAA:EGDA 16:1) nanocoating, d) randomly dispersed pristine PLGA/MWCNT nanocomposite, e) vertically aligned PLGA/MWCNT nanocomposite, f) PLGA/Poly(methyl vinyl ether-co-maleic acid)/montelukast nanofiber, g) PLA smooth nanofiber, h) PLA/cistanche polysaccharide nanofiber[17, 73, 87, 88]

REFERENCES

1.Daly AC, Pitacco P, Nulty J, Cunniffe GM, DJ. K. 3D printed microchannel networks to direct vascularisation during endochondral bone repair. Biomater. 2018; 162 (57): 34-46.

2.Dhanka M, Chaitra Shetty, Srivastava R. Injectable methotrexate loaded polycaprolactone microspheres:Physicochemical characterization, biocompatibility, and hemocompatibility evaluation. Mater Sci Eng C. 2017; 81: 542–550.

3.Fattahi FS, Khoddami A, Avinc O. Nano-Fibrous and Tubular Poly (lactic acid) Scaffolds for Vascular Tissue Engineering. Nanomed Res J. 2019; 4 (3): 141-156.

4.Thottappillil N, Nair PD. Scaffolds in vascular regeneration:current status. Vascular Heal Risk Man. 2015; 11: 79–91.

5.Ercolani E, Del Gaudio C, Bianco A. Vascular tissue engineering of small-diameter blood vessels: reviewing the electrospinning approach. J Tissue Eng Reg Med. 2015;9 (8):861-888.

6.Wang H, Hou W, Liu F, Han Q, Li T, Lin H, Deng G, He J. Preparation and evaluation of a self-anticlotting dialyzer via an interface crosslinking approach. J Mem Sci. 2018; 563: 115–125.

7.Ye K, Kuang H, You Z, Morsi Y, Mo X. Electrospun Nanofibers for Tissue Engineering with Drug Loading and Release. Pharm. 2019; 11.

8.Drews JD, Miyachi H, Shinoka T. Tissue-engineered vascular grafts for congenital cardiac disease: Clinicalexperience and current status. Trends Cardiovasc Med. 2017; 27: 521–531.

9.Wang H, Hou W, Liu F, Han Q, Li T, Lin H, Deng G, He J. Preparation and evaluation of a self-anticlotting dialyzer via an interface crosslinking approach. J Mem Sci. 2018: 115–125.

10.Horakova J, Mikes P, Saman A, Svarcova T, Jencova V, Suchy T, Heczkova B, Jakubkova S, Jirousova J, Prochazkova R. Comprehensive assessment of electrospun scaffolds hemocompatibility. Mat Sci Eng C. 2018; 82: 330-335.

11.H. E. Burton, J. M. Freij, Espino DM. Dynamic viscoelasticity and surface properties of porcine left anterior descending coronary arteries. Cardiovas Eng Tech. 2017; 8 (1): 41–56.

12.Wang H, Hou W, Liu F, Han Q, Li T, Lin H, Deng G, He J. Preparation and evaluation of a self-anticlotting dialyzer via an interface crosslinking approach. J Mem Sci. 2018; 563: 115–125.

13.Marbod Weber, Heidrun Steinle, Sonia Golombek, Ludmilla Hann, Christian Schlensak, Wendel HP, Avci-Adali M. Blood-Contacting Biomaterials: In Vitro Evaluation of the Hemocompatibility. Frontiers Bioeng Biotech. 2018; 6.

14.Blok SLJ, Engels GE, van Oeveren W. In vitro hemocompatibility testing. Imp fresh blood Biointer. 2016;11(2).

15.Elahi MF, Guan G, Wang L, MW. K. Improved hemocompatibility of silk fibroin fabric using layer- by-layer polyelectrolyte deposition and heparin immobilization. J Appl Polym Sci. 2014: 1–12.

16.Burton HE, Espino DM. The Effect of Mechanical Overloading on Surface Roughness of the Coronary Arteries. Appl Bionic Biomech. 2019.

17.Derakhshandeh H, Kashaf SS, Aghabaglou F, Ghanavati IO, Tamayol A. Smart Bandages: The Future of Wound Care. Trend Biotech. 2018; 36 (12).

18.ASTM E2524-08. Standard Test Method for Analysis of Hemolytic Properties of Nanoparticles West Conshohocken, PA: ASTM International, 2013 (Available online at: https://www.astm.org/Standards/E2524.htm) (accessed September 26, 2018).

19.Horakova J, Mikes P, Saman A, Svarcova T, Jencova V, Suchy T, Heczkova B, Jakubkova S, Jirousova J, Prochazkov R. Comprehensive assessment of electrospun scaffolds hemocompatibility. Mat Sci Eng C. 2018; 82: 330–335.

20.Balan V, Verestiuc L. Strategies to improve chitosan hemocompatibility: A review. Eur Polym J. 2014; 53: 171-188.

21.Mukesh D, Chaitra S, Srivastava R. Injectable methotrexate loaded polycaprolactone microspheres: Physicochemical characterization, biocompatibility, and hemocompatibility evaluation. Mat Sci Eng C. 2017; 81: 542–550.

22.Jung F, Braune S, Lendlein A. Haemocompatibility testing of biomaterials using human platelets. Clin Hem Microcir. 2013; 53: 97–115.

23.King RE, Lau HK, Zhang H, Sidhu I, Christensen MB, Fowler EW, Li L, Jia X, Kiick KL, Thibeault SL. Biocompatibility and Viscoelastic Properties of Injectable Resilin-Like Polypeptide and Hyaluronan Hybrid Hydrogels in Rabbit Vocal Folds. Reg Eng Tran Med. 2019.

24.Pankaj K-A-K-S, Atul D, Babita K, Subhasree R-C, Karmakar S. 1, 3β-Glucan anchored, paclitaxel loaded chitosan nanocarrier endows enhanced hemocompatibility with efficient anti-glioblastoma stem cells therapy. Carbohyd Polym. 2018; 180: 365–375.

25.Renee E, Ishnoor S-M, Christensen E-W-F, Linqing L, Xinqiao J-K-L, Kiick S-L-T. Biocompatibility and Viscoelastic Properties of Injectable Resilin-Like Polypeptide and Hyaluronan Hybrid Hydrogels in Rabbit Vocal Folds. Reg Eng Trans Med. 2019.

26.Gugutkov D, Gustavsson J, Cantini M, Salmeron-Sánchez M, Altankov G. Electrospun fibrinogen–PLA nanofibres for vascular tissue engineering. J Tissue Eng Reg Med. 2017; 11(10): 2774-2784.

27.Zhao X-W, Lin Y, Phil C, Fin C-R, Michase l-M. Structure and blood compatibility of highly oriented poly(lactic acid)/thermoplastic polyurethane blends produced by solid hot stretching. . Polym Adv Technol. 2013; 249: 853–860.

28.Fattahi F, Izadan H, Khoddami A. Deep Dyeing of Poly (lactic acid) and Poly (ethylene terephthalate) Fabrics Using UV/Ozone Irradiation. 4th International Color and Coatings Congress (ICCC 2011), November 22-24, Tehran-Iran, 2011.

29.Fattahi F, Izadan H, Khoddami A. Investigation into the Effect of UV/Ozone Irradiation on Dyeing Behaviour of Poly(Lactic Acid) and Poly(Ethylene Terephthalate) Substrates. Prog Color Colorants Coat. 2012; 5: 15-22.

30.Khoddami A, Avinc O, Ghahremanzadeh F. Improvement in poly(lactic acid) fabric performance via hydrophilic coating. Progress in Organic Coatings. 2011;72 (3):299-304.

31.Khoddami A, Avinc O, Mallakpour S. A novel durable hydrophobic surface coating of poly(lactic acid) fabric by pulsed plasma polymerization. Prog Org Coat. 2010; 67 (3): 311-316.

32.Avinc O, Khoddami A, Hasani H. A mathematical model to compare the handle of PLA and PET knitted fabrics after different finishing steps. Fiber Poly. 2011;12 (3):405-413.

33.Doustgani A, Ahmadi E. Melt electrospinning process optimization of polylactic acid nanofibers. J Ind Text. 2016; 45(4): 626-634.

34.Jain A, Kunduru KR, Basu A, Mizrahi B, Domb AJ, Khan

W. Injectable formulations of poly(lactic acid) and its copolymers in clinical use. Adv Drug Del Rev. 2016; 107: 213-227.
35.Alves PE, Soares BG, Lins LC, Livi S, Santos EP. Controlled delivery of dexamethasone and betamethasone from PLA electrospun fibers: A comparative study. Eur Polym J. 2019.
36.Sadat Fattahi F, Khoddami A, Avinc O, Poly (Lactic Acid) Nano-fibers as Drug-delivery Systems: Opportunities and Challenges. Nanomed Res J. 2019; 4 (3): 130-140.
37.Anna Magiera, JarosBaw Markowski, Elzbieta Menaszek, Jan Pilch, Blazewicz S. PLA-Based Hybrid and Composite Electrospun Fibrous Scaffolds as Potential Materials for Tissue Engineering. J Nanomater. 2017.
38.Scaffaro R, Lopresti F, Marino A, Nostro A. Antimicrobial additives for poly(lactic acid) materials and their applications: current state and perspectives. Appl Microb Biotech. 2018; 102: 7739–7756.
39.Zhou M, Yang J, Ye X, Zheng A, Li G, Yang P, Zhu Y, Cai L. Blood Platelet's Behavior on Nanostructured Superhydrophobic Surface. J Nano Res. 2008;2:129-136.
40.Awad NK, Niu H, Ali U, Morsi YS, 2 TL. Electrospun Fibrous Scaffolds for Small-Diameter Blood Vessels: A Review. Memb. 2018; 8(15).
41.Li G-C, Yang P, Qin W, Manfred F-M, Zhou S-N-H. The effect of coimmobilizing heparin and fibronectin on titanium on hemocompatibility and endothelialization. Biomater. 2011; 32: 4691–4703.
42.Fattahi F-S, Khoddami A, Izadian H. Review on Production, Properties, and Applications of Poly(lactic acid) Fibers. J Text Sci Techn. 2015; 5(1): 11-17.
43.Fattahi F-S, Khoddami A, Izadan H. A Review on Poly(lactic acid) Textile Goods Finishing: Plasma Treatment, UV/Ozone Irradiation, Superhydrophobic Surface Manufacturing and Enzymatic Treatment. J Apparel Text Sci Tech. 2017(2): 19-26.
44.Fattahi F, Poly (lactic acid) Nanofibers as novel drug delivery systems: A Birds Eye View. LAMBERT Academic Publishing, 978-620-0-49758-1, 2019.
45.Nofar M, Sacligil D, Carreau PJ, Kamal M-R, Heuzey M-C. Poly (lactic acid) blends: Processing, properties and applications. Int J Biol Macromol. 2019;125: 307-360.
46.Amani A, Kabiri T, Shafiee S, Hamidi A. Preparation and Characterization of PLA-PEG-PLA/PEI/DNA Nanoparticles for Improvement of Transfection Efficiency and Controlled Release of DNA in Gene Delivery Systems. Iran J Pharm Res. 2019; 18 (1): 125-141.
47.Handali S, Moghimipour E, Rezaei M, Saremy S, Dorkoosh FA. Co-delivery of 5-fluorouracil and oxaliplatin in novel poly(3-hydroxybutyrate-co-3-hydroxyvalerate acid)/ poly(lactic-co-glycolic acid) nanoparticles for colon cancer therapy. . Int J Biol Macromol. 2019;124: 1299–1311.
48.Ghasemi R, Abdollahi M, Zadeh EE, Khodabakhshi K, Badeli A, Bagheri H, Hosseinkhani S. mPEG-PLA and PLA-PEG-PLA nanoparticles as new carriers for delivery of recombinant human Growth Hormone (rhGH). Sci Rep. 2018.
49.Birhanu G, Tanha S, Akbari Javar H, Seyedjafari E, Zandi-Karimi A, Kiani Dehkordi B. Dexamethasone loaded multi-layer poly-l-lactic acid/pluronic P123 composite electrospun nanofiber scaffolds for bone tissue engineering and drug delivery. Pharm Dev Tech. 2018:1-10.
50.Mao Z, Li J, Huang W, Jiang H, Zimba B, Chen L, Wan J, Wu Q. Preparation of poly(lactic acid)/graphene oxide nanofiber membranes with different structures by electrospinning for drug delivery; 2018: 16619-16625.
51.Mohiti-Asli M, Saha S, Murphy S-V, Gracz H, Pourdeyhimi B, Atala A, Loboa E-G. Ibuprofen loaded PLA nanofibrous scaffolds increase proliferation of human skin cells in vitro and promote healing of full thickness incision wounds in vivo. J Biomed Mater Res B: Appl Biomater. 2015; 105 (2): 327-339.
52.Riggin C-N, Qu F, Kim D-H, Huegel J, Steinberg D-R, Kuntz A-F, Soslowsky L-J, Mauck R-L, Bernstein J. Electrospun PLGA Nanofiber Scaffolds Release Ibuprofen Faster and Degrade Slower after In Vivo Implantation. Ann Biomed Eng. 2017; 45(10).
53.Zhang L, Zhu H, Gu Y, XiaohuaWang, Wu P. Dual drug-loaded PLA nanoparticles bypassing drug resistance for improved leukemia therapy. J Nanopart Res. 2019; 21(83).
54.Neha-Atulkumar S, Abul-Kalam A-M, Khan Z-A. Fabrication of PLA-PEG Nanoparticles as Delivery Systems for Improved Stability and Controlled Release of Catechin. J Nanomater. 2017.
55.Foong CY, Hamzah MSA, Razak SIA, Saidin S, Nayan NHM. Influence of Poly(lactic acid) Layer on the Physical and Antibacterial Properties of Dry Bacterial Cellulose Sheet for Potential Acute Wound Healing Materials. Fiber Polym. 2018; 19 (2): 263-271.
56.Birhanu G, Tanha S, Akbari-Javar H, Seyedjafari E, Zandi-Karimi A, Dehkordi B-K. Dexamethasone loaded multi-layer poly-l-lactic acid/pluronic P123 composite electrospun nanofiber scaffolds for bone tissue engineering and drug delivery. Pharm Dev Tech. 2018.
57.Magiera A, Markowski J, Menaszek E, Pilch J, Blazewicz S. PLA-Based Hybrid and Composite Electrospun Fibrous Scaffolds as Potential Materials for Tissue Engineering. J Nanomater. 2017.
58.Moustafa H, El Kissi N, Abou-Kandil AI, Abdel-Aziz MS, Dufresne A. PLA/PBAT Bionanocomposites with Antimicrobial Natural Rosin for Green Packaging. ACS App Mater Inter. 2017; 9(23): 20132-20141.
59.Sho K, Okumura N, Junji K, Noriko K, Tabata Y. Development of Poly Lactic/Glycolic Acid (PLGA) Microspheres for Controlled Release of Rho-Associated Kinase Inhibitor. J Ophthal, 2017.
60.Mehdikhani M, Tavakoli E, Zargar-Kharazi A, Hashemibeni B. A novel nano-composite scaffold for cartilage tissue engineering. Scientia Iranica. 2018;25 (3):1815-1823.
61.Fattahi F-s, Khoddami A, Avinc O. Poly(lactic acid) (PLA) Nanofibers for Bone Tissue Engineering. J Text Polym. 2019; 7(2): 47-64.
62.G. Pitarresi, C. Fiorica, F. S. Palumbo, S. Rigogliuso, G. Ghersi, G. Giammona. Heparin functionalized polyaspartamide/ polyester scaffold for potential blood vessel regeneration,. J Biomed Mater Res A. 2014;102 (5):1334–1341.
63.Krawiec J-T. Adult stem cell-based tissue engineered blood vessels: a review. Biomater. 2012; 33: 3388–3400.
64.Reno F, Paul G, Rizzi M, Gatti G, L M. Poly (D,L) lactic acid blending with vitamin e increases polymer hemocompatibility: an hydrophilic effect. J Appl Polym Sci. 2013; 129(3):1527–1533.
65.Shalumon KT, Chennazhi KP, Anupama MS, Jayakumar R, Deepthi S, Nair SV. Fabrication of poly (l-lactic acid)/gelatin composite tubular scaffolds for vascular tissue engineering. Int J Biol macromol. 2015; 9.
66.Zhang C, Wen J, Yan J, Kao Y, Ni Z, Cui X, Wang H. In

situ growth induction of the corneal stroma cells using uniaxially aligned composite fibrous scaffolds. RSC Adv. 2015; 5: 12123–12130.
67.V M. After soft tissues, bone, drug delivery and packaging,PLA aims at blood. Eur Polym J. 2015; 68: 516–552.
68.Koh L-B, Rodriguez I, Venkatraman S-S. A novel nanostructured poly(lactic-co-glycolic-acid)–multi-walled carbon nanotube composite for blood-contacting applications: Thrombogenicity studies. Acta Biomaterialia. 2009; 5: 3411–3422.
69.Meng D, Yunpeng G-u, Zhenjun L, Yue Q, Gui E. Ma, Kang N. Endothelial Differentiation of Human Adipose-Derived Stem Cells on Polyglycolic Acid/Polylactic Acid Mesh. Stem Cell Int. 2015.
70.Jia L, Wei Z, Yu-Feng Z, Xia L. Cell responses and hemocompatibility of g-HA/PLA composites. Sci China Life Sci. 2011; 54: 366–371.
71.Silva J-D, Jesus S, Bernardi N, Colaço M, Borges O. Poly(D,L-Lactic Acid) Nanoparticle Size Reduction Increases Its Immunotoxicity. Frontier Bioeng Biotech. 2019; 7(137).
72.Chen J, Yu M, Guo B, Ma P-X, Yin Z. Conductive nanofibrous composite scaffolds based on in-situ formed polyaniline nanoparticle and polylactide for bone regeneration. J Colloid Interface Sci. 2018; 514: 517–527.
73.Soundararajan A, R-J-M, Dhandapani R, Radhakrishnan J, Manigandan A, Kalyanasundaram S, Sethuraman S, Subramanian A. Surface topography of polylactic acid nanofibrous mats: influence on blood compatibility. J Mater Scie: Mater Med. 2018; 29: 145-169.
74.Ailin Gao, FuLiu n, LixinXue. Preparationandevalua tionofheparin-immobilizedpoly(lacticacid) (PLA) membraneforhemodialysis. J Memb Sci. 2014: 390–399.
75.Li J, Liu F, Qin Y, He J, Xiong Z, Deng G, Li Q. A novel natural hirudin facilitated anti-clotting polylactide membrane via hydrogen bonding interaction. J Memb Sci. 2017; (523): 505–514.
76.Craparo E-F, D'Apolito R, Giammona G, Cavallaro G, Tomaiuolo G. Margination of Fluorescent Polylactic Acid–Polyaspartamide based Nanoparticles in Microcapillaries In Vitro: the Effect of Hematocrit and Pressure. Molecule. 2017; 22.
77.Wang H, Shi X, Gao A, Lin H, Chen Y, Ye Y, He J, Liu F, Deng G. Heparin free coating on PLA membranes for enhanced hemocompatibility via iCVD. Appl Surf Sci. 2018; 433:869–878.
78.Lv J, Yin X, Zeng Q, Dong W, Liu H, Zhu L. Preparation of carboxymethyl chitosan nanofibers through electrospinning the ball-milled nanopowders with poly (lactic acid) and the blood compatibility of the electrospun NCMC/PLA mats. J Polym Res. 2017; 24(60).
79.Weijie Z, Zhuo C, Sujuan M, Yonggang W, Fei Z, Keyi W, Chenguang Y, Xiuying P, Jianzhong M, Yuli W, Feifan L, Fen R, Yanbei K. Cistanche polysaccharide (CDPS)/polylactic acid (PLA) scaffolds based coaxial electrospinning for vascular tissue engineering. Int J Polym Mater Polym Biomater. 2016; 65(1):38–46.
80.Shao W, He J, Sang F, Wang Q, Chen L, Cui S, Ding B. Enhanced bone formation in electrospun poly(L-lactic-co-glycolic acid)–tussah silk fibroin ultrafine nanofiber scaffolds incorporated with graphene oxide. Mater Sci Eng C. 2016; 62: 823–834.
81.Shao W, He J, Han Q, Sang F, QianWang, Chen L, Cui S, Ding B. A biomimetic multilayer nanofiber fabric fabricated by electrospinning and textile technology from polylactic acid and Tussah silk fibroin as a scaffold for bone tissue engineering. Mater Sci Eng C. 2016; 67: 599–610.
82.He Z, Shi Z, Sun W, Ma J, Xia J, Zhang X, Chen W, Huang J. Hemocompatibility of folic-acid-conjugated amphiphilic PEG-PLGA copolymer nanoparticles for co-delivery of cisplatin and paclitaxel: treatment effects for non-small-cell lung cancer. Tumor Biol. 2016; 37: 7809–7821.
83.Yan Chen, Lin J, Yuqin Wan, Yanna Fei, Wang H, Gao W. Preparation and Blood Compatibility of Electrospun PLA/Curcumin Composite Membranes. Fiber Polym. 2012;13 (10): 1254-1258.
84.Sharkawi T, Darcos V, Vert M. Poly(DL-lactic acid) film surface modification with heparin for improving hemocompatibility of blood-contacting bioresorbable devices. J Biomed Mater Res. 2011; 98 (1).
85.Koh LB, Rodriguez I, Venkatraman S-S. A novel nanostructured poly(lactic-co-glycolic-acid)–multi-walled carbon nanotube composite for blood-contacting applications: Thrombogenicity studies. Acta Biomaterialia. 2009; 5: 3411–3422.
86.Li B-K, Isabel R, Zhou J. Platelet adhesion studies on nanostructured poly(lactic-co-glycolic-acid)–carbon nanotube composite. J Biomed Mater Res A. 2007.
87.Varshosaz J, Jahanian A, Maktoobian M. Montelukast Incorporated Poly(methyl vinyl ether-co-maleic acid)/Poly(lactic-co-glycolic acid) Electrospun Nanofibers for Wound Dressing. Fiber Polym. 2017; 18 (11): 2125-2134.
88.Weijie Z, Zhuo C, Sujuan M, Yonggang W, Fei Z, Keyi W, Chenguang Y, Xiuying P, Jianzhong M, Yuli W, Feifan L, Fenb R, Yanbei K. Cistanche polysaccharide (CDPS)/polylactic acid (PLA) scaffolds based coaxial electrospinning for vascular tissue engineering. Int J Polym Mater Polym Biomater. 2016; 65 (1): 38–46.