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Review Article

Polymers for Cardiovascular Stent Coatings

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Polymers have found widespread applications in cardiology, in particular in coronary vascular intervention as stent platforms (scaffolds) and coating matrices for drug-eluting stents. Apart from permanent polymers, current research is focussing on biodegradable polymers. Since they degrade once their function is fulfilled, their use might contribute to the reduction of adverse events like in-stent restenosis, late stent-thrombosis, and hypersensitivity reactions. After reviewing current literature concerning polymers used for cardiovascular applications, this review deals with parameters of tissue and blood cell functions which should be considered to evaluate biocompatibility of stent polymers in order to enhance physiological appropriate properties. The properties of the substrate on which vascular cells are placed can have a large impact on cell morphology, differentiation, motility, and fate. Finally, methods to assess these parameters under physiological conditions will be summarized.

1. Introduction

Cardiovascular diseases (CVDs) are known as a variety of disorders that involve the heart or blood vessels and are considered to be the leading cause of mortality worldwide [1]. Currently, percutaneous coronary intervention (PCI) is the main treatment for CVDs [2]. During PCI, an expandable coronary stent is placed inside the lesioned artery. Arterial injury is an inevitable consequence of all interventional procedures and initiates a cascade of cellular and molecular events resulting in an acute disruption of the endothelial layer [3]. Therefore, current research is focused on the safety of coronary stents, but side effects, such as late and very late stent-thrombosis and in-stent restenosis, remain problematic [4, 5].

In this context, polymers, which are capable of degrading, releasing drugs, or mimicking biological functionalities, are of great interest for the development of vascular implants. Thus, sophisticated biomaterials are required to fulfil special demands with their specific properties and biocompatibility. In this context, the present review is focused on polymers used as stent platforms and coating matrices for drug-eluting stents (DES), as well as on the description of parameters of vascular and blood cell function which are crucial for the evaluation of the biocompatibility of polymers. The last section deals with *in vitro* methods to assess these parameters under preferably physiological conditions and summarizes results of reports dealing with *in vitro* evaluation of polymers for cardiovascular implants.

2. Coronary Artery Stents

In 2002, DES were introduced to the European market with the aim to resolve adverse effects of PCI and subsequent stent implantation [6]. DES are vascular stents which allow the delivery of antiproliferative drugs to inhibit vascular smooth muscle cell (SMC) growth. Due to this controlled local drug delivery, events of stent-thrombosis and in-stent restenosis are supposed to be reduced or prevented [5]. Despite their high efficacy regarding the inhibition of in-stent restenosis, first-generation DES based on biostable polymeric drug carriers, such as poly(ethylene-co-vinyl acetate) (PEVA), poly(n-butyl methacrylate) (PBMA), and poly(styrene-b-isobutylene-b-styrene) block polymers (SIBS), were attributed to incidences of death or myocardial infarction after implantation [5]. Particularly late stent-thrombosis and delayed wound healing, caused by poor reendothelialisation and the persistence of polymer coatings after drug release, were identified as potential risks associated

with DES [7–10]. Furthermore, hypersensitivity reactions were observed [11, 12]. In this context, it has been stated that, besides the stent platform and the drug, the polymeric drug carrier might be a target for the improvement of biocompatibility of these devices. Therefore, DES coatings on the basis of biodegradable polymers were developed (second-generation DES). They are designed to offer the antirestenotic benefit of a standard DES, the safety of an uncoated bare metal stent (BMS) [13], and the ability of the coating polymer to degrade once its function is fulfilled. The latter of which might efficiently reduce observed late and very late stent-thrombosis and hypersensitivity reactions. In order to eliminate the presence of a permanent implant, completely bioresorbable coronary stents (scaffolds) on the basis of magnesium [14] and biodegradable polymers [15, 16] were developed. Polymers intended as scaffold materials degrade in a moderate period of 6–24 months. After resorption, there would be no triggers for stent-thrombosis, such as uncovered stent struts, durable polymers, or remnant drugs. The absence of foreign material may also reduce the requirement for long-term dual antiplatelet therapy and associated bleeding complications [14, 17].

3. Polymers for Cardiovascular Stents: Bioderived and Resorbable

In the past, synthetic polymers, such as poly(ethylene) (PE), polyurethanes (PUR), poly(glycolide) (PGA), and polylactides (PLA), have been the material of choice for implants and other medical devices. While PURs are well established as scaffold materials for vascular grafts due to their excellent hemocompatibility [18–21], PGA is commonly used as suture material for different surgical applications [22]. Further, PGA-containing scaffolds blended with poly(ϵ-caprolactone) (PCL) [23] are used for PGA-based drug delivery systems [24–26]. Overall, PLA has been intensely tested as temporary stent material in cardiology due to its long track records of *in vivo* biocompatibility [27–29].

The application of medical devices based on bioresorbable polymers is of increasing importance in the medical and pharmaceutical field [27]. These polymers, representing a suitable alternative for DES materials, are also considered as core material for fully resorbable scaffolds. In general, biopolymers from natural origin degrade physiologically by hydrolysis and are therefore supposed to be very biocompatible [30]. Typical representatives of biodegradable polymers are polyhydroxycarboxylic acids, such as PGA, PLA, poly(3-hydroxybutyrate) (P(3HB)), poly(4-hydroxybutyrate) (P(4HB)), and PCL. The chemical structure of the bioderived, resorbable polymer P(4HB) is quite similar to the synthetic polyesters PGA and PCL. P(4HB) belongs to the class of polyhydroxyalkanoatefs and is naturally produced by microorganisms [31, 32]. In addition to P(4HB), P(3HB) is another polyhydroxyalkanoate of interest. However, while P(4HB) is applicable for vascular grafts and heart valves [33], P(3HB) has not been accepted for vascular applications due to its capability to trigger extensive inflammatory responses in porcine models [34]. However, the biocompatibility of these polymers, specifically in vascular stenting, depends to a large extent on degradation kinetics [35]. Unfortunately, those that are considered to be more biocompatible, such as synthetic PLA, need years to degrade and therefore carry a risk of late and very late stent-thrombosis. Furthermore, degrading polymers, such as PGA, may generate fragments potentially leading to emboli [36, 37]. Clearly, bioresorbable polymers are not without challenges and are a work in progress [38].

3.1. Polymers for DES Coatings. DES are specialized vascular stents which allow the local delivery of drugs in a controlled manner with the purpose to reduce or prevent in-stent restenosis as a process of enhanced SMC proliferation [39, 40]. Furthermore, biomimetic polymers, such as phosphorylcholine (PC), poly(vinylidene fluoride)-hexafluoropropylene (PVDF-HFP), or the BioLinx polymer, do not interfere with stent reendothelialisation and are currently in use in second- and third-generation DES [41]. Beyond that, biodegradable polymers, such as PLA and poly(lactide-co-glycolide) (PLGA), were extensively studied to optimize their properties and biocompatibility. Due to the degradation of the polymeric coatings and the subsequent transformation into a BMS, DES are expected to cause lower stent-thrombosis. Intense work on stent development led to DES of next generations with further improved impact on endothelialisation and arterial healing.

While drug-elution from biodegradable polymers represents one approach to reduce hypersensitivity and late stent-thrombosis, an alternative is to avoid using any polymer at all. Polymer-free DES have been investigated where the drug was embedded mostly into microporous or nanoporous metallic stent surfaces [42, 43]. At present the efficacy and safety of polymer-free DES in clinical practice are subject of debate. Randomized controlled trials conducted so far provide conflicting results or are underpowered to address the question of their efficacy and safety [44]. However, several studies report that patients treated with polymer-free stents show similar clinical outcomes to those treated with durable polymer DES in terms of mortality, stent thrombosis, and long-term efficacy [45, 46]. On the other hand, it has been reported that new generation DES have proven superior or noninferior in terms of safety and efficacy compared with durable DES [47, 48]. The CHOICE trial might shed some light on this question [49]. Possibly, biocompatible, polymer-based abluminal or dual, and side-selective coatings as well as other innovative, polymer-free drug reservoirs might be applicable [14, 50, 51]. Common DES are summarized in Table 1.

3.2. Polymers for Vascular Scaffolds. Having questioned the role of the polymer, a further step is to question the role of the stent itself. The idea of a fully biodegradable scaffold is to provide a temporary mechanical support of the narrowed blood vessel. In consequence, the vessel is allowed to heal and recover its physiological function before the implant looses its mechanical integrity [64]. In addition, the absence of a permanent stent platform may reduce the requirements for a long-term dual antiplatelet therapy and facilitate the return of vessel vasomotion [14, 17]. Clinically approved scaffolds are mostly based on PLA (for review see [13, 27, 64]). Unfortunately, difficulties in replacing the mechanical properties

Table 1: Components and peformance of current clinically approved DES.

Type	DES	Coating	Drug	Clinical performance
Durable	Taxus Express [52, 53]	SIBS	Paclitaxel	Superior to BMS in reducing ISR and TLR
	Promus Element [54]	PBMA/PVDF-HFP	Everolimus	Comparable to Xience-V
	Endeavour [55–57]	PC	Zotarolimus	Similar safety and efficacy as Taxus with higher ST; impaired polymer integrity
	Xience-V [58]	PBMA/PVDF-HFP	Everolimus	Prevents ISR and restores vasomotion, low ST
Biodegradable	SymBio [59]	PLGA	Pimecrolimus/Paclitaxel	No beneficial effect compared to Taxus
	Endeavour Resolute [47]	BioLinx	Zotarolimus	Noninferior in safety and efficacy trials compared to durable DES
	BioMatrix [60–62]	PLA	Biolimus A9	reduced risk of CE compared to durable DES
Polymer-free	Janus Flex [63]		Tacrolimus	Higher rates of TLR and ST in comparison with Taxus
	Yukon Choice [45, 46]		Sirolimus, Trapidil	Similar to Taxus, no beneficial effects compared to durable DES

SIBS: poly(styrene-b-isobutylene-b-styrene) block copolymer, PBMA: poly(n-butyl methacrylate), PVDF-HFP: poly(vinylidene fluoride)-hexafluoropropylene, PC: phosphorylcholine polymer, PLGA: poly(lactide-co-glycolide), BioLinx: hydrophobic C10-polymer/hydrophilic C19-polymer/poly(vinyl-pyrrolidone) (PVP), and PLA: polylactide; DES: drug-eluting stent, BMS: bare metal stent, ISR: in-stent restenosis, TLR: target lesion revascularization, ST: stent thrombosis, and CE: cardiac events.

of the metallic cage and aggressive inflammatory reactions during polymer erosion—leading to in-stent restenosis—have been a drawback in the development of this field [65]. So far, the first clinically available scaffold is provided with a poly(L-lactide) (PLLA) frame and a poly(D,L-lactide) (PDLLA) coating carrying Everolimus (BVS, Abbott, USA).

4. Biocompatibility of Polymers Used for Cardiovascular Applications

Diagnostic and therapeutic devices implicate the contact between tissue, blood, and the implanted material. Using polymers for new technologies has been a revolutionary advance in the therapy of cardiovascular disease [13]. Nevertheless, there is increasing evidence that the polymer coating could be responsible for adverse effects (e.g., in-stent restenosis, stent-thrombosis, and hypersensitivity reactions). In order to improve clinical outcomes, a feasible biocompatible material should therefore promote the reendothelialisation of the polymeric surface and possess antithrombotic as well as anti-inflammatory properties. In this context, the term "biocompatibility" determines the interface reactions of blood and tissue cells with the surface of the polymer.

4.1. Polymer-Induced SMC Proliferation. After stenting, increased growth and migration of vascular SMCs can result in neointimal proliferation and present the key mechanisms of in-stent restenosis. Hereby, SMCs undergo complex phenotypic changes leading to impeded blood flow and cardiac symptoms [66, 67]. Additionally, the release of cytokines and growth factors from white blood cells may induce increased SMC growth and accumulation within the intima which is also an important contributor to in-stent restenosis. Several immunosuppressants administered via a coated stent platform (local drug delivery) have been tested for their potential to inhibit in-stent restenosis. In this regard, the deferred release of antiproliferative drugs such as Rapamycin (Sirolimus) or Taxol (Paclitaxel) is a viable method to control the rapid and undesired cell growth process (Figure 1) with the benefit of achieving higher tissue concentrations of the drug without systemic effects, at a precise site and time [68, 69]. The safety and efficacy of such an approach critically depends on the combination of drug, polymer, and kinetics of release [70]. The development of a polymeric carrier that meets all required criteria (biological inert, sterilisable, mechanically resistant, and flexible) is still extremely challenging.

Currently, other agents with potential benefits (e.g., statins and local gene-therapy) as well as improvements in polymer technology (biodegradable smart polymers, coatings for multiple-drug release) are under evaluation to overcome in-stent restenosis.

4.2. Polymer-Induced Endothelial Incompetence. During stenting, the endothelial layer is partially or completely destroyed. This disturbance of the normal endothelial structure and function is strongly implicated in the pathogenesis of atherosclerosis and the early, late, and very late thrombotic events that occur after intervention [71]. In addition, complete coverage of endothelial cells is associated with attenuation or even cessation of neointima growth [72, 73]. In

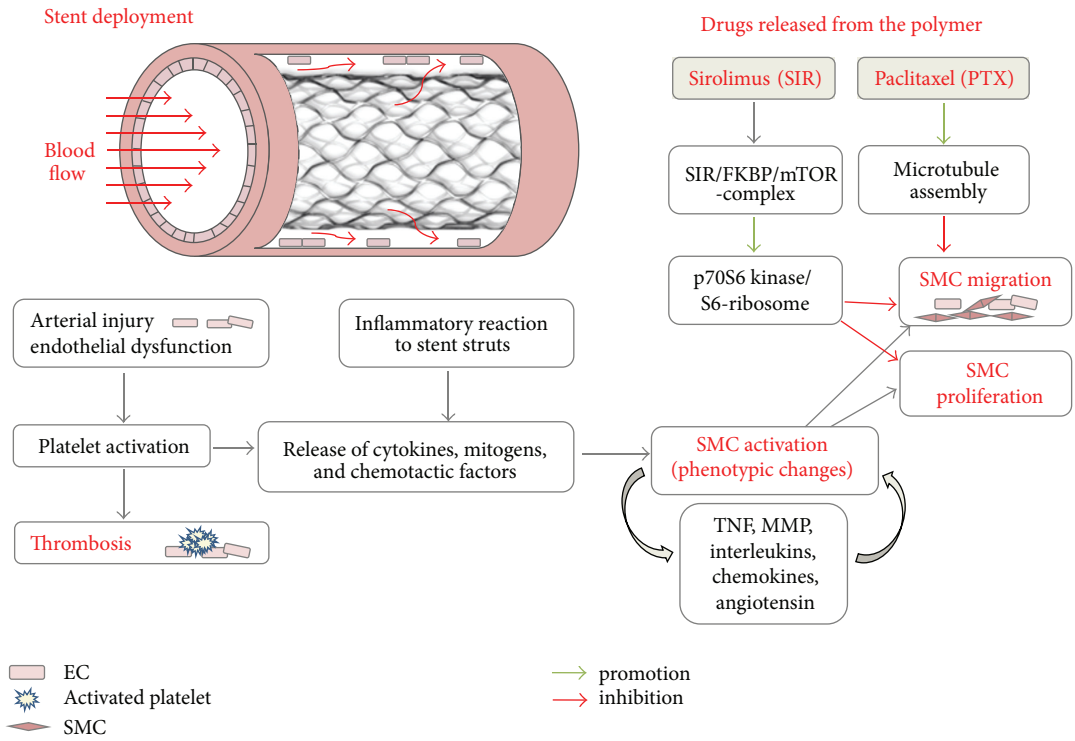

Figure 1: Drug-eluting stents: the impact of stent deployment and immunosuppressants Rapamycin (Sirolimus) and Taxol (Paclitaxel). EC = endothelial cell, SMC = smooth muscle cell, TNF = tumor necrosis factor, MMP = matrix metalloproteinase, FKBP = Rapamycin binding protein, and mTOR = mammalian target of Rapamycin. Modified by [68].

healthy vessels, the endothelial surface layer (ESL) is essential to maintain the antithrombotic and anti-inflammatory properties of the endothelium via inducing endothelial nitric oxide synthase (eNOS) and nitric oxide (NO) release [74]. A poor endothelialisation promotes platelet aggregation, thrombus formation, and finally stent-thrombosis.

Arterial healing involves regrowth of the denuded endothelium from the remaining endothelial cells and uninjured segments next to the stent. Circulating endothelial progenitor cells might also contribute to reendothelialisation after vessel injury [71, 75]. Furthermore, recent studies have demonstrated that proliferation, viability, and function of endothelial cells are dependent on the polymer surface [71, 76–80]. Therefore, the process of reendothelialisation on the surface material requires sufficient biocompatible qualities of the polymer surface underneath. The completion of endothelialisation on a BMS surface takes 3–6 months and more than 2 years in DES [2]. However, the regenerated endothelium does not completely mature and therefore remains incompetent in terms of barrier integrity and functionality [76, 81, 82].

It is well established that the subendothelial layers become stiff in cardiovascular disease [83, 84]. Evidence suggests that proper vessel compliance is critical for endothelial function in terms of eNOS expression and NO release [85]. The mechanical changes therefore may lead to dysregulation of the endothelium and may promote endothelial dysfunction [86]. Currently, the topographical properties of vascular implants are increasingly recognized as an important cue having an impact on the response of vascular cells in terms of adhesion, proliferation, viability, migration, differentiation, and mechanotransduction [87–89]. Cells attach to the polymer surface via focal adhesions, connecting the cytoskeleton to the polymer surface. The formation of these interfaces can be affected by the mechanical properties of the polymeric surface [90, 91]. Since most polymers, such as PLA [87], are extremely stiff polymers it might be conceivable that this is at least partly accountable for a regenerated but incompetent endothelium. Consequently, combining the biocompatibility of polymers with appropriate mechanical properties will increase their potential for use as implants.

4.3. Blood Cell-Material Interactions. Cell adhesion assays are frequently used to assess monocyte or platelet adhesion on polymeric surfaces [92, 93]. In this context Hezi-Yamit et al. [35] were able to show that polymer hydrophilicity should be considered as a parameter to assess the biocompatibility of polymer surfaces. They report that hydrophobic polymers such as PBMA or SIBS promote adhesion of inflammatory activated monocytes while more hydrophilic polymers (e.g., PC) lead to less proinflammatory responses. Cohen et al. [94] demonstrated differences in monocyte activity on poly(ethylene glycol) hydrogels, poly(dimethyl siloxane), and tissue culture polystyrene in cultures with conditioned medium priming. Khandwekar et al. [95] compared leukocyte adhesion on bare PCL surfaces and modified PCL surfaces. They showed that leukocyte adhesion on bare PCL could even be more reduced when converting to a heparin-modified PCL.

Platelet adhesion and leukocyte rolling on injured endothelium are key events of a process leading to platelet-leukocyte interaction, aggregation, and activation of the coagulation cascade. Leukocyte rolling is mainly mediated by selectins and by integrins such as Mac-1 [96]. It is conceivable that slow rolling supports adhesion strengthening and spreading of polymorphonuclear leukocytes, thus worsening blood cell compatibility. Following monocyte adhesion and transmigration into surrounding tissue, monocytes and monocyte-derived macrophages start to secrete proinflammatory cytokines. These reactions may lead to chronic inflammatory responses. Chronic inflammation has been described as foreign body reaction where monocytes, macrophages, and foreign body giant cells are present at the biomaterial interface for longer than two weeks [97].

Stent deployment induces arterial wall injury with subsequent platelet activation and thrombus formation. The kinetics of platelet adhesion to artificial surfaces have been revealed to be very rapid with initiation of adhesion taking less than 5 seconds on hydrophobic surfaces and less than 30 seconds on hydrophilic surfaces [98]. The degree of arterial injury and the stent material itself also influence these processes. Platelets adhere to polymeric surfaces through interaction with fibrinogen, von Willebrand factor, and fibronectin [98]. Activation of the GPIIb/IIIa receptor on platelets, with subsequent fibrinogen binding, represents the final common pathway of platelet activation and adhesion [99]. The role of fibrinogen in platelet adhesion also accounts for the direct effect of surface hydrophobicity, since fibrinogen is retained to a greater extent by hydrophobic than by hydrophilic surfaces [100, 101]. In addition the GPIIb/IIIa receptor is mainly involved in platelet adhesion which lead to the assumption that antagonists to this receptor bound to the polymeric stent surface are expected to prevent platelet adhesion and thrombus formation [99, 102]. However, the resultant GRII stent (Cook Cardiology, Bloomington, IN) has been withdrawn from the market due to high restenosis rates [99].

5. *In Vitro* Evaluation of Biocompatibility

Before developing the elaborated design for *in vivo* applications, it is of great importance to test various polymer characteristics in detail. Over the past years, a variety of methods have been established to determine biocompatibility of polymer implants.

5.1. Dynamic Testing. Cell interactions with polymers are usually studied using cell culture techniques. *In vitro* evaluation of surface materials by directly seeding ECs and SMCs onto the biopolymers represents a common procedure to assess biocompatibility and cytotoxicity as well as cell morphology [103–105]. In this context, most *in vitro* studies analysing the impact of certain materials on tissue cells involve experiments under static conditions. However, in healthy vessels especially ECs are exposed to the blood stream. This pulsatile, laminar blood flow exerts shear stress on the vascular endothelium, which induces antiapoptotic signals and preserves an anti-inflammatory and nonthrombotic endothelial phenotype compared to ECs cultured under static conditions [106, 107]. Therefore, the application of a cell perfusion system is strongly advisable when studying cell-material interactions *in vitro*. Such cell culture experiments allow for the investigation of specific mechanisms involved in the biologic responses of blood and tissue cells to materials.

5.2. Parallel Plate Flow Chamber. The parallel plate flow chamber (PPFC) is the design most frequently used to study vascular cells under flow conditions. Here, cell culture media is circulated through the chamber at adjustable flow rates creating a defined laminar shear stress. Prior to the flow experiment, the cells of interest need to be seeded on cover slips or polymer surfaces under static cell culture conditions. Additionally, these flow chambers are designed to allow microscopic observations of living cells under perfusion or fixed cells after perfusion. In this context, PPFCs are suitable to measure the kinetics of cell attachment, detachment, and rolling on surfaces under flow conditions. Hence, a broad range of studies refers to the adhesion of leukocytes and platelets on ECs [108, 109]. Recently, our group published studies which assessed a range of endothelial parameters in interaction with different stent materials using an *in vitro* perfusion system [79, 80]. However, these kinds of experiments are limited by the rectangular geometry of the flow channel and do only allow for the investigation of cell monolayers over several hours.

5.3. Bioreactors. To overcome the limitations of *2D* cell culture models vessel-simulating bioreactors have been developed. Typically, a *3D* bioreactor consists of a graft with an individual culture media reservoir to allow for a transversal gas and media exchange between the graft lumen and an outer chamber volume which simulates the interstitial tissue liquid. A porous graft (e.g., silicone, PTFE) is seeded with cells and the construct is perfused with culture media. This procedure enables *in vitro* cultivation of endothelial cells under fluid flow and can be regarded as a synthetic vessel [110, 111]. Furthermore, a special modification of a standard flow-through cell for tablets has been developed, which is particularly suitable for the evaluation of drug release and distribution from drug-eluting stents [112, 113]. This vessel-simulating flow-through cell was designed in order to overcome the limitations of *in vivo* examination of drug release from stents and distribution in the arterial wall [114] and improve the accuracy of prediction [112]. The system includes a hydrogel compartment forming a flow channel which represents the vessel wall. DES can be implanted into the flow channel which is then perfused at flow rates corresponding to the physiological blood flow in coronary arteries [113].

6. Biocompatibility Tests

6.1. Endothelial Cells. For most applications the adhesion and growth of vascular cells as well as the potential cytotoxicity of biomaterials are important aspects of biocompatibility. A simple method to quantify adherent cells is the direct incubation of the target cells on a surface of interest. However, our recent work [79, 80] underlines that common methods

to assess cell adhesion, proliferation, and cytotoxicity under static cell culture conditions alone are not always sufficient to investigate the biocompatibility of polymer surfaces. So far, particularly PLLA-based polymers and copolymers have proven to possess excellent biocompatibility in *in vitro* studies not only regarding cell growth and viability but also more importantly endothelial function. *In vitro*, ECs grown on PLLA-based polymers show an enhanced expression of eNOS and platelet endothelial cell adhesion molecule-1 (PECAM-1) under arterial flow conditions [79, 80], two factors which are both related to an improved vascular healing [115, 116]. In healthy vessels, the endothelial surface layer (ESL) of ECs functions as a vasculoprotective barrier which is related to eNOS expression and endothelium-dependent NO-release [74]. We report that ECs cultured on PLLA-based surfaces exhibit a well-marked ESL under arterial flow conditions, while biopolymers such as P(3HB) and P(4HB) exert a great impact on ESL width and therefore attenuate endothelial barrier function, which is accompanied by low eNOS and PECAM-1 expression [79, 80].

Only recently, atomic force microscopy (AFM) techniques have emerged to be suitable for probing micro- and nanomechanical properties in terms of cell elasticity and stiffness. AFM-techniques can be utilized to measure the elastic properties of cells that are attached to different surfaces [87, 117, 118].

6.2. Blood Cells. Injury induced during polymer implantation initiates an inflammatory response resulting in adhesion and extravasation of polymorphonuclear leukocytes to the implant site. Leukocyte rolling on the inner layer of the vessel wall is one of the first steps in this complex process. Therefore, it might be meaningful to measure leukocyte rolling velocity on polymer surfaces to estimate adherence of these blood cells to the material. In this regard, Goldmann [119] and Lawrence [120] introduced the definition of critical velocity implying the assumption that interaction between adhesion molecules takes place when a leukocyte moves with 70% of the velocity of a freely moving leukocyte with the same distance from the vessel wall. Despite the fact that leukocyte-platelet interactions are involved in tissue inflammation and thrombosis, especially after deposition of an implant, there is still little research experience when it comes to evaluating leukocyte-platelet interactions with surface materials. Further, CD11b/CD18 (Mac-1) represents a receptor for leukocyte activation as it supports interactions with platelets and ECs, respectively. Chang and Gorbet [121] showed that CD11b and leukocyte-platelet aggregates were upregulated upon contact with metal surfaces at pathological shear stress conditions.

Platelet adhesion and aggregation, as a marker for the prothrombotic potential of polymers, can be visualized by SEM imaging [80, 122]. Furthermore, platelet activation may be evaluated by the release of soluble P-selectin and collagen-induced platelet aggregation by the method of Born [123]. A further determinant to assess the activation of platelets upon exposure to polymers is the determination of the surface expression of cell adhesion molecules such as CD42b (GPIb). GPIb belongs to the GPIb-IX-V complex which binds to the von Willebrand factor and facilitates initial platelet adhesion to endothelial cells on sites of vascular injury [96]. Also, the expression of CD62P (P-selectin) can be used as a marker for leukocyte-platelet aggregates, since activated platelets bind to the leukocyte receptor PSGL-1 via P-selectin [96].

7. Summary and Conclusion

The issues regarding the implantation of vascular stents are mainly related to the induction of vascular injury, inflammation, and abnormal hemodynamics leading to the activation and growth of intimal SMCs. Further, incomplete reendothelialisation may raise the risk of in-stent restenosis and acute and late stent-thrombosis. The regenerated endothelium in stented segments is immature as demonstrated by poorly formed cell-cell contacts and reduced expression of PECAM-1 and eNOS. Thanks to their technical suitability and excellent biocompatibility, PLA-based polymers represent a promising class of materials for the development of fully resorbable stents. The polymer can thus perform a temporary mechanical function before degradation.

Biocompatibility is an important property of a polymer used for stent coatings or scaffolds. To date, biomaterials that have proven to be nontoxic and able to support cell growth and viability are generally considered biocompatible. However, the concept of biocompatibility for polymeric coatings and scaffolds has evolved due to multiple *in vitro* studies and the availability of clinical data. Mechanical properties as well as material hydrophilicity, blood cell activation, and endothelial cell function play a central role in the evaluation of stent polymers. The presence of a confluent and functional endothelium on the luminal surface of cardiovascular stents has been considered as an ideal approach to encounter in-stent restenosis and stent-thrombosis. Hence, it is important for cardiovascular stent materials to promote antithrombotic and anti-inflammatory properties and to accelerate endothelial growth and regeneration. Correlating these problems in biocompatibility to material properties is still insufficient. Therefore, the future tasks for the development of biomaterials intended for medical applications is not only to adapt stent designs and biomaterials to physiological needs but also to improve and develop *in vitro* methods for their adequate evaluation.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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