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Protein adsorption capability on polyurethane and modified-polyurethane membrane for periodontal guided tissue regeneration applications

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ABSTRACT

Periodontal disease if left untreated can result in creation of defects within the alveolar ridge. Barrier membranes are frequently used with or without bone replacement graft materials for achieving periodontal guided tissue regeneration (GTR). Surface properties of barrier membranes play a vital role in their functionality and clinical success. In this study polyetherurethane (PEU) membranes were synthesized by using 4,4′-methylene-diphenyl diisocyanate (MDI), polytetramethylene oxide (PTMO) and 1,4-butane diol (BDO) as a chain extender via solution polymerization. Hydroxyl terminated polydimethylsiloxane (PDMS) due to having inherent surface orientation towards air was used for surface modification of PEU on one side of the membranes. This resulting membranes had one surface being PEU and the other being PDMS coated PEU. The prepared membranes were treated with solutions of bovine serum albumin (BSA) in de-ionized water at 37 °C at a pH of 7.2. The surface protein adsorptive potential of PEU membranes was observed using Attenuated Total Reflectance Fourier Transform Infrared Spectroscopy (ATR-FTIR), Raman spectroscopy and Confocal Raman spectroscopy. The contact angle measurement, tensile strength and modulus of prepared membranes were also evaluated. PEU membrane (89.86 ± 1.62°) exhibited less hydrophobic behavior than PEU-PDMS (105.87 ± 3.16°). The ultimate tensile strength and elastic modulus of PEU (27 ± 1 MPa and 14 ± 2 MPa) and PEU-PDMS (8 ± 1 MPa and 26 ± 1 MPa) membranes was in required range. The spectral analysis revealed adsorption of BSA proteins on the surface of non PDMS coated PEU surface. The PDMS modified PEU membranes demonstrated a lack of BSA adsorption. The non PDMS coated side of the membrane which adsorbs proteins could potentially be used facing towards the defect attracting growth factors for periodontal tissue regeneration. Whereas, the PDMS coated side could serve as an occlusive barrier for preventing gingival epithelial cells from proliferating and migrating into the defect space by facing the soft tissue flaps. This study demonstrates the potential of a dual natured PEU barrier membrane for use in periodontal tissue engineering applications and further investigations are required.

1. Introduction

Periodontal disease results in creation of defects which if left untreated can lead to tooth and bone loss in the affected region. Recent advances in biomaterials research and new and improved surgical techniques have resulted in an ever increasing use of dental implants. The long-term success of dental implants is dependent upon the degree of osseointegration in healthy and sufficient bone [1–3]. Bone volume is often reduced due to extended time after tooth loss before implant placement [3,4]. The loss of bone in vertical and horizontal dimensions leads to surgical and anatomical limitations [3]. Various surgical techniques and biomaterials are frequently utilized for the augmentation of deficient ridges prior to placement of dental implants [5–7]. Such regenerative surgical treatments can include the utilization of barrier membranes [8].

The greatest challenge in periodontal tissue engineering is preventing gingival epithelial cell migration into the defect space and also the avoidance of adhesions forming between the barrier membrane and the regenerating tissues [5,9]. Certain cell populations residing in

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periodontal tissues have the potential to reverse periodontal destruction by creating new cementum, alveolar bone, and the PDL, provided they have the opportunity to populate the periodontal wound or defect [10,11]. Guided tissue regeneration (GTR) is a surgical technique that uses a barrier membrane to provide mechanical support [12] interfacing with the gingival connective tissue/epithelium on one side and PDL/alveolar bone tissues on the other side [13]. This membrane is expected to maintain space for clot stabilization and to promote periodontal tissue regeneration, while preventing postsurgical epithelial cell migration to the wound site [5].

Knowledge of the physical and mechanical properties of the periodontal ligament would be useful to help elucidate the role of the ligament in absorbing occlusal force [14]. Tooth movement under external forces shows nonlinear and time-dependent material behavior [15]. In GTR the mechanical properties of the membranes are of the utmost importance for the clinical success of the therapy. It is extremely important to know that an "ideal" periodontal membrane should balance two important materials properties (i.e. stiffness and elasticity) to sustain mechanical loading without membrane collapse and good manageability, respectively. The mechanical behavior in the wet state is important in predicting the mechanical properties of the membrane in vivo [16]. Previously, mechanical properties of synthetic periodontal membrane have been studied in both dry and wet conditions [12,17–19].

Various barrier membranes have been developed and tested for use in large defects with or without bone replacement graft materials to allow for migration of osteoblasts and ingrowth of blood vessels from adjacent osteogenic tissues (Table 1) [8,20]. Polyetherurethanes (PEUs) and PEU based composites are one of the commonly employed biomaterials for various biomedical applications [21–23] including ligament and meniscus reconstruction [24], blood-contacting materials [25], infusion pumps [26], heart valves [27], insulators for pacemaker leads [28] nerve guidance channels [29] and dental application [30,31]. The success of PEUs in medical devices over several decades gives a strong inclination towards investigating them as barrier membranes for periodontal GTR therapy.

Table 1
List of some commonly used barrier membranes for periodontal augmentation and regeneration.

Resorbability	Barrier membrane	Composition
1. Non-resorbable	Gore-Tex®	Expanded-polytetrafluoroethylene (ePTFE)
	Cytoplast® TXT-200	High-density PTFE (dPTFE)
	Cytoplast® Ti-250	Titanium-reinforced high-density PTFE
2. Resorbable - Natural	Alloderm®	Collagen Type-I derived from cadaveric human skin
	Bio-Gide®	Collagen derived from porcine skin (Type I & III)
	BioMend Extend®	Collagen Type-I derived from bovine tendon
	Paroguide®	Collagen Type I enriched with chondroitin-sulphate
	Avitene®	Microfibrillar hemostatic collagen Type-I derived from bovine corium
	Collistat®	Hemostatic collagen Type-I material
	Collagen membrane (modified)	Collagen Type-I cross-linked by diphenylphosphorylazide
	Cytoplast RTM®	Collagen Type-I derived from bovine tendon
3. Resorbable-Synthetic	Resolut LT®	Poly-DL-lactic/co glycolic acid
	Vicryl Penodontal Mesh®	Polyglactin 910
		Polyglycolide polylactide (9:1. w/w)
	Atrisorb®	Double-layered poly-DL-lactide and solvent (*N*-methyl-2- pyrrolidone)
	Guidor ®	Three layered polylactic acid and a citric acid ester acetyl tributylcitrate
	Epi-Guide®	D, D-L, L polylactic acid
	Polyurethane based barrier membrane	Polyetherurethane (–NH–CO–O–)
	Mempol®	Polydioxanon (PDS)

Protein adsorption occurs immediately on the biomaterial membrane surface as soon as it is implanted and comes in contact with blood [32]. The adsorbed proteins on the surface induce biological responses such as platelet accumulation or bone morphogenetic proteins (BMPs) migration [32]. Studying protein adsorption onto PEU membrane surface is of great importance in order to determine whether they can be used effectively for GTR applications. The adhesion of proteins to a surface is a time-dependent process that can involve relatively large energy scales in addition to dynamic conformational changes and reorientation following contact with the surface [33–35]. Surface chemistry influences the time dependent conformational changes in adsorbed proteins and mediate adsorption kinetics and binding strengths as well as subsequent protein activity [36]. The objective of our study was to prepare PEU barrier membranes with two differing surfaces via solution polymerization and characterization of their response with regards to protein adsorption.

2. Materials and methodology

2.1. Materials

All materials including, polytetramethylene oxide (PTMO) (Mw 2000), 4,4′-methylene-diphenyl diisocyanate (MDI), butane diol (1,4 BD), polydimethylsiloxane (PDMS, Mw 2000), calcium chloride, bovine serum albumin (BSA) (minimum purity 96% by electrophoresis), *N,N*, dimethyl formamide >99.8%, (DMF) and tetrahydrofuran >99% (THF) were purchased from Sigma-Aldrich Chemical Company, UK. All chemical reagents were used as received except PTMO which was purchased from Sigma Aldrich, UK dehydrated for 48 h at 80 °C in vacuum oven (10 mm Hg) before use.

2.2. Synthesis of PEU and PDMS modified PEU polymers

PEU membranes were synthesized with the ratio between reactants used was 1:2.16:1.06 (PTMO: MDI: 1.4 BD). 19.5 g of PTMO were mixed with 20 mL mixture of THF and DMF solvents (1:1) at 50 °C and left to stir for 60 min. Afterwards 5.5 g of MDI in 40 mL of THF and DMF solvents (1:1) was added drop wise. 60 min after adding MDI, the viscosity of the solution increased and 96 mg of chain extender 1,4 BD in 5 mL DMF solvent was added. Reaction proceeded overnight at 50 °C for 21 h with calcium chloride as hygroscopic material in the drying tube. Upon completion of the reaction the PEU polymer was isolated, dried in vacuum (10 mm Hg) at 80 °C for 24 h and stored. The PDMS modified PEU membranes were prepared as it was described previously by Rochery et al. [37].

2.3. Preparation of membranes

Synthesized PEU and PDMS modified PEU polymers were dissolved in THF solvent. 8 g polymer was dissolved in 200 mL solvent with magnetic stirring to make the polymer solution. After complete dissolution of the polymer into the solvent, the solution was cast as membranes in glass and quartz slides using micropipettes and left to dry for 48 h under cover. The dried membranes were peeled from the glass slides by immersing them in ice water, cut into 4cm x 8cm strips and stored between absorbent papers and marked. The membranes cast on quartz slides were not peeled as they were used for Raman spectroscopic characterizations. The membranes produced were PEU only and the PDMS modified PEU membranes that had one modified side due to surface orientation of PDMS and the other side just PEU.

2.4. BSA solution preparation and sample treatment

To determine whether the PEU membrane surfaces (unmodified and PDMS modified) have protein adsorptive ability, the membranes were subjected to a protein solution treatment [43]. 30 mg/mL of BSA