FEASIBILITY OF CARBONIC ANHYDRASE FACILITATED CO_2 REMOVAL FOR EXTRACORPOREAL LUNG SUPPORT SYSTEMS USING DOPAMINE AND POLYETHYLENEIMINE SURFACE FUNCTIONALIZATION

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Introduction

Extracorporeal membrane oxygenation (ECMO) and extracorporeal CO2 removal ($ECCO_2R$) offer potential solutions for respiratory failure by providing temporary lung support, using hollow fiber-based oxygenators. CO_2 is mainly transported in the body in form of bicarbonate (HCO_3^-). The enzyme carbonic anhydrase (CA) is naturally localized in the erythrocytes and catalyzes the conversion of bicarbonate (HCO_3^-) into CO_2 and vice versa. The covalent immobilization of CA on the surface of the hollow fiber membrane and the resulting direct conversion of HCO_3^- to CO_2 at the membrane interface facilitates gas exchange [1]. In contrast to previous studies with the same aim, the method employed in this work utilizes an amino group-rich surface, which is commonly used in carbon capture technology, for subsequent enzyme crosslinking. This approach was selected to transfer existing knowledge from another field and further profit from the potential hemocompatibility benefits of the coating.

Methods

Since enzyme cross-linking is not possible without prior surface functionalization, the membrane was modified using a dopamine (DA) and polyethyleneimine (PEI) coating, allowing the enzyme to be cross-linked. Carbonic anhydrase cross-linking was performed using glutaraldehyde. Membranes with different coating compositions were characterized using the spectrophotometrically measurement of esterase enzyme activity. Subsequent testing of the CO_2 removal capacity was conducted using PBS buffer as testing liquid. The test setup allowed low cost and continuous testing of different membranes in mini membrane modules (fiber number=90) under constant conditions. Hemocompatibility testing was performed in a static system using platelet-rich plasma (PRP) from abattoir pig blood anticoagulated with sodium citrate. Fixed membrane samples were analyzed using field emission scanning electron microscopy.

Results

We found a PEI/DA coating composition of 10 mg/mL DA and 10 mg/mL PEI with a coating/cross-linking time of 7 h/32 h is a reproducible and scalable method for production of biocatalytic active membranes with high enzyme activity values. Coatings using 600 Da and 800 Da PEI molecular weight showed comparable CO_2 removal capacities. Values between 30 % and 60 % were achieved for membrane improvement by the introduction of CA compared to coated membranes without CA. It has been demonstrated that within a storage period of four weeks at a temperature of 4 °C, the CO_2 removal capacities and thus the enzyme activity remain constant. Hemocompatibility test showed uncoated membranes exhibited disc-shaped platelet structures, while those with 600 Da PEI/DA showed less adhesion and rougher surfaces with CA cross-linking.

Discussion

Our data shows that a PEI/DA coating composition of 10/10 with 7 h/32 h coating/cross-linking is a feasible method for producing biocatalytic membranes, prioritizing reproducibility over higher enzyme activities. Despite variations in coating quality and flow dynamics, longer coating times prove to be decisive for effective CO_2 removal efficiency. The hydrophilized membrane showed biocompatible rough surface with less protein and platelet adhesions and is a promising solution for further surface modification research. The increased diffusion barrier of the coating is effectively compensated by the crosslinking of CA. Yet, an optimization of both coating and enzyme immobilization promises distinct potential for even better gas transfer.

References

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