IMMobilization of Human Neutrophil Elastase Inhibitors into Polysulfone Dialysis Membranes – a preliminary study

Rute Rebelo (rulesarabrandao@gmail.com), Faculty of Sciences, University of Porto, Portugal
Kristína Morgosová (morgosova.k@gmail.com), Faculty of Pharmacy, Hradec Králové, Czech Republic
Célia Amorim (camorim@ff.up.pt), Alberto Araújo (anaraujo@ff.up.pt), Maria Conceição Montenegro (mbranco@ff.up.pt), Susana Rocha (srocha@ff.up.pt), LAQV/REQUIMTE, Faculty of Pharmacy, University of Porto, Portugal
Rui Moreira (rmoreira@ff.ulisboa.pt), J. Med. Ulisboa, Faculty of Pharmacy, University of Lisbon, Portugal
Alice Santos Silva (assilva@ff.up.pt), UCIBIO/REQUIMTE, Faculty of Pharmacy, University of Porto, Portugal

INTRODUCTION

The contact of blood with dialysis membranes during hemodialysis (HD) therapy leads to neutrophil activation, with release of human neutrophil elastase (HNE), enhancing inflammation, a known risk factor for cardiovascular events. They are the main cause of mortality and morbidity in End-Stage Renal Disease patients. The specific modification of polysulfone (PSF) HD membranes might reduce inflammation.

AIM

This study aimed to dope PSF membranes with HNE inhibitors (HNEIs) and assess their bioactivity.

RESULTS

![Figure 1. Bioactivity of human neutrophil elastase inhibitors Sivelestat (A) and D4L-2 (B) in solution.](image)

![Figure 2. Bioactivity of human neutrophil elastase inhibitor modified polysulfone membranes.](image)

METHODOLOGY

Sivelestat (SIV), from Abcam, and an in house synthesized 4-oxo-5-lactam based compound (D4L-2) [1] were used as HNEIs. The PSF membranes were developed incorporating the HNEIs by adsorption according to [2]. In 3 independent assays, triplicates of PSF membrane circles (Ø = 0.6 cm) were incubated with HNEIs vehicle (2.5% DMSO) or with 10 - 2000 nM SIV or D4L-2. The IC50 of both HNEIs in solution was evaluated by a carrying out a HNE activity assay [1]. The same assay was used to determine the bioactivity of the modified PSF membranes. Statistical analysis was performed using GraphPad Prism 8 software. Accordingly, Student’s t test and One-Way Anova with Bonferroni Post – Hoc tests were used to compare groups.

CONCLUSION

- The successful adsorption of HNEIs into PSF membranes was achieved.
- HNE inhibition ability was directly dependent on the concentration utilized.
- The bioactivity of SIV and D4L-2 when immobilized into PSF membranes followed their inhibitory capacity in solution.

References


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