Stable Carbonic Anhydrase Hollow Fiber Membrane Coating Used in Conjunction with Dilute SO_2 Acidic Sweep Gas Increases Efficiency in Low Flow CO_2 Removal Devices

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Statement of Purpose: Current low-flow CO_2 removal ($ECCO_2R$) devices are limited in efficiency by the diffusional gradient across the gas exchange membranes. Since 90% of CO_2 in blood is in the form of bicarbonate (HCO_3^-), we previously reported the development of a Carbonic Anhydrase (CA) Hollow Fiber Membrane (HFM) that converts HCO_3^- to CO_2 directly at the HFM surface increasing CO_2 removal efficiency by 36% [(1)]. Subsequent work demonstrated creating an acidic microenvironment surrounding the HFM surface through infusion of dilute SO_2 sweep gas can further increase removal efficiency when used in combination with the CA coating, though the increase is short-lived due to coating solubility in acid. In this study we developed a stable CA-HFM coating and characterized its gas exchange efficiency in combination with dilute SO_2 acidic sweep gas.

Methods: CA was immobilized onto plasma aminated Polypropylene (PP from ALung Technologies®) HFMs with a low amine density (0.3 nmol/cm^2) and Polymethylpentene (PMP) HFMs with a high amine density (5.6 nmol/cm^2), through the tethering molecule glutaraldehyde activated chitosan with reducing agent sodium cyanoborohydride. Immobilized CA activity was measured with the esterase activity assay. Unmodified and CA-HFMs were potted in model $ECCO_2R$ devices and assessed for CO_2 removal (CO_2R) efficiency in a single pass gas exchange loop with a CO_2 inlet of 50mmHg under steady blood flow with oxygen and SO_2 acidic sweep gas. To assess CA-HFM stability, activity was measured before and after exposure to 1% SO_2 sweep gas.

Results: The esterase activity of CA-HFMs immobilized via chitosan was 11.9 U on low amine density PP and 9.3 U on high amine density PMP. After exposure to 1% SO_2 acidic sweep gas, CA-PP activity decreased by 84% to 2.0 U, while CA-PMP activity increased by 7% to 9.95 U. Retention of activity in the PMP CA-HFMs suggests that the presence of the reducing agent and the increased amination of the PMP HFMs are required to stabilize the CA-HFM coating. Using pure O_2 sweep gas, PMP CA-HFMs increased CO_2R by 31% (258 mL/min/m^2) compared to unmodified-HFMs (197 mL/min/m^2). Using 2.2% SO_2 sweep gas increased unmodified-HFM CO_2R by 17% (230 mL/min/m^2) compared to pure oxygen sweep gas control-HFMs, and decreased blood pH by 0.06 units. When employing both PMP CA-HFMs and 2.2% SO_2 sweep gas, CO_2 removal increased by 109% (411 mL/min/m^2) while blood pH decreased by 0.087 units. These findings suggest that dilute acidic sweep gas in combination with CA-HFMs significantly increases CO_2 removal and has minimal effect on blood pH.

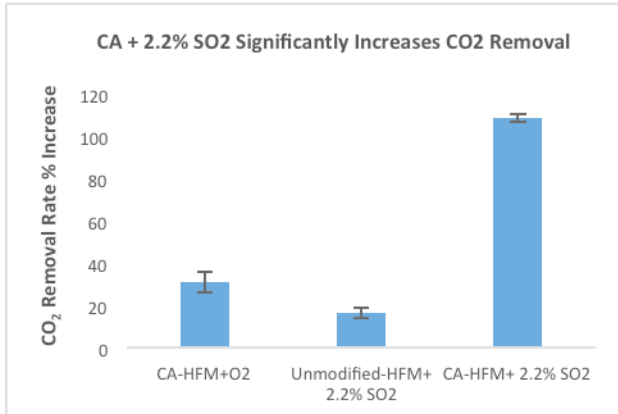

Figure 1. Acidic sweep gas used in combination with CA-HFMs significantly increases CO_2 removal rates in model $ECCO_2R$ devices

Conclusions: SO_2 sweep gas and CA-HFMs increase CO_2 removal in model $ECCO_2R$ devices, lending to the promise of commercial low flow, low surface area and lung preventative (less invasive and critical) ventilation. Further work will investigate the safety of blood sulfites and methods to mitigate toxicity.

References: [1] (Arazawa DT. J Memb Sci. 2012;404-404:25-31.)