Permeability of phospholipid membranes and human red blood cell membranes to hydrogen peroxide

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Hydrogen peroxide (H_2O_2) is an oxygen-derived oxidant involved in multiple redox processes in the cell, ranging from physiological signaling pathways to oxidative damage reactions when it is found at higher concentrations. In the vascular system, H_2O_2 is metabolized mainly by red blood cells (RBC) due to their very efficient antioxidant systems and high membrane permeability. However, the information regarding H_2O_2 transport in the human RBC membrane is limited, as neither the exact value of the permeability coefficient (Pm) nor the permeation mechanisms are known. To explore whether H_2O_2 permeates through the lipid fraction or protein channels, we studied H2O2 solubility in organic solvents and its permeability in lipid membranes, in order to compare with the RBC membrane. Through measurements of partition constants, we found that H_2O_2 is 14 and 122000 times less soluble in octanol and hexadecane than in water, anticipating a large thermodynamic barrier to H_2O_2 permeation by lipid membranes. The Pm in phospholipid membranes of different compositions, determined using the catalase-latency method, varied from 4×10^{-4} to 5×10^{-3} cm s^{-1}, at 37°C. On the other hand, in human RBC we determined a Pm of 1.6×10-3 cm s-1. After obtaining these results, we evaluated the potential role of aquaporins as H_2O_2 transporters by checking the effect of aquaporin inhibitors in H_2O_2 consumption by RBC, and also by studying H_2O_2 permeability in RBC devoid of either aquaporin 1 or aquaporin 3. Surprisingly, we could not detect any differences in H_2O_2 permeability in any case. Altogether, these results provide new information on lipid membrane permeability to H_2O_2 and a new value for the Pm in human RBC, which was previously unknown. Additionally, they indicate that H_2O_2 is not transported by aquaporins in human RBC membranes, suggesting simple diffusion or a still unidentified membrane protein as a more probable pathway.