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We investigated melatonin effects on red blood cell (RBC) metabolism in an H_2O_2-induced oxidative stress model. The study was carried out on three healthy adult donors by incubating RBCs in their own plasma at 37 °C, or under the influence of 1 mM H_2O_2 and 100 μM melatonin at different times (0, 1, 3 and 6 hours). We assessed incubation period, treatment, as well as interaction effects on oxidative stress markers, and adenine nucleotide and oxypurine levels. We found positive correlations between incubation times and hemolysis degree for each treatment. However, we did not observe any influence on RBC osmotic fragility and antioxidants tested. On the other hand, we found an increasing effect of incubation period on lipid peroxidation levels. Furthermore, oxidation induction regardless time more than doubled protein carbonyl groups in plasma but melatonin neutralized this H_2O_2 effect. Unexpectedly, we did not find any relevant alterations on energy expenditure or adenylate nucleotide metabolism regarding to treatments or incubation periods investigated. The results obtained for markers of lipid and protein injury validated the auto incubation model, as well indicated a protection effect of melatonin. This effect along with its exceptional multiplicity actions reinforced the hypothesis of pharmacological use of melatonin in oxidative blood disorders.

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P-036

Effect of urea in the reaction of nucleosides with hypobromous acid

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Keywords: Hypobromous acid; HOBr; urea; nucleoside

Hypobromous acid (HOBr) is generated by eosinophil peroxidase or myeloperoxidase using hydrogen peroxide, chloride, and bromide in the host defense system of humans, protecting against invading bacteria. Generally, HOBr can react with amines (R-NH2), resulting in bromamines (R-NHBr). Urea (CO(NH2)2) is a ubiquitous molecule with high concentrations (5 mM in plasma, 285 mM in urine) in humans. However, there is little information on the effect of urea in the reaction of HOBr. In the present study, we examined the reaction of nucleosides with HOBr in the absence and presence of urea using HPLC. Without urea, nucleosides immediately reacted with HOBr in the order of dG > dC > dT > dA. In the presence of 100 mM urea, the reaction was slow and carried out for several hours. 8-Br-dG, a reaction product from dG, increased by the addition of urea. Whereas, 100 mM lysine suppressed the reaction almost perfectly. The results suggest that urea reacts with HOBr resulting in urea bromamine, and which reacts with nucleosides slowly. Urea may have an importance for mutagenesis caused by the reaction of HOBr.

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P-037

Effect of Neutral Sphingomyelinase Inhibition on ER Stress and Apoptosis in Liver Ischemia–Reperfusion Injury

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Keywords: Liver; ischemia-reperfusion injury; ceramide; neutral sphingomyelinase

This study determined the role of selective neutral sphingomyelinase (N-SMase) inhibition on endoplasmic reticulum (ER) stress and apoptotic markers in a rat model of liver ischemia reperfusion (IR) injury. Liver IR injury was created by clamping blood vessels supplying the median and left lateral hepatic lobes for 60 min, followed by 60 min reperfusion. Sphingmyelin and ceramide levels in liver tissue were determined by tandem mass spectrometry. Spingomyelin levels were significantly increased in all IR groups compared to controls. Treatment with a specific N-SMase inhibitor significantly decreased all measured ceramides in IR injury. A significant increase was observed in ER stress markers C/EBP-homologous protein (CHOP) and 78 kDa glucose-regulated protein (GRP78) in IR injury, which was not significantly altered by N-SMase inhibition. Inhibition of N-SMase caused a significant reduction in phospho-NF-kB levels, hepatic TUNEL staining, cytosolic cytochrome c and caspase-3, -8 and -9 activities which were significantly increased in IR injury. Data herein confirm the role of ceramide in increased apoptotic cell death and highlight the protective effect of N-SMase inhibition in down-regulation of apoptotic stimuli responses occurring in hepatic IR injury.

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P-038

Role of the myeloperoxidase oxidant hypothiocyanous acid (HOSCN) in the adaption of cells to oxidative stress during inflammation

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Keywords: Inflammation; atherosclerosis; myeloperoxidase; protein oxidation; glycolysis

A host of chronic inflammatory diseases are accelerated by the formation of the powerful oxidant hypochlorous acid (HOCl) by myeloperoxidase (MPO). In the presence of thiocyanate (SCN^-), the production of HOCl by MPO is decreased in favour of the formation of a milder oxidant, hypothiocyanous acid (HOSCN). Unlike HOCl, HOSCN reacts selectively with thiols to result in reversible