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Ascorbic acid treatment leads to a decrease in NO levels in UV-irradiated human microvascular endothelial cells (HMEC-1)

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In several cell types UV light induces the synthesis of inducible nitric oxide synthase (iNOS) by activating a couple of transcription factors, first of all AP-1 and NF-κB. In the presence of molecular oxygen and other cofactors, iNOS converts the proteinogenic amino acid L-arginine to L-citrulline. A further product of this reaction is the free radical nitric oxide (NO), which reacts with reactive oxygen species (ROS) to yield reactive nitrogen species (RNS). RNS trigger nitrosative damage on proteins, lipids and even DNA and thus can lead to cellular dysfunction and death. Ascorbic acid (AA), as the main water-soluble antioxidant vitamin can limit the formation of ROS. Thus, also a subsequent reduced creation of RNS and a decrease of ROS-iNOS-mediated NO production should be the consequence. Furthermore the NO concentration should be reduced by a direct interaction of the free radical NO with AA as a scavenger.

Human microvascular endothelial cells (HMEC-1) were used as a model system for simulating UV-induced oxidative stress, e.g. like sunburn in the skin. Cells were supplemented with AA in two concentrations (50 and 100 μM) and subsequently irradiated with UV-A (25 J/cm^2) to investigate if this preventive supplementation can attenuate the increased NO levels in only UV-irradiated cells. NO concentration was visualized using the fluorescent probe DAF-2 DA on a life cell imaging system. Quantification was done using TILLVision software.

While NO concentrations – as expected – increased in UV-irradiated cells, the preventive supplementation with AA dose-dependently attenuated this increase. In addition, AA supplementation without subsequent irradiation led to decreased NO levels in the cells, indicating a direct interaction independent from ROS.

In conclusion, an adequate supply of ascorbic acid seems to protect endothelial cells against oxidative and nitrosative stress and its consequences at least in vitro. Maybe, the known effects of high-dosis AA infusion in burn patients to reduce water loss can be explained by comparable pathways.

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QSAR studies on di(hetero)arylamines derivatives of benzo(b)thiophenes as free radical scavengers

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Synthetic antioxidants are widely used in food industry, but because of toxic and carcinogenic effects revealed by some compounds such as BHA and BHT, their use is being restricted. The pursuit for novel compounds with antioxidant properties gained higher significance, since these compounds may contribute for the prevention of diseases in which free radicals are implicated. As reported in our previous papers, different series of novel di(hetero)arylamines derivatives of benzo(b)thiophenes were synthesized and studied as free radical scavengers [1,2]. In this study, a quantitative structure activity relationship (QSAR) model was developed to guide the synthesis of new potential radical scavengers. To increase the predictability of the QSAR model, DDPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging activity of 14 di(hetero)arylaminobenzo(b)thiophenes was assayed, and the results were pooled together with the DPPH radical activity results of 12 di(hetero)arylaminobenzo(b)thiophenes already reported by us. The 26 compounds used were divided in training set (18 compounds) and validation set (8 compounds). The antioxidant activity was correlated with 4 molecular descriptors calculated using DRAGON software tool, and the QSAR model was built using the partial least squares projection of latent structures (PLS) method. This QSAR model ($n = 18$; $r^2 = 0.958$; $q2 = 0.919$; $r2pred = 0.943$) properly predicted pEC50 values for the validation set of benzo(b)thiophene derivatives, and proved to be a useful tool for the screening of new potentially better di(hetero)arylaminobenzo(b)thiophenes free radical scavengers.

Research Project POCI/QUI/59407/2004 (FCT-Portugal).

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QSAR studies on di(hetero)arylamines derivatives of benzo(b)thiophenes as free radical scavengers

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