Study of the antioxidant action of morphine on the peroxidase cycle of MPO and HRP

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Inflammation is a complex physiological phenomenon involving chemical and enzymatic mechanisms. During this event, Polymorphonuclear Neutrophil Leukocytes (PMNs) play an important role by producing reactive oxygen species (ROS) and releasing myeloperoxidase (MPO), an oxidant enzyme. The latter one has two main activities : chlorination and peroxidase, which participate in the host defence against micro-organisms like bacteria and virus. However, an excessive amount of ROS and MPO released in the extracellular medium can cause damages on the surrounding tissues. A possible pathway to control this excessive inflammation is to regulate the neutrophil functions including MPO activity [4] [6] .

Besides its analgesic action, morphine presents antioxidant properties and has been shown to inhibit the ROS production and the PMN degranulation [1] [2] [3] [5]. However, there are few data about the potential effect of morphine on MPO activity

The aim of the study was to investigate the potential antioxidant activity of morphine on MPO activity in comparison to another peroxidase : Horseradish Peroxidase (HRP). Herein, we investigated the action of morphine on the different intermediates of the peroxidase cycle of MPO, using two spectroscopic techniques : EPR and UV-Visible absorption. As HRP belongs to the peroxidases and is characterized by a quite similar peroxidation cycle to MPO, the comparison with results obtained are also presented and can provide additional information on the mechanisms of action of morphine. The results show that morphine acts as a reducing agent in the peroxidase cycle of the two enzymes, like ascorbic acid. Morphine protects both enzymes from the adverse effect of their natural substrate, H_2O_2, which can act as a suicide inactivator at high concentration.

In conclusion, our findings show that morphine inhibits the formation of compound III for both enzymes and accelerates their peroxidase cycle, providing a competitive effet at high concentration for other substrates, like ABTS, having a high oxidant potential when oxidized by the enzymes.

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