

Inhibition of mitochondrial complex i by various non-steroidal anti-inflammatory drugs and its protection by quercetin via a coenzyme Q-like action

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Mitochondrial dysfunction plays a major role in the development of oxidative stress and cytotoxicity induced by non-steroidal anti-inflammatory drugs (NSAIDs). A major objective of the present study was to investigate whether in vitro the NSAIDs, aspirin, indomethacin, diclofenac, piroxicam and ibuprofen, which feature different chemical structures, are able to inhibit mitochondrial complex I. All NSAIDs were effective inhibitors when added both, directly to mitochondria isolated from rat duodenum epithelium (50 μ M) or to Caco-2 cells (250 μ M). In the former system, complex I inhibition was concentration-dependent and susceptible to competition and reversion by the addition of coenzyme Q (32.5-520 μ M). Based on reports suggesting a potential gastro-protective activity of quercetin, the ability of this flavonoid to protect isolated mitochondria against NSAIDs-induced complex I inhibition was evaluated. Low micromolar concentrations of quercetin (1-20 μ M) protected against such inhibiti