

Melatonin inhibits inflammatory response of stimulated intestinal epithelial cells

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Melatonin, oral-used in sleep disorders treatment, is the main secretory product of the pineal gland and in gastrointestinal tract (GIT) in which it has a local physiological poorly characterized role. Intraperitoneally-administered high dose has anti-inflammatory effects in experimental model of Inflammatory Bowel Diseases but the mechanisms is unclarified. Literature data show that melatonin inhibits the activation of neutrophils and monocytes and it is therefore conceivable that it has also inhibitory effect on mucosal inflammatory cell activation.

The aim of this study was to evaluate in an *in vitro* model of inflamed intestinal epithelium the potential protective effects of melatonin.

Differentiated monolayers of intestinal epithelial Caco-2 cells, in which the inflammatory response was induced by interleukin-1 β and interferon- γ , were exposed at concentrations of melatonin in the range from 1 nM to 50 μ M. We also exposed differentiated monolayers to melatonin in presence of luzindole, an antagonist of melatonin membrane receptors, to determine whether or not potential effect of melatonin involve membrane receptors.

Our results clearly show for the first time that melatonin decreased in release and expression some inflammatory mediators, including nitric oxide, interleukin-6, interleukin-8, cyclooxygenase-2, and that the treatment is associated with a reduced activation of the nuclear factor- κ B. Moreover, luzindole did not reverse the melatonin inhibition of stimulated- IL-6 release, indicating that the melatonin protective effect may be membrane receptor-independent.

Our findings suggest that assumption of pharmaceutical preparation of melatonin can also exert beneficial effects to gastrointestinal physiology.