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Antioxidant and antiapoptotic properties of melatonin restore intestinal calcium absorption altered by menadione

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Abstract The intestinal Ca^{2+} absorption is inhibited by menadione (MEN) through oxidative stress and apoptosis. The aim of this study was to elucidate whether the antioxidant and antiapoptotic properties of melatonin (MEL) could protect the gut against the oxidant MEN. For this purpose, 4-week-old chicks were divided into four groups: (1) controls, (2) treated i.p. with MEN (2.5 μmol/kg of b.w.), (3) treated i.p. with MEL (10 mg/kg of b.w.), and (4) treated with 10 mg MEL/kg of b.w after 2.5 μmol MEN/kg of b.w. Oxidative stress was assessed by determination of glutathione (GSH) and protein carbonyl contents as well as antioxidant enzyme activities. Apoptosis was assayed by the TUNEL technique, protein expression, and activity of caspase 3. The data show that MEL restores the intestinal Ca^{2+} absorption altered by MEN. In addition, MEL reversed the effects caused by MEN such as decrease in GSH levels, increase in the carbonyl content, alteration in mitochondrial membrane permeability, and enhancement of superoxide dismutase and catalase activities. Apoptosis triggered by MEN in the intestinal cells was arrested by MEL, as indicated by normalization of the mitochondrial membrane permeability, caspase 3 activity, and DNA fragmentation. In conclusion, MEL reverses the inhibition of intestinal Ca^{2+} absorption produced by MEN counteracting oxidative stress and apoptosis. These findings suggest that MEL could be a potential drug of choice for the reversal of impaired intestinal Ca^{2+} absorption in certain gut disorders that occur with oxidative stress and apoptosis.

Keywords Melatonin · Calcium absorption · Apoptosis · Oxidative stress · Menadione

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Introduction

Melatonin (MEL) is an ubiquitous hormone synthesized and secreted by the pineal gland in a circadian manner [1]. MEL is also synthesized in other extrapineal tissues like retina [2, 3] and gastrointestinal (GI) tract [4], which are related to paracrine and autocrine functions. In the gut, MEL is secreted by the enteroendocrine cells of mucosa with no circadian pattern, but conditioned by food intake, mainly by food enriched in tryptophan [5]. It is interesting to note that in this tissue MEL level is 400 times larger than that in the pineal gland [6], but its physiological significance is not completely understood. It was attributed several effects such as the regulation of food intake and digestion, stimulation of duodenal HCO_3^- secretion, improvement of the immune system in the gut, and prevention of GI mucosa ulcerations [7], among others. Recently, it was found that in the GI tract this hormone has a protective effect in ischemia and reperfusion experiments, stimulating the activity of certain antioxidant enzymes [8]. The protection of MEL appears to be

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