

## SUMMARY

### EFFECTS OF MELATONIN ON MATRIKS METALLOPROTEINASE-9, NITRIC OXIDE AND MALONDIALDEHYDE CONCENTRATIONS IN COLORECTAL CANCERS

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Colorectal cancers (CRC) are among the most common cancer types in today's world. In CRC, local and the metastatic invasions are the factors determining the prognosis of the disease. The most important barrier against invasion is collagen which is degraded mainly by matrix metalloproteinases (MMPs). MMPs play important roles in determining prognosis and new targets of therapy due to their important roles in metastasis. Melatonin, the most potent endogen antioxidant known, has been reported to inhibit tumour progression and to prevent the side effects caused by chemotherapy.

In this study, effects of melatonin on NO, MDA and MMP-9 production by CaCo-2 adenocancer cells were investigated. Different doses of melatonin ( $10^{-11}$ M- $10^{-3}$ M) were applied to CaCo-2 cells for various durations (24-48-72 hours). Control group did not receive any melatonin treatment. Culture medium was analysed for MDA by HPLC method, while NO levels were measured by Griess reaction. MMP-9 levels were measured using ELISA method. Presence of apoptosis was investigated by leukostat staining. Furthermore, biopsy materials from 15 patients with colorectal tumour diagnosis were evaluated for MMP-9 production by immunostaining.

Melatonin did not have any apoptotic effect on CaCo-2 cells. Melatonin treatment at a dose of 1mM caused a decrease in NO levels on the third day of treatment compared to the controls ( $p < 0.05$ ). There was no change in MDA levels by melatonin treatment. At day three, melatonin treatment at doses of 1mM, 0,01mM and 0,01nM caused an increase in MMP-9 levels compared to the control group ( $p < 0,05$ ).

Matrix metalloproteinase-9 levels play an important role in tumour development and metastasis in colorectal cancers. While inhibitory effects of

melatonin on NO production suggest a role for the antioxidant an antitumoral effect, it was surprising to see the effects of it on MMP-9 production. Further studies are needed to investigate the possible dual effects of melatonin on colorectal cancers.

**Keywords:**

Colorectal cancer, malondialdehyde, melatonin, matrix metalloproteinase-9, nitric oxide