

Effect of thymol and its derivatives on colorectal cell lines in *in vitro* system

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The beneficial effects of thymol (TY), a naturally occurring phenol monoterpene of essential oil from thyme, on human health are well known for many years. It is widely used in medical practices, cosmetics, agriculture, and as a natural remedy. However, due to its low solubility in aqueous media, its use e.g. in the food industry is limited. Our study is focused on the synthesis of hydrophilic derivatives of TY (acetic acid thymol ester, thymol β -D-glucoside) while the antioxidative and antiproliferative properties, as well as the effective cellular uptake, will remain intact. The biological activity was studied using colorectal cell models cultured *in vitro* (HT-29 and HCT-116).

The cytotoxic effect of the new derivatives on the colorectal cancer cell lines HT-29 and HCT-116 was assessed via MTT assay. The genotoxic effect was determined by comet assay and micronucleus analysis. ROS production was evaluated using ROS-Glo™ H₂O₂ assay. We confirmed that one of the thymol derivatives (acetic acid thymol ester) has the potential to have a cyto/genotoxic effect on colorectal cancer cells, even at much lower (IC₅₀ ~ 0.08 μ g/ml) concentrations than standard thymol (IC₅₀ ~ 60 μ g/ml) after 24 h of treatment. On the other side, the genotoxic effect of the second studied derivative - thymol β -D-glucoside was observed at a concentration of about 1000 μ g/ml. The antiproliferative effect of studied derivatives of thymol on the colorectal cancer cell lines was found to be both dose and time-dependent at 100 h. Moreover, thymol derivatives treated cells did not show any significantly increased rate of micronuclei formation. New derivatives of thymol significantly increased ROS production too.

The results confirmed that the effect of the derivative on tumor cells depends on its chemical structure, but further detailed research is needed. However, thymol and its derivatives have great potential in the prevention and treatment of colorectal cancer, which remains one of the most common cancers in the world.

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