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Determination of proliferation and genotoxic effect of thymol and acetyl thymol on in vitro intestinal model

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Thymol has a proven bioactive effect on colorectal cancer cells. However, its properties such as low solubility and cell penetration prevent its wider application. Therefore, a new hydrophilic derivative - acetylthymol - was synthesized. In our study, we treated colorectal cancer tumor cell lines (HT-29 and HCT-116) with thymol or acetylthymol on a concentration scale for 24 hours. Proliferation was determined using time-lapse microscopy with an Incucyte® Zoom device. The genotoxic effect of substances was analyzed by the comet assay method.

For a comprehensive assessment of the effect of thymol and the newly synthesized derivative - acetylthymol, the proliferative and genotoxic effect was also determined in 3D culture on colorectal cancer tumor cells. 3D cell culture ensures greater stability, while better representing real cell aggregation, morphology, and mutual cell interaction. As a result, the creation of a more complex microenvironment was ensured, which to a greater extent corresponds to the real conditions in vivo. Spheroids were formed after 5 days using ULA (ultra-low attachment) microplates. Subsequently, the proliferation and genotoxic effects of thymol and acetylthymol were analyzed and compared using the methods mentioned above.

Our results demonstrated that a newly synthesized hydrophilic derivative of thymol with targeted chemical structure modification acts more effectively on both colorectal cancer cell cultures in 3D at much lower concentrations than thymol alone. Comet assays have shown a significant increase in DNA damage for the newly synthesized derivative even at non-cytotoxic concentrations. The HCT-116 cell line showed higher DNA damage values than HT-29. Incucyte Zoom noted the effect of thymol and acetylthymol on the proliferation of both tumor cell lines. The results confirmed our assumption that the newly synthesized hydrophilic derivative can act more effectively than thymol. In the future, we would like to focus on determining the expression of selected proteins using the Western blot method.

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Thymol, acethyltymol, spheroids, proliferation, comet assay.