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**Toxicity of antiproliferative indole-steroid and 5-hydroxyindole in a yeast model system**

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Previously, we reported an indolamine-steroid conjugate to reduce rat C6 glioma proliferation by 52±8% at 10 μM and found a 5-hydroxyindole derivative to rapidly decrease glioma mitochondrial potential [1]. In this

work, we investigated the related indole compounds' toxicity towards *Saccharomyces cerevisiae* yeast, an eukaryote which can be used as a reliable model for some mammalian and cancer metabolic processes [2].

**The purpose of this work** was to investigate the effect of newly synthesized indoles on *S. cerevisiae* growth and redox condition and compare their relative toxicity towards glioma and healthy non-cancer cells.

**Experimental**. 16-(5-cyanoindol-3-yl)methylidene-DHEA (16-CIM-DHEA) was obtained by aldol condensation between DHEA and the corresponding indole aldehyde. 5-hydroxy-3-acetyl-2-methylindole (5-HIET) was obtained by Nenitzescu reaction between the corresponding enamine and 1,4-benzoquinone in nitromethane. Compounds were characterized by ESI-MS and IR spectroscopy. For yeast studies, the *YEp5117α* strain grown on minimum YPD medium was used. Cell growth after 24 hrs incubation was estimated by absorption at 600 nm. Cell viability was determined by tetrazolium dye reduction with detection at 520 nm. ROS generation was detected with the fluorescent probe 2',7'-dichlorodihydrofluorescein diacetate (DCF-DA).

**Results.** At 10 μM, 16-CIM-DHEA and 5-HIET reduce *S. cerevisiae* growth by 36±9% and 27±8% relative to control, respectively. The reference compound indole-3-carbinol did not affect yeast growth significantly. Neither compound decreased cell viability significantly as evidenced by tetrazolium assay. Therefore, a non-necrotic cell death is proposed. In addition, a 30±3% increase in ROS levels was detected for 16-CIM-DHEA.

**Conclusion.** Two compounds, 16-CIM-DHEA and 5-HIET, were found to moderately decrease *S. cerevisiae* yeast growth after 24 hrs without affecting cell viability. An increase in reactive oxygen species was detected in case of 16-CIM-DHEA, which suggests an adverse effect on metabolic function. Further study is underway to investigate the mechanism of the antiproliferative effect in rat C6 glioma and the compounds' side effects in non-cancer cells.

**References**

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