

Chemopreventive Measurements and Oxidative Stress Effects of Terpenoid-rich *Canarium odontophyllum* Miq. Leaf Extract (TRCO) in Ultraviolet B-Induced In-Vitro Skin Carcinogenesis Model

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The most common type of cancer found in the human outer and middle skin layers is keratinocyte carcinoma, often known as non-melanoma skin cancer. Although it can be aggressive, skin cancer is generally not fatal. This study aims to measure the chemopreventive and oxidative stress effects of terpenoid-rich *Canarium odontophyllum* Miq.'s leaf extract (TRCO) in the UVB-induced skin carcinogenesis model. The model involving human keratinocytes (HaCaT) was adapted with optimisations with pretreatment of 500 µg/ml TRCO (TRCO500) & 1000 µg/ml TRCO (TRCO1000). The HaCaT oncogenic transformation model's repetitive UVB exposure resulted in altered cell shape, according to our findings. Pretreatment of TRCO1000 significantly reduced tumour protein p53 (TP53) and marker of proliferation KI-67 (KI67) expression in UVB-induced HaCaT. Treatment with TRCO resulted in an overall reduction in oxidative stress. TRCO pretreatment showed reduced lipid peroxides, LPO and significantly reduced protein carbonyls. In conclusion, the promising results of this chemopreventive study using TRCO on this in-vitro skin carcinogenesis model suggested that it is worthwhile to conduct further isolations and assessments of terpenoids from *C. odontophyllum* Miq. leaf as a possible chemoprevention agent.

Keywords: *Canarium odontophyllum* Miq.; chemoprevention; skin cancer; HaCaT; human keratinocytes; in-vitro; terpenoids.

The most frequently occurring cancer in humans is non-melanoma skin cancer, also known as keratinocyte carcinoma. This cancer usually appears on skin areas exposed to the sun, including the head, neck, shoulders, back, and arms. These cancers have recently increased significantly

worldwide.¹ Solar ultraviolet radiation, especially ultraviolet-B (UVB) is a significant environmental carcinogen and the main culprit for human skin cancer.² UVB exerts more negative impact than beneficial to living organisms. UVB radiation triggers the skin to produce free radicals or reactive