

Natural antioxidants attenuate mycolactone toxicity to RAW 264.7 macrophages

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Abstract

Mycobacterium ulcerans produces a macrolide exotoxin, mycolactone which suppresses immune cells activity, is toxic to most cells and the key virulence factor in the pathogenesis of Buruli ulcer disease. Mycolactone is reported to mediate the production of reactive oxygen species in keratinocytes; cells that play critical role in wound healing. Increased levels of reactive oxygen species have been shown to disrupt the well-ordered process of wound repair; hence, the function of wound-healing cells such as macrophages, keratinocytes, and fibroblast could be impaired in the presence of the reactive oxygen species mediator, mycolactone. To ensure regeneration of tissues in chronic ulcers, with proper and timely healing of the wounds, natural antioxidants that can combat the effects of induced reactive oxygen species in wound-healing cells ought to be investigated. Reactive oxygen species activity was determined in mycolactone-treated RAW 264.7 macrophages and the scavenging ability of the antioxidants (ascorbic acid, gallic acid, and green tea kombucha) against mycolactone-induced reactive oxygen species (superoxide anions) was assessed using fluorescein probe (DCF-DA) and nitroblue tetrazolium dye. Cytotoxicity of the antioxidants, mycolactone, and the protective effect of the antioxidants on the cells upon treatment with mycolactone were determined using the Alamar blue assay. The expression levels of endogenous antioxidant enzyme genes (superoxide dismutase, catalase, and glutathione peroxidase) in response to mycolactone-

mediated reactive oxygen species were determined using RT-qPCR. Mycolactone induced the production of reactive oxygen species in RAW 264.7 macrophages, and the resulting superoxide anions were scavenged by some of the antioxidants. The selected endogenous antioxidant enzyme genes in the macrophages were upregulated in the presence of the antioxidants and mycolactone. The exogenously supplied ascorbic acid and green tea kombucha offered moderate protection to the macrophages against the toxicity of mycolactone. We conclude that the results provide insights into alternate and adjunct therapeutic approaches in Buruli ulcer treatment, which could significantly attenuate the toxicity of the pathogenic factor; mycolactone.