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Unveiling the impact of parabens on human neutrophils oxidative burst under hyperglycaemia conditions

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Abstract

Background: Parabens, also known as a family of alkyl esters of 4-hydroxybenzoic acid (4-HB), are natural or synthetic compounds that have been used as powerful antimicrobial agents across multiple industries such as cosmetic, pharmaceutical and food industries, since the 1920s [1]. Their widespread use stems from their low cost, broad-spectrum antimicrobial activity, chemical stability, and low risk of triggering allergic reactions [2]. However, concerns have arisen regarding their potential to disrupt the endocrine system and promote chronic inflammation, classifying them as endocrine-disrupting chemicals. Chronic tissue inflammation is implicated in the pathogenesis of numerous diseases, including Diabetes mellitus (DM), often involving the activation of neutrophils [3]. **Objective:** This study aims to unveil the effect of commonly used parabens and their metabolite on human neutrophils in physiological and hyperglycemia conditions, a common feature of DM. **Methods:** Isolated human neutrophils were exposed to four parabens (methyl-, ethyl-, propyl- and butyl paraben) and their metabolite, 4-HB. The production of reactive species, a marker of neutrophils' oxidative burst, was detected through a fluorescent probe, dihydrorhodamine 123. To disclose the mechanism involved in the production of reactive species by parabens and their metabolite, an inhibitor of NADPH oxidase, an inhibitor of myeloperoxidase (MPO), an inhibitor of protein kinase C (PKC) and an inhibitor of phospholipase C (PLC) were tested. **Results:** In general, it was demonstrated that parabens induced neutrophils' oxidative burst similarly under both physiological and hyperglycemic conditions. The mechanism of action of parabens involves the activation of PLC, followed by the subsequent activation of PKC, ultimately leading to the activation of NADPH oxidase and MPO. No effects were observed with the exposure of neutrophils to 4-HB. **Conclusions:** This study provides insights into the mechanisms by which parabens modulate neutrophil function under physiological and hyperglycemic conditions, potentially contributing to our understanding of their role in DM.

Keywords: parabens; neutrophils; inflammation; diabetes

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