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Título: *Corynebacterium diphtheriae* HETEROGENEOUS RESPONSES TO THE OXIDATIVE AGENTS H_2O_2, PARAQUAT AND K_2TeO_3: RESISTANCE PROFILES, ADAPTATIVE-RESPONSE/CROSS-RESISTANCE INDUCTION AND BIOFILM FORMATION

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Resumo

Corynebacterium diphtheriae is the main etiologic agent of diphtheria, an acute communicable infection of the upper respiratory tract, frequently fatal. As a result of increased vaccine coverage, the global incidence of diphtheria has reduced dramatically. Nevertheless, *C. diphtheriae* remains a concern worldwide due its potential to cause endocarditis, osteomyelitis and catheter-related infections. *C. diphtheriae* abilities to adhere to and survive within diverse host cells, including macrophages and respiratory cells were previously described. *C. diphtheriae* is also capable of resist to high doses of tellurite (TeO_3^{-2}), a general oxidant. These findings suggest that diphtheria bacilli tolerate high concentrations of reactive oxygen species (ROS). Nevertheless, *C. diphtheriae* oxidative stress response is poorly understood. In the present work, the resistance of ten *C. diphtheriae* strains to the oxidative agents, hydrogen peroxide (H_2O_2), paraquate and potassium tellurite (K_2TeO_3), was analyzed. Additionally, the ability of *C. diphtheriae* strains to adapt to ROS exposure through the induction of adaptive-response and/or cross-resistance and by modulation of biofilm formation was evaluated. *C. diphtheriae* strains exhibited different resistance levels to the oxidative agents tested. The two homologs strains ATCC 27010 and ATCC 27012, which differ in the presence of the corynephage β^{tox+}, showed a major difference in H_2O_2 resistance: the toxigenic strain, ATCC 27012, presented a higher susceptibility. The H_2O_2 induced an adaptive-response in three diphtheria bacilli strains. Among the two homologs strains, ATCC 27010 was the only H_2O_2-adaptive-response positive. Bacterial cross-resistance was not induced by any oxidative agents. The presence of H_2O_2, paraquate and K_2TeO_3 led to a diverse modulation of biofilm formation. Paraquate and K_2TeO_3 influenced antagonistically the adherence of *C. diphtheriae* to the glass surface despite both agent present the ability to generate superoxide anion. The H_2O_2 was able to potentiate the biofilm formation on polystyrene surface of the ATCC 27012 strain. The heterogeneous oxidative stress responses indicated that *C. diphtheriae* might express varied strategies that establish differences in host-pathogen interactions and in adaptation under stressing environmental conditions.

Palavras-chaves: adaptive-response, biofilm, *Corynebacterium diphtheriae*, cross-resistance, oxidative agents.

Agências de fomento: CNPq, CAPES, FAPERJ, SR-2 UERJ. *Bolsista do CNPq – Brasil.