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Influence of Menthol on Ion Fluxes and ATPase Activity in Antibiotic-Resistant *E. Coli* Under Aerobic and Anaerobic Conditions

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ABSTRACT

The rising rate of antibiotic resistance has become a worldwide problem, and plants are considered promising sources of new antibiotic agents due to the antibacterial activity of their extracts and essential oils. The *Lamiaceae* family of essential oil-bearing plants are known for their expressed antimicrobial activity. *Mentha arvensis* essential oil and its major component, menthol (comprising 70% of the oil's chemical composition), show antibacterial activity against a wide range of microbes, including *Escherichia coli* strains, particularly kanamycin-resistant ones. To understand the menthol mode of action, we studied its influence on the membranes of kanamycin-resistant *E. coli* pARG-25 and wild-type *E. coli* BW25113 strains, particularly, on ATPase activity, proton and potassium flux rates, extracellular and intracellular pH in both aerobic and anaerobic conditions, using two menthol concentrations: 125 µg/mL (the minimum inhibitory concentration, MIC) and 12.5 µg/mL. According to our results, menthol expresses its antibacterial effects through several mechanisms, mainly involving disruption of membrane-associated energy systems such as F_OF_1-ATPase, modulation of ion fluxes, which is, therefore. reflects on the changes in intracellular pH. These effects are concentration-, condition (aerobic/ anaerobic) and strain-dependent, with a greater impact on the kanamycin-resistant *E. coli* strain under anaerobic conditions. Compared to the *E. coli* BW25113 strain, *E. coli* pARG-25 has increased tolerance to menthol, particularly under aerobic conditions, where menthol effects on the Trk system are less pronounced. However, under anaerobic conditions, the menthol MIC decreased the specific growth rate, the ATPase activity and potassium flux by 40%, which confirmed its membrane-targeting mechanism of action.

Keywords: kanamycin-resistance, proton flux, potassium flux, ATPase activity

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