The effects of royal jelly derived exosomes on the proliferation rate of the MCF-7 breast cancer cell line and its antimicrobial effect on Staphylococcus aureus and Pseudomonas aeruginosa .

Abstract

Breast cancer, the most prevalent type of cancer among women globally, faces numerous challenges, including resistance to conventional treatments such as chemotherapy and their severe side effects. This resistance can lead to treatment failure and disease progression. Additionally, immunosuppression in these patients, particularly following chemotherapy, increases the likelihood of infections by bacteria such as *Staphylococcus aureus* and *Pseudomonas aeruginosa*, posing serious risks to cancer patients. This study aims to investigate the effects of exosomes derived from royal jelly on the proliferation of the MCF-7 breast cancer cell line and to evaluate their antimicrobial properties against *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Exosomes were extracted from royal jelly using precipitation methods and the "Exocib" isolation kit. The characteristics of the exosomes were assessed using Dynamic Light Scattering (DLS), Transmission Electron Microscopy (TEM), and flow cytometry to detect the surface marker CD63. The human breast cancer cell line MCF-7 was cultured in DMEM medium and, after the third passage, treated with varying concentrations of exosomes and doxorubicin. Cell viability was evaluated using the MTT assay, while cell migration and proliferation were assessed using the scratch assay. The expression levels of apoptosis-related genes (Caspase-3, Bax, and BCL2) were analyzed using Real-time PCR. Additionally, the antimicrobial effects of the exosomes on *Staphylococcus aureus* and *Pseudomonas aeruginosa* were evaluated by determining the Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC). The extracted exosomes exhibited an average size of approximately 96 nanometers and a spherical morphology, with the presence of the CD63 marker confirming their exosomal origin. In cytotoxicity assays, exosomes significantly reduced the viability of MCF-7 cells with an IC_{50} of 4.323 μg/ml, whereas doxorubicin demonstrated higher efficacy with an IC_{50} of 0.3363 μg/ml. In the scratch assay, both exosome and doxorubicin-treated groups showed a significant reduction in cell migration rates. Gene expression analysis revealed that exosomes increased the expression of Caspase-3 and Bax while decreasing the expression of BCL2, indicating the induction of apoptosis in cancer cells. In antimicrobial tests, exosomes exhibited MIC values of 8 mg/ml against *Staphylococcus aureus* and 4 mg/ml against *Pseudomonas aeruginosa*. The MBC for *Pseudomonas aeruginosa* was determined to be 8 mg/ml,

while for *Staphylococcus aureus*, it exceeded 8 mg/ml. Exosomes derived from royal jelly demonstrate high potential in inhibiting the proliferation of MCF-7 breast cancer cells and suppressing the growth of *Staphylococcus aureus* and *Pseudomonas aeruginosa* at the concentrations studied. These findings position royal jelly-derived exosomes as promising candidates for complementary or alternative therapeutic approaches in breast cancer treatment, particularly in conditions of drug resistance and reduced infection risk in patients.

Keywords:
Breast cancer, Exosome, Royal jelly, MCF-7, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, Apoptosis, Antimicrobial