ORT_27 - Evaluation of anticancer activity of silver nanoparticles on human leukemia, breast cancer, and melanoma cells

Gabriel Mustafá Misirli[1] ; Ana Paula Gregorio Alves Fontao[2]; Renata Ribeiro de Castro[2]; Shirley de Mello Pereira Abrantes[3]; André Luiz Franco Sampaio[2]; Edimilson Domingos da Silva[1]; Sotiris Missailidis[1].
[1]Fiocruz/Bio-Manguinhos
[2]Fiocruz/Farmanguinhos
[3]Ex-UNIAN (aposentada)/Assessoria Científica Independente (atual)

Introduction: According to WHO, Cancer is one of the leading causes of death with 10 million deaths occurred globally in 2020, and resistance to chemotherapy is a challenge. Metallic nanoparticles can accumulate in cancer tissue due to their size combined with the increased tissue/vascular permeability observed in cancer. Silver nanoparticles (AgNP), with an additional antimicrobial activity, poses as a promising antitumoral agent that can also be functionalized with natural products, biopharmaceuticals or monoclonal antibodies to increase its anticancer effects.

Objectives: To evaluate *in vitro* antitumor properties of AgNP on human leukemia, breast cancer and melanoma cell lines.

Methodology: Silver nanoparticles (AgNP) were synthesized by the borohydride reduction method and stabilized with boron and albumin (BSA) according to Misirli (2021; https://www.arca.fiocruz.br/handle/icict/51648) and later characterized by ultraviolet-visible spectroscopy, dynamic light scattering, laser doppler electrophoresis and transmission electron microscopy. AgNP were washed and stored in suspension in specific buffer (500 µg/mL). Leukemia (K562), breast cancer (MCF-7 and MDA-MB-231) and melanoma (SK-MEL-28) cell lines were seeded in 96-well plates ($5x10^3$ cells/mL), maintained in a 5% CO_2 atmosphere at 37°C for 24h and treated with AgNP in multiple concentrations (from 0.015 to 150 ppm), each in triplicate. Cytotoxicity was evaluated using MTT method 48h after treatment. Statistical analysis and IC50 calculations were performed using Graph Pad Prism 9.

Results: The AgNPs presented spherical, monodispersive particle, with an average size of 10 nm. When tested on SK-MEL-28 and MDA-MB-231 AgNP presented a cytotoxic effect at 150 ppm with a sharp decrease to basal values when tested at 15 ppm, from 86.66% to 2.36% in melanoma cell line SK-MEL-28, from 72.10% to 14.73% cytotoxicity. When tested on MCF7, a breast cancer cell line, AgNP displayed a cytotoxic effect from 1.5 to 150 ppm, with a IC50 of 19.06 ppm. We have observed that AgNP treatment on leukemia cell line K562, have had a maximum cytotoxic effect at 15 and 150 ppm (86.07 % and 71.11%, respectively) with a IC50 of 0.74 ppm. Comparison of different batches of AgNP resulted in similar IC50 for the cell lines tested.

Conclusion: AgNP have *in vitro* cytotoxic activity on leukemia (K562), breast cancer (MCF-7 and MDA-MB- 231) and melanoma (SK-MEL-28) cell lines. Further experiments are necessary to address selectivity index in non-tumorigenic cells and mechanism involved in AgNP-triggered cytotoxicity.

Keywords: Silver nanoparticle, Antitumoral, Cancer