Effect of Artesunate on Toxoplasma gondii:

In Vitro and In Vivo Experimental Studies

Thesis

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Abstract

gondii, the *Toxoplasma* causative agent toxoplasmosis, is an obligate intracellular protozoan able to infect a wide range of vertebrate cells. The most common therapy for toxoplasmosis is the combination of sulfadiazine and pyrimethamine. This treatment is associated with adverse reactions, thus, the development of new drugs is necessary. The effect of artesunate in vitro and in vivo was studied. In vitro experiments were performed with the VERO cell line infected with RH virulent T. gondii strain using multiple concentrations. A maximum reduction of tachyzoites viability of approximately 83.33% was obtained with a concentration of 0.1µg/ml artesunate after 48 hours. Transmission electron microscopic analysis morphological changes of the parasites including membrane damage, organelle vesiculation and then disruption. Also it revealed progressive vesiculation in the cytoplasm of treated parasites which did not occur in the host cell. Vesiculation inside the parasite resulted in its death, In vivo, artesunate produced a decrease in cerebral cyst count of approximately 48% after 8 days of treatment in immunocompetent group compared to untreated control group.

Key words: *Toxoplasma gondii*, artesunate, in vitro and in vivo

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List of Abbreviations

ACTs Artemisinin Combination Therapies Acquired immunodeficiency syndrome **AIDS** Artemisinin **ART** Carbon dioxide CO₂ Cytomegalovirus **CMV** Central nervous system **CNS CSF** Cerebrospinal fluid \mathbf{CT} Computed tomography Direct Agglutination test **DAT** Deoxyribonucleic acid **DNA** Dihydroartemisinin **DHA** Dihydrofolate reductase **DHFR** Dihydropteroate synthase **DHPS** Enzyme linked immunosorbent assay **ELISA IFAT** Indirect immunofluorescence Ig Immunoglobulin **IHAT** Indirect haemagglutination test HIV Human immunodeficiency virus Hrs Hours Interleukin IL **ISAGA** Immunosorbent Agglutination assay LAT Latex Agglutination Test