A Multimodality Therapeutic Application on Toxoplasmosis Encephalitis Utilizing Spiramycin and de novo *Ferula asafoetida* in immunodeficient mice

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Abstract

The poor absorption, blood-brain barrier, and activation of the parasite cysts in the CNS of immunocompromised patients defy toxoplasmosis therapy. This study investigates the parasite's behavior in a murine host over various scenarios of health conditions and treatment protocols. Female Swiss-Webster mice infected with *T. gondii ME49* cysts were divided into three batches as per the timetable of Dexamethasone administration. One batch of mice received no DMS (Batch I), another batch received DMS 14 days before infection (Batch II), and the third batch received it on the same day of infection for 14 days (Batch III). Each batch was split into four groups per the treatment protocol. One group was treated with Spiramycin (SP), another was treated with *Ferula asafoetida* (FA), a third group received a combined drug of SP and FA, and the fourth group was treated with neither. SP, FA, or FA+SP were orally given 35 days post-infection in batch (III) and on day zero of infection in batches (I) and (II). The treatments lasted for 14 days in all groups. All experimental mice were decapitated at day 60 pi. Our data showed a remarkable inhibitory effect by the combined drug (SP+FA) that resulted in a significant reduction $(p<0.0001)$ of cyst load, DNA concentrations, and normalization of T-cell subsets to zero alongside the amelioration of brain tissue. These findings demonstrate that a multimodality approach by combining *Ferula asafoetida* with spiramycin might be a powerful, safe, and neuroprotective regimen for controlling the development of toxoplasmosis encephalitis in all circumstances.

**Keywords:** *Toxoplasmosis encephalitis; drug discovery; Ferula asafoetida; spiramycin, T-cell expression, DNA expression, Dexamethasone; medicinal and complementary herbs*