Exploring the Potential of Repurposing Celecoxib with Chitosan Nanoparticles for Anti-Toxoplasmosis Effect: In Vitro and In Vivo Study (PP- 03)

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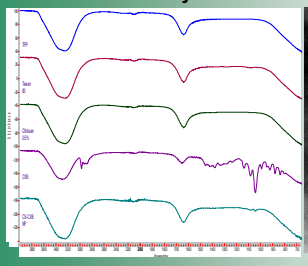
Introduction

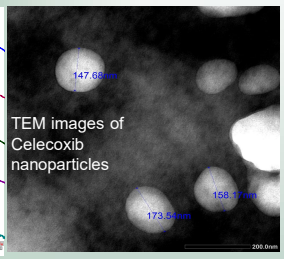
Toxoplasma gondii is a parasitic protozoan that can infect humans and animals. In healthy individuals, the infection may not cause severe symptoms, but it can be dangerous for pregnant women and individuals with weakened immune systems, such as undergoing chemotherapy. Toxoplasma gondii infection can cause serious complications, including encephalitis, pneumonia, and eye problems. In pregnant women, the parasite can be transmitted to the fetus, leading to congenital disabilities or even stillbirth. Celecoxib is a drug known for its anti-inflammatory properties, and chitosan nanoparticles can enhance drug delivery This combination may lead to improved efficacy and reduced side effects compared to traditional treatments for toxoplasmosis. The aim of this study was to explore the potential of repurposing celecoxib with chitosan nanoparticles for its anti- toxoplasmosis effect on the murine model of acute toxoplasmosis.

Materials and Methods

Chitosan nanoparticles encapsulated celecoxib were prepared using emulsion-ionic gelation technique and characterized by entrapment efficiency, particle size (PS), zeta potential (ZP), polydispersity index (PDI) and transmission electron microscope (TEM) images. The in vivo study was performed in a mouse model to monitor for infection progression, parasite load, survival rate and histopathological examinations of liver and spleen tissues.

FTIR analysis





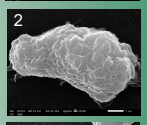
Results

The Celecoxib nanoparticles exhibited a spherical shape without aggregations, with PS, ZP, and PDI measuring 160.43±35.5 nm, 10.4725±2.09 mV, and 0.297, respectively. Fourier-transform infrared (FTIR) analysis indicated no excipient interaction. Transmission electron microscopy (TEM) images revealed nanoparticles adhering to the surface of tachyzoites, leading to disruption of plasma membranes and distortion of shape. In terms of efficacy, the survival rate analysis showed that treatment with celecoxib nanoparticles at a lower dose of 0.1 mg and shorter duration of 3 days resulted in a significantly higher survival rate compared to the standard treatment of sulfamethoxazole at 0.2 mg and longer duration of 7 days ($p<0.01$).

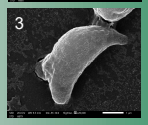
Histopathological Examination of the tachyzoite

1. Control infected group-the tachyzoite is normal without any change.

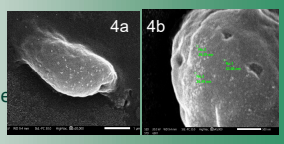
2. Sulfamethoxazole (the drug of choice) increase the particle size due to pores occurred on its surface.



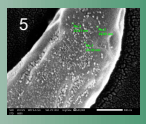
3. Celecoxib alone has small change on the tachyzoite.



4. (a) Celecoxib nanoparticles effectively cause damage of the tachyzoite, the nanoparticle precipitate on its surface,
(b) Pores occurred on the surface of tachyzoites due to the precipitation of the NP on its surface.



5. Pure NP has little effect on damaging the tachyzoite.



Conclusions

This study has demonstrated that chitosan nanoparticles encapsulating celecoxib represent a novel and potentially transformative approach to the treatment of acute toxoplasmosis. The unique physicochemical properties of the nanoparticles, characterized by their optimal particle size, zeta potential, and polydispersity index, have been shown to facilitate the targeted delivery of celecoxib, thereby enhancing its therapeutic efficacy. The in vivo results, particularly the observed survival rates and the histopathological examinations of liver and spleen tissues, provide compelling evidence of the enhanced anti-toxoplasmosis effect of this innovative formulation. This repurposed application has the potential to lower drug costs and promote sustainable drug use.

References

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