CRYPTOCOCCAL MENINGITIS, WHAT IT IS, AND TREATMENT ISSUES RELATED TO ITS MANAGEMENT

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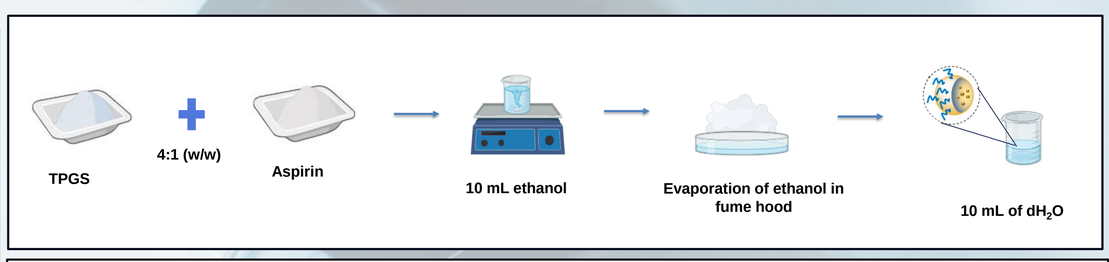
Introduction

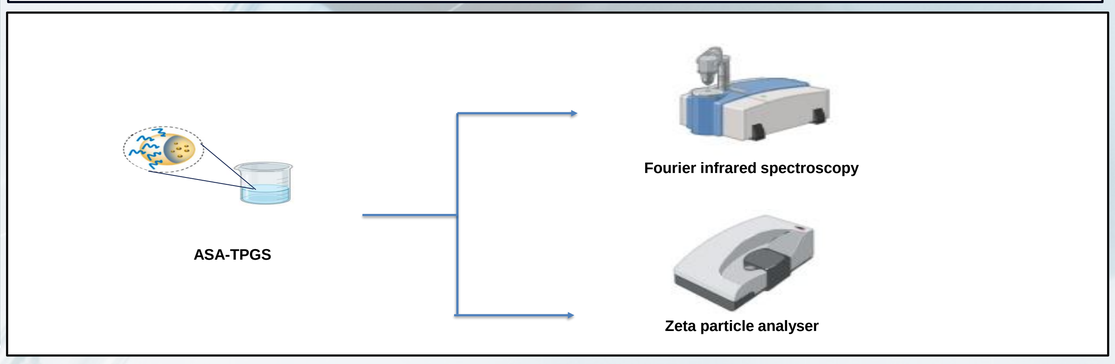
Cryptococcus neoformans **is the most common causative agent of fungal meningitis, resulting in cryptococcal meningitis. Cryptococcal meningitis manifests mostly in HIV-infected patients and is less common in individuals with non-HIV-related immunosuppression or immunocompetent hosts. Treatment of cryptococcal meningitis is limited by the selective permeability of the BBB, therefore, affecting the efficacy of the drugs. This structural organisation is a major impediment to treatment success as it excludes drugs, leading to their reduced bioavailability in the brain. This is compounded by treatment challenges associated with controlling cryptococcal growth in the brain. This is, in part, because under normal conditions, amphotericin B cannot cross the BBB, while fluconazole can cross the BBB; its use is limited by non-fluconazole susceptibility. Based on this latter, there is scope to explore other drugs that could be effective at treating cryptococcal meningitis.**

The solution to the above could be repurposing existing drugs already approved by the United States Food and Drug Administration as new antimicrobial agents. To this end, the objectives of this study were to reformulate aspirin by encapsulating it in D-α-tocopheryl polyethene glycol succinate (TPGS), characterise the encapsulated formulation of aspirin (ASA), and evaluate its *in vitro* and *in vivo* efficacy against *Cryptococcus neoformans.*

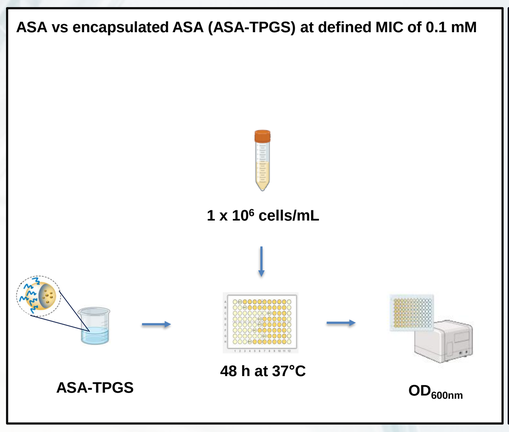
Methods

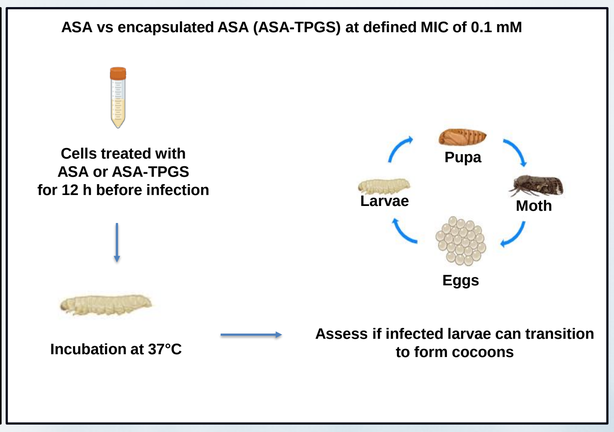
ASA encapsulation and characterisation



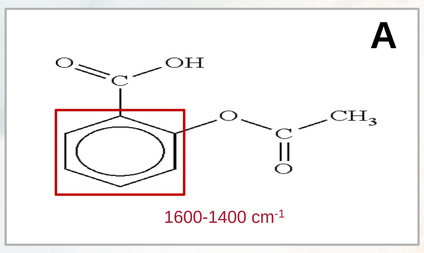


Potency of encapsulated ASA





Results



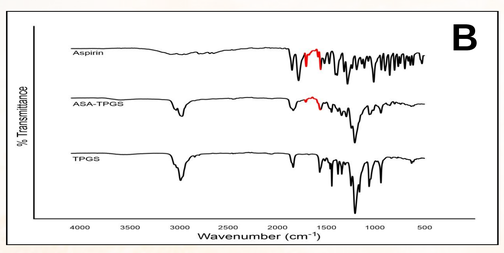


Figure 1. Fourier transform infrared spectroscopy spectrum confirming encapsulation of aspirin (ASA) in D-α-tocopheryl polyethene glycol succinate (TPGS) following the detection of the ASA's benzene ring **(A)** at a wavenumber of 1600-1400 cm^{-1} on the ASA-TPGS spectrum **(B)**. The ASA and TPGS spectra were included for comparison.

Table 1. Zeta particle analyser results representing particle size, polydispersity index and zeta potential.

Criteria	Definition/Description	Obtained readings	Deductions
Size	Nanoparticle (1 nm – 100 nm)	10.97 nm	ASA-TPGS is a nanoparticle
Polydispersity index (PDI)	Lower value shows narrow particle size distribution (0.1 – 0.25)	0.175 PI	ASA-TPGS has narrow size distribution
Zeta potential	Stable particle dispersed in PEG (-10 mV to +10 mV)	3.628 mV	ASA is stable in TPGS

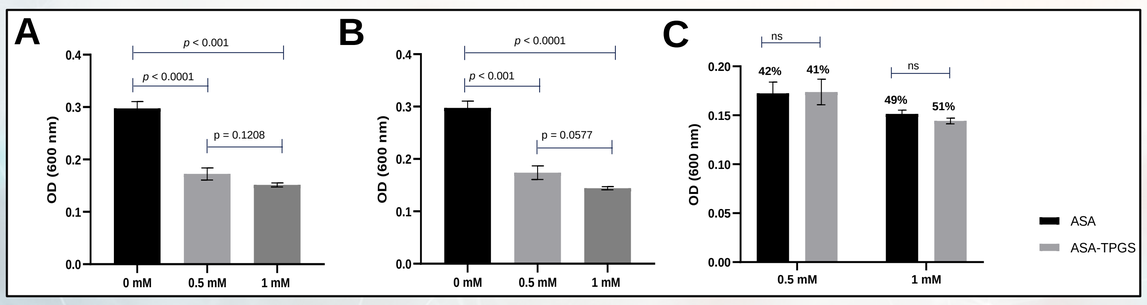


Figure 2. *In vitro* growth susceptibility results showing the inhibition of cryptococcal cells when tested against ASA **(A)** and ASA-TPGS **(B)**, while **(C)** summarises the effects of ASA vs ASA-TPGS at 0.5 and 1 mM.

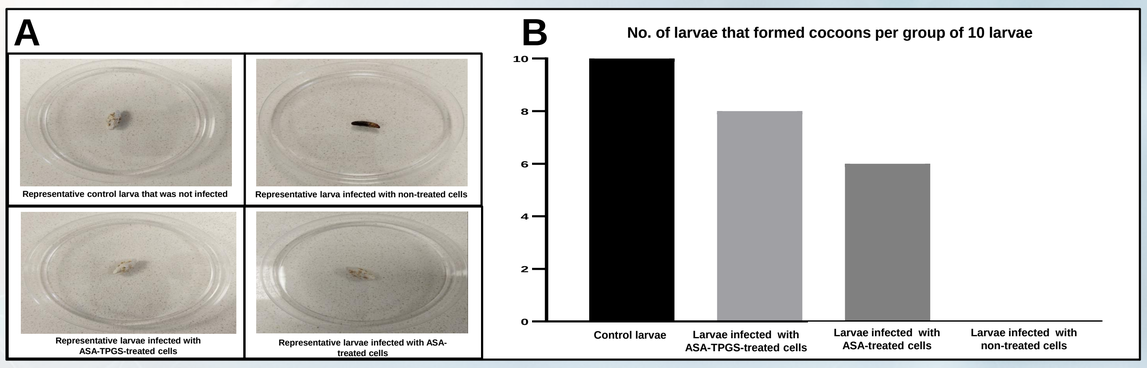


Figure 3. (A) is a depiction of the representative larvae that were either used as a control, infected with non-treated cells, infected with ASA-TPGS or ASA-treated cells, while **(B)** is a histogram that quantifies the number of larvae that formed cocoons per group of 10 larvae.

Conclusions

- **It was possible to prepare the micellar encapsulation of aspirin at a nano-scale (See Figure 1 and Table 1).**
- **The encapsulation did not result in aspirin exhibiting a reduction in its potency to inhibit cryptococcal growth (See figure 2 (C)).**
- **Moreover, the encapsulated aspirin attenuated cryptococcal disease in larvae infected with cryptococcal cells treated with encapsulated aspirin, as these infected larvae could complete their life cycle and transition to form pupa, while larvae infected with non-treated cryptococcal cells could not. succumbed to the infection and thus did not transition to form pupa (See Figure 3).**
- **These results demonstrate the potential of aspirin as an anti-*Cryptococcus* medicine.**