Citation

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Title - Preclinical evaluation of artemether loaded polymeric nanorods for the treatment of malaria

Publications –

1. Bhide, A. R., Surve, D. H., Guha, S., & Jindal, A. B. (2020). A sensitive RP-HPLC method for estimation of artemether from polymeric nanoparticles after pre-column acid treatment using UV-visible detector. Journal of Liquid Chromatography & Related Technologies, 43(15-16), 624-632.
2. Bhide, A. R., & Jindal, A. B. (2021). Fabrication and evaluation of artemether loaded polymeric nanorods obtained by mechanical stretching of nanospheres. International Journal of Pharmaceutics, 605, 120820.
3. Bhide, A. R., Suri, M., Katnoria, S., Kaur, S., Jirwankar, Y. B., Dighe, V. D., & Jindal, A. B. (2022). Evaluation of Pharmacokinetics, Biodistribution, and Antimalarial Efficacy of Artemether-Loaded Polymeric Nanorods. Molecular Pharmaceutics, 20(1), 118-127.
4. Bhide, A. R., Surve, D. H., & Jindal, A. B. Nanocarrier based active targeting strategies against erythrocytic stage of malaria. Journal of controlled release: official journal of the Controlled Release Society, S0168-3659.

Summary

The current study involves preparation and evaluation artemether-loaded PLGA nanorods by mechanical stretching of nanospheres. Artemether loaded PLGA nanospheres were fixed in a PVA film which was stretched using an *in-house* fabricated film stretching apparatus in one dimension while immersed in acetone or silicon oil, thus producing the nanorods. The effect of film thickness (100μm vs. 150μm), lactide to glycolide ratio in PLGA (50:50 vs. 75:25), extent of stretching (2x vs. 4x) on the resulting nanorods were studied. Nanorods exhibited a sustained drug release and were found to be non-toxic to the THP-1 cells and less haemolytic towards erythrocytes than nanospheres at concentrations between 0.001 to 100 μg/mL of artemether in the *in vitro* studies. Further, SEM and confocal microscopic analysis revealed that the nanospheres and nanorods adhere to the erythrocytes when incubated together. Intravenous administration of nanorods in rats displayed higher plasma drug concentration and lower elimination rate when compared with nanospheres in the pharmacokinetic study. In the

biodistribution of DiR loaded nanoparticles, nanospheres accumulated in the RES organs rapidly as compared to the nanorods indicating the longer circulation time of nanorods. In the *in vitro* schizont maturation inhibition assay, the formulations displayed a concentration dependent parasitic inhibition. Nanorods were more effective at lower concentrations whereas nanospheres were more effective at higher concentration. In the *in vivo* antimalarial efficacy study on *P. berghei* mouse model, nanorods exhibited highest chemosuppression on 5th and 7th day compared to the nanospheres and free drug. The survival rate of *P. berghei* infected mice was also found to be higher after treatment with artemether nanoformulations when compared with free artemether.

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