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Synthesis, characterization and in vitro analysis of polymer-based conjugaes containing dihydrofolate reductase inhibitors

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Malaria is an acute disease that is caused by the protozoanPlasmodiumparasites. Drug resistance is the majorproblem that is hindering the control of this disease. In order to overcome drug resistance to commonly usedantimalarials, nanocarriers which are biocompatible, non-toxic, and are able to deliver drugs to the target sitewere designed. Polyaspartamide-drug conjugates containing antimalarials that inhibit dihydrofolate reductasewere prepared and characterized by nuclear magnetic resonance spectroscopy (NMR), Fourier transform spec-troscopy (FTIR), X-ray diffraction (XRD), Thermogravimetric analysis (TGA), Scanning electron microscope(SEM), Energy-dispersive X-ray analysis (EDX), particle size analysis, as well asin vitroantiplasmodial analysisand drug release studies at physiological pH values. NMR and FTIR results confirmed the successful in-corporation of the drugs onto the conjugates. SEM images of the conjugates showed predominant spherical andcluster of globular morphologies.In vitrorelease mechanisms of the drugs from the conjugates were slow andsustained. Conjugates containing 4-aminosalicylic acid and pyrimethamine were found to be the most activeagainst the asexual stage of the parasite with an IC(sub50) value of 332.37±6.46 nM. Conjugate containing 4-aminoquinoline derivative, pyrimethamine and primaquine exhibited moderate antimalarial activity with anIC50value of 4.71 ± 0.70 nM.