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Synthesis and antimalarial activities of poly ethylene glycol derivatives of dihydroartemisinin

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Despite decades of effort to eradicate or at least control malaria, it remains endemic in all six WHO regions and the burden is heaviest in the African Region, where an estimated 90% of all malaria deaths occur; according to WHO, two countries – the Democratic Republic of the Congo and Nigeria – account for about 40% of estimated mortality due to malaria worldwide. The most recent additions to the drug therapy for malaria are artemisinin. However the therapeutic value of artemisinin is limited to a great extent by its low solubility in both oil and water. In the search for more effective and soluble drugs, a number of ether derivatives of dihydroartemisinin have been synthesized. The use of ethers of dihydroartemisinin and artemisinin itself in the treatment of *Plasmodium falciparum* malaria is restricted by their short plasma half-life. A search for new artemisinin derivatives with a better therapeutic index due to a better solubility and bio-availability has thus become an important target of many laboratories around the world. For this reason we prepared a new class of artemisinin derivatives using 4-Arm PEG-COOH and 8-Arm PEG-COOH (PEG-DHA); which are known for their high flexibilities, hydrophilic property and low toxicity. It is our belief that successful development of PEG-DHA via this study will reduce considerably the dosage regime of the artemisinin derivative, so that patient compliance will be easier.

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Terpenoids as promising therapeutic molecules against Alzheimer's disease: Amyloid beta and acetylcholinesterase directed pharmacokinetic and molecular docking analyses

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Alzheimer's disease (AD) is a progressive neurological disorder characterized by deterioration of cognitive functions and behavioral changes including dementia. Several attempts have been made to treat AD by combined drug therapy directed against acetylcholinesterase (AChE) and amyloid beta (Aβ) simultaneously for delaying the progression of the disease. However, the side-effects due to long-term administration of these drugs have motivated attempts for development of a new generation of therapeutics based on natural compounds. In this regard, one hundred terpenoids having neuroprotective properties were analyzed for their inhibitory potential against AChE and Aβ through molecular docking approach. In view of the fact that ADMET analyses of potential therapeutic compounds is essential for ensuring the development of safer drugs, the selected terpenoids were further screened for their pharmacokinetic properties, among which only twenty five terpenoids were found to fulfill all the ADMET descriptors and drug likeness properties. A triterpene, nimbolide, was found to be the most potent and safe inhibitor for both AChE and Aβ among the selected terpenoids as well as those of commonly used drug and known inhibitor, namely galanthamine and curcumin, respectively. Molecular dynamics simulation analysis of AChE-nimbolide and Aβ-nimbolide complexes also validated the results of docking. These findings well corroborated with the traditional knowledge of use of neem tree (Azadirachta indica), the source of nimbolide, in the treatment of AD. Thus, the present work makes a foundation for further clinical investigations of nimbolide as a drug for AD.

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