OMICS Group Conferences
Accelerating Scientific Discovery

2nd International Conference and Exhibition on
Neurology & Therapeutics
June 17-19, 2013 Hilton Chicago/Northbrook, Chicago, USA

Design and *in vitro* evaluation of nanostructured lipid carriers for management of cerebral malaria

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Curcumin is a polyphenol derived from the dietary spice turmeric and possesses diverse biological and pharmacological activities. The objective of the present investigation was to explore the potential of nanostructured lipid carriers (NLC) loaded curcumin to enhance the uptake of drug to brain via intranasal delivery for management of cerebral malaria. Curcumin loaded NLCs (C-NLC) were prepared using microemulsion technique. Compatibility studies of drug excipients were carried out using FTIR peak matching method. NLCs were characterized for surface morphology, particle size, and zeta potential by Scanning electron microscopy (SEM) and dynamic light scattering respectively. The NLCs showed average particle size of 85-190 nm with zeta potential of -31.4±0.61 mV. SEM studies confirmed that NLCs were spherical in shape and size was in agreement with results obtained from particle size analysis. NLCs were evaluated for the drug loading and encapsulation efficiency. The cytotoxicity value of C-NLC in SK-N-SH cell lines revealed that NLCs were non toxic by SRB assay. *In vitro* hemolytic activity was found within the acceptable range revealing low toxicity risk of the lipid nanoparticles. They were subjected to differential scanning calorimetry and x-ray diffraction which revealed that drug was present in amorphous form in NLCs. The *ex vivo* release studies of the formulated NLCs were carried out using sheep nasal mucosa in comparison with drug suspension in simulated nasal fluid. The results revealed that release rate was biphasic and faster from drug suspension as compared to NLCs. The nasal ciliotoxicity studies of prepared formulation were carried out using isolated bovine nasal mucosa which was further subjected to histopathological analysis. Results revealed that nanoparticles formulation had no harmful effect on the microscopic structures of nasal mucosa. Therefore NLCs nasal formulations have the potential to deliver curcumin through nasal mucosa to reach the brain for cerebral malaria.

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