Sustained release formulation of an anti-tuberculosis drug based on para-amino salicylic acid-zinc layered hydroxide nanocomposite

Abstract

Background: Tuberculosis (TB), is caused by the bacteria, Mycobacterium tuberculosis and its a threat to humans since centuries. Depending on the type of TB, its treatment can last for 6-24 months which is a major cause for patients non-compliance and treatment failure. Many adverse effects are associated with the currently available TB medicines, and there has been no new anti-tuberculosis drug on the market for more than 50 year, as the drug development is very lengthy and budget consuming process.Development of the biocompatible nano drug delivery systems with the ability to minimize the side effects of the drugs, protection of the drug from enzymatic degradation. And most importantly the drug delivery systems which can deliver the drug at target site would increase the therapeutic efficacy. Nanovehicles with their tendency to release the drug in a sustained manner would result in the bioavalibilty of the drugs in the body for a longer period of time and this would reduce the dosing frequency in drug administration. The biocompatible nanovehicles with the properties like sustained release of drug of the target site, protection of the drug from physio-chemical degradation, reduction in dosing frequency, and prolong bioavailability of drug in the body would result in the shortening of the treatment duration. All of these factors would improve the patient compliance with chemotherapy of TB.Result: An anti-tuberculosis drug, 4-amino salicylic acid (4-ASA) was successfully intercalated into the interlamellae of zinc layered hydroxide (ZLH) via direct reaction with zinc oxide suspension. The X-ray diffraction patterns and FTIR analyses indicate that the molecule was successfully intercalated into the ZLH interlayer space with an average basal spacing of 24 Å. Furthermore, TGA and DTG results show that the drug 4-ASA is stabilized in the interlayers by electrostatic interaction. The release of 4-ASA from the nanocomposite was found to be in a sustained manner. The nanocomposite treated with normal 3T3 cells shows it reduces cell viability in a dose- and time-dependent manner.Conclusions: Sustained release formulation of the nanocomposite, 4-ASA intercalated into zinc layered hydroxides, with its ease of preparation, sustained release of the active and less-toxic to the cell is a step forward for a more patient-friendly chemotherapy of Tuberculosis.

Keyword: 3T3 cell lines; MDR-TB; Nanocomposite; Para-Amino salicylic acid(PAS / 4-ASA); Zinc layered hydroxide.