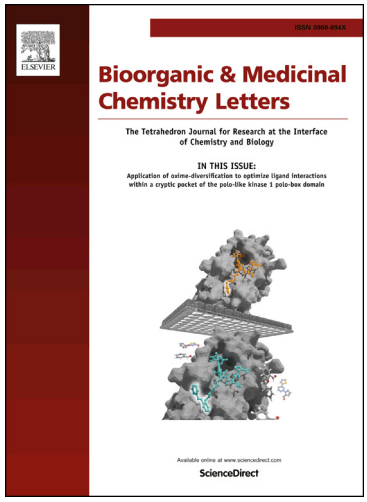

Digest

The long story of Camptothecin: From traditional medicine to drugs

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The long story of Camptothecin: From traditional medicine to drugs

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ABSTRACT

20-(S)-Camptothecin (CPT) is a natural alkaloid extracted from the bark of *Camptotheca acuminata* (Chinese happy tree). It acts as a DNA topoisomerase 1 poison with an interesting antitumor activity and its use is limited by low stability and solubility and unpredictable drug-drug interactions. Since the late 20th century, it has been widely used in cancer therapy and, since extraction yields from plant tissues are very low, various synthetic routes have been developed to satisfy the increase in demand for CPT. Moreover, SAR studies have allowed for the development of more potent CPT analogues topotecan and irinotecan. Unfortunately, resistance has already occurred in several tumour lines. Additional studies are needed to better understand the relationship between substituents and resistance, its clinical relevance and the impact of related gene polymorphism. One of the latest research approaches focuses on modifying the delivery mode to improve tumour cell uptake and reduce toxicity.

Keywords: Camptothecin, CPT-like compounds, *Camptotheca acuminata*, anticancer drugs, DNA Topoisomerase 1, drug-resistance, formulative studies.

Introduction Camptothecins are amongst the most important anticancer alkaloids of the 21st century as it is testified by their clinical applications.

20-(S)-Camptothecin (CPT) (***Figure 1***) was first discovered and isolated by Wall and Wani in 1966 from the bark of *Camptotheca acuminata* Decne., or Chinese Happy Tree, during a screening of various plant species with the aim to isolate novel steroids.[1] They found that this extract showed substantial antitumor activity in standard in vitro test systems as well as in a mouse leukaemia model; this finding was in agreement with the use in Traditional Chinese Medicine as a natural remedy against cancer. From a structural standpoint, CPT is a quinoline alkaloid consisting in a