Betulinic acid: a promising anticancer candidate.

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Source

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Abstract

Betulinic acid is a naturally occurring pentacyclic triterpenoid which has demonstrated selective cytotoxicity against a number of specific tumor types, a variety of infectious agents such as HIV, malaria and bacteria, and the inflammatory process in general. Biological activity was first demonstrated in melanoma cell lines and was confirmed in mice bearing human melanoma xenografts. These in vivo studies also established a favorable safety margin for betulinic acid, as systemic side effects were not observed at any dose. Recently, considerable in vitro evidence has demonstrated that betulinic acid is effective against small- and non-small-cell lung, ovarian, cervical, and head and neck carcinomas. Published data suggest that betulinic acid induces apoptosis in sensitive cells in a p53- and CD95-independent fashion. While the precise molecular target and mechanism of action remain elusive and are the focus of a number of ongoing research programs, accumulated experimental evidence indicates that betulinic acid functions through a mitochondrial-mediated pathway. Supplemental reports suggest that the generation of reactive oxygen species, inhibition of topoisomerase I, activation of the MAP kinase cascade, inhibition of angiogenesis, and modulation of pro-growth transcriptional activators and aminopeptidase N activity may play a role in betulinic acid-induced apoptosis. These potential mechanisms of action may enable betulinic acid to be effective in cells resistant to other chemotherapeutic agents. Arguments supporting the role of this agent in the treatment of cancers and other infectious conditions will be reviewed.

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