Recombinant human alpha fetoprotein synergistically potentiates the anti-cancer effects of 1′-S-1′-acetoxychavicol acetate when used as a complex against human tumours harbouring AFP-receptors

Norhafiza M. Arshad¹, Lionel L.A. In², T. L. Soh², Mohamad Nurul Azmi³, Halijah Ibrahim³, Khalijah Awang⁴, Elena Dudich⁵, Eduard Tatulov⁶ and Noor Hasima Nagoor¹,⁵

¹ Institute of Biological Science (Genetics and Molecular Biology), Faculty of Science, University of Malaya, Kuala Lumpur, Malaysia
² Department of Biotechnology, Faculty of Applied Sciences, UCSI University, Kuala Lumpur, Malaysia
³ Institute of Biological Science (Ecology and Biodiversity), Faculty of Science, University of Malaya, Kuala Lumpur, Malaysia
⁴ Centre for Natural Product Research and Drug Discovery (CENAR) and Department of Chemistry, Faculty of Science, University of Malaya, Kuala Lumpur, Malaysia
⁵ Centre for Research in Biotechnology for Agriculture (CEBAR), University of Malaya, Kuala Lumpur, Malaysia
⁶ Institute of Immunological Engineering, Lyubnuchany, Moscow, Russia

Correspondence to: Noor Hasima Nagoor, email: hasima@um.edu.my
Keywords: acetoxychavicol acetate; alpha fetoprotein; anti-cancer; alpinia conchigera; targeted cytotoxicity
Received: November 28, 2014 Accepted: April 08, 2015 Published: April 29, 2015

This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

ABSTRACT

Purpose: Previous in vitro and in vivo studies have reported that 1′-S-1′-acetoxychavicol acetate (ACA) isolated from rhizomes of the Malaysian ethnomedicinal plant Alpinia conchigera Griff (Zingiberaceae) induces apoptosis-mediated cell death in tumour cells via dysregulation of the NF-κB pathway. However, there were some clinical development drawbacks such as poor in vivo solubility, degradation of biological activity upon exposure to an aqueous environment and non-specific targeting of tumour cells. In the present study, all the problems above were addressed using the novel drug complex formulation involving recombinant human alpha fetoprotein (rhAFP) and ACA.

Experimental Design: To study the synergistic effect of both agents on human cancer xenografts, athymic nude (Nu/Nu) mice were used and treated with various combination regimes intraperitoneally. Serum levels of tumour markers for carcinoembryonic antigen (CEA) and prostate specific antigen (PSA) were assessed using sandwich ELISA. IHC and Western blotting were also conducted on in vivo tumour biopsies to investigate the involvement of NF-κB regulated genes and inflammatory biomarkers. Quantification and correlation between drug efficacies and AFP-receptors were done using IF-IC and Pearson’s correlation analysis.

Results: Mice exposed to combined treatments displayed higher reductions in tumour volume compared to stand alone agents, consistent with in vitro cytotoxicity assays. Milder signs of systemic toxicity, such as loss in body weight and inflammation of vital organs were also demonstrated compared to stand alone treatments. Tumour marker levels were consistent within all rhAFP/ACA treatment groups where levels of CEA and PSA were initially elevated upon commencement of treatment, and consecutively reduced corresponding to a decrease in tumour bulk volume. Both IHC and Western blotting results indicated that the combined action of rhAFP/ACA was not only able to down-regulate NF-κB activation, but also reduce the expression of...