Abstract

Characterization of Cycloartane-Type Sapogenol Derivatives for Prostate Cancer Chemoprevention †

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† Presented at the 2nd International Conference on Natural Products for Cancer Prevention and Therapy, Kayseri, Turkey, 8–11 November 2017.

Publish: 15 November 2017

Abstract: Inhibition of inflammation-induced carcinogenesis is an efficient therapeutic strategy for cancer chemoprevention as use of anti-inflammatories was reported to decrease the cancer risk. In this study, we aimed to investigate the inhibition potential of semi-synthetic derivations of cycloartane-type sapogenol molecules on inflammation-related tumorigenic mechanisms in LNCaP prostate cancer cells. Inflammatory microenvironment was stimulated by TNFα/inflammatory conditioned media (CM). WST1/Xcelligence (proliferation), luciferase reporter (NFκB activity), immunoblotting, DCFH (ROS) and Griess (NO release) methods were used. It has been found that TNFα-induced NFκB activation was suppressed by both astragenol and cycloastragenol derivatives through inhibition of IκB phosphorylation. Further, the loss of Androgen Receptor, NKX3.1 and p53 due to inflammatory microenvironment was partially restored. In addition, tumorigenic cellular events such as increased NO release and intracellular ROS levels were both suppressed by the molecules. Inhibition of B-catenin pathway at anti-inflammatory concentrations was determined through decreased levels of pAkt(S473), total B-catenin and B-catenin(S552) induced by both lipopolysaccharide and CM treatments in inflammatory microenvironment. Finally, saponin molecules were found to suppress the proliferation and migration of prostate cancer cells at apoptotic concentrations. Therefore, it is suggested that anti-inflammatory activity of these sapogenol derivatives through NFκB inhibition make them promising agents for chemoprevention of inflammation-related prostate carcinogenesis.

Keywords: saponin; cancer chemoprevention; androgen receptor; NKX3.1; astragenol; cycloastragenol
Acknowledgments: This study was supported by TUBITAK with the project number 113Z078 to BDB.

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