J Ginseng Res xxx (2017) 1–11

Contents lists available at ScienceDirect

Journal of Ginseng Research

journal homepage: http://www.ginsengres.org

Research article

Anticancer activity and potential mechanisms of 1C, a ginseng saponin derivative, on prostate cancer cells

Xu De Wang [1,2], Guang Yue Su [1,2], Chen Zhao [2,3], Fan Zhi Qu [1,2], Peng Wang [1,2], Yu Qing Zhao [1,2,*]

[1] School of Functional Food and Wine, Shenyang Pharmaceutical University, Shenyang, China
[2] Key Laboratory of Structure-based Drug Design and Discovery of Education, Shenyang Pharmaceurical University, Shenyang, China
[3] College of Life Science and Biological Pharmaceutical, Shenyang Pharmaceutical University, Shenyang, China

ARTICLE INFO

Article history:
Received 29 June 2016
Received in Revised form
27 October 2016
Accepted 26 December 2016
Available online xxx

Keywords:
1C
AD-2
apoptosis
reactive oxygen species
Wnt/β-catenin pathway

ABSTRACT

Background: AD-2 (20(*R*)-dammarane-3b, 12b, 20, 25-tetrol; 25-OH-PPD) is a ginsenoside and isolated from *Panax ginseng*, showing anticancer activity against extensive human cancer cell lines. In this study, effects and mechanisms of 1C ((20*R*)-3b-*O*-(L-alanyl)-dammarane-12b, 20, 25-triol), a modified version of AD-2, were evaluated for its development as a novel anticancer drug.
Methods: MTT assay was performed to evaluate cell cytotoxic activity. Cell cycle and levels of reactive oxygen species (ROS) were determined using flow cytometry analysis. Western blotting was employed to analyze signaling pathways.
Results: 1C concentration-dependently reduces prostate cancer cell viability without affecting normal human gastric epithelial cell line-1 viability. In LNCaP prostate cancer cells, 1C triggered apoptosis via Bcl-2 family-mediated mitochondria pathway, downregulated expression of mouse double minute 2, upregulated expression of p53 and stimulated ROS production. ROS scavenger, N-acetylcysteine, can attenuate 1C-induced apoptosis. 1C also inhibited the proliferation of LNCaP cells through inhibition on Wnt/β-catenin signaling pathway.
Conclusion: 1C shows obvious anticancer activity based on inducing cell apoptosis by Bcl-2 family-mediated mitochondria pathway and ROS production, inhibiting Wnt/β-catenin signaling pathway. These findings demonstrate that 1C may provide leads as a potential agent for cancer therapy.

1. Introduction

Prostate cancer is a great threat to human health. In the United States, prostate cancer is one of the most frequently diagnosed cancers and the third leading cause of cancer death in men [1]. Anti-androgen drugs can treat prostate cancers, but a lot of patients are more likely to develop androgen-independent tumors; these tumors are generally more aggressive, more resistant to currently used chemotherapeutic agents, and more metastasize than other tumor types [2–4]. Thus, novel therapeutic agents are needed to be developed to improve the treatment outcomes of prostate cancer.

Natural products obtained from medicinal herbs provide a rich source for developing novel anticancer agents and offer abundant and safe parent structures for synthetic drugs. We have recently been interested in evaluating the anticancer activity of modified compounds isolated from *Panax ginseng*. Ginseng is consumed in many countries, particularly in China and other Asian countries, to treat and prevent many diseases, such as cancer [5]. Individuals consume ginseng to reduce risks of cancers [6], including oral cavity, stomach, lung, pancreas, liver, ovary, and colon [7]. *P. ginseng* (Korean ginseng), *P. quinquefolius* (American ginseng), and other associated plants, including *P. notoginseng/pseudoginseng* (*P. notoginseng*, Buck FH Chen), are used to cure some diseases [8]. Ginseng is a widely used medicinal herb in the United States [9]. Although ginsenosides (saponins and triterpene glycosides) are only a part of the complex mixture of compounds present in these

* Corresponding author. School of Functional Food and Wine, Shenyang Pharmaceutical University, No. 103, Wenhua Road, Shenhe District, Shenyang 110016, Liaoning, China; Key Laboratory of Structure-based Drug Design and Discovery of Education, Shenyang Pharmaceurical University, No. 103, Wenhua Road, Shenhe District, Shenyang 110016, Liaoning, China.
E-mail address: zyq4885@126.com (Y.Q. Zhao).

http://dx.doi.org/10.1016/j.jgr.2016.12.014
p1226-8453 e2093-4947/$ – see front matter Copyright © 2017, The Korean Society of Ginseng, Published by Elsevier. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

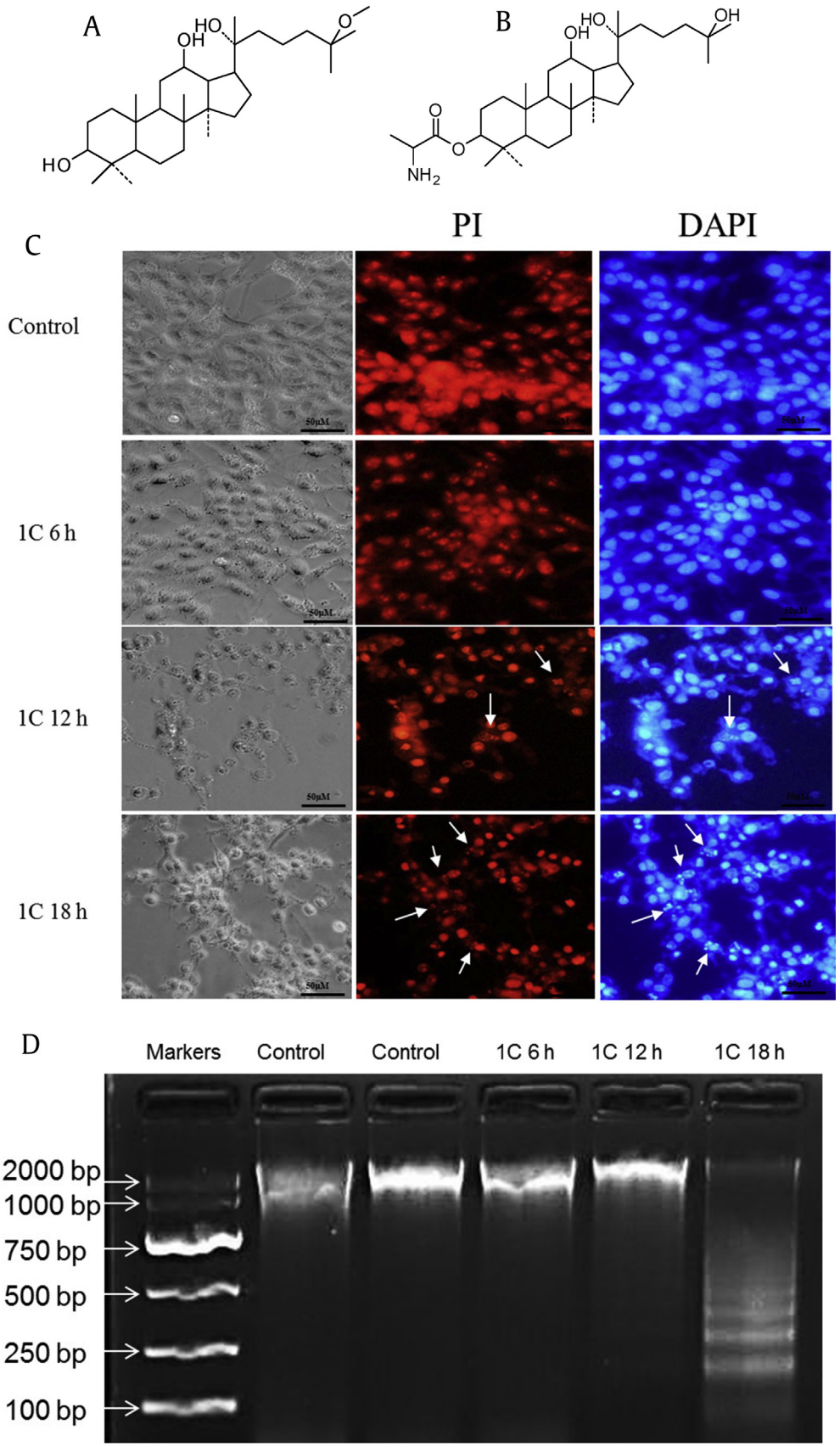

Fig. 1. 1C induced LNCaP cells apoptosis. Structures of (A) 1C and (B) AD-2. (C) The cells of nuclear morphology treated with 1C (25μM) for 0 h, 6 h, 12 h, and 18 h, as observed by a fluorescence microscope following staining with PI and DAPI. (D) DNA fragmentation analysis. DNA were separated in 2% agarose gel and visualized under ultraviolet light after staining with ethidium bromide. (E) Cell cycle analysis by flow cytometry. a (1C, 0h), b (1C, 6h), c (1C, 12h), d (1C, 18h). $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$. (F) The expression levels of apoptosis-related proteins, inducing caspase-9, cleaved-caspase-3, and PARP were examined by Western blotting assay.

Please cite this article in press as: Wang XD, et al., Anticancer activity and potential mechanisms of 1C, a ginseng saponin derivative, on prostate cancer cells, Journal of Ginseng Research (2017), http://dx.doi.org/10.1016/j.jgr.2016.12.014