European Food Research and Technology
https://doi.org/10.1007/s00217-020-03515-x

ORIGINAL PAPER

2-Benzhydrylsulfinyl-N-hydroxyacetamide-Na extracted from fig as a novel cytotoxic and apoptosis inducer in SKOV-3 and AMJ-13 cell lines via P53 and caspase-8 pathway

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Received: 5 March 2020 / Revised: 12 May 2020 / Accepted: 16 May 2020

Abstract

In this study, the fruits of both mature and air-dried figs were exposed to selective sequential extracting processes using soxhlet. Different polarity and non-polarity solvents were used to increase the yield of the isolated extracts. Methanol, ethyl acetate, chloroform, and *n*-hexane were used to precipitate and isolate the effective compound *2-benzhydrylsulfinyl-n-hydroxyacetamide-Na* from 11 extracts and 7 compounds extracted from the organic layer. Various spectral techniques were applied, including UV-spectroscopy, FT-IR, GC-Mass, ^{1}H-NMR, and ^{13}C-NMR for the detection of the precipitate. The aim of current work is to deal with the synthesis of a novel compound *2-benzhydrylsulfinyl-n-hydroxyacetamide-Na* from fig fruit and study its effect as anticancer and anti-proliferative agent against SKOV-3, and AMJ-13 cells. The effect of the active compound on breast cancer cells, ovarian cancer cell proliferation was measured by the MTT assay, while its ability to induce apoptosis was detected using DAPI, acridine orange/ethidium bromide (AO/EtBr) staining, flow cytometry assay and finally mitochondrial membrane potential (MMP). Real-Time PCR was used to detect changes in the expression of mRNA for Bax and Bcl-2, P53, caspase-8, and caspase-9. Treated cancer cells with *2-benzhydrylsulfinyl-n-hydroxyacetamide-Na* significantly increased ROS synthesis, with subsequent reduction of the MMP through mechanisms that included Bax upregulation P^{53}, Caspase-8, and Caspase-9 and Bcl-2 downregulation. The outcomes of the current study show that *2-benzhydrylsulfinyl-n-hydroxyacetamide-Na* extracted from fig fruit suppressed cancers cells' proliferation, resulting in apoptosis as a novel pathway that involves mitochondrial mechanism via activated P53 and caspase-8 signaling. In addition, the extract exerted no toxic effects, neither on serum levels of liver functional enzymes nor on the normal histological architecture of the lungs and spleen. We demonstrated how the *2-benzhydrylsulfinyl-n-hydroxyacetamide-Na* affects cancer cells along with a study the possible mechanisms involved in this effect which is mitochondrial damage and P^{53} pathway. We conclude that *2-benzhydrylsulfinyl-n-hydroxyacetamide-Na* holds a promising potential as an anticancer therapeutic agent.

Keywords *2-Benzhydrylsulfinyl-n-hydroxyacetamide-Na* · Anticancer activity · P53 · Caspase-8

Introduction

Cancer is ranked second among the global causes of death in humans, being a serious threat to health and livelihood [1]. The most common cancers surrounded by women are breast cancer and is another main cause of doom after lung cancer [2]. Breast cancer is triggered by frequent exposure of breast cells to prevalent ovarian hormones [3]. These hazard agents point across endogenous estrogen as possible players in the origination, development and promotion of breast cancer [4]. Amongst the gynecological malignancies, ovarian cancer is the principal cause of death in advanced countries. In spite of the global impact of this disease, the lifetime risk of evolving ovarian cancer in even in the postmenopausal population that

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Published online: 28 May 2020