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Deciphering the DNA-binding affinity, cytotoxicity and apoptosis induce as the anticancer mechanism of Bavachinin: An experimental and computational investigation

Mahvash Farajzadeh Dehkordi [a,b], Sadegh Farhadian [c,d,*], Mohammad Abdolvand [e,f], Ehsan Heidari Soureshjani [g,h], Babak Rahmani [a,b,*], Sina Darzi [i]

[a] Department of Molecular Medicine, Qazvin University of Medical Sciences, Qazvin, Iran
[b] Cellular and Molecular Research Center, Qazvin University of Medical Sciences, Qazvin, Iran
[c] Department of Biology, Faculty of Sciences, Shahrekord University, Shahrekord, Iran
[d] Central Laboratory, Shahrekord University, Shahrekord, Iran
[e] Cellular, Molecular and Genetics Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
[f] Medical Genetics Research Center of Genome, Isfahan University of Medical Sciences, Isfahan, Iran
[g] Young Researchers and Elite Club, Shahrekord Branch, Islamic Azad University, Shahrekord, Iran
[h] Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran, Iran
[i] Health Products Safety Research Center, Qazvin University of Medical Sciences, Qazvin, Iran

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ABSTRACT

One of the most important mechanism by which bioflavonoids can exert their effects in cancer treatment, is through their interaction with bio-macromolecules such as DNA. Recent literature emphasizes the role of Bavachinin (BVC) as an emerging anticancer agent. However, there are no reports on its ability to interact with DNA. The present study investigated the DNA binding properties of BVC by many spectroscopic and computational approaches. The evidences are provided from UV–visible and CD spectral analyses illustrated that BVC interacted with ctDNA through minor groove binding mode. Based on the thermodynamic analyses, it can be inferred that the binding process was spontaneous, and the hydrophobic interaction played a major role in BVC-ctDNA binding. *In silico* molecular docking and dynamic simulation finally strengthened our experimental results that BVC was located in the minor groove (AT- rich) region of B-DNA structure and resulted in the slight alteration in the secondary structure of DNA during the interaction process. Additionally, BVC indicated significant cytotoxicity against MCF-7 breast cancer cells. Furthermore, quantitative analyses demonstrate that BVC treatment significantly increased the expression of pro-apoptotic genes; *p53*, *caspase-3*, *-8*, and *-9* in MCF-7 cells. In order to further investigate the molecular targets of BVC, molecular docking studies indicated a relatively good binding affinity of BVC with pro-apoptotic proteins. In effect, BVC can be considered as a small organic compound with DNA binding property, appropriate cytotoxic activity, and potential of apoptotic inducing that can be adopted for medical science and pharmacy.

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1. Introduction

Cancer is one of the most important diseases. It is characterized by rapid growth of cells and abnormal cell division with the increased rate of DNA synthesis and very fast generation of metabolic energy in tumor cells [1]. Even after extensive research on the identification of cancer and its pathways, it is still a major cause of mortality all over the world [2]. Among the available strategies for cancer treatment, chemotherapy is the most commonly-used approach [3]. Despite the great advances in chemotherapy, chemotherapeutic agents have been limited because of their numerous side effects and drug resistance that lead to failure of treatment. [4]. In order to overcome the problems stated above, recognition of more effective and safer treatment options for cancer management, especially with the natural origin is essential [5]. For over half a century, natural products have

* Corresponding authors at: Department of Biology, Faculty of Science, Shahrekord University, Shahrekord, P. O. Box 115, Iran (S. Farhadian). Department of Molecular Medicine, Qazvin University of Medical Sciences, Qazvin, Iran (B. Rahmani).

E-mail addresses: farhadian@sku.ac.ir (S. Farhadian), b.rahmanigene@gmail.com (B. Rahmani).

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