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Title of the Article	Authors Name	Department	Name of Journal	Year	ISSN/ ISBN
An *in-silico* pharmacophore-based molecular docking study to evaluate the inhibitory potentials of novel fungal triterpenoid Astrakurkurone analogues against a hypothetical mutated main protease of SARS-CoV-2 virus	Anish Nag, Adhiraj Dasgupta, Sutirtha Sengupta, **Tapan Kumar Lai**, Krishnendu Acharya	Chemistry	Computers in Biology and Medicine	2023	0010-4825
Astrakurkurone, a sesquiterpenoid from wild edible mushroom, targets liver cancer cells by modulating Bcl-2 family proteins	Dasgupta, A.; Dey, D.; Ghosh, D.; Lai, T.K.; Bhuvanesh, N.; Dolui, S.; Velayutham, R.; Acharya, K	Chemistry	IUBMB Life	2019	1521-6551
Characterization and inception of a triterpenoid astrakurkurol, as a cytotoxic molecule on human hepatocellular carcinoma cells, Hep3B	Nandi, S.; Chandra, S.; Sikder, R.; Bhattacharya, S.; Ahir, M.; Biswal, D.; Adhikary, A.; Pramanik, N.R.; Lai, T.K.; Drew, M.G.B.; Acharya, K	Chemistry	Journal of Agriculture and Food Chemistry	2019	0021-8561

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Research Communication

Astrakurkurone, a Sesquiterpenoid from Wild Edible Mushroom, Targets Liver Cancer Cells by Modulating Bcl-2 Family Proteins

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Abstract

Induction of apoptosis is the target of choice for modern chemotherapeutic treatment of cancer, where lack of potent "target-specific" drugs has led to extensive research on anticancer compounds from natural sources. In our study, we have used astrakurkurone, a triterpene isolated from wild edible mushroom, *Astraeus hygrometricus*. We have discussed the structure and stability of astrakurkurone employing single-crystal X-ray crystallography and studied its potential apoptogenicity in hepatocellular carcinoma (HCC) cells. Our experiments reveal that it is cytotoxic against the HCC cell lines (Hep 3B and Hep G2) at significantly low doses. Further investigations indicated that astrakurkurone acts by inducing apoptosis in the cells, disrupting mitochondrial membrane potential and inducing the expression of Bcl-2 family proteins, for example, Bax, and the downstream effector caspases 3 and 9. A molecular docking study also predicted direct interactions of the drug with antiapoptotic proteins Bcl-2 and Bcl-xL. Thus, astrakurkurone could become a valuable addition to the conventional repertoire of future anticancer drugs. © 2019 IUBMB Life, 71(7):992–1002, 2019

Keywords: apoptosis; mitochondrial apoptosis; hepatocellular carcinoma; B-cell lymphoma-2 (Bcl-2) family; B-cell lymphoma-2 (Bcl-2); mitochondrial membrane potential; astrakurkurone

INTRODUCTION

Cancer is a well-recognized global health problem responsible for approximately 7.6 million deaths per annum (13% of all deaths) worldwide, which is expected to rise to 13.1 million by 2030 (1). Despite remarkable progress in the field of cancer research, both developing and developed countries are in the grip of this deadly disease, and still there is a need to discover and develop anticancer therapeutic agents. Apart from genetic causes, smoking, heavy metal pollution, and sedentary life style, coupled with increased affinity to low-fiber fast food, also contribute toward a leap in the incidences of cancer (1).

Decades of medical research have given us several treatment strategies for cancer, among which chemotherapy is the major line of choice. Chemotherapy usually targets cellular apoptosis, a pathway intrinsic to all cells. A chemotherapeutic agent can activate apoptosis in several ways, for example, by binding to cell death receptors onto the membrane or by modulating the Bcl-2 (B-cell lymphoma-2) family proteins at the intracellular level, both resulting in the release of cytochrome *c* in the cytosol followed by activation of caspases. The Bcl-2 family includes both proapoptotic and antiapoptotic proteins, and an intricate balance between these proapoptotic and antiapoptotic signals determines the fate of the cells. As the Bcl-2 family of proteins reside upstream of irreversible

Additional Supporting Information may be found in the online version of this article.

Abbreviations: *AO, acridine orange; Bcl-2, B-cell lymphoma-2; BH, Bcl homology domain; DAPI, 4′,6-diamidino-2-phenylindole; DCFDA, 2′,7′-dichlorofluorescein diacetate; DiOC6, 3,3′-dihexyloxacarbocyanine iodide; EB, ethidium bromide; FITC, fluorescein isothiocyanate; HCC, hepatocellular carcinoma; MMP, mitochondrial membrane potential; ROS, reactive oxygen species*

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Characterization and Inception of a Triterpenoid Astrakurkurol, as a Cytotoxic Molecule on Human Hepatocellular Carcinoma Cells, Hep3B

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ABSTRACT: Mushrooms are customary influential sources of pharmaceutically active metabolites. Usually lanostane-type triterpenoids from mushrooms had prospective for cancer disease treatments. Recently, a triterpenoid, astrakurkurol obtained from the fresh basidiocarps of the edible mushroom *Astraeus hygrometricus*, drew attention as a new cytotoxic therapeutic. The structural stability of this triterpenoid had been established with the amalgamation of density functional theory (DFT) calculations and study of single-crystal X-ray diffraction. To successfully manifest astrakurkurol as a potent cytotoxic therapeutics, a wide apprehension on the molecular and cellular mechanisms underlying their action is prerequisite. On this account, our study was directed to scrutinize the influence of this triterpenoid on human hepatocellular cancer cell model Hep3B. Encapsulating all experimental facts revealed that astrakurkurol had significantly decreased cell viability in a concentration-dependent manner. This effect was unveiled to be apoptosis, documented by DNA fragmentation, chromatin condensation, nuclear shrinkage, membrane blebing, and imbalance of cell cycle distribution. Astrakurkurol persuaded the expression of death receptor associated proteins (Fas), which triggered caspase-8 activation following tBid cleavage. Moreover, tBid mediated ROS generation, which triggered mitochondrial dysfunction and activated the mitochondrial apoptotic events. Astrakurkurol cytotoxicity was based on caspase-8-mediated intrinsic apoptotic pathway and was associated with inhibition at Akt and NF-κB pathway. Astrakurkurol had also inhibited the migration of Hep3B cells, indicating its antimigratory potential. These findings led us to introduce astrakurkurol as a feasible and natural source for a safer cytotoxic drug against hepatocellular carcinoma.

KEYWORDS: *astrakurkurol, triterpenoid, edible mushroom, liver cancer, apoptosis, migration*

INTRODUCTION

Cancer as a disease has become a huge concern worldwide, usually emerging from aberrant cells with unconstrained division and incursion through blood and lymph systems to other tissues. In the 21st century, overpowering cancer was one of the utmost challenges faced by mankind.[1] Among all cancers, hepatocellular carcinoma (HCC) is the biggest recurring malignancy on the globe, which accounts for almost 1 million deaths annually worldwide, and the numbers appear to be increasing substantially in America as well as in other developed western countries.[2] Despite major revolutions in modern medicine, the successful diagnosis and effective treatment of cancer still remains a significant challenge.[1] Modern cancer treatment involved chemotherapy, surgery, hormone therapy, radiation therapy, and immune therapy based on the stage of cancer progression,[3] and most of them pose significant toxic effects to unaffected tissue and the body as a whole.[4] Hence, considerable efforts were being given to identify therapeutic approaches appreciably from natural sources as they are more active as well as selective, less toxic with limited side effects, and capable of inhibiting growth and invasion of cancerous cells by simultaneously inducing apoptosis in early stage tumors.

Mushrooms have been consumed and valued for their inimitable taste, nutraceutical properties, and pharmacon utility. Various medicinal mushrooms known from ancient folklore had reports of use in conventional remedy, and fungal metabolites were popularly used to treat a broad range of diseases.[5] The latest studies revealed that there had been an

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NATURAL PRODUCT RESEARCH
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Structural elucidation and antimicrobial activity of a diketopiperazine isolated from a *Bacillus* sp. associated with the marine sponge *Spongia officinalis*

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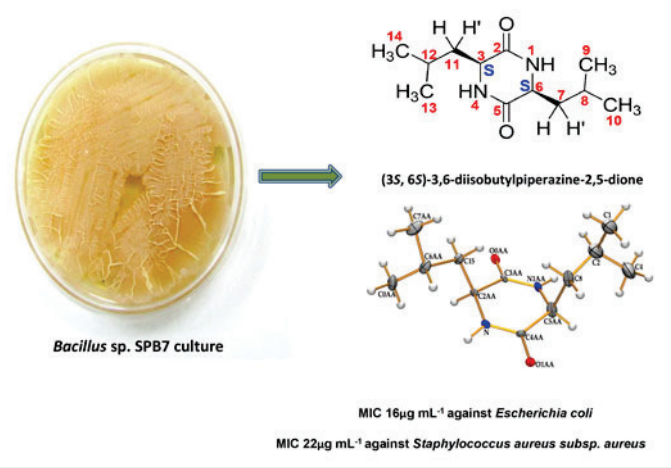
ABSTRACT

A diketopiperazine (3*S*, 6*S*)-3,6-diisobutylpiperazine-2,5-dione was isolated from a sponge-associated microbe for the first time and characterized by FTIR, HRESI-MS, ^{1}H, ^{13}C NMR and 2D NMR. The source is novel for this compound. Single crystal XRD of this diketopiperazine obtained as a natural product was analysed for the first time and its melting point was determined to be 262 °C. MICs of this cyclic dipeptide against *Escherichia coli* and *Staphylococcus aureus subsp. aureus* were 16 μg mL^{-1} and 22 μg mL^{-1} respectively, the first report of antibacterial activity of this diketopiperazine.



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