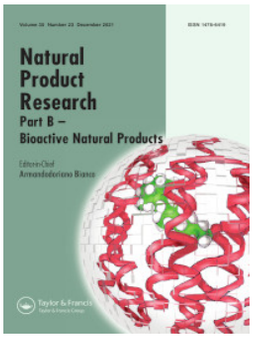

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SHORT COMMUNICATION

Jasminum azoricum L. leaves: HPLC-PDA/MS/MS profiling and *in-vitro* cytotoxicity supported by molecular docking

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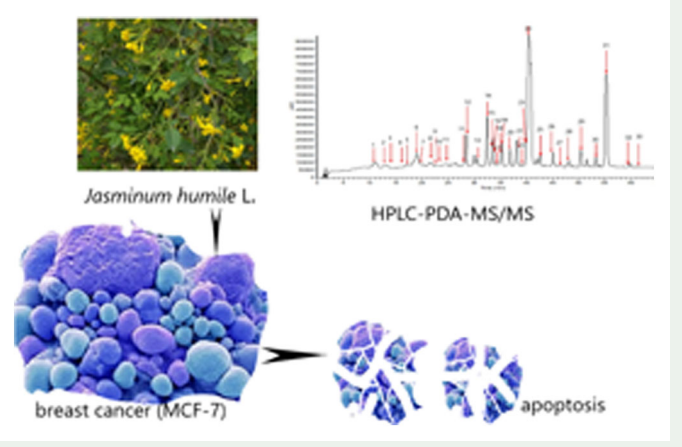
ABSTRACT

In this study chemical profiling of *Jasminum azoricum* L. (*J. azoricum*) using HPLC-PDA/MS/MS and evaluation of its *in-vitro* cytotoxicity towards the human breast cancer cell line (MCF-7), human colorectal cancer cell (HCT-116) and human hepatocellular carcinoma (Huh-7) cell lines. The viability % was determined by the neutral red uptake assay. The study led to the identification of 37 secondary metabolite; major nine compounds were subjected to virtual docking to determine their role in tumour growth inhibition by controlling apoptosis and cancer cell proliferation using the 3D crystal structure of MST3 ligand protein. Two compounds; sambacoside A and molihauside C, showed high-affinity values of (−9.91, −9.57) kcal/mol against MST3 protein. *In silico* prediction of absorption, distribution, metabolism, excretion and toxicity (ADMET) was performed and revealed no mutagenicity, no tumorigenicity and non-irritant actions of both compounds, so *J. azoricum* could be used as a beneficial source for cytotoxic compounds.



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1. Introduction

The screening of natural compounds using molecular docking identifies a primary configuration mechanism of action of a specific compound at the molecular level (Eissa et al. 2016; Hu et al. 2018).

Cancer is the leading cause of death around the world. Hepatocellular carcinoma is the most common form of cancer in patients with chronic liver disorders (Ji et al. 2009). There is a high incidence of breast cancer among women in the Middle East. Colorectal carcinoma is an invasive carcinoma and characterised by a high mutation rate (Collisson et al. 2012).

Jasminum azoricum L., commonly known as lemon-scented jasmine (Mifsud 2002), belongs to the Oleaceae family. It has white flowers and a pleasant aroma. It is found in the Middle East, India, China and Africa. There are limited data available concerning the chemical profile of *Jasminum azoricum* and its pharmacological activities (El-Hawary et al. 2019).

The aim of this study is to assess the *in-vitro* cytotoxic effects of the methanolic extract of *J. azoricum* leaves on MCF-7, HCT-116 and Huh-7 cell lines and identify metabolites by HPLC-PDA-MS/MS. In addition to molecular interactions of identified compounds with MST3 protein to evaluate the cytotoxic activities of major identified compounds.

2. Results and discussion

2.1. Cytotoxic activity

J. azoricum extract showed higher cytotoxicity towards Huh-7 > MCF-7> HCT-116 cell lines with IC_{50} values of 17.41 ± 3.60 μg/ml> 22.81 ± 2.63 μg/ml> 36.52 ± 3.66 μg/ml respectively.

2.2. HPLC-PDA-ESI-MS/MS

HPLC-PDA-ESI-MS/MS of *J. azoricum* leaves led to the identification of different groups of compounds. The major compounds identified were flavonoids (14 compounds) followed by secoiridoids (11 compounds) which were mainly oleoside derivatives and molihauside isomers A, C, E and F, in addition to one iridoid. The simple phenols identified were two phenylethanoid, 8 phenolic acids derivatives and a lignan (olivil hexoside). (Figures S2, S3 and S4) and (Table S1)

2.3. Molecular docking

The major identified compounds were docking them into MST3 protein for the cytotoxicity (Figures S4, S5, S6a, S6b, S7a, S7b), (Table S2). The superior binding capacity of two compounds, sambacoside A and molihauside C **(**each of 5 attachment hydrogen bonds**)** and decreasing the binding free energy of these two compounds with values of 9.91 kcal/mol and 9.57 kcal/mol respectively; were subjected to *in silico* ADMET and carcinogenicity analysis (Table S3).

J. azoricum extract has a potential selective anti-cancer effect in comparison to standard drug etoposide (Figure S1). The results were supported by studying the cytotoxic activities of major identified compounds by docking these identified compounds into MST3 protein, the high-affinity compounds towards the ligand-protein MST3 indicate higher cytotoxic activity, so sambacoside A (a trimeric secoiridoid) and molihauside C (a dimeric secoiridoid) are the most cytotoxic compounds proved by molecular docking.

3. Experimental

The experimental section is available online in supplementary material

4. Conclusion

The results of the study indicated that *Jasminum azoricum* L. is a cytotoxic plant and sambacoside A and molihauside C are considered potent epigenetic regulators on MST3. Further *in- vivo* studies on sambacoside A and molihauside C are needed to configure the mechanism of cytotoxic activity.

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Disclosure statement

The authors declare no conflict of interest.

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