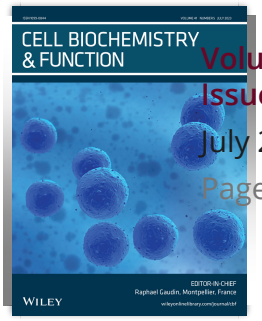
CELL BIOCHEMISTRY & FUNCTION



Volume 41, Issue 5
July 2023
Pages 573-589

RESEARCH ARTICLE

The inhibitory potential of chemical constituents of *Ficus carica* targeting interleukin-6 (IL-6) mediated inflammation

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First published: 24 May 2023 | https://doi.org/10.1002/cbf.3813

Abstract

Inflammation is an innate reaction of the body of an individual when subjected to the noxious factors repeatedly. Pharmacological approaches focused at disrupting cytokine signaling networks have become significant therapeutic alternatives for the treatment of inflammatory illnesses, cancer and autoimmune disorders. High levels of inflammatory mediators, particularly interleukin IL-1, IL-6, IL-18, IL-12, and tumor

References Related Information

Recommended

Activation of interleukin-6 and -8 expressions by methylmercury in human U937 macrophages involves RelA and p50

Megumi Yamamoto, Noureen Khan, Muflihatul Muniroh, Eriko Motomura, Rie Yanagisawa, Takami Matsuyama, Christoph F. A. Vogel

Journal of Applied Toxicology

necrosis factor alpha leads to a cytokine storm in the body. Among all the released cytokines in a patient suffering from inflammatory disorder, IL-6 mediator has a pivotal role in this inflammatory cascade which progresses to a cytokine storm. Therefore, the blockage of the IL-6 inflammatory mediator could be a promising treatment option for the patients with hyper inflammatory conditions. The phytochemicals could provide the new lead compounds against the IL-6 mediator. *Ficus carica* has been the ideal plant of research and investigation due to its commercial, economic and medical importance. The anti-inflammatory properties of *F. carica* were further investigated by in silico and in vivo approaches. The docking scores of Cyanidin-3,5-diglucoside, Kaempferol-7-O-rutinoside, Cyanidin-3-rhamnoglucoside, and Rutin are –9.231, –8.921, –8.840, and –8.335 Kcal/mole respectively. The free energy of binding and stability of the docked complexes of these top four phytochemicals with the IL-6 were further analyzed by Molecular Mechanics-Generalized Born Surface Area and Molecular Dynamic simulations, respectively. The in vivo anti-inflammatory carrageenan-induced rat paw edema model was used for the validation of in silico results. The maximum percentage paw edema inhibition with petroleum ether and ethyl acetate was 70.32% and 45.05%, respectively. The in vivo anti-inflammatory activity confirms the anti-inflammatory potential of *F. carica*. Therefore, it is predicted that Cyanidin-3,5-diglucoside, Kaempferol-7-O-rutinoside, Cyanidin-3-rhamnoglucoside, and Rutin have the potential to inhibit the IL-6 mediator which will aid in mitigating the cytokine storm in patients with acute inflammations.

[Inflammatory cytokine response in sulfur mustard-exposed mouse skin](#)

K. M. Ricketts, C. T. Santai, J. A. France, A. M. Graziosi, T. D. Doyel, M. Y. Gazaway, R. P. Casillas

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Significance statement

The Ficus carica plant has been included in traditional alternative systems of medicine for the treatment of various ailments since the ancient times. Plant leaves and fruits have profound chemical constituents possessing anti-inflammatory activity reported in numerous research publications. The current study is designed to evaluate and investigate further, the anti-inflammatory (IL-6 inhibitory) potential of *F. carica* from both computational (in silico) and in vivo methods for discovery of new and potentially better treatment. Both in vivo and in silico studies justify the IL-6 inhibitory activity of *F. carica* phytochemicals and show that they can prevent the hyper-inflammatory condition known as "cytokine storm" in the patients. The most effective IL-6 inhibitor phytochemicals include Cyanidin-3,5-diglucoside, Kaempferol-7-O-rutinoside, Cyanidin-3-rhamnoglucoside, and Rutin. In the future, these phytochemicals will require further pharmacokinetic and toxicity studies along with clinical trials to provide a new treatment option for patients with acute inflammatory conditions.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

Open Research

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Supporting Information

Filename	Description
cbf3813-sup-0001-Supporting_information_2.docx 2.5 MB	Supporting information.

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