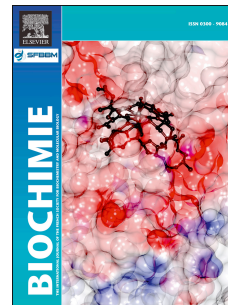


# Accepted Manuscript

S-allyl cysteine as potent anti-gout drug: Insight into the xanthine oxidase inhibition and anti-inflammatory activity

Johnson Preethi, Loganathan Chitra, Iruthayaraj Ancy, Poomani Kumaradhas, Thayumanavan Palvannan



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**Abstract**

S-allyl cysteine (SAC) is known for its various beneficial effects such as neuroprotection and immunomodulation. The beneficial effect of SAC against gout has not been explored. The present study aims to describe the two roles of SAC: (1) inhibitory effect against xanthine oxidase (XO) enzyme activity; and (2) anti-inflammatory property against MSU crystal-induced gouty inflammation in rat. The inhibitory effect of SAC against bovine XO enzyme activity was determined *in vitro*. *In silico* analysis was carried out to determine the intermolecular interaction between SAC and bovine XO. MSU crystal was injected in the right paw of the rat to induce gouty inflammation. SAC (40 mg/kg body weight) and colchicine (positive control; 1 mg/kg body weight) was given for 3 days. At the end of the treatment, the oxidative stress, antioxidant parameters and mitochondrial function were determined in the ankle joint tissue. The concentration of inflammatory cytokines such as TNF- $\alpha$  and IL-1 $\beta$  was measured in the serum using ELISA. SAC inhibited (IC<sub>50</sub> value, 33  $\mu$ g/ml) XO enzyme activity in a competitive mode with corresponding Ki value of 4  $\mu$ g/ml. *In silico* analysis predicted the interaction of SAC with the amino acids such as Arg880, Phe798, Phe914 and Phe1009 of XO enzyme. The root mean square deviation, root mean square fluctuation and free energy calculation values confirmed the stable SAC-XO interaction. The inhibition of SAC on XO enzyme activity in *in vivo* was further confirmed by silkworm model. SAC through reducing oxidative stress, enhancing antioxidants, protecting mitochondrial function has shown anti-inflammatory effect against MSU crystal-induced gout which was observed as reduced level of inflammatory markers in the serum. The medicinal potential of SAC as a preventive agent through its XO inhibitory property as well as curative agent through its anti-inflammatory property against gout has been understood from the present study.

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