Development and biological evaluation of C(60) fulleropyrrolidine-thalidomide dyad as a new anti-inflammation agent

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摘要.

Abstract

Research studies in the field of C60 fullerene derivatives have significantly increased due to the broad range of biological activities that were found for these compounds. We designed and prepared a new C60 fullerene hybrid bearing thalidomide as a potential double-action anti-inflammatory agent, capable of simultaneous inhibition of LPS-induced NO and TNF-α production. The C60 fulleropyrrolidine-thalidomide dyad, CLT, was an effective agent to suppress the release of NO and TNF-α by the LPS-stimulated macrophages RAW 264.7. Ten micromolars of CLT effectively inhibited LPS-induced NO and TNF-α production by 47.3 ± 4.2% and 70.2 ± 4% with respected to the control, respectively. Furthermore, preliminary biochemical investigation revealed that CLT was a potent agent to suppress both LPS-induced intracellular ROS production and iNOS expression, and CLT also inhibited the phosphorylation of ERK which is an important protein kinase involved in the activation of TNF-α synthesis in LPS-activated macrophages. We believed that the studies herein would hold promise for future development of a new generation of potent anti-inflammatory agents.