In vitro and *in silico* evaluation of the immunomodulatory effects of *Laurus nobilis* L. essential oil and eucalyptol on polymorphonuclear neutrophils

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Abstract:

Exaggerated activation of Polymorphonuclear neutrophils (PMNs) can lead to a harmful cycle of persistent inflammation. This study aims to investigate the *in vitro* and *in silico* immunomodulatory effects of *Laurus nobilis* essential oil (LEO) and its main compound eucalyptol on PMNs functions involved in inflammatory processes. The immunomodulation effects of LEO and eucalyptol, have been studied on both, fMLP-PMNs stimulated degranulation and oxidative burst, in addition to their antioxidant, anti-hemolytic and antiplatelet aggregation activities. We also performed an *in silico* analysis for LEO and eucalyptol to evaluate their potential inhibitory pathways. Firstly, we showed that LEO and eucalyptol have immunomodulatory activities on PMNs functions. Thus, LEO and eucalyptol inhibits in a dose-dependent both fMLP-induced degranulation of PMNs with maximal percentages of inhibition of 50.44 % and 74.69 %, respectively and in a same manner, they reduce oxidative burst with maximal percentages of inhibition of 61.07 % and 51.29 %, respectively ($p < 0.001$). Secondly, *in silico* docking of LEO studies showed that its selected major compounds (eucalyptol, α-terpinyl acetate, and β-phellandrene) have an energy change ranging between – 4.2 and – 7.4 kcal/mol on both NADPH oxidase, its subunits and PKC. In addition, LEO and eucalyptol were found to possess a significant antioxidant activity with various IC_{50}, protective capabilities against H_2O_2-induced hemolysis in erythrocytes ($p < 0.001$), and also inhibited collagen-induced platelet aggregation. The collective findings of this research shed light on the immunomodulatory effects on PMNs functions by LEO and eucalyptol that provide new insights to study the mechanism pathways of *Laurus nobilis* L., particularly in the modulation of the innate immunity and the inflammatory responses.

Keywords: Polymorphonuclear neutrophils; Immunomodulatory; Degranulation; Oxidative burst; *Laurus nobilis* L.