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Mode of pancreatic lipase inhibition activity *in vitro* by some flavonoids and non-flavonoid polyphenols

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Abstract

Numerous reports have shown plant metabolites as potential inhibitors of pancreatic lipase (PL). The most notable group is plant polyphenols. However, a limited number of reports diagnosed their mode of inhibition delineating conflicting results. To elucidate the kinetic mode of PL inhibition, some selected flavonoid and non-flavonoid polyphenols standards were first screened for their lipase inhibition potency by their half maximal inhibitory concentration (IC_{50}) followed by inhibition kinetic analysis. Of the phenolics tested, only Gallic acid (GA) and gallol moiety containing epicatechin, viz., Epigallocatechin (EGC) and Epigallocatechin gallate (EGCG) showed, comparative to others, higher PL inhibitions (IC₅₀, 387.2, 237.3, and 391.2 µM respectively). Analysis of enzyme inhibition modalities at various substrate concentrations revealed a dose-dependent inhibition of reaction velocity. Inhibitory rates decreased by the order of EGCG>EGC>GA (Ki, 13.29>35.0>44.61 µM respectively). The results, when verified by visual inspection of Lineweaver-Burk as well as Dixon plots, showed inhibitions of PL by GA, EGC, and EGCG that were best fit to competitive inhibitions. A role of the galloyl moiety in enzyme-inhibitor binding has been evident from their structural resemblance. Depicting it further, ethyl gallate (EG), showed a similar competitive inhibition, therefore, indicating a galloyl moiety driven competitive inhibition of PL.

Keywords: Lipase, *IC*₅₀ value, double-reciprocal plot, inhibition mode, Ki.

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