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Epigallocatechin-3-gallate inhibits the plasma membrane Ca^{2+}-ATPase: effects on calcium homeostasis

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Epigallocatechin-3-gallate (EGCG) and other catechins are the bioactive compounds present in green tea. These bioactives have been shown to be responsible to health benefits of green tea such as antiarthritic and anti-inflammatory effects as well as being involved in the prevention of cardiovascular diseases and cancer, among others. Different studies have shown that EGCG is involved in intracellular calcium (Ca^{2+}) homeostasis in excitable and in non-excitable cells. These findings hint at plasma membrane Ca^{2+}-ATPase (PMCA) involvement, as it transports Ca^{2+} actively to the extracellular medium coupled to ATP hydrolysis, maintaining the cellular homeostasis. The aim of this study was to investigate the catechins effect on the activity of isolated PMCA and the mechanism through which EGCG inhibits PMCA activity in the isolated protein and in living cells.

Results showed that (a) among catechins that inhibited PMCA activity, the most potent inhibitor was EGCG; (b) the measurement of partial reactions of phosphorylation of PMCA showed EGCG produced an increase in EP levels by a decrease in the rate of EP breakdown rather than an increase in the phosphorylation rate; (c) PMCA dephosphorylation was sensitive to ADP favoring the E1P intermediate; (d) docking simulations proposed that EGCG may bind to a site in the A domain; (e) EGCG inhibited PMCA activity in human embryonic kidney cells (HEK293T) that transiently overexpress hPMCA4, suggesting that the effects observed on isolated PMCA occur in living cells.

In conclusion, this study reveals the mechanism by which EGCG inhibits hPMCA4 isoform and shows that EGCG can inhibit PMCA activity in living cells. Therefore, the relevance of our study lies in the fact that the EGCG effects on Ca^{2+} homeostasis may involve the inhibition of PMCA among other mechanisms.

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