

Rottlerin despolariza membrana mitocondrial, reduz ATP celular, ativa AMPK e afeta produção de ROS e é considerado um ineficaz inibidor da PKC delta



Kamala tree – *Mallotus philippinensis*

## **Rottlerin: an inappropriate and ineffective inhibitor of PKCdelta.**

[Soltoff SP.](#)

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### **Source**

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### **Abstract**

Rottlerin has been used as a protein kinase Cdelta (PKCdelta)-selective inhibitor in hundreds of studies, on the basis of initial substrate phosphorylation studies in vitro. However, in more recent studies, rottlerin did not block PKCdelta activity but did block other kinase and non-kinase proteins in vitro and activated multiple Ca(2+)-sensitive K(+) channels with high potency. Rottlerin uncouples mitochondria, and this uncoupling depolarizes the mitochondrial membrane potential, reduces cellular ATP levels, activates 5'-AMP-activated protein kinase (AMPK) and affects mitochondrial production of reactive oxygen species (ROS). Classical mitochondrial uncouplers also produce these secondary changes, and reductions in ATP can block PKCdelta tyrosine phosphorylation and activation and generate effects resembling those produced by direct inhibition of kinase. Rottlerin also has effects in cells in which PKCdelta is downregulated or genetically deleted. These findings indicate that there have been gross misinterpretations in studies using rottlerin as a pharmacological tool to identify PKCdelta-dependent cellular events and indicate that rottlerin should not be used to determine the involvement of PKCdelta in biological processes.

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