ISSN: 2279 - 0594

Journal of Biomedical and Pharmaceutical Research

Available Online at www.jbpr.in

CODEN: - JBPRAU (Source: - American Chemical Society)

Volume 5, Issue 5: September-October;2016, 15-16

Short Communication

Does Rottlerin or its congeners have a potential as adjuvant to antidote therapy of spider/snake venom intoxication?

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Received 18August 2016; Accepted 05September 2016

ABSTRACT

Rottlerin is a polyphenol natural product isolated from the tree Mallotusphilippensis. Rottlerin displays a complex spectrum of pharmacology. Rottlerin has been shown to be an uncoupler of mitochondrial oxidative phosphorylation. It is also known to inhibit the NFAT-5/TonEBP expression. Apart from this it also inhibits thephospholipase A_2(PLA2) and phospholipase D enzyme (PLD). Both these enzymes are found in several venoms of the snakes and spider like the brown spider. Rottlerin has also neuroprotective and cardioprotective properties and thus is an ideal candidate for trial in the anti-dote therapy against the deleterious toxic effects of these venoms in humans. This article discusses the hypothetical possibility of its usage in toxic envenomation.

Keywords: Rottlerin, Phospholipase A2, Phospholipase D, TonEBP, Venom, toxic

Introduction:

Toxic bites from brown spiders (Loxosceles genus) have clinical manifestations including skin necrosis with rapid gravitational spreading, and systemic involvement that may include renal failure, hemolysis, and thrombocytopenia. Venoms of brown spiders in the genus *Loxosceles* contain phospholipase D enzyme toxins that can cause severe dermonecrosis and even death in humans[1]. These toxins cleave the substrates sphingomyelin and lysophosphatidylcholine in mammalian tissues, releasing the choline head group. Similarly, the snake venoms contain both the phospholipase A2 and phospholipase D enzymes[2]. One of the most important protein super-families present in snake venoms are the phospholipases A (PLA_2, E.C. 3.1.1.4), a class of heat-stable and highly homologous enzymes, which catalyse the hydrolysis of the 2-acyl bond of cell membrane phospholipids releasing arachidonic acid and lysophospholipids.There is a significant medical and scientific interest in these enzymes due to their involvement in a variety of inflammatory diseases and accidents caused by venomous animals. Ever since the first PLA_2activity was observed in NajaNajasnake venom, PLA_2s were characterized as the major component of snake venoms, being responsible for several pathophysiological effects caused by snake envenomation, such as neurotoxic, cardiotoxic, myotoxic, cytotoxic, hypotensive and anti-coagulant activities. On the other hand, Rottlerin is known to improve myocardial perfusion and cell viability[3]. These responses could partially be due to its effects on the NFAT-5. It is also a neuroprotectant and prevents neural and neurite**lossand in particular it was demonstrated that the rottlerin protects against MPTP-induced motor deficits, striatal dopamine depletion, and nigral dopaminergic neuronal loss[4].** Moreover, bradykininduced PLA_2 expression was attenuated by rottlerin, suggesting that the PLA_2 enzyme is amenable to its actions andmight be useful in its anti-venom responses[5,6]. Rottlerin also inhibits phospholipase D expression and thus rottlerin*per se* and its congeners like the tetrahydrorottlerin can be exploited for usage as adjuvant in the treatment of spider and snake envenomation and much more research work and experimental trials are required for this idea to be implemented[7].

Conclusion: It is suggested that Rottlerin because of its cardio/neuroprotective action and inhibitory effect on PLA_2/PLD enzymes can be used as an adjuvant in the treatment of spider/snake venom intoxication.

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