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## **Palmitoylethanolamide, endocannabinoids and related cannabimimetic compounds in protection against tissue inflammation and pain: potential use in companion animals.**

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### **Abstract**

Endocannabinoids have analgesic/anti-inflammatory properties. The biology of endocannabinoids, their receptors, signalling mechanisms and role in the regulation of physiological processes have been extensively reviewed. This review focuses on the role of palmitoylethanolamide (PEA), an endogenous fatty acid amide analogue of the endocannabinoid anandamide, in tissue protective mechanisms. PEA was first identified almost five decades ago in lipid extracts of various natural products, and its anti-inflammatory and antinociceptive effects were established later. Evidence exists that PEA is synthesised during inflammation and tissue damage and a number of beneficial effects, including the relief of inflammation and pruritus, have been shown to be useful in the control of neurogenic and neuropathic pain. The postulated hypotheses as to the mode of action of PEA include a possible local autacoid-like mediator activity regulating mast-cell activity and putative activation of cannabinoids and vanilloid TRPV1 receptors via "entourage" effects. The large number of scientific investigations into the effects of PEA and PEA-related compounds has given rise to new therapeutic opportunities. In spite of the multitude of therapies currently employed to control inflammation, pain, pruritus and tissue damage, the possibility of using a natural compound, such as PEA to manipulate endogenous protective mechanisms may be considered a beneficial novel therapeutic strategy in veterinary medicine.

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