

Abstract

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Biosynthesis of oleamide.

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BACKGROUND: Oleamide (cis-9-octadecenamide) is the prototype long chain primary fatty acid amide lipid messenger. The natural occurrence of oleamide was first reported in human serum in 1989. Subsequently oleamide was shown to accumulate in the cerebrospinal fluid of sleep-deprived cats and to induce sleep when administered to experimental animals. Accordingly, oleamide first became known for its potential role in the mechanisms that mediate the drive to sleep. Oleamide also has profound effects on thermoregulation and acts as an analgesic in several models of experimental pain. Although these important pharmacologic effects are well established, the biochemical mechanism for the synthesis of oleamide has not yet been defined.

SUMMARY OF FINDINGS: This chapter reviews the biosynthetic pathways that have been proposed and highlights two mechanisms which are most supported by experimental evidence: the generation of oleamide from oleoylglycine by the neuropeptide processing enzyme, peptidylglycine alpha-amidating monooxygenase (PAM), and alternatively, the direct amidation of oleic acid via oleoyl coenzyme A by cytochrome c using ammonia as the nitrogen source. The latter mechanism is discussed in the context of apoptosis where oleamide may play a role in regulating gap junction communication. Lastly, several considerations and caveats pertinent to the future study oleamide biosynthesis are discussed.

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