Pharmacol Rev. 2010 Mar;62(1):136-54. Epub 2010 Feb 4.

Oxidation of the endogenous cannabinoid arachidonoyl ethanolamide by the cytochrome P450 monooxygenases: physiological and pharmacological implications.

Snider NT, Walker VJ, Hollenberg PF.

Department of Molecular & Integrative Physiology, University of Michigan School of Medicine, 7720 Medical Science II, 1301 E. Catherine Street, Ann Arbor, MI 48109-5622, USA.
nsnider@umich.edu

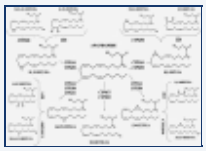
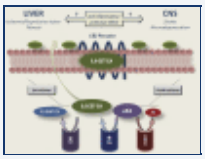
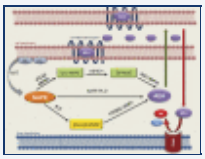
Abstract

Arachidonoyl ethanolamide (anandamide) is an endogenous amide of arachidonic acid and an important signaling mediator of the endocannabinoid system. Given its numerous roles in maintaining normal physiological function and modulating pathophysiological responses throughout the body, the endocannabinoid system is an important pharmacological target amenable to manipulation directly by cannabinoid receptor ligands or indirectly by drugs that alter endocannabinoid synthesis and inactivation. The latter approach has the possible advantage of more selectivity, thus there is the potential for fewer untoward effects like those that are traditionally associated with cannabinoid receptor ligands. In that regard, inhibitors of the principal inactivating enzyme for anandamide, fatty acid amide hydrolase (FAAH), are currently in development for the treatment of pain and inflammation. However, several pathways involved in anandamide synthesis, metabolism, and inactivation all need to be taken into account when evaluating the effects of FAAH inhibitors and similar agents in preclinical models and assessing their clinical potential. Anandamide undergoes oxidation by several human **cytochrome** P450 (P450) enzymes, including CYP3A4, CYP4F2, CYP4X1, and the highly polymorphic **CYP2D6**, forming numerous structurally diverse lipids, which are likely to have important physiological roles, as evidenced by the demonstration that a P450-derived epoxide of anandamide is a potent agonist for the cannabinoid receptor 2. The focus of this review is to emphasize the need for a better understanding of the P450-mediated pathways of the metabolism of anandamide, because these are likely to be important in mediating endocannabinoid signaling as well as the pharmacological responses to endocannabinoid-targeting drugs.

PMID: 20133390 [PubMed - indexed for MEDLINE] PMCID: PMC2835397

Images from this publication. See all images (3)

Free text

Publication Types, MeSH Terms, Substances, Grant Support

LinkOut - more resources