



Review

## Biochemistry, biology and chemistry of the 5-lipoxygenase product 5-oxo-EETE

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### Abstract

5-Oxo-EETE (5-oxo-6,8,11,14-eicosatetraenoic acid) is an arachidonic acid metabolite formed by the oxidation of 5S-hydroxy-6,8,11,14-eicosatetraenoic acid (5-HETE) by 5-hydroxyeicosanoid dehydrogenase (5-HEDH), a microsomal enzyme found in leukocytes and platelets. 5-HEDH is highly selective for 5S-HETE, and displays little activity for other monohydroxy metabolites of arachidonic acid. The synthesis of 5-oxo-EETE requires NADP<sup>+</sup> and can be stimulated by activation of the respiratory burst and by oxidative stress. 5-Oxo-EETE is a chemoattractant for eosinophils and neutrophils, and elicits a variety of responses in these cells, including actin polymerization, calcium mobilization, integrin expression, and degranulation. Its primary target appears to be the eosinophil, and among lipid mediators it is the strongest chemoattractant for these cells. It is also a chemoattractant for monocytes and stimulates the proliferation of prostate tumor cells. Its actions are mediated by a G<sub>i</sub> protein-coupled receptor (OXE receptor) that is highly expressed by eosinophils > neutrophils > monocytes. When administered *in vivo* in both humans and rodents it elicits tissue eosinophilia, suggesting that it may be an important mediator in allergic diseases such as asthma, and that the development of drugs designed to prevent its formation or effects may be useful therapeutic agents in these diseases.

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## Nomenclature

5-HEDH	5-hydroxyeicosanoid dehydrogenase
5-HETE	5 <i>S</i> -hydroxy-6 <i>E</i> ,8 <i>Z</i> ,11 <i>Z</i> ,14 <i>Z</i> -eicosatetraenoic acid
5-HpETE	5 <i>S</i> -hydroperoxy-6 <i>E</i> ,8 <i>Z</i> ,11 <i>Z</i> ,14 <i>Z</i> -eicosatetraenoic acid
5-LO	5-lipoxygenase
5-oxo-15-HETE	15-hydroxy-6 <i>E</i> ,8 <i>Z</i> ,11 <i>Z</i> ,13 <i>E</i> -eicosatetraenoic acid
5-oxo-ETE	5-oxo-6 <i>E</i> ,8 <i>Z</i> ,11 <i>Z</i> ,14 <i>Z</i> -eicosatetraenoic acid
5-oxo-ETrE	5-oxo-8 <i>Z</i> ,11 <i>Z</i> ,14 <i>Z</i> -eicosatrienoic acid (6,7-dihydro-5-oxo-ETE)
AA	arachidonic acid
cPLA <sub>2</sub>	cytosolic phospholipase A <sub>2</sub>
diHETE	dihydroxyeicosatetraenoic acid
ECL	eosinophil chemotactic lipid
FLAP	5-LO activating protein
FOG <sub>7</sub>	5-oxo-7-glutathionyl-8,11,14-eicosatrienoic acid
GM-CSF	granulocyte-macrophage colony stimulating factor
LT	leukotriene
PAF	platelet-activating factor
PG	prostaglandin
PKC	protein kinase C
PMA	phorbol myristate acetate
PPP	pentose phosphate pathway
TX	thromboxane

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