Bioavailable Dual sEH/PDE4 Inhibitor for Inflammatory Pain

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CONTACT

Amir J. Kallas
ajkallas@ucdavis.edu
tel: .

INVENTORS

- Bloecher, Rene
- Hammock, Bruce D.
- Harris, Todd R.
- Morisseau, Christophe H.
- Reddy, Gopireddy
- Wagner, Karen M.
- Xiang, Yang

OTHER INFORMATION

KEYWORDS

soluble epoxide hydrolase, sEH, phosphodiesterase 4, PDE4, dual inhibitor, endogenous cytochrome P450s derived epoxy-fatty acids, CYP450, EpFAs, epoxyeicosatrienoic acids, EETs, arachidonic acid

ABSTRACT

Researchers at the University of California, Davis, have developed a dual soluble epoxide hydrolase (sEH)/ phosphodiesterase 4 (PDE4) inhibitor for the treatment of inflammatory pain.

FULL DESCRIPTION

Soluble epoxide hydrolase (sEH) is an enzyme that metabolizes endogenous cytochrome P450s (CYP450) derived epoxy-fatty acids (EpFAs). Inhibition of sEH elevates EpFA levels, which has anti-hypertensive, anti-inflammatory, and analgesic properties. In general, however, the bioavailability of potent sEH inhibitors is poor while efforts to improve pharmacokinetics results in decreased potency.

Phosphodiesterase 4 (PDE4) is an enzyme involved in the inflammatory response in immune cells and is a major target for inflammatory diseases such as psoriasis, psoriatic arthritis, chronic obstructive pulmonary diseases, and asthma. PDE4 activation is also correlated with symptoms of neuronal disorders such as depression, schizophrenia and Alzheimer's disease. Currently, PDE4 Inhibitors are used to block the PDE4 enzyme in inflammatory pain therapies but have limited use due to side effects such as nausea and vasculitis.

Researchers at the University of California, Davis, have developed a new drug that inhibits both soluble epoxide hydrolase (sEH) and phosphodiesterase 4 (PDE4). This drug has been shown to reduce inflammatory pain in rats after oral application. Co-administration of PDE4 and sEH inhibitors resulted in an enhanced analgesic effect compared to the individual treatment and, by inhibiting both enzymes, the new sEH/PDE4 dual compound has the potential to provide rapid relief of inflammatory pain while improving bioavailability, mitigating vasculitis and limiting side effects such as nausea. Additionally, based on the current knowledge of the involved single targets and their inhibitors, diseases such as hypertension, COPD, neuropathic pain and depression could also potentially be addressed by this compound.

APPLICATIONS

- Inflammatory diseases such as psoriasis, psoriatic arthritis, chronic obstructive pulmonary diseases, and asthma
- Neuropathic pain
- Hypertension
- Depression

FEATURES/BENEFITS

- Orally bioavailable
- Synergistic analgesic effect
- Potent dual ligands with IC_{50} values ranging from subnano to submicromolar concentrations

RELATED MATERIALS

- Blöcher, René et al. "Orally Available Soluble Epoxide Hydrolase/Phosphodiesterase 4 Dual Inhibitor Treats Inflammatory Pain." Journal of Medicinal Chemistry. EPub 03 Apr 2018. doi: 10.1021/acs.jmedchem.7b01804. - 04/03/2018

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Published Application	20010395202	12/23/2001	2018-039

CATEGORIZED AS

- **Medical**
  - Disease: Autoimmune and Inflammation
  - New Chemical Entities, Drug Leads
  - Therapeutics

RELATED CASES

2018-039-0

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Method of Preventing Bone Loss and Periodontal Disease
- Multi-Target Inhibitors for Pain Treatment
- Improved Dioxin Detection and Measurement
- Detection System for Small Molecules
- Small Molecule sEH Inhibitors to Treat Alpha-Synuclein Neurodegenerative Disorders
- Soluble Epoxide Hydrolase-Conditioned Stem Cells for Cardiac Cell-Based Therapy
- Beneficial Effects of Novel Inhibitors of Soluble Epoxide Hydrolase as Adjuvant Treatment for Cardiac Cell-Based Therapy
- Antibodies: Bacillus Delta Endotoxin PAbs
- Antibodies: Bromacil Herbicide PAbs
- Novel Neuropathy Treatment Using Soluble Epoxide Inhibitors
- Novel and Specific Inhibitors of p21
- Antibodies for Pseudomonas (P.) aeruginosa
- Antibodies: Urea Herbicide Pabs
- Chemical Synthesis of Lipid Mediator 22-HDoHE and Structural Analogs
- Antibodies: Triazine Herbicide Pabs
- Optimized Non-Addictive Biologics Targeting Sodium Channels Involved In Pain Signaling
- Soluble Epoxide Hydrolase Inhibitors For The Treatment Of Arrhythmogenic Cardiomyopathy And Related Diseases
- A New Pharmaceutical Therapy Target for Depression and Other Central Nervous System Diseases

University of California, Davis
Technology Transfer Office
1 Shields Avenue, Mrak Hall 4th Floor,
Davis,CA 95616

Tel:
530.754.8649
techtransfer@ucdavis.edu
https://research.ucdavis.edu/technology-transfer/
Fax:
530.754.7620