# A class of small-molecule therapeutics for hypertension and inflammatory diseases

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Technology description

Summary

Epoxyeicosatrienoic acids (EETs) are lipid metabolites that regulate blood pressure and inflammation. EETs are metabolized by soluble epoxide hydrolase (sEH); therefore, inhibition of sEH may treat hypertension and other medical conditions caused by irregularities in blood pressure, vasodilation, endothelial cell function, and inflammation. However, treatments for these conditions, based on this strategy, do not currently exist because the best-known inhibitors of sEH have poor bioavailability. This technology is a class of potent sEH inhibitors with improved biocompatibility. These inhibitors may potentially be used to treat hypertension, metabolic syndrome, atherosclerosis, erectile dysfunction, stroke, diabetes, and aging in humans. Additionally, these inhibitors may be used to treat laminitis disease in horses.

## Non-urea-based sEH inhibitors preserve functionality of lipids that regulate blood pressure and inflammation

The most potent sEH inhibitors are urea-based and are readily metabolized in vivo, limiting their use as pharmaceuticals. The inhibitors described by this technology are based on a stronger and less metabolically active chemical functionality, and are thus more attractive drug candidates. These small molecules are potent inhibitors of sEH in low nanomolar concentrations (IC50's < 2 nM).

Studies investigating the pharmacokinetic profile of these molecules are currently underway.

Tech Ventures Reference: IR 2436

## Publications

Pecic S, Pakhomova S, Newcomer ME, Morisseau C, Hammock BD, Zhu Z, Rinderspacher A, Deng SX. "Synthesis and structure-activity relationship of piperidine-derived non-urea soluble epoxide hydrolase inhibitors." Bioorg Med Chem Lett. 2013 Jan 15;23(2):417-21.

Pecic S, Deng SX, Morisseau C, Hammock BD, Landry DW. "Design, synthesis and evaluation of non-urea inhibitors of soluble epoxide hydrolase." Bioorg Med Chem Lett. 2012 Jan 1;22(1):601-5.

Xie Y, Liu Y, Gong G, Smith DH, Yan F, Rinderspacher A, Feng Y, Zhu Z, Li X, Deng SX, Branden L, Vidovic D, Chung C, Schuerer S, Morisseau C, Hammock BD, Landry DW. "Discovery of potent non-urea inhibitors of soluble epoxide hydrolase." Bioorg Med Chem Lett. 2009 Apr 15;19(8):2354-9.

## Application area

Treatment for hypertension

Treatment for inflammation

Treatment for metabolic syndrome and syndrome X

Treatment for erectile dysfunction

Treatment for atherosclerosis

Treatment for stroke

Preventative treatment for stroke and diabetes

Potential anti-aging treatment

## Advantages

Novel approach to treatment of hypertension

No treatments for metabolic syndrome currently exist

Improved bioavailability and potentially improved pharmacokinetic profile

## Institution

Columbia University

## Inventors

Stevan Pecic


联系我们

叶先生

电 话：021-65679356

手 机：13414935137

邮 箱：yeyingsheng@zf-ym.com