



Yohimbine Derivatives for the Treatment of Raynaud's Phenomenon

The Technology

Raynaud's Phenomenon is a condition in which exposure to cold temperatures decreases blood flow to the extremities. Often associated with systemic sclerosis (scleroderma), the reduction in blood flow can eventually lead to necrosis or gangrene of the fingertips, with significant effects on quality-of-life. Current research has shown that the α_2c adrenergic receptor is responsible for cold-induced vasoconstriction, but in the absence of specific inhibitors, pharmacological treatment has focused on using non-specific agents, such as antihypertensive drugs, to control vasospasm. Unsurprisingly, these treatments often have undesirable side effects due to their systemic actions.

Researchers at the University of Tennessee and the University of Mississippi have discovered that bivalent yohimbine is a highly selective α_2c adrenergic receptor antagonist and have created novel derivatives. Whereas monomeric yohimbine is selective for α_2 -AR but not specific between α_2 -AR subtypes, select yohimbine dimers were found to be highly specific for the α_2c -AR. Antagonistic activity was demonstrated *in vitro* at sub- μ M concentration and vasodilatory activity was demonstrated *in vivo* (mouse studies). In the course of studying these yohimbine dimers, the researchers have also developed a series of monomeric yohimbine derivatives which are also highly subtype selective, with antagonistic activity 40 to 2000 times more potent against α_2c than either α_2a or α_2b .

Related publications:

- [J Pharmacol Exp Ther. 2006 Nov;319\(2\):739-48.](#)
- [Bioorg Med Chem Lett. 2005 Jun 2;15\(11\):2758-60](#)

Benefits

- Expected to reduce side effects by targeting the Raynaud's-specific adrenergic receptor subtype
- Reduced research and development costs as well as reduced time to market, as chemistry is proven and simple to implement.
- Issued patent with broad claims to yohimbine dimers

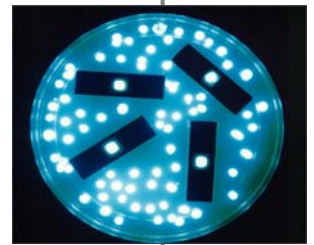
The Inventor

Dr. Duane Miller is the Harriett S. Van Vleet Professor, the Associate Dean for Research and Graduate Programs, and the Chair of the Department of Pharmaceutical Sciences in the College of Pharmacy at the University of Tennessee Health Sciences Center. In addition to his extensive record of academic research, his work has also been used as the foundation for two startup companies, and is a fundamental platform technology for a third.

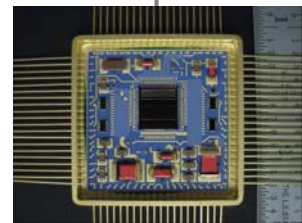
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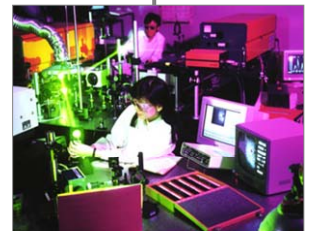
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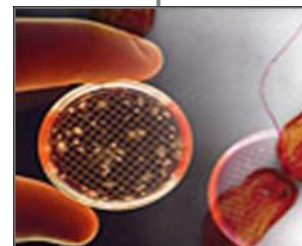
ENGINEERING



MATERIALS



MEDICINE





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Patents

- One issued US patent (6,638,943) and one pending application

Contact

The University of Tennessee Research Foundation (UTRF) is a non-profit corporation responsible for commercializing University of Tennessee technologies and for supporting University research. UTRF is seeking parties interested in learning more about this technology and in exploring possible research and/or commercialization arrangements.

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