Novel Compounds for the Treatment of Alcohol Addiction and Anxiety

OTT ID #1147

TECHNOLOGY

The inventors have developed novel aza-beta carboline compounds that are useful for the treatment of several diseases and conditions including chemical addiction (alcohol, nicotine, and opioids), anhedonia, anxiety, and other conditions associated with withdrawal. These compounds are designed to bind selectively to the α1 subtype $GABA_A$ receptor. Evidence has shown that the α1 $GABA_A$ receptor subtype in the striato-pallidal and extended amygdala system regions of the brain regulates alcohol seeking behaviors. GABA systems have been implicated in both the physical/somatic and the motivational symptoms of ethanol withdrawal. Alcohol dependence and anxiety frequently co-occur in psychiatric patients and can significantly complicate treatment outcomes. It has been found that those with anxiety disorders are more likely to be diagnosed with alcohol dependence. The inventors have shown that α1-preferring ligands reduce ethanol intake and produce anxiolysis in alcoholic rats. The lead compounds also show a reduced capacity to potentiate GABA in *Xenopus* oocytes and HEK cells assays, demonstrate fewer sedative effects with alcohol, and can antagonize the reinforcing actions of alcohol in both nondependent and dependent rats. Recent experiments in primates show that 3-PBC, the lead compound for the design of these aza-beta carbolines, diminished alcohol self-administration and craving.

Drug addiction is a disease that affects brain circuits involved in reward and motivation, learning and memory, and inhibitory control over behavior. Drug and alcohol dependence remain a significant public health concern. These addictions impact the physical and mental well-being, family structure, and occupational stability of those affected. Some efficacy has been observed with current medications for alcoholism, opiate addiction, and nicotine addiction, but for the most part the effect has been limited. Opioid antagonists can be dysphoric or anxiogenic in some patients. Classically used benzodiazepine α1 agonists are addictive, sedating, ataxic, and amnesic. Patient compliance is also often a problem due to the anxiety and depression experienced during withdrawal. Alcohol-dependent individuals represent a heterogeneous group, and it is unlikely that a single pharmacological treatment will be effective for all alcoholics. It is predicted that genetic variation will emerge as an important factor in substance abuse treatments, thus the addition of multiple appropriately targeted novel treatments will be critical in improving patient outcomes.

FEATURES/BENEFITS

- **More Specific** – Compounds targeted to the α1 subunit of the GABA receptor
- **Less Sedation** – Lead compounds show fewer sedative effects with alcohol
- **Reduced Anxiety** – Animal studies demonstrate anxiolysis
- **Unmet Medical Need** – Current medications for chemical abuse are limited in effect

INTELLECTUAL PROPERTY

U.S. Utility Patent 8,268,854; Aza-Beta Carbolines and Methods of Using Same

This technology is part of an active and ongoing research program and is seeking partners for development of the final product. It is available for developmental research support/licensing under either exclusive or non-exclusive terms.

UWM RESEARCH FOUNDATION

Technology Overview

MARKETS

Over 14 million people in the U.S. have an alcohol addiction, and the condition affects more than 12% of the population at some point during life. The costs of alcohol abuse in the U.S. were estimated to be $185 billion in 1998. In the U.S. more than 13,000 specialized drug treatment facilities provide counseling and medical treatment to persons with substance abuse disorders in addition to those treated in physician's offices and mental health clinics. Alcohol withdrawal delirium will result in the death of 1 out of every 5 alcoholics who stop drinking without professional medical intervention.

According to BCC research reports, the U.S. market for substance abuse treatment and diagnosis should reach $3.1 billion in 2013 with a compound annual growth rate of 2.7%. Pharmaceutical treatments have the largest share with an estimate of $2.8 billion in 2013. Recent health care reform has mandated that health insurance coverage for mental health illnesses include drug and alcohol disorders, making treatments more widely available to the public. In 2014 the Mental Health Parity Act's reach will also extend to include small group insurance plans and plans for individuals. There is clearly a need for safe and effective therapies to fill the medication void.

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PUBLICATIONS

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INVENTORS

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Dr. James Cook is a University Distinguished Professor in the Department of Chemistry & Biochemistry at the University of Wisconsin-Milwaukee. He obtained his Ph.D. in Organic Chemistry from the University of Michigan followed by postdoctoral research at the University of British Columbia. Professor Cook's group works in several fields including Natural Products, Medicinal Chemistry, and Organic Synthesis. A large focus of the Cook laboratory revolves around anti-anxiety drugs. However, his laboratory is currently seeking drugs to treat schizophrenia as well as alcohol abuse. In a related program, they have a compound in pre-clinical development for Alzheimers disease. His goal is to create drugs that are better and safer than those currently on the market.

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