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<sub>A</sub> receptor. Evidence has shown that the α1 GABA<sub>A</sub> 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-prefering 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.

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.

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.
MARKETS
The National Council on Alcoholism and Drug Dependency estimates that over 23 million Americans (age 12 and older) are addicted to alcohol and other drugs. According to the Substance Abuse and Mental Health Services Administration (SAMHSA), just under 11% (2.5 million) received care at an addiction treatment facility in 2012. SAMHSA also estimates that the market for addiction treatment is about $35 billion per year. Six in 10 American adults take prescription drugs, creating a vast market for new meds to treat the side effects of the old ones. Opioid prescriptions alone have skyrocketed from 112 million in 1992 to nearly 249 million in 2015, the latest year for which numbers are available, and America’s dependence on the drugs has reached crisis levels. Millions are addicted to or abusing prescription painkillers such as OxyContin, Vicodin and Percocet. Statistics from the Centers for Disease Control and Prevention show that, from 1999 to 2014, more than 165,000 people died in the United States from prescription-opioid overdoses, which have contributed to a startling increase in early mortality among whites, particularly women — a devastating toll that has hit hardest in small towns and rural areas.

The market for substance abuse treatment in the U.S., is projected to progress to $12 billion by 2024.

PUBLICATIONS
Kaminski, B., et al. Effects of the benzodiazepine GABA_A α1 selective ligand, 3-propoxy- β-carboline hydrochloride (3-PBC), on alcohol seeking and self-administration in baboons. Psychopharmacology, manuscript submitted.


INVENTORS
James Cook, Ph.D., Michael Van Linn, Ph.D., Wenyuan Yin, Ph.D.

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. His goal is to create drugs that are better and safer than those currently on the market.

For further information please contact:
Jessica Silvaggi, Ph.D.
Senior Licensing Manager
UWM Research Foundation
1440 East North Avenue
Milwaukee, WI 53202
Tel: 414-906-4654
Please reference: OTT ID. 1147