Novel Compounds for Treatment of Alcohol Addiction and Anxiety

(OTT ID 1147)

Inventor: James Cook, Ph.D.
Dep't of Chemistry and Biochemistry
UW-Milwaukee

Smruti Patil, Ph.D., IPMM
Licensing Associate
1440 East North Ave.
Milwaukee, WI 53202
Tel: 414-906-4657
smruti@uwmrf.org

Problems

- Opioid antagonists employed for the treatment of alcohol abuse can cause mood disorders, depression, anxiety, and dysphoria
- Addiction to the medications are common
- Anxiety and depression during withdrawal
- Patient compliance is a severe problem
- Classical benzodiazepines employed to treat alcohol abuse are sedating, ataxic, and amnesic with abuse liabilities
- SSRIs employed in treatment of alcoholism are limited because they cause sexual dysfunction in many patients and take 3-4 weeks to take effect; they also cause anxiety in some patients

Solutions to the Problem

- The inventors have developed novel aza-beta carboline compounds useful in chemical addiction, anhedonia, anxiety, and other conditions associated with withdrawal from alcohol
- Compounds specifically target the alpha 1 subunit of the GABA(A) receptor
- Alpha 1-preferring antagonists have been shown to reduce ethanol intake, reduce craving (baboon study), and reduce any anxiety/anhedonia during withdrawal in P and HAD rats

Development of Novel $GABA_A$ Subtype Specific Agents

- To elucidate the role of specific $GABA_A$/benzodiazepine receptor subtypes in regulating alcohol reinforcement, a number of active-carbolines have been synthesized and evaluated
- Preliminary studies with the benzodiazepine receptor antagonists, 3-propoxy-beta-carboline (3-PβC) and beta-carboline-3-carboxylic acid *t*-butyl ester (βCCt), was carried out to examine the role of α1 receptor subtypes within the ventral pallidum (VP) on alcohol self-administration
- Examination of the data indicated a reduced rate in alcohol self-administration in P and HAD rats as well as reduced alcohol consumption and increased latency to gain access to alcohol in baboons
- Studies on 3-PβC (administered as the HCl salt) indicated that it was active against alcohol craving in baboons

Key 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
- **Animal Models for Addiction** – Available on request

Intellectual Property and Licensing

- U.S. Utility Patent 8,268,854

  Aza-Beta Carbolines and Methods of Using Same. Issues on 09/18/2012

Current Status

- Technology is available for licensing under exclusive or non-exclusive terms
- Looking for a development partner to aid in the development of a final product

In Summary

- The results of the present study demonstrate that the α1 selective ligands βCCt and 3-PBC · HCl are highly effective in suppressing ethanol responding in P and HAD rats
- βCCt and 3-PBC are highly effective anti-anxiety agents in P and HAD rats but not normal rats
- βCCt and 3-PBC are equally effective orally as Naltrexone when administered acutely; furthermore, βCCt and 3-PBC remain effective 24 hours post administration, unlike Naltrexone
- The α1 receptor clearly plays a role in alcohol-motivated behaviors; however, it also plays a role in normal ingestive behaviors
- βCCt and 3-PBC may represent prototypes of novel pharmacotherapeutic agents that can be used to treat alcohol abuse and alcoholism

Novel Compounds for Treatment of Alcohol Addiction and Anxiety

(OTT ID 1147)

Inventor: James Cook, Ph.D.
Dep't of Chemistry and Biochemistry
UW-Milwaukee

For further information please contact:

Smruti Patil, Ph.D., IPMM
Licensing Associate
1440 East North Ave.
Milwaukee, WI 53202
Tel: 414-906-4657
smruti@uwmrf.org