Research & Innovation Services (RIS)

UNIVERSITY OF BATH

NOVEL ORVINOL COMPOUNDS

For the treatment of anxiety, depression and polydrug abuse

TECHNOLOGY

Researchers at the University of Bath have designed a series of compounds combining the beneficial effects of buprenorphine and naltrexone for the treatment of poly drug abuse, anxiety and depression.

Buprenorphine is well established as a treatment for opiate abuse. Buprenorphine displays complex pharmacology, it is a partial mu opioid receptor (MOPr) agonist (depending on the assay it can be an agonist or antagonist) and has low or no efficacy at kappa opioid receptors (KOPr) and delta opioid receptors. It is also a partial agonist at NOP receptors.

Naltrexone is used clinically for the treatment of opiate and alcohol dependence and is predominantly a MOPr antagonist. Sustained release naltrexone has been shown to be very useful for the treatment of alcohol dependence.

The novel compounds combine the beneficial effects of both buprenorphine and naltrexone and are therefore KOPr and MOPr antagonists with ORL-1 receptor agonist activity, i.e. buprenorphine with MOPr partial agonism replaced by MOPr antagonism.

Drug Abuse: The lead compound BU10119 suppresses opioid self-administration (Fig 1) and heroin induced reinstatement (relapse) in primates.

Depression: BU10119 is active in behavioural assays predictive of anxiolytic and antidepressant activity (e.g Fig 2).

Drug - likeness: Promising safety and DMPK profile

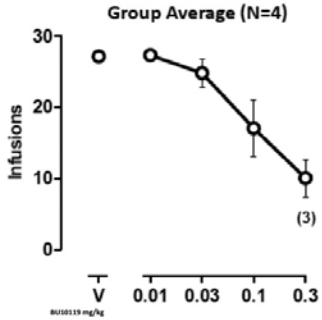


Fig 1. Suppression of opioid self-administration

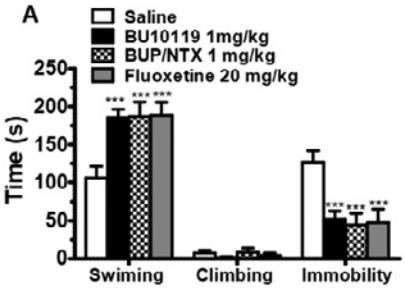
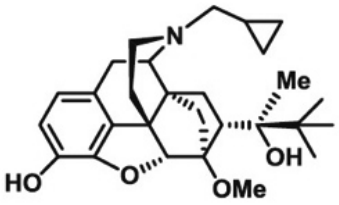
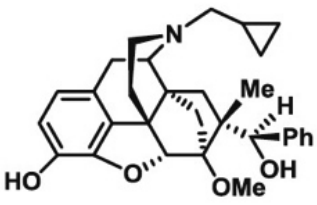


Fig 2. BU10119 is effective in the forced swim test - a model of antidepressant activity



Buprenorphine



BU10119

UNIQUE SELLING POINTS

- In vitro pharmacology that resembles the combination of buprenorphine/naltrexone: high affinity/zero efficacy at κ receptors, high affinity/little efficacy at μ receptors and a weak partial agonist profile at NOP receptors
- Potential for treatment-resistant depression and drug- abuse relapse prevention
- No MOPr agonism so no abuse liability, avoids side effects of respiratory depression and euphoria
- Issued IP in the US, Europe, Canada and Japan for composition and method of use in substance abuse treatment, relapse prevention and treatment of depression and anxiety

OPPORTUNITIES

- The University of Bath is seeking collaborative partners or licensees for the clinical development of these compounds.
- The academic team have considerable commercial experience with Professor John Lewis having been the Research and Development Director for Reckitt Benckiser (then Reckitt & Colman) during the clinical development of buprenorphine.

COMMERCIAL APPLICATIONS

These compounds are available to licence for the treatment of depression, anxiety and polydrug abuse (including cocaine, alcohol and opiate dependence). Depression is extremely common with 15% of the population experiencing a period of depression in their life time and 11% of people experiencing either depression or anxiety at any point in time (NHS Clinical Knowledge Summaries). Depression, especially treatment-resistant depression, remains a significant unmet clinical need.

Alcohol, cocaine and opiate dependence are significant problems; the US Substance Abuse and Mental Health Services Administration's (SAMHSA's) National Survey on Drug Use and Health identified 21.6 million persons aged 12 or older needed treatment for an illicit drug or alcohol abuse problem in 2019. The Centers for Disease Control and Prevention estimates that the total "economic burden" of prescription opioid misuse alone in the United States is $78.5 billion a year, including the costs of healthcare, lost productivity, addiction treatment, and criminal justice involvement.

A single compound that combines the beneficial effects of buprenorphine and naltrexone has advantages over coadministration of the individual compounds, in particular avoiding the risk of buprenorphine diversion and simplifying dosing schedules.

CONTACT

The University of Bath is seeking collaborative partners or licensees for the clinical development of these compounds.

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