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Declarations under Rule 4.17:

— *as to the identity of the inventor (Rule 4.17(i))*

[Continued on next page]

(54) Title: COMPOSITIONS AND METHODS FOR ENHANCING ANALGESIC POTENCY OF COVALENTLY BOUND COMPOUNDS, ATTENUATING ITS ADVERSE SIDE EFFECTS, AND PREVENTING THEIR ABUSE

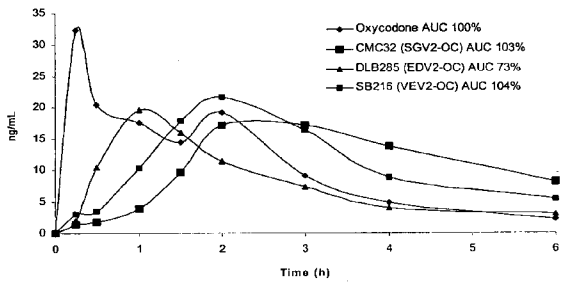


Figure 11

(57) Abstract: The invention generally relates to compositions and methods with covalently bound compounds, such as controlled substances covalently attached to a chemical moiety, and opioid antagonists or covalently bound opioid antagonists to enhance analgesic potency and/or attenuate one or more adverse effects of covalently bound compounds, including adverse side effect(s) in humans such as nausea, vomiting, dizziness, headache, sedation (somnolence), physical dependence or pruritis. This invention relates to compositions and methods for selectively enhancing the analgesic potency of a covalently bound compound and simultaneously attenuating anti-analgesia, hyperalgesia, hyperexcitability, physical dependence and/or tolerance effects associated with the administration of a covalently bound compound. The methods of the invention comprise administering to a subject an analgesic or sub-analgesic amount of a covalently bound compound and an amount of excitatory opioid receptor antagonist such as naltrexone or nalmefene effective to enhance the analgesic potency of a covalently bound compound and attenuate the anti-analgesia, hyperalgesia, hyperexcitability, physical dependence and/or tolerance effects of covalently bound compound. The invention also relates to the addition of covalently-bound opioid antagonists to the compositions containing covalently bound compounds such that if the compositions are subjected to manipulation by illicit chemists, the opioid antagonist is released effectively reducing or eliminating the euphoric effect of the covalently bound compounds.

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— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

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USPC: 514/282;424/465
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 514/282; 424/465

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EAST

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US2003/0004177 A1 (KAO et al.) 02 January 2003 (02.01.2003), whole document	3-11,18-19,22-27,31,33
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A		1-2,12-17,20-21,28-30,32
Y	US 2004/0106636 A1 (KREAM) 03 June 2004 (03.06.2004), whole document	3-11,18-19,22-27,31,33
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A		1-2,12-17,20-21,28-30,32
Y	US 2002/0094947 A1 (CRAIN et al.) 18 July, 2002 (18.07.2002), whole document	3-11,18-19,22-27,31,33
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A		1-2,12-17,20-21,28-30,32

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