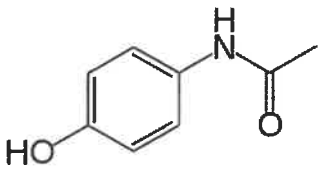
METHODS OF TREATING PAIN USING PHARMACEUTICALLY ACTIVE ACETAMINOPHEN DIMERS LINKED THROUGH PHENOLIC HYDROXYL GROUPS

CROSS-REFERENCES TO RELATED APPLICATIONS

[0001] This application claims the benefit of priority under 35 U.S.C. § 119(e) of U.S. Application No. 14/922,362 filed October 26, 2015, the disclosure of which is incorporated herein by reference.

BACKGROUND OF THE INVENTION

[0002] Acetaminophen (Formula 1), chemically named N-acetyl-p-aminophenol, is one of the most widely used medications in the United States.



Formula 1

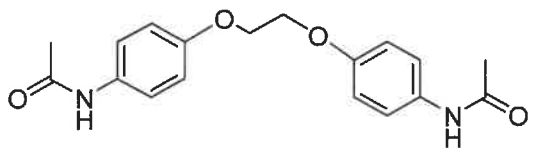
[0003] Acetaminophen is an over-the-counter analgesic and antipyretic, commonly sold under the trade name Tylenol®. Acetaminophen is classified as a mild analgesic. It is commonly used for the relief of headaches and other minor aches and pains and is a major ingredient in numerous cold and flu remedies. In combination with opioid analgesics such as codeine, oxycodone, and hydrocodone, acetaminophen can also be used in the management of more severe pain such as post-surgical pain and providing palliative care in advanced cancer patients.

[0004] When administered in proper therapeutic doses, acetaminophen is considered safe and harmless. Unfortunately, misuse and overdose of the drug can lead to hepatotoxicity and even, death.

[0005] Acetaminophen induced hepatotoxicity arises from impaired metabolism of acetaminophen monomers by the liver. Acetaminophen has a single phenolic hydroxyl group

BRIEF SUMMARY OF THE INVENTION

[0011] In one aspect, provided herein is a method of treating pain (acute or chronic pain) in a patient having a risk of hepatotoxicity if administered an acetaminophen monomer. The method includes administering to the patient in need thereof a therapeutically effective amount of a pharmaceutical composition comprising a pharmaceutically acceptable carrier or excipient and an acetaminophen dimer compound having Formula (1):



(1)

or a pharmaceutically acceptable salt or solvate thereof.

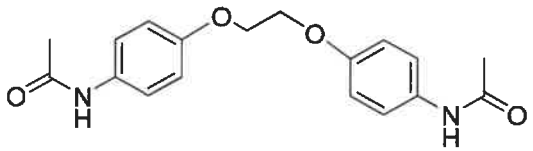
[0012] In some embodiments, the patient is an adult human patient. In other embodiments, the patient is a pediatric (*i.e.*, infant, child or adolescent) human patient. A pediatric patient may be an individual from birth to up to 18-21 years of age. The patient may be experiencing a fever. Alternatively, the patient may suffer from pain (acute pain or chronic pain). In some embodiments, the patient is receiving treatment for cancer. In other embodiments, the patient suffers from gastrointestinal acidity or gastrointestinal reflux disease (GERD). The subject may be in need of palliative care.

[0013] The pharmaceutical composition can also include a barbiturate, opioid, antihistamine, caffeine, diphenhydramine, dextromethorphan, pseudoephedrine, biosimilar thereof, pharmaceutical equivalent thereof, or any combination thereof. In some embodiments, the pharmaceutical composition is administrated orally, rectally, sublingually, subcutaneously, intramuscularly, intravenously, transdermally, or transmucosally. The therapeutically effective amount administered may be about 500 mg to about 1000 mg. The pharmaceutical composition may be formulated as an oral tablet or extended release oral tablet.

[0014] In another aspect, provided herein is a method of treating pain (acute or chronic pain) or fever in a patient in need thereof without risking hepatotoxicity. The method includes administering to the patient a therapeutically effective amount of a pharmaceutical composition comprising a pharmaceutically acceptable carrier or excipient and an acetaminophen dimer compound having Formula (1):

CLAIMS:

1. Use of an acetaminophen dimer compound having the Formula (1):



(1)

or a pharmaceutically acceptable salt or solvate thereof and a pharmaceutically acceptable carrier or excipient, in the preparation of a pharmaceutical composition for the treatment of acute or chronic pain in a subject which subject's symptoms stem from a condition other than fascioliasis.

2. The use of claim 1 wherein the subject is experiencing acute pain.

3. The use of claim 1 wherein the subject is experiencing chronic pain.

4. The use of claim 1 wherein the subject suffers from gastrointestinal acidity or gastrointestinal reflux disease.

5. The use of claim 1 wherein the subject suffers from cancer.

6. The use of claim 1 wherein the pharmaceutical composition further comprises a barbiturate, opioid, antihistamine, caffeine, diphenhydramine, dextromethorphan, pseudoepinephrine or combinations thereof.