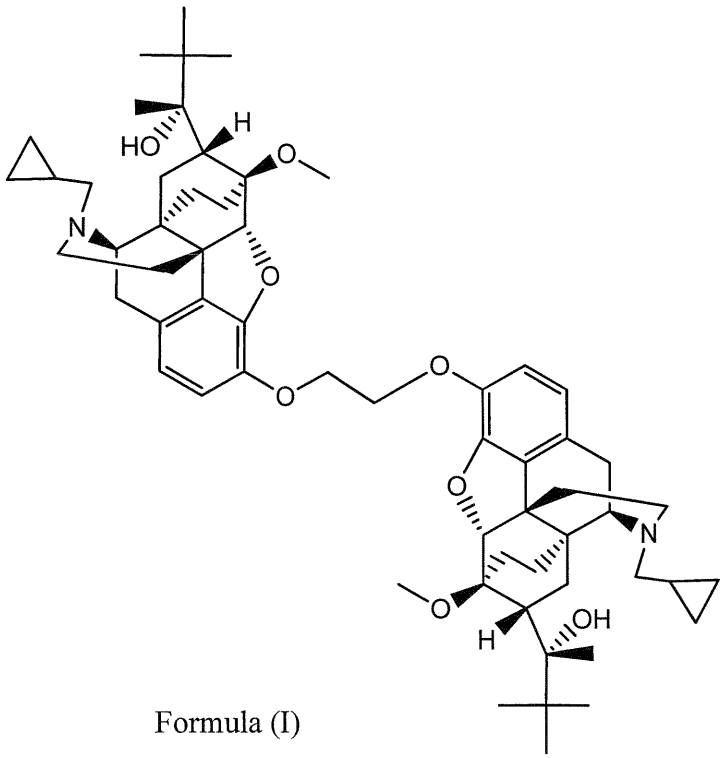
[0014] There has accordingly been a long-standing need for a chronic treatment of IBS-D that decreases intestinal motility, thereby decreasing the incidence of diarrhea, is an analgesic, is not associated with pancreatitis, and more than merely treating symptoms, potentially addresses underlying hypersensitivity and resulting hyperalgesia associated with IBS-D.

BRIEF SUMMARY

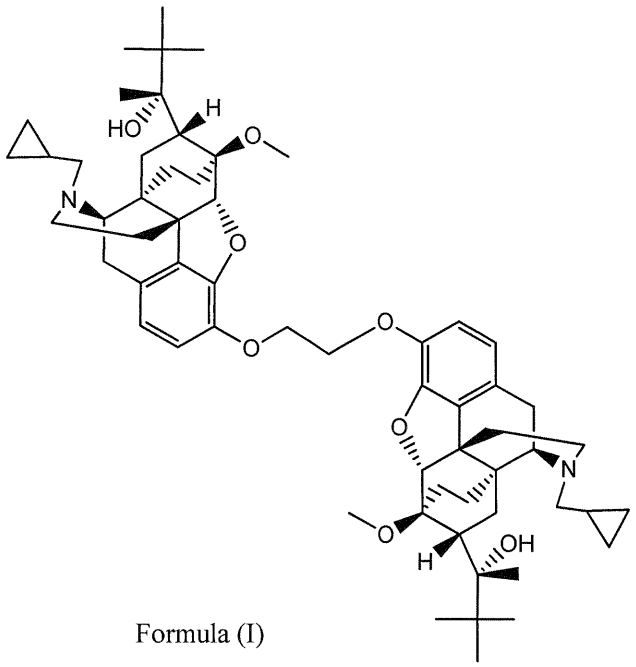
[0015] The present disclosure provides a novel dimer comprising two buprenorphine drug molecules, conjugated to each other by *O*-alkylation through their phenolic groups to yield the structure of Formula (I):



Formula (I)

or a pharmaceutically acceptable salt or solvate thereof.

[0015a] In one aspect of the present disclosure, there is provided a buprenorphine dimer compound having Formula (I):



Formula (I)

or a pharmaceutically acceptable salt or solvate thereof.

[0015b] In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising a pharmaceutically acceptable carrier or excipient and a buprenorphine dimer compound disclosed herein.

[0015c] In a further aspect of the present disclosure, there is provided a use of a buprenorphine dimer compound disclosed herein in the manufacture of a medicament for treating or managing gastrointestinal hyperalgesia.

[0015d] In another aspect of the present disclosure, there is provided a use of a buprenorphine dimer compound disclosed herein in the manufacture of a medicament for treating IBS-D in a patient in need thereof.

[0015e] In a further aspect of the present disclosure, there is provided a buprenorphine dimer compound disclosed herein for use in treating or managing gastrointestinal hyperalgesia.

[0015e] In a further aspect of the present disclosure, there is provided a buprenorphine dimer compound disclosed herein for use in treating IBS-D.

[0016] In Formula (I), the compound is: 2,2'-((4aR,4a'R,6S,6'S,7S,7'S,12bR,12b'R)-9,9'-(ethane-1,2-diylbis(oxy))bis(3-(cyclopropylmethyl)-7-methoxy-1,2,3,4,5,6,7,7a-octahydro-

[0020] The novel compound of the present disclosure addresses a long-felt need for an effective treatment of IBS-D that addresses both pain and diarrhea, reduces visceral (colonic) hypersensitivity, does not have the drawbacks of other agents utilized for this purpose and that can be prescribed safely on a chronic basis. Accordingly, the present disclosure comprises the use of the compound for the treatment of IBS-D, especially when visceral hypersensitivity and hyperalgesia are present. The compound may also find application as an adjuvant with other drugs such as teduglutide for treating other intestinal conditions such as short bowel syndrome, to safely reduce intestinal transit time. Pharmaceutical compositions according to the present disclosure comprise a buprenorphine dimer of Formula (I) formulated as an oral tablet or capsule, extended release oral tablet or capsule, intramuscular or subcutaneous depot injection, or transdermal patch.

BRIEF DESCRIPTION OF THE DRAWINGS

[0021] **Figure 1** provides a bar chart illustrating the stability of buprenorphine dimer when exposed to CYP enzymes in the presence and absence of a co-factor.

[0022] **Figure 2** provides a bar graph showing the stability of buprenorphine dimer to aqueous conditions, as well as acidic and basic condition, each at room temperature and at 140°F for the indicated period of time.

[0023] **Figure 3** provides the results of buprenorphine dimer receptor binding experiments – μ receptor.

[0024] **Figure 4** provides the results of buprenorphine dimer receptor binding experiments – κ receptor.

[0025] **Figure 5** provides μ agonist functional assay results for the buprenorphine dimer.

[0026] **Figure 6** provides μ antagonist functional assay results for the buprenorphine dimer.

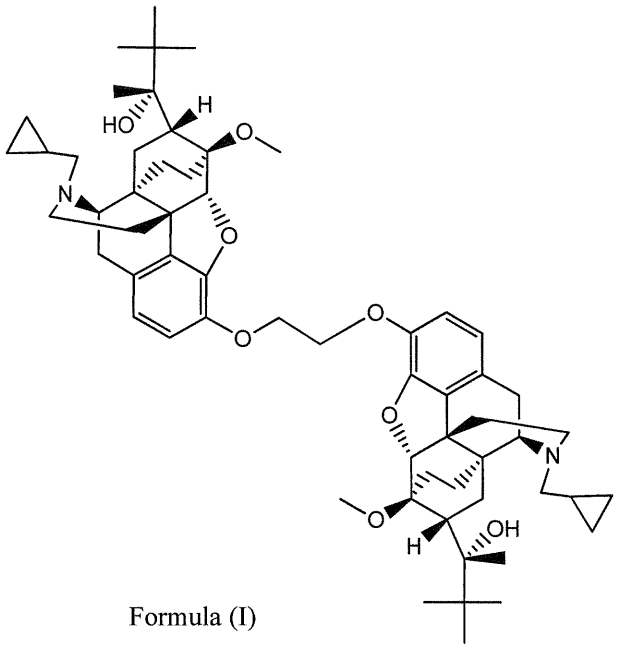
[0027] **Figure 7** provides the results of oral and IV bioavailability for buprenorphine and the buprenorphine dimer.

[0028] **Figures 8 and 9** provide the graphs for stress-induced fecal output of male CD-1 mice according to the evaluation of Example 7.

[0029] **Figure 10** demonstrates that buprenorphine dimer decreases fecal output in a dose-dependent manner.

WHAT IS CLAIMED IS:

1. A buprenorphine dimer compound having Formula (I):



Formula (I)

or a pharmaceutically acceptable salt or solvate thereof.

2. The buprenorphine dimer compound of claim **1,** wherein the compound is in the form of a pharmaceutically acceptable salt.

3. A pharmaceutical composition comprising a pharmaceutically acceptable carrier or excipient and a buprenorphine dimer compound of claim **1**.

4. Use of a buprenorphine dimer compound of claim **1** in the manufacture of a medicament for treating or managing gastrointestinal hyperalgesia.

5. Use of a buprenorphine dimer compound of claim **1** in the manufacture of a medicament for treating IBS-D in a patient in need thereof.

6. The use in accordance with claim **5**, wherein the patient is a human and wherein the dose of buprenorphine dimer compound to be administered is about 0.1 mg/kg of the patient's body weight to about 7.2 mg/kg of the patient's body weight

7. The use in accordance with claim **5**, wherein the patient is a human and wherein the dose of buprenorphine dimer compound to be administered is about 10 to about 50 mg daily.

8. A buprenorphine dimer compound of claim **1** for use in treating or managing gastrointestinal hyperalgesia.

9. A buprenorphine dimer compound of claim **1** for use in treating IBS-D.