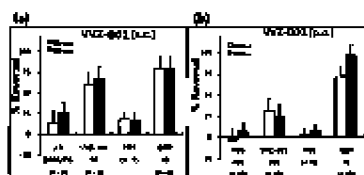


## Abstract:



(EN)The present invention relates to a novel benzamide derivative and a pharmaceutical use thereof, and more specifically, to a novel benzamide derivative of formula 1 or a pharmaceutically acceptable salt thereof, and a composition containing same for the prevention and treatment of pain and itching. The benzamide derivative and the pharmaceutically acceptable salt according to the present invention have a remarkable effect on the suppression of pain. The benzamide derivative and the pharmaceutically acceptable salt have an effect on the suppression of pain not only in a neuropathic animal model but also in a formalin model and other pain-induced models, and thus can be used for the suppression of various kinds of pain such as nociceptive pain and chronic pain. Further, it is confirmed that the present invention has an antipruriginous effect on an itch model in which an established mechanism of pain and concept of treatment is applied, and therefore the antipruriginous composition is useful since the composition can be used for the radical treatment of atopy by suppressing and treating the early itching phase to prevent skin damage and inflammatory response after the scratching phase.

**FORM 2**

THE PATENTS ACT, 1970  
(39 of 1970)  
AND  
THE PATENTS RULES, 2003

**COMPLETE  
SPECIFICATION**

(See Section 10; rule 13)

TITLE OF THE INVENTION

“NOVEL BENZAMIDE DERIVATIVE AND USE THEREOF”

**APPLICANT**

**VIVOZON, INC.**

of (Jeongneung-dong, Korea Univ. health science Univ. Jinrigwan 5F), 161,  
Jeongneung-ro Seongbuk-gu, Seoul 136-855 , Republic of Korea; Nationality: Korea

The following specification particularly describes  
the invention and the manner in which  
it is to be performed

## DECLARATION

We hereby declare that the attached complete specification has been provided by the applicant as the true, correct and complete English translation of the as filed specification of PCT Application No. PCT/KR2012/010257.



(S. Anitha Shirmila Elizabeth)  
Reg. No. IN/PA-1847  
Of De Penning & De Penning  
Agent for the Applicants

【DESCRIPTION】

【Invention Title】

NOVEL BENZAMIDE DERIVATIVE AND USE THEREOF

【Technical Field】

5           The present invention relates to a novel benzamide derivative and pharmaceutical use thereof, and more particularly, to a novel benzamide derivative having a structure of Formula 1 or pharmaceutically acceptable salts thereof, and a composition for prevention or treatment of pain or itching including the above material.

10   【Background Art】

          Although a variety of neuropathological studies on pain have been actively conducted and pain treatment methods have been extensively studied, pain treatment still mostly depends upon use of narcotic analgesics already developed in the art.

15           Currently developed pain relievers affect peripheral or central nerves to decrease pain, and may typically include non-steroidal anti-inflammatory drugs (NSAID), COX-2 inhibitors, opiates and morphinomimetics, flupirtin, etc.

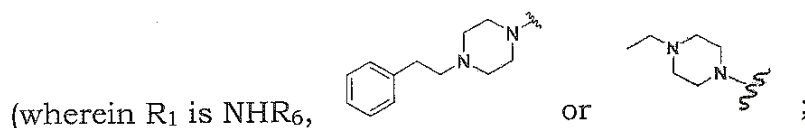
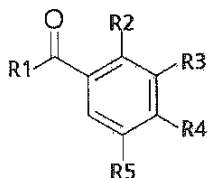
          Representative examples of NSAID are paracetamol, and  
20   acetaminophen, which are presumed to affect the central nervous system and to inhibit cyclooxygenase, thus suppressing production of prostaglandin, and therefore, are known to reduce inflammation as well as pain. In particular, paracetamol shows fewer side effects and is relatively safe, however, when administered in doses higher than  
25   recommended, has a problem of inducing potentially fatal damage to

# **[CLAIMS]**

## **[Claim 1]**

A benzamide derivative represented by Formula 1 below or pharmaceutically acceptable salt thereof.

5 [Formula 1]



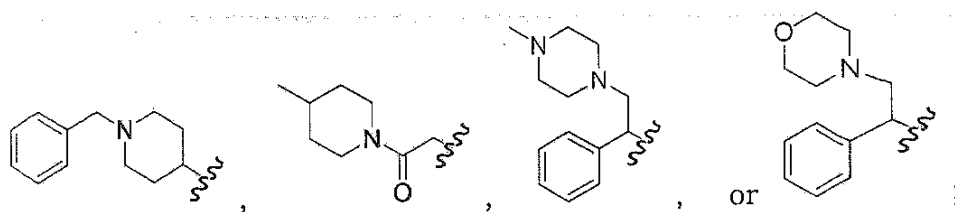
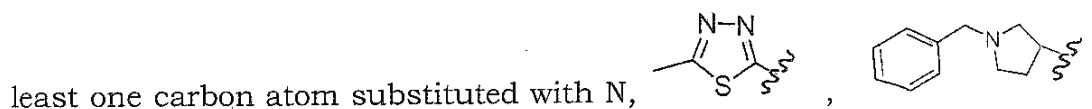
R<sub>2</sub> is hydrogen, (C<sub>1</sub>-C<sub>6</sub>) alkyl or (C<sub>1</sub>-C<sub>6</sub>) alkoxy;

R<sub>3</sub> is hydrogen, (C<sub>1</sub>-C<sub>6</sub>) alkyl or (C<sub>1</sub>-C<sub>6</sub>) alkoxy having at least one  
10 hydrogen atom substituted or unsubstituted with halogen;

R<sub>4</sub> is hydrogen, hydroxyl group, amino group (NH<sub>2</sub>), (C<sub>1</sub>-C<sub>6</sub>) alkoxy, (C<sub>3</sub>-C<sub>6</sub>) aromatic cycloalkoxy, (C<sub>3</sub>-C<sub>6</sub>) aliphatic cycloalkoxy, or (C<sub>1</sub>-C<sub>6</sub>) alkylalkoxy having at least one (C<sub>3</sub>-C<sub>6</sub>) aromatic ring or aliphatic ring;

15 R<sub>5</sub> is hydrogen, (C<sub>1</sub>-C<sub>6</sub>) alkyl, (C<sub>1</sub>-C<sub>6</sub>) alkoxy or halogen;

R<sub>6</sub> is CH<sub>2</sub>R<sub>11</sub>, CH<sub>2</sub>CHR<sub>12</sub>R<sub>13</sub>, quinuclidine, naphthalene having at



R<sub>11</sub> is a (C<sub>5</sub>-C<sub>6</sub>) aliphatic cyclic or aromatic cyclic compound or (C<sub>5</sub>-C<sub>6</sub>) aliphatic heterocyclic or aromatic heterocyclic compound having at least one carbon atom substituted with O or N, wherein the aliphatic ring, aromatic ring, aliphatic hetero-ring or aromatic hetero-ring of R<sub>11</sub> may be one substituted with at least one substituent selected from a group consisting of; (C<sub>1</sub>-C<sub>6</sub>) alkyl, hydroxy, NR<sub>21</sub>R<sub>22</sub>, halogen and (C<sub>5</sub>-C<sub>6</sub>) aliphatic heterocyclic or aromatic heterocyclic compound having at least one carbon atom substituted with O or N, wherein R<sub>21</sub> and R<sub>22</sub> are independently each hydrogen, (C<sub>1</sub>-C<sub>6</sub>) alkyl or phenyl;

R<sub>12</sub> and R<sub>13</sub> are independently each hydrogen, NR<sub>23</sub>R<sub>24</sub>, an (C<sub>5</sub>-C<sub>6</sub>) aliphatic cyclic or aromatic cyclic compound, or a (C<sub>5</sub>-C<sub>6</sub>) aliphatic heterocyclic or aromatic heterocyclic compound having at least one carbon atom substituted with O or N, wherein the aliphatic ring, aromatic ring, aliphatic hetero-ring or aromatic hetero-ring of R<sub>12</sub> and R<sub>13</sub> may be one substituted with at least one substituent of (C<sub>1</sub>-C<sub>6</sub>) alkyl or (C<sub>1</sub>-C<sub>6</sub>) alkoxy, wherein R<sub>23</sub> and R<sub>24</sub> are independently each hydrogen or (C<sub>1</sub>-C<sub>6</sub>) alkyl or, otherwise, are coupled together to form a (C<sub>5</sub>-C<sub>6</sub>) aliphatic cyclic or heterocyclic compound, or a (C<sub>5</sub>-C<sub>6</sub>) aliphatic heterocyclic or aromatic heterocyclic compound having at least one carbon atom substituted with O.)

**【Claim 2】**

The benzamide derivative or pharmaceutically acceptable salt thereof according to claim 1, wherein R<sub>2</sub> in Formula 1 is hydrogen or methoxy (-OCH<sub>3</sub>),

R<sub>3</sub> is hydrogen, methyl (-CH<sub>3</sub>), methoxy (-OCH<sub>3</sub>) or

trifluoromethyl (-CF<sub>3</sub>),

R<sub>4</sub> is hydrogen, amino group (-NH<sub>2</sub>), butoxy (-O(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>) or benzyloxy (-OCH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), and

R<sub>5</sub> is hydrogen, methyl (-CH<sub>3</sub>), methoxy (-OCH<sub>3</sub>) or chlorine (-Cl).

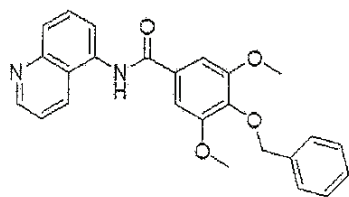
5    **【Claim 3】**

The benzamide derivative or pharmaceutically acceptable salt thereof according to claim 1, wherein R<sub>1</sub> is NHR<sub>6</sub>, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>5</sub> are each methoxy (-OCH<sub>3</sub>), R<sub>4</sub> is butoxy (-O(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>) or benzyloxy (-OCH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>).

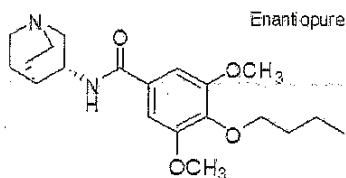
10    **【Claim 4】**

The benzamide derivative or pharmaceutically acceptable salt thereof according to claim 3, wherein the compound represented by Formula 1 is selected from a group consisting of Formula 2 to Formula 46.

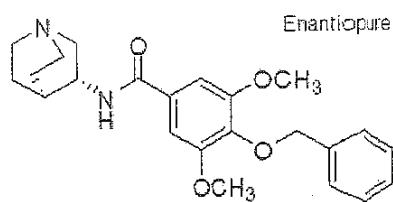
15    **[Formula 2]**



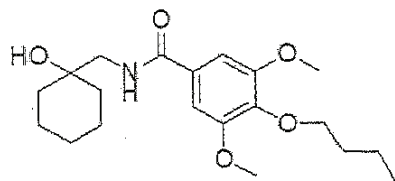
**[Formula 3]**



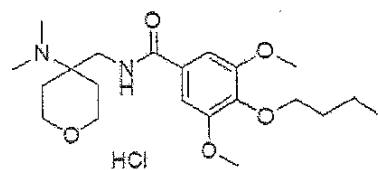
**[Formula 4]**



[Formula 5]

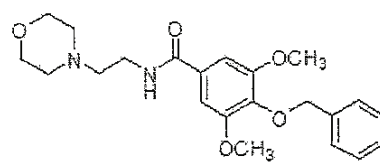


[Formula 6]

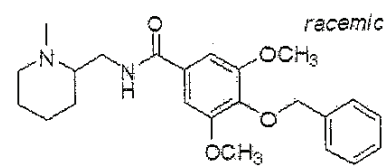


5

[Formula 7]

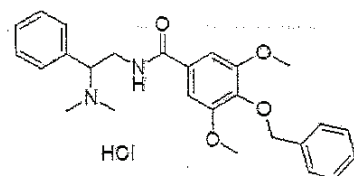


[Formula 8]



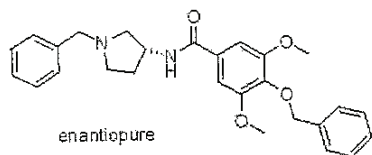
10

[Formula 9]

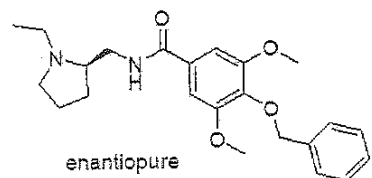


[Formula 10]

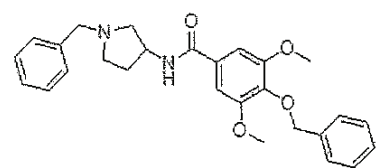




[Formula 11]

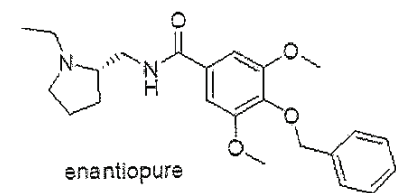


[Formula 12]

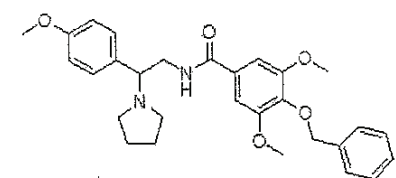


5

[Formula 13]

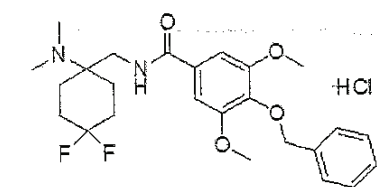


[Formula 14]

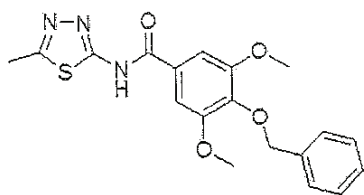


10

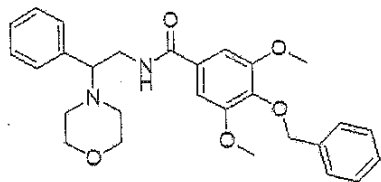
[Formula 15]



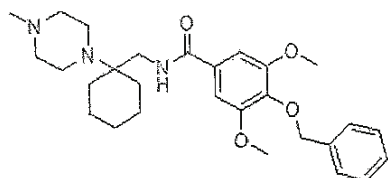
[Formula 16]



[Formula 17]

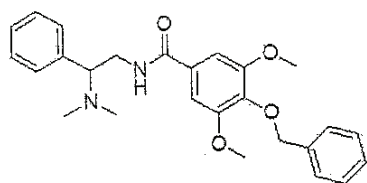


[Formula 18]

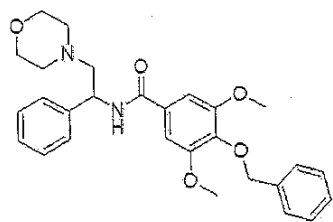


5

[Formula 19]

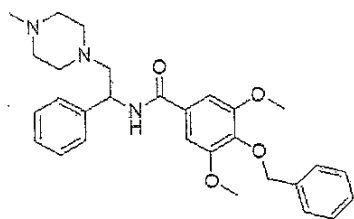


[Formula 20]

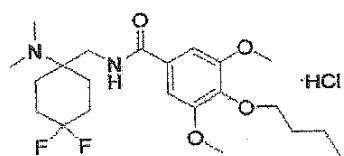


10

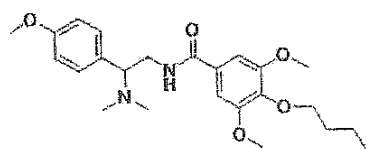
[Formula 21]



[Formula 22]

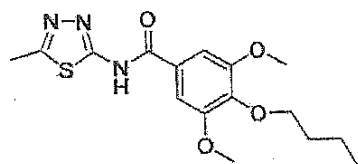


[Formula 23]

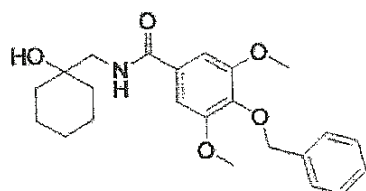


5

[Formula 24]

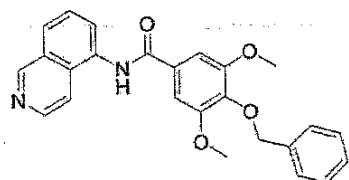


[Formula 25]

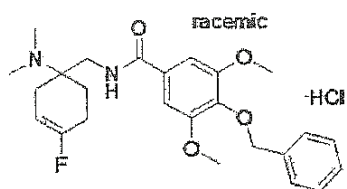


10

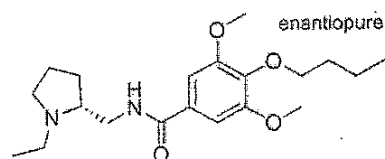
[Formula 26]



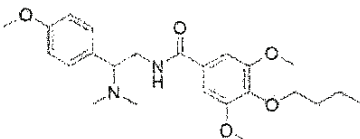
[Formula 27]



[Formula 28]

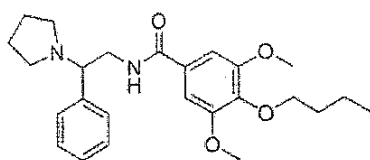


[Formula 29]

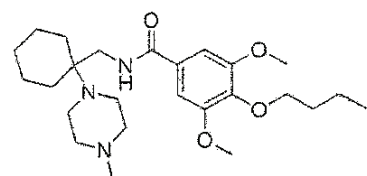


5

[Formula 30]

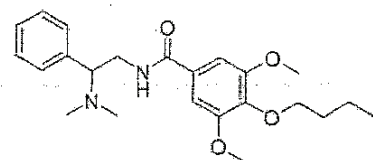


[Formula 31]

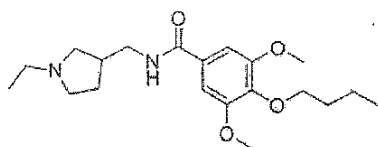


10

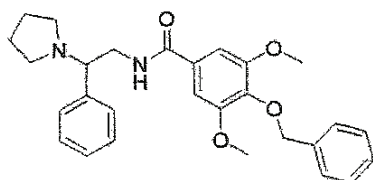
[Formula 32]



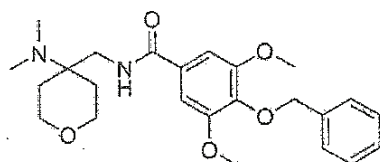
[Formula 33]



[Formula 34]

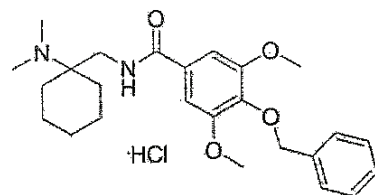


[Formula 35]

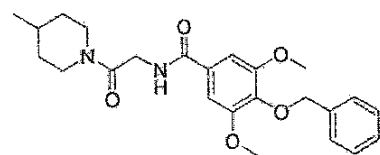


5

[Formula 36]

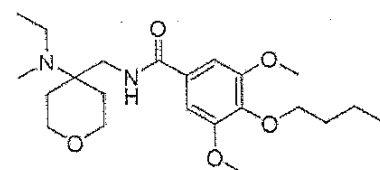


[Formula 37]

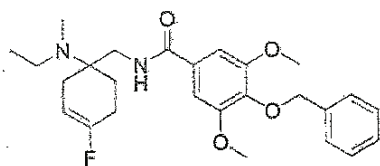


10

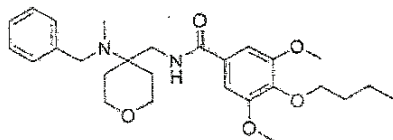
[Formula 38]



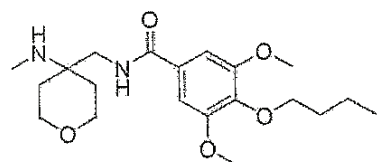
[Formula 39]



[Formula 40]

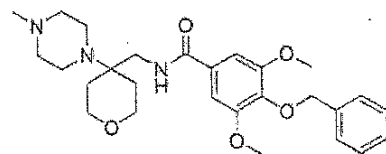


[Formula 41]

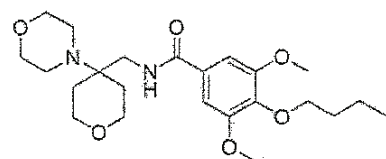


5

[Formula 42]

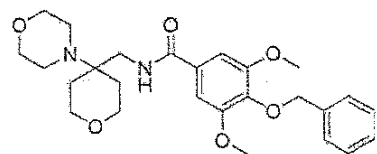


[Formula 43]

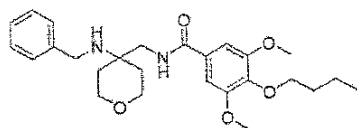


10

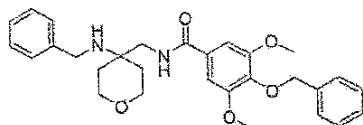
[Formula 44]



[Formula 45]



[Formula 46]



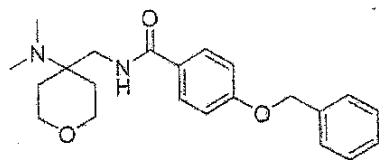
【Claim 5】

- 5        The benzamide derivative or pharmaceutically acceptable salt thereof according to claim 1, wherein  $R_1$  is  $NHR_6$ ,  $R_2$ ,  $R_3$  and  $R_5$  are each hydrogen, and  $R_4$  is butoxy ( $-O(CH_2)_3CH_3$ ) or benzyloxy ( $-OCH_2C_6H_5$ ).

【Claim 6】

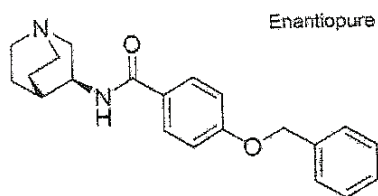
- 10       The benzamide derivative or pharmaceutically acceptable salt thereof according to claim 5, wherein the compound represented by Formula 1 is selected from a group consisting of compounds represented by Formula 47 to Formula 62.

[Formula 47]

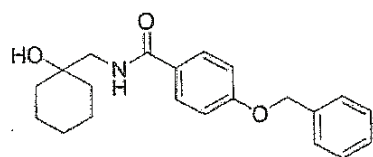


15

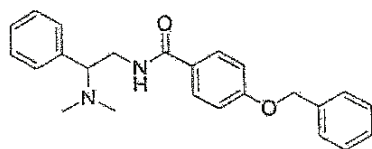
[Formula 48]



[Formula 49]

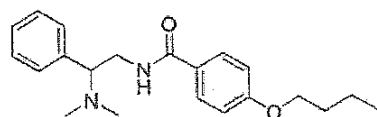


[Formula 50]

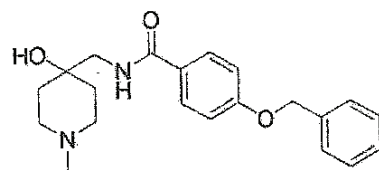


5

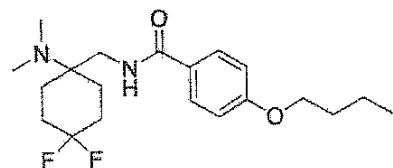
[Formula 51]



[Formula 52]

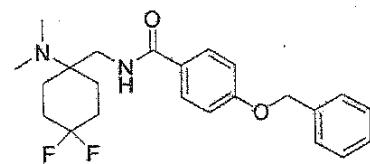


[Formula 53]



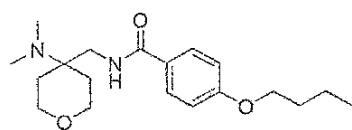
10

[Formula 54]

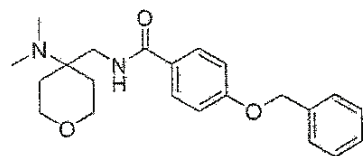


[Formula 55]

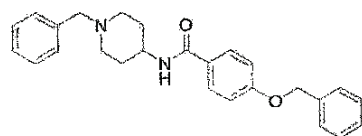




[Formula 56]

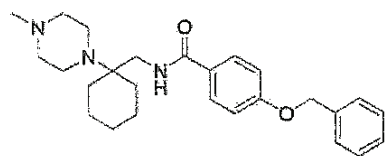


[Formula 57]

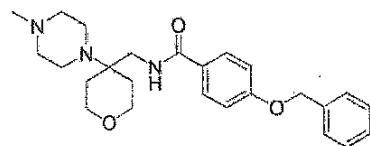


5

[Formula 58]

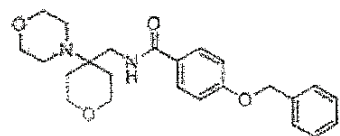


[Formula 59]

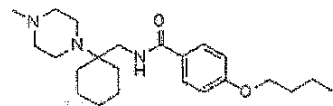


10

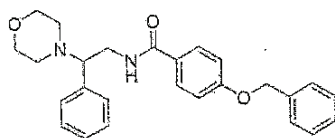
[Formula 60]



[Formula 61]



[Formula 62]



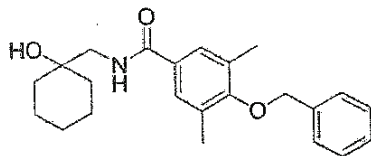
【Claim 7】

The benzamide derivative or pharmaceutically acceptable salt  
5 thereof according to claim 1, wherein  $R_1$  is  $NHR_6$ ,  $R_2$  is hydrogen,  $R_3$  and  
 $R_5$  are each methyl ( $-CH_3$ ),  $R_4$  is butoxy ( $-O(CH_2)_3CH_3$ ) or benzyloxy ( $-$   
 $OCH_2C_6H_5$ ).

【Claim 8】

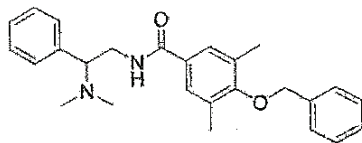
The benzamide derivative or pharmaceutically acceptable salt  
10 thereof according to claim 7, wherein the compound represented by  
Formula 1 is selected from a group consisting of compounds  
represented by Formula 63 to Formula 75.

[Formula 63]

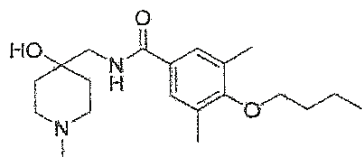


15

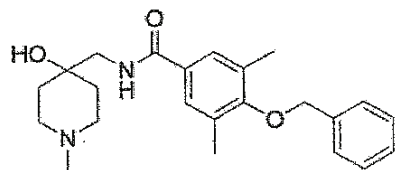
[Formula 64]



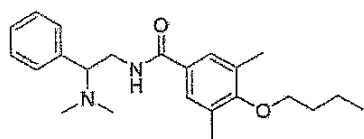
[Formula 65]



[Formula 66]

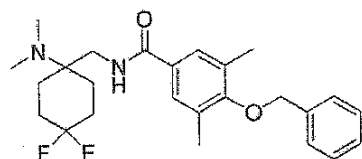


[Formula 67]

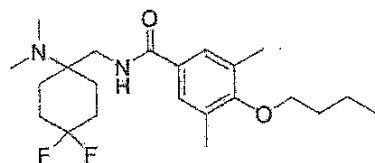


5

[Formula 68]

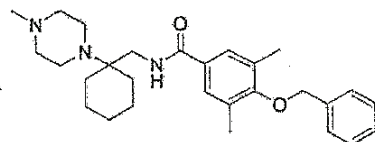


[Formula 69]

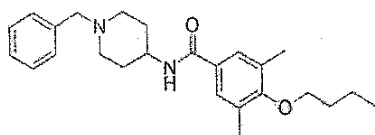


10

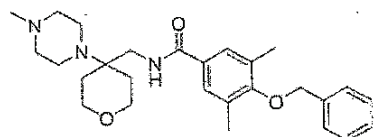
[Formula 70]



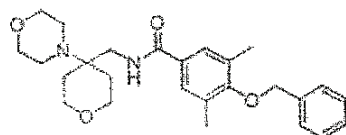
[Formula 71]



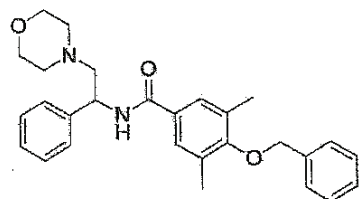
[Formula 72]



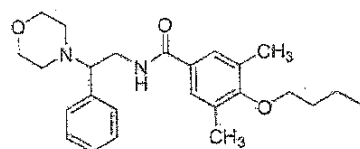
[Formula 73]



[Formula 74]



[Formula 75]



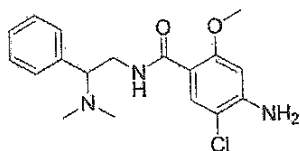
10 【Claim 9】

The benzamide derivative or pharmaceutically acceptable salt thereof according to claim 1, wherein R<sub>1</sub> is NHR<sub>6</sub>, R<sub>2</sub> is methoxy (-OCH<sub>3</sub>), R<sub>3</sub> is hydrogen, R<sub>4</sub> is amino group (-NH<sub>2</sub>), and R<sub>5</sub> is chlorine (-Cl).

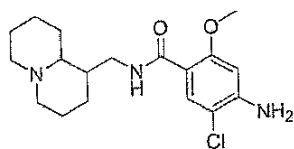
【Claim 10】

The benzamide derivative or pharmaceutically acceptable salt thereof according to claim 9, wherein the compound represented by Formula 1 is selected from a group consisting of compounds represented by Formula 76 to Formula 80.

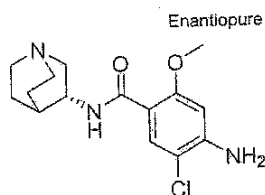
5 [Formula 76]



[Formula 77]

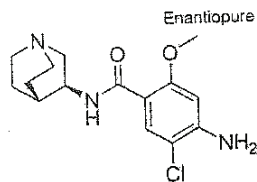


[Formula 78]

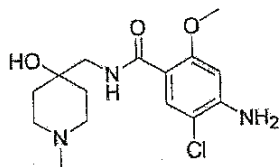


10

[Formula 79]



[Formula 80]



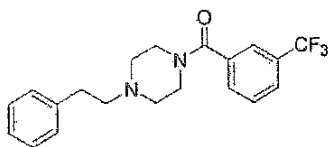
【Claim 11】

The benzamide derivative or pharmaceutically acceptable salt thereof according to claim 1, wherein R<sub>2</sub>, R<sub>4</sub> and R<sub>5</sub> are each hydrogen, and R<sub>3</sub> is trifluoromethyl (-CF<sub>3</sub>).

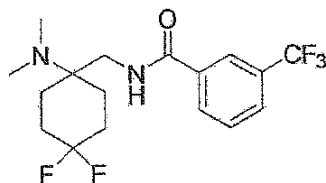
5 【Claim 12】

The benzamide derivative or pharmaceutically acceptable salt thereof according to claim 11, wherein the compound represented by Formula 1 is selected from a group consisting of compounds represented by Formula 81 to Formula 83.

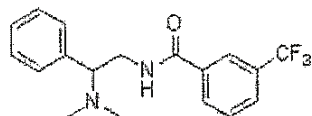
10 【Formula 81】



【Formula 82】



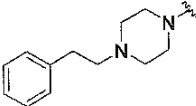
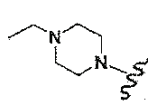
【Formula 83】



15

【Claim 13】

The benzamide derivative or pharmaceutically acceptable salt thereof according to claim 1,

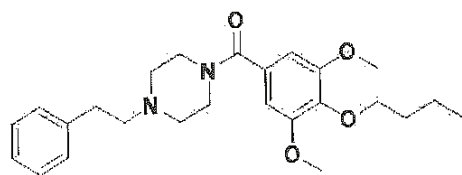
Wherein R<sub>1</sub> is  or , R<sub>2</sub> is hydrogen, R<sub>3</sub>

and R<sub>5</sub> are each methoxy (-OCH<sub>3</sub>), R<sub>4</sub> is butoxy (-O(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>) or benzyloxy (-OCH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>).

【Claim 14】

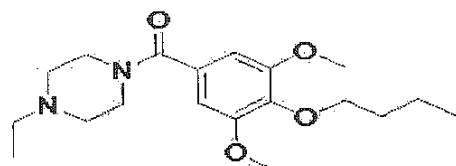
The benzamide derivative or pharmaceutically acceptable salt thereof according to claim 13, wherein the compound represented by Formula 1 is selected from a group consisting of compounds represented by Formula 155 to Formula 157.

[Formula 155]

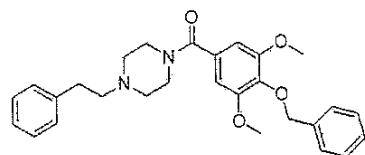


10

[Formula 156]



[Formula 157]



【Claim 15】

15

The benzamide derivative or pharmaceutically acceptable salt thereof according to any one of claims 1 to 14, wherein the benzamide derivative or its pharmaceutically acceptable salt has antagonist activity of Glycine Transporter 2 (GlyT2) and antagonist activity of 5-hydroxytryptamine subtype 2 (5HT2) receptor, simultaneously.

【Claim 16】

A composition for prevention or treatment of pain or pruritus, comprising the benzamide derivative or pharmaceutically acceptable salt thereof according to any one of claims 1 to 14.



## 【ABSTRACT】

Disclosed are a novel benzamide derivative and pharmaceutical use thereof, and more particularly, a novel benzamide derivative having a structure of Formula 1 or pharmaceutically acceptable salts thereof, and a composition for prevention or treatment of pain or itching including the above material. The novel benzamide derivative and pharmaceutically acceptable salt thereof according to the present invention exhibit excellent pain-suppressive effect and, in particular, pain-suppressive effect in not only a neuropathic animal model but also other models such as a formalin model, and therefore, may be used in suppression of different pains such as nociceptive pain, chronic pain, etc. Further, since it was demonstrated that the present invention displays anti-pruritic efficacy even in an itching model, to which a mechanism and treatment concept established with respect to pain is applied, the present invention may also be effectively used in radical treatment of atopic dermatitis by applying the inventive product to an anti-pruritic composition in order to suppress an initial itching stage and treat symptoms thereof, thus preventing skin damage or inflammation after the scratching stage.

FIG.1

