New compounds for the treatment of acute pain

INVENTORS: Katia Varani
Flavia Varano
Vittoria Colotta
Daniela Catarzi
Pier Andrea Borea
Fabrizio Vincenzi

CONTITOLARI: Università degli Studi di Ferrara

STATUS PATENT: Concesso

N° Priority: 102016000070952

Date:2 gennaio 2019

Patent Family: EP3481836A1; EP3481836B1; IT201600070952A1; US2020308192A1; WO2018007957A1

The invention

The invention consists of a series of novel compounds for the treatment of acute pain. Current therapeutic approaches for pain management include the use of opioids with which many side effects are known to be associated including tolerance and potential dependence. The present invention serves the development of new therapeutic strategies and new non-opioid drugs for the treatment of pain.The invention describes the development of new compounds with a thiazolo[5,4-d]pyrimidine structure that are found to be A2A adenosine receptor blockers and more potent than those already on the market. Affinity and potency of the compounds were evaluated by receptor binding experiments and cyclic AMP assays. It is evident from these assays that the new compounds have high affinity (femtomolar order) for the A2A receptor, associated with high potency (picomolar order). In addition, the new derivatives have been tested in widely used and validated animal models of acute pain, such as the writhing and tail immersion tests, and have been found to be similarly or more effective than morphine.

The Inventors

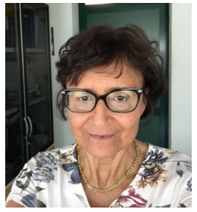
Prof.ssa Katia Varani, Ordinario di Farmacologia, Università di Ferrara

Prof. Pier Andrea Borea, Ordinario di Farmacologia, Università di Ferrara

Prof. Fabrizio Vincenzi, Associato di Farmacologia, Università di Ferrara

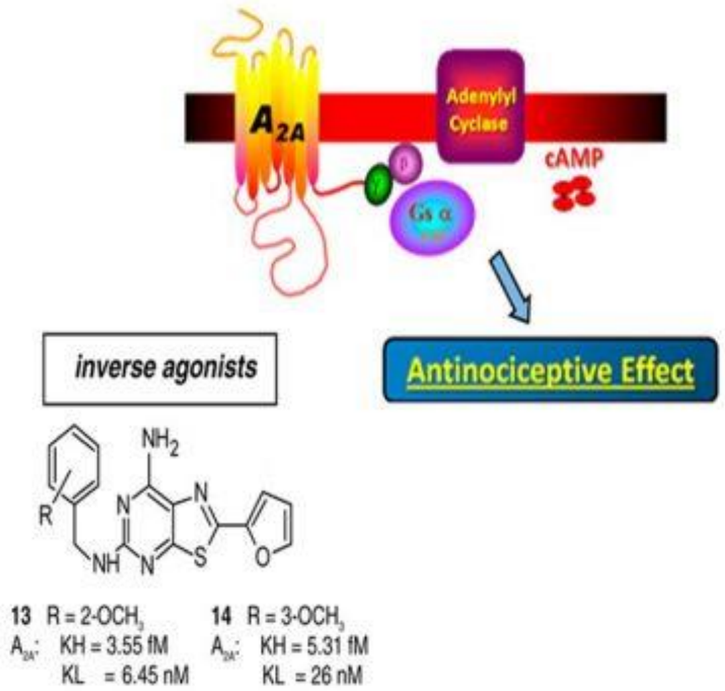
Prof. ssa Flavia Varano, Associato di Chimica Farmaceutica, Università di Firenze

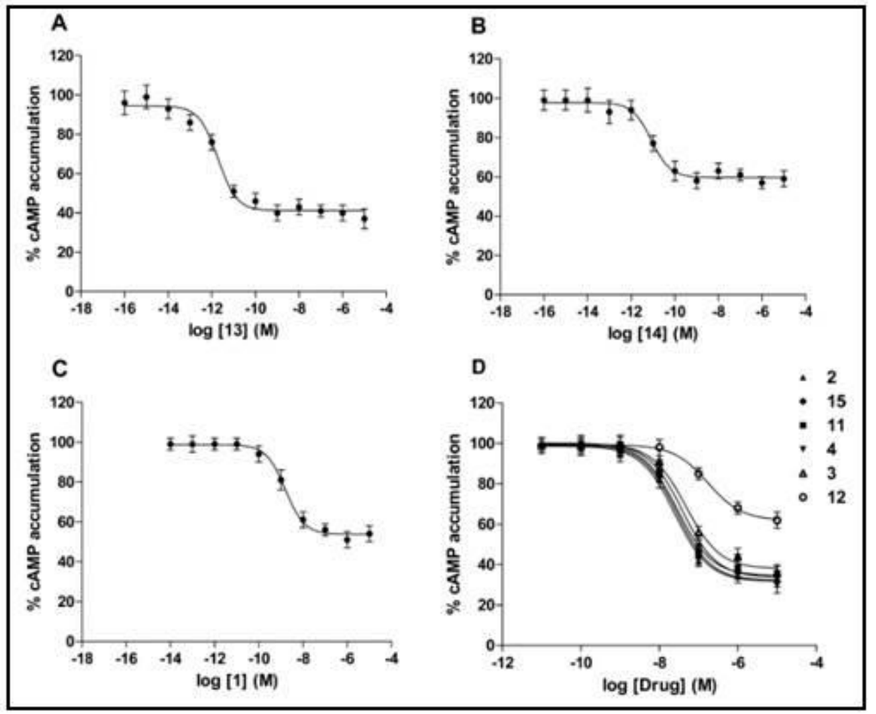
Prof. ssa Daniela Catarzi, Associato di Chimica Farmaceutica, Università di Firenze



Prof. ssa Vittoria Colotta, Associato di Chimica Farmaceutica, Università di Firenze

Images


A2A
Adenylyl Cyclase
cAMP
Gs α
inverse agonists
Antinociceptive Effect
NH2
R
N
N
NH
N
S
O
13 R = 2-OCH3
A2A: KH = 3.55 fM
KL = 6.45 nM
14 R = 3-OCH3
A2A: KH = 5.31 fM
KL = 26 nM


A
B
C
D
% cAMP accumulation
log [13] (M)
log [14] (M)
log [1] (M)
log [Drug] (M)
2
15
11
4
3
12

Industrial application

The patented technology is designed for the following fields of application:

1. Treatment of acute pain;
2. Treatment of inflammatory processes;
3. Treatment of fibrosis;
4. Oncological treatments;
5. Treatments of neurodegenerative diseases.

Among the advantages of the technology, it is possible to highlight that two compounds among those patented showed picomolar-order potency in functional tests of cyclic AMP, superior to that of already commercially available A2A receptor blockers, with antinociceptive action equal to or greater than morphine and the reference compound in writhing and tail immersion tests.

Possible Developments

The patent is available for outright assignment, as well as for exclusive and non-exclusive licensing. Licenses are available for the remaining term of the patent titles.

The Research Group is available for new collaborative and third-party research activities, in-depth technical investigations, scientific advice, also aimed at raising the TRL of the technology.

The TRL of the invention is 3.

For further information:

Ufficio di Trasferimento Tecnologico dell'Università degli Studi di Firenze

Sede: Piazza S. Marco 4 – 50121 Firenze

Sito web: www.unifi.it

E-mail: brevetti@unifi.it

For further information:

Ufficio Regionale di Trasferimento Tecnologico

Sede: Via Luigi Carlo Farini, 8 50121 Firenze (FI)

E-mail: urtt@regione.toscana.it

UNIVERSITÀ DEGLI STUDI FIRENZE

Università degli Studi di Ferrara

REGIONE TOSCANA

urtt Ufficio Regionale di Trasferimento Tecnologico