dose will depend on the condition being treated, the route of administration and the age, weight and condition of the patient and will be the doctor's discretion.

Compounds of the present invention may be used in the manufacture of medicaments for the treatment of any diseases disclosed herein. The compounds and pharmaceutical compositions described herein are useful for modulating TRPA1 receptors, wherein modulation is believed to be related to a variety of disease states.

The compound of the present invention can be administered alone or in combination with other therapeutic agents. For instance, the TRPA1 modulator is administered conjointly with one or more of an anti-inflammatory agent, anti-acne agent, anti-wrinkle agent, anti-scarring agent, anti-psoriatic agent, anti-proliferative agent, anti-fungal agent, anti-viral agent, anti-septic agent, anti-migraine agent, keratolytic agent, or a hair growth inhibitor

~~In accordance with another aspect, the present patent application further provides a method of inhibiting TRPA1 receptors in a subject in need thereof by administering to the subject one or more compounds described herein in the amount effective to cause inhibition of such receptor.~~

Detailed Description of the Invention

Definitions

The terms "halogen" or "halo" means fluorine (fluoro), chlorine (chloro), bromine (bromo), or iodine (iodo).

The term "alkyl" refers to a hydrocarbon chain radical that includes solely carbon and hydrogen atoms in the backbone, containing no unsaturation, having from one to eight carbon atoms (i.e. C_{1-8}alkyl), and which is attached to the rest of the molecule by a single bond, e.g., methyl, ethyl, n-propyl, 1-methylethyl (isopropyl), n-butyl, n-pentyl and 1,1-dimethylethyl (t-butyl). The term "C_1-C_6alkyl" refers to an alkyl chain having 1 to 6 carbon atoms. The term "C_1-C_4alkyl" refers to an alkyl chain having 1 to 4 carbon atoms. Unless set forth or recited to the contrary, all alkyl groups described or claimed herein may be straight chain or branched, substituted or unsubstituted.

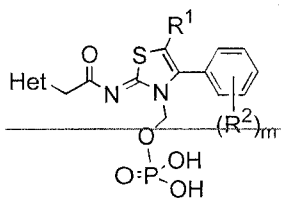
The term "alkoxy" refers an alkyl group attached via an oxygen linkage to the rest of the molecule (i.e. C_{1-8}alkoxy). Examples of such alkoxy moiety include, but are not limited to, $-OCH_3$ and $-OC_2H_5$. Unless set forth or recited to the contrary, all alkoxy groups described herein may be straight chain or branched, substituted or unsubstituted.

5. A pharmaceutical composition comprising one or more compounds selected from the compounds of any one of claims 1 to 4, and one or more pharmaceutically acceptable excipients, carriers, diluents or mixture thereof.

6. Use of the compound according to any one of claims 1 to 4 in the manufacture of a medicament for the treatment of the symptoms of a disease or condition associated with TRPA1 function which is selected from pain, chronic pain, complex regional pain syndrome, neuropathic pain, postoperative pain, rheumatoid arthritic pain, osteoarthritic pain, back pain, visceral pain, cancer pain, algesia, neuralgia, migraine, neuropathies, diabetic neuropathy, sciatica, HIV-related neuropathy, post-herpetic neuralgia, fibromyalgia, nerve injury, ischaemia, neurodegeneration, stroke, post stroke pain, multiple sclerosis, asthma, cough, COPD, oesophagitis, gastroeosophagal reflux disorder (GERD), irritable bowel syndrome, inflammatory bowel disease, pelvic hypersensitivity, urinary incontinence, cystitis, burns, psoriasis, eczema, emesis, stomach duodenal ulcer and pruritus.

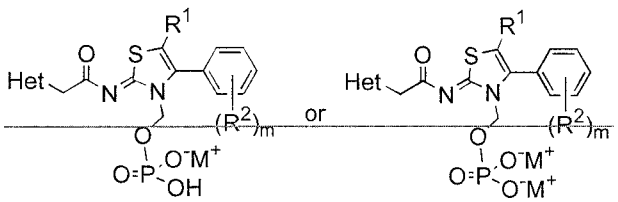
7. Use of the compound according to any one of claims 1 to 4 in the manufacture of a medicament for the treatment of chronic pain, neuropathic pain, rheumatoid arthritic pain or osteoarthritic pain.

~~8. A process for preparing a compound of formula Ic-1~~



(Ic-1)

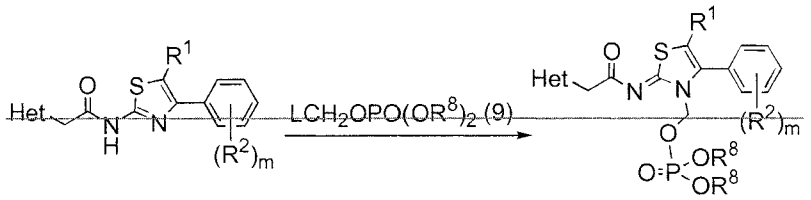
~~or a pharmaceutically acceptable salt thereof (Id-1 or Id),~~



(Id-1) (Id)

~~comprising:~~

a. reacting a compound of formula (1) or its salt with a compound of formula (9) to form a compound of formula Ic;



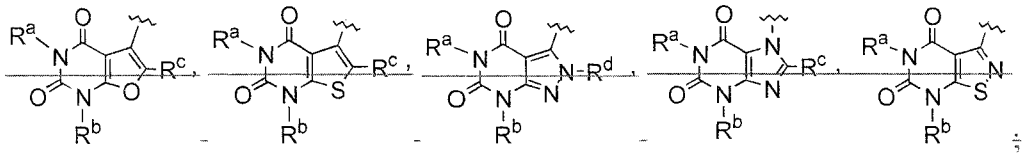
(1) (Ic)

b. converting compound of formula Ic to corresponding compound of formula Ic-1; and

c. optionally converting compound of formula Ic-1 to a pharmaceutically acceptable salt of formula Id-1 or Id,

wherein,

Het is selected from the group consisting of



R^1 is hydrogen;

at each occurrence, R^2, which may be the same or different, is independently selected from halogen, haloC_1-C_8alkyl and haloC_1-C_8alkoxy;

R^8 is selected from hydrogen, C_1-C_4alkyl, C_6-C_{14}arylC_1-C_6alkyl and pharmaceutically acceptable cation (M^+ or M^{2+});

R^a, R^b and R^d, which may be the same or different, are each independently selected from hydrogen and C_1-C_4alkyl;

R^c is selected from hydrogen and C_1-C_4alkyl;

'm' is an integer ranging from 0 to 5, both inclusive;

L is Cl, Br, OTs or I and

M^+ is a pharmaceutically acceptable cation.

9. The process of claim 8, wherein the step 'a' is performed in presence of a base selected from sodium hydride or sodium *tert*-butoxide or potassium *tert*-butoxide in a solvent and compound of formula (9) is di-*tert*-butyl iodomethyl phosphate.