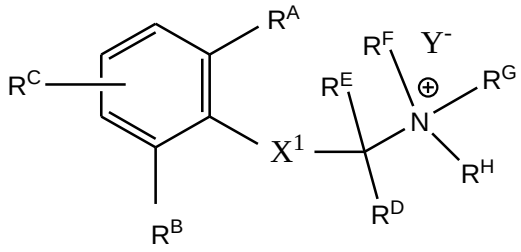
CLAIMS

What is claimed is:

1. A compound represented by Formula (**I**)



(**I**),

wherein:

Y^- is a pharmaceutically acceptable anion;

R^A is CO_2R^T;

R^T is substituted or unsubstituted alkyl ~~(preferably methyl or ethyl)~~;

R^B is H, D, halogen, or substituted or unsubstituted alkyl~~, preferably methyl or ethyl~~;

R^C is selected from as H, D, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, OR^I, CN, NR^JR^K, $NR^LC(O)R^M$, $S(O)R^N$, $S(O)_2R^N$, $SO_2R^OR^P$, $SO_2NR^QR^R$, SO_3R^S, CO_2R^T; $C(O)R^U$, and $C(O)NR^VR^W$~~, (preferably H, F, Cl, or CN and more preferably H)~~;

each of R^I, R^J, R^K, R^L, R^M, R^N, R^O, R^P, R^Q, R^R, R^S, R^U, R^V, and R^W is independently selected from H, D, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, or R^J and R^K or R^V and R^W or R^Q and R^R can also be taken together with the nitrogen to which they are attached to form a substituted or unsubstituted 5, 6, 7, or 8 membered ring;

X^1 is —$NR^ZC(O)$—;

R^Z is H, D, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, and substituted or unsubstituted heteroalkyl ~~(preferably H)~~;

each of R^D and R^E is independently selected from H, D, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted heteroalkyl, and substituted or unsubstituted cycloalkyl;

or R^D and R^E together with the carbon to which they are attached form a substituted or unsubstituted cycloalkyl ~~(such as a C_3-C_6 cycloalkyl)~~ or a substituted or unsubstituted heterocyclic ~~(such as a 3- to 15-membered heterocyclic ring)~~;

or R^D and R^Z together with the carbon and the —NC(O)— to which they are attached form a substituted or unsubstituted lactam;

~~each of R^F, R^G and R^H is independently selected from absent, H, D, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted C_6-C_{10} aryl, substituted or unsubstituted 5- to 10-membered heteroaryl, substituted or unsubstituted CH_2-C_5-C_{10} aryl, and substituted or unsubstituted CH_2-C_5-C_{10} heteroaryl; or alternatively, two or three of R^F,~~ wherein R^{GF} and R^{HG} together with the N^+ to which they are attached form an optionally substituted ~~heterocyclyl (such as a 3~~5- to ~~15~~10-membered heterocyclic ring~~)~~ having~~,~~ zero, one, or more heteroatoms in addition to the N^+, ~~including, but not limited to, an optionally substituted heteroaryl ring;~~

~~or two or three of R^D, R^E, R^F, R^G~~ and R^H ~~together with the N^+ form an optionally substituted heterocyclic ring having, zero, one or more heteroatoms in addition to the N^+, including but not limited to, a~~ is a substituted or unsubstituted –CH_2-C_5-C_{10} aryl, or substituted or unsubstituted –CH_2-C_5-C_{10} heteroaryl ~~ring; for example, two of R^E, R^F, and R^G are taken together with the N^+ to form a heterocyclic ring having, zero, one or more heteroatoms in addition to the N^+~~.

2. The compound of claim 1, wherein R^T is methyl or ethyl.

3. The compound of claim 1 ~~or 2~~, wherein X^1 is —NHC(O)—.

4. The compound of ~~any one of~~ claim~~s~~ 1 ~~to 3~~, wherein R^B is methyl, and R^C is selected from the group consisting of hydrogen, methyl, halogen, nitrile, methoxy, and ethoxy.

5. The compound of ~~any one of~~ claim~~s~~ 1 ~~to 3~~, wherein R^B are methyl and R^C is hydrogen.

6. The compound of ~~any one of~~ claim~~s~~ 1~~ to 5~~, wherein each of R^D and R^E is independently selected from hydrogen, D, substituted or unsubstituted alkyl; or R^D and R^E together form a substituted or unsubstituted C_3-C_6 cycloalkyl or substituted or unsubstituted heterocyclic.

7. The compound of claim 6, wherein R^D and R^E are both hydrogen.

8. The compound of claim 6, wherein R^D is hydrogen and R^E is a C_1-C_4 alkyl.

9. The compound of claim 8, wherein R^D is hydrogen and R^E is methyl, ethyl, n-propyl, or n-butyl.

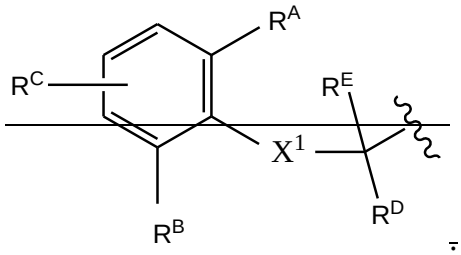
10. The compound of claim 6, wherein R^D and R^E are taken together with the carbon to which they are attached to form a substituted or unsubstituted C_3-C_6 cycloalkyl.

~~11. The compound of any one of claims 1 to 10, wherein each of R^F, R^G and R^H is the same or different and is selected from a substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, or a substituted or unsubstituted heteroaryl.~~

~~12. The compound of claim 11, wherein each of R^F, R^G and R^H is the same.~~

~~13. The compound of any one of claims 1 to 10, wherein R^F and R^G are the same or different and are each independently a substituted or unsubstituted alkyl, and R^H is a substituted or unsubstituted arylalkyl, or a substituted or unsubstituted heteroarylalkyl.~~

~~14. The compound of any one of claims 1 to 10, wherein R^F and R^G are the same or different and are each a substituted or unsubstituted alkyl, and R^H is:~~



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15. The compound of any one of claims 1 to 10, wherein two of R^F, R^G and R^H together with the N^+ to which they are attached form an optionally substituted 5- to 10-membered heterocyclic ring having, zero, one, or more heteroatoms in addition to the N^+.

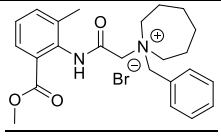
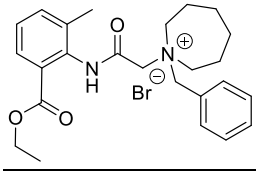
16. The compound of claim 15, wherein R^F and R^G are taken together with the N^+ to which they are attached to form a 5-, 6-, or 7-membered heterocyclyl, and R^H is an aralkyl or a heteroaralkyl.

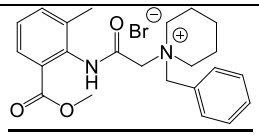
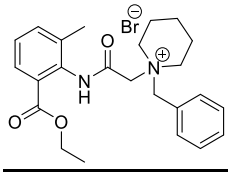
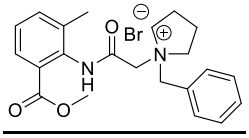
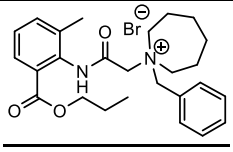
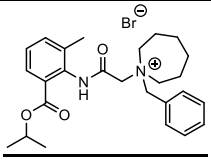
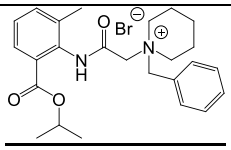
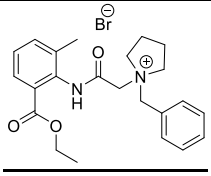
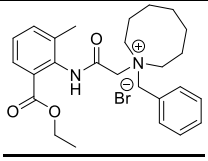
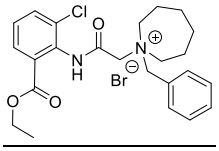
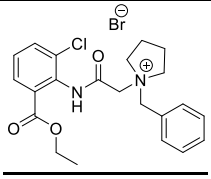
17. The compound of claim 15, wherein R^F and R^G together with the N^+ to which they are attached form an optionally substituted 5- to 10-membered heterocyclic ring having zero, one, or more heteroatoms in addition to the N^+, and R^H is $-CH_2-Z$; wherein Z is a substituted or unsubstituted aryl or a substituted or unsubstituted heteroaryl.

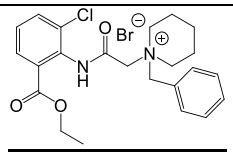
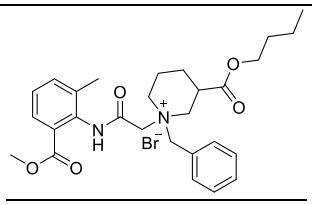
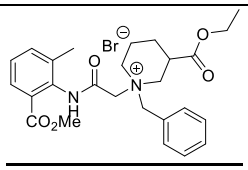
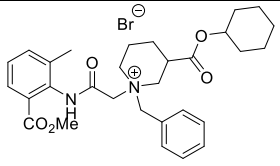
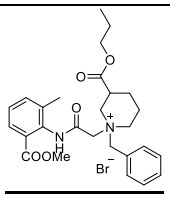
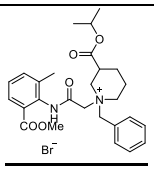
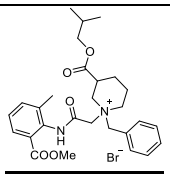
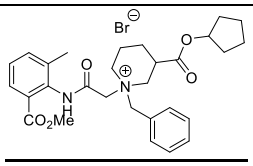
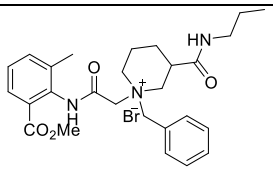
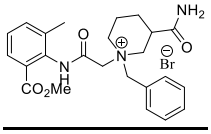
18. The compound of claim 17, wherein Z is selected from the group consisting of unsubstituted phenyl, phenyl substituted by a C_1-C_4 alkyl, halogen, methoxy, ethoxy, and cyano.

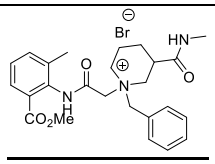
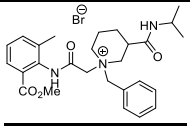
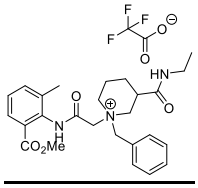
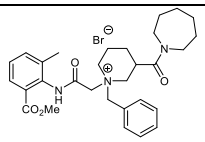
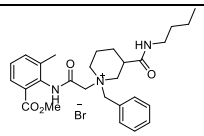
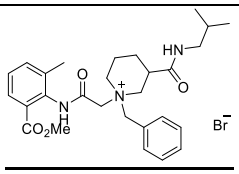
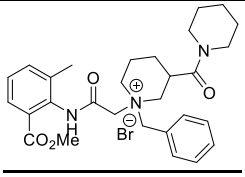
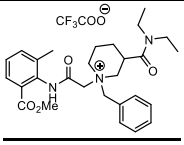
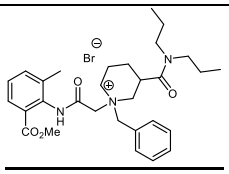
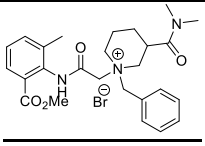
19. The compound of any one of claims 15 to 18, wherein R^F and R^G together with the N^+ to which they are attached form a five, six, or seven- membered ammonium-containing heterocyclic ring.

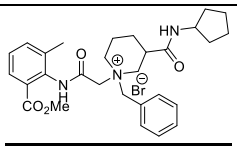
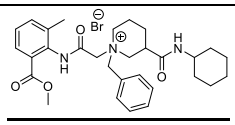
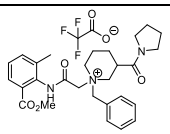
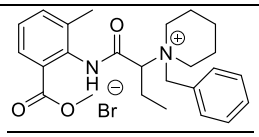
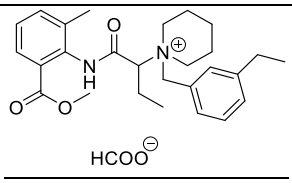
2011. The compound of ~~any one of~~ claim~~s~~ 1~~–19~~, wherein the compound is selected from those in the Table~~s described herein~~ below

Compound	**Structure**
1A	
2A	

3A	
4A	
5A	
6A	
7A	
8A	
9A	
10A	
11A	
12A	

13A	
14A	
16A	
17A	
18A	
19A	
20A	
21A	
28A	
30A	

31A	
32A	
33A	
34A	
35A	
36A	
37A	
38A	
39A	
40A	

41A	
42A	
43A	
57	
58A	

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~~21~~12. A pharmaceutical composition comprising the compound of ~~any one of~~ claim~~s~~ 1~~ to 20~~ or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

~~22~~13. The composition of claim ~~21~~13, wherein said composition is formulated for oral, intravenous, intramuscular, rectal, cutaneous, subcutaneous, topical, transdermal, sublingual, nasal, inhalation, vaginal, intrathecal, epidural, or ocular administration.

~~23~~14. Use of a compound of any one of claims 1 to ~~20~~ 11 or a composition of any one of claims ~~21~~ 12 to ~~22~~13 in the manufacture of a medicament for treating pain, cough, itch, or a neurogenic inflammatory disorder.

~~24~~15. The use of claim ~~23~~14, wherein said pain is selected from the group consisting of pain due to back and neck pain, lower back pain, cancer pain, gynecological and labor pain, fibromyalgia, arthritis, rheumatoid arthritis, osteoarthritis, rheumatological pains, orthopedic pains, acute and post herpetic neuralgia and other neuropathic pains ~~(including peripheral neuropathy)~~, sickle cell crises, vulvodynia, peri-anal pain,

irritable bowel disease, irritable bowel syndrome, inflammatory bowel disease, oral mucositis, esophagitis, interstitial cystitis, urethritis and other urological pains, dental pain, headaches, trigeminal trophic syndrome, erythromelalgia, abdominal wall pain, chronic abdominal wall pain, allergic rhinitis, muscle pain, rectal pain, Levator ani syndrome, proctalgia fugax, hemorrhoid pain, stomach pain, skin ulcers, stomach ulcers, burn pain, ophthalmic irritation, conjunctivitis ~~(e.g., allergic conjunctivitis)~~, eye redness, dry eye, dry eye syndrome ~~(chronic ocular pain)~~, complex regional pain syndrome, post-surgical ocular pain, postoperative pain, acute postoperative pain, and procedural pain ~~(i.e., pain associated with injections, draining an abscess, surgery, dental procedures, ophthalmic procedures, ophthalmic irritation, conjunctivitis (e.g., allergic conjunctivitis), eye redness, dry eye, arthroscopies and use of other medical instrumentation, cosmetic surgical procedures, dermatological procedures, setting fractures, biopsies, and the like)~~.

~~25~~16. The use of claim ~~23~~15, wherein said cough is selected from the group consisting of cough in patients with asthma, COPD, asthma-COPD overlap syndrome (ACOS), interstitial pulmonary fibrosis (IPF), idiopathic pulmonary fibrosis, post viral cough, post-infection cough, chronic idiopathic cough and lung cancer.

~~26~~17. The use of claim ~~23~~15, wherein said itch is selected from the group consisting of itch due to pruritus, brachioradial pruritus, chronic idiopathic pruritus, genital/anal pruritus, notalgia paresthetica, scalp pruritus, allergic dermatitis, contact dermatitis, atopic dermatitis, hand eczema, poison ivy, infections, parasites, insect bites, pregnancy, metabolic disorders, liver or renal failure, drug reactions, allergic reactions, eczema, genital and anal itch, hemorrhoid itch, and cancer.

~~27~~18. The use of claim ~~23~~15, wherein said neurogenic inflammatory disorder is selected from the group consisting of allergic inflammation, asthma, chronic cough, conjunctivitis, rhinitis, psoriasis, inflammatory bowel disease, interstitial cystitis, arthritis, colitis, contact dermatitis, diabetes, eczema, cystitis, gastritis, migraine headache, rosacea, sunburn, pancreatitis, chronic rhinosinusistis, traumatic brain injury, polymicrobial sepsis, tendinopathies, chronic urticaria, rheumatic disease,

acute lung injury, exposure to irritants, inhalation of irritants, pollutants, chemical warfare agents, and atopic dermatitis.

~~28. The use of claim 23, wherein a compound represented by Formula (**I**) is used in combination with one or more exogenous large pore receptor agonists.~~