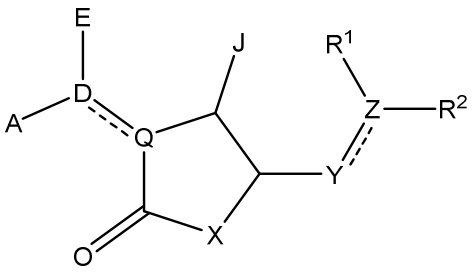
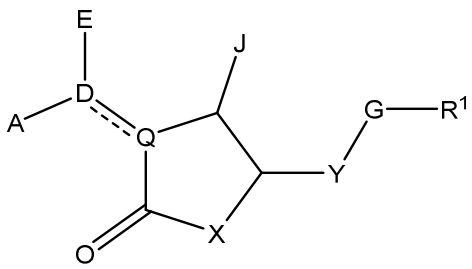
CLAIMS

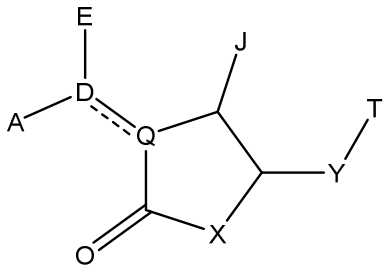
1. Compounds of formula I, II, III and IV, pharmaceutically acceptable salts or prodrug thereof,



(I)



(II)



(III)

wherein

------ represents a carbon–carbon single bond or a carbon–carbon double bond;

X is selected from O, S, NH, CH_2;

Y is selected from CH, CH_2;

Z is selected from C, N;

G is selected from O, S;

T is selected from OH, SH, NH_2, halogen;

R^1 and R^2 are independently selected from H, alkyl, alkenyl, cycloalkyl, aryl or $-CH_2-R^3$; wherein R^3 is selected from aryl, cycloalkyl, heteroaryl, $-R^4-R^5$; wherein R^4 is selected from alkyl, alkenyl; wherein R^5 is selected from aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted gama–lactone;

Q is selected from C, CH;

D is selected from C, CH, CH_2;

One of A and E is H and the other is selected from H, OH, SH, aryl, alkyl, alkenyl, R^6–R^7, wherein R^6 is selected from alkyl, alkenyl, and R^7 is selected from alkyl, alkenyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted gama-lactone;

J is selected from H, OH, SH, NH_2, halogen;

wherein the compound is not nitenin, dihydronitenin nor their respective isomers, enantiomers and stereoisomers.

2. The compounds of formula II according to claim 1, wherein

X is O;

Y is CH_2;

G is O;

R^1 is H;

J is H;

Q is C;

D is C;

E is H;

A is $-R^6-R^7$; wherein R^6 is alkyl and R^7 is heteroaryl.

3. The compounds of formula II according to claim 1, wherein

X is O;

Y is CH_2;

G is O;

R^1 is H;

J is H;

Q is C;

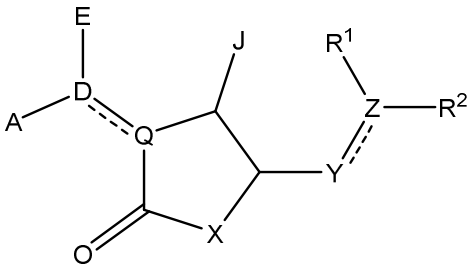
D is C;

E is $-R^6-R^7$; wherein R^6 is alkyl and R^7 is heteroaryl;

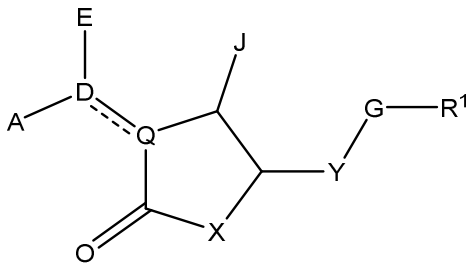
A is H.

4. The compounds of formula I, II and III, according to claim 1, wherein R^7 is not furan-3-yl.

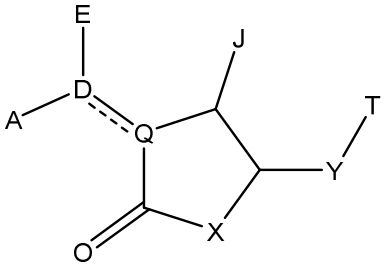
5. The compounds of formula I, II and III, pharmaceutically acceptable salts or prodrug thereof,



(I)



(II)



(III)

wherein

------ represents a carbon-carbon single bond or a carbon-carbon double bond;

X is selected from O, S, NH, CH_2;

Y is selected from CH, CH_2;

Z is selected from C, N;

G is selected from O, S;

T is selected from OH, SH, NH_2, halogen;

R^1 and R^2 are independently selected from H, alkyl, alkenyl, cycloalkyl, aryl or $-CH_2-R^3$; wherein R^3 is selected from aryl, cycloalkyl, heteroaryl, $-R^4-R^5$; wherein R^4 is selected from

alkyl, alkenyl; wherein R^5 is selected from aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted gama-lactone;
Q is selected from C, CH;
D is selected from C, CH, CH_2;
One of A and E is H and the other is selected from H, OH, SH, aryl, alkyl, alkenyl, R^6-R^7, wherein R^6 is selected from alkyl, alkenyl, and R^7 is selected from alkyl, alkenyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted gama-lactone;
J is selected from H, OH, SH, NH_2, halogen;
for use as a pharmaceutical ingredient.

6. The compounds of formula I for use as pharmaceutical ingredient according to claim 5, wherein;
X is O;
Y is CH;
Z is C;
R1 is alkyl;
R2 is $-CH_2-R^3$; wherein R^3 is $-R^4-R^5$; wherein R^4 is alkyl and R5 is heteroaryl;
Q is C;
D is C;
A is $-R^6-R^7$; wherein R^6 is alkyl and R^7 is heteroaryl;
E is H; and
J is H.

7. The compounds of formula II for use as pharmaceutical ingredient according to claim 5, wherein;
X is O;
Y is CH_2;
G is O;
R^1 is H;

J is H;

Q is C;

D is C;

E is H;

A is $-R^6-R^7$; wherein R^6 is alkyl and R^7 is heteroaryl.

8. The compounds of formula II for use as pharmaceutical ingredient according to claim 5, wherein;

X is O;

Y is CH_2;

G is O;

R^1 is H;

J is H;

Q is C;

D is C;

E is $-R^6-R^7$; wherein R^6 is alkyl and R^7 is heteroaryl;

A is H.

9. The compound of formula I, II and III according to any of claims 5 through 8, for use in the treatment, prevention or reduction of pain in an individual in need thereof.

10. The compound of formula I, II and III according to any of claims 5 through 8, for use in the treatment of at least one of the following acute and chronic pain types: neuropathic pain, nociceptive pain , psychogenic or somatogenic pain, diabetic neuropathic pain, post-herpetic pain, low-back pain, radiculopathy pain, musculoskeletal pain, post-operative and post-traumatic pain, phantom pain, surgical pain, wound associated pain, chemotherapy-induced peripheral neuropathic pain, short-term/acute or long-term/chronic inflammatory pain, rheumatic pain, arthritic pain, pain associated with osteoarthritis, myofascial pain, migraine, orofacial chronic pain, trigeminal neuralgia, pain

associated with cancer, pain associated with fibromyalgia, hyperalgesia syndromes, pain associated with infections, HIV related pain, sprains and strains, hyperalgesia, somatogenic pain, psychogenic pain, heat induced pain, physical pain, nociceptive pain, rheumatic pain, headache, pelvic pain, bladder pain, myofascial, vascular pain, migraine wound, wound associated pain, arthritic pain, somatic visceral pain, phantom pain, radiculopathy, lumbar pain, visceral pain, bowel pain, and pain associated with osteoarthritis.

11. The compound of formula I, II and III according to any of claims 5 through 8, for use in the treatment or prophylaxis of a disease in which Kv1.3 channels are involved.

12. The compound of formula I, II and III according to any of claims 5 through 8, for use in the treatment of autoimmune disorders.

13. The compound of formula I, II and III according any of claims 5 through 8, for use in the treatment of diabetes and insulin resistance syndromes.

14. The compounds of formula I, II and III and pharmaceutical salts or prodrug thereof are used as antiepileptic and antiseizures agents.

15. The compound of formula I, II and III according to any of claims 5 through 8, wherein the compound is administered in a therapeutically effective dose between 0.0018 and 1.8mg/kg.

16. Pharmaceutical composition comprising a pharmacologically acceptable diluent or carrier and a

combination of active ingredients, wherein said active ingredients comprise at least one compound as described in formula I, II and III in anyone of claims 5-8 or a pharmacologically acceptable salt or prodrug thereof.

~~17. A method of treating pain in a subject in need thereof, comprising administering to the subject having pain a therapeutically effective amount of a compound of formula I, II and III of any one of claims 5 through 8.~~

17. Use of a compound comprising Formula I, II and III of any of claims 5 through 8 in the manufacture of a medicament for treating pain wherein the medicament is to be administered at a therapeutically effective amount.

18. The use ~~method~~ according to claim 17, wherein the pain is of an acute or chronic pain type selected from neuropathic pain, nociceptive pain , psychogenic or somatogenic pain, diabetic neuropathic pain, post-herpetic pain, low-back pain, radiculopathy pain, musculoskeletal pain, post-operative and post-traumatic pain, phantom pain, surgical pain, wound associated pain, chemotherapy-induced peripheral neuropathic pain, short-term/acute or long-term/chronic inflammatory pain, rheumatic pain, arthritic pain, pain associated with osteoarthritis, myofascial pain, migraine, orofacial chronic pain, trigeminal neuralgia, pain associated with cancer, pain associated with fibromyalgia, hyperalgesia syndromes, pain associated with infections, HIV related pain, sprains and strains, hyperalgesia, somatogenic pain, psychogenic pain, heat induced pain, physical pain, nociceptive pain, rheumatic pain, headache, pelvic pain, bladder pain, myofascial, vascular pain, migraine wound, wound associated pain, arthritic pain, somatic visceral pain, phantom pain, radiculopathy, lumbar pain, visceral pain, bowel pain, and pain associated with osteoarthritis.

~~19. A method of treatment or prophylaxis of a disease in which Kv1.3 channels are involved in a subject in need thereof, comprising administering a therapeutically effective amount of a compound of formula I, II and III of anyone of claims 5 through 8 to a subject in need of treatment or prophylaxis of a disease in which Kv1.3 channels are involved.~~

19. Use of a compound comprising Formula I, II and III of any of claims 5 through 8 in the manufacture of a medicament for treating prophylaxis of a disease in which Kv1.3 channels are involved wherein the medicament is to be administered at a therapeutically effective amount.

~~20. A method of treatment of an autoimmune disease in a subject in need thereof, comprising administering a therapeutically effective amount of a compound of anyone of claims 5 through 8 to a subject having an autoimmune disease.~~

20. Use of a compound comprising Formula I, II and III of any of claims 5 through 8 in the manufacture of a medicament for treating autoimmune disease wherein the medicament is to be administered at a therapeutically effective amount.

~~21. A method of treatment of diabetes or insulin resistance syndromes in a subject in need thereof, comprising administering a therapeutically effective amount of a compound of anyone of claims 5 through 8 to a subject having diabetes or an insulin resistance syndrome.~~

21. Use of a compound comprising Formula I, II and III of any of claims 5 through 8 in the manufacture of a medicament for treating diabetes or an insulin resistance syndrome wherein the medicament is to be administered at a therapeutically effective amount.

~~22. A method of treatment of epilepsy or seizures in a subject in need thereof, comprising administering a therapeutically effective amount of a compound of anyone of claims 5 through 8 to a subject having epilepsy or seizures.~~

22. Use of a compound comprising Formula I, II and III of any of claims 5 through 8 in the manufacture of a medicament for treating epilepsy or seizures wherein the medicament is to be administered at a therapeutically effective amount.

~~23. The method according to anyone of claims 17 through 21, wherein the compound is administered in a therapeutically effective amount between 0.018 and 1.8 mg/kg.~~

23. Use of a compound comprising Formula I, II and III of any of claims 17 through 21 in the manufacture of a medicament having a therapeutically effective amount between 0.018 and 1.8 mg/kg.

24. The compound, composition, or use~~, or method~~ of anyone of claims 1 through 23, wherein the compound is a compound of formula I, wherein

X is O;

Y is CH;

Z is C;

R^1 is alkyl;

R^2 is $-CH_2-R^3$; wherein R^3 is $-R^4-R^5$; wherein R^4 is alkyl and R^5 is heteroaryl;

Q is C;

D is C;

A is $-R^6-R^7$; wherein R^6 is alkyl and R^7 is heteroaryl;

E is H; and

J is H.

25. The compound of anyone of claims 1 through 4, wherein the compound is isolated or synthetically produced.

26. The compound of anyone of claims 5 through 24, wherein the compound is nitenin or dihydronitenin.