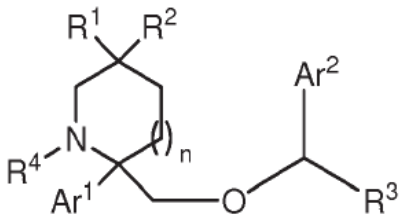
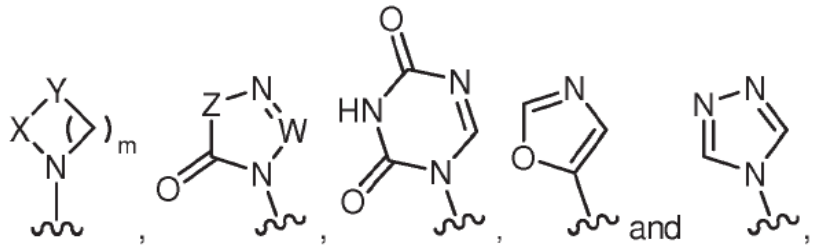
What is claimed is:

1. A compound of the formula:



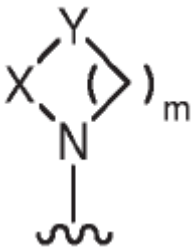
or pharmaceutically acceptable salts and/or solvates thereof, wherein:

R^1 and R^2 are each independently selected from the group consisting of H, alkyl, haloalkyl, alkyl substituted with one or more hydroxyl groups, -CN, alkynyl, $-N(R^6)_2$, $-N(R^6)-S(O_2)-$alkyl, $-N(R^6)-C(O)-N(R^9)_2$, -alkylene-CN, -cycloalkylene-CN, -alkylene-O-alkyl, -C(O)-alkyl, $-C(=N-OR^5)$-alkyl, $-C(O)-N(R^9)_2$, -C(O)-O-alkyl, -alkylene-C(O)-alkyl, -alkylene-C(O)-O-alkyl, -alkylene-$C(O)-N(R^9)_2$,



with the proviso that at least one of R^1 and R^2 is -CN;
W is $=C(R^8)-$ or =N-;
X is -C(O)- or $-S(O_2)-$;
Y is selected from the group consisting of $-CH_2-$, -O-, and $-N(R^6)-C(O)-$, with the proviso that:

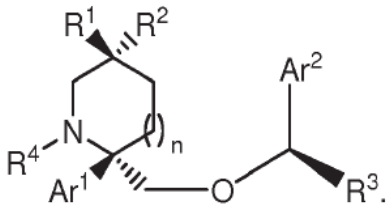
(a) the nitrogen atom of $-N(R^6)-C(O)-$ is bonded to X, and
(b) if R^1 or R^2 is



and Y is -O-, X is not -$S(O_2)$-;

Z is -$C(R^7)_2$-, -$N(R^6)$-, or -O-;
R^3 is selected from the group consisting of H, -CH_2OR^5, and alkyl;
R^4 is selected from the group consisting of H, alkyl, cycloalkyl, heterocycloalkyl, heteroaryl, aryl, acyl, aroyl, alkylsulfonyl, and arylsulfonyl;
R^5 is H or alkyl;
R^6 is selected from the group consisting of H, alkyl, cycloalkyl, and aryl;
each R^7 is independently H or alkyl; or
each R^7, together with the ring carbon to which they are shown attached, form a cycloalkylene ring;
R^8 is selected from the group consisting of H, alkyl, alkyl substituted with one or more hydroxyl groups, -$N(R^6)_2$, -$N(R^6)$-$S(O_2)$-alkyl, -$N(R^6)$-$S(O_2)$-aryl, -$N(R^6)$-C(O)-alkyl, -$N(R^6)$-C(O)-aryl, alkylene-O-alkyl, and -CN;
R^9 is selected from the group consisting of H, alkyl, and aryl, or each R^9, together with the nitrogen to which they are shown attached, form a heterocycloalkyl ring;
Ar^1 and Ar^2 are each independently selected from the group consisting of unsubstituted aryl and aryl substituted with 0 to 3 substituents selected from the group consisting of halogen, alkyl, alkoxy, haloalkyl, haloalkoxy, -CN, -OH, and -NO_2;
n is 0, 1, or 2; and
m is 1, 2, or 3.

2. The compound according to claim 1, wherein the compound has the following structure:



3. The compound according to claim 1, wherein:

R^3 is alkyl;
R^4 is H;
Ar^1 is substituted or unsubstituted phenyl;
Ar^2 is substituted or unsubstituted phenyl; and
n is 1.

4. The compound according to claim 2, wherein:

R^3 is alkyl;
R^4 is H;
Ar^1 is unsubstituted phenyl;
Ar^2 is substituted phenyl; and
n is 1.

5. The compound according to claim 1, wherein:

R^3 is alkyl;
R^4 is H;
Ar^1 is monosubstituted phenyl;
Ar^2 is substituted phenyl; and
n is 1.

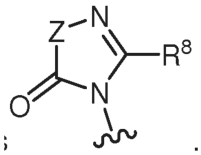
6. The compound according to claim 4, wherein:

Ar^2 is 3,5-bis(trifluoromethyl)phenyl, 3,5-bis(fluoro)phenyl, 3,5-bis(chloro)phenyl, 3,5-bis(methyl)phenyl, or 3,5-bis(methoxy)phenyl.

7. The compound according to claim 6, wherein:

R^3 is $-CH_3$.

8. The compound according to claim 7, wherein:
one of R^1 or R^2 is



;

9. The compound according to claim 8, wherein:

Z is -NH-; and
R^8 is H.

10. The compound according to claim 8, wherein:

Z is -NH-; and
R^8 is $-NH-S(O_2)-CH_3$.

11. The compound according to claim 8, wherein:

Z is -NH-; and
R^8 is $-CH_2-OH$.

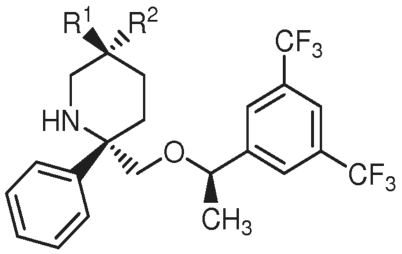
12. The compound according to claim 8, wherein:

Z is -NH-; and
R^8 is $-CH_2-O-CH_3$.

13. The compound according to claim 8, wherein:

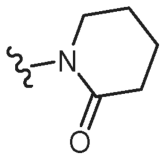
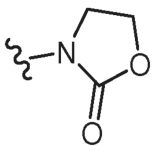
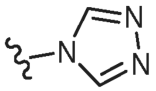
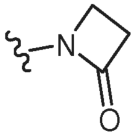
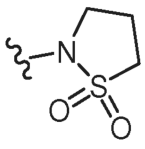
Z is -NH-; and
R^8 is $-NH_2$.

14. The compound according to claim 1, having the formula:

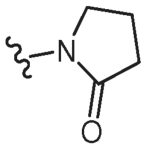
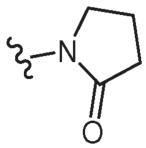
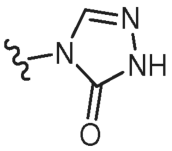
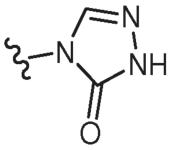


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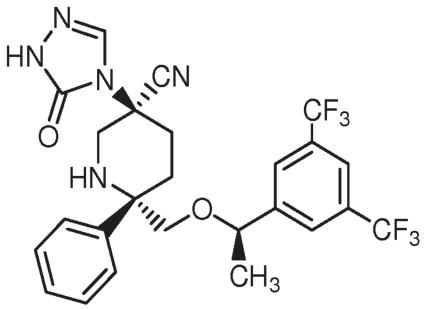
wherein R^1 and R^2 are selected from the group consisting of:

Compound	R^1	R^2
1		-CN
2		-CN
7	-CN	
9		-CN
32		-CN

(continued)

Compound	R^1	R^2
33		-CN
34	-CN	
35	-CN	
36	-NH-S(O_2)-CH_3	-CN
37	-CN	-NH-S(O_2)-CH_3
39	-CN	-NH_2
40	-NH_2	-CN
41	-NH-C(O)-NH_2	-CN
42		-CN

15. The compound according to claim 2, represented by the following formula:



or a pharmaceutically acceptable salt and/or solvate thereof.

16. A pharmaceutical composition comprising:

at least one compound of any one of claims 1-15 or a pharmaceutically acceptable salt and/or solvate thereof, and at least one pharmaceutically acceptable carrier.

17. A pharmaceutical composition comprising a pharmaceutically acceptable carrier, at least one serotonin reuptake inhibitor, and at least one compound of any one of claims 1-15 or a pharmaceutically acceptable salt and/or solvate

thereof.

18. A compound of any one of claims 1-15 or a pharmaceutically acceptable salt and/or solvate thereof, for use in a method of treating a physiological disorder, symptom or disease selected from the group consisting of respiratory diseases, inflammatory diseases, skin disorders, ophthalmological disorders, central nervous system conditions, depression, anxiety, phobia, bipolar disorder, addictions, alcohol dependence, psychoactive substance abuse, epilepsy, nociception, psychosis, schizophrenia, Alzheimer's disease, AIDS related dementia, Towne's disease, stress related disorders, obsessive/compulsive disorders, eating disorders, bulimia, anorexia nervosa, binge eating, sleep disorders, mania, premenstrual syndrome, gastrointestinal disorders, atherosclerosis, fibrosing disorders, obesity, Type II diabetes, pain related disorders, headache, neuropathic pain, post-operative pain, chronic pain syndrome, bladder disorders, genitourinary disorders, cough, emesis, and nausea.

19. The compound for use of claim 18, wherein the physiological disorder, symptom or disease is emesis, depression, anxiety or cough.

20. The compound for use of claim 19, wherein the physiological disorder, symptom or disease is depression or anxiety.

21. The compound for use of claim 18, wherein the physiological disorder, symptom or disease is emesis and/or nausea.

22. The compound for use of claim 19, wherein the physiological disorder, symptom or disease is cough.

23. The compound for use of claim 20, wherein the treatment comprises administering said compound and at least one anti-depressant agent and/or at least one anti-anxiety agent.

24. The compound for use of claim 20, wherein the treatment comprises administering said compound and at least one selective serotonin reuptake inhibitor, and wherein the physiological disorder, symptom or disease is depression.

25. A compound of any one of claims 1-15 or a pharmaceutically acceptable salt and/or solvate thereof for use in a method of antagonizing an effect of a Substance P at a neurokinin-1 receptor site or for blocking at least one neurokinin-1 receptor, in a patient in need of such treatment.

26. The compound for use of claim 18, wherein the treatment comprises administering said compound and at least one active ingredient selected from the group consisting of other NK_1 receptor antagonists, selective serotonin reuptake inhibitors, dopamine receptor agonists, serotonin 5-HT_3 receptor antagonists, serotonin 5-HT_{2c} receptor agonists, nociceptin receptor agonists, glucocorticoids and inhibitors of multidrug resistance protein 5; and
wherein the physiological disorder, symptom or disease is selected from the group consisting of: a respiratory disease, depression, anxiety, phobia, bipolar disorder, alcohol dependence, psychoactive substance abuse, nociception, psychosis, schizophrenia, stress related disorder, obsessive/compulsive disorder, bulimia, anorexia nervosa, binge eating, sleep disorder, mania, premenstrual syndrome, gastrointestinal disorder, obesity, headache, neuropathic pain, post-operative pain, chronic pain syndrome, bladder disorder, genitourinary disorder, cough, emesis and nausea.

27. A compound according to any one of claims 1-15 or a pharmaceutically acceptable salt and/or solvate thereof for use in a method of treating emesis and/or nausea, wherein the treatment comprises administering said compound in combination with at least one serotonin 5-HT_3 receptor antagonist and/or at least one glucocorticoid.

28. The compound for use of claim 27, wherein the serotonin 5-HT_3 receptor antagonist is ondansetron and the glucocorticoid is dexamethasone.

29. A kit, comprising:

    two or more separate containers in a single package, wherein each container comprises a pharmaceutical composition;
    wherein a first container of said package comprises a first pharmaceutical composition comprising a compound of any one of claims 1-15 and/or a pharmaceutically acceptable salt and/or solvate thereof in a pharmaceutically acceptable carrier,
    a second container of said package comprises a second pharmaceutical composition comprising another therapeutic agent in a pharmaceutically acceptable carrier, and