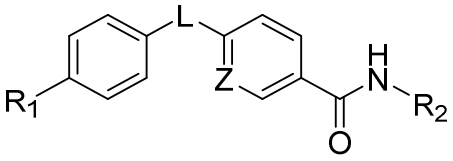
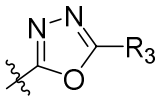
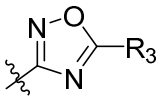
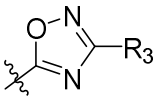
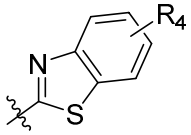
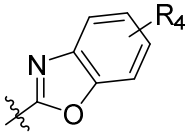
SUMMARY

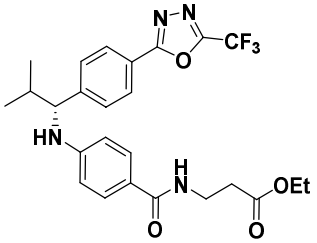
The present invention relates to certain amide compounds as glucagon receptor modulators for treating glucagon-associated disorders. Unexpectedly, these compounds, acting as antagonists or inverse agonists of the glucagon receptor, produce higher efficacy in modulating the glucagon receptor for reducing the glycemic level, as compared to known therapeutic agents.

An aspect of this invention is drawn to the compounds of formula (I) below and pharmaceutically acceptable salts thereof:



(I).

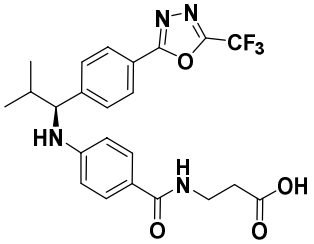
In this formula, R_1 is , , , , or ; R_2 is $-CH_2CH_2CO_2R_5$ or $-CH_2CH_2SO_3H$; L is $–X-CH(R_6)-$ or $–CH(R_6)-X-$, X being NH or O; and Z is C or N, in which R_3 is C_{1-6} alkyl, aryl, or heteroaryl, the C_{1-6} alkyl being optionally substituted with one to three halo moieties and each of the aryl and heteroaryl being optionally substituted with one to three moieties selected from the group consisting of C_{1-6} alkyl, C_{3-10} cycloalkyl, aryl, halogen substituted C_{1-6} alkyl, C_{1-6} alkoxy, and halo; R_4 represents one to three moieties selected from H, halo, hydroxyl, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxy, halogen substituted C_{1-6} alkyl, and C_{3-10} cycloalkyl; R_5 is H, C_{1-6} alkyl, , C_{3-10} cycloalkyl or halogen substituted C_{1-6} alkyl; and R_6 is C_{1-6} alkyl, C_{3-10} cycloalkyl, or C_{1-10} heterocycloalkyl, the C_{1-6} alkyl being optionally substituted with one to three moieties selected from halo, hydroxyl, C_{1-6} alkoxy, and aryl, and each of the C_{3-10} cycloalkyl and C_{1-10} heterocycloalkyl being optionally substituted with one to two moieties selected from the group consisting of C_{1-6} alkyl, C_{1-6} alkoxy, and halo.



^{1}H NMR (400MHz, DMSO-d_6): δ 7.94-8.07 (m, 3H), 7.60-7.64 (m, 2H), 7.45-7.53 (m, 2H), 6.65-6.73 (m, 1H), 6.52-6.60 (m, 2H), 3.99-4.07 (m, 2H), 1.97-2.11 (m, 3H), 1.14 (s, 4H), 1.00-1.06 (m, 3H), 0.77-0.86 (m, 3H). MS(M+1):505.

Compound 1-57.

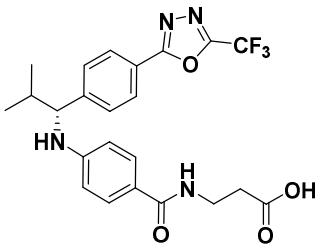
(S)-3-(4-((2-methyl-1-(4-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)phenyl)propyl)amino)benzamido)propanoic acid



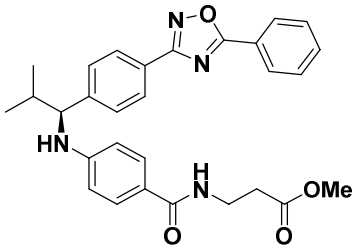
^{1}H NMR (400MHz, DMSO-d_6): δ 8.02 (d, J = 8.3 Hz, 2H), 7.98 (t, J = 5.4 Hz, 1H), 7.62 (d, J = 8.3 Hz, 2H), 7.48 (d, J = 8.8 Hz, 2H), 6.68 (d, J = 7.8 Hz, 1H), 6.55 (d, J = 8.8 Hz, 2H), 4.30 (t, J = 7.6 Hz, 1H), 2.41 (t, J = 7.1 Hz, 2H), 1.98-2.11 (m, 1H), 1.03 (d, J = 6.4 Hz, 3H), 0.81 (d, J = 6.8 Hz, 3H). MS(M+1):477.

Compound 1-58.

(R)-3-(4-((2-methyl-1-(4-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)phenyl)propyl)amino)benzamido)propanoic acid



methyl (S)-3-(4-((2-methyl-1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)propyl)amino)benzamido)propanoate



1H NMR (400MHz, DMSO-d6) : δ 8.14-8.19 (m, 2H), 7.97-8.03 (m, 3H), 7.70-7.76 (m, 1H), 7.62-7.69 (m, 2H), 7.53-7.59 (m, 2H), 7.45-7.50 (m, 2H), 6.64-6.68 (m, 1H), 6.54-6.59 (m, 2H), 4.22-4.28 (m, 1H), 3.55-3.56 (m, 3H), 2.68 (s, 8H), 1.99-2.09 (m, 1H), 1.01-1.06 (m, 3H), 0.79-0.84 (m, 3H) MS(M+1): 499.

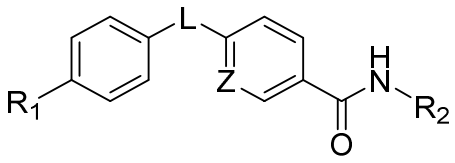
EXAMPLE 3: Synthesis of the compounds shown in the following Table 3

The following scheme was followed for synthesizing Compounds 3-1 to 3-15.

Scheme III

WHAT IS CLAIMED IS:

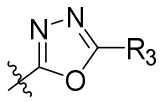
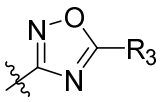
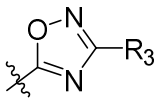
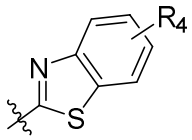
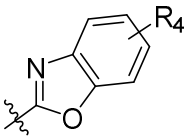
1. A compound of formula (I):



(I),

or a pharmaceutically acceptable salt thereof,

wherein

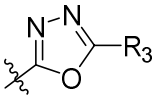
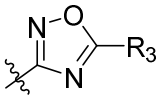
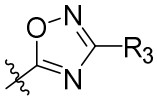
R_1 is , , , , or ;

R_2 is $-CH_2CH_2CO_2R_5$ or $-CH_2CH_2SO_3H$;

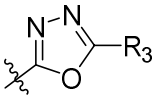
L is $–X-CH(R_6)-$ or $–CH(R_6)-X-$, X being NH or O; and

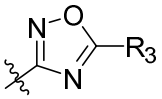
Z is C or N,

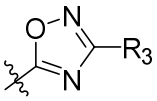
in which R_3 is C_{1-6} alkyl, aryl, or heteroaryl, the C_{1-6} alkyl being optionally substituted with one to three halo moieties and each of the aryl and heteroaryl being optionally substituted with one to three moieties selected from the group consisting of C_{1-6} alkyl, C_{3-10} cycloalkyl, aryl, halogen substituted C_{1-6} alkyl, C_{1-6} alkoxy, and halo; R_4 represents one to three moieties selected from the group consisting of H, halo, hydroxyl, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxy, halogen substituted C_{1-6} alkyl, and C_{3-10} cycloalkyl; R_5 is H, C_{1-6} alkyl, C_{3-10} cycloalkyl or halogen substituted C_{1-6} alkyl; and R_6 is C_{1-6} alkyl, C_{3-10} cycloalkyl, or C_{1-10} heterocycloalkyl, the C_{1-6} alkyl being optionally substituted with one to three moieties selected from the group consisting of halo, hydroxyl, C_{1-6} alkoxy, and aryl, and each of the C_{3-10} cycloalkyl and C_{1-10} heterocycloalkyl being optionally substituted with one to two moieties selected from the group consisting of C_{1-6} alkyl, C_{1-6} alkoxy, and halo.

2. The compound or salt of claim 1, wherein R_1 is , , or .

3. The compound or salt of claim 2, wherein L is –CH(R_6)-X-, X being NH or O.

4. The compound or salt of claim 3, wherein R_1 is .

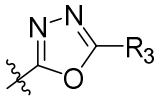
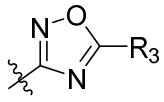
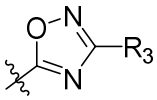
5. The compound or salt of claim 3, wherein R_1 is .

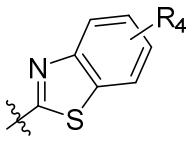
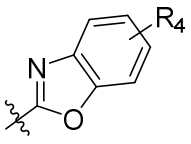
6. The compound or salt of claim 3, wherein R_1 is .

7. The compound or salt of claim 2, wherein L is –X-CH(R_6)-, X being NH or O.

8. The compound or salt of claim 2, wherein R_3 is C_{1-6} alkyl, optionally substituted phenyl or pyridinyl.

9. The compound or salt of claim 2, wherein L is –CH(R_6)-X-, R_6 being C_{1-6} alkyl.

10. The compound or salt of claim 1, wherein R_1 is , , or , R_3 being C_{1-6} alkyl, optionally substituted phenyl or pyridinyl; L is –X-CH(R_6)- or –CH(R_6)-X-, R_6 being C_{1-6} alkyl; and Z is C.

11. The compound or salt of claim 1, wherein R_1 is  or .

12. The compound or salt of claim 11, wherein L is –CH(R_6)-X-.

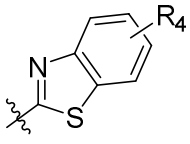
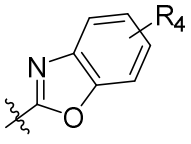
13. The compound or salt of claim 12, wherein X is NH and Z is N.

14. The compound or salt of claim 12, wherein R_6 is C_{1-6} alkyl.

15. The compound or salt of claim 11, wherein L is –X-CH(R_6)- and Z is C.

16. The compound or salt of claim 15, wherein R_6 is C_{1-6} alkyl.

17. The compound or salt of claim 11, wherein R_4 is H.

18. The compound or salt of claim 1, wherein R_1 is  or , R_4 being H; and L is –X-CH(R_6)- or –CH(R_6)-X-, R_6 being C_{1-6} alkyl.

19. The compound or salt of claim 1, wherein R_3 is C_{1-6} alkyl, aryl, or 6-membered heteroaryl, the C_{1-6} alkyl being optionally substituted with one to three halo moieties and each of the aryl and 6-membered heteroaryl being optionally substituted with one to three moieties selected from the group consisting of methyl, trifluoromethyl, ethyl, propyl, isopropyl, butyl, tert-butyl, F and Cl.

20. The compound or salt of claim 1, wherein R_6 is C_{1-6} alkyl or C_{3-10} cycloalkyl, the C_{1-6} alkyl being optionally substituted with one to three moieties selected from the group consisting of fluoro, hydroxyl, methoxy, and phenyl.

21. The compound or salt of claim 1, which is any one selected from the group consisting of.

3-(4-((2-Methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)propyl)amino)benzamido) propanoic acid;

Methyl 3-(4-((2-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)propyl)amino) benzamido)propanoate;

Ethyl 3-(4-((2-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)propyl)amino) benzamido)propanoate;

3-(4-((2-Methyl-1-(4-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)phenyl)propyl)amino) benzamido)propanoic acid;

3-(4-((3-Methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)butyl)amino)benzamido) propanoic acid;

Ethyl 3-(4-((1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)butyl)amino)benzamido) propanoate;

3-(4-((1-(4-(5-Phenyl-1,3,4-oxadiazol-2-yl)phenyl)butyl)amino)benzamido)propanoic acid;

3-(4-((1-(4-(5-(Trifluoromethyl)-1,3,4-oxadiazol-2-yl)phenyl)butyl)amino)benzamido) propanoic acid;

3-(4-((3-Methyl-1-(4-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)phenyl)butyl)amino) benzamido)propanoic acid;

Ethyl 3-(4-((2-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)butyl)amino) benzamido)propanoate;

3-(4-((2-Methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)butyl)amino)benzamido) propanoic acid;

3-(4-((1-(4-(5-(tert-butyl)-1,3,4-oxadiazol-2-yl)phenyl)-3-methylbutyl)amino)benzamido) propanoic acid;

2-(4-((1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)pentyl)amino)benzamido)ethane-1-sulfonic acid;

3-(4-((1-(4-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)phenyl)pentyl)amino)benzamido)propanoic acid;

Ethyl 3-(4-((1-(4-(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)phenyl)pentyl)amino) benzamido)propanoate;

3-(4-((1-(4-(5-(Pyridin-2-yl)-1,3,4-oxadiazol-2-yl)phenyl)pentyl)amino)benzamido) propanoic acid;

Ethyl 3-(4-((1-(4-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)phenyl)-2-methylpropyl) amino)benzamido)propanoate;

3-(4-((1-(4-(5-(4-Fluorophenyl)-1,3,4-oxadiazol-2-yl)phenyl)-2-methylpropyl)amino) benzamido)propanoic acid;

Ethyl 3-(4-((1-(4-(5-(tert-butyl)-1,3,4-oxadiazol-2-yl)phenyl)pentyl)amino) benzamido) propanoate;

3-(4-((1-(4-(5-(tert-butyl)-1,3,4-oxadiazol-2-yl)phenyl)pentyl)amino)benzamido) propanoic acid;

Ethyl 3-(4-((1-(4-(5-(tert-butyl)-1,3,4-oxadiazol-2-yl)phenyl)-2-methylbutyl)amino) benzamido)propanoate;

3-(4-((1-(4-(5-(tert-butyl)-1,3,4-oxadiazol-2-yl)phenyl)-2-methylbutyl)amino)benzamido)propanoic acid;

ethyl 3-(4-((1-(4-(5-(tert-butyl)-1,3,4-oxadiazol-2-yl)phenyl)-2-methylpropyl)amino) benzamido)propanoate;

3-(4-((1-(4-(5-(tert-butyl)-1,3,4-oxadiazol-2-yl)phenyl)-2-methylpropyl)amino)benzamido)propanoic acid;

ethyl 3-(4-((1-(4-(5-(4-methoxyphenyl)-1,3,4-oxadiazol-2-yl)phenyl)-2-methylpropyl) amino)benzamido)propanoate;

3-(4-((1-(4-(5-(4-methoxyphenyl)-1,3,4-oxadiazol-2-yl)phenyl)-2-methylpropyl)amino)benzamido)propanoic acid;

ethyl 3-(4-((1-(4-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)phenyl)-3-methylbutyl) amino)benzamido)propanoate;

3-(4-((1-(4-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)phenyl)-3-methylbutyl)amino)benzamido)propanoic acid;

ethyl 3-(4-((1-(4-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)phenyl)-2-methylbutyl) amino)benzamido)propanoate;

3-(4-((1-(4-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)phenyl)-2-methylbutyl)amino)benzamido)propanoic acid;

ethyl 3-(4-((2-methyl-1-(4-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)phenyl)butyl)amino)benzamido)propanoate;

3-(4-((2-methyl-1-(4-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)phenyl)butyl)amino)benzamido)propanoic acid;

ethyl 3-(4-((1-(4-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)phenyl)pentyl)amino)benzamido)propanoate;

ethyl 3-(4-(((1S)-2-methyl-1-(4-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)phenyl)butyl)amino)benzamido)propanoate;

ethyl 3-(4-(((1R)-2-methyl-1-(4-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)phenyl)butyl)amino)benzamido)propanoate;

3-(4-(((1S)-2-methyl-1-(4-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)phenyl)butyl)amino)benzamido)propanoic acid;

3-(4-(((1R)-2-methyl-1-(4-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)phenyl)butyl)amino)benzamido)propanoic acid;

methyl 3-(4-((1-(4-(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)phenyl)pentyl)amino)benzamido)propanoate;

(S)-ethyl 3-(4-(2-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)propylamino)benzamido)propanoate;

(R)-ethyl 3-(4-(2-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)propylamino)benzamido)propanoate;

(S)-3-(4-(2-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)propylamino)benzamido)propanoic acid;

(R)-3-(4-(2-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)propylamino)benzamido)propanoic acid;

ethyl (S)-3-(4-((1-(4-(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)phenyl)pentyl)amino)benzamido)propanoate;

ethyl (R)-3-(4-((1-(4-(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)phenyl)pentyl)amino)benzamido)propanoate;

(S)-3-(4-((1-(4-(5-(pyridin-2-yl)-1,3,4-oxadiazol-2yl)phenyl)pentyl)amino)benzamido)propanoic acid;

(R)-3-(4-((1-(4-(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)phenyl)pentyl)amino)benzamido)propanoic acid;

ethyl 3-(4-(((1S)-2-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)butyl)amino) benzamido)propanoate;

ethyl 3-(4-(((1R)-2-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)butyl)amino) benzamido)propanoate;

3-(4-(((1S)-2-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)butyl)amino)benzamido)propanoic acid;

3-(4-(((1R)-2-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)butyl)amino)benzamido)propanoic acid;

ethyl (S)-3-(4-((1-(4-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)phenyl)pentyl)amino) benzamido)propanoate;

ethyl (R)-3-(4-((1-(4-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)phenyl)pentyl)amino) benzamido)propanoate;

(S)-3-(4-((1-(4-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)phenyl)pentyl)amino)benzamido)propanoic acid;

(R)-3-(4-((1-(4-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)phenyl)pentyl)amino)benzamido)propanoic acid;

ethyl (S)-3-(4-((2-methyl-1-(4-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)phenyl) propyl)amino)benzamido)propanoate;

ethyl (R)-3-(4-((2-methyl-1-(4-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)phenyl) propyl)amino)benzamido)propanoate;

(S)-3-(4-((2-methyl-1-(4-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)phenyl)propyl)amino)benzamido)propanoic acid;

(R)-3-(4-((2-methyl-1-(4-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)phenyl)propyl)amino)benzamido)propanoic acid;

ethyl (S)-3-(4-((3-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)butyl)amino) benzamido)propanoate;

ethyl (R)-3-(4-((3-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)butyl)amino) benzamido)propanoate;

(S)-3-(4-((3-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)butyl)amino)benzamido)propanoic acid;

(R)-3-(4-((3-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)butyl)amino)benzamido)propanoic acid;

methyl (S)-3-(4-((2-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)propyl)amino)benzamido)propanoate;

(S)-2-(4-((2-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)propyl)amino)benzamido)ethane-1-sulfonic acid;

ethyl 3-(4-((1-(4-(5-(tert-butyl)-1,2,4-oxadiazol-3-yl)phenyl)-2-methylpropyl)amino) benzamido)propanoate;

3-(4-((1-(4-(5-(tert-butyl)-1,2,4-oxadiazol-3-yl)phenyl)-2-methylpropyl)amino)benzamido)propanoic acid;

ethyl 3-(4-((1-(4-(5-(tert-butyl)-1,2,4-oxadiazol-3-yl)phenyl)pentyl)amino)benzamido) propanoate;

3-(4-((1-(4-(5-(tert-butyl)-1,2,4-oxadiazol-3-yl)phenyl)pentyl)amino)benzamido)propanoic acid;

ethyl 3-(4-((1-(4-(5-(tert-butyl)-1,2,4-oxadiazol-3-yl)phenyl)-3-methylbutyl)amino) benzamido)propanoate;

3-(4-((1-(4-(5-(tert-butyl)-1,2,4-oxadiazol-3-yl)phenyl)-3-methylbutyl)amino)benzamido)propanoic acid;

ethyl 3-(4-((1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)pentyl)amino)benzamido) propanoate;

3-(4-((1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)pentyl)amino)benzamido)propanoic acid;

ethyl 3-(4-((3-methyl-1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)butyl)amino)benzamido)propanoate;

3-(4-((3-methyl-1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)butyl)amino)benzamido)propanoic acid;

ethyl 3-(4-((2-methyl-1-(4-(5-(thiophen-2-yl)-1,2,4-oxadiazol-3-yl)phenyl)propyl)amino)benzamido)propanoate;

3-(4-((2-methyl-1-(4-(5-(thiophen-2-yl)-1,2,4-oxadiazol-3-yl)phenyl)propyl)amino)benzamido)propanoic acid;

3-(4-((1-(4-(5-(thiophen-2-yl)-1,2,4-oxadiazol-3-yl)phenyl)pentyl)amino)benzamido)propanoic acid;

3-(4-((3-methyl-1-(4-(5-(thiophen-2-yl)-1,2,4-oxadiazol-3-yl)phenyl)butyl)amino)benzamido)propanoic acid;

3-(4-((cyclopentyl(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)methyl)amino)benzamido)propanoic acid;

ethyl 3-(4-((cyclohexyl(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)methyl)amino)benzamido)propanoate;

3-(4-((cyclohexyl(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)methyl)amino)benzamido)propanoic acid;

ethyl 3-(4-(((1S)-2-methyl-1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)butyl)amino)benzamido)propanoate;

3-(4-(((1S)-2-methyl-1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)butyl)amino)benzamido)propanoic acid;

Ethyl 3-(4-(((1R)-2-methyl-1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)butyl)amino)benzamido)propanoate;

3-(4-(((1R)-2-methyl-1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)butyl)amino)benzamido)propanoic acid;

ethyl (R)-3-(4-((2-methyl-1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)propyl)amino)benzamido)propanoate;

(R)-3-(4-((2-methyl-1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)propyl)amino)benzamido)propanoic acid;

ethyl 3-(4-((1-(4-(5-(4-fluorophenyl)-1,2,4-oxadiazol-3-yl)phenyl)-2-methylpropyl)amino)benzamido)propanoate;

3-(4-((1-(4-(5-(4-fluorophenyl)-1,2,4-oxadiazol-3-yl)phenyl)-2-methylpropyl)amino)benzamido)propanoic acid;

3-(4-((2-methyl-1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)propyl)amino)benzamido)propanoic acid;

ethyl (S)-3-(4-((2-methyl-1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)propyl)amino) benzamido)propanoate;

(S)-3-(4-((2-methyl-1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)propyl)amino)benzamido)propanoic acid;

ethyl 3-(4-(((1S)-2-methyl-1-(4-(5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl)phenyl) butyl) amino)benzamido)propanoate;

3-(4-(((1S)-2-methyl-1-(4-(5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl)phenyl)butyl)amino)benzamido)propanoic acid;

methyl 3-(4-((2-methyl-1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)propyl)amino) benzamido)propanoate;

methyl 3-(4-((1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)pentyl)amino)benzamido) propanoate;

ethyl (S)-3-(4-((1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)pentyl)amino)benzamido) propanoate;

(S)-3-(4-((1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)pentyl)amino)benzamido)propanoic acid;

ethyl (R)-3-(4-((1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)pentyl)amino)benzamido) propanoate;

(R)-3-(4-((1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)pentyl)amino)benzamido) propanoic acid;

ethyl (S)-3-(4-((1-(4-(5-(pyridin-2-yl)-1,2,4-oxadiazol-3-yl)phenyl)pentyl)amino) enzamido)propanoate;

(S)-3-(4-((1-(4-(5-(pyridin-2-yl)-1,2,4-oxadiazol-3-yl)phenyl)pentyl)amino)benzamido)propanoic acid;

ethyl (R)-3-(4-((1-(4-(5-(pyridin-2-yl)-1,2,4-oxadiazol-3-yl)phenyl)pentyl)amino) benzamido)propanoate;

(R)-3-(4-((1-(4-(5-(pyridin-2-yl)-1,2,4-oxadiazol-3-yl)phenyl)pentyl)amino)benzamido)propanoic acid;

ethyl (S)-3-(4-((3-methyl-1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)butyl)amino) benzamido)propanoate;

ethyl (R)-3-(4-((3-methyl-1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)butyl)amino) benzamido)propanoate;

(S)-3-(4-((3-methyl-1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)butyl)amino) benzamido)propanoic acid;

(R)-3-(4-((3-methyl-1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)butyl)amino)benzamido)propanoic acid;

ethyl (S)-3-(4-((1-(4-(5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl)phenyl)pentyl)amino) benzamido)propanoate;

ethyl (R)-3-(4-((1-(4-(5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl)phenyl)pentyl)amino) benzamido)propanoate;

(S)-3-(4-((1-(4-(5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl)phenyl)pentyl)amino)benzamido)propanoic acid;

(R)-3-(4-((1-(4-(5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl)phenyl)pentyl)amino)benzamido)propanoic acid;

methyl (S)-3-(4-((2-methyl-1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)propyl)amino)benzamido)propanoate;

3-(4-(1-((4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)amino)pentyl)benzamido)propanoic acid;

3-(4-(2-methyl-1-((4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)amino)propyl)benzamido)propanoic acid;

ethyl 3-(4-(1-((4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)amino)pentyl)benzamido) propanoate;

ethyl 3-(4-(2-methyl-1-((4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)amino)propyl) benzamido)propanoate;

ethyl 3-(4-(2-methyl-1-((4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)amino)butyl) benzamido)propanoate;

3-(4-(2-methyl-1-((4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)amino)butyl)benzamido)propanoic acid;

ethyl 3-(4-(1-((4-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)phenyl)amino)-2-methylbutyl)benzamido)propanoate;

3-(4-(1-((4-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)phenyl)amino)-2-methylbutyl)benzamido)propanoic acid;

ethyl 3-(4-(1-((4-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)phenyl)amino)-2-methylpropyl) benzamido)propanoate;

3-(4-(1-((4-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)phenyl)amino)-2-methylpropyl)benzamido)propanoic acid;

3-(4-(2-methyl-1-((4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)amino)propyl)benzamido)propanoic acid;

(S)-ethyl 3-(4-(2-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenylamino)propyl) benzamido)propanoate;

(R)-ethyl 3-(4-(2-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenylamino)propyl) benzamido)propanoate;

(S)-3-(4-(2-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenylamino)propyl)benzamido)propanoic acid;

(R)-3-(4-(2-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenylamino)propyl)benzamido)propanoic acid;

ethyl 3-(4-((1-(4-(benzo[d]oxazol-2-yl)phenyl)-2-methylpropyl)amino)benzamido) propanoate;

ethyl 3-(4-((1-(4-(benzo[d]oxazol-2-yl)phenyl)pentyl)amino)benzamido)propanoate;

3-(4-((1-(4-(benzo[d]oxazol-2-yl)phenyl)-2-methylpropyl)amino)benzamido) propanoic acid;

3-(4-((1-(4-(benzo[d]oxazol-2-yl)phenyl)pentyl)amino)benzamido)propanoic acid;

ethyl (S)-3-(4-((1-(4-(benzo[d]oxazol-2-yl)phenyl)-2-methylpropyl)amino)benzamido) propanoate;

ethyl (R)-3-(4-((1-(4-(benzo[d]oxazol-2-yl)phenyl)-2-methylpropyl)amino) benzamido)propanoate;

(S)-3-(4-((1-(4-(benzo[d]oxazol-2-yl)phenyl)-2-methylpropyl)amino)benzamido)propanoic acid;

(R)-3-(4-((1-(4-(benzo[d]oxazol-2-yl)phenyl)-2-methylpropyl)amino)benzamido)propanoic acid;

ethyl (R)-3-(4-((1-(4-(benzo[d]oxazol-2-yl)phenyl)pentyl)amino)benzamido) propanoate;

(R)-3-(4-((1-(4-(benzo[d]oxazol-2-yl)phenyl)pentyl)amino)benzamido)propanoic acid;

ethyl (R)-3-(4-(((4-(benzo[d]oxazol-2-yl)phenyl)(cyclopentyl)methyl)amino) benzamido)propanoate;

(R)-3-(4-(((4-(benzo[d]oxazol-2-yl)phenyl)(cyclopentyl)methyl)amino)benzamido)propanoic acid;

ethyl (R)-3-(4-((1-(4-(benzo[d]oxazol-2-yl)phenyl)-3-methylbutyl)amino)benzamido) propanoate;

(R)-3-(4-((1-(4-(benzo[d]oxazol-2-yl)phenyl)-3-methylbutyl)amino)benzamido) propanoic acid;

ethyl (S)-3-(4-((1-(4-(benzo[d]oxazol-2-yl)phenyl)pentyl)amino)benzamido) propanoate;

(S)-3-(4-((1-(4-(benzo[d]oxazol-2-yl)phenyl)pentyl)amino)benzamido)propanoic acid;

ethyl (S)-3-(4-((1-(4-(benzo[d]oxazol-2-yl)phenyl)-3-methylbutyl)amino)benzamido) propanoate;

(S)-3-(4-((1-(4-(benzo[d]oxazol-2-yl)phenyl)-3-methylbutyl)amino)benzamido)propanoic acid;

Ethyl 3-(4-(((1S)-1-(4-(benzo[d]oxazol-2-yl)phenyl)-2-methylbutyl)amino)benzamido)propanoate;

3-(4-(((1S)-1-(4-(benzo[d]oxazol-2-yl)phenyl)-2-methylbutyl)amino)benzamido)propanoic acid;

Ethyl 3-(4-(((1R)-1-(4-(benzo[d]oxazol-2-yl)phenyl)-2-methylbutyl)amino)benzamido)propanoate;

3-(4-(((1R)-1-(4-(benzo[d]oxazol-2-yl)phenyl)-2-methylbutyl)amino)benzamido)propanoic acid;

ethyl (S)-3-(4-(((4-(benzo[d]oxazol-2-yl)phenyl)(cyclopentyl)methyl)amino)benzamido)propanoate;

(S)-3-(4-(((4-(benzo[d]oxazol-2-yl)phenyl)(cyclopentyl)methyl)amino)benzamido)propanoic acid;

ethyl (S)-3-(4-((1-(4-(benzo[d]thiazol-2-yl)phenyl)-2-methylpropyl)amino)benzamido) propanoate;

(S)-3-(4-((1-(4-(benzo[d]thiazol-2-yl)phenyl)-2-methylpropyl)amino)benzamido)propanoic acid;

ethyl (S)-3-(6-((1-(4-(benzo[d]thiazol-2-yl)phenyl)-2-methylpropyl)amino)nicotinamido) propanoate;

(S)-3-(6-((1-(4-(benzo[d]thiazol-2-yl)phenyl)-2-methylpropyl)amino)nicotinamido)propanoic acid;

ethyl (S)-3-(6-((1-(4-(benzo[d]oxazol-2-yl)phenyl)-2-methylpropyl)amino)nicotinamido) propanoate;

(S)-3-(6-((1-(4-(benzo[d]oxazol-2-yl)phenyl)-2-methylpropyl)amino)nicotinamido)propanoic acid;

ethyl (S)-3-(4-((3-methyl-1-(4-(3-phenyl-1,2,4-oxadiazol-5-yl)phenyl)butyl)amino) benzamido)propanoate;

(S)-3-(4-((3-methyl-1-(4-(3-phenyl-1,2,4-oxadiazol-5-yl)phenyl)butyl)amino)benzamido)propanoic acid;

ethyl (S)-3-(4-((2-methyl-1-(4-(3-phenyl-1,2,4-oxadiazol-5-yl)phenyl)propyl)amino) benzamido)propanoate;

(S)-3-(4-((2-methyl-1-(4-(3-phenyl-1,2,4-oxadiazol-5-yl)phenyl)propyl)amino)benzamido)propanoic acid;

ethyl 3-(4-(((1S)-2-methyl-1-(4-(3-phenyl-1,2,4-oxadiazol-5-yl)phenyl)butyl)amino) benzamido)propanoate;

3-(4-(((1S)-2-methyl-1-(4-(3-phenyl-1,2,4-oxadiazol-5-yl)phenyl)butyl)amino) benzamido)propanoic acid;

ethyl (S)-3-(4-((1-(4-(3-phenyl-1,2,4-oxadiazol-5-yl)phenyl)pentyl)amino)benzamido) propanoate;

(S)-3-(4-((1-(4-(3-phenyl-1,2,4-oxadiazol-5-yl)phenyl)pentyl)amino)benzamido) propanoic acid;

Ethyl 3-(4-(1-(4-(benzo[d]thiazol-2-yl)phenyl)-2-methylpropoxy)benzamido)propanoate;

3-(4-(1-(4-(Benzo[d]thiazol-2-yl)phenyl)-2-methylpropoxy)benzamido)propanoic acid;

Ethyl 3-(4-(1-(4-(benzo[d]oxazol-2-yl)phenoxy)-2-methylpropyl)benzamido)propanoate;

3-(4-(1-(4-(Benzo[d]oxazol-2-yl)phenoxy)-2-methylpropyl)benzamido)propanoic acid;

Ethyl 3-(4-(1-(4-(benzo[d]thiazol-2-yl)phenoxy)-2-methylpropyl)benzamido)propanoate; and

3-(4-(1-(4-(Benzo[d]thiazol-2-yl)phenoxy)-2-methylpropyl)benzamido)propanoic acid.

22. The compound or salt of claim 21, which is any one selected from the group consisting of:.

Methyl 3-(4-((2-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)propyl)amino) benzamido)propanoate;

methyl 3-(4-((1-(4-(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)phenyl)pentyl)amino) benzamido)propanoate;

(S)-ethyl 3-(4-(2-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)propylamino) benzamido)propanoate;

(S)-3-(4-(2-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)propylamino)benzamido)propanoic acid;

ethyl (S)-3-(4-((1-(4-(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)phenyl)pentyl)amino) benzamido)propanoate;

(S)-3-(4-((1-(4-(5-(pyridin-2-yl)-1,3,4-oxadiazol-2yl)phenyl)pentyl)amino)benzamido)propanoic acid;

ethyl 3-(4-(((1S)-2-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)butyl)amino) benzamido)propanoate;

3-(4-(((1S)-2-methyl-1-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)phenyl)butyl)amino)benzamido)propanoic acid;

ethyl 3-(4-(((1S)-2-methyl-1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)butyl)amino)benzamido)propanoate;

3-(4-(((1S)-2-methyl-1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)butyl)amino)benzamido)propanoic acid;

ethyl (S)-3-(4-((2-methyl-1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)propyl)amino) benzamido)propanoate;

(S)-3-(4-((2-methyl-1-(4-(5-phenyl-1,2,4-oxadiazol-3-yl)phenyl)propyl)amino)benzamido)propanoic acid;

ethyl (S)-3-(6-((1-(4-(benzo[d]thiazol-2-yl)phenyl)-2-methylpropyl)amino)nicotinamido) propanoate;

(S)-3-(6-((1-(4-(benzo[d]thiazol-2-yl)phenyl)-2-methylpropyl)amino)nicotinamido)propanoic acid;

ethyl (S)-3-(6-((1-(4-(benzo[d]oxazol-2-yl)phenyl)-2-methylpropyl)amino)nicotinamido) propanoate; and

(S)-3-(6-((1-(4-(benzo[d]oxazol-2-yl)phenyl)-2-methylpropyl)amino)nicotinamido)propanoic acid.

23. A pharmaceutical composition comprising a compound or salt of claim 1 and a pharmaceutically acceptable carrier.

24. Use of a compound or salt of claim 1 in the manufacture of a medicament for reducing the glycemic level in a subject in need thereof.

25. Use of a compound or salt of claim 1 in the manufacture of a medicament for treating a disorder associated with glucagon in a subject in need thereof, , wherein the disorder associated with glucagon is selected from the group consisting of hyperglycemia, Type II diabetes, metabolic syndrome, impaired glucose tolerance, glucosuria, diabetic nephropathy, diabetic neuropathy, diabetic retinopathy, hyperinsulinemia, insulin resistance syndrome, cataracts, obesity, dyslididemia, hypertension and myocardial infarction.