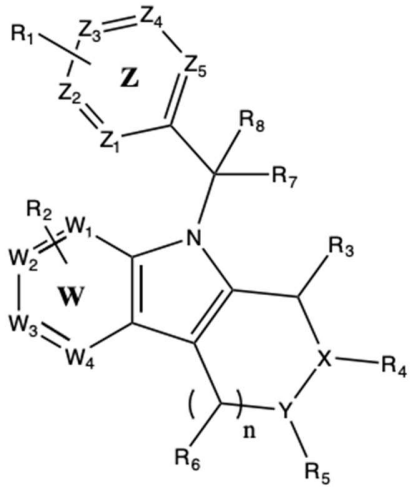
counterparts. (Shaughnessy et al., Diabetes 2000 Jun; 49(6): 904-911). Thus, increasing glucose consumption in adipocytes can be achieved by targeting FABP4.

While the literature and certain prior art patent applications (e.g., WO 00/47734, WO 00/15229, WO 00/15230, WO 02/40448, WO 01/54694, WO 00/59506 and WO 2004/063156) have provided various presentations of the concept of the FABP inhibition, in general, and that of the FABP4 inhibition, in particular, none of the discussions in these prior art documents provides solution(s) of all of the unmet needs, as does the present invention. Specifically, the present invention describes a novel class of compounds that bind to FABP4 and modulate adipocyte metabolism to drive enhanced glucose utilization.

Summary

The present disclosure relates to a compound of Formula (I):



Formula (I)

Wherein:

W_{1-4} and Z_1-Z_5 are each independently -C, -CH, CH_2, O, S, or N;

X is independently CH_2, N or CHR_4;

Y is independently CH_2, or CHR_5;

n is a number between 0 and 3;

One or more R_1's on the ring Z are independently selected from the group consisting of: CN, OH, COOH, OCH_3, CF_3, $CONH_2$, $B(OH)_2$, $B(OR)_2$, an acid isostere, a substituted amine, ethers, and a halogen, substituted or unsubstituted alkyl, substituted or unsubstituted cyclic or

heterocyclic, substituted or unsubstituted cycloaryl or cychloheteroaryl, wherein the substituted cycloaryl or cychloheteroaryl may be substituted with hydrogen, CN, OH, COOH, OCH_3, CF_3, $CONH_2$, $B(OH)_2$, $B(OR)_2$, an acid isostere, a substituted amine, ethers, and a halogen, substituted or unsubstituted alkyl, substituted or unsubstituted cyclic or heterocyclic, substituted or unsubstituted cycloaryl or cychloheteroaryl, SO_2NH_2;

One or more R_2's on the ring W are independently selected from the group consisting of: CN, OH, CHF2, CH2F, CF_3, COOH, $CONH_2$, $B(OH)_2$, $B(OR)_2$, an acid isostere, a halogen, and a bicyclic heteroaryl;

R_7 is hydrogen or CN, COOH, $CONH_2$, $B(OH)_2$, $B(OR)_2$ or an acid isostere;

R is alkyl;

R_3, R_4, R_5 or R_8, or R_6 when n is not zero, is each independently selected from:

(1) hydrogen;

(2) alkyl or ether having 1 to 12 carbon atoms,

(3) a substituted amine, or

(4) --$(CH_2)_m$ G, wherein m is 1 to 12 and G is independently selected from:

(a) cycloalkyl containing 3 to 6 carbon atoms,

(b) aryl or heteroaryl,

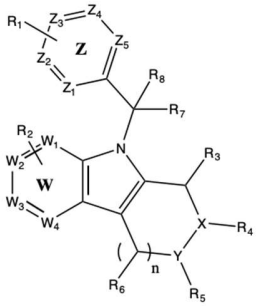
(c) CF_3, CF_2H or CFH_2, or

(d) a heterocycle,

provided that R_3, R_4, R_5, R_8, or R_6 are not all hydrogen;

or pharmaceutically acceptable salts or stereoisomers thereof.

In one aspect, the present disclosure relates to a compound of Formula I:



Formula (I)

wherein:

W_{1-4} and Z_1-Z_5 are each independently -C, -CH, O, S, or N;

X is independently CH_2, N or CHR_4;

Y is independently CH_2, or CHR_5;

n is a number between 0 and 3;

one or more R_1's on the ring Z are independently selected from the group consisting of one or more of: CN, OH, COOH, OCH_3, CF_3, $CONH_2$, $B(OH)_2$, $B(OR)_2$, an acid isostere, a substituted amine, ethers, a halogen, a substituted or unsubstituted alkyl, a substituted or unsubstituted cyclic or heterocyclic, a substituted or unsubstituted cycloaryl or cycloheteroaryl, wherein the substituted cycloaryl or cycloheteroaryl may be substituted with one or more of hydrogen, CN, OH, COOH, OCH_3, CF_3, $CONH_2$, $B(OH)_2$, $B(OR)_2$, an acid isostere, a substituted amine, an ether, a halogen, a substituted or unsubstituted alkyl, a substituted or unsubstituted cyclic or heterocyclic, a substituted or unsubstituted cycloaryl or cycloheteroaryl, and SO_2NH_2;

one or more R_2's on the ring W are independently selected from the group consisting of one or more of: CN, OH, CHF2, CH2F, CF_3, COOH, $CONH_2$, $B(OH)_2$, $B(OR)_2$, an acid isostere, a halogen, and a bicyclic heteroaryl;

R_7 is hydrogen,CN, COOH, $CONH_2$, $B(OH)_2$, $B(OR)_2$ or an acid isostere;

R is alkyl;

R_3, R_4, R_5 or R_8, or R_6 when n is not zero, is each independently selected from:

(1) hydrogen;

(2) substituted or unsubstituted alkyl or ether having 1 to 12 carbon atoms,

(3) a substituted amine, or

(4) $-(CH_2)_m$ G wherein m is 1 to 12 and G is independently:

(a) cycloalkyl containing 3 to 6 carbon atoms,

(b) aryl or heteroaryl,

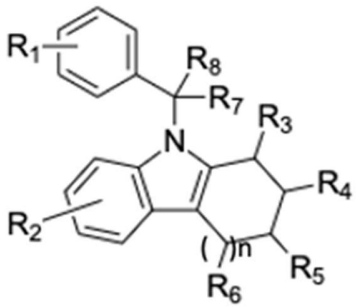
(c) CF_3, CF_2H or CFH_2, or

(d) a heterocycle,

provided that R_3, R_4, R_5, R_8, or R_6 are not all hydrogen;

or pharmaceutically acceptable salts or stereoisomers thereof.

In another aspect, the present disclosure relates to a compound of Formula II:



Formula II

wherein:

n = 0, 1, or 2;

R_1 is selected from the group consisting of: CN, COOH, $CONH_2$, $B(OH)_2$, $B(OR)_2$, an acid isostere, and a halogen;

R_2 is selected from the group consisting of: CN, COOH, $CONH_2$, $B(OH)_2$, $B(OR)_2$, an acid isostere, a halogen, and a bicyclic compound;

R_7 is hydrogen or CN, COOH, $CONH_2$, $B(OH)_2$, $B(OR)_2$ or an acid isostere;

R is alkyl;

R_3, R_4, R_5 or R_8, or R_6 when n is not zero, is each independently selected from:

(1) hydrogen;

(2) alkyl having 1 to 12 carbon atoms, or

(3) $-(CH_2)_m$ G, wherein m is 1 to 12 and G is independently:

(a) cycloalkyl containing 3 to 6 carbon atoms,

(b) aryl or heteroaryl, or

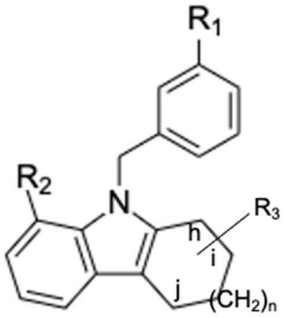
(c) CF_3, CF_2H or CFH_2;

provided that G is not a nitrogen or oxygen-containing group; and

provided that R3, R4, R5, R8, or R6 are not all hydrogen;

or pharmaceutically acceptable salts thereof.

In another aspect, the present disclosure relates to a compound of Formula III comprising:



wherein:

n = 0, 1 or 2;

R_1 and R_2 are each independently CN, COOH or $CONH_2$;

R_3 is independently selected from:

(1) alkyl having 1 to 12 carbon atoms;

(2) $-(CH_2)_mG$ wherein m is 1 to 12 and G is independently:

(a) cycloalkyl containing 3 to 6 carbon atoms; or

(b) phenyl;

or pharmaceutically acceptable salts thereof.

In another aspect, the present disclosure relates to a compound selected from the group consisting of: 5-[(3-cyanophenyl)methyl]-2-fluoro-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(6-cyanopyridin-2-yl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(6-carbamoylpyridin-2-yl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 6-({4-carboxy-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indol-5-yl}methyl)pyridine-2-carboxylic acid, 5-[(3-cyano-2-fluorophenyl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(1,3-benzoxazol-6-yl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(1,3-benzoxazol-5-yl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(6-fluoropyridin-2-yl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(2-fluoropyridin-4-yl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 7-hexyl-5-{[6-(trifluoromethyl)pyridin-2-yl]methyl}-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 7-hexyl-5-{[2-(trifluoromethyl)pyridin-4-yl]methyl}-5H,6H,7H,8H,9H,10H-

cyclohepta[b]indole-4-carboxylic acid, 5-[(5-cyanopyridin-3-yl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(5-cyanothiophen-2-yl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(4-cyanothiophen-2-yl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(5-cyanofuran-2-yl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(3,5-dimethyl-1,2-oxazol-4-yl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-(3-cyanobenzoyl)-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(1,3-benzoxazol-7-yl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(5-cyanothiophen-3-yl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 7-hexyl-5-[(1H-indol-4-yl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(3-carbamoylphenyl)methyl]-7-propyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 7-butyl-5-[(3-carbamoylphenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 7-butyl-5-[(3-cyanophenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 7-butyl-5-[(pyridin-3-yl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 7-butyl-5-[(3-methylphenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 7-butyl-5-[(3-methoxyphenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 7-butyl-5-[(3-chlorophenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 7-butyl-5-[(3-hydroxyphenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 7-butyl-5-[(2-methoxypyridin-4-yl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 7-butyl-5-[(4-carbamoylphenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 7-butyl-5-[(2-carbamoylphenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 7-butyl-5-[(4-methylphenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 7-butyl-5-[(2-cyanophenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 7-butyl-5-[(2-methylphenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 7-butyl-5-[(2-fluorophenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(3-carbamoylphenyl)methyl]-7-pentyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(3-cyanophenyl)methyl]-7-pentyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(3-carbamoylphenyl)methyl]-

7-(2-phenylethyl)-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(3-cyanophenyl)methyl]-7-(2-phenylethyl)-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(3-carbamoylphenyl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(3-cyanophenyl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(3-carbamoylphenyl)methyl]-7-octyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(3-cyanophenyl)methyl]-7-octyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(3-fluorophenyl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 7-hexyl-5-[(pyridin-3-yl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 7-hexyl-5-[(3-methylphenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 7-hexyl-5-[(3-methoxyphenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(3-chlorophenyl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 7-hexyl-5-[(2-methoxypyridin-4-yl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(3-carboxyphenyl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(4-carbamoylphenyl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(2-carbamoylphenyl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 7-hexyl-5-[(4-methylphenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(4-cyanophenyl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(2-cyanophenyl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 7-hexyl-5-[(2-methylphenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(2-fluorophenyl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(4-fluorophenyl)methyl]-7-hexyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 9-[(3-carbamoylphenyl)methyl]-2-hexyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-cyanophenyl)methyl]-2-hexyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-carboxyphenyl)methyl]-2-hexyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-fluorophenyl)methyl]-2-hexyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 2-hexyl-9-[(pyridin-3-yl)methyl]-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 2-hexyl-9-[(3-methylphenyl)methyl]-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 2-hexyl-9-[(3-methoxyphenyl)methyl]-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-

chlorophenyl)methyl]-2-hexyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 2-hexyl-9-[(3-hydroxyphenyl)methyl]-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 2-hexyl-9-[(2-methoxypyridin-4-yl)methyl]-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-carboxyphenyl)methyl]-2-hexyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(4-carbamoylphenyl)methyl]-2-hexyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(2-carbamoylphenyl)methyl]-2-hexyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 2-hexyl-9-[(4-methylphenyl)methyl]-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(4-cyanophenyl)methyl]-2-hexyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(2-cyanophenyl)methyl]-2-hexyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 2-hexyl-9-[(2-methylphenyl)methyl]-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(2-fluorophenyl)methyl]-2-hexyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-carbamoylphenyl)methyl]-2-(2-phenylethyl)-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-cyanophenyl)methyl]-2-(2-phenylethyl)-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-carbamoylphenyl)methyl]-4-(2-phenylethyl)-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-cyanophenyl)methyl]-4-(2-phenylethyl)-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-carbamoylphenyl)methyl]-2-propyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-cyanophenyl)methyl]-2-propyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 2-butyl-9-[(3-carbamoylphenyl)methyl]-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-carbamoylphenyl)methyl]-2-pentyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-cyanophenyl)methyl]-2-pentyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 1-butyl-9-[(3-carbamoylphenyl)methyl]-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-carbamoylphenyl)methyl]-1-(pentyloxy)-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-cyanophenyl)methyl]-1-(pentyloxy)-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 1-butyl-9-[(3-cyanophenyl)methyl]-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 6-butyl-5-[(3-carbamoylphenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 6-butyl-5-[(3-cyanophenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 9-[(3-carbamoylphenyl)methyl]-1-ethyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-cyanophenyl)methyl]-1-ethyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-carboxyphenyl)methyl]-1-ethyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-carbamoylphenyl)methyl]-1-propoxy-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-carbamoylphenyl)methyl]-4-ethyl-

2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 4-[(3-carbamoylphenyl)methyl]-3-ethyl-1H,2H,3H,4H-cyclopenta[b]indole-5-carboxylic acid, 4-[(3-cyanophenyl)methyl]-3-ethyl-1H,2H,3H,4H-cyclopenta[b]indole-5-carboxylic acid, 3-butyl-4-[(3-carbamoylphenyl)methyl]-1H,2H,3H,4H-cyclopenta[b]indole-5-carboxylic acid, 3-butyl-4-[(3-cyanophenyl)methyl]-1H,2H,3H,4H-cyclopenta[b]indole-5-carboxylic acid, 2-butyl-4-[(3-carbamoylphenyl)methyl]-1H,2H,3H,4H-cyclopenta[b]indole-5-carboxylic acid, 2-butyl-4-[(3-cyanophenyl)methyl]-1H,2H,3H,4H-cyclopenta[b]indole-5-carboxylic acid, 5-[(3-carbamoylphenyl)methyl]-10-ethyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(3-cyanophenyl)methyl]-10-ethyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(3-carbamoylphenyl)methyl]-10-propyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(3-cyanophenyl)methyl]-10-propyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 9-[(3-carboxyphenyl)methyl]-4-ethyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-carbamoylphenyl)methyl]-3-ethyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 10-butyl-5-[(3-carbamoylphenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 10-butyl-5-[(3-cyanophenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(3-carbamoylphenyl)methyl]-10-pentyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(3-cyanophenyl)methyl]-10-pentyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 4-[(3-carbamoylphenyl)methyl]-2-pentyl-1H,2H,3H,4H-cyclopenta[b]indole-5-carboxylic acid, 4-[(3-cyanophenyl)methyl]-2-pentyl-1H,2H,3H,4H-cyclopenta[b]indole-5-carboxylic acid, 9-[(3-carbamoylphenyl)methyl]-2-ethyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-carboxyphenyl)methyl]-2-ethyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 5-[(3-carbamoylphenyl)methyl]-7-ethyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 5-[(3-cyanophenyl)methyl]-7-ethyl-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, 9-[(3-cyanophenyl)methyl]-3-ethyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-carbamoylphenyl)methyl]-4-propyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-carbamoylphenyl)methyl]-3-propyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-cyanophenyl)methyl]-3-propyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 4-butyl-9-[(3-carbamoylphenyl)methyl]-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 4-butyl-9-[(3-cyanophenyl)methyl]-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 3-butyl-9-[(3-carbamoylphenyl)methyl]-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 3-butyl-9-[(3-

cyanophenyl)methyl]-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-carbamoylphenyl)methyl]-4-pentyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-cyanophenyl)methyl]-4-pentyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-carbamoylphenyl)methyl]-3-pentyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 9-[(3-cyanophenyl)methyl]-3-pentyl-2,3,4,9-tetrahydro-1H-carbazole-8-carboxylic acid, 4-[(3-carbamoylphenyl)methyl]-3-propyl-1H,2H,3H,4H-cyclopenta[b]indole-5-carboxylic acid, 4-[(3-cyanophenyl)methyl]-3-propyl-1H,2H,3H,4H-cyclopenta[b]indole-5-carboxylic acid, 2-({7-butyl-5-[(3-carbamoylphenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indol-4-yl}formamido)acetic acid, 2-({7-butyl-5-[(3-cyanophenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indol-4-yl}formamido)acetic acid, 7-butyl-5-[(3-carbamoylphenyl)methyl]-N-(2-hydroxyethyl)-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxamide, 7-butyl-5-[(3-cyanophenyl)methyl]-N-(2-hydroxyethyl)-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxamide, 7-butyl-5-[(3-fluorophenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, and 7-butyl-5-[(3-carboxyphenyl)methyl]-5H,6H,7H,8H,9H,10H-cyclohepta[b]indole-4-carboxylic acid, or pharmaceutically acceptable salts or stereoisomers thereof.

It is an object of the present disclosure is the compound according to Formula (I), (II), or (III) for use in the treatment of disorders acting on the fatty acid binding protein (FABP4).

In another aspect, the present disclosure relates to a compound as defined herein for use in therapy.

Yet another object of the present disclosure is a pharmaceutical composition comprising a compound according to Formula (I), (II), or (III) as active ingredient, in combination with a pharmaceutically acceptable diluent or carrier for use in the treatment of disorders acting on the FABP4. Here, the pharmaceutical composition can further comprise an additional therapeutically active agent.

In another aspect, the present disclosure relates to a pharmaceutical composition comprising a compound as defined herein for use in the prophylaxis or treatment of disorders acting on the fatty acid binding protein FABP4.

In another aspect, the present disclosure relates to a pharmaceutical composition comprising a compound as defined herein as the active ingredient, in combination with a pharmaceutically acceptable diluent or carrier.

Yet another object of the present disclosure is a method for the treatment of disorders acting on the FABP4, which comprises administering to a subject in need of such treatment

(preferably, a human) an effective amount of a compound according to Formula (I), (II), or (III) including, optionally, the co-administration with other therapeutic agents, either as a single (or multiple) dosing, and either simultaneously or sequentially.

Yet another object of the present disclosure is a method for inhibiting FABP4, which comprises administering to a subject in need of such treatment (preferably, a human) an effective amount of a compound according to Formula (I), (II), or (III).

Yet another object of the present disclosure is the use of a compound according to Formula (I), (II), or (III) for the manufacture of a medicament for use in the treatment of disorders acting on the fatty acid binding protein FABP4. Examples of such disorders include type 2 diabetes, hyperglycemia, metabolic syndrome, obesity, atherosclerosis, intracranial atherosclerotic disease, non-alcoholic steatohepatitis, asthma, vascular dementia, multiple sclerosis, Alzheimer's disease, other chronic inflammatory and autoimmune/inflammatory diseases, chronic heart disease, polycystic ovary syndrome, preeclampsia, and cancer.

In another aspect, the present disclosure relates to use of a compound as defined herein in the manufacture of a medicament for inhibiting the fatty acid binding protein FABP4 in a subject.

In another aspect, the present disclosure relates to use of a compound as defined herein in the manufacture of a medicament for the prophylaxis or treatment of disorders acting on the fatty acid binding protein FABP4 in a subject.

Other features and advantages of the disclosure will be apparent from the detailed description and the claims.

Description of the Preferred Embodiments

The preferred embodiments of the present invention will now be described with reference to the drawings. Identical elements in the various figures are identified with the same reference numerals.

Reference will now be made in detail to each embodiment of the present invention. Such embodiments are provided by way of explanation of the present invention, which is not intended to be limited thereto. In fact, those of ordinary skill in the art may appreciate upon reading the present specification and viewing the present drawings that various modifications and variations can be.

The invention, in one embodiment, is a compound of Formula (I) comprising: