Abstract:
The present invention relates to compounds of the general Formula I their pharmaceutically acceptable salts, pharmaceutically acceptable solvates, enantiomers, diastereomers, prodrugs, their N-oxide, metabolites, polymorphs, use of these compounds in medicine and the intermediates involved in their preparation.

Formula I


Declarations under Rule 4.17:
— as to applicant’s entitlement to apply for and be granted a patent (Rule 4.17(4))

Published:
— with international search report (Art. 21(3))
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))
NOVEL COMPOUNDS FOR TREATMENT OF DIABETES, OBESITY OR RELATED DISORDERS

FIELD OF THE INVENTION

The present invention relates to compounds of the general Formula I their pharmacologically acceptable salts, pharmacologically acceptable solvates, enantiomers, diastereomers, prodrugs, their N-oxide, metabolites, polymorphs, use of these compounds in medicine and the intermediates involved in their preparation. The compounds of the invention are suitable for the treatment of diabetes and associated disorders. Additionally, these compounds may also be useful in the management of obesity.

\[
\begin{array}{c}
R^1 \\
\text{N} \\
R^2 \\
Y \\
R^3 \\
\text{T}_n \\
R^6 \\
R^5 \\
\text{T}_m \\
R^4
\end{array}
\]

Formula I

SUMMARY OF THE RELATED ART

Diabetes is a major worldwide health problem. In 2000, 171 million people were living with diabetes, and this number is projected to rise to 366 million in 2030. [Wild, S.; Roglic, G.; Green, A.; Sicree, R.; King, H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care 2004, 27, 1047-53.] Type II diabetes, also known as diabetes mellitus, is now internationally recognized as one of the major threats to human health in the 21st century. According to the International Diabetes Federation (IDF), diabetes is expected to cause 3.8 million deaths worldwide in 2007, roughly 6% of total world mortality, about the same as HIV/AIDS and malaria combined. Those that suffer from type II diabetes have too little insulin or cannot use insulin effectively. As a result, glucose levels build up in the blood and urine and, if left untreated, can cause life-threatening complications, including blindness, kidney failure, and heart disease. The huge human and economic costs of diabetes and associated complications prompted the research for appropriate and efficient treatments.

While, bile acids (BAs) have long been known to be essential in dietary lipid absorption and cholesterol catabolism, in recent years an important role for BAs as
signalling molecules has emerged. BAs activate mitogen-activated protein kinase pathways, are ligands for the G-protein-coupled receptor (GPCR) TGR5 and activate nuclear hormone receptors such as farnesoid X receptor alpha (FXR-alpha; NR1H4). TGR5 is a novel GPCR mediating several non-genomic functional responses induced by binding of bile acids. TGR5, also known as BG37, M-BAR, or hGPCR19, is a bile acid G protein-coupled receptor primarily expressed in monocytes and macrophages, lung, spleen, and the intestinal tract. Bile acids are known to be key regulators of lipid, glucose and overall energy metabolism. TGR5 is a G protein-coupled receptor that is activated by bile acids, resulting in an increase in cAMP levels and the subsequent modulation of energy expenditure in brown adipose tissue and muscle. Therefore, the development of a TGR5-specific agonist could lead to the prevention and treatment of various metabolic disorders related to obesity. [Thomas et al. Nature 2008, 7, 678.] Bile acid activation of the G protein-coupled receptor TGR5 has been shown to induce energy expenditure in muscle and brown fat, thereby conferring resistance to weight gain. An article published in Cell Metabolism (Vol. 10, Issue 3, Sept. 2, 2009) elaborates on a separate TGR5-regulated mechanism in the gut that drives secretion of the hormone glucagon-like peptide (GLP-1) and resulting insulin sensitization. Binding of TGR5 agonist increases cAMP stimulates the secretion of GLP-1 from intestinal endocrine cells. [Katsuma, et al, Biochem. Biophys. Res. Commun. 2005, 329(1), 386-390.] GLP-1 has an insulinotropic effect in the pancreas and reduces the appetite. The combined effects of FXR and TGR5 in metabolically-active tissues leads to a reduction of hyperglycaemia and insulin resistance.

Upon ligand binding, TGR5 activation is followed by release of the Gas subunit and activates the transcription of target genes by binding to cAMP response elements (CREs) contained in their promoter. In the brown adipose tissue (BAT) and muscle, activation of TGR5 leads to the activation of type 2 iodothyronine deiodinase 2 (D2) which converts thyroxine (T4) to triiodothyronine (T3) and up-regulates (PPARa), uncoupling protein (UCP-1, UCP2) and PPAR-coactivator (PGClα) activity inducing beta-oxidation, oxidative phosphorylation and energy uncoupling. [Watanabe et al, Nature 2006, 439(7075) 484-489.] FXR in the liver stimulates beta-oxidation, down regulates FA synthesis. FXR also stimulates adipocyte differentiation, augmenting the production of leptin and adiponectin. These two hormones enhance energy uncoupling, β-oxidation, oxidative phosphorylation and reduce appetite.
TGR.5 modulators have been the subject of a several patent applications listed below:

- WO/2008/097976 - Heterocyclic Modulators of TGR5 for Treatment of Disease
- WO/2008/091540 - Substituted Bile Acids as TGR5 Modulators and Methods of Use
- WO/2008/067219 - Quinazolinone Modulators of TGR5
- WO/2008/067222 - Heterocyclic Modulators of TGR5
- WO/2004/067008 - Receptor Agonists
- WO/2004/043468 - Screening Method
- US 2006/0199795 - Receptor Agonists
- WO/2010/016846 - Heterocyclic Modulators of TGR5
- WO/2010/016845 - Heterocyclic Modulators of TGR5
- WO/2011/071565 - Heterocyclic Modulators of TGR5
- WO/2012/117000 - Heterocyclic Modulators of TGR5

All of the above disclosed compounds are in various stages of development and looking at the high unmet needs and the therapeutic potential of selective TGR5 modulators, there remains a need to develop further compounds as TGR5 modulators having superior therapeutic properties which can be possibly developed as potential treatment of diabetes and allied diseases.

SUMMARY OF THE INVENTION

The present invention relates to new heterocyclic compounds which are effective modulators of TGR5 agonists of structural Formula I,

![Formula I](image)

wherein, Y, T, R¹, R², R³, R⁴, R⁵, and R⁶ are defined herein below and pharmaceutically acceptable salts thereof.

The invention further comprises compositions comprising the compounds and/or pharmaceutically acceptable salts thereof. The invention also comprises use of
the compounds and compositions for treating diseases or disorders in which TGR5 is a mediator or is implicated.

The invention also comprises use of the compounds in and for the manufacture of medicaments, particularly for treating diseases and disorders in which TGR5 is a mediator or it's implicated.

The present invention also provides compositions and combinations thereof and methods for using such compounds, compositions and combinations to treat these and related disorders.

**DETAILED DESCRIPTION OF THE INVENTION**

All of the compounds of Formula I disclosed herein may have quaternary ammonium ion moieties, and it is understood to one skilled in the art that these compounds may preferably be in the presence of a pharmaceutically acceptable counter ion. The pharmaceutically acceptable counter ion for each of the quaternary ammonium ion moieties present in the compounds of the invention can be any pharmaceutically acceptable counter ion. It is also understood that the source of the counter ions can be from either intermolecular sources, or, when possible, intramolecular sources.

In accordance with one aspect of the invention compounds are provided having structure of Formula I:

![Formula I](image)

or an isotope, enantiomer, diastereomer or pharmaceutically acceptable salt thereof, wherein,

- Y is = S, -S(0)-, -S(0)₂⁻;
- T is = -(CO)NH⁻, -NH(CO)⁻, -NR⁻;
- n is 0, 1, 2, 3 or 4; m is 0, 1, 2 or 3;
- R¹ is selected from aryl, heteroaryl, heterocyclyl or aryl(C₁-C₆)alkyl, wherein said aryl, heteroaryl, heterocyclyl or aryl(C₁-C₆)alkyl can optionally be substituted with one, two, or three R¹a groups, wherein R¹a at each occurrence independently represents halogen, C₁-C₄alkyl, C₃-C₄ haloalkyl, C₃-C₆cycloalkyl, heteroaryl, heterocyclyl, the group representing -R¹b, -C₁-C₄ alkyl-R¹b, or -OC₁-C₄ alkyl-R¹b wherein
R^{1b} at each occurrence independently represents cyano, nitro, -N(R^{15})_2, -OR^{15}, -SR^{1c}, -C(0)R^{1c}, -C(0)OR^{1c}, -C(0)OR^{1c}, -S(0)N(R^{15})_2, -S(0)_2N(R^{15})_2, or -S(0)_2R^{1c}, -OC(0)R^{1c}, -OC(0)OR^{1c}, -OC(0)N(R^{1c})_2, -N(R^{1c})C(0)R^{1c}, -N(R^{1c})C(0)OR^{1c}, -N(R^{1c})C(0)N(R^{1c})_2, or -N(R^{1c})C(=NR^{15})N(R^{1c})_2, wherein each R^{1c} is independently hydrogen, C{1-C}_4 alkyl, or C{1-C}_4 haloalkyl.

R^2 is selected from -Z - R^Z, wherein

Z is -C(R^Y)_2-, -C(H)(OH)-, -N(R^Y)-, -O-, -C(R^Y)O-, -S-, -S(0)-, -S(0)_2-, -C(O)- wherein R^Y at each occurrence independently represents hydrogen, C{1-C}_4 haloalkyl, C{1-C}_4 alkyl, or hydroxy(C{1-C}_4 alkyl) groups; and R^Z is aryl or heteroaryl, heterocyclul wherein said aryl or heteroaryl or heterocyclyl groups can optionally substituted with one, two, or three R^Z groups,

wherein R^Z at each occurrence is cyano, halogen, nitro, -R^{Zib} -N(R^{Zib})_2, -O R^{Zib}, -S R^{Zib}, -C(O) R^{Zib}, -C(0)0 R^Zb, -C(0)N(R^{Zib})_2, -S(0)N(R^{Zib})_2, -S(0)_2N(R^{Zib})_2, or -S(0)_2R^{Zib}, -OC(O) R^{Zib}, -OC(O)0 R^{Zib}, -OC(O)N(R^{Zib})_2, -N(R^{15})C(0) R^{Zib}, -N(R^{Zib})C(0)0 R^{Zib}, -N(R^{Zib})C(0)N(R^{Zib})_2, or -N(R^{Zib})C(=NR^{2b})N(R^{Zib})_2, wherein at each occurrence R^{2b} is independently hydrogen, C{1-C}_4 alkyl, or CrC {1-C}_4 haloalkyl groups and R^{15} is as defined earlier;

R^3 is (i) aryl, heteroaryl, or aryl(C{1-C}_2)alkyl, wherein said aryl, heteroaryl, or aryl(C{1-C}_2)alkyl can optionally be substituted with one, two, or three R^3 groups,

wherein R^3 at each occurrence independently represents hydrogen, halogen, cyano, nitro, C{1-C}_4 alkyl, C{1-C}_4 haloalkyl, acyl, optionally substituted C{3-C}_8 cycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocyclyl, the group representing -R^{3b}, -C{1-C}_4 alkyl-R^{3b}, or -O-C{1-C}_4 alkyl; wherein the substituted group on C{3-C}_8 cycloalkyl, aryl, heteroaryl or heterocyclyl are selected from hydrogen, cyano, halogen, acyl, C{1-C}_4 alkyl, aryl, or heteroaryl; wherein, R^{3b} at each occurrence is independently selected from cyano, nitro, -N(R^{3c})_2, -OR^{3c}, -SR^{3c}, -C(0)R^{3c}, -C(0)OR^{3c}, -C(0)N(R^{3c})_2, -C(0)N(R^{3c})-N[(d-C_3)alkyl]_3, -S(0)N(R^{3c})_2, -S(0)_2N(R^{3c})_2, or -S(0)_2R^{3c}, -S(0)_2R^{3c}, -R^{3c} N-S(0)_2R^{3c}, -S(0)_2N[(d-C_3)alkyl]_3, -OC(O)R^{3c}, -OC(O)OR^{3c}, -OC(O)N(R^{3c})_2, -N(R^{3c})C(0)R^{3c}, -N(R^{3c})C(0)OR^{3c}, -N(R^{3c})C(0)N(R^{3c})_2, or -N(R^{3c})C(=NR^{3c})N(R^{3c})_2, wherein R^{3c} at each occurrence independently selected from hydrogen, C{1-C}_4 alkyl, C{1-C}_4 haloalkyl, cycloalkyl, heteroaryl, aryl heterocyclyl, -C(0)OR^{3d} or -N(R^{3d})C(=NR^{3d})N(R^{3d})_2 groups, wherein R^{3d} is defined hereinafter; or,
(ii) \( \text{Ci-C}_4 \text{alkyl}, \text{-CrC}_4 \text{alkyl-N(R)} \), \(-\text{d-C}_4 \text{alkyl-SR}_1\), \(\text{C}_3 \text{-C cycloalkyl}, \) or heterocyclyl groups, wherein the cycloalkyl, and heterocyclyl groups are each optionally substituted with 1 to 6 groups which are each independently selected from \(-\text{R}^5\) or \(-\text{C}_4 \text{alkyl-R}^3\), wherein \(\text{R}^3\) at each occurrence is independently selected from hydrogen, \(\text{Ci-C}_4 \text{alkyl, or Cj-C}_4 \text{haloalkyl groups and R}^3\) at each occurrence is independently selected from cyano, nitro, \(-\text{N(R)}^3\), \(-\text{OR}^3\), \(-\text{SR}^3\), \(-\text{C}_4 \text{alkyl-R}^3\), \(-\text{C}_4 \text{alkyl-N(R)}^3\), \(-\text{C}_4 \text{alkyl-alkyl-R}^3\), \(-\text{C}_4 \text{alkyl-SR}^3\), \(-\text{C}_3 \text{-C cycloalkyl, or heterocyclyl, the group representing-R, C -}\)

\(\text{Ci-C}_4 \text{alkyl, -CrC}_4 \text{alkyl-N(R)}_1\) from \(\text{C}_3 \text{-C cycloalkyl, or heterocyclyl groups, wherein the cycloalkyl, and heterocyclyl groups are each optionally substituted with 1 to 6 groups which are each independently selected from -R^5 or -C_4alkyl-R^3, wherein R^3 at each occurrence is independently selected from hydrogen, Ci-C_4alkyl, or Cj-C_4haloalkyl groups and R^3 at each occurrence is independently selected from cyano, nitro, cyano, halogen, acyl, Ci-C_4alkyl, C_1-C_4 haloalkyl, aryl, or heteroaryl heterocyclyl, or -N(R^4) groups; wherein R^4 at each occurrence is independently selected from hydrogen, acyl, C_1-C_4alkyl or -S(0)R^4b; wherein R^4b at each occurrence is independently selected from amino, acyl or Ci-C_4alkyl groups; R^5 and R^6 each independently represents hydrogen, C_1-C_4alkyl or alternatively, R^5 and R^6 together with carbon atom to which they are attached form a 3-7 membered ring, optionally comprising 1 or 2 heteroatom selected from O, N and S. R^7 is independently absent or represents hydrogen, Ci-C_4alkyl or Cj-C_4haloalkyl.

In a preferred embodiment R^1 is selected from aryl wherein aryl is substituted with one, two, or three R^1a group, wherein R^1a group is independently selected from halogen or CrC_4alkyl.

In another preferred embodiment R^2 is selected from -Z-R^Z, wherein Z is \(\text{-C(R^Y)}_2\), wherein R^Y at each occurrence independently represents hydrogen, C_1-

C_4alkyl; and R^2 is aryl wherein said aryl can optionally substituted with one, two, or three R^1l groups selected from cyano, halogen, -O R^2l, wherein R^2l is independently selected from hydrogen or Cj-C_4alkyl.

In a still preferred embodiment R^3 is aryl, heteroaryl, or aryl(Ci-C_2)alkyl, wherein said aryl, heteroaryl, or aryl(Ci-C_2)alkyl can optionally be substituted with one, two, or three R^3a groups, wherein R^3a at each occurrence independently represents hydrogen, halogen, cyano, nitro, Ci-C_4alkyl, C_1-C_4 haloalkyl, acyl, optionally substituted C_3-C_6cycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocyclyl, the group representing -R^3b, -C_1-
C₄ alkyl-R³b, or -OC₁-C₄ alkyl; wherein the substituted group on C₃-C₈ cycloalkyl, aryl, heteroaryl or heterocyclyl are selected from hydrogen, nitro, cyano, halogen, acyl, C₅-Qalkyl, aryl, or heteroaryl; wherein, R³b at each occurrence is independently selected from cyano, nitro, -NR³c, -OR³c, -SR¹e, -C(0)R³e, -C(0)OR³e, -C(0)N(R³c)₂, -C(0)N[(C₃-C₅ alkyl)]³⁺, -S(0)²N[(C₃-C₅ alkyl)]³⁺, -S(0)²N[(C₃-C₅ alkyl)]³⁺, -OC(0)R³e, -OC(0)OR³e, -OC(0)N(R³c)₂, -N[(R³e)C(0)]R³e, -N[(R³e)C(0)]R³e, -N[(R³e)C(0)]N(R³c)³⁺ or -N[(R³e)C(0)]N(R³c)³⁺, wherein R³c at each occurrence independently selected from hydrogen, C₅-Qalkyl, C₄-C₄ haloalkyl, cycloalkyl, heteroaryl, aryl heterocyclyl, -C(0)OR³d or -N(R³d)C(=NR³d)N(R³b)₂ groups, wherein R³b at each occurrence is independently selected from hydrogen, C₅-Qalkyl, or C₁-C₄ haloalkyl groups.

In a still further preferred embodiment R³ is selected from C₁-C₄ alkyl, -C₁-C₄ alkyl-OR³d, wherein R³b at each occurrence is independently selected from hydrogen, C₅-Qalkyl, or C₁-C₄ haloalkyl groups.

In an embodiment, the various groups as defined above may be selected from: "Alkyl", as well as other groups having the prefix "alk", such as alkoxy and alkanoyl, means carbon chain which may either be linear or branched, and combinations thereof, unless the carbon chain is defined otherwise. Examples of alkyl group include, but not limited to, methyl, ethyl, propyl, isopropyl, butyl, sec-butyl, tert.-butyl, pentyl, hexyl etc. Where the specified number of carbon atoms permits e.g. from C₃-i₉, the term alkyl also includes cycloalkyl groups, and combinations of linear or branched alkyl chains combined with cycloalkyl structures. In an embodiment, the alkyl group may be optionally substituted with nitro, cyano, halogen, cycloalkyl, acyl, aryl, or heteroaryl or heterocyclyl groups; "Amino" or "amine" refers to a -N(R)₂ radical group, where each R is independently hydrogen, alkyl, aryl, acyl, heterocyclyl, or heteroaryl group. In a preferred embodiment, an amino group may be optionally substituted by one or more substituents which independently are with nitro, cyano, halogen, cycloalkyl, acyl, aryl, or heteroaryl or heterocyclyl groups.

"Cycloalkyl" is the subset of alkyl and means saturated carbocyclic ring having a specified number of carbon atoms, preferably 3-10 carbon atoms. Examples of cycloalkyl include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl etc. In a embodiment, cycloalkyl group may be optionally substituted with nitro, cyano, halogen, C₅-Qalkyl, cycloalkyl, acyl, aryl, or heteroaryl or heterocyclyl groups.
"Aryl" means a mono- or polycyclic aromatic ring system containing carbon ring atoms. The preferred aryls are monocyclic or bicyclic 6-10 membered aromatic ring systems. In a preferred embodiment the aryl group may be selected from but not limited to phenyl and naphthyl. In an embodiment, aryl group may be optionally substituted with nitro, cyano, halogen, C1-C4 alkyl, cycloalkyl, acyl, aryl, or heteroaryl or heterocyclyl groups.

"Acyl" used herein, refers to group R-C(O)-, wherein R is independently selected from hydrogen or alkyl, cycloalkyl, aryl as defined elsewhere in the specification. In a preferred embodiment the acyl group represents formyl, acetyl and the like. In an embodiment, acyl group may be optionally substituted with nitro, cyano, halogen, C1-C4 alkyl, cycloalkyl, acyl, aryl, or heteroaryl or heterocyclyl groups.

"Heterocycle" and "heterocyclyl" refer to saturated or unsaturated non-aromatic rings or ring systems containing at least one heteroatom selected from O, S, N further including the oxidized forms of sulfur and nitrogen, namely SO, SO2, NO, NO2. In a preferred embodiment the heterocyclyl group may be selected from but not limited to tetrahydrofuran (THF), dihydrofuran, 1,4-dioxane, morpholine, 1,4-dithiane, piperazine, piperidine, pyridine, 1,3-dioxolane, imidazoline, imidazolidine, pyrrolidine, pyrrole, tetrahydropyran, dihydropyran, oxathiolane, dithiolane, 1,3-dioxane, 1,3-dithiane, oxathiane, thiomorpholine. In an embodiment, the heterocycle group may be optionally substituted with nitro, cyano, halogen, C1-C4 alkyl, cycloalkyl, acyl, aryl, or heteroaryl or heterocyclyl groups.

"Heteroaryl" means an aromatic or partially aromatic heterocycle that contains at least one ring heteroatom selected from O, S and N. In an embodiment heteroaryl group includes heteroaryl fused to the other kinds of rings, such as aryls, cycloalkyls, and heterocycles that are not aromatic. In a preferred embodiment the heteroaryl group may be selected from but not limited to pyrrolyl, isoazolyl, isothiazolyl, pyrazolyl, pyridyl, oxazolyl, oxadiazolyl, thiazolyl, oxadiazolyl, imidazolyl, triazolyl, tetrazolyl, furyl, triazinyl, thienyl, pyrimidyl, benzoxazolyl, benzothiazolyl, benzothiazolyl, dihydrobenzofuranyl, indoliny1, pyridazinyl, indazolyl, benzimidazolyl, indolizinyl, cinnolinyl, phthalazinyl, quinazolinyl, naphthyridinyl, carbazolyl, benzodioxolyl, quinoxalinyl, purinyl, furazanyl, isobenzofuranyl, benzimidazolyl, benzofuranyl, benzothienyl, quinolyl, indolyl, isoquinolyl, dibenzofuranyl etc. For
heterocyclyl and heteroaryl groups, rings and ring systems containing from 3-15 carbon atoms are included, forming 1-3 rings. In an embodiment, the heteroaryl group may be optionally substituted with nitro, cyano, halogen, Cl-C₄alkyl, cycloalkyl, acyl, aryl, or heteroaryl or heterocyclyl groups.

The term "halogen" refers to fluorine, chlorine, bromine and iodine. Chlorine and fluorine are generally preferred.

The term "substituted," as used herein, means that any one or more hydrogens on the designated atom is replaced with a selection from the indicated group, provided that the designated atom's normal valency is not exceeded, and that the substitution results in a stable compound. The term "substituted," as used herein, means that any one or more hydrogens on the designated atom is replaced with a selection from the indicated group, provided that the designated atom's normal valency is not exceeded, and that the substitution results in a stable compound.

The term "Pharmaceutically acceptable salts" refer to derivatives of the disclosed compounds wherein the parent compound is modified by making acid or base salts thereof. Examples of pharmaceutically acceptable salts include, but are not limited to, mineral or organic acid salts of the basic residues. The pharmaceutically acceptable salts include the conventional quaternary ammonium salts of the parent compound formed, for example, from non-toxic inorganic or organic acids.

The term "combination therapy" means the administration of two or more therapeutic agents to treat a therapeutic condition or disorder described in the present disclosure. Such administration encompasses co-administration of these therapeutic agents in a substantially simultaneous manner, such as in a single capsule having a fixed ratio of active ingredients or in multiple, separate capsules for each active ingredient. In addition, such administration also encompasses use of each type of therapeutic agent in a sequential manner. In either case, the treatment regimen will provide beneficial effects of the drug combination in treating the conditions or disorders described herein.

The phrase "therapeutically effective" is intended to qualify the amount of active ingredients used in the treatment of a disease or disorder. This amount will achieve the goal of reducing or eliminating the said disease or disorder.

The term "therapeutically acceptable" refers to those compounds (or salts, prodrugs, tautomers, zwitterionic forms, etc.) which are suitable for use in contact with
the tissues of patients without undue toxicity, irritation, and allergic response, are commensurate with a reasonable benefit/risk ratio, and are effective for their intended use.

As used herein, reference to "treatment" of a patient is intended to include prophylaxis. The term "patient" means all mammals including humans. Examples of patients include humans, cows, dogs, cats, goats, sheep, pigs, and rabbits. Preferably, the patient is a human.

The term "prodrug" is meant to indicate a compound that may be converted under physiological conditions or by solvolysis to a biologically active compound described herein. Thus, the term "prodrug" refers to a precursor of a biologically active compound that is pharmaceutically acceptable. A prodrug may be inactive when administered to a subject, but is converted in vivo to an active compound, for example, by hydrolysis. The prodrug compound often offers advantages of solubility, tissue compatibility or delayed release in a mammalian organism (see, e.g., Bundgard, H., Design of Prodrugs (1985), pp. 7-9, 21-24 (Elsevier, Amsterdam). A discussion of prodrugs is provided in Higuchi, T., et al., "Pro-drugs as Novel Delivery Systems," A.C.S. Symposium Series, Vol. 14. and in Bioreversible Carriers in Drug Design, ed. Edward B. Roche, American Pharmaceutical Association and Pergamon Press, 1987, both of which are incorporated in full by reference herein. The term "prodrug" is also meant to include any covalently bonded carriers, which release the active compound in vivo when such prodrug is administered to a mammalian subject. Prodrugs of an active compound, as described herein, may be prepared by modifying functional groups present in the active compound in such a way that the modifications are cleaved, either in routine manipulation or in vivo, to the parent active compound. Prodrugs include compounds wherein a hydroxy, amino or mercapto group is bonded to any group that, when the prodrug of the active compound is administered to a mammalian subject, cleaves to form a free hydroxy, free amino or free mercapto group, respectively. Examples of prodrugs include, but are not limited to, acetate, formate and benzoate derivatives of an alcohol or acetamide, formamide and benzamide derivatives of an amine functional group in the active compound and the like.

The term 'optional' or 'optionally' means that the subsequent described event or circumstance may or may not occur, and the description includes instances where the event or circumstance occur and instances in which it does not. For example,
'optionally substituted alkyl' means either 'alkyl' or 'substituted alkyl'. Further an optionally substituted group includes the unsubstituted group also.

Unless otherwise stated in the specification, structures depicted herein are also meant to include compounds which differ only in the presence of one or more isotopically enriched atoms. For example, compounds having the present structures wherein hydrogen is replaced by deuterium or tritium, or wherein carbon atom is replaced by $^{13}$C- or $^{14}$C- enriched carbon, are within the scope of this invention.

Other terms used in defining compounds of formula (I) in their various embodiments, which are not specifically defined are those which are well understood by a skilled person.

Particularly preferred compounds may be selected from:

2-((5-(2-(3,4-dichlorophenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-N-(pyridin-4-ylmethyl)acetamide;
N-(2,4-dichlorophenyl)-2-((5-(2-(3,4-dichlorophenyl)propan-2-yl)-1-(4-fluorophenyl)-IH-imidazol-2-yl)thio)acetamide;
2-((5-(2-(3,4-dichlorophenyl)propan-2-yl)-1-(4-fluorophenyl)-IH-imidazol-2-yl)thio)-N-phenyl acetamide;
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-IH-imidazol-2-yl)thio)-N-phenylacetamide;
N-(3-chloro-4-methylphenyl)-2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-IH-imidazol-2-yl)thio)acetamide;
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-IH-imidazol-2-yl)thio)-N-(4-fluorophenyl)acetamide;
N-(IH-benzo[d]imidazol-2-yl)-2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-IH-imidazol-2-yl)thio)acetamide;
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-IH-imidazol-2-yl)thio)-1-(4-methylpiperazin-1-yl)ethanone;
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-IH-imidazol-2-yl)thio)-1-(4-(4-fluorophenyl)piperazin-1-yl)ethanone;
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-IH-imidazol-2-yl)thio)-N-(4-(2-methyl-IH-imidazol-1-yl)phenyl)acetamide;
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-l-(3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)ethanone;
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-l-(3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)ethanone;
N-(1H-benzo[d]imidazol-2-yl)-2-((5-(2-(4-chloro-3-methoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)acetamide;
2-((5-(2-(4-chloro-3-methoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-l-(3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)ethanone;
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-2-methyl-N-(4-(2-methyl-1H-imidazol-1-yl)phenyl)propanamide;
1-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-N-(4-(2-methyl-1H-imidazol-1-yl)phenyl)cyclobutanecarboxamide;
2-((5-((2-(3-cyano-4-fluorophenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-2-methyl-N-(4-(2-methyl-1H-imidazol-1-yl)phenyl)propanamide;
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-N-(4-(2-methyl-1H-imidazol-1-yl)phenyl)acetamide;
(S)-methyl 5-amino-2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)acetamido)-5-oxopentanoate;
2-((1-(4-fluorophenyl)-5-(2-(3-methoxyphenyl)propan-2-yl)-1H-imidazol-2-yl)thio)-N-(4-(2-methyl-1H-imidazol-1-yl)phenyl)acetamide;
(S)-methyl 2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)acetamido)-4-methylpentanoate;
(S)-methyl 2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)acetamido)-3-phenylpropanoate;
2-((5-(2-(4,5-dimethoxy-2-nitrophenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-N-(4-(2-methyl-1H-imidazol-1-yl)phenyl)acetamide;
2-((5-(2-(4,5-dimethoxy-2-(methylsulfonyl)phenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-N-(4-(2-methyl-1H-imidazol-1-yl)phenyl)acetamide;
(S)-dimethyl 2-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)acetamido)pentanedioate;
(S)-dimethyl 2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)acetamido)succinate;
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-N-(4-(2-methyl-1H-imidazol-1-yl)phenyl)acetamide;
N-(3,4-dimethoxyphenyl)-2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)acetamido)acetamide;
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-N-isopentylacetamide;
N-(cyclohexylmethyl)-2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)acetamido)acetamide;
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-N-(pyridine-3-ylmethyl)acetamide;
N-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl)-thiophene-3-carboxamide;
N-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl)-4-fluorobenzamide;
N-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl)-1H-benzo[d]imidazole-5-carboxamide;
N-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl)-2-(2,4,5-trifluorophenyl)acetamide;
N-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl)-1H-indazole-5-carboxamide;
N-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl)-6-methylnicotinamide;
N-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl)-4-(1H-imidazol-1-yl)benzamide;
2-((2-(1H-imidazol-1-yl)ethyl)thio)-5-(2-(3,4-dichlorophenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazole;
1-((5-(2-(3,4-dichlorophenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl) piperidine;
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-N-(pyridine-3-ylmethyl)ethanamine;
N-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl) aniline;
5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-2-((2-(2-methyl-1H-imidazol-1-yl)ethyl)thio)-1H-imidazole;
1-((2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl)-4-methylpiperazine;
1-((2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl)-1H-indole;
1-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl)-1H-benzo[d]imidazole;
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-1-(4-methoxyacetyl) piperazin-1-yl) ethanone;
4-((1-((2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl)-1H-imidazol-4-yl)phenol.

GENERAL PROCESS FOR PREPARATION

The compounds of present invention may be prepared by different synthetic schemes as described herein below wherein the groups R²₁, R¹, R³, X, & Y are as defined earlier. Synthesis of the compounds of Formulae (I) disclosed herein, and embodiments thereof, are not limited by these examples and schemes. One skilled in the art will know that other modifications/alterations that can be used to synthesize the compounds of Formula (I) disclosed herein, in combination with the processes described herein. In the descriptions below, one of ordinary skilled in the art would recognize that specific reaction conditions, added reagents, solvents, and reaction temperatures can be modified for the synthesis of specific compounds that fall within the scope of this disclosure.
GENERAL METHOD OF SYNTHESIS:

Compounds of formula (2) are commercially available or may be prepared from known compounds using standard methodologies.

Step (I): An aldehyde of formula (3) may be prepared by reaction of nitrile (2) with diisobutylaluminum hydride in a suitable solvent, such as THF(tetrahydrofuran) or toluene. Step (II): Formation of carbinol (4) may be achieved by treatment of corresponding aldehyde (3) with methylmagnesium bromide in a suitable solvent, such as diethyl ether or THF. Step (III): Conversion of carbinol (4) to corresponding ketone (5) may occur under standard conditions, such as the Swern oxidation — known to one skilled in the art of synthetic organic chemistry. Step (IV): Bromoketone (6) may be prepared by bromination of ketone (5) under typical conditions, such as with tetrabutylammonium tribromide in a solvent mixture of MeOH(methanol)/DCM(dichloromethane). Step (V): Reaction of bromoketone (6) with hexamethylenetetramine in a suitable solvent, such as DCM, followed by acidic treatment under standard conditions, such as hydrochloric acid in ethanol, may afford amino-ketone hydrochloride (6). Step (VI): Substituted isothiocyanate, which may be optionally suitably substituted, may react with amino-ketone hydrochloride (7) in a suitable solvent, such as DCM or toluene, and in the presence of a base, such as triethylamine, at room temperature to yield the corresponding thiourea derivative, which may condense upon treatment with HOAc(acetic acid) at elevated temperature to give a compound of formula (8) (Scheme-1).
Alkylation of imidazol-2-thione (8) with suitable reagents such as chloroethylamine hydrochloride or substituted chloro or bromo alkyl amine or protected amine in a suitable solvent, such as acetone, DMF (dimethylformamide) or MeCN (acetonitrile), and in the presence of a base, such as triethylamine, may afford a compound of formula 9. Coupling of compound of formula 9 with a substituted aryl or alkyl carboxylic acid which may be optionally suitably substituted, in a suitable solvent, such as dichloromethane, DMF or MeCN, and in the presence of reagents, such as HBTU (0-Benzotriazole-N,N,N',N'-tetramethyl-uronium-hexafluoro-phosphate) or EDC(1-ethyl-3-(3-dimethylaminopropyl)carbodiimide)/HOBt(1-Hydroxybenzotriazole), may afford a compound of formula (1) (Scheme-2).

Scheme-3

Alkylation of imidazol-2-thione (8) with a reagent such as chloroacetic acid or substituted chloro or bromo alkyl carboxylic acid or protected carboxylic acid in a suitable solvent, such as acetone, DMF or MeCN, and in the presence of a base, such as triethylamine, may afford a compound of formula 10. Coupling of compound of formula 10 with substituted alkyl or aryl amine which may be optionally substituted suitably, in a suitable solvent, such as dichloromethane, DMF or MeCN, and in the presence of reagents, such as HBTU or EDC/HOBt, may afford a compound of formula (1) (Scheme-3).

The following compounds were prepared using the process described above in combination, when required, with other processes, reagents, conditions as are well known to persons skilled in the art. Such obvious modifications/alterations etc. carried out to obtain further compounds of formula (1), should, based on the disclosures herein
provided in combination with the knowledge of a skilled person be considered to be within the scope of the invention.

EXPERIMENTAL

Melting points were recorded on a scientific melting point apparatus and are uncorrected. IR spectra were recorded as neat (for oils) or on KBr pellet (for solid) on FT-IR 8300 Shimadzu and are expressed in ν (cm⁻¹). All H spectral data are recorded on a 400 MHz ¹H NMR spectrometer using DMSO-d₆ or CDCl₃, as solvent with tetramethylsiiane (TMS) as an internal standard. Chemical shifts are given in δ downfield from tetramethylsiiane. Multiplicities are recorded as a s (singlet), br s (broad singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), or m (multiplet). Coupling constants (J) are expressed in hertz. Mass spectra are recorded on Perkin-Elmer Sciex API 3000. HPLC analysis were carried out at λmax 220 nm using column ODS C-18, 150 mm x 4.6 mm x 4 µm on AGILENT 1100 series. Elemental analyses were performed on a Thermo Quest EA 1110 CHNS. All reactions involving air or moisture sensitive compounds were performed under nitrogen atmosphere. Thin layer chromatography (TLC) was performed on aluminum sheets precoated with silica gel 60 F254, and spots were visualized with UV light. Flash chromatography (FC) was performed using silica gel 230-400 mesh.

Example 1

2-((5-(2-(3,4-dichlorophenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-N-(pyridin-4-ylmethyl)acetamide

To a solution of 2-((5-(2-(3,4-dichlorophenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)acetic acid (1.0 eq.) in DMF (5mL) was added pyridin-4-ylmethanamine (1.2 eq.) at 0°C followed by addition of HBTU (O-Benzotriazole-N,N,N',N'-tetramethyl-uronium-hexafluoro-phosphate) (1.1 eq.), DIPEA (3.0 eq.) and stirred for 5-6 h at room temperature. Reaction mixture was quenched with water and extracted with ethyl acetate, combined organic layers were dried over sodium sulphate and distilled the solvent under vacuum. Crude product was purified by column chromatography to afford the desired product.
IR (cm⁻¹) (CDCl₃): 2926, 1666, 1602, 1510.

¹H NMR (CDCl₃, 400MHz): 9.16 (s, 1H), 8.57 (d, J = 3.6Hz, 2H), 7.27 - 7.25 (m, 3H), 7.08 (s, 1H), 6.98 (d, J = 2Hz, 1H), 6.92 - 6.87 (m, 2H), 6.81 - 6.79 (dd, J₁ = 8Hz, J₂ = 2Hz, 1H), 6.59 - 6.55 (m, 2H), 4.51 (d, J = 6Hz, 2H), 3.67 (s, 2H), 1.49 (s, 6H).

MS: m/z Relative intensities = 529.0, (M+)100%, (+ve-mode)

The following compounds were prepared by following a similar process as described in Example 1 along with suitable modifications as are well known to those skilled in the art.

**Example 2**

N-(2,4-dichlorophenyl)-2-((5-(2-(3,4-dichlorophenyl)propan-2-yl)-l-(4-fluorophenyl)-lH-imidazol-2-yl)thio)acetamide

IR (cm⁻¹) (CDCl₃): 1687, 1583, 1527, 1510.

¹H NMR (CDCl₃, 400MHz): 10.70 (s, 1H), 7.39 (d, J = 2.8Hz, 1H), 7.24 - 7.22 (m, 2H), 7.14 (s, 1H), 7.00 (d, J = 2.8Hz, 1H), 6.92 - 6.68 (m, 2H), 6.84 - 6.82 (dd, J₁ = 8.4Hz, J₂ = 2.4Hz, 1H), 6.61 - 6.58 (m, 2H), 3.87 (s, 2H), 1.50 (s, 6H).

MS: m/z Relative intensities = 582.0, (M+l)+ 100%, (+ve-mode)

**Example 3**

2-((5-(2-(3,4-dichlorophenyl)propan-2-yl)-l-(4-fluorophenyl)-lH-imidazol-2-yl)thio)-N-phenyl acetamide.

IR (cm⁻¹) (CDCl₃): 2968, 1689, 1626, 1599, 1510.

¹H NMR (CDCl₃, 400MHz): 10.95 (s, 1H), 7.61 (d, J = 8.4Hz, 2H), 7.36 - 7.32 (m, 2H), 7.24 - 7.21 (m, 2H), 7.10 (t, J = 7.2Hz, 1H), 7.01 (d, J = 2Hz, 1H), 6.91 - 6.87 (m, 2H), 6.85 - 6.82 (dd, J₁ = 8.4Hz, J₂ = 2.4Hz, 1H), 6.60 - 6.57 (m, 2H), 3.73 (s, 2H), 1.52 (s, 6H).

MS: m/z Relative intensities = 514.1, (M+l)+ 100%, (+ve-mode)

**Example 4**

2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-l-(4-fluorophenyl)-lH-imidazol-2-yl)thio)-N-phenylacetamide

IR (cm⁻¹) (CDCl₃): 1030, 1442, 1688, 2834, 2970, 1333, 3192, 3416.

¹H NMR (CDCl₃, 400MHz): 11.06 (s, 1H), 7.62 (d, J = 7.6Hz, 2H), 7.34 (t, J = 7.6Hz, 2H), 7.21 (s, 1H), 7.09 (d, J = 7.6Hz, 1H), 6.88-6.82 (m, 2H), 6.66 (d, J = 9.2Hz, 1H), 6.57-6.53 (m, 2H), 6.50-3.46 (m, 2H), 3.87 (s, 3H), 3.74 (s, 2H), 3.68 (s, 3H), 1.51 (s, 6H).
MS: m/z Relative intensities = 506.2 (M+)^+100%.

Example 5
N-(3-chloro-4-methylphenyl)-2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1H-imidazol-2-yl)thio)acetamide
IR (cm⁻¹) (CDCl₃): 2926, 2965, 3092.

¹H NMR (DMSO, 400MHz): 10.40 (s, 1H), 7.72 (d, J=1.6Hz, 1H), 7.29 - 7.26 (m, 2H), 7.12 (s, 1H), 7.02 - 6.98 (m, 2H), 6.72 (d, J=8.4Hz, 1H), 6.68 - 6.64 (m, 2H), 6.42 - 6.40 (dd, J₁=9.6Hz, J₂=2Hz, 2H), 3.85 (s, 2H), 3.17 (s, 3H), 3.57 (s, 3H), 2.26 (d, J=3.6Hz, 3H), 1.42 (s, 6H).

MS: m/z Relative intensities = 554.1 (M+H)+100%.

Example 6
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1H-imidazol-2-yl)thio)-N-(4-fluorophenyl)acetamide
IR (cm⁻¹) (CDCl₃): 839, 1258, 1506, 1769, 2835, 3443.

¹H NMR (CDCl₃, 400MHz): 11.75 (s, 1H), 7.60-7.56 (m, 2H), 7.19 (s, 1H), 7.05-6.99 (m, 2H), 6.88-6.82 (m, 2H), 6.67 (d, J = 8.4Hz, 1H), 6.56-6.53 (m, 2H), 6.50-6.47 (m, 2H) 3.85 (s, 3H), 3.70 (s, 3H), 1.51 (s, 6H).

MS: m/z Relative intensities = 524.1 (M+^+100%, (+ve-mode)

Example 7
N-(1H-benzo[d]imidazol-2-yl)-2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1H-imidazol-2-yl)thio)acetamide
IR (cm⁻¹) (CDCl₃): 843, 1028, 1154, 1269, 1510, 1632, 2855, 2930, 2967, 3117, 3215, 3341.

¹H NMR (DMSO, 400MHz): 12.02 (s, 1H), 11.83 (s, 1H), 7.44 (s, 2H), 7.12-7.08 (m, 1H), 7.04 (d, J=3.2Hz, 2H), 7.00 (d, J=8.8Hz, 2H), 6.73 (d, J=8.4Hz, 1H), 6.70 - 6.66 (m, 2H), 6.43 (t, J= 7.6Hz, 2H), 3.98 (s, 2H), 3.69 (s, 3H), 3.55 (s, 3H), 1.49 (s, 6H).

MS: m/z Relative intensities = 546(M+H)^+ 100%, (+ve-mode)

Example 8
2-((5-(2-(3J-dimethoxyphenyl)propan-2-yl)-1H-imidazol-2-yl)thio)-l-(4-methylpiperazin-l-yl)ethanone
IR (cm⁻¹) (CDCl₃): 2967, 2928, 2853, 1641, 1510, 1262, 1221, 1152, 1026, 845.

¹H NMR (CDCl₃, 400MHz): 7.11 (s, 1H), 6.82 (t, J=8.4Hz, 2H), 6.65 (d, J=8.8Hz, 1H), 6.58-6.55 (m, 2H), 6.47 (t, J= 7.2Hz, 2H), 4.01 (s, 2H), 3.85 (s, 3H), 3.73 (s, 3H),
3.60 (t, J = 4.8Hz, 2H), 3.55 (t, J=4.8Hz, 2H), 2.46 (t, J=4.4Hz, 2H), 2.40 (t, J =
4.8Hz, 2H), 2.33 (s, 3H), 1.48 (s, 6H).
MS: m/z Relative intensities = 513 (M+) 100 %, (+ve-mode).

Example 9
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-
yl)thio)-1-(4-(4-fluorophenyl)piperazin-1-yl)ethanone
IR (cm⁻¹) (CDCl₃): 2967, 2928, 2855, 1647, 1510, 1258, 1223, 1153, 1030, 843.
¹H NMR (CDCl₃, 400MHz): 7.12 (s, IH), 6.98 (t, J=8 Hz, 2H), 6.88-6.85 (m, 2H),
6.82 (t, J=8.8Hz, 2H), 6.64 (d, J=8.8 Hz, IH), 6.58-6.55 (m, 2H), 6.47 (t, J= 7.6Hz,
2H), 4.07 (s, 2H), 3.85 (s, 3H), 3.73-3.69 (m, 4H), 3.68 (s, 3H),
3.09-3.02 (m, 4H), 1.48 (s, 6H).
MS: m/z Relative intensities = 593 (M+)+100 %, (+ve-mode).

Example 10
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-
yl)thio)-N-(4-(2-methyl-1H-imidazol-1-yl)phenyl)acetamide
IR (cm⁻¹) (CDCl₃): 2967, 2928, 2855, 1647, 1510, 1258, 1223, 1153, 1030, 843.
¹H NMR (CDCl₃, 400MHz): 1.60 (s, IH), 7.75 (d, J = 8.8Hz, 2H), 7.28-7.25 (m, 2H),
7.22 (s, IH), 7.04 (s, IH), 6.99 (s, IH), 6.88-6.83 (m, 2H), 6.68 (d, J = 8.4Hz, IH),
6.58-6.53 (m, 2H), 6.52-6.48 (m, 2H), 3.86 (s, 3H), 3.73-3.72 (m, 5H), 2.37 (s, 3H),
1.52 (s, 6H).
MS: m/z Relative intensities = 586.3 (M+H)+, 100%, (+ve-mode).

Example 11
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-
yl)thio)-l-(3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-
yl)ethanone
IR (cm⁻¹) (CDCl₃): 3435, 3119, 1728, 1656, 1602, 1440, 1410.
¹H NMR (DMSO-D₆, 400MHz): 7.04-7.01 (m, IH), 6.96-6.92 (m, 2H), 6.73 (d, J =
8.4Hz, IH), 6.68-6.62 (m, 2H), 6.41-6.38 (m, 2H), 5.01 (s, IH), 4.81 (s, IH), 4.19-4.18
(m, IH), 4.12-4.11 (m, IH), 4.03-3.91 (m, 4H), 3.71 (s, 3H), 3.59 (s, 3H), 3.32 (s, 6H).
MS: m/z Relative intensities = 605.1 (M+H)+, 100%, (+ve-mode).
Example 12

\[
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yithio)-l-(3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)ethanone
\]

IR (cm\(^{-1}\)) (CDCl\(_3\)): 3433, 2926, 1693, 1606, 1512, 1411, 1222, 844.

\(^{1}\)H NMR (CDCl\(_3\), 400MHz): 11.50 (s, 1H), 7.74 (d, J = 8.8 Hz, 2H), 7.29-7.27 (m, 2H), 7.23 (s, IH), 7.18 (d, J = 8.4 Hz, IH), 7.04 (d, J = 1.2 Hz, IH), 6.997-6.990 (m, IH), 6.90-6.86 (m, 1H), 6.60-6.54 (m, 3H), 6.48 (d, J = 2.0 Hz, IH), 3.73 (s, 2H), 3.71 (s, 3H), 2.36 (s, 3H), 1.54 (s, 6H).

MS: m/z Relative intensities = 590.1 (M+H)+, 100%, (+ve-mode).

Example 13

N-(1H-benzo[d]imidazol-2-yl)-2-((5-(2-(4-chloro-3-methoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yithio)acetamide

IR (cm\(^{-1}\)) (CDCl\(_3\)): 3350, 1683, 1629, 1575.

\(^{1}\)H NMR (CDCl\(_3\), 400MHz): 12.04 - 11.84 (m, 2H), 7.44 (s, 2H), 7.20 (d, J = 8Hz, IH), 7.15 (s, IH), 7.10 - 7.08 (m, 2H), 7.04 - 7.00 (m, 2H), 6.77-6.74 (m, 2H), 6.53-6.51 (m, 2H), 3.98 (s, 2H), 3.64 (s, 3H), 1.90 (s, 6H).

MS: m/z Relative intensities = 549.9, (M)+100%, (+ve-mode).

Example 14

2-((5-(2-(4-chloro-3-methoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yithio)-l-(3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)ethanone

\(^{1}\)H NMR (CDCl\(_3\), 400MHz): 7.14 (d, J = 8.4Hz, IH), 6.87-6.82 (m, 3H), 6.77-6.74 (m, 2H), 6.53-6.51 (m, 2H), 3.90-3.84 (m, 2H), 3.71 (s, 3H), 2.36 (s, 3H), 1.47 (s, 6H).

MS: m/z Relative intensities = 608.9, (M)+100%, (+ve-mode).

Example 15

2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yithio)-2-methyl-N-(4-(2-methyl-1H-imidazol-1-yl)phenyl)propanamide

IR (cm\(^{-1}\)) (CDCl\(_3\)): 3439, 1745, 1681, 1510.

\(^{1}\)H NMR (CDCl\(_3\), 400MHz): 12.13 (s, IH), 7.92-7.88 (m, 2H), 7.33-7.26 (m, 2H), 7.03-7.00 (m, 2H), 6.87-6.83 (m, 2H), 6.67 (d, J = 8Hz, IH), 6.49-6.45 (m, 4H), 3.86 (s, 3H), 3.71 (s, 3H), 2.36 (s, 3H), 1.52 (s, 6H), 1.46 (s, 6H).

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MS: m/z Relative intensities = 614, (M)+100%, (+ve-mode).

Example 16

1-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1H-imidazol-2-y1)thio)-N-(4-(2-methyl-1H-imidazol-1-yl)phenyl)cyclobutanecarboxamide

IR (cm⁻¹) (CDC₃): 3435, 1730, 1681, 1604, 1510.

¹H NMR (CDC₁₃, 400MHz): 12.0 (s, IH), 7.84 (d, J = 8.8Hz, IH), 7.27-7.25 (m, 3H), 7.03-6.99 (m, 2H), 6.87 (t, J = 8.4Hz, 2H), 6.68 (t, J = 8.0Hz, IH), 6.56-6.47 (m, 4H), 3.86 (s, 3H), 3.70 (s, 3H), 2.88-2.86 (m, 2H), 2.36 (s, 3H), 2.02-1.92 (m, 3H), 1.47 (s, 6H).

MS: m/z Relative intensities = 626.2, (M)+100%, (+ve-mode).

Example 17

2-((5-(2-(3-cyano-4-fluorophenyl)propan-2-yl)-1H-imidazol-2-y1)thio)-2-methyl-N-(4-(2-methyl-1H-imidazol-1-yl)phenyl)propanamide

IR icm⁻¹) (CDC₁₃): 3417, 3390, 2235, 1730, 1681, 1471.

¹H NMR (CDC₁₃, 400MHz): 12.00 (s, IH), 7.88 (d, J = 8.4Hz, 2H), 7.35 (s, IH), 7.29-7.26 (m, 2H), 7.24-7.21 (m, IH), 7.20-7.18 (m, IH), 7.09-6.99 (m, 3H), 6.95-6.90 (m, 2H), 6.53-6.50 (m, 2H), 2.38 (s, 3H), 1.57 (s, 6H), 1.52 (s, 6H).

MS: m/z Relative intensities = 597.1 (M+H)+, 100%, (+ve-mode).

Example 18

2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1H-imidazol-2-y1)thio)-N-(1H-indazol-5-yl)acetamide

IR (cm⁻¹) (CDC₁₃): 3021, 2967, 2897, 1738, 1672, 1512, 1385, 1212, 1153, 1045, 1030, 845.

¹H NMR (CDC₁₃, 400MHz): 8.96 (d, J=8Hz, IH), 7.13 (s, IH), 6.85-6.81 (m, 2H), 6.66 (d, J=8.8Hz, IH), 6.59 (m, IH), 6.54-6.50 (m, IH), 4.59 (m, IH), 3.86 (s, 3H), 3.75 (s,
3H), 3.73 (s, 3H), 3.70-3.67 (m, 4H), 3.59 (s, IH), 2.41-2.35 (m, 3H), 2.05 (s, IH), 1.49 (s, 6H).

MS: m/z Relative intensities = 573 (M+) +100 %, (+ve-mode).

**Example 20**

2-(l-(4-fluorophenyl)-5-(2-(3-methoxyphenyl)propan-2-yl)-lH-imidazol-2-yl)thio)-N-(4-(2'-methyl- lH-imidazol-1-yl)phenyl)acetamide.

$^1$H NMR (CDCl$_3$, 400MHz): 11.51 (s, IH), 7.74 (d, J = 8.8 Hz, 2H), 7.29-7.25 (m, 3H), 7.23 (s, IH), 7.18 (d, J = 1.2 Hz, IH), 7.04 (d, J = 1.2 Hz, IH), 6.99 (d, J = 8.0 Hz, 2H), 6.60-6.54 (m, 3H), 6.48 (d, J = 2.0 Hz, IH), 3.74-3.71 (m, 5H), 2.37 (s, 3H), 1.54 (s, 6H).

**Example 21**

(S)-methyl 2-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-l-(4-fluorophenyl)-lH-imidazol-2-yl)thio)acetamido)-4-methylpentanoate.

IR (cm$^{-1}$) (CDC$_3$): 3441, 3021, 1647, 1468, 1028, 669.

$^1$H NMR (CDCl$_3$, 400MHz): 8.74 (d, J = 5.8 Hz, IH), 7.11 (s, IH), 6.86-6.81 (m, 2H), 6.66 (d, J= 8.4 Hz, IH), 6.56-6.52 (m, 2H), 6.50-6.47 (m, 2H), 4.53 (d, J= 8 Hz, IH), 3.85 (s, 3H), 3.74-3.70 (m, 7H), 3.56 (d, J= 14.4 Hz, IH), 1.68-1.60 (m, 3H), 1.57 (s, 3H), 1.49 (d, J= 4.8 Hz, 6H).

MS: m/z Relative intensities = 558.2 (M+) +100 %, (+ve-mode).

**Example 22**

(S)-methyl 2-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-lH-imidazol-2-yl)thio)acetamido)-3-phenylpropanoate.

IR (cm$^{-1}$) (CDCl$_3$): 3435, 2961, 1611, 1412, 1389, 1333, 1514, 1082, 973, 849, 669.

$^1$H NMR (CDCl$_3$, 400MHz): 8.1 (d, J = 7.6 Hz, IH), 7.27 - 7.24 (m, 2H), 7.16 - 7.14 (m, 2H), 7.01 (s, IH), 6.82 (t, J = 8.4 Hz, 2H), 6.66 (d, J = 9.2 Hz, IH), 6.56 - 6.47 (m, 4H), 4.84 - 4.82 (m, IH), 3.85 (s, 3H), 3.73 - 3.68 (m, 6H), 3.63 (d, J = 9.2 Hz, 2H), 3.14 (d, J = 5.6 Hz, IH), 3.10 (d, J = 7.6 Hz, IH), 1.49 (s, 6H).

MS: m/z Relative intensities = 592.1 (M+) +100 %, (+ve-mode).

**Example 23**

2-(5-(2-(4,5-dimethoxy-2-nitrophenyl)propan-2-yl)-l-(4-fluorophenyl)-lH-imidazol-2-yl)thio)-N-(4-(2'-methyl- lH-imidazol-1-yl)phenyl)acetamide

IR (cm$^{-1}$) (CDCl$_3$): 2974, 1689, 1608, 1514.
$^1$H NMR (CDCl$_3$, 400MHz): 11.34 (s, 1H), 7.74 (d, $J$ = 8.8Hz, 2H), 7.26 - 7.21 (m, 2H), 7.04 - 7.02 (m, 2H), 6.99 - 6.98 (m, 4H), 6.83 (s, 1H), 6.41 (s, 1H), 3.86 (s, 3H), 3.77 (s, 2H), 3.74 (s, 3H), 2.35 (s, 3H), 1.71 (s, 6H).

MS: m/z Relative intensities = 613.2 (M$^+$)$^+$100 %, (+ve-mode).

**Example 24**

2-((5-(2-(4,5-dimethoxy-2-(methylsulfonamido)phenyl)propan-2-yl)-l-(4-fluorophenyl)- 1H-imidazol-2-yl)thio)-N-(4-(2-methyl- 1H-imidazol- 1-yl)phenyl)acetamide

IR (cm$^{-1}$) (CDCl$_3$): 3308, 1606, 1514.

$^1$H NMR (CDCl$_3$, 400MHz): 11.10 (s, 1H), 7.72 - 7.69 (m, 2H), 7.35 (s, 1H), 7.27 - 7.25 (m, 4H), 7.1 1 (s, 1H), 7.02 - 6.98 (m, 2H), 6.86 - 6.69 (m, 3H), 6.24 (s, 1H), 3.87 (s, 3H), 3.79 (s, 2H), 3.58 (s, 3H), 2.99(s, 3H), 2.35(s, 3H), 1.66 (s, 6H).

MS: m/z Relative intensities = 679.3 (M$^+$)$^+$100 %, (+ve-mode).

**Example 25**

(S)-dimethyl 2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-l-(4-fluorophenyl)- 1H-imidazol-2-yl)thio)acetamido)pentanedioate

IR icm$^{-1}$ (CDCl$_3$): 3620, 2974, 2874, 1740, 1603, 1439, 1385, 1153, 1030, 669.

$^1$H NMR (CDCl$_3$, 400MHz): 8.96 (d, $J$ = 7.6Hz, 1H), 7.13 (s, 1H), 6.84 (d, $J$ =7.6Hz, 2H), 6.76 (d, $J$ = 8.8Hz, IH), 6.59 (s, 1H), 6.50 - 6.48 (m, 3H), 4.60 (d, $J$ = 5.2Hz, 1H), 3.86 (s, 3H), 3.75 (s, 3H), 3.73 (s, 3H), 3.67 (s, 4H), 3.56 (s, IH), 2.40 - 2.37 (d, d, $J_1$ = 8.8Hz, $J_2 = 2Hz$, 2H), 2.08 -2.04 (m, IH), 2.03 - 2.00 (m, IH), 1.49 (s, 6H).

MS: m/z Relative intensities = 588.2 (100) (M+H)$^+$, (+ve-mode).

**Example 26**

(S)-dimethyl 2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-l-(4-fluorophenyl)- 1H-imidazol-2-yl)thio)acetamido)succinate

IR (cm$^{-1}$) (CDCl$_3$): 3620, 2976, 2899, 1742, 1603, 1439, 1410, 1385, 1153, 1028, 878, 845, 669.

$^1$H NMR (CDCl$_3$, 400MHz): 8.92 (d, $J$ = 7.6Hz, IH), 7.12 (s, IH), 6.84 (d, $J$ =8.4Hz, 2H), 6.66 (d, $J$ = 8.4Hz, IH), 6.59-6.56 (m, 2H), 6.48 (d, $J$ = 2.4Hz, 2H), 4.86 - 4.81 (m, IH), 3.86 (d, $J$ =4Hz, 3H), 3.75 -3.73 (m, 7H), 3.64 (d, $J$ =4.4Hz, 5H), 3.00 - 2.95 (d, d, $J_1$ = 5.2Hz, $J_2 = 4.8Hz$, IH), 2.90 - 2.84 (d,d, $J_1 = 16.8Hz$, $J_2 = 5.2Hz$, IH), 1.48 (s, 6H).

MS: m/z Relative intensities = 574.1 (100) (M+H)$^+$, (+ve-mode).
Example 27

2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-l-(4-fluorophenyl)-4-methyl-lH-imidazol-2-yl)thio)-N-(4-(2-methyl- lH-imidazol- 1-yl)phenyl)acetamide

IR (cm⁻¹) (CDCl₃): 3431, 2993, 2931, 1698, 1606, 1552, 141 1.

1H NMR (CDCl₃, 400MHz): 7.68 (d, J = 8.8Hz, 2H), 7.38 (d, J = 8.8Hz, 2H), 7.19 (d, J = 1.2Hz, IH), 6.99 (d, J = 1.2Hz, IH), 6.71 - 6.66 (m, 3H), 6.62 - 6.59 (m, 2H), 6.52 (d, J = 2Hz, IH), 6.47-6A4 (dd, J₁ = 8.4Hz, J₂ = 2Hz, IH), 4.60 (s, IH), 3.75 (s, 3H), 3.60 (s, 3H), 2.48 (s, 3H), 2.35 (s, 3H), 1.54 (s, 6H).

MS: m/z Relative intensities = 600.2 (100) (M+H)⁺, (+ve-mode).

Example 28

2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-l-(4-fluorophenyl)-4-methyl-lH-imidazol-2-yl)thio) - N-isopropylacetamide

1H NMR (DMSO-d₆, 400MHz): 8.15 (d, J = 6.4Hz, IH), 6.86 - 6.80 (m, 2H), 6.66 (d, J = 7.6Hz, IH), 6.58 - 6.53 (m, 2H), 6.48 (d, J = 4Hz, IH), 6.47 - 6.44 (m, IH), 4.0 - 3.94 (m, IH), 3.85 (s, 3H), 3.72 (s, 3H), 3.64 (S, 3H), 2.45 (S, 3H), 1.52 (S,6H), 1.15 (d, J = 6.4Hz, 6H).

Example 29

N-(3,4-dimethoxyphenyl)-2-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)- (4-fluorophenyl)-1H-imidazol-2-yl)thio)-acetamido)acetamide

1H NMR (CDCl₃, 400MHz): 8.93 (s, IH), 8.75 (t, J = 6.4Hz, IH), 7.29 (d, J = 2.4Hz, IH), 7.01 (s, IH), 6.96 - 6.93 (dd, J₁ = 8.8Hz, J₂ = 2.4Hz, IH), 6.87 - 6.81 (m, 3H), 6.65 (d, J = 8.4Hz, IH), 6.54 - 6.51 (m, 2H), 6.45 - 6.42 (m, 2H), 4.13 (d, J = 6.4Hz, 2H), 3.89 (s, 3H), 3.87 (s, 3H), 3.85 (s, 3H), 3.70 (s, 3H), 3.60 (s, 2H), 3.49 (s, 3H), 1.48 (s, 6H), 1.29 (s, 3H).

MS: m/z Relative intensities = 623.3 (100%) (M+H)⁺, (+ve-mode).

Example 30

2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)- 1-(4-fluorophenyl)- lH-imidazol-2- yl)thio)-N-isopentylacetamide

IR (cm⁻¹) (CDCl₃): 2972, 2935, 2856, 1710, 1629, 1600, 1589, 1541.

1H NMR (DMSO-D₆, 400MHz): 8.07 (t, J = 5Hz, IH), 7.08 - 7.02 (m, 3H), 6.75 (d, J = 8Hz, IH), 6.67-6.64(m, 2H), 6.44 - 6.41 (m, 2H), 3.71 (s, 3H), 3.64 (s, 2H), 3.58 (s, 3H), 3.05-3.00 (m, 2H), 1.54-1.49 (m, IH), 1.42 (s, 6H), 1.27-1.22 (m,2H), 0.84 (d, J = 6.8Hz, 6H).
Example 31

N-(cyclohexylmethyl)-2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yI)-1-(4-fluorophenyl)-H-imidazol-2-yl)thio)acetamide

Example 32

2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yI)-1-(4-fluorophenyl)-H-imidazol-2-yI)thio)-N-(pyridine-3-ylmethyl)acetamide

Example 33

2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yI)-1-(4-fluorophenyl)-H-imidazol-2-yI)thio)-1-morpholinoethanone

Example 34

N-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yI)-1-(4-fluorophenyl)-H-imidazol-2-yI)thio)ethyl) thiophene-3-carboxamide
To a solution of 2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethanamine (1.0 eq.) in DMF (5mL) was added thiophene-3-carboxylic acid (1.2 eq.) at 0°C followed by addition of HBTU (O-Benztetramethyl-uronium-hexafluoro-phosphate) (1.1 eq.), DIPEA (3.0 eq.) and stirred for 5-6 h at room temperature. Reaction mixture was quenched with water and extracted with ethyl acetate; combined organic layers were dried over sodium sulphate and distilled the solvent under vacuum. Crude product was purified by column chromatography to afford the desired product.

**Example 35**

N-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-((4-fluorophenyl)imidazol-2-yl)thio)ethyl)-1H-benzo[d]imidazole-5-carboxamide

IR (cm⁻¹) (CDCl₃): 843, 1260, 1510, 1645, 2833, 2932, 2969, 3379.

^1H NMR (CDCl₃, 400MHz): 8.78 (brs, 1H), 8.00-7.99 (dd, J₁ = 1Hz, J₂ = 2.8Hz, 1H), 7.57-7.56(dd, J₁ = 1.2Hz, J₂ = 5.2Hz, 1H), 7.36-7.34 (m, 1H), 7.15 (s, 1H) 6.83 (t, J = 7.2Hz, 2H), 6.65 (d, J = 8.5Hz, 1H), 6.54-6.50 (m, 2H), 6.47-6.45 (m, 2H), 3.85(s, 3H), 3.78-3.74 (m 2H), 3.68 (d, 3H), 3.21-3.18 (m, 2H), 1.63 (s, 6H).

MS: m/z Relative intensities = 526.1 (M+), (+ve-mode).

The following compounds were prepared by following a similar process as described in Example 34 along with suitable modifications as are well known to those skilled in the art.

**Example 36**

N-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-((4-fluorophenyl)imidazol-2-yl)thio)ethyl)-1H-benzo[d]imidazole-5-carboxamide
IR (cm$^{-1}$) (CDCl$_3$): 3437, 3117, 2967, 2330, 1605, 1464, 1244, 1049.

$^1$H NMR (CDCl$_3$, 400MHz): 8.97 (t, $J = 4$Hz, IH), 8.30 (s, IH), 8.17 (s, IH), 7.86 (d, $J = 5.6$ Hz, IH), 7.73 (d, $J = 8$Hz, IH), 7.20 (s, IH), 6.86 - 6.80 (m, 2H), 6.63 - 6.61 (m, IH), 6.55-6.43 (m, 4H), 3.86-3.80 (m, 5H), 3.65 (s, 3H), 3.27-3.24 (m, 2H), 1.47(s, 6H).

MS: m/z Relative intensities = 560.1 (M$^+$)*, (+ve-mode).

**Example 37**

N-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl)-2-(2,4,5-trifluorophenyl)acetamide

IR (cm$^{-1}$) (CDCl$_3$): 3620, 3021, 2974, 2874, 1668, 1603, 1435, 1256, 1153, 1028.

$^1$H NMR (CDCl$_3$, 400MHz): 8.20 (s, IH), 7.24-7.18 (m, IH), 7.04 (s, IH), 6.96-6.90 (m, IH), 6.86-6.82 (m, 2H), 6.66 (d, $J = 8.4$Hz, IH), 6.54-6.46 (m, 4H), 3.88 (s, 3H), 2.59 (s, 3H), 3.10-3.07 (m, 2H), 1.50 (s, 6H).

MS: m/z Relative intensities = 588.1 (M$^+$)*, (+ve-mode).

**Example 38**

N-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl)-1H-indazole-5-carboxamide

IR (cm$^{-1}$) (CDCl$_3$): 3430, 3221, 3154, 2967, 2835, 1641, 1460, 1260, 1026, 845.

$^1$H NMR ((DMSO, 400MHz): 13.28 (s, IH), 8.69 (t, $J = 5.2$Hz, IH), 8.29 (s, IH), 8.20 (s, IH), 7.83-7.80 (dd, $J_1 = 1.2$Hz, $J_2 = 8.8$Hz, IH), 7.57 (d, $J = 8.8$Hz, IH), 7.13 (s, IH), 7.00-6.96 (m, 2H), 6.72 (d, $J = 8.4$Hz, IH), 6.66-6.63 (m, 2H), 6.42-6.40 (m, 2H), 3.70 (s, 3H), 3.56 (s, 3H), 3.54-3.50 (q, $J = 6$Hz, 2H), 3.17 (t $J = 6.4$Hz, 2H), 1.42 (s, 6H).

MS: m/z Relative intensities = 560 (M$^+$)*, (+ve-mode).

**Example 39**

N-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl)-6-methylnicotinamide

$^1$H NMR (CDCl$_3$, 400MHz): 9.52 (s, IH), 9.10 (d, $J = 2$Hz, IH), 8.20 -8.18 (dd, $J_1 = 2$Hz, $J_2 = 8$Hz, IH), 7.28 (s, IH), 7.18 (s, IH), 7.10 (d, $J = 8.8$Hz, IH), 6.53-6.50 (m, 2H), 6.47-6.44 (m, 2H), 3.86 (s, 3H), 3.86-3.80 (m, 2H), 3.68 (s, 3H), 3.24-3.21 (m, 2H), 2.64 (s, 3H), 1.49 (s, 6H).

MS: m/z Relative intensities = 535.1 (M$^+$)*, (+ve-mode).
Example 40

N-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl)-4-(1H-imidazol-1-yl)benzamide.

IR (cm⁻¹) (CDCl₃): 3439, 3117, 1649, 1608, 1552, 1460.

¹H NMR (CDCl₃, 400MHz): 9.36 - 9.35 (m, 1H), 8.13 (d, J = 8.8Hz, 2H), 7.96 (s, 1H), 7.57 (d, J = 8.4Hz, 2H), 8.37 (s, 1H), 7.96 (s, 1H), 7.57 (d, J = 8.4Hz, 2H), 6.88 - 6.82 (m, 2H), 3.85 (s, 3H), 3.84 - 3.80 (m, 2H), 3.69 (s, 3H), 3.25 - 3.22 (m, 2H), 1.50 (s, 6H).

MS: m/z Relative intensities = 586.1 (M⁺)⁺, (+ve-mode).

Example 41

2-((2-(1H-imidazol-1-yl)ethyl)thio)-5-(2-(3,4-dichlorophenyl)propan-2-yl)-1-(4-fluorophenyl)-IH-imidazole.

To a solution of 5-(2-(3,4-dichlorophenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazole-2-thiol (1.0 eq.) in DMF (5mL) was added 2-(1H-imidazol-1-yl)ethyl methanesulfonate (1.2 eq.) at followed by addition of K₂CO₃ (3.0 eq.) and stirred for 3 h at 90 °C. Reaction mixture was quenched with water and extracted with ethyl acetate; combined organic layers were dried over sodium sulphate and distilled the solvent under vacuum. Crude product was purified by column chromatography to afford the desired product.

IR (cm⁻¹) (CDCl₃): 3416, 2972, 1645, 1600, 1508.

¹H NMR (CDCl₃, 400MHz): 7.55 (s, 1H), 7.44 (d, J = 8.4Hz, 1H), 7.17 (s, 1H), 7.12 (s, 1H), 7.08 - 7.02 (m, 3H), 6.97 - 6.94 (m, 1H), 6.85 (s, 1H), 6.74 - 6.71 (m, 2H), 4.22 (t, J = 6.4Hz, 2H), 3.36 - 3.31 (m, 2H), 1.47 (s, 6H).

MS: m/z Relative intensities = 474.9 (M⁺)⁺, (+ve-mode).

The following compounds were prepared by following a similar process as described in Example 41 along with suitable modifications as are well known to those skilled in the art.
Example 42

r-((5-(2-(3,4-dichlorophenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl) piperidine.

IR (cm⁻¹) (CDCl₃): 2931; 2852, 1597, 1504, 1220.

NMR (DMSO-d₆, 400MHz): 7.43 (d, J = 8.4Hz, 1H), 7.13 (s, 1H), 7.09 - 7.05 (m, 2H), 7.01 (d, J = 2Hz, 1H), 6.96 - 6.93 (dd, J₁ = 8.4Hz, 1H, J₂ = 2Hz, 1H), 6.73 - 6.70 (m, 2H), 3.04 - 3.15 (m, 2H), 2.47 - 2.18 (m, 5H), 1.46 - 1.23 (m, 13H).

MS: m/z Relative intensities = 492.0 (M⁺)*, (+ve-mode).

Example 43

2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-N-(pyridine-3-ylmethyl)ethanamine

IR (cm⁻¹) (CDCl₃): 629, 669, 770, 843, 928, 1028, 1215, 1256, 1410, 1512, 1603, 2839, 2974, 3021.

NMR (DMSO-d₆, 400MHz): 8.46 (S, 1H), 8.43 (d, J = 4Hz, 1H), 7.67 (d, J = 8Hz, 1H), 7.33-7.30 (m, 1H), 7.07 (s, 1H), 7.01(t, J = 8.4Hz, 2H), 6.74 (d, J = 8.8Hz, 1H), 6.62-6.59 (m, 2H), 6.42 (d, J = 6.4Hz, 2H), 3.71 (s, 3H), 2.67 (t, J = 7.6Hz, 2H), 2.67 (t, J = 7.6Hz, 3H), 1.48 (s, 6H).

MS: m/z Relative intensities = 507.1 (M⁺)*, (+ve-mode).

Example 44

N-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl)aniline

IR (cm⁻¹) (CDCl₃): 2936, 2976, 3020.

NMR (CDCl₃, 400MHz): 7.17-7.13 (m,3H), 6.83-6.78 (m,2H), 6.70-6.67 (t,J=7.2Hz,1H), 6.63 (t,J=6.8Hz,1H), 6.57 (t,J=4.4Hz,2H), 6.51-6.46 (m,4H), 3.84 (s,3H), 3.70 (s,3H), 3.42 (t,J=6.4Hz,2H), 3.22 (t,J=6.4Hz,2H), 1.48 (s,6H).

MS: m/z Relative intensities = 492.2 (M+H)+100 %, (+ve-mode).

Example 45

5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-2-(2-(2-methyl-1H-imidazol-1-yl)ethyl)thio)-1H-imidazole

IR (cm⁻¹) (CDCl₃): 845, 1026, 1151, 1221, 1260, 1512, 1630, 2855, 2927, 2967, 3117.

NMR (CDCl₃, 400MHz): 7.14 (s,1H), 6.90 (s, 1H), 6.85-6.81 (m, 3H), 6.67-6.65 (dd, J₁ = 6Hz, J₂ = 2.8Hz, 1H), 6.51-6.48 (m,4H), 4.22 (t, J = 7.2Hz, 2H), 3.84 (s, 3H), 3.73 (s,3H), 3.30 (t, J = 7.2Hz, 2H), 2.37 (s,3H), 1.49 (s, 6H).
MS: m/z Relative intensities = 480.9 (M⁺)⁺, (+ve-mode).

**Example 46**

1-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1H-imidazol-2-yl)thio)ethyl)-4-methylpiperazine

**Example 47**

1-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl)-1H-indole

**Example 48**

1-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1H-imidazol-2-yl)thio)ethyl)-1H-benzo[d]imidazole

**Example 49**

2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-l-(4-(2-methoxyacetyl) piperazin-l-yl) ethanone
$^1$H NMR (CDCl$_3$, 400MHz): 7.12 (d, J = 6.4Hz, 1H), 6.89 - 6.81 (m, 2H), 6.67 (d, J = 7.2Hz, 1H), 6.58 - 6.53 (m, 2H), 6.47 (d, J = 6.8Hz, 2H), 4.12 (s, 2H), 4.00 - 3.99 (m, 2H), 3.85 (s, 3H), 3.73 (s, 3H), 3.70 - 3.49 (m, 8H), 3.42 (s, 3H), 1.48 (s, 6H).

MS: m/z Relative intensities = 571.1 (40%) (M+H) $^+$, 593.4 (100%) (M+Na) $^+$

**Example 50**

4-(1-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1H-imidazol-2-yl)thio)ethyl)-lH-imidazol-4-yl)phenol.

IR (cm$^{-1}$) (CDCl$_3$): 3435, 3079, 2414, 1710, 1442, 1238, 1026.

$^1$H NMR (DMSO, 400MHz): 9.37 (s, 1H), 7.52 - 7.47 (m, 2H), 7.35 (s, 1H), 7.14 (s, 1H), 6.99 (t, J = 8.4Hz, 2H), 6.74 - 6.61 (m, 2H), 6.65 - 6.61 (m, 2H), 6.44 - 6.42 (m, 2H), 4.21 (t, J = 6.4Hz, 2H), 3.71 (s, 3H), 3.57 (s, 3H), 3.38 (t, J = 6.4Hz, 2H), 1.42 (s, 6H).

MS: m/z Relative intensities = 559.4 (40%) (M)$^+$, (+ve-mode).

Biological studies:

**In-vitro studies: hTGR5 Reporter Gene Assay:**

Chinese Hamster Ovarian (CHO) K1 cells were plated in 24 well tissue culture plate at a density of 4 X $10^4$ cells/well in a Nutrient Mixture F-12 HAM containing 10% Fetal Bovine Serum, cultured for 24 hrs at 37°C/5% C0$_2$, and then transfected with 50 ng of human (h) TGR5 expression plasmid (pCMV SPORT6 - hTGR5), 300 ng of cAMP-responsive element (CRE)-driven luciferase reporter plasmid (pCRE-Luc) and 100 ng of /?-galactosidase reporter vector in each well using Polyfect Transfection Reagent (QIAGEN, Cat. No.: 301107) according to the manufacturer's instructions. After 4 hrs of incubation, cells were washed once with phosphate-buffered saline (PBS) and medium was exchanged to Nutrient Mixture F-12 HAM containing 0.5% Fatty acid free bovine serum albumin (FAFBSA) and ImM Sodium Pyruvate Solution. After incubation for another 18 hrs, cells were treated for 5 hrs with different concentrations of each compound. After treatment, the cells were lysed with 100 µL of Glo Lysis buffer (Promega, Cat. No.: E2661) and subjected to Luciferase and /?-Galactosidase assays as described below.

**Luciferase and /?-Galactosidase Assays.**

For luciferase assays, 20 µL of cell lysate was mixed with 100 µL of Luciferase Assay Substrate (Promega, Cat. No.: E1501) & Luminescence was measured in HIDEW Multitechnology Plate Reader. For galactosidase assays, 30 µL of cell lysate...
was mixed with 30 μL of 2X ONPG Buffer [20 mM sodium phosphate buffer - pH 7.3, 2 mM MgCl₂, 100 mM β-mercaptoethanol, and 1.33 mg/mL o-nitrophenyl-β-D-galactopyranoside (ONPG)] and incubated at 37°C for 2-10 mins. The optical density at 415 nm was determined in SpectraMax 190.

Normalized luciferase values were determined by dividing the luciferase activity by the galactosidase activity and expressed as fold induction with respect to (w.r.t.) DMSO control.

**TGR5 Assay Results**

In the following table, EC₅₀ values determined according to the TGR5/CRE-Luciference Assay described herein (CRE-Luc). Table below display h-TGR5 CRE-Luc percentage activity of the compounds at 100 nM and 1µM w.r.t. control (RG-239 at 1µM) data. The following compounds in Table 1 were made by procedure described in above scheme and examples, and, where applicable, by making any necessary substituent of known material that one skilled in the art would ordinarily understand.
<table>
<thead>
<tr>
<th>Example Number</th>
<th>In-vitro (hCRE Luciference assay) % control wrt RG239 (1 µM)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>100 nM</td>
</tr>
<tr>
<td>2</td>
<td>29.4</td>
</tr>
<tr>
<td>4</td>
<td>68.6</td>
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<tr>
<td>5</td>
<td>81.9</td>
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<td>6</td>
<td>96.2</td>
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<td>7</td>
<td>62.7</td>
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<td>8</td>
<td>89.8</td>
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<td>9</td>
<td>96.1</td>
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<td>10</td>
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<td>11</td>
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<td>45</td>
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<td>46</td>
<td>61.3</td>
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<tr>
<td>47</td>
<td>112.8</td>
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<tr>
<td>48</td>
<td>75.8</td>
</tr>
</tbody>
</table>

Protocol for GLP-1 secretion activity in C57 mice Model

Male C57 mice of 8-12 week age, bred in Zydus research Centre Animal house will be used for this experiment. Animal will be issued and subjected for 3-7 days acclimatization. On first day animal will be grouped based on non-fasting serum...
glucose levels and kept on fasting for overnight. On second day of the experiment, formulation of test compounds will be prepared and fasting body weight of animals will be recorded. Each animal will receive a single dose of vehicle/test compounds administered per orally as per specified group and dose levels. Exactly 15 min post dosing glucose load (3gm/kg/10ml) will be administered orally to all the groups. Then exactly after 10 min of glucose load animal will bled from retro orbital plexus. Blood collection will be done in micro centrifuge tube containing 30µl of 2% EDTA and 5µl of DPP-IV inhibitor. Blood samples immediately after collection will be centrifuged and plasma will be separated and analyzed for Total GLP-1 level using ELISA kit. The percent or fold change Vs Vehicle will be calculated to determine the total GLP-1 secretion activity for the test compound. Following table shows the total GLP-1 secretion activity for the selected test compound:

<table>
<thead>
<tr>
<th>Test Substance (Dose 30 mg/kg)</th>
<th>Model</th>
<th>Route</th>
<th>Active/Total</th>
<th>Fold change Vs vehicle control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Example 43</td>
<td>C57-N</td>
<td>Oral</td>
<td>Active</td>
<td>3.20 ± 0.90</td>
</tr>
</tbody>
</table>

The novel compounds of the present invention can be formulated into suitable pharmaceutically acceptable compositions by combining with suitable excipients by techniques and processes and concentrations as are well known.

The compounds of Formula (I) or pharmaceutical compositions containing them are useful as antidiabetic and antiobesity compounds suitable for humans and other warm blooded animals, and may be administered either by oral, topical or parenteral administration.

In certain instances, it may be appropriate to administer at least one of the compounds described herein or a pharmaceutically acceptable salt, ester, or prodrug thereof in combination with another therapeutic agent. Several reasons can be attributed for using a combination therapy depending on the need of the patient. As an example, if one of the side effects experienced by a patient upon receiving one of the compounds herein is hypertension, then it may be appropriate to administer an anti-hypertensive agent in combination with the initial therapeutic agent. Or, by way of example only, the benefit experienced by a patient may be increased by administering one of the compounds described herein with another therapeutic agent (which also includes a therapeutic regimen) that also has therapeutic benefit. Several such instances are well known to a skilled person and the use of combination therapy may be envisaged for all such
situations. In any case, regardless of the disease, disorder or condition being treated, the overall benefit experienced by the patient may simply be additive of the two therapeutic agents or the patient may experience a synergistic benefit.

Specific, non-limiting examples of possible combination therapies include use of certain compounds disclosed herein with agents found in the following pharmacotherapeutic classifications as indicated below. These lists should not be construed to be closed, but should instead serve as illustrative examples common to the relevant therapeutic area at present. Moreover, combination regimens may include a variety of routes of administration and should include oral, intravenous, intraocular, subcutaneous, dermal, and inhaled topical.

For the treatment of metabolic disorders, compounds disclosed herein may be administered with an agent selected from the group comprising: insulin, insulin derivatives and mimetics, insulin secretagogues, insulin sensitizers, biguanide agents, alpha-glucosidase inhibitors, insulinotrophic sulfonylurea receptor ligands, meglitinides, GLP-1 (glucagon like peptide-1), GLP-1 analogs, DPPIV (dipeptidyl peptidase IV) inhibitors, GPR-19 inhibitors, sodium-dependent glucose co-transporter (SGLT2) inhibitors, PPAR modulators, non-glitazone type PPAR.deltal agonist, HMG-CoA reductase inhibitors, cholesterol-lowering drugs, rennin inhibitors, anti-thrombotic and anti-platelet agents and anti-obesity agents.

For the treatment of metabolic disorders, compounds disclosed herein may be administered with an agent selected from the group comprising: insulin, metformin, Glipizide, glyburide, Amaryl, gliclazide, meglitinides, nateglinide, repaglinide, amylin mimetics (for example, pramlintide), acarbose, miglitol, voglibose, Exendin-4, vildagliptin, Liraglutide, naliglutide, saxagliptin, pioglitazone, rosiglitazone, HMG-CoA reductase inhibitors (for example, rosuvastatin, atrovastatin, simvastatin, lovastatin, pravastatin, fluvastatin, cerivastatin, rosuvastatin, pitavastatin and like), cholesterol-lowering drugs (for example, fibrates which include: fenofibrate, benzaafibrate, clofibrate, gemfibrozil and like; cholesterol absorption inhibitors such as Ezetimibe, eflucimibe etc.

From the foregoing description, one skilled in the art can easily ascertain the essential characteristics of this invention, and without departing from the spirit and scope thereof, can make various changes and modifications of the invention to adapt it
to various usages and conditions. Such different embodiments are also to be considered to be within the scope of the present invention.
Claims:

1. A compound of Formula I, including their pharmaceutically acceptable salts, their enantiomers, their diastereomers, and pharmaceutical compositions containing:

![Diagram of Formula I]

wherein, Y is = S, -S(O)-, -S(O)₂⁻; T is = -(CO)NH-, -NH(CO)-, -NR₁²⁻; n is 0, 1, 2, 3 or 4; m is 0, 1, 2 or 3; R¹ is selected from aryl, heteroaryl, heterocyclyl or aryl(C₆-C₆)alkyl, wherein said aryl, heteroaryl, heterocyclyl or aryl(C₆-C₆)alkyl is optionally to be substituted with one, two, or three R¹ groups, wherein R¹ at each occurrence independently represents halogen, Ci-Gjalkyl, Ci-C₄ haloalkyl, C₃-C₅ cycloalkyl, heteroaryl, heterocyclyl, the group representing -R¹b, -Ci-C₄ alkyl-R¹b, or -OC₁-C₄alkyl-R¹b wherein R¹b at each occurrence independently represents cyano, nitro, -N(R²c)₂, -OR₃, -SR₄, -C(0)R₅, -C(0)OR₆, -C(0)N(R₇c)₂, -S(0)N(R₈c)₂, -S(0)₂N(R₉c)₂, or -S(0)₂R¹b, -OC(0)R¹b, -OC(0)OR₁b, -OC(0)N(R₁b)₂, or -N(R₁b)cOC(0)N(R₁b)₂, wherein each R¹b is independently hydrogen, Ci-C₄alkyl, or Ci-C₄ haloalkyl; R² is selected from -Z- R³, wherein

Z is = -C(R²b)₂⁻, -C(H)(OH)-, -N(R²b)⁻, -O-, -C(R²b)₂0-, -S-, -S(O)⁻, -S(O)₂-, -C(O)-

wherein: R² at each occurrence independently represents hydrogen, C₁-C₄ haloalkyl, Ci-Gjalkyl, or hydroxy(Ci-C₄)alkyl groups; and R³ is aryl or heteroaryl, heterocyclyl wherein said aryl or heteroaryl or heterocyclyl groups is optionally substituted with one, two, or three R²b groups;

wherein R²b at each occurrence is cyano, halogen, nitro, -R²b, -N(R²b)₂⁻, -O R³b, -S R³b, -C(O) R³b, -C(O)0, -R³b, -C(O)N(R³b)₂⁻, -S(0)N(R³b)₂⁻, -S(0)₂N(R³b)₂⁻, or -S(0)₂R³b, -OC(O) R³b, -OC(0)0, -R³b, -OC(O)N(R³b)₂⁻, -N(R-C)C(0) R³b, -N(R³b)C(0)0, -R³b, -N(R³b)C(0)N(R³b)₂⁻, or -N(R³b)C(0)N(R³b)₂⁻,

wherein at each occurrence R³b is independently hydrogen, Ci-C₄alkyl, or C₁-C₄ haloalkyl groups;
R³ is

(i) aryl, heteroaryl, or aryl(C₁-C₂)alkyl, wherein said aryl, heteroaryl, or aryl(QQC₂)alkyl is optionally be substituted with one, two, or three R³a groups, wherein R³a at each occurrence independently represents hydrogen, halogen, cyano, nitro,

5 Ci-C₄alkyl, C₁-C₄ haloalkyl, acyl, optionally substituted C₃-C₈cycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocycl, the group representing -R³b, -Ci-C₄alkyl-R³b, or -oc1-c₄ alkyl; wherein the substituted group on C₃-C₈cycloalkyl, aryl, heteroaryl or heterocycl are selected from hydrogen, nitro, cyano, halogen, acyl, Ci-C₄alkyl, aryl, or heteroaryl;

wherein, R³b at each occurrence is independently selected from cyano, nitro, -N(R³c)₂, -OR³c, -SR³c, -C(0)OR³c, -C(0)N(R³c)₂, -C(0)N(R³c)=N[(C,-C₃)alkyl]⁺, -S(0)N(R³c)₂, -S(0)₂N(R³c)₂, or -S(0)₂R³c-, (R³c)-N-S(0)₂R³c⁻, -S(0)₂N[R³c⁺]-N[(C,-C₃)alkyl]⁺, -OC(0)R³c⁻, -OC(0)OR³c⁻, -OC(0)N(R³c)₂⁻, -N(R³c)C(0)R³c⁻, -N(R³c)C(0)OR³c⁻, -N(R³c)C(0)N(R³c)₂⁻, or -N(R³c)=N[R³c⁺]N(R³c)₂⁻, wherein R³c at each occurrence independently selected from hydrogen, Ci-C₄alkyl, C₁-C₄ haloalkyl, cycloalkyl, heteroaryl, aryl heterocycl, -C(0)OR³d or -N(R³d)C(=NR³d)N(R³d)₂ groups, wherein R³d at each occurrence is independently selected from hydrogen, Ci-C₄alkyl, or C₁-C₄
cycloalkyl groups; or the groups selected from C₃-C₈alkyl, -Ci-C₄alkyl-N(R³d)₂⁻, -Ci-C₄alkyl-OR³d⁻, -Ci-C₄alkyl-SR³d⁻, C₃-C₈ cycloalkyl, or heterocycl groups, wherein the cycloalkyl, and heterocycl groups are each optionally substituted with 1 to 6 groups which are each independently selected from - R³e or -Cic-C₄alkyl-R³e⁻, wherein R³e at each occurrence is independently selected from cyano, nitro, -N(R³e)₂⁻, -OR³e⁻, -SR³e⁻, -C(0)R³e⁻, -C(0)OR³e⁻, -C(0)N(R³e)₂⁻, -C(0)N(R³e)-N[(C,-C₃)alkyl]⁺, -S(0)N(R³e)₂⁻, -S(0)₂N(R³e)₂⁻, -S(0)₂N[R³e⁺]-N[(C,-C₃)alkyl]⁺, -S(0)₂R³e⁻, -OC(0)R³e⁻, -OC(0)OR³e⁻, -OC(0)N(R³e)₂⁻, -N(R³e)C(0)R³e⁻, -N(R³e)C(0)OR³e⁻, -N(R³e)C(0)N(R³e)₂⁻, or -N(R³e)=N[R³e⁺]N(R³e)₂⁻, wherein R³e at each occurrence independently represent hydrogen, CrQalkyl, or CrQhaloalkyl
groups;

R⁴ is selected from hydrogen, nitro; cyano, halogen, acyl, Ci-C₄alkyl, Ci-C₄
cycloalkyl, aryl, or heteroaryl heterocycl, or -N(R⁴d)₂ groups; wherein R⁴d at each occurrence is independently selected from hydrogen, acyl, Ci-C₄alkyl or -
S(0)2R₃⁺; wherein R₃⁺ at each occurrence is selected from amino, acyl or C₁-C₄alkyl groups; R⁵ and R⁶ each independently represents hydrogen, C₁-C₄alkyl or alternatively, R⁵ and R⁶ together with carbon atom to which they are attached form a 3-7 membered ring, optionally comprising 1 or 2 hetroatom selected from O, N and S; R⁷ is independently absent or represents hydrogen, C₁-C₄alkyl or C₄₋₄ haloolkyl.

2. The compound as claimed in claim 1, wherein R¹ is selected from optionally substituted aryl group.

3. The compound as claimed in claim 2, wherein the substitution on the aryl group is selected from halogen or C₄₋₄ alkyl.

4. The compound as claimed in claim 1, wherein R² is selected from -Z-R₂⁻, wherein Z is -C(R⁴)₂⁻, wherein R⁴ at each occurrence independently represents hydrogen, C₁-C₄alkyl; and R²⁻ is aryl wherein said aryl is optionally substituted with one, two, or three R²⁻ groups independently selected from cyano, halogen or -O R²⁻b, wherein R²⁻b is independently selected from hydrogen or C₄₋₄ alkyl.

5. The compound as claimed in claim 1, wherein R³ is aryl, heteroaryl, or aryl(C₁-C₄)alkyl, wherein said aryl, heteroaryl, or aryl(C₁-C₄)alkyl is optionally substituted with one, two, or three R³⁻ groups, wherein R³⁻ at each occurrence independently represents hydrogen, halogen, cyano, nitro, C₁-C₄alkyl, C₁₋₄ haloalkyl, acyl, optionally substituted C₃₋₈ cycloalkyl, optionally substituted heteroaryl, optionally substituted heterocyclyl, the group representing -R³⁻, -C₁₋₄alkyl-R³⁻, or -OC₁₋₄ alky; wherein, R³⁻ at each occurrence is independently selected from cyano, nitro, -N(R³⁻)₂⁻, -OR³⁻, -SR⁻, -C(0)R³⁻, -C(0)N(R³⁻)₂⁻, -C(0)N[(C₁₋₄)alkyl]⁻, -S(0)N(R³⁻)₂⁻, S(0)₂N(R³⁻)₂⁻, or -S(0)₂R³⁻⁻, (R³⁻⁻)⁻S(0)₂⁻R³⁻⁻, -S(0)₂N(R³⁻)⁻N[(C₁₋₄)alkyl]⁺, -OC(0)R³⁻⁻, -OC(0)OR³⁻⁻, -OC(0)N(R³⁻)₂⁻, -N(R³⁻)C(0)⁻R³⁻⁻, -N(R³⁻)C(0)OR³⁻⁻, -N(R³⁻)C(0)N(R³⁻)₂⁻, or -N(R³⁻)C(=NR³⁻)N(R³⁻)₂⁻, wherein R³⁻ at each occurrence independently selected from hydrogen, C₁₋₄ alkyl, C₁₋₄ haloalkyl, cycloalkyl, heteroaryl, aryl heterocyclyl, -C(0)OR³⁻⁻ or -N(R³⁻)C(=NR³⁻⁻)N(R³⁻)₂⁻ groups, wherein R³⁻ at each occurrence is independently selected from hydrogen, C₁₋₄ alkyl, or C₁₋₄ haloalkyl groups.
6. The compound as claimed in claim 5, wherein the substituents on C₃-
C₆cycloalkyl, aryl, heteroaryl or heterocyclyl groups are selected from hydrogen, nitro, cyano, halogen, acyl, Ci-C₄alkyl, aryl, or heteroaryl.

7. The compound as claimed in claim 1, wherein R³ is selected from Ci-C₄alkyl, -Ci-
C₄alkyl-OR, wherein R³ at each occurrence is independently selected from hydrogen, d-Cialkyl, or C1-C4 haloalkyl groups.

8. The compounds of Formula I selected from
2-((5-(2-(3,4-dichlorophenyl)propan-2-yl)-l-(4-fluorophenyl)-lH-imidazol-2-
yl)thio)-N-(pyridin-4-ylmethyl)acetamide;
N-(2,4-dichlorophenyl)-2-((5-(2-(3,4-dichlorophenyl)propan-2-yl)-1-(4-fluorophenyl)-lH-imidazol-2-yl)thio)acetamide;
2-((5-(2-(3,4-dichlorophenyl)propan-2-yl)-1-(4-fluorophenyl)-lH-imidazol-2-yl)thio)-N-phenyl acetamide;
2-((5-(2,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-lH-imidazol-2-
yl)thio)-N-phenylacetamide;
N-(3-chloro-4-methylphenyl)-2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-lH-imidazol-2-yl)thio)acetamide;
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-lH-imidazol-2-
yl)thio)-N-(4-fluorophenyl)acetamide;
N-(1H-benzo[d]imidazol-2-yl)-2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-lH-imidazol-2-yl)thio)acetamide;
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-lH-imidazol-2-
yl)thio)-1-(4-methylpiperazine-1-yl)ethanone;
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-
yl)thio)-1-(4-(4-fluorophenyl)piperazine-1-yl)ethanone;
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-
yl)thio)-N-(4-(2-methyl-1H-imidazol-1-yl)phenyl)acetamide;
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-
yl)thio)-1-(3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)ethanone;
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-
yl)thio)-1-(3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)ethanone;
N-(1H-benzo[d]imidazol-2-yl)-2-((5-(2-(4-chloro-3-methoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)acetamide;

2-((5-(2-(4-chloro-3-methoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-1-(3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-alpyrazin-7(8H)-yl)ethanone;

2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-2-methyl-N-(4-(2-methyl-1H-imidazol-1-yl)phenyl)propanamide;

1-(5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-N-(4-(2-methyl-1H-imidazol-1-yl)phenyl)cyclobutanecarboxamide;

2-((5-(2-(3-cyano-4-fluorophenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-2-methyl-N-(4-(2-methyl-1H-imidazol-1-yl)phenyl)propanamide;

2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-N-(1H-indazol-5-yl)acetamide;

(S)-methyl 5-amino-2-(5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)acetamido)-5-oxopentanoate;

2-((1-(4-fluorophenyl)-5-(2-(3-methoxyphenyl)propan-2-yl)-1H-imidazol-2-yl)thio)-N-(4-(2-methyl-1H-imidazol-1-yl)phenyl)acetamide;

(S)-methyl 2-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)acetamido)-4-methylpentanoate;

(S)-methyl 2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)acetamido)-3-phenylpropanoate;

2-((5-(2-(4,5-dimethoxy-2-nitrophenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-N-(4-(2-methyl-1H-imidazol-1-yl)phenyl)acetamide;

2-((5-(2-(4,5-dimethoxy-2-(methylsulfonamido)phenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-N-(4-(2-methyl-1H-imidazol-1-yl)phenyl)acetamide;

(S)-dimethyl 2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)acetamido)pentanedioate;

(S)-dimethyl 2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)acetamido)succinate;

2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-4-methyl-1H-imidazol-2-yl)thio)-N-(4-(2-methyl-1H-imidazol-1-yl)phenyl)acetamide;
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-4-methyl-1H-imidazol-2-yl)thio) - N-isopropylacetamide;  
N-(3,4-dimethoxyphenyl)-2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)acetamidoacetamide;  
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-N-isopentylacetamide;  
N-(cyclohexylmethyl)-2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)acetamide;  
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-N-(pyridine-3-ylmethyl)acetamide;  
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-1-morpholinoethanone;  
N-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl) thiophene-3-carboxamide;  
N-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl)-4-fluorobenzamide;  
N-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl)-IH-benzo[d]imidazole-5-carboxamide;  
N-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl)-2-(2,4,5-trifluorophenyl)acetamide;  
N-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl)-IH-indazole-5-carboxamide;  
N-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl)-6-methylnicotinamide;  
N-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl)-4-(IH-imidazol-1-yl)benzamide;  
2-((2-(IH-imidazol-1-yl)ethyl)thio)-5-(2-(3,4-dichlorophenyl)propan-2-yl)-1-(4-fluorophenyl)-IH-imidazole;  
1-(2-(5-(2-(3,4-dichlorophenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)ethyl piperidine;  
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-yl)thio)-N-(pyridine-3-ylmethyl)ethanamine;
N-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-y1)thio) ethyl)aniline;
5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-2-((2-(2-methyl-1H-imidazol-1-y1)ethyl)thio)-1H-imidazole;
1-(2-((5-2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-y1)thio)ethyl)-4-methylpiperazine;
1-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-y1)thio)ethyl)-1H-indole;
1-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-y1)thio)ethyl)-1H-benzo[d]imidazole;
2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-y1)thio)-1-(4-(2-methoxyacetyl) piperazin-1-y1) ethanone;
4-(1-(2-((5-(2-(3,4-dimethoxyphenyl)propan-2-yl)-1-(4-fluorophenyl)-1H-imidazol-2-y1)thio)ethyl)-1H-imidazol-4-y1)phenol.

9. The compounds of formula (I) or their pharmaceutical compositions for the treatment of diabetes and associated disorders.
10. Use of the compounds of formula (I) or their pharmaceutical compositions for the treatment of diabetes or its associated disorders.
11. A method of treating disorders caused by metabolic disorder comprising administering to a patient in need thereof an effective amount of a compound of formula (I) according to any of the preceding claims or its pharmaceutical composition according to any of the preceding claims.
12. A pharmaceutical composition comprising a therapeutically effective amount of formula (I) or salt thereof along with one or more additional therapeutically active compounds for the treatment of metabolic disorders.
13. The pharmaceutical composition as claimed in Claim 12, wherein one or more additional therapeutically active compounds for the treatment of metabolic disorders are selected from insulin, insulin derivatives or mimetics, insulin secretagogues, insulin sensitizers, biguanide agents, alpha-glucosidase inhibitors, insulinotropic sulfonylurea receptor ligands, meglitinides, GLP-1 (glucagon like peptide-1), GLP-1 analogs, DPPIV (dipeptidyl peptidase IV) inhibitors, GPR-119 inhibitors, sodium-dependent glucose co-transporter (SGLT2) inhibitors, PPAR modulators, non-glitazone type PPAR delta agonist, HMG-CoA reductase
inhibitors, cholesterol-lowering drugs, rennin inhibitors, anti-thrombotic and anti-platelet agents or anti-obesity agents.

14. The pharmaceutical composition as claimed in claim 12, wherein therapeutically effective amount of formula (I) is combine with agents selected from insulin, metformin, Glipizide, glyburide, amaryl, gliclazide, meglitinides, nateglinide, repaglinide, amylin mimetics wherein amylin mimetics is selected from pramlintide; acarbose, miglitol, voglibose, Exendin-4; vildagliptin, Liraglutide, naliglutide, saxagliptin, pioglitazone, rosiglitazone, HMG-CoA reductase inhibitors, wherein HMG-CoA reductase inhibitors are selected from rosvastatin, atrovastatin, simvastatin, lovastatin, pravastatin, fluvastatin, cerivastatin, rosuvastatin, pitavastatin; cholesterol-lowering drugs wherein cholesterol-lowering drugs are selected from fenofibrate, benzaflibrate, clofibrate, gemfibrozil; cholesterol absorption inhibitors wherein cholesterol absorption inhibitors are selected from ezetimibe, efucimibe or suitable mixture thereof.

15. Use of the compounds of formula (I) or their pharmaceutical compositions along with additional therapeutically active compounds as claimed in claim 12, 13 and 14 for the treatment of metabolic disorders.
## INTERNATIONAL SEARCH REPORT

**International application No**
PCT/IN2012/000821

### A. CLASSIFICATION OF SUBJECT MATTER

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According to International Patent Classification (IPC) or to both national classification and IPC

### B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

- C07D  A61K  A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

- Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
  - EPO-Internal, CHEM ABS Data, WPI Data

### C. DOCUMENTS CONSIDERED TO BE RELEVANT

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Further documents are listed in the continuation of Box C. See patent family annex.

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### Date of the actual completion of the international search

**23 April 2013**

### Date of mailing of the international search report

**03/05/2013**

### Name and mailing address of the ISA/

**Authorized officer**

- Weisbrod, Thomas

**European Patent Office, P.B. 5818 Patentlaan 2**

- NL - 2280 HV Rijswijk
- Tel. (+31-70) 340-2040
- Fax: (+31-70) 340-3016

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