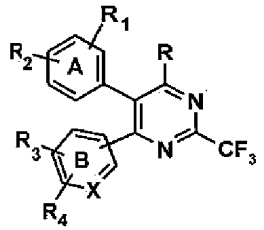
aryloxy and heterocyclyl groups such as morpholine, piperazine, piperidine, pyrrolidine, thiazolidine and the like; Rl, R2, R3 and R4 represents hydrogen, hydroxy, nitro, azido, halogens, substituted or unsubstituted groups selected from alkyl, haloalkyl, alkoxy, aryl, aryloxy, acyloxy, amino, hydrazine, alkylthio, alkoxycarbonyl, alkoxyalkyl, sulfamoyl, -SO2NHNH2, -SO2Cl, carboxylic acid and its derivatives.

Objectives

We have focused our research to identify cytokine inhibitors predominantly acting through the inhibition of the TNF-α, which are devoid of any side effects normally associated with TNF-α inhibitors and to identify novel small molecule anticancer agents. Our sustained efforts have resulted in novel heterocyclic compounds of the formula (I). The derivatives may be useful in the treatment of inflammation, cancer and immunological diseases. Particularly the compounds of the present invention are useful for the treatment of immunological diseases those mediated by cytokines such as TNF-α, IL-1, IL-6, IL-lβ, IL-8, IL-12 and inflammation. More particularly, the compounds of the present invention are useful as PDE4 inhibitors, and are useful for treating PDE4 mediated diseases. The compounds of the present invention are also useful in the treatment of rheumatoid arthritis; osteoporosis; multiple myeloma; uveititis; acute and chronic myelogenous leukemia; ischemic heart disease; atherosclerosis; ischemic-induced cell damage; pancreatic β-cell destruction; osteoarthritis; rheumatoid spondylitis; gouty arthritis; inflammatory bowel disease; adult respiratory distress syndrome (ARDS); asthma, chronic obstructive pulmonary disorder (COPD), psoriasis; Crohn's disease; allergic rhinitis; ulcerative colitis; anaphylaxis; contact dermatitis; asthma; muscle degeneration; cachexia; bone resorption diseases; ischemia reperfusion injury; brain trauma; multiple sclerosis; sepsis; septic shock; toxic shock syndrome; fever and myalgias due to infection.

Summary

In one example, there is disclosed the use of a compound of formula (I),



(I)

their tautomeric forms, stereoisomers, polymorphs, solvates, pharmaceutically acceptable salts and compositions thereof in the manufacture of a medicament for treating COPD;

wherein: A represents substituted or unsubstituted aryl group;

B represents substituted or unsubstituted groups selected from aryl or pyridyl;

X represents carbon or nitrogen atom;

R represents substituted or unsubstituted groups selected from azido; halogens; linear or branched alkyl groups comprising methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, *t*-butyl, n-pentyl, isopentyl and hexyl; alkoxy groups comprising methoxy, ethoxy,

hydrazine; monoalkylamino; dialkylamino; acylamino; alkylsulfonyl; alkylsulfinyl; alkylthio; alkoxycarbonyl; alkoxyalkyl; sulfamoyl; $-SO_2NHNH_2$; $-SO_2Cl$; carboxylic acid and its derivatives; R, R_1, R_2, R_3, R_4 and R' groups are optionally substituted by one or more substituents selected from halogens; hydroxy; nitro; cyano; ureas; azido; amino; imino-1-phenyl butanone; amide groups comprising acetamide and benzamide; thioamide; hydrazine; linear or branched alkyl groups comprising methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, *t*-butyl, n-pentyl, isopentyl and hexyl; alkoxy groups comprising methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy and *t*-butoxy; haloalkyl groups comprising dichloromethyl, difluoromethyl, trifluoromethyl and trichloromethyl; acyl groups comprising acetyl, propanoyl and benzoyl; haloalkoxy groups comprising trifluoromethoxy, trifluoroethoxy, trichloromethoxy; cycloalkyl groups comprising cyclopropyl and cyclobutyl; haloacyl groups comprising trifluoroacetyl and trichloroacetyl; acyloxyacyl; heterocyclyl; aryl; heteroaryl; monoalkylamino; dialkylamino; acylamino; aryloxy groups comprising phenoxy and naphthoxy; alkoxycarbonyl groups comprising methoxycarbonyl and ethoxycarbony; aryloxycarbonyl; alkylsulfonyl; haloalkylsulfonyl; $-SO_2Cl$; arylsulfonyl; alkylsulfinyl; arylsulfinyl; thioalkyl; thioaryl; sulfamoyl; alkoxyalkyl groups; carboxylic acids and its derivatives comprising hydroxamic acids; hydroxamates; esters; amides and acid halides; these substituents are further optionally substituted with substituents selected from hydroxy; alkoxy; halogens; alkylsulfonyl; haloalkyl; alkyl and aryl group which in turn is optionally further substituted by halogens and alkyl.

In one aspect, the present invention refers to use of a compound in the manufacture of a medicament for treating chronic obstructive pulmonary disorder (COPD), wherein the compound is selected from the group consisting of Ethyl-1-[5-(3-aminosulfonylphenyl)-6-(4-fluorophenyl)-2-(trifluoromethyl)pyrimidin-4-yl]piperidine-4-carboxylate; 5-(3-Aminosulfonylphenyl)-4-(4-fluorophenyl)-2-(trifluoromethyl)-6-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}pyrimidine; 3-[4-(4-Fluorophenyl)-6-(1,3-thiazolidin-3-yl)-2-(trifluoromethyl)pyrimidin-5-yl]benzenesulfonamide; 3-[4-Morpholin-4-yl-2-(trifluoromethyl)-6-phenyl-pyrimidin-5-yl] benzenesulfonamide; 3-{4-[4-(2-Cyanoethyl)piperazin-1-yl]- 6-(4-fluorophenyl)-2-(trifluoromethyl) pyrimidin-5-yl}benzenesulfonamide; and 3-{6-(4-Fluorophenyl)-4-[4-(trifluoroacetyl)piperazin-1-yl]-2-(trifluoromethyl) pyrimidin-5-yl}benzenesulfonamide. In another aspect, the present invention refers to a compound, 3-[4-morpholin-4-yl-2-(trifluoromethyl)-6-phenyl-pyrimidin-5-yl]benzenesulfonamide and its pharmaceutically acceptable salts. In yet another aspect, the present invention refers to use of the compound as disclosed herein the manufacture of a medicament for the treatment of a pain disorder, inflammation and immunological diseases selected from rheumatoid arthritis, uveitis, osteoporosis, osteoarthritis, rheumatoid spondylitis, gouty arthritis, inflammatory bowel disease, adult respiratory distress syndrome (ARDS), psoriasis, Crohn's disease, allergic rhinitis, ulcerative colitis, contact dermatitis, asthma, chronic obstructive pulmonary disorder (COPD), multiple myeloma, multiple sclerosis, sepsis and septic shock. In a further aspect, the present invention refers to use of

the compound as disclosed herein in the manufacture of a medicament for the treatment of rheumatoid arthritis; osteoporosis; multiple myeloma; uveitis; acute and chronic myelogenous leukemia; ischemic heart disease; atherosclerosis; cancer; ischemic-induced cell damage; pancreatic beta cell destruction; osteoarthritis; rheumatoid spondylitis; gouty arthritis; inflammatory bowel disease; ARDS; psoriasis; Crohn's disease; allergic rhinitis; ulcerative colitis; anaphylaxis; contact dermatitis; muscle degeneration; cachexia; asthma; chronic obstructive pulmonary disorder (COPD); bone resorption diseases; ischemia reperfusion injury; brain trauma; multiple sclerosis; sepsis; septic shock; toxic shock syndrome; fever and myalgias due to infection in a mammal. Also described are novel heterocyclic compounds of the formula (I),

We Claim:

1. Use of a compound in the manufacture of a medicament for treating chronic obstructive pulmonary disorder (COPD), wherein the compound is selected from the group consisting of:
Ethyl-1-[5-(3-aminosulfonylphenyl)-6-(4-fluorophenyl)-2-(trifluoromethyl) pyrimidin-4-yl]piperidine-4-carboxylate;
5-(3-Aminosulfonylphenyl)-4-(4-fluorophenyl)-2-(trifluoromethyl)-6-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}pyrimidine;
3-[4-(4-Fluorophenyl)-6-(1,3-thiazolidin-3-yl)-2-(trifluoromethyl) pyrimidin-5-yl]benzenesulfonamide;
3-[4-Morpholin-4-yl-2-(trifluoromethyl)-6-phenyl-pyrimidin-5-yl] benzenesulfonamide;
3-{4-[4-(2-Cyanoethyl)piperazin-1-yl]- 6-(4-fluorophenyl)-2-(trifluoromethyl) pyrimidin-5-yl}benzenesulfonamide; and
3-{6-(4-Fluorophenyl)-4-[4-(trifluoroacetyl)piperazin-1-yl]-2-(trifluoromethyl) pyrimidin-5-yl}benzenesulfonamide.

2. A compound, 3-[4-morpholin-4-yl-2-(trifluoromethyl)-6-phenyl-pyrimidin-5-yl]benzenesulfonamide and its pharmaceutically acceptable salts.

3. Use of the compound as claimed in claim 2 in the manufacture of a medicament for the treatment of a pain disorder, inflammation and immunological diseases selected from rheumatoid arthritis, uveitis, osteoporosis, osteoarthritis, rheumatoid spondylitis, gouty arthritis, inflammatory bowel disease, adult respiratory distress syndrome (ARDS), psoriasis, Crohn's disease, allergic rhinitis, ulcerative colitis, contact dermatitis, asthma, chronic obstructive pulmonary disorder (COPD), multiple myeloma, multiple sclerosis, sepsis and septic shock.

4. Use of the compound as claimed in claim 2 in the manufacture of a medicament for the treatment of rheumatoid arthritis; osteoporosis; multiple myeloma; uveitis; acute and chronic myelogenous leukemia; ischemic heart disease; atherosclerosis; cancer; ischemic-induced cell damage; pancreatic beta cell destruction; osteoarthritis;

rheumatoid spondylitis; gouty arthritis; inflammatory bowel disease; ARDS; psoriasis; Crohn's disease; allergic rhinitis; ulcerative colitis; anaphylaxis; contact dermatitis; muscle degeneration; cachexia; asthma; chronic obstructive pulmonary disorder (COPD); bone resorption diseases; ischemia reperfusion injury; brain trauma; multiple sclerosis; sepsis; septic shock; toxic shock syndrome; fever and myalgias due to infection in a mammal.

5. Use of the compound, as claimed in claim 2 in the manufacture of a medicament for treating chronic obstructive pulmonary disorder (COPD).

6. Use of a compound, as claimed in claim 2 in the manufacture of a medicament for treating asthma.

7. Use of the compound, 3-[4-morpholin-4-yl-2-(trifluoromethyl)-6-phenyl-pyrimidin-5-yl]benzenesulfonamide or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating chronic obstructive pulmonary disorder (COPD).

8. Use of the compound, 3-[4-morpholin-4-yl-2-(trifluoromethyl)-6-phenyl-pyrimidin-5-yl]benzenesulfonamide or its pharmaceutically acceptable salts thereof in the manufacture of a medicament for the treatment of asthma.

9. A pharmaceutical composition comprising a compound as claimed in claim 2, as an active ingredient, along with a pharmaceutically acceptable carrier, diluent, excipient or solvate.

10. A pharmaceutical composition according to claim 9, wherein the composition is in the form of a tablet, capsule, powder, syrup, solution, aerosol or suspension.