been described (a) James et al., ACS Chem. Biol. 2016, 11, 3179; b) Waszkowycz et al., J. Med. Chem. 2018, 61, 10767).

Certain compounds that are useful as PARG inhibitors are further disclosed in documents WO 2016/092326, WO 2016/097749 and WO 2021/055744.

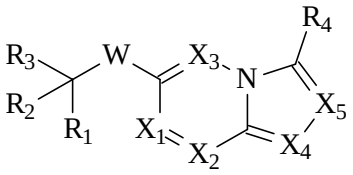
Document US 2019/233411 discloses certain Gcn2 inhibitors and uses thereof.

Document WO 2009/050183 discloses certain imidazo[1,2-a]pyridine derivatives which are useful for treating diseases mediated by the ALK-5 and/or ALK-4 receptor.

Summary of the invention

It was an objective technical problem of the present invention to provide compounds that are cell-permeable inhibitors of PARG. The technical problem of the present invention is solved by the embodiments described herein and as characterized by the claims.

Accordingly, in a first embodiment, the present invention provides a compound of formula (I):



(I)

or an enantiomer, diastereoisomer, tautomer, pharmaceutically acceptable solvate, pharmaceutically acceptable crystal form, pharmaceutically acceptable salt or a prodrug thereof. It is understood that thought the present description the term “a compound of formula (I)” preferably encompasses also a compound of formula (Ia) to (Ibo), unless indicated to the contrary.

A further embodiment of the present invention relates to a pharmaceutical composition comprising the compound of formula (I) or a pharmaceutically acceptable salt, hydrate or solvate thereof, and a pharmaceutically acceptable carrier.

In a further embodiment, the present invention relates to the compound of formula (I) of the present invention or a pharmaceutically acceptable salt, hydrate or solvate thereof, or a pharmaceutical composition of the present invention, for use in therapy.

The compounds of formula (I) are useful for treating a disease or disorder in which PARG activity is implicated.

In one aspect, there is provided a use of the compound as described herein or the pharmaceutical described herein, in the manufacture of a medicament for treatment of a disease or disorder in which PARG activity is implicated.

The compounds of formula (I) are useful for a method of treating a proliferative disorder. In a preferred embodiment of the present invention, the proliferative disorder is cancer, preferably a human cancer.

In another aspect, there is provided a use of the compound as described herein or the pharmaceutical composition described herein, in the manufacture of a medicament for treatment of a proliferative disorder, preferably wherein the proliferative disorder is cancer, preferably a human cancer.

Definitions

The following definitions apply throughout the present specification and the claims, unless specifically indicated otherwise.

The term “hydrogen” is herein used to refer to protium, deuterium and/or tritium, preferably to protium. Accordingly, the term “non-hydrogen atom” refers to any atoms that is not hydrogen, i.e. that is not protium, deuterium or tritium.

The term “hydrocarbon group” refers to a group consisting of carbon atoms and hydrogen atoms.

The term “alicyclic” is used in connection with cyclic groups and denotes that the corresponding cyclic group is non-aromatic.

As used herein, the term “alkyl” refers to a monovalent saturated acyclic (i.e., non-cyclic) hydrocarbon group which may be linear or branched. Accordingly, an “alkyl” group does not comprise any carbon-to-carbon double bond or any carbon-to-carbon triple bond. A “C_{1-5} alkyl” denotes an alkyl group having 1 to 5 carbon atoms. Preferred exemplary alkyl groups are methyl, ethyl, propyl (e.g., n-propyl or isopropyl), or butyl (e.g., n-butyl, isobutyl, sec-butyl, or tert-butyl). Unless defined otherwise, the term “alkyl” preferably refers to C_{1-4} alkyl, more preferably to methyl or ethyl, and even more preferably to methyl.

As used herein, the term “alkenyl” refers to a monovalent unsaturated acyclic hydrocarbon group which may be linear or branched and comprises one or more (e.g., one or two) carbon-to-carbon double bonds while it does not comprise any carbon-to-carbon triple bond. The term “C_{2-5} alkenyl” denotes an alkenyl group having 2 to 5 carbon atoms. Preferred exemplary alkenyl groups are ethenyl, propenyl (e.g., prop-1-en-1-yl, prop-1-en-2-yl, or prop-2-en-1-yl), butenyl, butadienyl (e.g., buta-1,3-dien-1-yl or buta-1,3-dien-2-yl), pentenyl, or pentadienyl (e.g., isoprenyl). Unless defined otherwise, the term “alkenyl” preferably refers to C_{2-4} alkenyl.

As used herein, the term “alkynyl” refers to a monovalent unsaturated acyclic hydrocarbon group which may be linear or branched and comprises one or more (e.g., one or two) carbon-to-carbon triple bonds and optionally one or more (e.g., one or two) carbon-to-carbon double bonds. The term “C_{2-5} alkynyl” denotes an alkynyl group having 2 to 5 carbon atoms. Preferred exemplary alkynyl groups are ethynyl, propynyl (e.g., propargyl), or butynyl. Unless defined otherwise, the term “alkynyl” preferably refers to C_{2-4} alkynyl.

As used herein, the term “alkylene” refers to an alkanediyl group, i.e. a divalent saturated acyclic hydrocarbon group which may be linear or branched. A “C_{1-5} alkylene” denotes an alkylene group having 1 to 5 carbon atoms, and the term “C_{0-3} alkylene” indicates that a covalent bond (corresponding to the option “C_0 alkylene”) or a C_{1-3} alkylene is present. Preferred exemplary alkylene groups are methylene (-CH_2-), ethylene (e.g., -CH_2-CH_2- or -CH(-CH_3)-), propylene (e.g., -CH_2-CH_2-CH_2-, -CH(-CH_2-CH_3)-, -CH_2-