pyrrolobenzodiazepines (PhD Thesis; University of Antwerp, Belgium; Faculty of Pharmaceutical, Biomedical and Veterinary Sciences; Department of Biomedical Sciences; 2011; 220 p.).

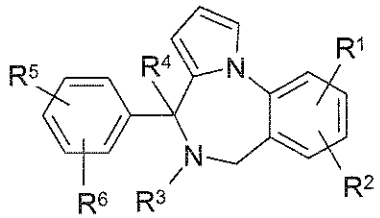
The antifungal compounds of the present invention or part of the compounds of the present invention are structurally different and may have improved metabolic stability properties, improved PK (pharmacokinetic) properties, improved plasma binding, reduced hERG channel inhibition, reduced cytochrome P450 liabilities, or improved bioavailability compared with compounds disclosed in the prior art. Preferably said compounds have a broad antifungal spectrum, and maintain adequately hight thereapeutic efficacy and adequately low toxicity or other side effects.

It is accordingly an object of the present invention to provide novel compounds with antifungal activity to overcome or ameliorate at least one of the disadvantages of the prior art, or to provide useful alternative compounds.

Summary ~~of the invention~~

It has been found that the compounds of the present disclosure~~invention~~ are useful as antifungal compounds.

The present disclosure, in a first aspect,~~invention~~ concerns novel compounds of Formula (*I*):



(I)

and stereoisomeric forms thereof, wherein

R^1 is hydrogen, halo, C_{1-4}alkyl or C_{1-4}alkyloxy;

R^2 is hydrogen or halo;

R^3 and R^4 are hydrogen;

or R^3 and R^4 taken together form a bond;

R^5 is C_{1-4}alkylcarbonyl, C_{1-4}alkylsulphonyl, C_{1-4}alkylsulphinyl, or C_{1-4}alkyl substituted with one hydroxyl moiety;

R^6 is hydrogen or halo;

and the pharmaceutically acceptable addition salts, and the solvates thereof.

The present disclosure~~invention~~ also concerns methods for the preparation of compounds of Formula (I) and pharmaceutical compositions comprising them.

The present compounds are useful agents for combating fungi *in vivo*.

In a second aspect, there is provided a pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as active ingredient, a therapeutically effective amount of a compound as defined above.

The novel compounds described in the present disclosure~~invention~~ may be useful in the treatment or prevention of infections caused by dermatophytes, systemic fungal infections and onychomycosis.

The novel compounds described in the present disclosure~~invention~~ may be active against a wide variety of fungi, such as *Candida* spp., e.g. *Candida albicans, Candida glabrata, Candida kruceï, Candida parapsilosis, Candida kefyr, Candida tropicalis; Aspergillus* spp., e.g. *Aspergillus fumigatus, Aspergillus niger, Aspergillus flavus; Cryptococcus neoformans; Sporothrix schenckii; Epidermophyton floccosum; Microsporum* spp., e.g. *Microsporum canis, Microsporum gypseum; Trichophyton* spp., e.g. *Trichophyton mentagrophytes, Trichophyton rubrum, Trichophyton quinckeanum, Trichophyton tonsurans, Trichophyton verrucosum, Trichophyton violaceum, Trichophyton interdigitale, Trichophyton soudanense*; *Fusarium* spp., e.g. *Fusarium solani, Fusarium oxysporum, Fusarium proliferatum, Fusarium verticillioides*; *Rhizomucor* spp., e.g. *Rhizomucor miehei, Rhizomucor pusillus*; *Mucor circinelloides; Rhizopus* spp., e.g. *Rhizopus oryzae, Rhizopus microspores; Malassezia furfur; Acremonium* spp.; *Paecilomyces; Scopulariopsis; Arthrographis* spp.; *Scytalidium; Scedosporium* spp., e.g. *Scedosporium apiospermum, Scedosporium prolificans*; *Trichoderma* spp.; *Penicillium spp.*; *Penicillium marneffei; Blastoschizomyces.*

In view of the aforementioned pharmacology of the present compounds, it follows that they are suitable for use as a medicament as defined in a third aspect.

The disclosure, in a fourth aspect,~~invention~~ also relates to a compound according to the general Formula (I), the stereoisomeric forms thereof and the pharmaceutically acceptable addition salts and the solvates thereof, for use in the treatment or prevention of fungal infections.

One advantage of the compounds or a part of the compounds of the present disclosure~~invention~~ may lie in their enhanced bioavailability, improved metabolic stability properties, improved PK properties, reduced hERG channel inhibition, or reduced cytochrome P450 liabilities compared with the compounds disclosed in the prior art.

The present invention will now be further described. In the following passages, different aspects of the invention are defined in more detail. Each aspect so defined may be combined with any other aspect or aspects unless clearly indicated to the contrary. In particular, any feature indicated as being preferred or advantageous may be combined with any other feature or features indicated as being preferred or advantageous.