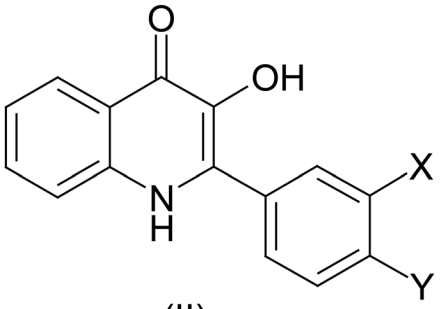
Derivatives of 2-phenyl-3-hydroxyquinoline-4(1H)-one and methods of their preparation and utilization

Introduction:
2-Phenyl-3-hydroxy-4(1H)-quinolinones can be considered as aza-analogues of flavones, compounds which are known for the wide-range of their biological activities. These quinolinones were studied as inhibitors of topoisomerase, gyrase and IMPDH. They were tested for anticancer activity invitro and were also shown to possess immunosuppressive properties.

Technology description:
Derivatives of 2-phenyl-3-hydroxyquinoline-4(1H)-one of the general formula (II) where X represents a nitro group, amino group, and Y represents an atom of halogen, oxygen or sulphur substituted by C1 to C6 alkyl or phenyl group, whereby both the alkyl and phenyl group may be further substituted and the substituents may be identical or different, or by nitrogen substituted independently by hydrogen, C1 to C6 alkyl, C1 to C6 alkyl, which may be substituted among others by halogen, hydroxy, C1 to C4 alkoxy or C1 to C4 alkylamino group, or may form a saturated or unsaturated heterocyclic ring with 5 to 7 atoms, where the individual ring atoms comprise atoms of carbon, and any of the carbon atoms may be substituted by an atom of nitrogen, sulphur or oxygen, X and Y together form an imidazo group, or imidazo group substituted by C1 to C6 alkyl, which may be substituted among others by halogen, hydroxy, C1 to C4 alkoxy or C1 to C4 alkylamino group, CHO or acetylgroup, or a heterocyclic ring with 5 to 6 atoms, where the ring atoms may be further substituted. Methods of preparation of these compounds are described. In addition, their cytostatic, cytotoxic, antiproliferation and immunosuppressive activity is described including examples of their potential pharmacological and pharmaceutical utilization.



(II)

Advantages:
The invention provides a novel class of compounds possessing a cytotoxic activity to a wide range of tumor cell lines. Our recent data demonstrate that selected compounds covered by these patents modulate protein-protein interactions of EF1A1. These compounds will be useful as medicaments for the treatment of cancer and other diseases connected with abnormal proliferation of cells/tissues.

Development status:
Laboratory scale, data on cell lines, limited ADME/Tox data, *in vivo* pharmacology and pharmacodynamics.

Publications:
Kadric, J., K. Motyka, P. Dzubak, M. Hajduch, M. Soural. Synthesis, cytotoxic activity, and fluorescence properties of a set of novel 3-hydroxyquinolin-4(1H)-ones. Tetrahedron Letters. 2014, 55(26), 3592-3595. ISSN 0040-4039. IF: 2.379.
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Hradil, P., J. Hlavac, M. Soural, M. Hajduch, M. Kolar, R. Vecerova. 3-Hydroxy-2-phenyl-4(1H)-quinolinones as Promising Biologically Active Compounds. Mini-reviews in Medicinal Chemistry. 2009, 9(6), 696-702. ISSN 1389-5575. IF: 3.132. PMID: 19519495
Soural, M., J. Hlavac, P. Hradil, I. Frysova, M. Hajduch, V. Bertolasi, M. Malon. Synthesis and Cytotoxic Activity of Substituted 2-Phenyl-3-Hydroxy-4(1H)-Quinolinones-7- Carboxylic Acids and their Phenacyl Esters. European Journal of Medicinal Chemistry. 2006, 41(4), 467-474. ISSN 0223-5234. IF: 2.022. PMID: 16540209

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