



Novel PPAR α antagonists bearing Stilbene or Bioisosteres endowed with antiproliferative effects in cancer cell lines

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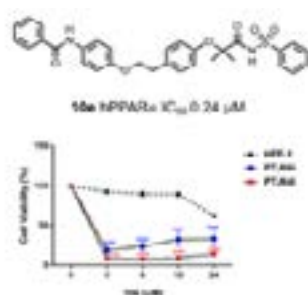
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Abstract

Peroxisome Proliferator-Activated Receptors (PPARs) have been widely studied in the last decades, and they attracted the attention of scientists as promising therapeutic targets. Intensive efforts by researchers produced a wide panel of drugs targeting the three PPAR subtypes (PPAR α PPAR γ PPAR δ) able to modulate important metabolic functions. PPAR activation is involved in several physiologic pathways, as lipid and glucose metabolism, insulin sensitivity, energy homeostasis, and cell differentiation. Fibrates and thiazolidinediones, respectively synthetic PPAR α and PPAR γ agonists, are currently used for the treatment of hyperlipidemia and hyperglycemia, in patients affected by type 2 diabetes and metabolic syndrome.

In recent years, an increased expression of PPAR α has been found in different tumors: it is well known that cancer cells present altered metabolic pathways, switching from the glycolysis to fatty acid oxidation metabolism. In this scenario, PPAR α antagonists emerged as novel potential drugs in tumors overexpressing PPAR α by interfering with cellular survival and metastasis formation.[2] In vitro anticancer effects were found for PPAR α antagonists in chronic lymphocytic leukemia [3], renal cancer, colorectal and pancreatic cancer [4], paraganglioma [5].

In this study we report on the synthesis of novel PPAR α antagonists bearing stilbene or its bioisosteres, starting from the structure of a dual PPAR α / γ agonist, previously synthesized in our laboratory. We explored the cytotoxicity of the novel compounds in different cancer cell lines (colorectal, pancreatic, renal, paraganglioma) expressing PPAR α .



Biography

Alessandra Ammazalorso obtained her PhD in Pharmaceutical Sciences from the University of Chieti, Italy, in 2001. Since 2004 she has been an Assistant Professor of Medicinal Chemistry at the University of Chieti, Department of Pharmacy. Her research interests include the design and synthesis of small-molecule drugs, mainly compounds targeting Peroxisome Proliferator-Activated Receptors, aromatase and nitric oxide synthase.

Publications

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