The influence of R substituents in triphenylphosphinegold(I) carbonimidothioates, Ph 3PAu[SC(OR) = NPh] (R = Me, Et and iPr), upon in vitro cytotoxicity against the HT-29 colon cancer cell line and upon apoptotic pathways

ABSTRACT

The Ph3PAu[SC(OR) = NPh], R = Me (1), Et (2) and iPr (3), compounds are significantly cytotoxic to the HT-29 cancer cell line with1 being the most active. Based on human apoptosis PCR-array analysis, caspase activities, DNA fragmentation, cell apoptotic assays, intracellular reactive oxygen species (ROS) measurements and human topoisomerase I inhibition, induction of apoptosis is demonstrated and both the extrinsic and intrinsic pathways of apoptosis have been shown to occur. Compound1 activates the p73 gene, whereas each of2 and3 activates the p53 gene. An additional apoptotic mechanism is exhibited by2, that is, via the JNK/MAP pathway.

Keyword: Phosphinegold(I) compounds; Carbonimidothioate; Thiolate; Apoptosis; Cancer; Cell cycle