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Biological potential of new molecular hybrids of thiohydantoin and zingerone derivatives

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Molecular hybridization is one of the most valuable structure modification tools currently used in drug construction. The concept of hybridization is usually achieved via chemical connection of two or more biologically active pharmacophoric moieties to form a new molecular hybrid with potentially higher activity and efficacy compared to the parent moieties. In general, a symmetrical hybrid connects two identical fragments and is expected to produce more potent and/or selective pharmacological effects compared to single molecules, whereas the nonsymmetrical hybrid drug is perceived to show both pharmacological activities resulting from the individual pharmacophores (dual action) with additional synergic effect. Zingerone is a natural compound present in significant amounth in ginger. Both natural and synthetic zingerone derivatives exhibit different biological and pharmacological activities such as anti-inflammatory, antimicrobial, anti-cancer, and hepatoprotective. On the other hand, many synthesized thiohydantoin derivatives exhibit a wide range of biological and pharmacological potentials, such as antimicrobial, anti-convulsive, anti-proliferative, anti-metastatic, anti-diabetic, and anti-HIV. In this study, a short series of new zingerone-thiohydantoin molecular hybrids were synthesized from *O*-alkyl zingerone derivatives for evaluation of their potential biological activity. Obtained new potentially bioactive compounds were tested for their antimicrobial and *in vitro* anticancer activities. These compounds showed low to moderate antimicrobial activity. The difference in the cytotoxic activity of the hybrid compounds depends on the nature of the *O*-alkyl substituent of the benzene ring. Among the tested compounds, zingerone-thiohydantoin hybrid with an *O*-buthyl substituent exerted the significant cytotoxic activity on colon HCT-116 cancer cells without toxicity on healthy MRC-5 cells.

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