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SG 10 - Hypericin under ultrasound exposure is able to provoke a significant anticancer effect on an in vitro three-dimensional colon cancer model

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Abstract

One of the main advantages of using ultrasound (US) in combination with a chemical agent (sonosensitizer) is the ability to maximize its anticancer activity in the so called sonodynamic therapy (SDT). SDT shares common features with the clinically approved photodynamic therapy (PDT), distinguishing itself by the use of US instead of light to achieve a better tissue penetration. The way in which SDT achieves cytotoxic effects remains still under debate, but one of the main activities involves the sonosensitizer-mediated reactive oxygen species (ROS) production [1]. In this work the anticancer activity of hypericin (HYP), a well-known photosensitizer, was investigated under US stimulation on an in vitro three-dimensional (3D) colon cancer model. The focus on 3D model is important since cancer cells organized into 3D structure share similar aspects of solid tumour, serving as a more feasible tool before moving to the in vivo setting compared to two-dimensional (2D) cell culture models [2]. The effects of US exposure of HYP have been studied on a human colon cancer (HT-29) cell line grown into 2D monolayers or 3D spheroids by coating 96-well plate with agarose. The synergic activity of HYP in combination with US was assessed by evaluating treatment effects on cell growth and cell death, by cytofluorimetric assays and confocal imaging. In order to select the proper non-cytotoxic concentration of HYP and the proper time to perform SDT, cytotoxicity assays and cytofluorimetric evaluations of cellular uptake were performed, resulting for 2D cell cultures 0.1 μ M HYP for 24 h incubation, and for 3D spheroid cultures 0.2 μ M HYP for 24 h of incubation. On 2D HT-29 cell cultures, SDT showed a strong effect 48 h after the treatment, and on 3D HT-29 spheroids, SDT induced a significant decrease in spheroid volumes also 48 h after the treatment. Moreover, it was also investigated the effect of SDT with HYP on HT-29 cells resistant to chemotherapeutic drugs such as doxorubicin. Data point out that the US exposure of HYP is able to trigger a significant anticancer activity on 2D and 3D colon cancer models.

Keywords

Sonodynamic therapy (SDT); ultrasound (US); hypericin (HYP); three-dimensional (3D) spheroids.

References

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