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QHMEM, a Quinazolinone Compound, Inhibits Proliferation and Induces Apoptosis in Human Colon Cancer HCT116 Cells

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***SUMMARY*. QHMEM, 4(3H)-Quinazolinone, 2-[2-(4-hydroxy-3-methoxyphenyl)ethenyl]-3-(2-methoxyphenyl), is a newly synthesized quinazolinone compound without any reports regarding its biological activities. For the first time, we report the anti-proliferative effect of the compound against human colon cancer cells. Using sulforhodamine B (SRB) assay, we demonstrated that QHMEM inhibited cell growth both dose- and time-dependently. The inhibitory activity of QHMEM on cell growth was further confirmed by colony formation assay. The cell cycle distribution of HCT116 cells was not significantly affected by QHMEM using flow cytometry analysis. But the fraction of apoptotic cells was increased dose-dependently as assessed by annexin V/propidium iodide (PI) double staining. Furthermore, we found that the ration of pro-apoptotic protein Bax over anti-apoptotic protein Bcl-2 was significantly increased, indicating permeabilization of mitochondrion membrane and triggering of apoptosis by QHMEM. In conclusion, the quinazolinone compound QHMEM inhibited the proliferation of human colon cancer HCT116 cells through induction of apoptosis.**

RESUMEN. QHMEM, 4 (3H)-quinazolinona,2-[2-(4-hidroxi-3-metoxifenil)etenil]-3-2-metoxifenil), es un compuesto de quinazolinona recién sintetizado sin ningún informe sobre sus actividades biológicas. Por primera vez, informamos el efecto antiproliferativo del compuesto contra las células de cáncer de colon humano. Usando el ensayo de sulforodamina B (SRB), demostramos que QHMEM inhibía el crecimiento celular tanto de forma dependiente de la dosis como del tiempo. La actividad inhibitoria de QHMEM sobre el crecimiento celular se confirmó adicionalmente mediante un ensayo de formación de colonias. La distribución del ciclo celular de las células HCT116 no se vio afectada significativamente por QHMEM mediante el análisis de citometría de flujo. Pero la fracción de células apoptóticas se incrementó de manera dependiente de la dosis según lo evaluado por la doble tinción anexina V/yoduro de propidio (PI). Además, encontramos que la ración de la proteína pro-apoptótica Bax sobre la proteína anti-apoptótica Bcl-2 aumentó significativamente, lo que indica la permeabilización de la membrana mitocondria y la activación de la apoptosis por QHMEM. En conclusión, el compuesto de quinazolinona QHMEM inhibió la proliferación de células HCT116 de cáncer de colon humano mediante la inducción de la apoptosis.

INTRODUCTION

Colorectal cancer is one of the most common malignancies in the world with the incidence rate ranking the third among all the tumors [1]. At present, the major treatments of the disease include surgery, radiation therapy, chemotherapy, and immunotherapy [2]. Surgical treatment is the first choice for the treatment of colorectal cancer. With the continuous improvement of surgical techniques, the 5-year overall survival rate after colon cancer resection has been increased from 50% in the 1970s to 64% currently. Unfortunately, the tumor will eventually metastasis and relapse in 50% of patients [3]. Chemotherapy follows the first-order kinetic principle of killing a certain percentage of cancer cells with a certain concentration of drugs, and is an important first-line treatment for patients with relapsed and advanced colon cancer [4]. However, the efficacies of the chemotherapeutic agents currently used in clinic against colon cancer are limited, while the side effects

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