The Roles of Endoplasmic Reticulum Stress and Mitochondrial Apoptotic Signaling Pathway in Quercetin-Mediated Cell Death of Human Prostate Cancer PC-3 Cells

Kuo-Ching Liu,1 Chun-Yi Yen,2 Rick Sai-Chuen Wu,3 Jai-Sing Yang,4 Hsu-Feng Lu,5 Kung-Wen Lu,6 Chyi Lo,7 Hung-Yi Chen,8 Nou-Ying Tang,7 Chih-Chung Wu,9 Jing-Gung Chung2,10

1Department of Medical Laboratory Science and Biotechnology, China Medical University, Taichung 404, Taiwan
2Department of Biological Science and Technology, China Medical University, Taichung 404, Taiwan
3Department of Anesthesiology, Critical Care and Pain Service, China Medical University Hospital, Taichung 404, Taiwan
4Department of Pharmacology, China Medical University, Taichung 404, Taiwan
5Department of Clinical Pathology, Cheng Hsin General Hospital, Taipei 112, Taiwan
6School of Post-Baccalaureate Chinese Medicine, China Medical University, Taichung 404, Taiwan
7School of Chinese Medicine, China Medical University, Taichung 404, Taiwan
8School of Pharmacy, China Medical University, Taichung 404, Taiwan
9Department of Nutrition and Health Sciences, Chang Jung Christian University, Tainan 711, Taiwan
10Department of Biotechnology, Asia University, Taichung 413, Taiwan

Received 10 November 2011; revised 29 January 2012; accepted 1 February 2012

ABSTRACT: Prostate cancer has its highest incidence and is becoming a major concern. Many studies have shown that traditional Chinese medicine exhibited antitumor responses. Quercetin, a natural polyphenolic compound, has been shown to induce apoptosis in many human cancer cell lines. Although numerous evidences show multiple possible signaling pathways of quercetin in apoptosis, there is no report to address the role of endoplasmic reticulum (ER) stress in quercetin-induced apoptosis in PC-3 cells. The purpose of this study was to investigate the effects of quercetin on the induction of the apoptotic pathway in human prostate cancer PC-3 cells. Cells were treated with quercetin for 24 and 48 h and at various doses (50–200 μM), and cell morphology and viability decreased significantly in dose-dependent manners. Flow cytometric assay indicated that quercetin at 150 μM caused G0/G1 phase arrest (31.4–49.7%) and sub-G1 phase cells (19.77%) for 36 h treatment and this effect is a time-dependent manner. Western blotting analysis indicated that quercetin induces the G0/G1 phase arrest via decreasing the levels of CDK2, cyclins E, and D proteins. Quercetin also stimulated the protein expression of ATF, GRP78, and GADD153 which is a hallmark of ER stress. Furthermore, PC-3 cells after incubation with quercetin for 48 h showed an apoptotic cell death and DNA damage which are confirmed by DAPI and Comet assays, leading to decrease the antiapoptotic Bcl-2 protein and level of DΨm, and increase the...