Cinnamomum cassia Suppresses Caspase-9 through Stimulation of AKT1 in MCF-7 Cells but Not in MDA-MB-231 Cells

Sima Kianpour Rad1, M. S. Kanthimathi1,2*, Sri Nurestri Abd Malek3, Guan Serm Lee3, Chung Yeng Looi4, Won Fen Wong5

1 Department of Molecular Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia, 2 University of Malaya Centre for Proteomics Research, UMCPR, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia, 3 Institute of Biological Sciences, Faculty of Science, University of Malaya, Kuala Lumpur, Malaysia, 4 Department of Pharmacology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia, 5 Department of Medical Microbiology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

* kanthi@ummc.edu.my

Abstract

Background

Cinnamomum cassia bark is a popular culinary spice used for flavoring and in traditional medicine. C. cassia extract (CE) induces apoptosis in many cell lines. In the present study, particular differences in the mechanism of the anti-proliferative property of C. cassia on two breast cancer cell lines, MCF-7 and MDA-MB-231, were elucidated.

Methodology/Principal Findings

The hexane extract of C. cassia demonstrated high anti-proliferative activity against MCF-7 and MDA-MB-231 cells (IC50, 34±3.52 and 32.42 ±0.37 μg/ml, respectively). Oxidative stress due to disruption of antioxidant enzyme (SOD, GPx and CAT) activity is suggested as the probable cause for apoptosis initiation. Though the main apoptosis pathway in both cell lines was found to be through caspase-8 activation, caspase-9 was also activated in MDA-MB-231 cells but suppressed in MCF-7 cells. Gene expression studies revealed that AKT1, the caspase-9 suppressor, was up-regulated in MCF-7 cells while down-regulated in MDA-MB-231 cells. Although, AKT1 protein expression in both cell lines was down-regulated, a steady increase in MCF-7 cells was observed after a sharp decrease of suppression of AKT1.

Trans-cinnamaldehyde and coumarin were isolated and identified and found to be mainly responsible for the observed anti-proliferative activity of CE (Cinnamomum cassia).

Conclusion

Activation of caspase-8 is reported for the first time to be involved as the main apoptosis pathway in breast cancer cell lines upon treatment with C. cassia. The double effects of C. cassia on AKT1 gene expression in MCF-7 cells is reported for the first time in this study.