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# Caffeic acid phenethyl ester suppresses TNF-α mediated activation of NF-κB and induces apoptosis

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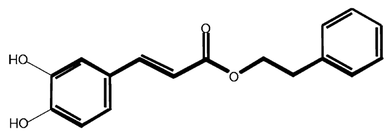
## Abstract

Caffeic acid phenethyl ester (CAPE) is an active component of Propolis and has antiviral, anti-inflammatory and immunomodulatory properties. We aimed to investigate the effects of CAPE on the inhibition of NF-κB(p65 subunit) translocation. CAPE displayed a strong growth inhibition effect on human hepatoblastoma (HepG2) cell lines in a dose-dependent manner. Flow cytometry analysis showed that the ratio of sub-G1 phase cells increased when exposed to CAPE for 24 h. When HepG2 cells were treated with CAPE (20~100 μM) for 24h, DNA ladders were visible at 60 μM. Moreover, CAPE significantly induced morphological changes of typical apoptosis. In immunofluorescence assay, CAPE significantly blocked the TNF-α-mediated NF-κB translocation to the nucleus. In conclusion, the results of the present study indicates that CAPE suppresses TNF-α-induced NF-κB activity and leading to the apoptosis of HepG2 cells.

## Introduction

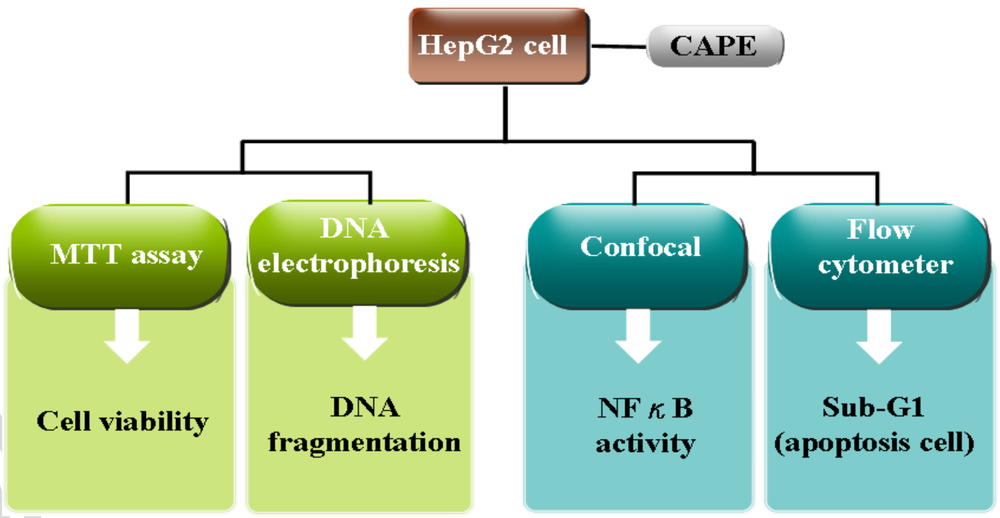
Cancer mortality rates have risen throughout most of the past century and into the new millennium. Cancer is already the leading cause of death in some countries. This observation has engendered much research activity aimed at identifying cancer chemopreventive agents, especially naturally occurring compounds derived from the diet, which have the advantage of being relatively nontoxic(1). Hepatocellular carcinoma is one of the most lethal malignancies and ranks as the second leading cause of cancer deaths in Asia. Apoptosis is a cell death process that plays a critical role in development, tissue homeostasis and development of various human diseases. Lack of apoptotic induction and inappropriate-controlled apoptosis process have been implicated in tumor development and progression as well as chemoresistance. NF-κB is a transcription factor that is associated with tumorigenesis, and its increased activity has been associated with evasion of apoptosis, malignant transformation, sustained cell proliferation, metastasis, and angiogenesis(2).

Honey-bee propolis




Caffeic acid phenethyl ester

## Experimental design




## Results

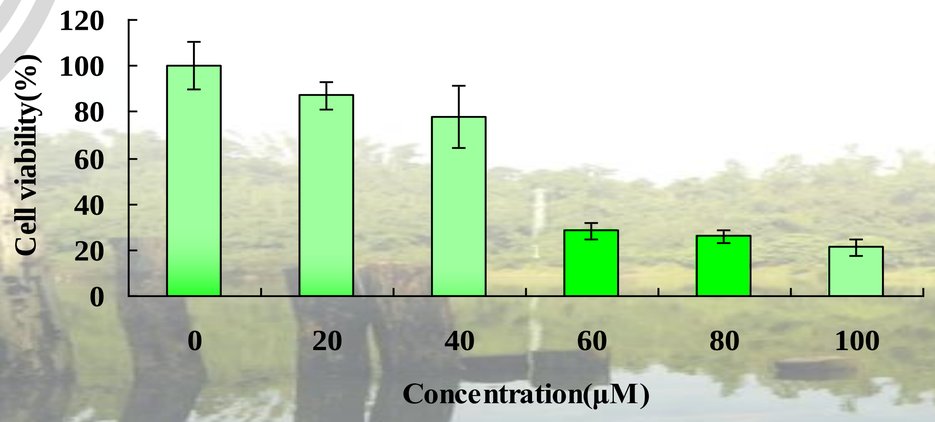



**Fig.1** Effects of CAPE on viability of HepG2 cells. Cells were treated with the indicated concentrations of CAPE (0, 20, 40, 60, 80 or 100 μM) for 24 h. Cell viability was assessed using an MTT reduction assay. *$p$<0.05, **$p$<0.01 vs. control.

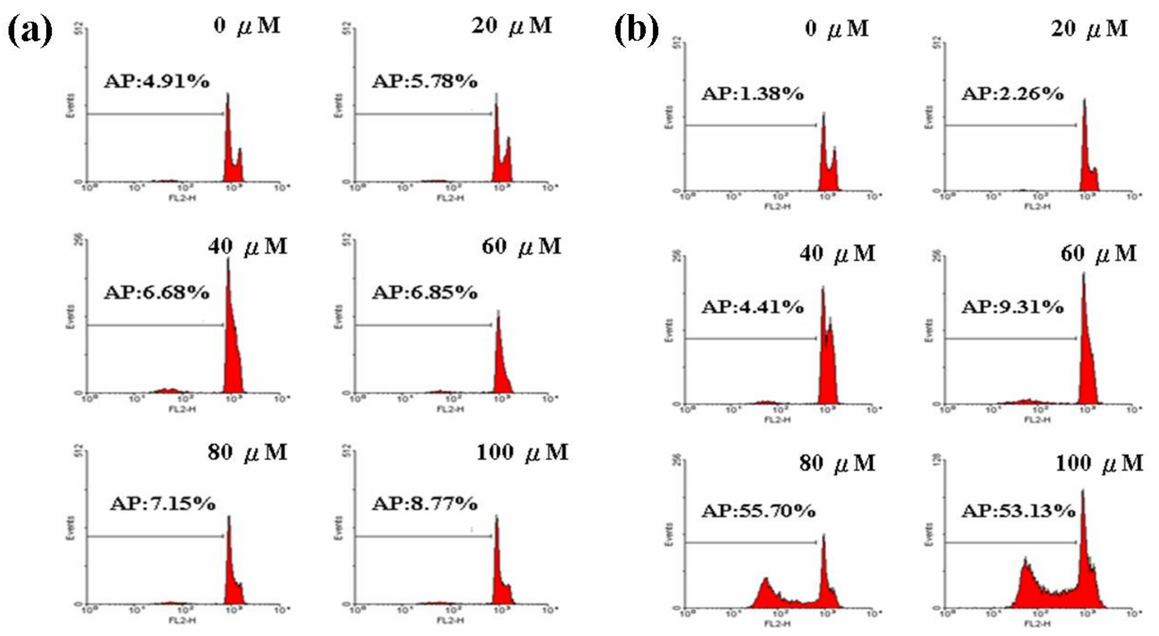



**Fig. 2** Flow cytometric analysis of DNA content in HepG2 cells treated with different concentrations of CAPE for (a)12 h, (b)24 h.

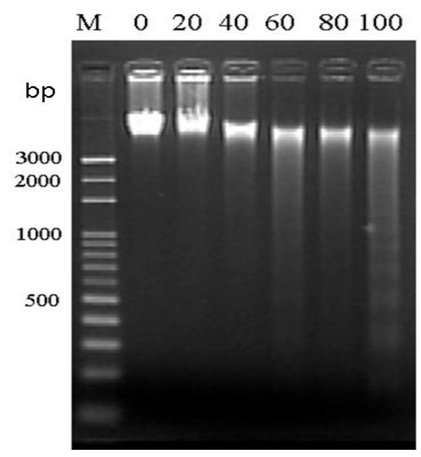



**Fig. 3** DNA fragmentation was detected by gel electrophoresis following 0~ 100 μM CAPE stimulation for 24 h.

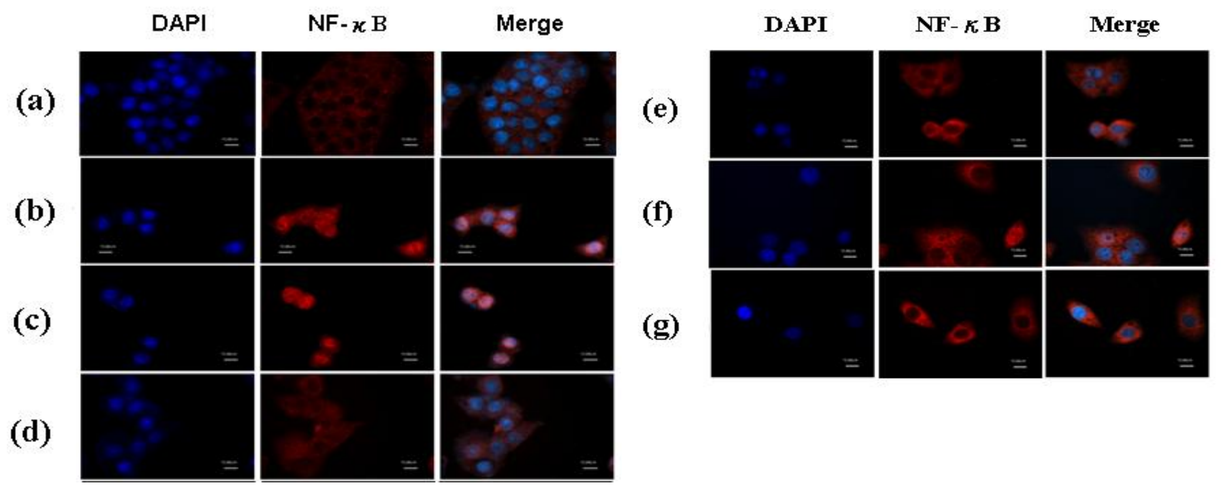



**Fig.4** CAPE inhibited TNF-α-induced nuclear translocation of NF-κB. HepG2 cells were incubated with 10 ng/ml TNF-α for 30 min in the presence or absence of CAPE for 24 h. (a) control, (b) TNF-α(alone), (c) CAPE 20 μM, (d) CAPE 40μM, (e) CAPE 60 μM, (f) CAPE 80 μM, (g) CAPE 100 μM .

## Conclusion

Our results demonstrate that CAPE is a potent inhibitor of cell proliferation and an inducer of apoptosis in HepG2 cell through suppression of TNF-α mediated NF-κB activation.

## Reffrences

1. Cao J, Jia L, Zhou HM, Liu Y, Zhong LF. 2006. Mitochondrial and nuclear DNA damage induced by curcumin in human hepatoma G2 cells. Toxicol Sci. 91(2):476–483.
2. Karin M. 2006. Nuclear factor-κB in cancer development and progression. Nature. 441:431–436.