CARDY-05

HUMAN T LYMPHOCYTES ACTIVATED BY TISSUE NECROSIS FACTOR-ALPHA ARE INHIBITED BY GINKGO BILOBA EXTRACT THROUGH DOWN-REGULATION OF ACTIVATOR PROTEIN-1

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BACKGROUND/AIMS: Ginkgo biloba extract has been used in cardiovascular diseases. However, it was unknown whether Ginkgo biloba extract has regulatory effects on human T lymphocytes activated by tissue necrosis factor-alpha, which has important roles on the progression of atherosclerotic plaques. We evaluated whether Ginkgo biloba extract can modulate the activated human peripheral T lymphocytes by tissue necrosis factor-alpha.

METHODS: Primary human T lymphocytes were isolated from whole blood. Both activator protein-1 (AP-1) and nuclear factor-kappa B were determined by electrophoretic mobility shift assays. Their relative protein activities were determined by kinase assays and Western blotting.

RESULTS: Molecular investigation indicated that the inhibition of activated human T lymphocyte specifically correlated with the down-regulation of AP-1 DNA-binding activities. We also revealed that Ginkgo biloba extract was unique in its ability to inhibit the activation of c-Jun NH_2-terminal protein kinase.

DISCUSSION/CONCLUSION: Via down-regulation of AP-1 activity, Ginkgo biloba extract may have novel therapeutic effects on inflammation-based diseases associated with tissue necrosis factor-alpha-activated human T lymphocytes.

Key words: Activator protein-1, Ginkgo biloba extract, Tissue necrosis factor-alpha.

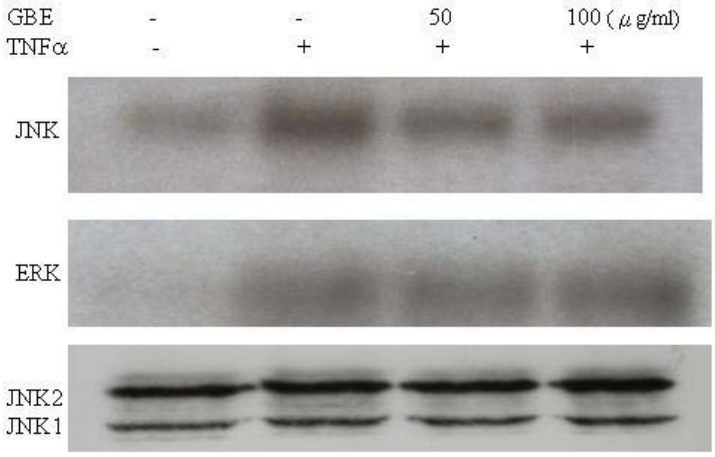

Figure: GBE treatment inhibits the JNK, but a lesser extent the ERK, signaling pathway. Human peripheral blood T cells at $2x10^6$/ml were pretreated or not with 100 μ g/ml GBE for 2 hours and then stimulated with TNF-α for various time points. TNF-α activated JNK in a time-dependent manner and GBE pretreatment can suppress the activity of JNK. Their kinase activities were measured based on phosphorylation of GST-c-Jun fusion protein (c-Jun) substrate. Analysis of JNK band density showed GBE at 100μg/ml time-dependently decrease the fold of band density markedly. Under these conditions, GBE had no effect on total JNK protein levels. GBE treatment affects the activity of ERK not much. Their kinase activities were measured based on phosphorylation of myelin basic protein (MBP) substrate. The representative data out of three are shown. * denotes statistical significance (p value < 0.05) as compared with cells stimulated alone in indicated parallel time.

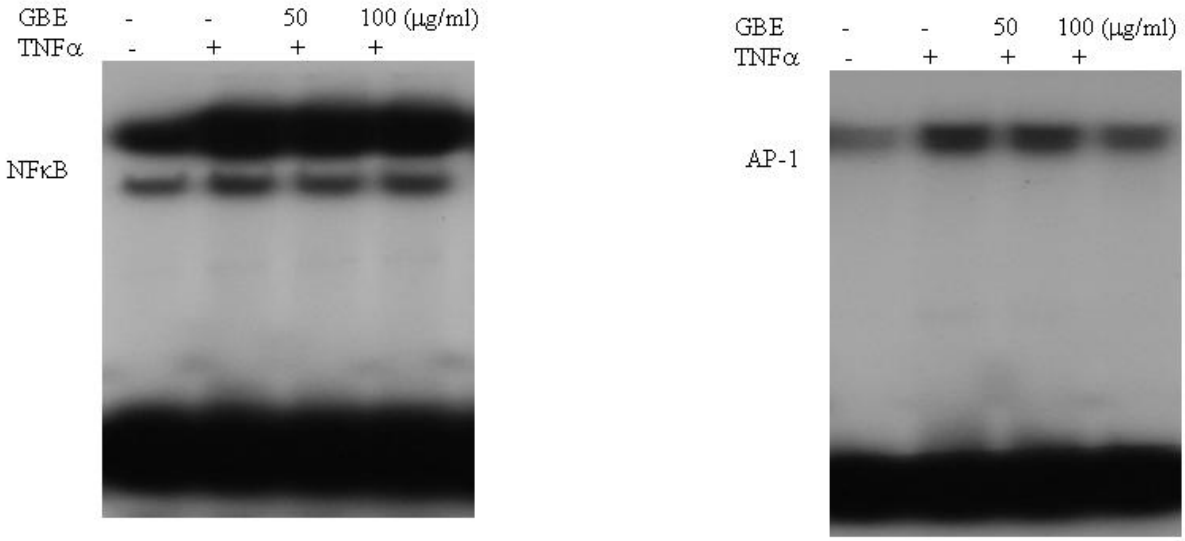

Figure: GBE blocked AP-1 DNA-binding activity stimulated by TNF-α, but not NFκB. Human peripheral blood T cells at $2x10^7$/ml were pretreated with various concentrations of GBE for 2 hours and then stimulated or not with TNF-α for one hour. We found that GBE can inhibit AP-1 DNA-binding activity. At least three independent experiments were performed.