



## The effect of Carvacrol on apoptotic factors in the cancer cells line DU145 by Experiment and molecular dynamic simulation

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### Abstract

**Introduction & Aim:** The apoptotic factors such as BID, BIM and APAF1 have a main role in inducing apoptotic pathways. Furthermore, some compounds such as Carvacrol can active these apoptotic factors to cause apoptosis. In this study, the comet assay technique and molecular dynamics simulations were applied to investigate the effects of Carvacrol on induction of apoptotic pathway.

**Methods:** In the comet assay technique, different concentrations including 130, 230, and 360  $\mu\text{M}$  of Carvacrol were selected according to IC50 using MTT assay on the cell line DU145. Alkaline electrophoresis was performed and 100 comet pictures were analyzed using CASP software. Data were analyzed by SPSS statistical software. Molecular dynamics simulations on BID, BIM and APAF1 were performed with the GROMACS 5.4.7 package. Carvacrol was closed in a fully hydrated simulation box with a protein (Bak, Bax, Bim, Apaf1, Bid and P38).

**Results:** The IC50 for Carvacrol was determined at 360  $\mu\text{M}$  by MTT test. Rate of tail to head in alkaline electrophoresis at 130, 230, and 360  $\mu\text{M}$  of Carvacrol concentrations were  $13.8 \pm 0.3$ ,  $40.6 \pm 0.3$ , and  $47.6 \pm 0.5$  percent, respectively. Molecular dynamic simulation shown that carvacrol can actives the Bim factor.



**Conclusion:** Statistical analysis of the molecular dynamics and calculated potential energy, radius of gyration (Rg), temperature, root mean square fluctuation (RMSF) and root mean square deviation (RMSD) indicated that Carvacrol affected protein which stimulated the apoptotic cascade. Therefore, both experimental and theoretical results demonstrate that Carvacrol directly affects factors initiating apoptosis. This combined approach avoids the necessity for quantum mechanical calculations.

**Keywords:** Simulation, Carvacrol, the DU145 Cells line, Prostate cancer, Comet assay