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Apoptotic Effect of Petroselinum crispum (parsley) on AKT/mTOR Pathway in Human Prostate Cancer Cell Line

Mehmet Kadir Erdoğan¹, Hakan Aşkın²

¹Department of Biology, Faculty of Arts and Sciences, Bingol University, 12000, Bingol, Turkey
²Department of Molecular Biology and Genetics, Faculty of Sciences, Ataturk University, 25240, Erzurum, Turkey

Prostate cancer (PCa) is the most common cancer in elderly males (>70 years of age). It is a major health problem, especially in developed countries with their greater proportion of elderly men in the general population. Petroselinum crispum (parsley) is a member of Apiaceae family that is cultivated and consumed throughout the world as a seasoning condiment. Studies have shown that P. crispum has antioxidant, antimicrobial, anti-coagulant, hepatoprotective and anti-proliferative activities [1,2]. AKT/mTOR pathway is nearly related with p53 and play a central role in tumorigenesis and apoptosis [3].

In the present study, antiproliferative and apoptotic effects of parsley was examined with various methods. PC-3 human prostate cancer cell line was used for assays and cells were grown in DMEM (Dulbecco's Modified Eagle Medium) supplemented with 5 ml of penicillin-streptomycin and 10% fetal bovine serum and in a humidified incubator containing 5% CO2. Parsley was obtained from local market and extracted with methanol. Cell viability was determined by MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay (Roche). PC-3 cells were treated with the different concentrations of parsley (0-500 µg/ml). Cell Death Detection Elisa assay was performed according to the manufacturer’s (Roche) protocol for detect the apoptotic effect of parsley. To extract the total RNA Pure Link RNA Mini Kit (Life Technologies) and for cDNA synthesis High Capacity cDNA Reverse Transcription Kit (Thermo Fisher) was used. Primer sequences were as follows: β-actin, forward 5’ ctctttcagctctctctc t3’, reverse S’ acaacatgttggctacag 3’; p53, forward 5’ gtccaaacaccacagtctct 3’, reverse S’ cctctctcctctcctctc t3’, reverse S’ cctctctcctctcctctc t3’; AKT, forward 5’ cacaccacctgaccaagatg 3’, reverse 5’ ctggccgagtaggagaactg 3’; and mTOR, forward 5’ tgtctgcgtggctgaaagt 3’ and reverse S’ tcacgctgtctgtcaggg 3’. Gene expression levels of AKT, mTOR and p53 were measured by RT-qPCR (real-time quantitative polymerase chain reaction), 2 x qPCRBIO SyGreen Mix Lo-ROX Kit (PCR Biosystems). β-actin was used as house-keeping gene for optimization. Each independent experiments were performed in triplicate.

When PC-3 cells treated with 500 µg/ml concentration of P.crispum methanolic extract, the inhibition rate was 71%. IC50 (half maximal inhibitory concentration) value was determined as 297,5 µg/ml. IC50 of P. crispum was used further analysis. Apoptotic rate was 11,3 fold higher than control group when the cells treated with IC50 value of methanolic extract of P. crispum (p<0,05). Also AKT and mTOR expressions significantly decreased, while p53 level significantly increased (p<0,05).

In conclusion, treatment with P. crispum can significantly inhibit the growth of prostate carcinoma cells, downregulate the AKT/mTOR pathway and increase p53 expression in vitro. These findings suggest that P. crispum might be an appropriate therapeutic in treatment of cancer.

Keywords: mTOR, parsley, prostate cancer, MTT, RT-qPCR