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## 56 - Anti-HSV-1 Activity of natural raw and roasted unsalted pistachio kernels in human monocytic THP-1 and Vero cells.

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### **Anti-HSV-1 Activity of natural raw and roasted unsalted pistachio kernels in human monocytic THP-1 and Vero cells.**

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**Introduction.** A great interest is globally devoted to the search for alternative treatment for HSV infections. To date, acyclovir and related nucleoside analogues are effective viral DNA polymerase inhibitors, though their intensive use has led to the increase of drug-resistance. Plants are rich sources of pharmacologically active agents, which provide several advantages such as reduced side effects, less resistance, low toxicity and various mechanisms of action. The purpose of the current study was to investigate the effects of natural raw (NRRE) and roasted unsalted (RURE) pistachio polyphenols-rich extracts in both human monocytic cells THP-1 and epithelial VERO cells on HSV-1 replication. **Materials and Methods.** Pistachio polyphenolic extracts were prepared following two different extraction methods, with or without *n*-hexane. Cell viability was measured by monitoring the metabolic activity over time following NRRE and RURE dose-dependent (0.2, 0.4, 0.8 mg/mL) treatment. Cells and virus dilutions were pre-treated with both extracts for 1h and mixed to allow viral adsorption. After 1 h, any unabsorbed virus was aspirated and the monolayer covered with Dulbecco's Modified Eagle's Medium containing 0.8% methylcellulose in presence of both extracts, separately. **Results and Conclusions.** The identification and quantification of phenolic compounds showed that the NRRE extracts were generally richer in polyphenolic compounds compared with RURE extracts. A better profile of cellular tolerability was reported for both NRRE and RURE extracts obtained without using *n*-hexane in both cell lines. Non-toxic concentrations of NRRE and/or RURE (0.6, 0.4 and 0.3 mg/mL) were employed to verify the antiviral effect by plaque reduction assay. In Vero cells, NRRE and RURE exhibited a significant inhibitory activity at 0.6 mg/mL and in particular, treatment with the mixture extracted with *n*-hexane determined a significant reduction of plaque numbers and size, as reported by change of morphology and by detection of micro plaques. Based on this, NRRE and RURE *n*-hexane were used to treat cells and virus suspension and detect the viral DNA and genes. We report that NRRE significantly reduced viral DNA and genes, whereas RURE mildly affected the viral DNA but partially reduced viral transcripts and protein at 0.6 mg/mL. A strong reduction was also detected in the intracellular virus production in THP-1 cells pre-treated with NRRE and RURE *n*-hexane and infected with HSV-1 by plaque assay. These data support the potential use of pistachio extracts as antiherpetic agents.

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