

Different Plant Extracts Effect Proliferation and NO Activity in NSCLC Cell Lines

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Aim of the study: Geophyte is a general name given to plants which under the ground body such as bulbs, tubers and rhizomes, gained ability to store nutrients. *Cyclamen* L., belonging to the Primulaceae family, is a tuberous perennial geophyte, and some taxa of this genus have been used for their biological activities in folk medicine. In Turkey, this genus is represented with 12 taxa, 5 of which are endemic. Nitric oxide (NO) is a potent pleiotropic mediator of physiological process such as smooth muscle relaxant, neuronal signaling and regulation of cell mediated toxicity. It is a diffusible free radical, which plays many roles as an effector molecule in diverse biological systems including neuronal messenger, vasodilatation, antimicrobial and antitumor activities. Although NO radical is involved in host defense, over production of this radical contributes to the pathogenesis of some diseases. *To the best of our knowledge*, this study is the *first to investigate* the effects of some *Cyclamen* taxa on proliferation and NO inhibitory activity in LPS-activated non-small cell lung cancer (NSCLC) cell lines.

Material and Methods: In the present study, three *Cyclamen* taxa; *C. pseudibericum* Hildebr. (endemic), *C. mirabile* Hildebr. (endemic) and *C. persicum* Mill. were collected from different localities in Turkey. The tubers of plants were air-dried and grounded to fine powder and then extracted with ethanol. The effect of three *Cyclamen* taxa on cell viability of human NSCLC cell lines (H1975 and HCC78) was determined by using CellTiter Glo assay. Experiments were conducted along with control and seven different concentrations (1, 10, 30, 50, 75, 100, 200 µg/ml) of the test extracts. The nitric oxide assay was performed as described by Yang et al. (2009). After preincubation of H1975 and HCC78 cells (5×10^3 cells/well) with LPS (1 µg/ml) for 24h, the plant extracts (1, 10, 30, 50, 75, 100, 200 µg/ml) were added and incubated for 48h. The quantity of nitrite in the culture medium was measured as an indicator of NO production. Amount of nitrite, a stable metabolite of NO, was measured using Griess reagent.

Results: Among the three *Cyclamen* tuber extracts evaluated, the highest cytotoxic activity was obtained from *C. persicum* compared to other two *Cyclamen* taxa. We found that *C. persicum* has cytotoxic effects on H1975 and HCC78 cell lines and IC₅₀ values are 17.27 µg/ml and 34.15 µg/ml. Inhibition of NO production was measured as nitrite in the cell free culture supernatant. NO production by LPS-activated cells was found to be significantly inhibited by the plant extracts in a dose dependent manner. Among the different *Cyclamen* taxa, *C. persicum* exhibited the significant reduction of nitrite level to 203.75 µM at the concentration of 200 µg/ml in H1975 cells. The amount of nitrite in HCC78 cells was found as 198.75 µM at the concentration of 200 µg/ml for *C. pseudibericum*.

Keywords: *Cyclamen*, proliferation, nitric oxide assay, LPS, NSCLC cell lines.