**The role of phytopharmaceuticals and reactive oxygen species (ROS) in cancer therapy**

Salehe Biniaz 1

Soheila Rahgozar1\*

1- Department of Cell and Molecular Biology & Microbiology, Faculty of Biological Sciences and Technologies, Isfahan University

[rahgozar@sci.ui.ac.ir](mailto:rahgozar@sci.ui.ac.ir)

**‌ Statement of Problem:** Phytochemicals are widely used in combination with chemotherapy drugs in order to reduce their diverse side effects. Increased cytotoxic levels of ROS induce different signaling pathways contributing to cell cycle arrest and cell death. Phytochemicals may destroy cancer cells by possibly generating intracellular ROS.

**Research Purpose:** The aim of this studywas to introduceseveral phytopharmaceuticals which may be potentially considered in cancer therapy by inducing ROS in the malignant cells.

**Research Method:** All the related academic articles and research papers published from 1990 to 2022 were collected and precisely reviewed from PubMed, Google scholar and ScienceDirect.

**Results and Conclusion:** 6-Shogaol, a ginger plant derivative, induces p53 activation in leukemic cells, leading to apoptosis and cell-cycle arrest. Moreover, 6-Shogaol generates ROS and downregulates fatty acid synthase. Luteolin is a flavonoid which promotes ROS and cause cell cycle arrest by suppressing CDK2 in melanoma and colorectal cancer cells. Moreover, luteolin may restrain the proliferation and expression of p-STAT3, p-EGFR, p-Akt, and p-Erk1/2 in breast cancer cells. Resveratrol, a dietary phytophenol, generates ROS and ER stress in melanoma. Elevated ROS production leads to the phosphorylation of p38 MAPK and cell cycle arrest by activating p53 and preventing cyclinB expression. Resveratrol may then accelerate apoptosis by inhibiting Bcl-2 and upregulating Bax. Curcumin, a food flavoring phenolic compound enhances ROS by inducing JNK and ERK1/2 pathways and potentiates p53-mediated apoptosis in choriocarcinoma cells. ROS may also activate PTEN, constrain PI3K/Akt pathway and upregulate NF‐κB activity in different cancer cells. In conclusion, a growing body of evidence shows that plant medicines may increase the intracellular levels of ROS in cancer cells contributing to cell death. The present study may help selecting new cancer therapeutic strategies by using plant medicines as herbal supplements in cancer treatment.

**Keywords:** Phytopharmaceuticals, reactive oxygen species, cancer therapy.