

## **Dietary flavonoid modulates epigenetic markers and miRNA in triple negative breast cancer**

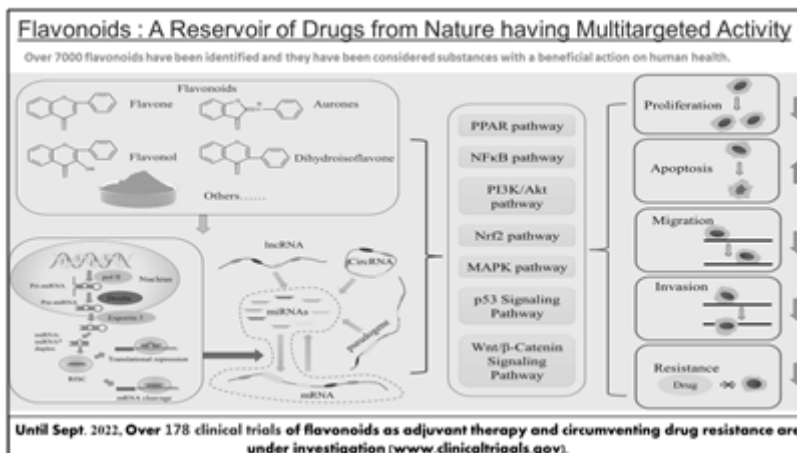
**Rajesh N Gacche, Nimal Snehal and Kumbhar Navanath**  
Savitribai Phule Pune University, India

**Statement of the Problem:** Triple-negative breast cancer (TNBC) is a heterogeneous group of breast carcinomas distinguished by rapid metastatic growth and aggressive tumor invasion ability, leading to high female mortality. On the eve of emerging drug resistance, there is a need to identify candidate drugs that will improve the efficacy of conventional therapeutic regimes. The purpose of this study was to investigate the effect of dietary flavonoids on regulation of epigenetic markers and miRNAs involved in progression of TNBC.

**Methodology & Theoretical Orientation:** Series of in vitro cell culture assays such as MTT assay for cell viability, cell migration assay, ROS assay, cell cycle inhibition and apoptosis assay was carried out FACs analysis. The gene expression profile of HDAC 1-11 isomers, DNMT-1/3 and HMT, Onco- and tumor suppressor miRNAs and MRP1 & BCRP was determined using RT-qPCR. The protein expression analysis of HDACs 1, 3, 4 & 6 and apoptosis marker proteins was analyzed using immunoblotting.

**Findings:** The Apigenin, Galangin and luteolin, showed good potential to modulate the expression profiles of epigenetic regulators in TNBC (MD-MB-231) cells. The HDAC1, HDAC2, HDAC3, HDAC4, HDAC5, HDAC6 and HDAC8 were downregulated in MD-MB-231 cells after treatment with dietary flavonoids such as Apigenin, Galangin and Luteolin. The results were normalized with GAPDH. The protein expression level of HDAC1, HDAC3, HDAC4 and HDAC6 were reduced after the treatment of Apigenin, Galangin and Luteolin. The expression of DNMT1 and HMT downregulated after the treatment of Apigenin, Galangin and Luteolin. The oncomiR-21 was downregulated after the treatment of Apigenin and Luteolin. Whereas, the tumor suppressor miRNAs such as miR34 and miR200b was significantly upregulated after the treatment of Apigenin, Galangin and Luteolin. The combinatorial studies suggested the synergistic effect (CI<1) between flavonoids and SAHA against MDA-MB-231 cells. The qRT-PCR and Western analysis results were supported by molecular docking and MD simulation studies.

**Conclusion & Significance:** On the eve of evolving drug resistance, tumor heterogeneity, and off target toxicities there is need to find alternative candidate adjuvant therapeutic molecules which will augment the efficacy of conventional drugs and circumvent the drug resistance. The results of the present study clearly indicate the significance of lead flavonoid molecules as adjuvant drug molecules for effective treatment of TNBC.



## Biography

Rajesh N. Gacche is a senior professor in the Department of Biotechnology, Savitribai Phule Pune University, India. Prof. Rajesh is a Fellow of Royal Society of Medicine, London, UK. His research focuses on cancer biology, especially exploring natural products and promising plant-derived lead fractions as adjuvants or complementary and alternative medicine for improving the efficacy of conventional drugs and amelioration of emerging drug resistance and off-target toxicities. Prof. Rajesh has published over 150 research papers in reputed international journals. Prof. Rajesh is an author of a book titled as 'Dietary Research and Cancer (1st, 1). Singapore: Springer Nature 2022. ISBN: 9789811660498. Oncologist, health care & food industry, nursing is widely using this book and the word media has taken cognizance of this book in the mainstream of diet and cancer research.

**Received:** May 10, 2023; **Accepted:** May 12, 2023; **Published:** July 17, 2023