

## Summary:

Cancer is a disease that progresses gradually with the loss of growth control. Chronic myeloid leukemia (CML) is the most common hematopoietic neoplasm. CML is a myeloproliferative neoplasm characterized by an increase in myeloid cells. The pathogenesis of CML includes the translocation of the ABL1 gene on chromosome 9 with the BCR gene on chromosome 22. This leads to the production of a fusion oncoprotein called BCR-ABL1. BCR-ABL1 is an active tyrosine kinase that induces growth and proliferation through downstream signaling pathways. Activation of various intracellular signaling pathways increases proliferation and decreases apoptosis. Cancer treatment with chemotherapeutic agents has two major problems, the development of tumor resistance to time-dependent treatment and non-specific toxicity to normal cells. Therefore, trying to find new therapeutical strategies is under evaluation. Tannic acid belongs to a subset of tannin compounds that have chemopreventive, chemosensitizing, and antitumor properties. The Hippo signaling pathway, which controls cell growth, proliferation, apoptosis, differentiation, and organ size, is actually a tumor suppressor pathway, and dysfunctional Hippo signaling has been shown to be involved in a variety of biological processes and tumor development. MicroRNAs are small (21-25 nucleotides), single-stranded, non-coding RNA molecules that bind to messenger RNA to inhibit protein production. MicroRNAs are involved in normal physiological processes, including cell proliferation, differentiation, and apoptosis, as well as several pathological conditions such as tumors. The aim of this study is to evaluate the expression of some microRNAs affecting the Hippo signaling pathway in tannic acid-treated K562 cells. The results showed that cell viability in K562 cells treated with 10  $\mu$ M tannic acid is 50%. evaluation of reactive oxygen species using the DCFH-DA method led us to treat the cells with tannic acid for 12 and 48 hours. Evaluation of the expression of effective microRNAs and mRNAs in the hippo pathway using real-time polymerase chain reaction showed that the expression levels of miR-29b-3p and miR-103a-3p increased after 12 hours; While the expression levels of miR-590-3p, miR-135a-5p, miR-182-5p, and miR-125b-2-3p decreased after 12 hours. The expression levels of miR-135a-5p, miR-182-5p, and miR-103a-3p increased after 48 hours; While the expression levels of miR-125b-2-3p, miR-590-3p and miR-29b-3p decreased after 48 hours. Regarding the expression of hippo pathway genes, the expression levels of STK4, MOB1B, and LATS1 increased after 12 hours; While the expression levels of SAV1, STK3, MOB1A, LATS2, and YAP decreases after 12 hours. The expression levels of all genes increased after 48 hours and no decrease in expression was observed. Overall, our results suggest that tannic acid can be proposed as a therapeutic strategy alongside chemotherapeutic agents by regulating the hippo signaling pathway through microRNAs.

Keywords: Chronic myeloid leukemia, microRNA, Hippo signaling pathway, Tannic acid