

EFFECTS OF METHANOLIC AND AQUEOUS EXTRACTS OF *Carica papaya* LEAF ON MIRNA-MEDIATED TRANSCRIPTIONAL REGULATION OF FETAL HEMOGLOBIN

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Introduction: Hemoglobinopathies are genetic blood disorders resulting characterized by abnormal hemoglobin that disrupts oxygen transport and leads to diverse health complications. Raising fetal hemoglobin (HbF) levels is one possible therapeutic approach. But the current main therapy based on the use of hydroxyurea (HU), faces limitations related to cost and safety, especially in underserved areas. To overcome these constraints, researchers are investigating natural alternatives like *Carica papaya* (CP) leaf extracts to boost HbF production with fewer side effects.

Methodology: We conducted a comparative study using aqueous (AECP) and methanolic (MECP) CP leaf extracts to evaluate their impact on HbF regulation in K562 myeloid cells. Gene expression changes were assessed using RT-qPCR after 24-hour exposure to varying extract concentrations (0,05 µg/ml, 0,5µg/ml and 5µg/ml).

Results: The transcriptional analysis of hemoglobin genes (HBA, HBB and HBG1) as well as that of its epigenetic regulators (HDAC1, HDAC2, HDAC3, DNMT1 and DNMT3b), transcription inhibitors (BCL11A and KLF1), transcription activators (MYC and HIC2) and miRNA-mediated regulators (miR-30a-3p, miR-29C-3p and miR-148b-3p) has revealed distinct expression patterns in K562 cells exposed to AECP when compared to MECP. While the expression levels of some genes were affected by one extract, other genes were affected by the other extract and some remained unaffected suggesting that the concentration and specific composition of AECP or MECP has a different impact on hemoglobin expression.

Discussion: The differential effects of MECP and AECP exposure on hemoglobin related genes expressed in K562 cells indicates that complex regulatory mechanisms underly their action. The concentration-dependent responses observed emphasize the need for further research to comprehend their implications in hemoglobinopathies. Overall, this study highlights the potential of extracts of CP leaf as modulators of HbF gene expression in K562 cells. Further investigation into their gene modulation mechanisms is warranted.

Acknowledgements: This project was supported by the grant IDI&CA-IPL/2022/miRCa/ESTeSL