GLUCOMORINGIN, A GLUCOSINOLATES EXTRACTED FROM *MORINGA OLEIFERA* SEEDS, INDUCES ANTIPROLIFERATIVE EFFECT IN HUMAN NEUROBLASTOMA CELLS

Santa Cirmi[1], Nadia Ferlazzo[1], Laura Musumeci[2], Caterina Russo[3], Alessandro Maugeri[1], Giovanni Enrico Lombardo[3], Michele Navarra[1]

[1]Department of Chemical, Biological, Pharmaceutical and Environmental Sciences, University of Messina, Messina - Italy, [2]Department of Chemical, Biological, Pharmaceutical and Environmental Sciences, University of Messina; "Prof. Antonio Imbesi" Foundation, Messina - Italy, [3]Department of Chemical, Biological, Pharmaceutical and Environmental Sciences, University of Messina; "Prof. Antonio Imbesi" Foundation, Messina - Italy

Introduction: Neuroblastoma (NB) is a tumour of the sympathetic nervous system which occurs mainly in early childhood, representing the most aggressive tumor of infancy. It accounts for approximately 6-10% of all infant malignancies. Although the improvements recently obtained in the treatment of NB, the prognosis of patients with NB is still poor. In addition, conventional cancer therapies cause serious side effects and extend the patient's lifespan only by a few years. Therefore, cancer control may benefit from the potential that resides in alternative therapies. In the last decades, glucosinolates (GLs) have been studied mostly for their anticancer properties. The aim of our research was to study the antiproliferative effect of 4-(α-L-rhamnopyranosyloxy) benzyl glucosinolate (glucomoringin; GMG) in SH-SY5Y human neuroblastoma cells. GMG is an atypical member of the GL family present mainly in Moringa oleifera Lam, a vegetable belonging to the Moringaceae family.

Materials and methods: To estimate the anti-proliferative activity of GMG in SH-SY5Y cells, we performed both the MTT test and the cell count assay. Potential drugs cytotoxicity was evaluated by both LDH assay and trypan blue test. Cell death induced by GMG was also assessed by fluorescence-activated cell sorting (FACS) analysis using the annexin-V/iodide propidium (PI) staining. Cytofluorimetric studies were also used to check the progression of cells through the cell cycle, using the PI. In order to evaluate the effect of GMG on the expression of proteins and genes involved in apoptotic processes, we performed both western blotting and Real Time-PCR analyses, respectively. Finally, we investigated any possible involvement of NF-κB in the inhibition of SH-SY5Y cell growth caused by GMG.

Results: We found that GMG significantly reduced SH-SY5Y cell growth through a mechanism involving the activation of apoptotic machinery. In addition, it increased the cell population in both G2and S phases, as well as decreased that in the G1phase. Studying the drug mechanism of action, we found that GMG was able to enhance the expression of p53, p21, and Bax at both protein and transcriptional level. Moreover, exposure of SH-SY5Y cells to GMG significantly increased the gene expression of both caspase 3and 9and induced their cleavage, thereby initiating an intrinsic apoptotic cascade. Finally, GMG inhibited nuclear translocation of NF-κB.

Discussion and conclusion: Our study demonstrates the ability of GMG to reduce the growth of SH-SY5Y cells and reveals its mechanism of action, suggesting its promising role as an anticancer drug.