Nano-Formulated Quercetin: A Novel Therapy for Neuroblastoma by the Re-expression of RIZ1

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Neuroblastoma is an aggressive pediatric cancer, with two thirds of all cases found in children ages five or younger. Current drugs cause adverse side effects which greatly affects the developmental milestones in children. Therefore, a new therapeutic drug will be needed to treat neuroblastoma effectively and reduce a patient's side effects. Studies found that RIZ1, a tumor suppressor gene is silenced in the aggressive neuroblastoma cell line, IMR-32, while SK-N-SH and GM-11027 (less aggressive) showed moderate expression. Studies identified that RIZ1 is silenced in the aggressive forms of neuroblastoma is due to promoter methylation. Quercetin, a natural flavonoid, re-expressed RIZ1 and inhibited the growth and division of neuroblastoma cells. These studies determined that quercetin is able to demethylate the promoter region of RIZ1 and further confirmed that Quercetin dose dependently inhibited DNMT enzyme with an IC50 of 50 µM using a DNA methyl transferase (DNMT) enzyme assay. This is the first report indicating that Quercetin has DNMT inhibitor activity. As a natural product, Quercetin requires a higher concentration to exert a significant therapeutic effect and therefore increases the possibility of unwanted side effects. Quercetin was successfully encapsulated to the chitosan nanoparticle (CNP- Q) and which resulted in the nanoformulation with a size of 152 nm and an action potential of 43 mV. The cellular internalization of CNP-Q is greater than Quercetin itself and has also shown that it induces cytotoxicity and re-expresses RIZ1 in IMR-32 using a lower dose. Results indicate that nanoformulation of Quercetin has a great potential to develop into a drug for the future treatment of neuroblastoma.