Rosmarinic Acid Attenuates Malignant Phenotypes in vivo via DNMT1 Gene Pathway: Implications for Cancer Therapeutics

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Despite increasing cancer incidence globally, few alternative treatments to chemotherapy and radiation exist. These standard therapies require specialized equipment, are costly, and have serious side effects. Recent research into natural polyphenols as anticancer agents has been inconclusive. This study synthesized pure rosmarinic acid (RosA) from spearmint (Mentha spicata) and evaluated its ability to inhibit blastema formation in planarians (Schmidtea mediterranea), modeling growth and metastasis in breast and colon cancers. Overexpression of DNA methyltransferase-1 (DNMT-1) promotes aberrant methylation in these cancers. Furthermore, planarians regenerate using pluripotent stem cells, identical to tumor formation. Planarians were split into groups A (with RA) and B (control). Blastema size was quantified by imaging software. Regeneration was tracked over 2 weeks, approximating percentage regeneration. A western blot evaluated RA's effect on DNMT-1 levels. Results showed RA reduced blastema formation by ~96%, likely by inhibiting DNMT-1 expression. Western blot analysis revealed 96% lower DNMT-1 levels in group A vs B and cytotoxicity was under 5%. The significant DNMT-1 decrease suggests RA may reduce DNMT-1 transcription/translation, normalizing methylation. These findings strongly support pure RA's potential as an alternative, natural therapy for cancers involving DNMT-1 dysregulation, with minimal cytotoxicity.