Anacardic Acid Analogs as Inhibitors of Matrix Metalloproteinase-2 for the Prevention of Cancer Metastasis

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Cancer metastasis is the cause of ninety percent of cancer deaths. The collagenase, Matrix Metalloproteinase-2 (MMP-2) has been identified to have a critical role in the proliferation of cancer metastases. Recent studies have identified anacardic acid, the primary constituent of Cashew Nut Shell Extract (CNSE), to be an effective inhibitor of MMP-2. However, anacardic acid has been found to have a very low cellular permeability, generating a need for analogs with increased inhibition of MMP-2 that would be more suitable as drug compounds. Therefore, analogs of anacardic acid that have increased inhibition of MMP-2 can be identified and developed into potential drug-like lead compounds for the prevention of cancer metastasis. Computational docking studies and enzymatic inhibition studies were utilized to identify analogs of anacardic acid and assess their inhibitory strength. Anacardic acid's binding energy and half maximal Inhibitory Concentration value (IC50) to MMP-2 was used as a standard of comparison for the analogs tested. Fourteen (14) analogs labeled A-N were identified and screened through computational docking studies, generating two (2) analogs, Analog G and Analog H, with higher predicted binding strengths to MMP-2 as compared to anacardic acid. Inhibition of MMP-2 was found at higher concentrations with IC50 values of 15.10 μM for anacardic acid, 75.10 μM for Analog G, and 13.03 μM for Analog H, indicating that Analog G was a weaker inhibitor of MMP-2, and Analog H was a stronger inhibitor of MMP-2. Therefore, Analog H has significant potential for development into a leading drug compound for the prevention of cancer metastasis.

Awards Won:
American Chemical Society: Second Award of $3,000