

Synthesis A Series of Anthra[1,2-*d*]imidazole-6,11-dione Derivatives as Telomerase Inhibitors

Chun-Liang Chen (陳俊良)¹, Fong-Chun Huang (黃豐淳)², Jing-Jer Lin (林敬哲)^{2*}, Hsu-Shan Huang (黃旭山)^{1*}

¹*School of Pharmacy, National Defense Medical Center, Taipei 114, Taiwan;* ²*Institute of Biopharmaceutical Sciences, National Yang-Ming University, Taipei 112, Taiwan*

huanghs@ndmctsgh.edu.tw

Telomere is the nucleoprotein structure at the end of eukaryotic chromosomes, and functional telomeres are essential for continued cell proliferation. Because of the end replication problem, telomere is shortened by 50-60 bases whenever cell division happens, and this erosion induces apoptosis when its length became critically short. The enzyme telomerase is able to perform this function of length extension, since it is a specialized reverse transcriptase with an endogenous RNA template on which successive telomeric repeats are synthesized. Most human tumors not only express telomerase but also have very short telomeres, whereas telomerase activity is either reduced or absent in normal tissues, making the inhibition of telomerase an attractive target for cancer therapeutics. In the recent research shown that inhibition of telomerase can be achieved with appropriately planar aromatic structure such as anthraquinone derivatives. This inhibition is believed to occur as a result of the stabilization of telomeric DNA by these compounds as folded G-quadruplex structures. A series of anthra[1,2-*d*]imidazole-6,11-dione derivatives were synthesized for the development of human telomerase inhibitors as potential anticancer agents, which will be evaluated for their effects by TRAP assay, cell proliferations and cytotoxicity by MTT assay, hTERT expression by SEAP assay.