

Design and Synthesis of 1-Arylpyrrolo[3,2-c]quinoline Derivatives as Potential Anticancer Agents

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Combrestastatin A4 (CA-4) is a well known potent tubulin polymerization inhibitor. It is structurally similar to colchicines and competes on the position of microtubule with colchicines. The structural features of CA-4 possess two aryl rings in the *cis* conformation with methoxy groups on the aryl rings. The derivatives of CA-4 have been proved to have great inhibitor activity against tubulin polymerization. Quinoline derivatives have great biological activities in many aspects, and our results have shown that quinazoline derivatives with anilino substituents on the 2-position exhibited good anticancer activity. A benzoyl group was introduced onto the 4-position of quinazoline to mimic CA-4. However, our results showed that even methoxy groups introduced onto the benzoyl moiety and 6,7-position of quinazoline could not achieve a good anticancer activity. It was reasoned that the two aromatic rings are not in *cis* conformation. Therefore, derivatives of 1-arylpyrrolo[3,2-c]quinoline were designed to force the two aromatic rings in *cis* conformations. The biological results showed that 3-OMe, 4-OMe, 3,4-OMe and 3-OH-4-OMe on the 1-phenyl group played an important role in 1-aryl-4-methyl-2,3-dihydropyrrolo[3,2-c]quinoline derivatives. The aromatic planar structure is assumed essential to the inhibitory activity. We hope that the results presented here will promote further research on this series of compounds as potential anticancer therapeutic agents.

