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Design and synthesis of new 1,3,4-benzotriazepin-5-one derivatives and their biological evaluation as tubulin polymerase inhibitors

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During mitosis, tightly regulated microtubule dynamics is essential for spindle formation and chromosomal separation. Microtubules are cylinder-shaped protein polymers composed of α -tubulin and β -tubulin heterodimers arranged head to tail. Microtubules are elements of the cell cytoskeleton that play key roles in cell division and cell shape. Indeed, targeting tubulin is a successful strategy for cancer therapy. Many natural and synthetic products of varied structures bind to the colchicine site of tubulin, thus suggesting a high plasticity of tubulin at the colchicine site. Combretastatins are strong inhibitors of tubulin polymerization, which have attracted much attention owing to their potent cytotoxic and vascular disrupting activities. Many SAR studies have established the key structural elements responsible for high antitubulin and cytotoxic activities in combretastatins and related compounds are the trimethoxyphenyl ring. Several rings were synthesized as tubulin polymerase inhibitors in addition to inducing apoptosis. 1,3,4-benzotriazepine ring system was previously synthesized and was found to have anti-tumor effect by inhibition of several enzymes. Combining both colchicine and combrestatins structures new 1,3,4-benzotriazepine analogues were designed, their docking to the tubulin site has been studied, finally their inhibition of tubulin polymerase and anti-tumor effect were screened.

Biography

Lamia W Mohamed has completed her PhD in the year 2005 from Cairo University and Postdoctoral studies from Faculty of Pharmacy, Cairo University (FOPCU). She is the Director of Career Center, FOPCU. She has published more than 10 papers in reputed journals and has been serving as member in the American Chemical Society. She is also a Reviewer at Science Publishing Group. In addition, she has participated in organizing both 5th and 6th International conferences of Faculty of Pharmacy, Cairo University.

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