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Discovery of anticancer agents-synthetic scaffolds

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As part of a program aimed at the development of selective estrogen receptor modulators (SERMs), novel chromene scaffolds, benzopyranobenzoxapanes, were discovered. Many compounds showed binding affinity as low as 1.6-200 nM, displayed antagonist behaviors in the MCF-7 human breast adenocarcinoma cell line as well in Ishikawa cell line with IC50 values in the range 0.2-360 nM. On the basis of the side chain substitution, various compounds demonstrated strong inhibitory activity in anti-uterotropic assay. Many compounds were evaluated in several in vivo models of estrogen action. Relative to a full estrogen agonist (ethynyl estradiol) and the SERM raloxifene, one of the molecule was found to be a potent SERM that behaved as antagonist in the uterus and exhibited estrogen agonistic activity on bone, plasma lipids, hot flush, and vagina. The overall pharmacokinetic profile and stability were significantly improved compared to those of the phase 2 development compound.

Biography

Prior to completing her doctoral thesis, Dr. Bhoga was a senior chemist in an industrial position. For her doctoral thesis project, Dr. Bhoga developed various new synthetic approaches to various biologically active natural products, evaluated them as antimicrobial agents and human platelet aggregation inhibitors. Her doctoral work was published in internationally reputed scholarly journals: Tetrahedron Letters, 2005, 46, 5239-5242, European Journal of Medicinal Chemistry, 2007, 42(8), 1144-1150, Tetrahedron Letters, 2004, 45, 9483- 9485. After earning her Ph.D., Dr. Bhoga served as a researcher in several prestigious research institutions in Germany, Spain and South Africa. Her work in these countries focused on the development of new bioactive agents against cancer. Dr. Bhoga developed selective inhibitors of 17ß-Hydroxy Steroid Dehydrogenase type 1, a steroidogenic enzyme that catalyzes the formation of the most active estrogen to estradiol (E2). Her work was published in Journal of Medicinal Chemistry, 2008, 51, 4685–4698. Dr. Umadevi Bhoga's research in the area of supramolecular chemistry focused on the synthesis and characterization of 2,2,6,6-tetramethylpiperidine N-oxide (TEMPO) functionalized G(4)-PAPAM dendrimers. Because dendrimers are being applied for many applications including drug delivery, antibacterials, and materials chemistry, their characterization is important. Dr. Umadevi Bhoga worked on the synthesis protocol for obtaining TEMPO-functionalized PAMAM dendrimers. Studies with these dendrimers are extremely important because they provide researchers with a high level of understanding of the influence of molecular structures on binding interactions.