Synthesis and biological activity of natural product (±)-hibiscone B: discovery of a potential new class of chemotherapeutics

Goess, B.[1], Rawlings, J.[2], *Roth, P.[3], Johar, S.[3,4], Rudd, H.[3], Tryon, H.[3]

[1]Professor, Department of Chemistry, Furman University, [2]Associate Professor, Department of Biology, Furman University, [3]Undergradate Research Assistant, Department of Chemistry, Furman University, [4]Undergraduate Research Assistant, Department of Biology, Furman University
peyton.roth@furman.edu

Keywords: Furanosesquiterpenoid, Furanosteroid, Hibiscone B, Total Synthesis, PI(3)K

Abstract: Despite remarkable progress in cancer treatment since the first chemotherapeutics were developed in the 1940s, the desire for more efficient and selective treatments necessitates the search for new classes of chemotherapeutics. Small molecules that inhibit enzymatic pathways associated with cell proliferation are invaluable, since cancers are characterized by rapid cell division. The PI3K pathway has recently garnered considerable interest in pharmaceutical industries, because mutated PI3K contributes to rapid cell proliferation in many cancers. Accordingly, discovering small molecules that inhibit PI3K could lead to the production of a new class of chemotherapeutics. We have previously established an efficient synthesis of hibiscone C and demonstrated that hibiscone C readily inhibits PI3K; however, the synthetic pathways to other members of the hibiscone family have yet to be explored. Herein, we present a novel and efficient synthesis of hibiscone B starting with hibiscone C. Additionally, we report on the ability of hibiscone B to inhibit PI3K activity in mice T-cells, which closely mimic cancer cells. Our discovery that hibiscone B significantly impedes PI3K function supports the potential of hibiscone family products as chemotherapeutics, suggesting an exciting new synthetic route in chemotherapeutic development.