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Taming tumor growth with plant-derived natural compounds: A case study with noscapinoids

Joshi Harish
Emory University School of Medicine, USA

Meadow saffron plant (*genus-Colchicum*) was known to be toxic because of an orally available toxin, colchicine. Colchicine led to the discovery of the major protein, tubulin that assembles into cellular microtubules (MTs). MTs are responsible for maintaining fidelity of chromosome segregation during cell division and axonal integrity and transport in post-mitotic neurons. Using a chemical-genetic approach, we identified noscapine as a "mutant" colchicine that binds tubulin, but unlike colchicine that depolymerizes MTs, noscapine alters only subtle Microtubule behaviors (e.g., polymerization/depolymerization dynamics). This has led to the development of a series of a novel class of anti-cancer compounds that mitigate Mt dynamics enough to activate cell cycle checkpoints that halt the progression of cell cycle in normal cells. Cancer cells with compromised checkpoints lead to gain or loss of many chromosomes, a prelude to cellular self-destruction. We will present the discovery methods and synthesis of these compounds, and also elucidate the behavior of prostate cancer cells under compromised Mt-dynamics by novel class of chemicals. This is an example of natural small molecules combined with *in silico* analyses leading to discovery important plant-derived chemotherapeutic intervention of disease.