# Design and Evaluation of Betulin-Based Anti-Cancer Compounds

Chakradhar, Anjali

Betulin is a compound found in the bark of birch trees. Betulinic acid, a betulin derivative, exhibits ready availability and selective cytotoxicity as an anti-cancer agent, as designated by the National Cancer Institute (NCI). However, there are no betulin-based anti-cancer drugs today because of betulin's poor solubility in aqueous media like blood and weak activity against cancer cell lines in low (nM) concentrations. There is a critical need to modify the molecular structure of betulinic acid to increase its efficacy against cancer cells. This project designs and evaluates novel betulin-based anti-cancer compounds. To extract betulin from the birch bark, several organic solvents were considered, and chloroform produced the highest crude yield. To purify the crude solid, several solvents were considered and ethanol produced the most pure product. Betulonic acid was synthesized from betulin through an oxidation reaction where the primary and secondary alcohol groups were replaced by a carboxyl group and ketone respectively. The ketone was then reduced to a hydroxyl group to produce betulinic acid. To improve bioavailability, the molecular structure of betulinic acid was modified to realize different analogs. Specifically, betulinic acid was combined with several different amines to synthesize amides. The potency of three betulin analogs were evaluated in-vitro on prostate cancer cell-lines. The tests showed the compounds are effective on cancer cells in micro-molar concentrations. However, for approval as a drug, it is necessary that the compounds are effective in the nano-molar concentrations. The design is being further modified by exploring the addition of other active agents to betulin and the synthesis of betulin-based salts to further increase solubility.

**Awards Won:**
Fourth Award of $500