

Anticancer Podostatin Compounds

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Technology description

The promise of natural compounds as productive sources of new anticancer and antiproliferative drugs continues to expand. Dr. Pettit and his team have been at the forefront of discovering, isolating and synthesizing natural compounds for anticancer and antimicrobial activities as well as other indications for a long time. With the recent developments in the antibody-drug conjugate (ADC) space, there is a renewed interest in natural products as a source of potent payload for ADCs. Dr. Pettit is one of the key players that helped advance the ADC space.

Bridelia ferruginea has been used for many years in African traditional medicine for the treatment of many ailments including diarrhea, dysentery and sterility. The plant genus has over 60 species and has been extensively studied. Several compounds have been discovered that lower fasting blood sugar levels, treat liver disorders as well as promote rheumatic pain relief. While many constituents were discovered, including podophyllotoxin compounds, there is a need to identify new analogs that have suitable cancer cell growth inhibition values and that contain an easily derivatizable group for conjugation.

Dr. Pettit and his team at Arizona State University evaluated the *B. ferruginea* cancer cell growth inhibitory constituents and developed 4-azapodophyllotoxins, pharmaceutical compositions with an easily derivatizable group for conjugation. These compounds have exceptional cell growth inhibition values. SAR studies were conducted focusing on 4-aza-podophyllotoxin structural modifications resulting in even more potent cancer cell growth inhibition. The method of action appears to center around arresting cell division at the metaphase by inhibition of tubulin polymerization.

These potent cancer cell growth inhibitors have a long patent life and are highly amenable to conjugation to further increase their utility and selectivity as well as reduce potential side effects.

Application area

- Cancer cell growth inhibitors
- o Potential application as a free drug
- Anti-insect, antiparasitic, DNA damaging & vascular-disrupting targets

Advantages

Potent inhibitors of cancer cell growth (GI50 0.1 to <0.03 $\mu\text{g/mL}$)
Derivatizable group for convenient conjugation to antibodies through a linker
Potential application as a free drug
Intrinsic tumor targeting property
Total and efficient synthesis achieved

Institution

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