Novel Derivatives of Withanolides as Anticancer Agents

Summary:
The invention is a novel composition of matter showing potent anti-cancer properties.

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Applications:
Cancer treatment.

Overview:
Withanolides are present primarily in the Solanaceae family, and have attracted interest in recent years mainly due to their exhibition of significant biological activities, inclusive of antimicrobial, antitumor, anti-inflammatory, immunomodulatory, and insect-antifeedant activities. It has been reported that those withanolides displaying the most promising antitumor characteristics contain an α,β-unsaturated ketone in ring A, a 5β,6β-epoxy group in ring B, and a nine-carbon side chain with an α,β-unsaturated δ-lactone group. The typical withanolide, withaferin A contains these three moieties and has been shown in vitro and in vivo to suppress the growth of an array of tumor cells, including breast, pancreatic, prostate, lung, leukemia, and head and neck squamous cell carcinoma (HNSCC), by inducing apoptosis.

How it works:
As part of an ongoing study of withanolides from plant sources at University of Kansas, a library of 224 native plant extracts from the U.S. Great Plains was evaluated for cytotoxic activities against HNSCC and melanoma cell lines using the MTS viability assay. One of the most promising leads, Physalis longifolia, commonly known as “long leaf groundcherry”, was subjected to a phytochemical investigation. Several novel compounds were isolated from the aerial parts ofPhysalis longifolia. Novel derivatives of these compounds were designed and synthesized that showed potent cytotoxicity against human head and neck squamous cell carcinoma (JMAR and MDA-1986), melanoma (B16F10 and SKMEL-28), and normal fetal fibroblast (MRC-5) cells with IC50 values as low as 67 nM.

Additional Web Content:
Contact the inventor, Jeffrey Aube, Mark Cohen, Abbas Samadi, Barbara Timmermann.

Patents:
US 2012/0196815