**Anticancer and Neuroprotective Agents**

**Summary:**
The invention is a group of novel analogs and derivatives of novobiocin that inhibit heat shock protein 90 (Hsp90) protein. Hsp90 is the master regulator of the heat shock response and assists in folding proteins. These novel analogs have been shown to be effective anticancer and neuroprotective agents.

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**Overview & Applications:**
Diabetic Peripheral Neuropathy (DPN) is a common complication in diabetic patients. Consequences of DPN include sensory deficits and microvascular disease, which leads to foot ulcers and gangrene. KU-32, a novobiocin analog has been shown to reverse the effects of DPN in mice. Mice were rendered diabetic and developed increasing severe mechanical hypoalgesia and thermal hypoalgesia. Upon KU-32 administration these conditions were reversed.

Hsp90 assists in the proper folding of numerous mutated or over expressed signal transduction proteins that are involved in cancer. Consequently, there is considerable interest in developing chemotherapeutic drugs that specifically disrupt the function of Hsp90 thus hindering the proliferation of cancer cells. One of the novobiocin analogs, KU-135, has been used to induce anti-proliferative effects in Jurakat Tlymphocytes (Human Leukemic Cells).

**Why it is better:**
The new Hsp90 inhibitors have decreased toxicity, increased solubility, and/or increased selectivity for Hsp90. In addition to being nontoxic, KU-32 absorbs into the blood stream very well. The potency of KU-135 was compared to that of 17-AAG, an established HSP90 inhibitor. Results indicate that KU-135 more potently inhibits cell proliferation by regulating signaling pathways that are mechanistically different that those targeted by 17-AAG.

**Patents:**
AU 20053/3001957; Europe 1807440; 2438078; US 7,622,451; 7,608,594; 7,811,998; 7,960,353; 8,212,011; 8,212,012; 2012/0252745.

**Additional Web Content:**
Contact the inventor, Brian Blagg.