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DDD-028: A potent, neuroprotective, non-opioid medication for the treatment of chemotherapy induced peripheral neuropathy (CIPN)

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Chemotherapy induced peripheral neuropathy (CIPN) is a painful and major dose-limiting side effect of cancer treatment that can interrupt or lead to discontinuation of therapy. Current CIPN medications, including *oxycodone* and *duloxetine*, relieve pain but have no effect on underlying CNS tissue damage. Disease modifying medications to treat CIPN as well as other neuropathies remains a critical unmet need, and our extensive work on pentacyclic *pyridoindole* scaffolds resulted in the identification of DDD-028 (1) for the treatment of CIPN. DDD-028 displays potent analgesic activity CIPN and other well-accepted models of neuropathy. DDD-028 displays no activity at any of the key off-target receptors, including opioid, cannabinoid, NMDA, or dopamine receptors. Chronic administration of paclitaxel along with DDD-028 over an 18-day period demonstrated that DDD-028 is exerting a prophylactic effect against CIPN. Plasma neurofilament assay and intraepidermal nerve fiber (iENF) density demonstrated that DDD-028 is neuroprotective. Histopathological analysis of tissues from the spinal cord and the key areas of the brain involved in pain sensation indicates that DDD-028 is preventing astrocyte proliferation and damage. DDD-028 is well tolerated in all of the tests and does not induce sedation in any

of the animals tested.

Recent Publications

1. Raghavan Rajagopalan (2021): Pain Relieving and Neuroprotective Effects of Non-opioid Compound, DDD-028, in the Rat Model of Paclitaxel-Induced Neuropathy. *Neurotherapeutics*. 18(7).
2. Raghavan Rajagopalan (2013). The synthesis and comparative receptor binding affinities of novel, isomeric pyridoindolobenzazepine scaffolds: *Bioorg Med Chem Letter*; 24(2):576-9

Biography

Raghavan Rajagopalan has over 35 years of experience in diagnostic and therapeutic drug discovery and developmental research. He has considerable medicinal chemistry expertise in oncology, nephrology, and pain, focusing on radiotherapy and phototherapy. He has made a pioneering contribution to Type 1 phototherapy of tumors. He was principally responsible for IND and NDA applications for 4 drug candidates, of which one is in the market and the other is undergoing Phase 2 clinical trials. In addition to his research work, he is a Registered Patent Agent with the United States Patent & Trademark Office. He has over 100 patents and 30 publications, of which four are pioneering works in oncology, pain, and nephrology.

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