

Synthesis of analogs of natural tubulin polymerization inhibitors using Parsley and Dill seed extracts

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Abstract

Analogs of antimitotic natural products combretastatin A-4 (CA4), podophyllotoxin (PT) and flavanoids were synthesized using allylpolyalkoxybenzenes from Dill and Parsley seed essential oils. The targeted molecules were evaluated *in vivo* in a phenotypic sea urchin embryo assay for antimitotic and microtubule destabilizing activity. Structure activity relationship studies identified mostly active molecules with polymethoxyphenyl rings as potent antiproliferative agents. The effective threshold concentrations (EC) resulting in mitotic abnormalities in the sea urchin embryos were 0.25-1 nM. These molecules displayed high cytotoxicity against a panel of 60 human cancer cell lines including multi drug resistant cells. Cytotoxic effect of tested compounds was attributed to microtubule destabilization resulted in cell cycle arrest followed by apoptotic cell death. Considering encouraging data from phenotypic and mechanistic studies, some compounds may prove to be lead candidates for further *in vivo* studies to assess its potential as anti-tumor agents.

Biography:

V V Semenov is working as the Head of Medicinal Chemistry Laboratory from N D Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences. He is the author of 25 patents and 280 scientific articles. His research project is on application of nitrogen heterocycles and nitrocompounds in drug design; synthesis of analogs of natural antimitotics using

allylpolyalkoxybenzenes from dill and parsley seed essential oils; biological evaluation of compounds as tubulin modulators in the original sea urchin embryo assay and; development of chemical library for screening for anticancer, antibacterial, and antifungal activities in cooperation with National Cancer Institute (Bethesda, USA) and the University of Queensland (Brisbane, Australia).