A Natural Organic Compound “Decursin” Exhibits Antitumor and Renoprotective Effects in Osteosarcoma

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Introduction:
Combination chemotherapy including cisplatin is the standard treatment for osteosarcoma. However, high-dose cisplatin can cause severe side effects, such as nephrotoxicity. Enhancing the efficacy of cisplatin could allow dose reduction and minimize adverse events. Decursin is a plant-derived natural compound that has been reported to exert antitumor effects in several cancers. The aim of this study was to investigate both the sensitizing effect of decursin on cisplatin activity and its direct antitumor effects in osteosarcoma cells.

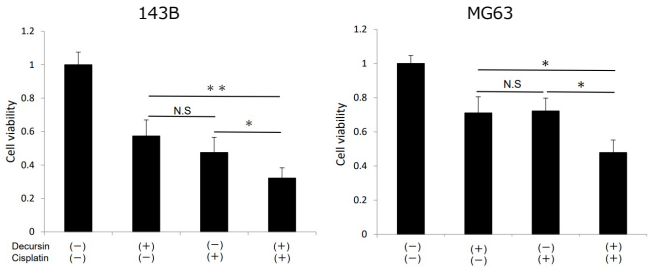
Methods:
In vitro, human osteosarcoma cell lines were treated with decursin, cisplatin, or a combination of both. Synergistic effects were quantified using the Combination Index. Antitumor effects of decursin alone were evaluated by assays of cell proliferation, apoptosis, cell cycle distribution, and signaling pathway analysis.
In vivo, subcutaneous xenograft models were established using human osteosarcoma cells. Mice were divided into vehicle, decursin monotherapy, cisplatin monotherapy, and combination groups. Tumor volume was monitored, and at 3 weeks post-treatment, blood biochemistry, kidney weight, and histological evaluation were performed.

Results:
In vitro, co-treatment with decursin and cisplatin significantly enhanced growth inhibition and apoptosis compared with cisplatin alone. Decursin alone inhibited osteosarcoma cell proliferation in a dose- and time-dependent manner, induced apoptosis, and reduced the proportion of cells in S phase. Mechanistically, decursin suppressed phosphorylation in the Akt–NF-κB–COX2 pathway and downregulated downstream effectors, including Bax/Bcl-2 and Cyclin D1/CDK4, in a dose-dependent manner.
In vivo, the combination group exhibited the smallest tumor volume compared with all other groups. Moreover, compared with cisplatin alone, the combination group showed lower serum creatinine and blood urea nitrogen levels, and histological evaluation revealed attenuated renal atrophy and proximal tubular cell degeneration.

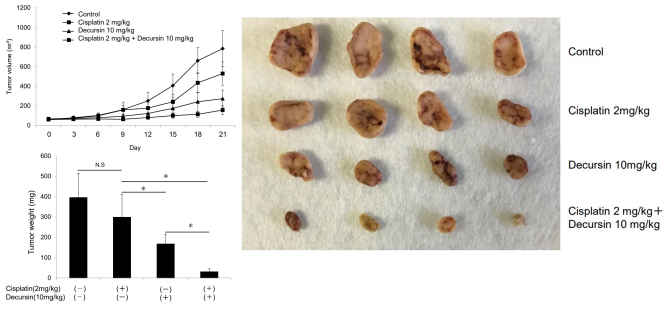
Discussion:
Decursin not only exerted intrinsic antitumor effects on osteosarcoma cells but also enhanced the therapeutic efficacy of cisplatin. Importantly, decursin demonstrated a renal protective effect, mitigating cisplatin-induced nephrotoxicity. These findings support the potential of decursin as a novel therapeutic agent for osteosarcoma.

Significance/Clinical Relevance:
This study highlights decursin as a promising adjunct to cisplatin-based chemotherapy in osteosarcoma. By simultaneously enhancing antitumor efficacy and reducing nephrotoxicity, decursin may improve both the therapeutic index and tolerability of current treatment regimens. Translation of these findings into clinical practice could significantly impact patient outcomes by offering a safer and more effective therapeutic strategy for osteosarcoma.

RealTime-Glo™ MT Cell Viability Assay



Tumor Volume and Weight



Effects on kidney