

Effects of polysaccharide peptide (PSP) from *Coriolus versicolor* on the pharmacokinetics of cyclophosphamide in the rat and cytotoxicity in HepG2 cells.

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Polysaccharide peptide (PSP), isolated from *Coriolus versicolor* COV-1, has been shown to restore the immunological effects against cyclophosphamide-induced immuno-suppression, although the mechanism(s) involved remain uncertain. This study investigated the PSP-cyclophosphamide interaction by studying the effects of PSP on the pharmacokinetic of cyclophosphamide in the rat and the effect of PSP on the cytotoxic effects of cyclophosphamide on a cancer cell line (HepG2 cells). In the pharmacokinetic studies in the rat, acute pre-treatment of PSP (4 micromol/kg/day, i.p.) decreased the clearance (CL) of cyclophosphamide by 31%, with a concomitant increase in the area under concentration-time curve (AUC) by 44%, and prolongation of the plasma half-life ($T(1/2)$) by 43%. Sub-chronic pre-treatment of PSP (2 micromol/kg/day, i.p., 3 days) decreased the CL of cyclophosphamide by 33%, with a concomitant increase in the AUC by 50%, and prolongation of the plasma $T(1/2)$ by 34%. In cytotoxicity studies using HepG2 cells, non-toxic dose of PSP (1-10 microM) enhanced the cytotoxicity of cyclophosphamide. PSP at 10 microM further decreased HepG2 cell viability by 22% compared to when cyclophosphamide was present alone. In summary, PSP enhanced the cytotoxic effect of cyclophosphamide on a cancer cell line in vitro and altered the pharmacokinetics of cyclophosphamide in vivo in the rat. Both of these effects may be beneficial in the use of PSP as an adjunct to cyclophosphamide treatment.