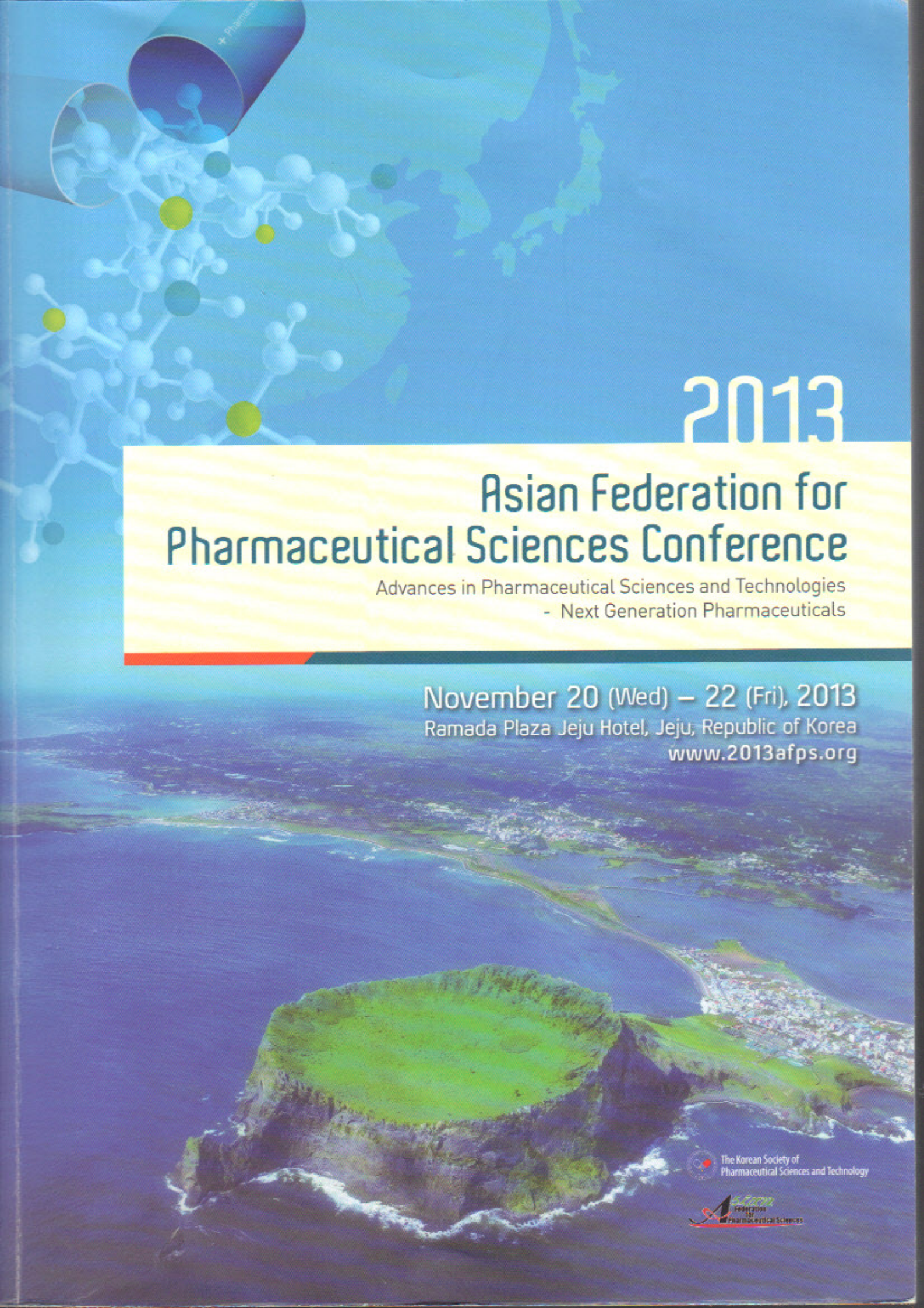

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Sphingolipid and pluronic® polymer based solid lipid nanoparticles of docetaxel for enhanced bioavailability and to overcome MDR

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Purpose. Ceramide or TMP-I based docetalxel solid lipid nanoparticles were prepared using Trymyristin as main lipid containing P85 for intravenous delivery to overcome multi drug resistance.

Methods. The prepared nanoparticles were characterized by TEM, particle size analysis, drug content, cellular uptake and cytotoxicity in resistant breast cancer cell line MCF-7 ADR. The docetaxel nanoparticles composed of ceramide or TMP-I with P85 and Trimyristine with a mean diameter of 80 -150 nm were prepared by hot high pressure homogenization. The drug release was low compared to Taxotere® ensure a long time drug release profile. The prepared SLNs showed higher cellular uptake compared to control formulation in the resistant cell line MCF-7 ADR. This is further ensured by the confocal laser scanning microscopy (CLSM) study using coumarin 6 (C6) cellur uptake studies. The in vitro cytotoxicity study showed that the prepared nanoparticles significantly increased cytotoxic effect in the resistant cell line than that of control.

Results. In vivo pharmacokinetic study in rats at 10 mg/Kg dose showed that the nanoparticles significantly increased the bioavailability (2 fold) than Taxotere®. Antitumore activity of the prepared nanoparticles was assessed in MCF-7ADR cancer Xenograft BALB/C nude mice models showed that the ceramide and TMP-I SLNs significantly reduced the tumor size than Taxotere®.

Conclusion. This study showed that TMP-I and ceramide6 based SLNs significantly enhanced the bioavailability and effective on the resistant tumor. Thus, these formulations could be effective in the treatment of resistant tumors.