Novel α-fetoprotein (AFP) third domain-conjugated PLGA nanoparticles with paclitaxel: pharmacokinetics and biodistribution study

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Intoduction

Paclitaxel (PTX) is a highly hydrophobic anticancer drug, therefore cremophor EL solution is applied for its clinical administration, which causes serious allergic reactions to the subjects after intravenous use [1]. Moreover, PTX implementation is limited due to non-specific distribution throughout the body; toxicity to healthy tissues, limiting the dose and frequency of the treatment. Drug encapsulation into PLGA nanoparticles (NPS) conjugated with vector molecule is a well-known strategy, allowing to rich its active targeted delivery and to enhance its bioavailability [2]. Thus, we developed a novel PTX PLGA nanoparticles conjugated with recombinant α-fetoprotein third domain (rAFP3d-NPs), which is known as a tumor-specific biomarker [3].

Methods

In pharmacokinetics experiments 180 female Wistar rats were randomly divided into three groups, each group being received 6 mg/kg of paclitaxel injection through tail vein in the form of rAFP3d-NPs or PTX cremophor EL solution. At certain time points after dosing, blood samples were collected and organs were harvested followed by extraction and HPLC analysis.

Results

Favorable chromatography conditions allowing the baseline separation of the analyte with the internal standard and other exogenous materials were developed and the HPLC method was validated. All the PTX formulations demonstrated a gradual declining trend after reaching maximum of the concentrations. Pharmacokinetics parameters such as $AUC_{(0-\infty)}$ and $t_{1/2}$ were 3 times higher for rAFP3d-NPs with low clearance rate, compared with PTX cremophor EL solution, indicating longer retention of PTX in systemic circulation. In addition, accumulation of rAFP3d-NPs was predominantly observed in liver and spleen over a period of 12 hours.

Conclusion

A simple and effective HPLC method was provided for the determination of rAFP3d-NPs in rats with good accuracy and precision. Novel PTX delivery system demonstrated prolonged release profile, when compared with PTX cremophor EL solution. Our findings indicate an increase in PTX bioavailability and pharmacokinetics profile improvement and also are the basis for determining the optimal dosing regimen in rAFP3d-NPs further studies on immunodeficiency models *in vivo*.

References

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