7.1 ± 0.6 days. The two drugs showed totally different release behaviors, which can be employed in combination to treat restenosis.

Conclusion Sandwich-type ethylcellulose films loaded with probucol or aspirin were successfully prepared and showed ability to release the two drugs in different ways: rapid release of aspirin to treat thrombus and inflammation typical of early-stage restenosis, and sustained release of probucol for inhibition of VSMC proliferation frequently seen in the later stage of restenosis. These drug-loaded ethylcellulose films provide new insight into restenosis therapy.

47 GAMBOGIC ACID DELIVERY USING LIPID NANOPARTICLES MODIFIED WITH CELL-PENETRATING PEPTIDE

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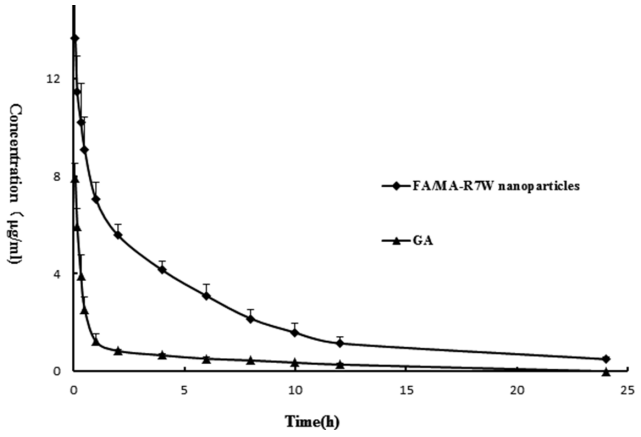
Objectives Gambogic acid (GA) is a novel tissue-specific proteasome inhibitor which can potentially be used to treat cancer with low toxicity. However, poor aqueous solubility (~10 μg/mL) and low tumor cell-specific delivery have limited its clinical application. Clinical application of GA requires the development of delivery vehicles.

Methods In this study, we developed a novel nanoparticle GA delivery system. The nanoparticles incorporate a cell-penetrating peptide conjugated to myristic acid (MA-R7W), a folate modified lipid (FA-PEG2000-DSPE), a pH-sensitive lipid (PEG1000-hyd-PE), eggPC and cholesterol. The lipids formed the nanoparticle shells, and GA was loaded into the lipid bilayer of the nanoparticles. PEG on the surface of the nanoparticles provides a long circulation time. Folate is incorporated to enable targeting of tumor cells with amplified folate receptor expression. PEG1000-hyd-PE can shield/unshield R7W on the nanoparticle surface according to the pH difference between normal tissues and cancer.



Abstract 47 Figure 1 Plasma concentration-time curves in rats for FA/MA-R7W nanoparticles and free gambogic acid (1 mg/kg)

Results In vitro, FA/MA-R7W nanoparticles improved cellular uptake 2.5-fold compared to GA liposomes (without FA-PEG2000-DSPE, AA-R8 and PEG1000-hyd-PE) at pH 5. In vivo, GA encapsulated in FA/MA-R7W nanoparticles induced potent tumor inhibition (62.6%), showed lengthy circulation (Figure 1) and tumor cell targeting.

Conclusions In conclusion, FA/MA-R7W nanoparticles are promising vehicles for GA delivery and warrant further investigation.

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48 TRANSFERRIN-MODIFIED SELF-ASSEMBLED HSA (HUMAN SERUM ALBUMIN) NANOPARTICLES ENHANCE DRUG DELIVERY TO TUMORS

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Objectives Taxanes like paclitaxel (Tax), docetaxel and cabazitaxel are effective chemotherapeutic drugs which have been used in various types of cancer in recent years. Taxanes are highly lipophilic and practically insoluble in water. In addition, their clinical applications are limited by their toxicity to normal tissues. Human serum albumin (HSA) nanoparticles (HSA-Nps) have been shown to be a promising drug delivery system. They act by enhancing the drug's bioavailability in tumors via SPARC. To further improve the targeting efficiency of HSA-Nps, transferrin (Tf) was covalently coupled to the HSA-Nps using NHS-PEG2000-MAL as a bifunctional cross-linking agent, since transferrin receptor is highly expressed in most tumor cells.

Methods HSA-Nps encapsulating paclitaxel (HSA-Nps-Tax) were obtained using the salting-out method. The cross-linking agent was then added to react with the amino groups of HSA-Nps. Meanwhile, sulfhydryl groups were introduced to Tf by 2-iminothiolane, which reacts with the amino groups of transferrin. In the third step, sulfhydryl-reactive transferrin was covalently coupled to the HSA-Nps.

Results Tf-modified HSA-Nps-Tax (Tf-HSA-Nps-Tax) had an excellent mean particle size (180 nm) and stability, and had greater cytotoxicity and apoptosis-inducing activity in MCF-7 cells than HSA-Nps-Tax in vitro. Furthermore, Tf-HSA-Nps-Tax showed greater tumor growth inhibition than HSA-Nps-Tax in vivo, which highlighted the advantage of transferrin targeting of tumor cells.

Conclusions Tf-modified self-assembled HSA Nps are promising targeted carriers for tumor therapeutics.

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