were significantly enhanced by LF. Increased expression of nuclear factor kappa-light-chain-enhancer of activated B cells (NFκB) and inducible nitric oxide synthase (iNOS) was noted in spleen lysates after LF treatment.
Conclusions *L. japonicae flos* extracts exert immumodulatory activity by improving cellular as well as innate immunity in immunosuppressed mice and promoting the secretion of immune-related cytokines via iNOS-related signaling pathways.

Biochemical Pharmacy

44 CORE-SHELL NANOSPHERES FOR PH-RESPONSIVE RELEASE OF ANTICANCER DRUGS AND NEAR-INFRARED IMAGING

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Objectives Nanoscaled drug carriers with pH-responsiveness have attracted extensive interest in view of the acidic environment in cancerous cells. Rapid response to pH changes plays a key role in efficient intracellular drug release. In addition, real-time tracking of drug carriers is important for understanding distribution and targeted accumulation of the drug carriers. This work aims at developing silver selenide quantum dots (Ag_2Se QDs)@carboxymethyl chitosan (CMCS) core-shell nanospheres with encapsulated paclitaxel (PTX) for cancer therapy and bioimaging.
Methods Oleic acid-capping Ag_2 Se QDs were synthesized by a one-pot strategy, washed with ethanol, and obtained by centrifugation. The as-synthesized Ag_2Se QDs were reacted with N-hydroxysuccinimide and conjugated with CMCS at the amino sites. In an aqueous solution of PTX, the hydrophobic oleoyl groups tended to aggregate locally and entrap PTX by hydrophobic interaction, spontaneously producing Ag_2Se QDs (PTX) @CMCS nanospheres.
Results By conjugating the oleic acid-capping Ag_2 Se QDs with pH-sensitive CMCS at a degree of substitution (DS) of 13%, biocompatible core-shell nanospheres loaded with PTX were successfully prepared, which had an average size of 36.3 ± 0.2 nm. The drug loading content (DLC) and drug loading efficiency (DLE) for the PTX was 5.01 ± 0.8% and 52.4 ± 3.2%, respectively. The PTX release half-life was 4.1 hours under conditions resembling the intracellular environment of cancerous cells (37°C, pH 5.0).
Conclusions Core-shell structured Ag_2Se QDs (PTX)@CMCS nanospheres capable of releasing PTX in an acidic environment and emitting NIR fluorescence under NIR laser excitation were synthesized and characterized. The hydrophobic oleoyl groups entrapped PTX via hydrophobic interaction and the oleoyl-CMCS chains were extended at lowered pH to release the otherwise encaged drug. In addition, the encapsulated Ag_2Se QDs can emit bright NIR fluorescence for bioimaging by which nanosphere distribution in a patient can be monitored. This study provides a new approach for developing nanocomposite drug carriers for cancer therapy.

45 PREVENTIVE EFFECT OF *SPARASSIS CRISPA* ON TYPE I DIABETES

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Objectives The purpose of this study was to investigate the preventive effect of *Sparassis crispa* on type I diabetes.
Methods The preventive effect of *S. crispa* extract (0.6 g/kg/day) was investigated using a rat model of type I diabetes established by streptozotocin after 3-week oral administration. The diabetes-related factor index was examined using the ELISA test.
Results Compared to the model group, the *S. crispa* extract administration group showed lower diabetic weight lost ($p < 0.01$), lower fasting glucose levels and lower postprandial 2-hour blood glucose levels ($p < 0.001$). *S. crispa* extract administration can significantly alleviate STZ-induced decrease in glucose tolerance and reduce STZ-induced elevation in endotoxin and iNOS levels. It also effectively suppresses glycosylated hemoglobin accumulation and reduces total bile acid level.
Conclusions *S. crispa* extract has a good preventive effect on type I diabetes. This study provides a theoretical basis for its use in healthcare products and drugs for type I diabetes.

46 SANDWICH-TYPE ETHYLCELLULOSE FILMS FOR CONTROLLED RELEASE OF ANTI-RESTENOSIS DRUGS

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Objectives Restenosis is a response of the vessel wall to balloon-induced injury and is characterized primarily by elastic recoil of the vessel wall and a series of pathological processes including thrombus, inflammation and vascular smooth muscle cell (VSMC) proliferation. To treat restenosis, appropriate drug delivery vehicles are needed which can release therapeutic agents targeting different symptoms into blood vessels in a controlled manner. The main objective of the present study was to prepare sandwich-type ethyl cellulose films with high performance for efficient drug loading and controlled drug release for restenosis treatment.
Methods Sandwich-type ethyl cellulose films loaded with probucol for treating coronary artery disease, or aspirin as an antithrombotic drug, were prepared by casting three individual layers in sequence using an ethyl cellulose/toluene solution. On a glass plate, the first ethyl cellulose layer (bottom layer) was cast without drugs, on to which the middle layer containing probucol or aspirin was then cast. After solvent evaporation at room temperature, a third top layer was cast on to the middle layer. The obtained drug-loading films were further dried at room temperature under vacuum.
Results The sandwich-type ethyl cellulose films exhibited a drug loading content (DLC) of 12.1 ± 0.9% and a drug loading efficiency (DLE) of 73.5 ± 3.6% for aspirin, and a DLC of 11.0 ± 0.8% and a DLE of 69.3 ± 3.4% for probucol. Under physiological conditions (37°C, pH 7.4), the release half-life of aspirin from the films was 2.7 ± 0.2 hours, while that of probucol was

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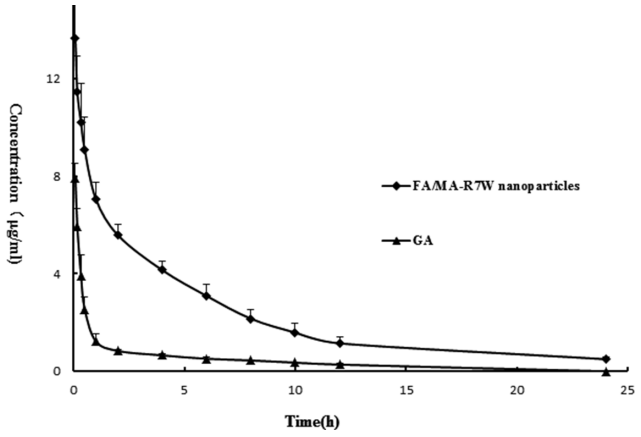
Objectives Gambogic acid (GA) is a novel tissue-specific proteasome inhibitor which can potentially be used to treat cancer with low toxicity. However, poor aqueous solubility (~10 μg/mL) and low tumor cell-specific delivery have limited its clinical application. Clinical application of GA requires the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