学生代表性成果

1. 学生代表性论文

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In vitro/vivo antitumor study of modified-chitosan/carboxymethyl chitosan "boosted" charge-reversal nanoformulation

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Chitosan derivatives
Antitumor nanosystem

ABSTRACT

Major obstacles in the development of nanoformulations as efficient drug delivery systems are the rapid clearance from blood circulation and lysosomal entrapment. To overcome these problems, a polysaccharide-based core-shell type charge-switchable nanoformulation (CS-LA-DMMA/CMCS/PAMAM@DOX) is constructed to improve antitumor efficacy of DOX. By applying carboxymethyl chitosan (CMCS) as bridge polymer and negatively charged chitosan-derivative as outer shell, the stability and pH-sensitivity of this nanoformulation is promisingly enhanced. Furthermore, the positively charged PAMAM@DOX could escape from lysosomes via "proton sponge effect" and "cationic-anionic interaction with lysosome membranes". Admirable cellular uptake and high apoptosis/necrosis rate were detected in this study. *In vitro* assays demonstrate that the CS-LA-DMMA/CMCS/PAMAM@DOX was internalized into HepG2 cells predominantly via the clathrin-mediated endocytosis pathway. Excitingly, *in vivo* studies showed that high accumulation of CS-LA-DMMA/CMCS/PAMAM@DOX in tumor tissue led to enhanced tumor inhibition. Compared with free DOX, the tumor inhibition rate of nanoformulation was improved up to 226%.

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REVIEW | Open Access

Charge reversal nano-systems for tumor therapy

Peng Zhang[1*], Daoyuan Chen[1], Lin Li[1] and Kaoxiang Sun[1,2]

Abstract
Surface charge of biological and medical nanocarriers has been demonstrated to play an important role in cellular uptake. Owing to the unique physicochemical properties, charge-reversal delivery strategy has rapidly developed as a promising approach for drug delivery application, especially for cancer treatment. Charge-reversal nanocarriers are neutral/negatively charged at physiological conditions while could be triggered to positively charged by specific stimuli (i.e., pH, redox, ROS, enzyme, light or temperature) to achieve the prolonged blood circulation and enhanced tumor cellular uptake, thus to potentiate the antitumor effects of delivered therapeutic agents. In this review, we comprehensively summarized the recent advances of charge-reversal nanocarriers, including: (i) the effect of surface charge on cellular uptake; (ii) charge-conversion mechanisms responding to several specific stimuli; (iii) relation between the chemical structure and charge reversal activity; and (iv) polymeric materials that are commonly applied in the charge-reversal delivery systems.

Keywords: Charge reversal, Stimuli-responsive, Nano systems, Surface charge, Antitumor therapy

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Research paper

Design and synthesis of novel hederagonic acid analogs as potent anti-inflammatory compounds capable of protecting against LPS-induced acute lung injury

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ARTICLE INFO

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STING
Acute lung injury

ABSTRACT

Acute lung injury (ALI) presents a significant clinical challenge due to its high mortality rates and the lack of effective treatment strategies. The most effective approaches to treating ALI include disrupting inflammatory cascades and associated inflammatory damage within the lung. Hederagenin was utilized as a core skeleton to design and synthesize 33 hederagonic acid derivatives. Among these derivatives, compound 29 demonstrated potent anti-inflammatory activity without inducing cytotoxicity, inhibiting nitric oxide (NO) release by 78–86 %. Detailed structure-activity relationship studies and the reverse virtual screening of ALI-related targets revealed that compound 29 exhibits a high affinity for the STING protein. Mechanistic studies revealed that compound 29 suppresses macrophage activation, inhibits the nuclear translocation of IRF3 and p65, and disrupts the STING/IRF3/NF-κB signaling pathway, thereby attenuating the inflammatory response. The *in vivo* administration of compound 29 was sufficient to protect against lipopolysaccharide (LPS)-induced ALI by suppressing the production of inflammatory mediators, including IL-6, TNF-α, and IFN-β, thereby preserving lung tissue integrity. These results substantiate the anti-inflammatory efficacy of compound 29, both *in vitro* and *in vivo*, indicating its potential as a promising lead compound in ALI treatment strategies.

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Ocotillol Derivatives Mitigate Retinal Ischemia-Reperfusion Injury by Regulating the Keap1/Nrf2/ARE Signaling Pathway

Xin Zhang,[†] Wen Zhang,[†] Laien Zhao, Gongshan Ma, Yanmei Huang, Zhiyuan Geng, Qian Jiang, Xiaomei Wen, Yuqi Lin, Qingguo Meng, Zhuhong Zhang,* and Yi Bi*

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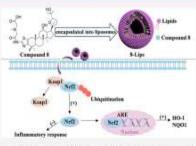

ABSTRACT: Retinal ischemia-reperfusion (RIR) injury can lead to various retinal diseases. Oxidative stress is considered an important pathological event in RIR injury. Here, we designed and synthesized 34 ocotillol derivatives, then examined their antioxidant and anti-inflammatory capacities; we found that compounds **7** (C24-*R*) and **8** (C24-*S*) were most active. To enhance their water solubility, sustained release, and biocompatibility, compounds **7** and **8** were encapsulated into liposomes for *in vivo* activity and mechanistic studies. *In vivo* studies indicated that compounds **7** and **8** protected normal retinal structure and physiological function after RIR injury, reversed damage to retinal ganglion cells, and the *S*-configuration exhibited significantly stronger activity compared with the *R*-configuration. Mechanistic studies showed that compound **8** exerted a therapeutic effect on RIR injury by activating the Keap1/Nrf2/ARE signaling pathway; compound **7** did not influence this pathway. We also demonstrated that differential isomerization at the C-24 position influenced protection against RIR injury.

2. 学生代表性发明专利

证书号第3290441号

发明专利证书

发明名称：具有肿瘤耐药逆转活性的α-常春藤皂苷元衍生物及其制备方法和用途

发明人：毕毅;王洪波;刘现轩;杨延婷;傅风华;倪敬轩;王晓马金波;雷蕾

专利号：ZL 2017 1 0065183.9

专利申请日：2017年02月06日

专利权人：烟台大学

地址：264005 山东省烟台市莱山区清泉路32号

授权公告日：2019年03月12日　　授权公告号：CN 106749494 B

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局长
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2019年03月12日

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其他事项参见背面

证书号第7236325号

专利公告信息

发明专利证书

发明名称：靶向蛋白降解嵌合体分子自组装纳米材料及制备方法与应用

专利权人：烟台大学;烟台市疾病预防控制中心

地址：264005 山东省烟台市莱山区清泉路30号

发明人：刘沙;王晓雯;张晓瑜;楚永超

专利号：ZL 2024 1 0614511.6　　授权公告号：CN 118203646 B

专利申请日：2024年05月17日　　授权公告日：2024年07月26日

申请日时申请人：烟台大学;烟台市疾病预防控制中心

申请日时发明人：刘沙;王晓雯;张晓瑜;楚永超

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2024年07月26日

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证书号第4838993号

发明专利证书

发明名称：基于自组装的电荷反转型核/壳药物载体、其制备方法及应用

发明人：张蓬;李琳;郭妍;孙粤祥

专利号：ZL 2020 1 1320453.4

专利申请日：2020年11月23日

专利权人：烟台大学

地址：264003 山东省烟台市莱山区清泉路30号

授权公告日：2021年12月07日　　授权公告号：CN 112438988 B

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其他事项参见续页

证书号第6492920号

发明专利证书

发明名称：一种组蛋白甲基转移酶抑制剂及其制备方法

发明人：芦静;范哲;浣淑容;巫鑫屿;谢艳秋

专利号：ZL 2023 1 0437364.5

专利申请日：2023年04月18日

专利权人：烟台大学

地址：264005 山东省烟台市莱山区清泉路30号

授权公告日：2023年11月17日　　授权公告号：CN 116478111 B

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2023年11月17日

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