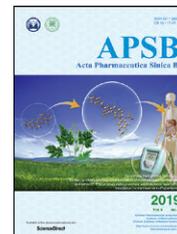




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Reviews

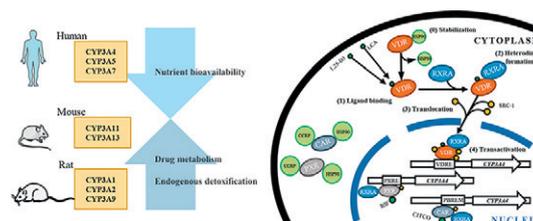
Role of vitamin D receptor in the regulation of CYP3A gene expression

Xuan Qin, Xin Wang

Shanghai Key Laboratory of Regulatory Biology, Institute of Biomedical Sciences and School of Life Sciences, East China Normal University, Shanghai 200241, China

Vitamin D receptor (VDR) regulates the expression of cytochrome P450 3A (CYP3A) in human, mouse and rat. VDR-response elements are found in the promoters of CYP3A genes in different species. This transactivation effect is a potential modulator of nutrient bioavailability and drug metabolism.

Acta Pharmaceutica Sinica B, 9 (2019) 1087



Development and application of hyaluronic acid in tumor targeting drug delivery

Zhijian Luo^a, Yan Dai^b, Huile Gao^c

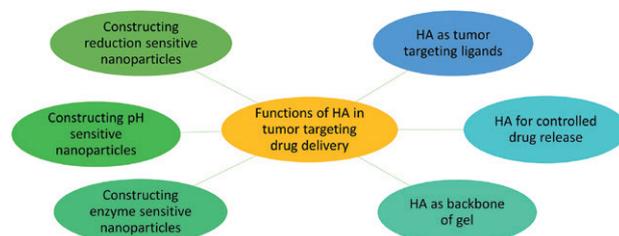
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The review summarizes various applications of hyaluronic acid in tumor targeting drug delivery systems based on the specific CD44-targeting capacity and the hyaluronidase degradation property.

Acta Pharmaceutica Sinica B, 9 (2019) 1099



Annual reviews

Current trends in drug metabolism and pharmacokinetics

Yuhua Li^{a,b}, Qiang Meng^c, Mengbi Yang^d, Dongyang Liu^e, Xiangyu Hou^f, Lan Tang^g, Xin Wang^h, Yuanfeng Lyu^d, Xiaoyan Chen^f, Kexin Liu^c, Ai-Ming Yuⁱ, Zhong Zuo^d, Huichang Bi^a

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^hSchool of Life Sciences, East China Normal University, Shanghai 200241, China

ⁱUC Davis School of Medicine, Sacramento, CA 95817, USA

Understanding of DMPK properties is essential for drug development and precision medication. In this article, we provided an overview of recent research on DMPK with focuses on the regulatory mechanisms of pharmacokinetics, drug–drug interaction, mathematical modeling, non-classical metabolism and so on. Existing challenges and perspectives on future directions are also discussed.

Acta Pharmaceutica Sinica B, 9 (2019) 1113



Recent progress in drug delivery

Chong Li^a, Jiancheng Wang^b, Yiguang Wang^b, Huile Gao^c, Gang Wei^d,
Yongzhuo Huang^e, Haijun Yu^e, Yong Gan^e, Yongjun Wang^f, Lin Mei^g,
Huabing Chen^h, Haiyan Huⁱ, Zhiping Zhang^j, Yiguang Jin^k

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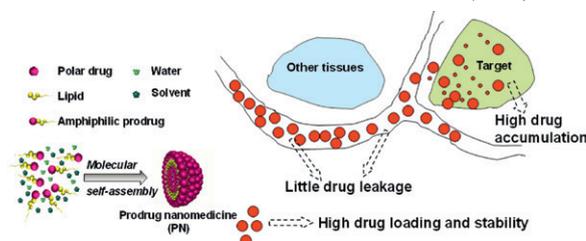
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^jSchool of Pharmacy, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China

^kDepartment of Pharmaceutical Sciences, Beijing Institute of Radiation Medicine, Beijing 100850, China

This review makes a concise overview of current progress in the research of drug delivery systems that focused on the delivery strategies, construction techniques and specific representatives.



Original articles

PEP06 polypeptide 30 is a novel cluster-dissociating agent inhibiting α v integrin/FAK/Src signaling in oral squamous cell carcinoma cells

Gulnara Tuguzbaeva^{a,c,d,e}, Er Yue^b, Xi Chen^b, Lina He^d, Xinlei Li^c,
Jiaming Ju^c, Ying Qin^c, Valentin Pavlov^a, Yanjie Lu^{b,c}, Wenting Jia^{b,c},
Yunlong Bai^{b,c}, Yumei Niu^d, Baofeng Yang^{b,c}

^aCentral Laboratory of Scientific Research, Bashkir State Medical University, Ufa 450008, Russian Federation

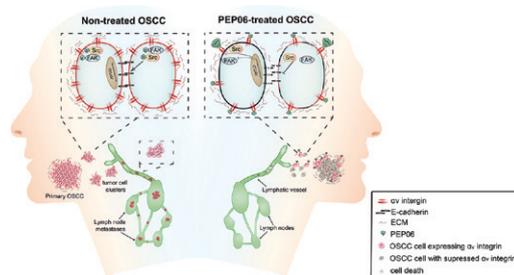
^bDepartment of Pharmacology (State-Province Key Laboratories of Biomedicine-Pharmaceutics of China, Key Laboratory of Cardiovascular Research, Ministry of Education), College of Pharmacy, Harbin Medical University, Harbin 150081, China

^cTranslational Medicine Research and Cooperation Center of Northern China, Heilongjiang Academy of Medical Sciences, Harbin 150081, China

^dDepartment of Endodontics, the First Affiliated Hospital of Harbin Medical University, Harbin 150081, China

^eDepartment of Orthopedic Dentistry and Maxillofacial Surgery, Bashkir State Medical University, Ufa 450008, Russian Federation

PEP06 polypeptide 30, acting as a cluster-dissociating therapeutic agent, possesses the effect of anti-metastatic potential in oral squamous cell carcinoma by inhibiting α v integrin/FAK/Src signaling and disrupting E-cadherin-based intercellular junctions.



Hypericin enhances β -lactam antibiotics activity by inhibiting *sarA* expression in methicillin-resistant *Staphylococcus aureus*

Genzhu Wang^{a,b}, Liang Li^a, Xiukun Wang^b, Xue Li^b, Youwen Zhang^b, Jie Yu^b,
Jiandong Jiang^{b,d}, Xuefu You^b, Yan Q. Xiong^{a,c}

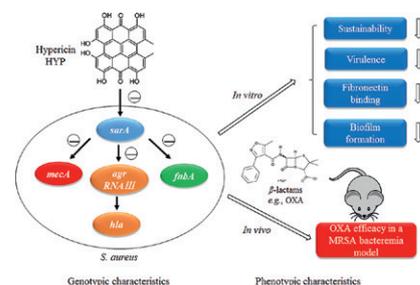
^aLos Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, CA 90502, USA

^bBeijing Key Laboratory of Antimicrobial Agents, Institute of Medicinal Biotechnology, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China

^cGeffen School of Medicine at UCLA, Los Angeles, CA 90095, USA

^dState Key Laboratory of Bioactive Substances and Function of Natural Medicine, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China

In this study, the authors demonstrated that hypericin, as a *sarA* inhibitor, had synergistic activity with β -lactams both *in vitro* and in a murine bacteremia model due to MRSA. The mechanisms may be related to significantly reduced biofilm formation, fibronectin binding and expression of virulence genes (e.g., *fnbA* and *hla*).

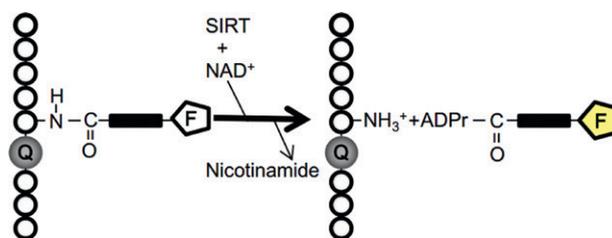


A one-step specific assay for continuous detection of sirtuin 2 activity

Qi Dai, Zhihua Zheng, Fan Xia, Peiqing Liu, Min Li

School of Pharmaceutical Sciences, Sun Yat-Sen University, National and Local United Engineering Lab of Druggability and New Drugs Evaluation, Guangdong Provincial Key Laboratory of New Drug Design and Evaluation, Guangzhou 510006, China

Sirtuins (SIRT2s) are NAD⁺-dependent histone deacetylases with extensive physiological functions. We established a novel strategy for detecting the activity of SIRT2 *in vitro* and in cell lysate. Fluorescence increment of these probes is based on SIRT2-mediated removal of the acyl side chain with fluorophore.



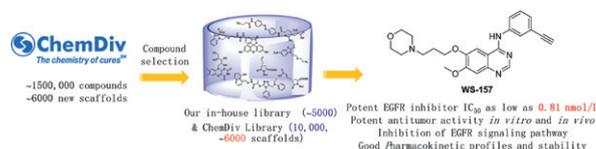
Discovery of WS-157 as a highly potent, selective and orally active EGFR inhibitor

Pengxing He^a, Shenghui Niu^a, Shuai Wang^a, Xiaojing Shi^a, Siqi Feng^a, Linna Du^a, Xuyang Zhang^a, Zhilu Ma^a, Bin Yu^{a,b}, Hongmin Liu^a

^aSchool of Pharmaceutical Sciences, Zhengzhou University, Zhengzhou 450001, China

^bState Key Laboratory of Pharmaceutical Biotechnology, Nanjing University, Nanjing 210023, China

WS-157 identified from our in-house diverse compound library was fully characterized as a potent and selective EGFR-TKI. WS-157 showed excellent inhibitory activities against EGFR (IC₅₀ = 0.81 nmol/L), EGFR^[d746-750] (IC₅₀ = 1.2 nmol/L) and EGFR^[L858R] (IC₅₀ = 1.1 nmol/L), good *in vivo* antitumor activity and acceptable pharmacokinetic properties.



Novel radioligands for imaging sigma-1 receptor in brain using positron emission tomography (PET)

Yu Lan^{a,d}, Ping Bai^a, Zude Chen^a, Ramesh Neelamegam^b, Michael S. Placzek^a, Hao Wang^a, Stephanie A. Fiedler^a, Jing Yang^a, Gengyang Yuan^b, Xiying Qu^b, Hayden R. Schmidt^c, Jinchun Song^d, Marc D. Normandin^b, Chongzhao Ran^a, Changning Wang^a

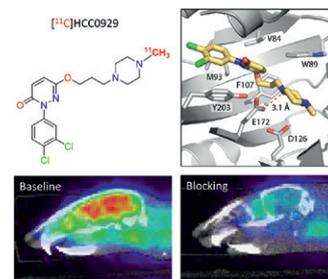
^aAthinoula A. Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Charlestown, MA 02129, USA

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^dDepartment of Pharmacy, Renmin Hospital of Wuhan University, Wuhan 430060, China

Of the two novel ¹¹C-labeled sigma-1 receptor radioligands, [¹¹C]HCC0929 has possessed better kinetic property and specificity, which could potentially accelerate preclinical research and medical development in sigma-1 receptor-related center nervous systems disease.



Design, synthesis, and biological evaluation of novel tetrahydroprotoberberine derivatives (THPBs) as proprotein convertase subtilisin/kexin type 9 (PCSK9) modulators for the treatment of hyperlipidemia

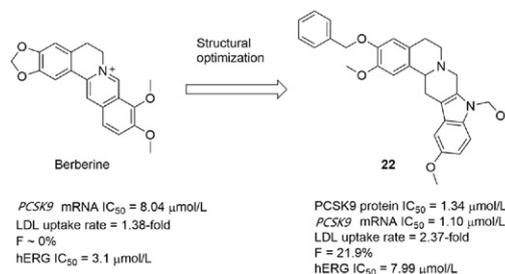
Chenglin Wu^{a,b}, Cong Xi^{a,c}, Junhua Tong^{a,c}, Jing Zhao^{a,c}, Hualiang Jiang^{a,c}, Jiang Wang^{a,c}, Yiping Wang^{a,c}, Hong Liu^{a,c}

^aState Key Laboratory of Drug Research and CAS Key Laboratory of Receptor Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, China

^bSchool of Pharmacy, China Pharmaceutical University, Nanjing 210009, China

^cUniversity of Chinese Academy of Sciences, Beijing 100049, China

A novel series of tetrahydroprotoberberine derivatives (THPBs) were designed, synthesized, and evaluated as PCSK9 modulators for the treatment of hyperlipidemia. Compound **22** demonstrated significant reductions of TC and LDL-C in hyperlipidemic hamsters, which is a promising lead compound for the development of PCSK9 modulator for the treatment of hyperlipidemia.



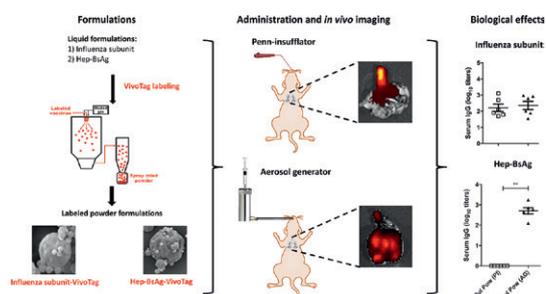
Pulmonary immunization: deposition site is of minor relevance for influenza vaccination but deep lung deposition is crucial for hepatitis B vaccination

Jasmine Tomar^a, Wouter F. Tonnis^a, Harshad P. Patil^b, Anne H. de boer^a, Paul Hagedoorn^a, Rita Vanbever^b, Henderik W. Frijlink^a, Wouter L.J. Hinrichs^a

^aDepartment of Pharmaceutical Technology and Biopharmacy, University of Groningen, Groningen 9713 AV, the Netherlands

^bAdvanced Drug Delivery and Biomaterials, Louvain Drug Research Institute (LDRI), Université catholique de Louvain, Brussels 1200, Belgium

The influence of pulmonary deposition on immune response was investigated for influenza and hepatitis B (Hep-B) vaccine candidates. Powder vaccines were targeted to different regions of the respiratory tract by Penn-insufflator (commercial) and in-house aerosol generator. Site of deposition was of minor relevance for influenza but of major importance for Hep-B vaccine.

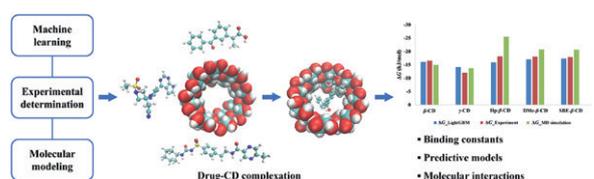


Predicting complexation performance between cyclodextrins and guest molecules by integrated machine learning and molecular modeling techniques

Qianqian Zhao, Zhuyifan Ye, Yan Su, Defang Ouyang

State Key Laboratory of Quality Research in Chinese Medicine, Institute of Chinese Medical Sciences (ICMS), University of Macau, Macau, China

Current research presented an alternative to traditionally trial-and-error experimentation for drug-CD formulation development. It revealed that the integration of experimental determinations, molecular modeling calculation and data-driven machine learning techniques could provide a new solution for highly efficient and accurate formulation development in the future.



Short Communication

Immunosuppressant mycophenolic acid biosynthesis employs a new globin-like enzyme for prenyl side chain cleavage

Xiwei Chen^a, Lu Wang^b, Jinmei Zhang^a, Tao Jiang^a, Changhua Hu^a, Dehai Li^{b,c}, Yi Zou^{a,d}

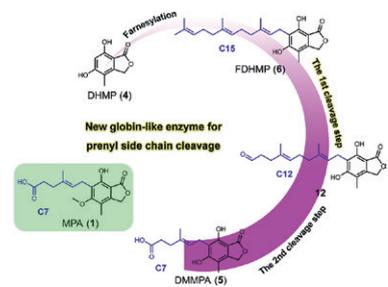
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^bKey Laboratory of Marine Drugs, Chinese Ministry of Education, School of Medicine and Pharmacy, Ocean University of China, Qingdao 266003, China

^cLaboratory for Marine Drugs and Bioproducts of Qingdao, National Laboratory for Marine Science and Technology, Qingdao 266237, China

^dBiological Science Research Center, Southwest University, Chongqing 400715, China

Collaborative biosynthesis—a new globin-like enzyme (PgMpaB) is responsible for the first pivotal C–C bond cleavage step in mycophenolic acid (MPA, **1**) biosynthesis. The second cleavage step is a *PgMpa* cluster-independent process *in vivo*.



Cover story**Front**

Cardiovascular diseases are a major cause of death throughout the world. Proprotein convertase subtilisin/kexin type 9 (PCSK9) modulators may attenuate PCSK9-induced low-density lipoprotein receptor (LDLR) degradation in lysosome and promote the clearance of circulating low-density lipoprotein cholesterol (LDL-C). Berberine, extracted from the traditional Chinese herb, has been shown cholesterol-lowering effect, and can reduce PCSK9 protein expression in HepG2 cells. A novel series of tetrahydroprotoberberine derivatives (THPBs) were designed, synthesized, and evaluated as PCSK9 modulators for the treatment of hyperlipidemia. Among them, compound **22** exhibited effects of downregulating PCSK9 expression, increasing LDLR expression, and promoting LDL uptake in HepG2 cells. In addition, compound **22** reduced total cholesterol (TC) and LDL-C in hyperlipidemic hamsters with a good pharmacokinetic profile, being a promising lead compound for the development of PCSK9 modulator for the treatment of hyperlipidemia.

Jiang Wang, Yiping Wang, Hong Liu

Back

Administration of vaccines *via* the pulmonary route might be an advantageous immunization approach as compared to conventional parenteral administration. However, the optimal antigen deposition site within the lungs to induce optimal immune responses has thus far hardly been addressed. In this study, we investigated whether deep lung deposition is crucial for vaccines against diseases that do or do not spread *via* the respiratory tract *i.e.* influenza and hepatitis-B, respectively. To explore this, spray dried vaccine formulations were targeted to trachea/central airways using commercially available Penn-Century insufflator and to the deep lungs *via* an in-house built aerosol generator. Comparable magnitude of immune responses was induced against influenza vaccine regardless of the site of deposition. However, for hepatitis-B vaccine, deep lung deposition was found to be crucial as upper airways targeting did not elicit any immune response at all while deep lung deposition did. This study demonstrates that the optimal site for antigen deposition within the respiratory tract is crucial and depends upon the type of antigen.

Wouter L.J. Hinrichs