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Reviews

Acta Pharmaceutica Sinica B, 9 (2019) 1087

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

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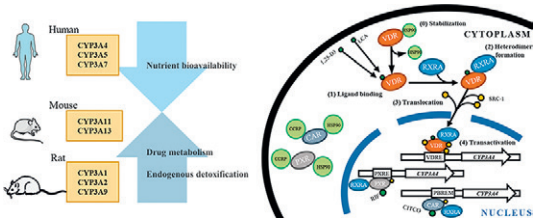

Vitamin D receptor (VDR) regulates the expression of cytochrome P450 3A (CYP3A) in human, mouse and rat. VDR-response elements are found in the promoters of *CYP3A* genes in different species. This transactivation effect is a potential modulator of nutrient bioavailability and drug metabolism.

Acta Pharmaceutica Sinica B, 9 (2019) 1099

Development and application of hyaluronic acid in tumor targeting drug delivery

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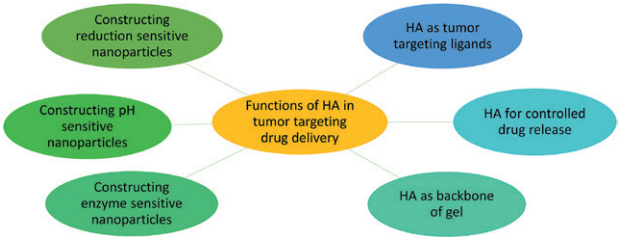

The review summarizes various applications of hyaluronic acid in tumor targeting drug delivery systems based on the specific CD44-targeting capacity and the hyaluronidase degradation property.

Annual reviews

Acta Pharmaceutica Sinica B, 9 (2019) 1113

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 Yu[i], Zhong Zuo[d], Huichang Bi[a]

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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.

Original articles

Acta Pharmaceutica Sinica B, 9 (2019) 1183

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

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

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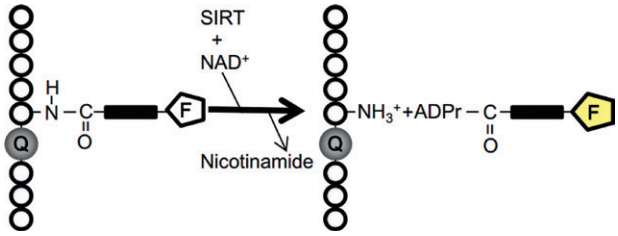

Sirtuins (SIRTs) are NAD^+-dependent histone deacetylases with extensive physiological functions. We established a novel strategy for detecting the activity of SIRT2 *in vitro* and in cell lysate. Fluorescence increment of these probes is based on SIRT-mediated removal of the acyl side chain with fluorophore.

Acta Pharmaceutica Sinica B, 9 (2019) 1193

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]

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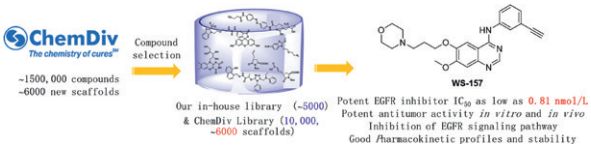


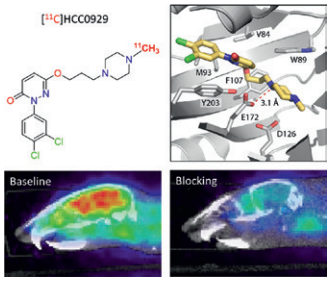
WS-157 identified from our in-house diverse compound library was fully characterized as a potent and selective EGFR-TKI. **WS-157** showed excellent inhibitory activities against EGFR (IC_{50} = 0.81 nmol/L), $EGFR^{[d746–750]}$ (IC_{50} = 1.2 nmol/L) and $EGFR^{[L858R]}$ (IC_{50} = 1.1 nmol/L), good *in vivo* antitumor activity and acceptable pharmacokinetic properties.

Acta Pharmaceutica Sinica B, 9 (2019) 1204

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]

[a]*Athinoula A. Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Charlestown, MA 02129, USA*
[b]*Gordon Center for Medical Imaging, Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Charlestown, MA 02129, USA*
[c]*Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, MA 02129, USA*
[d]*Department of Pharmacy, Renmin Hospital of Wuhan University, Wuhan 430060, China*



Of the two novel ^{11}C-labeled sigma-1 receptor radioligands, [^{11}C]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.

Acta Pharmaceutica Sinica B, 9 (2019) 1216

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]

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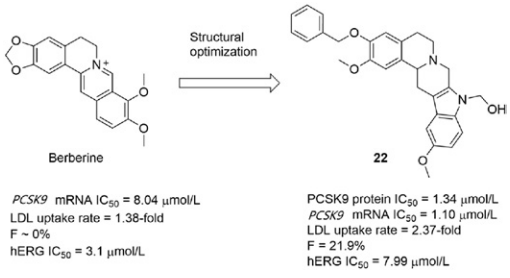

A novel series of tetrahydroprotoberberine derivatives (THPBs) were designed, synthesized, and evaluated as PCSK9 modulators for the treatment of hyperlipidemia. Compound **22** demonstrated significant reductions of TC and LDL-C in hyperlipidemic hamsters, which is a promising lead compound for the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

Acta Pharmaceutica Sinica B, 9 (2019) 1231

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]

[a]*Department of Pharmaceutical Technology and Biopharmacy, University of Groningen, Groningen 9713 AV, the Netherlands*
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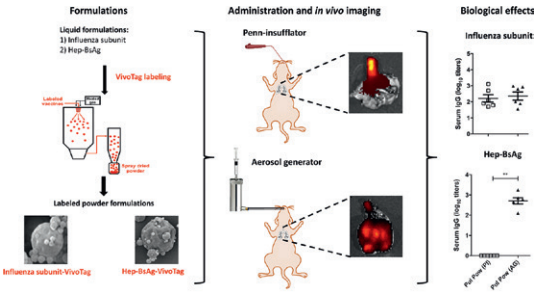

The influence of pulmonary deposition on immune response was investigated for influenza and hepatitis B (Hep-B) vaccine candidates. Powder vaccines were targeted to different regions of the respiratory tract by Penn-insufflator (commercial) and in-house aerosol generator. Site of deposition was of minor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

Acta Pharmaceutica Sinica B, 9 (2019) 1241

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

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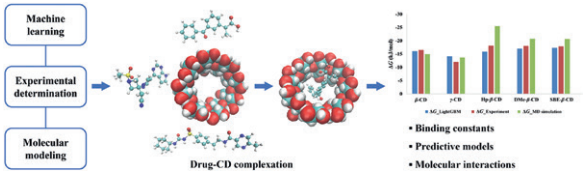

Current research presented an alternative to traditionally trial-and-error experimentation for drug–CD formulation development. It revealed that the integration of experimental determinations, molecular modeling calculation and data-driven machine learning techniques could provide a new solution for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

Short Communication

Acta Pharmaceutica Sinica B, 9 (2019) 1253

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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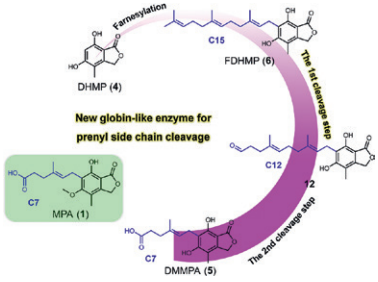

Collaborative biosynthesis—a new globin-like enzyme (PgMpaB) is responsible for the first pivotal C–C bond cleavage step in mycophenolic acid (MPA, **1**) biosynthesis. The second cleavage step is a *PgMpa* cluster-independent process *in vivo*.

Acta Pharmaceutica Sinica B, 9 (2019)

Cover story

Front

Cardiovascular diseases are a major cause of death throughout the world. Proprotein convertase substilisin/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 tetrahedroprotoberberine 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