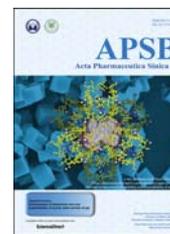




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Special Column: Enhancement of Dissolution and Oral Bioavailability of Poorly Water-Soluble Drugs

Editor Profiles

Guest Editors of Special Column: Wei Wu, Yi Lu, and Jianping Qi

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Editorial

Persistent endeavors for the enhancement of dissolution and oral bioavailability

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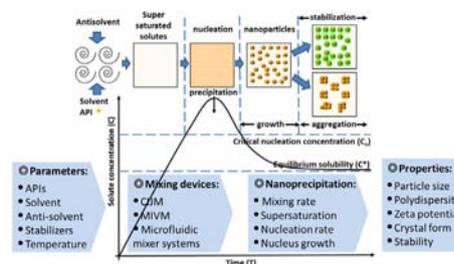
Application of flash nanoprecipitation to fabricate poorly water-soluble drug nanoparticles[☆]

Jinsong Tao^a, Shing Fung Chow^b, Ying Zheng^a

^aState Key Laboratory of Quality Research in Chinese Medicine, Institute of Chinese Medical Science, University of Macau, Macau, China

^bDepartment of Pharmacology and Pharmacy, The University of Hong Kong, Hong Kong, China

Flash nanoprecipitation (FNP) via mixing devices, such as confined impinging jets mixer (CIJM), multi-inlet vortex mixer (MIVM) and microfluidic mixer systems could tailor drug nanoparticles with various properties by controlling the mixing rate and supersaturation level during the FNP process, as well as the parameters of APIs, solvent, anti-solvent, stabilizers and temperature.



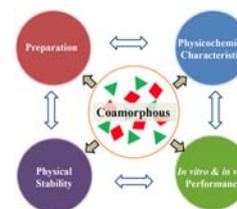
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Advances in coamorphous drug delivery systems[☆]

Qin Shi, Sakib M. Moinuddin, Ting Cai

State Key Laboratory of Natural Medicines, Department of Pharmaceutics, School of Pharmacy, China Pharmaceutical University, Nanjing 210009, China

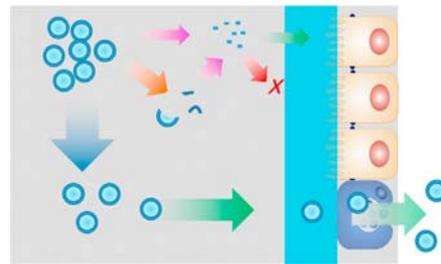
This review provides a comprehensive overview of coamorphous drug delivery systems from the perspectives of preparation, physicochemical characteristics, physical stability, *in vitro* and *in vivo* performance. Furthermore, the challenges and strategies in developing robust coamorphous drug products of high quality and performance are also briefly discussed.



[☆]Invited for Special Column

Adapting liposomes for oral drug delivery[☆]Haisheng He^a, Yi Lu^{a,b}, Jianping Qi^{a,b}, Quangang Zhu^b, Zhongjian Chen^b, Wei Wu^{a,b}^aKey Laboratory of Smart Drug Delivery of MOE and PLA, School of Pharmacy, Fudan University, Shanghai 201203, China^bShanghai Dermatology Hospital, Shanghai 200443, China

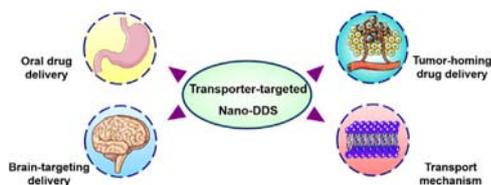
Despite the success of parenteral liposomes, oral delivery of liposomes is impeded by various barriers such as instability, poor permeability and mass production difficulties. By modulating bilayer compositions and decorating with polymers or ligands, both the stability and permeability of liposomes can be greatly improved, bettering liposomes for oral delivery.

**Emerging transporter-targeted nanoparticulate drug delivery systems**

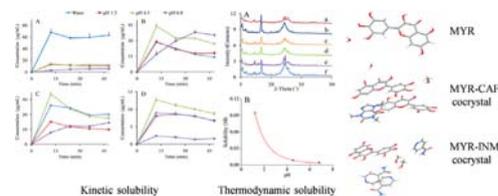
Hongyan Su, Yan Wang, Shuo Liu, Yue Wang, Qian Liu, Guangxuan Liu, Qin Chen

Department of Pharmacy, Cancer Hospital of China Medical University, Liaoning Cancer Hospital & Institute, Shenyang 110042, China

The recent trends in transporter-targeted nano-DDS is reviewed: (i) the emerging transporter-targeted nano-DDS developed to facilitate oral drug delivery; (ii) the recent advances in transporter-assisted brain-targeting nano-DDS; (iii) recent developments in transporter-mediated tumor-targeting drug delivery; and (iv) the possible transport mechanisms involved in the transporter-mediated endocytosis.

**Original Articles****The effects of pH, surfactant, ion concentration, cofomer, and molecular arrangement on the solubility behavior of myricetin cocrystals**[☆]Shuzhen Ren^a, Mingyu Liu^{a,b}, Chao Hong^a, Guowen Li^c, Jiabin Sun^a, Jianying Wang^d, Lei Zhang^d, Yan Xie^a^aResearch Center for Health and Nutrition, Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China^bInstitute of Chinese Materia Medica, Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China^cPharmacy Department, Shanghai TCM-Integrated Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai 200082, China^dShanghai Innovation Center of TCM Health Service, Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China

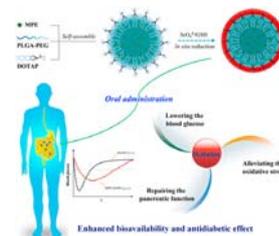
The myricetin (MYR) cocrystals solubility was systematically elucidated by investigating its kinetic solubility, thermodynamic solubility, and intrinsic dissolution rate. The improved solubility of MYR cocrystals was probably related to the alternate arrangements of MYR and isonicotinamide/caffeine (INM/CAF) molecules and increased intermolecular distance.

**Selenium-layered nanoparticles serving for oral delivery of phytochemicals with hypoglycemic activity to synergistically potentiate the antidiabetic effect**[☆]

Wenji Deng, Huan Wang, Baojian Wun, Xingwang Zhang

Department of Pharmaceutics, College of Pharmacy, Jinan University, Guangzhou 510632, China

Selenium-layered nanoparticles (SeNPs) were developed by self-assembly/in situ reduction technique to orally deliver mulberry leaf and *Pueraria Lobata* extracts (MPE) and enhanced antidiabetic efficacy was achieved through the synergy between selenium and hypoglycemic phytochemicals.

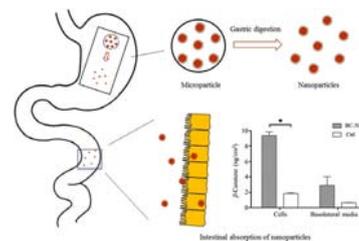


Intestinal uptake of barley protein-based nanoparticles for β -carotene delivery[☆]

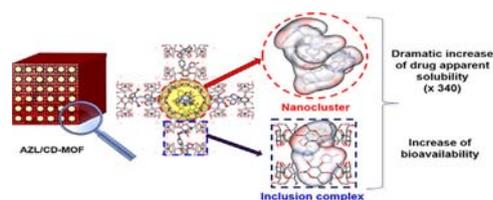
Guangyu Liu, Ying Zhou, Lingyun Chen

Department of Agricultural, Food and Nutritional Science, University of Alberta, Alberta T6G 2P5, Canada

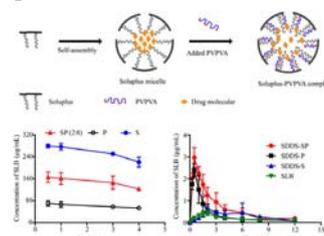
Barley protein microparticles could protect encapsulated compounds and prevent nanoparticles from aggregation during storage. Barley protein nanoparticles can be liberated from microparticles upon gastric digestion and demonstrate absorption improving effect in both Caco-2 cell and rat jejunum models. These vehicles show significant potential in the delivery of hydrophobic compounds.

**Drug nanoclusters formed in confined nano-cages of CD-MOF: dramatic enhancement of solubility and bioavailability of azilsartan[☆]**Yuanzhi He^{a,b}, Wei Zhang^{b,c}, Tao Guo^b, Guoqing Zhang^b, Wei Qin^{a,b}, Liu Zhang^b, Caifen Wang^b, Weifeng Zhu^a, Ming Yang^a, Xiaoxiao Hu^b, Vikramjeet Singh^d, Li Wu^{b,e}, Ruxandra Gref^d, Jiwen Zhang^{a,b,c,e}.^aKey Laboratory of Modern Preparation of TCM, Ministry of Education, Jiangxi University of Traditional Chinese Medicine, Nanchang 330004, China^bCenter for Drug Delivery Systems, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201210, China^cSchool of Chemistry and Environmental Engineering, Shanghai Institute of Technology, Shanghai 201418, China^dInstitut des Sciences Moléculaires d'Orsay, UMR 8214 CNRS, Université Paris-Sud, Université Paris-Saclay, Orsay 91400, France^eSchool of Pharmacy, Key Laboratory of Molecular Pharmacology and Drug Evaluation, Ministry of Education, Yantai University, Yantai 264005, China

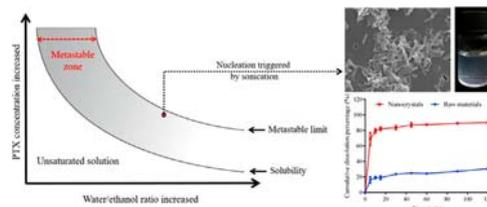
The solubility and bioavailability of AZL loaded in CD-MOF have been significantly improved to 340-fold and 9.7-fold, respectively, compared with the raw API. A dual molecule mechanism of complexation and nanoclusterization was first proposed and experimentally verified.

**Supersaturated polymeric micelles for oral silybin delivery: the role of the Soluplus-PVPVA complex[☆]**Chunliu Zhu^{a,c}, Shuang Gong^{b,c}, Jinsong Ding^b, Miaorong Yu^c, Ejaj Ahmad^c, Yi Feng^a, Yong Gan^c^aEngineering Research Center of Modern Preparation Technology of Traditional Chinese Medicine, Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China^bXiangya School of Pharmaceutical Science, Central South University, Changsha 410000, China^cShanghai Institute of Materia Medica, Chinese Academy of Science, Shanghai 201203, China

The study reported a supersaturated complex, formed by Soluplus and PVPVA, for oral silybin (SLB) delivery. The adsorption of PVPVA on the hydrophilic-hydrophobic interface of the Soluplus micelle endowed the complex with the ability to maintain proper stability of SLB supersaturated solution, and thus improved the oral bioavailability of SLB.

**Development of carrier-free nanocrystals of poorly water-soluble drugs by exploring metastable zone of nucleation[☆]**Xiaoting Ren^a, Jianping Qi^b, Wei Wu^b, Zongning Yin^a, Tonglei Li^c, Yi Lu^b^aKey Laboratory of Drug Targeting and Drug Delivery Systems, West China School of Pharmacy, Sichuan University, Chengdu 610041, China^bDepartment of Pharmaceutics, School of Pharmacy, Fudan University, Shanghai 201203, China^cDepartment of Industrial and Physical Pharmacy, College of Pharmacy, Purdue University, West Lafayette, IN 47907, USA

A solution may stay supersaturated without forming any nuclei and become metastable. When nucleation is triggered directly from the metastable zone, it helps to produce homogeneous nuclei leading to uniform carrier-free nanocrystals. Avoiding disadvantages related to the carrier materials, carrier-free nanocrystals offer numerous benefits for drug delivery.



Preparation and characterization of multimodal hybrid organic and inorganic nanocrystals of camptothecin and gold[☆]

Christin P. Hollis^a, Alan K. Dozier^b, Barbara L. Knutson^c, Tonglei Li^d

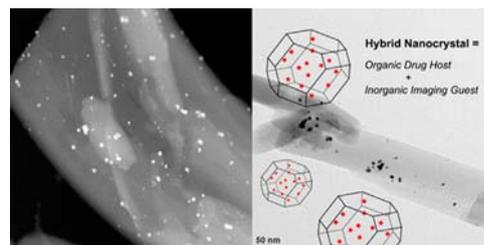
^aDepartment of Pharmaceutical Sciences, University of Kentucky, Lexington, KY 40506, USA

^bElectron Microscopy Center, University of Kentucky, Lexington, KY 40506, USA

^cDepartment of Chemical Engineering and Material Sciences, University of Kentucky, Lexington, KY 40506, USA

^dDepartment Industrial & Physical Pharmacy, College of Pharmacy, Purdue University, West Lafayette, IN 47907, USA

Gold atoms and clusters were integrated physically into the crystal lattices as defects of camptothecin nanocrystals to achieve potential applications of concurrent bioimaging and anticancer therapy.



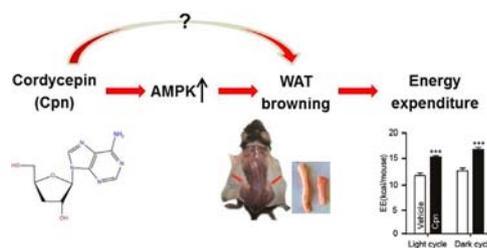
Cordycepin promotes browning of white adipose tissue through an AMP-activated protein kinase (AMPK)-dependent pathway

Guihong Qi^a, Yue Zhou^a, Xiaopo Zhang^b, Jiaqi Yu^a, Xin Li^a, Xiaoxue Cao^a, Chongming Wu^a, Peng Guo^a

^aPharmacology and Toxicology Research Center, Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100193, China

^bSchool of Pharmaceutical Science, Hainan Medical University, Hainan 571199, China

Cordycepin increases energy expenditure *via* promoting white adipose tissue browning in mice, in which AMPK activation may play an important role.

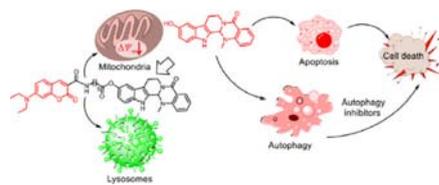


Novel fluorescent probes of 10-hydroxyevodiamine: autophagy and apoptosis-inducing anticancer mechanisms

Shuqiang Chen, Guoqiang Dong, Shanchao Wu, Na Liu, Wannian Zhang, Chunquan Sheng

School of Pharmacy, Second Military Medical University, Shanghai 200433, China

Novel fluorescent probes were designed to elucidate the antitumor mode of action of 10-hydroxyevodiamine, which was proven to be distributed in the mitochondria and lysosomes and acted by autophagy and apoptosis mechanisms.



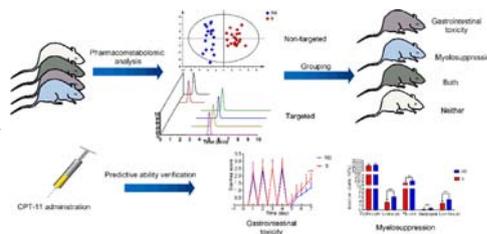
Pharmacometabolomic prediction of individual differences of gastrointestinal toxicity complicating myelosuppression in rats induced by irinotecan

Yiqiao Gao^{a,b}, Wei Li^{a,b}, Jiaqing Chen^{a,b}, Xu Wang^{a,b}, Yingdong Lv^{a,b}, Yin Huang^{a,b}, Zunjian Zhang^{a,b}, Fengguo Xu^{a,b}

^aKey Laboratory of Drug Quality Control and Pharmacovigilance (Ministry of Education), State Key Laboratory of Natural Medicine, China Pharmaceutical University, Nanjing 210009, China

^bJiangsu Key Laboratory of Drug Screening, China Pharmaceutical University, Nanjing 210009, China

Mass spectrometry-based non-targeted and targeted metabolomics were conducted in sequence to screen the exclusive biomarkers in predose serums. Based on the pharmacometabolomic analysis, two prediction models were constructed to predict gastrointestinal toxicity and myelosuppression of CPT-11 simultaneously, followed by verification of relevant chemotherapeutic toxicity evaluation indexes.



Cover story**Front**

Insoluble azilsartan (AZL) was successfully loaded in biocompatible versatile γ -cyclodextrin metal-organic framework (CD-MOF). In a typical cage-like unit of CD-MOF, three AZL molecules formed a nanocluster inside the 1.7 nm sized cavity surrounded by six γ -CDs, whilst other three molecules of AZL were included by γ -CD pairs. AZL clusters formed in the confined spaces exhibit uniform size distributions which are hard to be achieved by conventional techniques. The strategy improved the bioavailability of pure AZL in Sprague–Dawley rats by 9.7-fold and 1.5-fold higher than that of AZL/ γ -CD complex, respectively. The apparent solubility of AZL was enhanced by 340-fold after loading into CD-MOF, while only 9.4-fold increment was recorded when forming γ -CD inclusion complexes. Thus, the nanoclusters played a key role in the solubility and bioavailability enhancement of AZL/CD-MOF. The dual molecular mechanism of nanoclusterization and complexation in CD-MOF was demonstrated by molecular modeling and experimental characterizations.

Li Wu, Ruxandra Gref, and Jiwen Zhang

Back

Carrier-free nanocrystals offer numerous benefits for drug delivery concerning drug loading, stability and carrier associated side-effects. However, it is full of challenges to produce carrier-free nanocrystals with controllable size. A solution may stay supersaturated without forming any nuclei and become metastable. When nucleation is triggered directly from the metastable solution, it helps to produce homogeneous nuclei leading to uniform nanocrystals. With paclitaxel as a model drug, a wide range of metastable compositions are found to be applicable to prepare carrier-free paclitaxel nanocrystals with particle size smaller than 250 nm and PDI less than 0.25. The study demonstrates the importance of nucleation in producing organic nanocrystals and a novel preparation technique of high-quality pure drug nanocrystals.

Zongning Yin, Tonglei Li, and Yi Lu
