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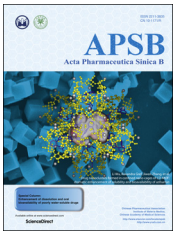

Editorial: Persistent endeavors for the enhancement of dissolution and oral bioavailability

More than 50% of marketed drugs and 90% drug candidates are believed to be poorly water-soluble, and these figures keep growing due to input of new drug entities into the pool, thanks to the fast development in drug discovery. It has long been recognized that poor solubility poses problems of retarded dissolution rate and thereby poor bioavailability. Enhancement of dissolution and oral bioavailability remains a challenge not only in formulation but also for early-stage development despite years of efforts and progress. According to the canonical Noyes–Whitney equation, the dissolution rate of drug crystals or particles is positively proportionate to the solubility and the surface area of a specific drug entity[1]. Based on this rationale, efforts have been made in the past to increase inherent solubility and surface area or dispersity of drug entities. Optional strategies include, but not limited to, salt formation, microsizing or nanosizing, solid dispersion, amorphorization and inclusion complexation[2]. While improving dissolution works very well for enhancement of oral bioavailability of BCS II drugs, it fails for BCS IV drugs whose oral absorption calls for enhancement of dissolution and permeation across gastrointestinal biomembrane simultaneously[1]. In the past decades, novel approaches have been investigated towards this end. This area continues to be active with new methods and theories proposed and put into practice. In this special issue, we bring together prominent scientists to showcase the most recent advances in the big field of enhancement of dissolution and oral bioavailability.

Albeit well documented in literature, down-sizing of drug particles and amorphorization continuously draws attention from both academics and industries. However, research interest has shifted towards understanding of the performance of drug crystals, especially nanocrystals, both *in vitro* and *in vivo*, as well as development of new methods for efficient production of nanocrystals and cocrystals. As a continuation of their series of works, Hollis et al.[3] reported camptothecin nanocrystals hybridized with gold, which renders the drug nanocrystals detectable by CT, suggesting potential usage in simultaneous cancer therapy and bioimaging. Ren et al.[4] reported a new method to prepare carrier-free nanocrystals by exploiting the metastable zone. The goal is to trigger nucleation from metastable supersaturation, which produces homogenous nuclei that lead to uniform nanocrystal[4]. Ren and Liu et al.[5] studied the variables influencing the dissolution behavior of myricetin cocrystals. Physical characterization of single crystal structure reveals alternate arrangement of drug molecules/co-formers and increased intermolecular distance as the leading factor that results in dissolution enhancement[5]. In addition, Shi et al.[6] provided an overview on various aspects of coamorphous drug delivery systems.

Carrier, especially nanocarrier, systems emerges as novel alternative options in recent years for enhancement of dissolution and oral bioavailability. The rest articles of this special issue address versatile nanocarriers. Among various nanocarriers, lipid-based ones remain a good option due to good maintaining of a solubilized state of the poorly water-soluble drugs and facilitated absorption upon lipid digestion and structural transformation. The review article by He et al.[7] provides an overview on the challenges, promises and strategies involved in oral delivery of liposomes. Jørgensen et al.[8] investigated the composition of SNEDDS on the chasing principle, a theory involved with co-administration of drug suspension and drug-free lipid vehicles, which was proposed by the same group and aimed to solve the problem of low loading and poor stability for some drugs. Liu et al.[9] studied barley protein-based nanoparticles, which are protein-stabilized nanoemulsions based on canola oil, and found greatly improved absorption or beta-carotene. He et al.[10] reported a very interesting azilsartan nanoclusters formed in confined nanocages of CD-MOF with greatly improved apparent solubility by 340-fold and oral bioavailability in rats by 9.7-fold. Molecular modeling suggested dual molecular mechanism of nanoclusterization and complexation of the drug inside the CD-MOF cages[10]. Polymeric micelles based on Solupus–Copovidone complex system were employed in Zhu et al.'s work to maintain a supersaturated state of silybin and thereby enhance oral absorption[11]. Deng et al.[12] developed PLGA-PEG/DOTAP-based polymeric micelles and coated the

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systems with selenium *via in situ* reduction. The selenium-layered core-shell nanoconstructs demonstrate synergistic hypoglycemic effect of selenium and mulberry leaf and *Pueraria lobata* extract[12]. Moreover, Tao et al.[13] provided an overview to a very useful method, the flash nanoprecipitation method, for the fabrication of nanoparticles for poorly water-soluble drugs.

In a word, novel strategies are emerging to counter the challenges with poor dissolution and poor bioavailability, and this special issue aims to set up a platform for scientist to share the most recent advances.

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