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Preface

Self-emulsifying drug delivery systems (SEDDS) – The splendid comeback of an old technology

Although having been pioneered already in the 1980s, self-emulsifying drug delivery systems (SEDDS) have recently moved back into the limelight of global pharmaceutical research. This renaissance is primarily based on numerous discoveries and substantial improvements in the field of SEDDS having been made within the last five years, resulting in encouraging *in vivo* studies confirming the enormous potential of this formulation approach. This special issue is addressing these recent developments and should motivate both academic and industrial scientists to keep an eye out on this rapidly developing scientific area.

Based on new studies of lipase activities, pH and bile salts levels in the gastrointestinal tract of both healthy volunteers, paediatrics and diseased populations, a better understanding of *in vivo* SEDDS digestion has been enabled, and is reviewed in this special issue [1]. In addition, recent studies, using new and advanced techniques, on the colloidal phases generated upon dispersion and digestion of SEDDS have shed light on the importance of such structures for the solubilisation and absorption of poorly water-soluble drugs [2]. Based on the improved understanding of gastrointestinal digestion of SEDDS, new *in vitro* lipolysis models are in development, also taking into account the specific gastro-intestinal physiology of special populations, and drug absorption during SEDDS digestion, is also reviewed in this special issue [3]. Moreover, new techniques for the direct examination of kinetic changes during the process of drug supersaturation as a result of lipase digestion have been established. Thereby obtained kinetic data open the door to mathematic modelling of supersaturation and precipitation *versus* permeation [4]. For drug release studies a new approach has been introduced [5] and mucus diffusion studies for SEDDS have been established allowing the development of highly mucus permeating oil droplets that can reach the absorptive membrane in high quantities [6]. Furthermore, imaging techniques, such as Laser microscopic analyses, have recently provided first insights regarding the fate of SEDDS on the absorption membrane [7]. All these newly established and strongly improved analytical tools have contributed to our understanding of the *in vivo* fate of SEDDS and have resulted in numerous improvements in SEDDS formulation development, that are reviewed in this special issue.

Within recent years the first lipase stable SEDDS have been generated, either by changing the composition [8] or by incorporation of lipase inhibitors [9] in both cases making them less susceptible to gastrointestinal variability. Microemulsions containing hydrophobic ion pairs such as timolol-octanoate or methothrexate-docusate, pioneered by Gasco and Trotta thirty years ago [10,11], currently experience a revival. New salts of approved drugs fall now under the 505(b)(2) regulatory approval pathway of the FDA allowing for fewer clinical and toxicity studies in order to obtain approval. Within this special issue an overview of the formation and potential of hydrophobic ion pairs, referred to as lipophilic salts/ionic liquid forms is provided [12]. Another recent comeback for SEDDS is their application for oral peptide delivery systems. Although the very first commercial product based on SEDDS was developed in order to improve the oral bioavailability of the peptide drug cyclosporine [13], it took also almost thirty years to bring SEDDS back into focus for the delivery of peptide drugs and hydrophilic macromolecular drugs in general [14]. In view of these developments, solid SEDDS providing in particular long term storage stability regained significant commercial interest. Within this special issue opportunities and challenges regarding the solidification of SEDDS are discussed in this special issue [15].

A bridge between academic and industrial research is built and an overview of the industrial focused scientific gaps related to lipid-based formulations is provided [16]. Furthermore, excipients listed in the IIG database of the FDA that can be used for the formulation of SEDDS are summarized and discussed regarding their properties [17].

Finally, the Guest-Editors of this special issue wish to thank all the contributing authors for their excellent reviews that were certainly not easy to write in such a complex and currently fast developing field. A special thank you also goes to the referees for their very prompt and expert comments and advice for revision. Furthermore, we wish to thank the ADDR Editor-In-Chief Hamid Ghandehari for inviting us to edit this special issue.

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