

# Oral Lipid Based Formulations Enhancing The Bioavailability Of Poorly Water Soluble Drugs Drugs And The Pharmaceutical Sciences

*This text book is a guide for pharmaceutical academics (students and teachers) as well as industry professionals learning about drug delivery and formulation. Chapters presents comprehensive information about self-emulsifying formulations by providing an in-depth understanding of the basic concepts and formulation mechanisms. This information is supplemented by details about current research and development in this field. Readers will learn about the types of self-emulsifying drug delivery systems, evaluation parameters and digestion models, among other topics. Key Features: - 9 chapters organized in a reader-friendly layout - complete guide on self-emulsifying drug delivery formulations, including lipid based systems, SMEDOs, surfactants, and oral dosage forms - includes basic concepts and current developments in research and industrial applications - presents information on conventional and herbal formulations - references for further reading*

*Oral lipid-based formulations are attracting considerable attention due to their capacity to facilitate gastrointestinal absorption and reduce or eliminate the effect of food on the*

absorption of poorly water-soluble,  
lipophilic drugs. Despite the obvious and  
demonstrated utility of these formulations  
for addressing a persistent and growing  
problem

Provides a comprehensive review of all types  
of medical therapeutic delivery solutions from  
traditional pharmaceutical therapy development  
to innovative medical device therapy  
treatment to the recent advances in cellular  
and stem cell therapy development • Provides  
information to potentially allow  
future development of treatments with greater  
therapeutic potential and creativity •  
Includes associated regulatory requirements  
for the development of these therapies •  
Provides a comprehensive developmental  
overview on therapeutic delivery solutions •  
Provides overview information for both the  
general reader as well as more detailed  
references for professionals and specialists  
in the field

The goal of any novel drug delivery system is  
to provide therapeutic benefits to the  
patients by increasing duration of drug  
action, reducing dosing frequency, and  
controlling drug release rate at the target  
site, thereby reducing unwanted side effects.  
Advanced Technology for Delivering  
Therapeutics is a reference book that covers  
recent developments in the field of drug  
delivery science and technology. The purpose  
of this book is to bring together  
descriptions of some selective technologies

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Sciences

*including new and promising nanotechnology  
currently being investigated for drug  
delivery applications. This book is a useful  
source of information for graduate and post-  
graduate students of pharmacy and biomedical  
science; pharmaceutical*

*Lipid-Based Nano-Delivery for Oral  
Administration of Poorly Water Soluble Drugs  
(PWSDs): Design, Optimization and in Vitro  
Assessment*

*Oral Drug Absorption*

*Basic Principles and Biological Examples  
Water-Insoluble Drug Formulation, Third  
Edition*

*Self-Emulsifying Systems for Oral  
Bioavailability Enhancement of Drugs  
Salts, Cocrystals, and Polymorphism*

The absorption and oral bioavailability of poorly water-soluble drugs is often limited by poor aqueous solubility and slow dissolution in the gastrointestinal (GI) tract. Lipid-based formulations are a popular formulation approach to enhance oral bioavailability for drugs where water solubility is the primary limitation to absorption. The research undertaken in this thesis examines the use of different types and masses of lipids to improve drug solubilisation and absorption, and investigates the contribution of gastric processing to the improvements in oral bioavailability typically seen after co-

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administration of poorly water-soluble drugs with lipids and lipid-based formulations. A simple in vitro lipid digestion model was used to assess the effect of lipid type and mass on the solubilisation of three model lipophilic drugs (danazol, cinnarizine and halofantrine). Digestion of medium chain triacylglyceride (MCT) formulations yielded improved drug solubilisation (and resulted in drug supersaturation) at high lipid mass (250 mg). In contrast, for long chain triacylglyceride (LCT) formulations, drug concentrations in the aqueous phase of the digests were higher after digestion of the smallest lipid masses, regardless of drug lipophilicity. In all cases, digestion of the LCT formulations was incomplete, resulting in a residual oil phase. At low masses of LCT lipid (50 mg), digestion was more complete, resulting in increased drug transfer into the aqueous phase. For the more lipophilic drugs, partitioning into the residual oil phase increased. Drug lipophilicity, the choice and quantity of lipid, and the need for complete digestion of the formulation were therefore important indicators of the performance of the in vitro lipid digestion assay. Cinnarizine (CZ) was subsequently chosen as a model poorly

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water-soluble drug to exemplify the effects of lipid load on drug exposure in in vivo studies and to compare in vitro and in vivo performance. In vivo bioavailability studies were undertaken at fixed and varied lipid:CZ ratios and after administration with LCT and MCT. In all cases, the bioavailability of CZ was higher after administration of LCT rather than MCT formulations, regardless of lipid mass. At a fixed lipid:CZ ratio, increasing the quantity of formulation did not affect oral bioavailability, and linear pharmacokinetics were observed. When the lipid:CZ ratio was increased, CZ absorption increased at lipid doses from 50 mg to 250 mg, but did not increase further beyond 250 mg. The data suggest that the type and mass of lipid co-administered are important, but that in most cases, LCT formulations outperform the equivalent MCT formulation. The same lipids were also given by intraduodenal administration as both a lipid solution and as a dispersed lipid formulation, to assess the contribution of gastric processing to oral bioavailability. CZ bioavailability was reduced when either formulation was administered intraduodenally and similar trends were evident for MCT and LCT. The data suggest

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that gastric and intestinal processing contribute to improved CZ absorption. Finally, aspiration of GI content after formulation administration revealed that the digestion of MCT was more prevalent in the stomach than LCT. Gastric processing may explain the improvements in bioavailability when MCT formulations (both solution and dispersion) were administered orally when compared to intraduodenally. Surprisingly, LCT formulations were seemingly less dependent on gastric processing. In summary, the research described in this thesis highlights the potential utility (and drawbacks) of in vitro lipid digestion models to predict in vivo absorption, and further shows that the mass and type of lipid, and processing in both the stomach and the intestine are important determinants of oral bioavailability from lipid-based formulations.

Solid State Development and Processing of Pharmaceutical Molecules A guide to the latest industry principles for optimizing the production of solid state active pharmaceutical ingredients Solid State Development and Processing of Pharmaceutical Molecules is an authoritative guide that covers the entire pharmaceutical value chain. The

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authors-noted experts on the topic-examine the importance of the solid state form of chemical and biological drugs and review the development, production, quality control, formulation, and stability of medicines. The book explores the most recent trends in the digitization and automation of the pharmaceutical production processes that reflect the need for consistent high quality. It also includes information on relevant regulatory and intellectual property considerations. This resource is aimed at professionals in the pharmaceutical industry and offers an in-depth examination of the commercially relevant issues facing developers, producers and distributors of drug substances. This important book: Provides a guide for the effective development of solid drug forms Compares different characterization methods for solid state APIs Offers a resource for understanding efficient production methods for solid state forms of chemical and biological drugs Includes information on automation, process control, and machine learning as an integral part of the development and production workflows Covers in detail the regulatory and quality control aspects of drug development Written for medicinal

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chemists, pharmaceutical industry professionals, pharma engineers, solid state chemists, chemical engineers, Solid State Development and Processing of Pharmaceutical Molecules reviews information on the solid state of active pharmaceutical ingredients for their efficient development and production. This thesis has explored the use of lipid-based formulations (LBF) to enhance the oral bioavailability of the cholesteryl ester transfer protein (CETP) inhibitor CP-532,623, used here as a model poorly water soluble drug (PWSD), and the impact of dispersion and digestion on formulation performance. A particular focus has been the use of the in vitro lipid digestion model as a tool to predict the oral bioavailability of PWSDs, by investigating the relationship between drug solubilisation after in vitro digestion and in vivo exposure after oral administration. Dispersion and digestion of LBFs are both events that challenge the solubilisation of a co-administered drug. The data show that the development of LBFs can be informed by the dispersion and solubilisation properties of individual excipients after in vitro digestion. Different patterns of solubilisation were observed with changes in the type of

excipient employed. Lipids and lipophilic co-surfactants retained drug in an oily phase but were nonetheless resistant to drug precipitation. Hydrophilic surfactants (particularly Kolliphor RH 40) maintained higher drug solubilisation levels after digestion, a characteristic that was maintained within composite formulations containing Kolliphor and additional excipients. Conversely, co-solvents supported high initial drug loading, but provided no ongoing solubilisation when introduced to aqueous media. A series of formulations based on medium chain (MC) lipids and were initially developed to provide for effective drug loading and good dispersion properties. Assessment of these MC-LBFs using the in vitro digestion model revealed varying degrees of susceptibility to precipitation during in vitro digestion, and a broad correlation between drug solubilisation after in vitro digestion and drug absorption after oral administration in beagle dogs. Subsequent modification of the formulations to include long chain (LC) lipids rather than MC lipids generally resulted in higher levels of CP-532,623 solubilisation after in vitro digestion. In all cases the LBFs greatly enhanced in vitro solubilisation

and in vivo oral bioavailability of CP-532,623 in fasted beagle dogs when compared to a simple powder formulation. Within related groups of formulations in vitro solubilisation on lipid digestion was also found to correlate with in vivo exposure. Notably, formulations based on LC-LBFs required higher levels of drug solubilisation to achieve similar levels of in vivo exposure, when compared to MC-LBFs. Re-evaluation of the in vitro data to measure drug supersaturation rather than drug solubilisation, however, resulted in improved correlations, especially for formulations containing a common surfactant. Thus, formulations containing Kolliphor RH 40 were absorbed more readily at lower supersaturation levels than formulations containing polysorbate 80 or vitamin E TPGS. The data suggest that the degree of drug solubilisation and supersaturation during in vitro lipid digestion provides some indication of formulation performance but that this alone is insufficient to completely explain patterns of drug absorption. Further investigations into the factors contributing to the high bioavailability obtained in beagle dogs also suggested that drug absorption from LBFs may vary in beagle and greyhound

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dogs, with drug absorption typically being higher in beagles. In summary, the studies presented here further demonstrate the utility of the in vitro digestion model in formulation development. In conjunction with solubility studies, calculation of drug supersaturation, and characterisation of the physical state of precipitated drug, in vitro lipolysis tests provide useful in vitro indicators of formulation performance. Interestingly, the current studies suggest that whilst the overall patterns of in vitro-in vivo correlation that have previously been described in the literature, may be maintained, they appear to exist in parallel with excipient specific effects on drug absorption and bioavailability. Thus, in addition to concentration or thermodynamic activity, the nature of the solubilised phases formed on lipid formulation digestion appears to be a significant driver of differences in patterns of drug absorption from LBF.

Modern drug discovery technique led to the consistent increase in the number of new pharmacologically active lipophilic compounds that are poorly water soluble. A great challenge facing the pharmaceutical scientist is making these molecules into orally administered medications with

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sufficient bioavailability. One of the most popular approaches to improve the oral bioavailability of these molecules is the utilization of a lipid based drug delivery system. Development and optimization of formulation is an integral part of manufacturing and marketing of any therapeutic agent which is indeed a time consuming and costly process. Optimization process may require alteration in formulation composition, manufacturing process, equipment and batch sizes. If these types of changes are applied to a formulation, studies in human healthy volunteers may be required to prove that the new formulation is bioequivalent with the old one. IVIVC includes in vivo relevance to in vitro dissolution specifications and can serve as surrogate for in vivo bioavailability and to support biowaivers. This book provides the information about the use of biorelevant media as media an alternative for in vivo studies.

Prediction and Assessment, Second Edition  
Lipid Nanocarriers for Drug Targeting  
Molecular Dynamics Simulations of Lipid-  
based Drug Delivery Systems  
An Evidence Based Approach  
Understanding the Determinants of Drug  
Absorption Following Oral Administration

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Soluble Drugs Drugs And The Pharmaceutical  
Sciences  
of Lipid-based Drug Delivery Systems  
Advanced Technology for Delivering  
Therapeutics

This volume is intended to provide the reader with a breadth of understanding regarding the many challenges faced with the formulation of poorly water-soluble drugs as well as in-depth knowledge in the critical areas of development with these compounds. Further, this book is designed to provide practical guidance for overcoming formulation challenges toward the end goal of improving drug therapies with poorly water-soluble drugs. Enhancing solubility via formulation intervention is a unique opportunity in which formulation scientists can enable drug therapies by creating viable medicines from seemingly undeliverable molecules. With the ever increasing number of poorly water-soluble compounds entering development, the role of the formulation scientist is growing in importance. Also, knowledge of the advanced analytical, formulation, and process technologies as well as specific regulatory considerations related to the formulation of these compounds is increasing in value. Ideally, this book will serve as a useful tool in the education of current and future generations of scientists,

and in this context contribute toward providing patients with new and better medicines.

Properties and Formulation: From Theory to Real-World Application Scientists have attributed more than 40 percent of the failures in new drug development to poor biopharmaceutical properties, particularly water insolubility. Issues surrounding water insolubility can postpone or completely derail important new drug development. Even the much-needed reformulation of currently marketed products can be significantly affected by these challenges. More recently it was reported that the percentage increased to 90% for the candidates of new chemical entities in the discovery stage and 75% for compounds under development. In the most comprehensive resource on the topic, this third edition of *Water-Insoluble Drug Formulation* brings together a distinguished team of experts to provide the scientific background and step-by-step guidance needed to deal with solubility issues in drug development. Twenty-three chapters systematically describe the detailed discussion on solubility theories, solubility prediction models, the aspects of preformulation, biopharmaceutics,

pharmacokinetics, regulatory, and discovery support of water-insoluble drugs to various techniques used in developing delivery systems for water-insoluble drugs. This book includes more than 15 water-insoluble drug delivery systems or technologies, illustrated with case studies and featuring oral and parenteral applications. Highlighting the most current information and data available, this seminal volume reflects the significant progress that has been made in nearly all aspects of this field. The aim of this book is to provide a handy reference for pharmaceutical scientists in the handling of formulation issues related to water-insoluble drugs. In addition, this book may be useful to pharmacy and chemistry undergraduate students and pharmaceutical and biopharmaceutical graduate students to enhance their knowledge in the techniques of drug solubilization and dissolution enhancement.

Gegenstand dieser Dissertation war das Ermitteln der Verbesserung der peroralen Bioverfügbarkeit Fenofibrat (FFB) durch lipid-basierte Formulierung (LBF). Eine weitere Aufgabe bestand darin, verschiedene analytische Methoden zur Bewertung der Verbesserung der oralen Bioverfügbarkeit

von Fenofibrat einzusetzen. Diese schlossen in vitro biorelevante Löslichkeits-, Dispersions-, Auflösungs- und Präzipitationstests ein. Auf Basis der analytischen Ergebnisse wurden dann PBPK-Modelle verwendet, um menschliche Plasmaprofile nach der Verabreichung der FFB-Formulierungen zu simulieren. Die daraus resultierenden in silico-Vorhersagen stimmten mit den in vivo-Beobachtungen überein. Durch Anwendung der Parametersensitivitätsanalyse war es weiterhin möglich, ein mechanistisches Verständnis der beteiligten geschwindigkeitsbegrenzenden Schritte zu erreichen. Formulierungen auf Lipidbasis können nach dem Pouton-Klassifizierungssystem eingeteilt werden. Typ I Formulierungen bestehen ausschließlich aus Ölen, während am anderen Ende der Skala die Typ IV Formulierung weitestgehend aus Tensiden ist. In dieser Arbeit wurden in erster Linie Lipidformulierungen Typ IIIA und Typ IIIB untersucht. Es wurde gezeigt, dass Dispersionstests an FFB-Lipidformulierungen am besten unter Verwendung der USP 3-Apparatur durchgeführt werden, da in diesem Apparat die GI-Motilität in vivo am besten reflektiert wird. Um die

Hydrodynamik in verschiedenen Auflösungsapparaten zu vergleichen, wurde der Auflösungsversuch von LBF Nr. 1 - Nr. 4 von FFB auch unter Verwendung von USP 2 durchgeführt. Ungeachtet von kompendialen oder biorelevanten Medien führten die meisten dieser Lipidformulierungen zur Auflösung eines Großteils des beladenen Medikaments, im Gegensatz zum unformulierten Fenofibrat, das sich in nüchternem Zustand kaum auflöst. Weiter zeigten die Transfermodellexperimente an den Lipidformulierungen von FFB, dass eine intestinale Präzipitation nach einer Magenauflösung unwahrscheinlich ist. Durch mathematische Transformation der Noyes-Whitney-Gleichung kann ein Excel-Toolkit zur Berechnung des z-Werts aus in-vitro-Auflösungsprofilen verwendet werden. Die z-Werte werden dann in physiologisch-basierte pharmakokinetische in silico Modelle, STELLA® und Simcyp®, eingesetzt. Anhand der erforderlichen post-absorptiven Parameter kann mithilfe dieser Modelle die Plasma-Arzneistoff-Konzentration nach oraler Verabreichung von verschiedenen Formulierungen vorhergesagt werden. Darüber hinaus ermöglicht der Simcyp®-Simulator eine Reihe von virtuellen

Versuchen, die PK-Variabilität vom Wirkstoff in verschiedenen Bevölkerungsgruppen zu bestimmen. Um diese Möglichkeiten für LBF von Fenofibrat zu testen, wurde LBF Nr. 4 modelliert. Das Simulationsergebnis von Simcyp® entsprach dem aus der STELLA®-Software. Weiterhin wurden die Plasmafenofibrinsäure-Konzentrationsprofile von den Modellen genau vorhergesagt. Die Punktschätzwerte für C<sub>max</sub> und AUC, berechnet aus den In-silico und in vivo Plasmaprofilen, lagen sogar im Bereich von 0,8-1,25 für die SMEDDS Lösung und Kapselformulierungen. Diese Übereinstimmung von in vitro-in silico mit in vivo wurde weiterhin durch Berechnung der jeweiligen f<sub>2</sub> Faktoren unterstützt. Basierend auf diesen Ergebnissen scheint es, dass der In-vitro-In-Silico-In-vivo-Ansatz ein nützliches Werkzeug zum Identifizieren und Vergleichen von Beschränkungen der oralen Absorption für Formulierungen auf Lipidbasis und zum Optimieren der Lipidformulierungsentwicklung von schlecht löslichen Arzneimitteln darstellt.

Background: The work presented in this thesis was designed as a part of an ongoing research project to develop a formulation strategy to enhance the oral bioavailability of

lycopene. As a natural antioxidant derived from dietary sources, lycopene has attracted considerable attention as a potent chemopreventative agent. Lycopene is an extremely lipophilic compound and absorption from dietary sources is estimated to be low and highly variable. The purpose of this thesis is to perform a systematic assessment of lycopene absorption from the gastrointestinal tract and to design a novel oral formulation strategy of lycopene. Methods: A mechanistic evaluation of the route of absolute absorption and absolute bioavailability of lycopene was evaluated in the mesenteric lymph duct cannulated rat model. Lycopene was formulated in a range of self micro-emulsifying drug delivery system and then characterised. A solid dispersion was also investigated. Finally, the in vivo bioavailability was evaluated in conscious pig model. Results: The absolute bioavailability of lycopene is  $1.85 \pm 0.39\%$  and the intestinal lymphatic route is the major uptake mechanism of lycopene from gastrointestinal tract. A novel LBSDF formulation which developed resulted in a 2.2-fold higher bioavailability compared to the commercial lycopene product, lycovit®. Conclusion: The data obtained in this study illustrate a

number of design concepts that might usefully be incorporated into formulation strategies for lipid-based formulations of poorly water soluble drugs. In the case of lycopene, an optimised formulation, which allows for efficient and reproducible dosing may serve as the basis for a prospective case controlled study into the potential benefits of this potent antioxidant.

Emulsion-based Systems for Delivery of Food Active Compounds

Oral Lipid-Based Formulations

SNEDDS for Improved Oral Bioavailability of BCS ClassII Drug-IVIVC

Nanocolloids

Pharmacokinetics and Pharmacodynamics of Nanoparticulate Drug Delivery Systems

Therapeutic Delivery Solutions

This authoritative volume provides a contemporary view on the latest research in molecules with optimal drug-like properties. It is a valuable source to access current best practices as well as new research techniques and strategies.

Written by leading scientists in their fields, the text consists of fourteen chapters with an underlying theme of early collaborative opportunities between pharmaceutical and discovery sciences. The book explores the practical realities of performing physical pharmaceutical and biopharmaceutical research in the context of drug discovery with short timelines and low compound availability. Chapters cover strategies and tactics to enable discovery as well as predictive approaches to

establish, understand and communicate risks in early development. It also examines the detection, characterization, and assessment of risks on the solid state properties of advanced discovery and early development candidates, highlighting the link between solid state properties and critical development parameters such as solubility and stability. Final chapters center on techniques to improve molecular solubilization and prevent precipitation, with particularly emphasis on linking physiochemical properties of molecules to formulation selection in preclinical and clinical settings. *Pharmaceutical Drug Delivery Systems and Vehicles* focuses on the fundamental principles while touching upon the advances in the pharma field with coverage of the basic concepts, fundamental principles, biomedical rationales, preparative and characterization techniques, and potential applications of pharmaceutical drug delivery systems and vehicles.

The current project has explored the determinants of drug absorption following oral administration of lipid-based drug delivery systems (LBDDS) and the role of intestinal digestive processes on formulation performance. Particular focus has been directed to the role of formulation excipients and drug loading on the generation and maintenance of drug supersaturation during LBDDS processing and the subsequent impact on drug bioavailability. The data show that initiation of digestion by pancreatic enzymes functions as an effective supersaturation trigger and that addition of polymeric precipitation inhibitors (PPI) may be utilised to stabilise supersaturation for longer periods and therefore to enhance absorption. Formulation performance was highly correlated with the maximum degree of supersaturation that the

formulation generated on dispersion and digestion. In vitro, increasing drug dose initially increased drug thermodynamic activity in the aqueous colloidal phases formed by formulation digestion. Above a critical drug loading, however, supersaturation 'pressure' increased to a point above which nucleation and crystal growth dominated, resulting in drug precipitation. The utilisation of lower drug loads, higher surfactant levels, reduced cosolvent and the addition of PPI all enhanced formulation performance in vitro (i.e. supported ongoing solubilisation), however, subsequent studies showed that only in some cases was the addition of PPI able to support enhanced absorption in vivo. Consistent with the potential for increases in thermodynamic activity with increase in drug dose, non-linear increases in bioavailability were evident after administration of a series of LBDDS containing increasing quantities of drug to beagle dogs. In further alignment with the in vitro data, non-linear increases in bioavailability were also only evident up to a critical point, beyond which further increases in drug dose resulted in a reduction in bioavailability. The initial in vivo studies were therefore highly consistent with the in vitro supersaturation data. Replication of the in vivo study in a younger cohort of animals, however, was not able to reproduce the same trends and linear increases in exposure with dose were apparent in this animal cohort. Further studies failed to show a significant difference in hepatic function across the two cohorts, and instead suggested that age-related changes in GI solubilisation, potentially through increased bile salt secretion in the older cohort, may have led to better stabilisation of supersaturation and therefore increases in danazol absorption. Increases in the quantity of drug absorbed at higher doses in the older cohort

may have also magnified differences in exposure due to greater saturation of first pass metabolism. The latter data led to a more detailed evaluation of the role of drug dose on the bioavailability of danazol from LBDDS. These studies were conducted in rats to allow more direct exploration of the role of first pass metabolism, and gastric and intestinal processing on danazol bioavailability. Surprisingly, danazol exposure in the rat following oral administration of danazol formulated in similar LBDDS as those used in the dog studies was low ( 12%), and incorporation of PPI had limited effect. In contrast, co-administration of an inhibitor of CYP450 enzymes resulted in a large increase in bioavailability suggesting that the major limitation to oral bioavailability was first pass metabolism. The applicability of previous in vitro models of lipid digestion to events in the rat was also examined, and a number of modifications to the model suggested. The data obtained indicate that in the rat, lipid digestion may be less efficient than it is in the dog (or human), and therefore that digestion-mediated reductions in solubilisation capacity are less important, that danazol absorption from LBDDS formulations is high ( 50%) and that the principle limitation to danazol bioavailability in the rat is first pass metabolism. In summary, this thesis contributes to a better understanding of the mechanisms by which LBDDS promote drug solubilisation and absorption and specifically to the influence of drug dose, animal model and the inclusion of polymeric precipitation inhibitors (PPI) on supersaturation generation and stabilisation.

Highly lipophilic and poorly water soluble drug candidates are common outcomes of drug discovery programs in recent years, presenting drug development challenges through poor

gastrointestinal absorption and insufficient systemic exposure after oral administration. Co-administration with lipodic excipients presents an apparent strategy to improve the oral bioavailability of these compounds by stimulating enhanced solubilisation in the gut and recruitment of intestinal lymphatic drug transport. The impact of stimulating intestinal lymphatic transport to improve oral bioavailability on systemic drug exposure, clearance and deposition has been poorly understood. The interpretation of lymphatic drug transport data is further complicated by variations in dosing excipients and dispersed states, study models, prandial (fed/fasted) states, intravenous dosing conditions and formulations used for the assessment of absolute bioavailability. The studies described in this thesis investigated various factors affecting the intestinal lymphatic transport and oral bioavailability assessment of highly lipophilic compounds using lymph-cannulated and non lymph-cannulated animals. These factors examined included subtle differences in lipophilicity and lipid solubility of chemically similar drug analogues, lipid and non-lipid based oral formulations, intravenous dosing states and dosing conditions. The impact of lymphatic drug delivery on systemic exposure, clearance and drug deposition was also examined in comparison with portal route of drug absorption in this thesis. Oral bioavailability of highly lipophilic analogues was significantly enhanced after administration in long chain lipid-based formulations via stimulation of intestinal lymphatic transport and significantly influenced by subtle differences in lipid solubility, however, not lipophilicity as indicated by log P. After delivery in lymph or the lipid-based emulsion, systemic clearance (Cl) and volume of distribution (Vd) of a

highly lipophilic, lymphatically transported model drug, halofantrine (Hf) were significantly lower than when delivered in plasma or lipid-free co-solvent formulation. However, where drug and lipid entered the systemic circulation coincidentally,  $Cl$  and  $V_d$  were unaffected by the route of entry, but significantly altered by total plasma lipid levels. These findings suggest that a mismatch in plasma lipid levels after intravenous and oral administration may lead to differences in drug clearance and errors in bioavailability assessment. This thesis also investigated the influence of absorption route (lymphatics vs. blood) on drug pharmacokinetics and tissue distribution. Brain to blood ratios were found to be significantly lower after stimulation of intestinal lymphatic delivery suggesting that drug association with intestinal lymph lipoproteins might limit brain drug access. Lipophilic model compounds (DDT, Hf) and lipids were assessed following delivery to the systemic circulation in association with lymph lipoproteins or plasma, and were found to differ significantly. For DDT,  $Cl$  and  $V_d$  were higher whereas for Hf, these parameters were lower due, in particular, to differences in adipose tissue uptake and liver uptake. For compounds like DDT, changes to the route of absorption may thus directly impact on pharmacokinetics and tissue distribution, whereas for Hf, factors which influence lymphatic transport may, by altering systemic lipoprotein concentrations, indirectly impact pharmacokinetics and tissue distribution. Ultimately, careful control of dosing conditions and thus the extent of lymphatic transport may be important in assuring reproducible efficacy and toxicity for lymphatically transported drugs.

Developing Solid Oral Dosage Forms

Recent trends in solubility and bioavailability enhancement for poorly water-soluble drugs

Pharmaceutical Drug Delivery Systems and Vehicles

Self Nanoemulsifying Drug Delivery System of Poorly

Soluble Drug Olanzapine for Enhanced Oral Bioavailability and IVVC

Enhancing the Bioavailability of Poorly Water-Soluble Drugs

Lipid Based Formulation Approaches to Enhance

Bioavailability of Lycopene

Advances in technology permeates every aspect of life, including the healthcare system. Nanotechnology based systems have gained popularity based upon their promise, size, and other characteristics. Multifunctional Nanocarriers for Contemporary Healthcare Applications is a critical academic publication that explores advancements in nanostructured systems, applications of these systems in healthcare, and biomedical applications of these systems. Featuring coverage on a wide range of topics, such as hydrogels, controlled drug delivery systems, and nanomedicine, this book is geared toward researchers, students, and academicians seeking current research on advancements and applications of nanostructured systems in the healthcare industry.

Nearly 40% of new drug candidates exhibit low solubility in water, which leads to poor oral bioavailability, high intra- and inter-subject variability and lack of dose proportionality. Modification of the physicochemical properties, such as salt formation and particle size reduction of the compound may be one approach to improve the dissolution rate. . In recent years, much attention has focused on lipid based formulations to improve the oral bioavailability of poorly water soluble drug compounds. In fact, the most popular approach is the incorporation of the drug compound into

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inert lipid vehicles such as oils, surfactant dispersions, self-emulsifying formulations, emulsions and liposomes with particular emphasis on self microemulsifying drug delivery systems (SMEDDS).

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Pharmaceutical Preformulation and Formulation: A Practical Guide from Candidate Drug Selection to Commercial Dosage Form reflects the mounting pressure on pharmaceutical companies to accelerate the new drug development and launch process, as well as the shift from developing small molecules to the growth of biopharmaceuticals. The book meets the need for advanced information for drug preformulation and formulation and addresses the current trends in the continually evolving pharmaceutical industry. Topics include: Candidate drug selection Drug discovery and development Preformulation predictions and drug selections Product design to commercial dosage form Biopharmaceutical support in formulation Development The book is ideal for practitioners working in the pharmaceutical arena—including R&D scientists, technicians, and

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managers—as well as for undergraduate and postgraduate courses in industrial pharmacy and pharmaceutical technology.

An in Vitro Model of Lipid Digestion for Assessing the Oral Bioavailability Enhancement Potential of Lipidic Formulations

Oral Drug Delivery for Modified Release Formulations  
Design and Development of Self Microemulsifying Drug  
Delivery System of Clopidogrel Bisulphate

Filtration and Purification in the Biopharmaceutical Industry  
Role of Lipid Excipients in Modifying Oral and Parenteral  
Drug Delivery

Discovering and Developing Molecules with Optimal Drug-Like Properties

Developing Solid Oral Dosage Forms is intended for pharmaceutical professionals engaged in research and development of oral dosage forms. It covers essential principles of physical pharmacy, biopharmaceutics and industrial pharmacy as well as various aspects of state-of-the-art techniques and approaches in pharmaceutical sciences and technologies along with examples and/or case studies in product development. The objective of this book is to offer updated (or current) knowledge and skills required for rational oral product design and development. The specific goals are to provide readers with: Basics of modern

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Sciences

theories of physical pharmacy,  
biopharmaceutics and industrial  
pharmacy and their applications  
throughout the entire process of  
research and development of oral dosage  
forms Tools and approaches of  
preformulation investigation,  
formulation/process design,  
characterization and scale-up in  
pharmaceutical sciences and  
technologies New developments,  
challenges, trends, opportunities,  
intellectual property issues and  
regulations in solid product  
development The first book (ever) that  
provides comprehensive and in-depth  
coverage of what's required for  
developing high quality pharmaceutical  
products to meet international  
standards It covers a broad scope of  
topics that encompass the entire  
spectrum of solid dosage form  
development for the global market,  
including the most updated science and  
technologies, practice, applications,  
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with case studies in every chapter A  
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established authors/co-authors of diverse background, knowledge, skills and experience from industry, academia and regulatory agencies

Filtration and Purification in the Biopharmaceutical Industry, First Edition greatly expands its focus with extensive new material on the critical role of purification and the significant advances in filtration science and technology. This new edition provides state-of-the-science information on all aspects of filtration and purification, in Oral lipid-based formulations are attracting considerable attention due to their capacity to facilitate gastrointestinal absorption and reduce or eliminate the effect of food on the absorption of poorly water-soluble, lipophilic drugs. Despite the obvious and demonstrated utility of these formulations for addressing a persistent and growing problem of major significance, the pharmaceutical industry has been slow to apply and further develop this technology. This title provides a comprehensive summary of the theoretical and practical

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aspects of oral lipid-based formulations for use in industry, and provides further insights into a developing technology expected to assume increasing prominence in years to come.

A suitable drug delivery system is an essential element in achieving efficient therapeutic responses of drug molecules. With this desirability in mind, the book unites different techniques through which extremely small-sized particles can be utilized as a successful carrier for curing chronic as well as life-threatening diseased conditions. This is a highly informative and prudently organized book, providing scientific insight for readers with an interest in nanotechnology. Beginning with an overview of nanocarriers, the book impetuses on to explore other essential ways through which these carriers can be employed for drug delivery to varieties of administrative routes. This book discusses the functional and significant features of nanotechnology in terms of Lymphatic and other drug targeting deliveries. The book is

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presenting depth acquaintance for various vesicular and particulate nano-drug delivery carriers, utilized successfully in Pharmaceutical as well as in Cosmeceutical industries along with brief information on their related toxicities. In addition, the work also explores the potential applications of nanocarriers in biotechnology sciences for the prompt and safe delivery of nucleic acid, protein, and peptide-based drugs. An exclusive section in the book illuminates the prominence and competent applicability of nanotechnology in the treatment of oral cancer. The persistence of this book is to provide basic to advanced information for different novel carriers which are under scale-up consideration for the extensive commercialization. The book also includes recent discoveries and the latest patents of such nanocarriers. The cutting-edge evidence of these nanocarriers available in this book is beneficial to students, research scholars, and fellows for promoting their advanced research.

Nanoarchitectonics for Smart Delivery

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Sciences  
and Drug Targeting

A Practical Guide from Candidate Drug  
Selection to Commercial Dosage Form  
Formation, Application, Health and  
Safety

Mechanistic Understanding of Enhanced  
Human Oral Bioavailability of  
Fenofibric Acid from Novel Lipid  
Carriers Using Semi- Physiologically  
Based Pharmacokinetic Model and Various  
Analytical Approaches Including  
Biorelevant Dissolution Testing  
Concepts and Applications

Investigation of Formulation Variables  
and Physiological Processing on the  
Behaviour of Lipid-based Formulations  
for Poorly Water-soluble Drugs

***With the advance of combinational chemistry  
and high throughput screening, an increasing  
number of pharmacologically active compounds  
have been discovered and developed. A  
significant proportion of those drug candidates  
are poorly water-soluble, thereby exhibiting  
limited absorption profiles after oral  
administration. Therefore, advanced formulation  
and processing technologies are demanded in  
order to overcome the biopharmaceutical limits  
of poorly water-soluble drugs. A number of  
pharmaceutical technologies have been***

***investigated to address the solubility issue, such as particle size reduction, salt formation, lipid-based formulation, and solubilization. Within the scope of this dissertation, two of the pharmaceutical technologies were investigated names thin film freezing and hot-melt extrusion. The overall goal of the research was to improve the oral bioavailability of poorly water-soluble drugs by producing amorphous solid dispersion systems with enhanced wetting, dissolution, and supersaturation properties. In Chapter 1, the pharmaceutical applications of hot-melt extrusion technology was reviewed. The formulation and process development of hot-melt extrusion was discussed. In Chapter 2, we investigated the use of thin film freezing technology combined with template emulsion system to improve the dissolution and wetting properties of itraconazole (ITZ). The effects of formulation variables (i.e., the selection of polymeric excipients and surfactants) and process variables (i.e., template emulsion system versus cosolvent system) were studied. The physic-chemical properties and dissolution properties of thin film freezing compositions were characterized extensively. In Chapter 3 and Chapter 4, we investigated hot-melt extrusion technology for producing amorphous solid dispersion systems and improving the***

***dissolution and absorption of ITZ. Formulation variables (i.e., the selection of hydrophilic additives, the selection of polymeric carriers) and process variables (i.e., the screw configuration of hot-melt extrusion systems) were investigated in order to optimize the performance of ITZ amorphous solid dispersions. The effects of formulation and process variables on the properties of hot-melt extrusion compositions were investigated. In vivo studies revealed that the oral administration of advanced ITZ amorphous solid dispersion formulations rendered enhanced oral bioavailability of the drug in the rat model. Results indicated that novel formulation and processing technologies are viable approaches for enhancing the oral absorption of poorly water-soluble drugs.***

***Nanoarchitectonics for Smart Delivery and Drug Targeting is one of the first books on the market to exclusively focus on the topic of nanoarchitectonics, a rapidly developing area of nanotechnology which allows scientists to arrange nanoscale structural units, typically a group of atoms or molecules, in an intended configuration. This book assesses novel applications of nanomaterials in the areas of smart delivery and drug targeting using nanoarchitectonics and discusses the***

**advantages and disadvantages of each application. Provides a scholarly introduction to the uses of nanoarchitectonics in drug delivery and targeting Explores novel opportunities and ideas for developing and improving nanoscale drug delivery systems through the use of nanoarchitectonics, allowing scientists to see how this exciting new technology is used in practice Assesses the pros and cons of each application, allowing readers to assess when it is most appropriate to use nanoarchitectonics in drug delivery**

**Nanocolloids: A Meeting Point for Scientists and Technologists presents an easy-to-read approach to current trends in nanoscale colloid chemistry, which offers relatively simple and economically feasible ways to produce nanomaterials. Nanocolloids have been the subjects of major development in modern technology, with many current and future applications. The book helps scientists and technologists to understand the different aspects of modern nanocolloid science. It outlines the underlying fundamental principles of nanocolloid science and covers applications ranging from emulsions to dispersions and suspensions. You will find details on experimental techniques and methods for the synthesis and characterization of nanocolloids,**

***including the latest developments in nanoemulsions and nanoparticles. Edited by leading academics with over 10 years' experience in the field of colloid and surfactant science. Each chapter is authored by recognized experts in the field. Outlines the underlying fundamental science behind nanocolloids. Provides comprehensive coverage of current topics and potential applications in nanocolloid science. Presents a multidisciplinary approach to help chemical engineers, chemists, physicists, materials scientists and pharmacologists, form an in-depth understanding of nanocolloid science.***

***Lipid Nanocarriers for Drug Targeting presents recent advances in the area of lipid nanocarriers. The book focuses on cationic lipid nanocarriers, solid lipid nanocarriers, liposomes, thermosensitive vesicles, and cubosomes, with applications in phototherapy, cosmetic and others. As the first book related to lipid nanocarriers and their direct implication in pharmaceutical nanotechnology, this important reference resource is ideal for biomaterials scientists and those working in the medical and pharmaceutical industries that want to learn more on how lipids can be used to create more effective drug delivery systems. Highlights the most commonly used types of lipid nanocarriers***

***and explains how they are applied in pharmacy***

***Shows how lipid nanocarriers are used in  
different types of treatment, including oral  
medicine, skin repair and cancer treatment***

***Assesses the pros and cons of using different  
lipid nanocarriers for different therapies***

***Nanocarriers for Drug Delivery***

***Multifunctional Nanocarriers for Contemporary  
Healthcare Applications***

***Advanced Formulation and Processing***

***Technologies in the Oral Delivery of Poorly  
Water-soluble Drugs***

***Novel Paediatric Formulation for the Drug  
Sodium Benzoate***

***Solid State Development and Processing of  
Pharmaceutical Molecules***

***A Meeting Point for Scientists and Technologists***

***Self-nanoemulsifying drug delivery systems  
(SNEDDS) have been proved as***

***technologically worthwhile, effortlessly  
scalable and economically sound delivery  
systems for enhancing the oral  
bioavailability of highly lipophilic drugs.***

***Distinct merits of smaller globule size,  
higher solubilization tendency and robust  
formulation advantages have made them as  
one of the most promising alternatives  
among the diverse lipid-based  
nanostructured systems. In the last two  
decades, the phenomenal success of***

**SNEDDS as a potential delivery platform for oral delivery of drugs has gained phenomenal interest in academia and industry with utility of them in non-oral drug delivery too. The current book manuscript provides an overview account on the recent advances in the development of self-nanoemulsifying formulations along with their characterization and applications in enhancing biopharmaceutical performance of the drugs. Besides, the book highlights two research case studies as instances to the pharmaceutical formulation scientists for development of solid self-nanoemulsifying systems of two poorly water soluble drugs, ondansetron and valsartan, for enhancing their oral bioavailability.**

**This book covers basic aspects of different nanoparticles, including type of materials, lipid, polymeric and inorganic structures, synthesis strategies, as well as the main physicochemical characterization techniques. Moreover, this book addresses applications for both treatment and diagnosis of diseases, highlighting in vitro and in vivo findings and clinical evaluation. The chapters highlight the main barriers for drug delivery which can benefit from nanoencapsulation: the topical and oral routes. The main innovations in the field,**

such as gene therapy and functionalization of nanoparticles with a variety of moieties, including monoclonal antibodies for selective delivery, are discussed and illustrated with examples. Finally, the application of nanoparticles for drug delivery to cancer is reviewed considering toxicology and regulatory aspects.

This comprehensive resource covers the fundamentals, formulation, and biopharmaceutical issues of lipid-based drug delivery. It presents the principles of lipid absorption and covers formulation issues, such as dissolution testing and stability testing, and physiological and biopharmaceutical issues, including the role of specific enzymes, the evaluation of transport systems in the body, and the mechanisms governing the transport of water-insoluble drugs.

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- 1. Silymarin-loaded solid nanoparticles with excellent hepatic protection: physicochemical characterization and in vivo evaluation.**
- 2. The Influence of Bile Salt on the Chemotherapeutic Response of Docetaxel-loaded Thermosensitive Nanomicelles.**
- 3. Enhanced oral bioavailability of fenofibrate using polymeric nanoparticulated systems: Physicochemical characterization and in**

**vivo investigation. 4. Tumor-targeting. pH-sensitive nanoparticles for docetaxel delivery to drug-resistant cancer cells. 5. Comparative study on solid self-nanoemulsifying drug delivery and solid dispersion system for enhanced solubility and bioavailability of ezetimibe. 6. Novel electrosprayed nanospherules for enhanced aqueous solubility and oral bioavailability of poorly water-soluble fenofibrate. 7. Receptor-targeted. drug-loaded. functionalized graphene oxides for chemotherapy and photothermal therapy. 8. Progressive slowdown/prevention of cellular senescence by CD9-targeted delivery of rapamycin using lactose-wrapped calcium carbonate nanoparticles. 9. Optimization and physicochemical characterization of a cationic lipid-phosphatidylcholine mixed emulsion formulated as a highly efficient vehicle that facilitates adenoviral gene transfer. 10. Combination of NIR therapy and regulatory T cell modulation using layer-by-layer hybrid nanoparticles for effective cancer photoimmunotherapy. 11. Cyclic RGD-conjugated Pluronic® blending system for active. targeted drug delivery. 12. Transferrin-Conjugated Polymeric Nanoparticle for Receptor-Mediated Delivery of Doxorubicin in Doxorubicin-Resistant Breast Cancer Cells. 13. Self-**

**microemulsifying drug delivery system (SMEDDS) for improved oral delivery and photostability of methotrexate. 14.**

**Comparison of 1-palmitoyl-2-linoleoyl-3-acetyl-rac-glycerol-loaded self-emulsifying granule and solid self-nanoemulsifying drug delivery system: powder property, dissolution and oral bioavailability. 15.**

**Liposomal Formulations for Nose-to-Brain Delivery: Recent Advances and Future Perspectives. 16. Development of folate-functionalized zein nanoparticles for ligand-directed delivery of paclitaxel.**

**Examination of the Relationship Between Solubilisation, Supersaturation and Drug Absorption from Lipid-based Formulations Nanocarriers: Drug Delivery System Development of Self Microemulsifying Drug Delivery System**

**Pharmaceutical Theory and Practice Formulating Poorly Water Soluble Drugs An Investigation of the Impact of Intestinal Lymphatic Transport on Bioavailability, Systemic Clearance and Disposition of Lipophilic Drugs**

**ORAL DRUG DELIVERY FOR MODIFIED RELEASE FORMULATIONS** Provides pharmaceutical development scientists with a detailed reference guide for the development of MR formulations Oral Drug Delivery for Modified Release Formulations is an up-to-

date review of the key aspects of oral absorption from modified-release (MR) dosage forms. This edited volume provides in-depth coverage of the physiological factors that influence drug release and of the design and evaluation of MR formulations. Divided into three sections, the book begins by describing the gastrointestinal tract (GIT) and detailing the conditions and absorption processes occurring in the GIT that determine a formulation's oral bioavailability. The second section explores the design of modified release formulations, covering early drug substance testing, the biopharmaceutics classification system, an array of formulation technologies that can be used for MR dosage forms, and more. The final section focuses on in vitro, in silico, and in vivo evaluation and regulatory considerations for MR formulations. Topics include biorelevant dissolution testing, preclinical evaluation, and physiologically-based pharmacokinetic modelling (PBPK) of in vivo behaviour. Featuring contributions from leading researchers with expertise in the different aspects of MR formulations, this volume: Provides authoritative coverage of physiology, physicochemical determinants, and in-vitro in-vivo

correlation (IVIVC) Explains the different types of MR formulations and defines the key terms used in the field Discusses the present status of MR technologies and identifies current gaps in research Includes a summary of regulatory guidelines from both the US and the EU Shares industrial experiences and perspectives on the evaluation of MR dosage formulations Oral Drug Delivery for Modified Release Formulations is an invaluable reference and guide for researchers, industrial scientists, and graduate students in general areas of drug delivery including pharmaceuticals, pharmaceutical sciences, biomedical engineering, polymer and materials science, and chemical and biochemical engineering.

Currently, more than 90% of compounds identified are water insoluble and or poorly water soluble, which is a bottle neck in the development of many new drug candidates. These poorly soluble drug molecules are difficult to formulate using conventional approaches and are associated with numerous formulation-related performance issues. Formulating these compounds using lipid-based systems is one of the rapidly growing interests and suitable drug delivery strategies. Lipid

formulations such as self-emulsifying/microemulsifying/nanoemulsifying drug delivery systems (SEDDS/SMEDDS/SNEDDS) have been attempted in many researches to improve the bioavailability and dissolution rate for their better dispersion properties.

One of the greatest advantages of incorporating the poorly soluble drug into such formulation products is their spontaneous emulsion and or microemulsion/nanoemulsion formation in aqueous media. The performance and ongoing advances in manufacturing technologies have rapidly introduced lipid-based drug formulations as commercial products into the marketplace with several others in clinical development. The current chapter aims to present the characteristics feature, development and utilization of oral lipid-based nanoformulations within the drug delivery regime. The content of the chapter also provides an insight into the in vitro evaluation of lipid-based nanosystems and their limitations.

Oral Drug Absorption, Second Edition thoroughly examines the special equipment and methods used to test whether drugs are released adequately when administered orally. The contributors discuss methods for accurately establishing and validating in vitro/in vivo correlations for both MR

and IR formulations, as well as alternative approaches for MR an Molecular dynamics (MD) simulation is a powerful technique to investigate molecular self-assembly. It can be used to model and understand the interactions of biological membranes, proteins, and lipids. Above their critical micelle concentration (CMC), molecules that are composed of hydrophilic head group and hydrophobic tail group aggregate spontaneously to form a wide variety of assemblies ranging from micelles, rodlike structures, and bilayers to more complex phases such as hexagonal and cubic phases. These self-assembly processes are of fundamental importance in drug discovery and development. In the area of drug discovery and development, it is vital to have an effective means of improving the bioavailability of poorly water-soluble drugs (PWSD). Lipid-based delivery systems (LBDDS) are one of the important approaches of improving the bioavailability of PWSD. The nature of gastrointestinal (GI) fluids strongly influences the absorption of PWSDs. The dissolution rate and the amount of drugs dissolved is determined by the nature of the GI fluids and their solubilisation capacity. Within the GI tract there are

endogenous as well as exogenous solubilising components. The endogenous components are secreted from the gall bladder, whereas the exogenous components are those which are administered in the drug formulation as well as resulting from meals. After oral administration, drugs must remain dissolved within the GI tract before partitioning into and then across the enterocyte. Although the self-assembly process of lipids and lipophilic excipients within the GI tract are thought to have a significant influence on drug solubilisation and the degree of drug supersaturation, the molecular understanding of these structures is limited. The first section of this work describes the modification of the GROMOS 53A6 united atom force field particularly for polyethylene glycol (PEG). Then, using MD simulations and experimental methods such as turbidity, particle size measurement, cross-polarized light microscopy and NMR, the current study explores the phase behaviour of (i) the 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC), sodium glycochenodeoxycholate (GDX), and water system, and (ii) the 1-palmitoyl-2-hydroxy-sn-glycerol-3-phosphocoline (Lyso PC), GDX and water system and constructs ternary

phase diagrams of these mixtures. It also investigates part of the quaternary phase diagram of Lyso PC, glycerol 1-monooleate (GMO), GDX and water, which was used to investigate the structures formed in the intestine after digestion of triglycerides. The solubilisation capacity of the lipidic microenvironment on PWSD has also been investigated using LC-MS and MD simulation. The association structures of these various systems have been modelled and compared to the experimental phase behaviour of the analogous systems. It is indicated in these studies that digestion and digested products have a significant impact on the phase behaviour of the contents of the small intestine and on solubilisation and bioavailability of PWSDs. In summary, this thesis contributes to a better understanding of the performance of lipid-based formulations (LBF) and shines a light on the use of MD simulations as a prediction tool to model LBDDS.

Pharmaceutical Preformulation and Formulation

Preparation and Evaluation of Lovastatin Self Microemulsifying Drug Delivery System  
A Comprehensive Text Book on Self-emulsifying Drug Delivery Systems

**A comprehensive text that offers a review of the delivery of**

**food active compounds through emulsion-based systems**  
**Emulsion-based Systems for Delivery of Food Active Compounds** is a comprehensive recourse that reviews the principles of emulsion-based systems formation, examines their characterization and explores their effective application as carriers for delivery of food active ingredients. The text also includes information on emulsion-based systems in regards to digestibility and health and safety challenges for use in food systems. Each chapter reviews specific emulsion-based systems (Pickering, multiple, multilayered, solid lipid nanoparticles, nanostructured lipid carriers and more) and explains their application for delivery of food active compounds used in food systems. In addition, the authors – noted experts in the field – review the biological fate, bioavailability and the health and safety challenges of using emulsion-based systems as carriers for delivery of food active compounds in food systems. This important resource: Offers a comprehensive text that includes detailed coverage of emulsion-based systems for the delivery of food active compounds Presents the most recent development in emulsion-based systems that are among the most widely-used delivery systems developed to control the release of food active compounds Includes a guide for industrial applications for example food and drug delivery is a key concern for the food and pharmaceutical industries Emulsion-based Systems for Delivery of Food Active Compounds is designed for food scientists as well as those working in the food, nutraceutical and pharmaceutical and beverage industries. The text offers a comprehensive review of the essential elements of emulsion-based systems for delivery of food active compounds.