Biography (2021)

Professor of Biopharmaceutics and Industrial Pharmacy

Dr. Fassihi is a professor of biopharmaceutics and industrial pharmacy at Temple University, School of Pharmacy, where he has taught and done research in the pharmaceutical sciences since 1992. He has worked as an assistant professor at Isfahan University (1979-1982), a postdoctoral fellow at Brighton University (1983), a Senior Scientist at Welsh School of Pharmacy (1984), and Senior Lecturer at Rhodes University in South Africa (1984-1988). He was Founder and Head of School of Pharmacy, and Professor and Chair of Department, at University of the Witwatersrand in Johannesburg, South Africa (1988-1992), where he was awarded with gold medals by both the Academy of Pharmaceutical Sciences and the Society of Cosmetic Chemists. In 1991 he was a visiting professor at Cincinnati University undertaking research in advanced biopharmaceutics with Professor Wolfgang A. Ritschel and in 1992 he joined Temple University, School of Pharmacy, where he has served as professor, director of graduate programs, chair of various university committees and professional organizations. His research emphasizes on design, development, evaluation (*in-vitro and in-vivo*), optimization and scale-up operations of oral dosage forms, oral-soluble films, orally disintegrating tablets, capsules, tablets, enteric coated, osmotic pumps, tampered resistant systems, controlled and modified release drug delivery(CR), dispersed systems, topical products, gels, parenteral and advanced delivery systems, some of which are presented in Figure-1.

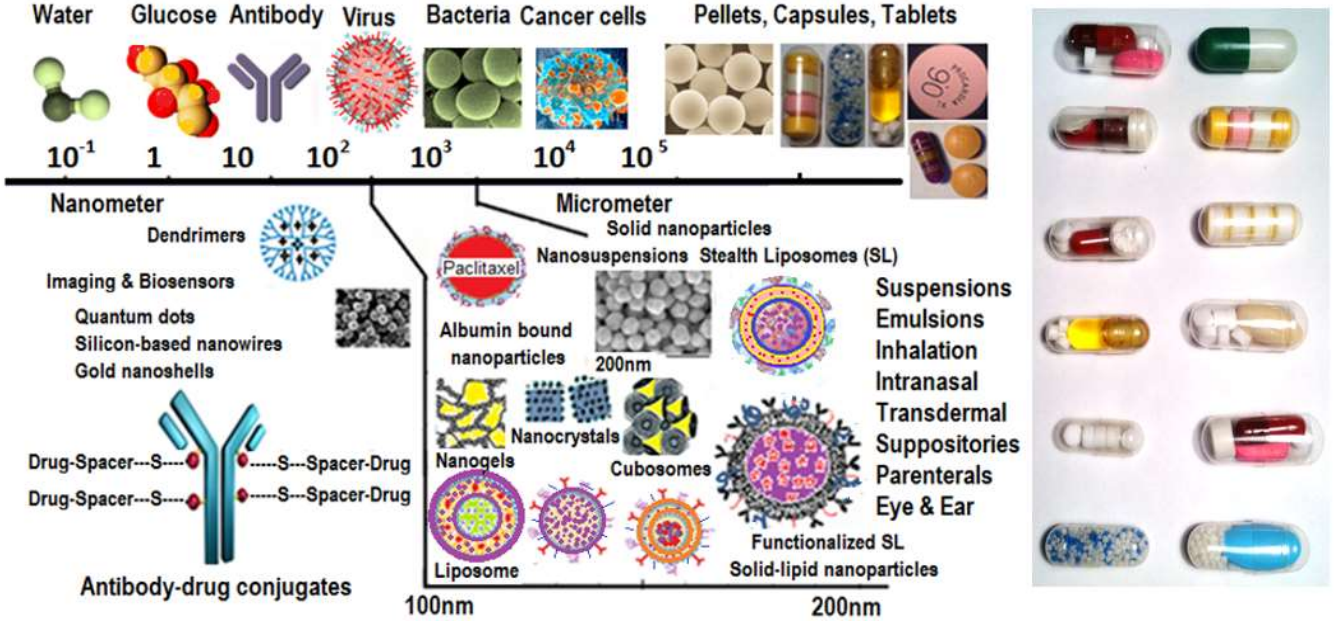

Figure 1. Approximate size spectrum of drug carriers and drug delivery systems (R.Fassihi; Pharmaceutical Dosage Forms Capsules, Edited by L. L. Augsburger & S. W. Hoag; (2017) Taylor & Francis Group, LLC.).

Oral CR systems were introduced in the 1950's and 100's of products with significant clinical benefits have been FDA approved. However, growth of CR parenteral has been slow. PLGA based depot CR delivery systems especially for delivery of anticancer drugs, opioids, antipsychotics, drugs used in the treatment of opioid use disorder, and antimicrobials in periodontal diseases including gingivitis and periodontitis, constitute a major area of research. Since its introduction in 1989 only twenty PLGA based formulations are FDA approved with no generic product approvals. This is due to the absence of standard dissolution methods and full understanding of PLGAs in complex depot formulations. It is critical to identify the same inactive ingredients (Q1) and in the same concentration (Q2) as the reference listed drug in reverse engineering for generic product development. There are diverse types of PLGA depot formulations including micro-particles, solid implant, and in situ gel implant. We developed in-situ gel depot formulations of PLGA-naltrexone and determined their drug release rate based on a novel dissolution method referred to as "Shape Controlled Basket in Tube", (see Fig.2). Results obtained with the developed method demonstrated accuracy, reproducibility and simplicity of the method for investigating release over weeks or months when compared with other cumbersome methods (i.e. USP 1; 4; dialysis-based and continuous flow methods), see Fig. 3. This can provide greater opportunity to compare drug release from various formulations (brand vs generic) during delivery system development and the FDA approval process with discriminatory power of dissolution method and use of an integrated fiber-optic UV dip probe for ease of release rate determination.

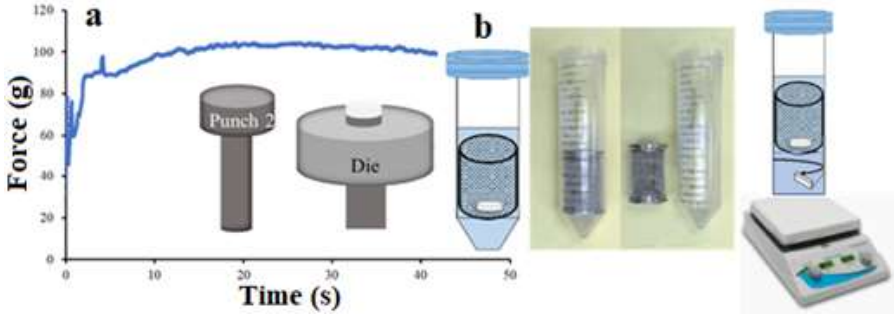

Fig.2. (a)-Schematics of the in-situ gel disk preparation for shape control using a mold assembly with application of 100 g force observed for highly viscous SC or IM injectable formulations, (AAPS PharmSciTech, Feb, 20, (2018). (b)-Use of USP basket fitted in tube(s) method for full surface exposure and in-situ quantification using shaker or magnetic stirrer; (AAPS-2019 & J. Pharm. Pharmacology 2020).

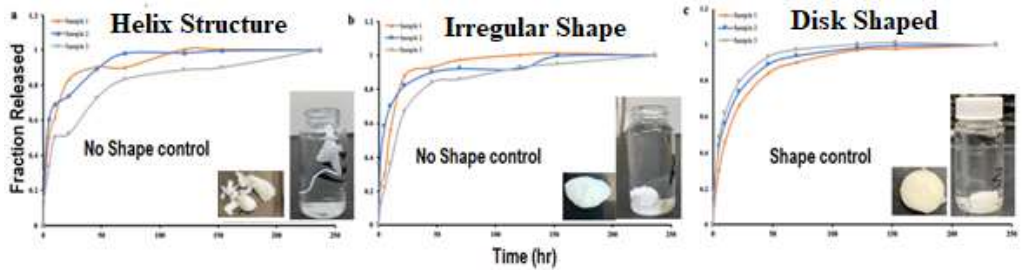

Fig. 3. Using sample and separate method, various in-situ geometries formed upon injection of formulation with needle, without needle and with shape control. Release profiles embody (a) irregular helix structure, (b) irregular sphere like shape, and (c) controlled shape disk-like implant. Reproducibility of drug release is clearly apparent (see Figure 3C; N=3); (Journal of Pharmacy and Pharmacology, Pages 1-11, April-27 (2020). **https://doi.org/10.1111/jphp.13277).**

Development of Modified Release Tamper-resistant Microchip Embedded (MRTME) and patient specific formulations of opioids, antipsychotics and restricted drugs intended to prevent dosage form manipulation by making them harder to "crush, chew, inhale, insufflate, extract, snort, & inject", has been promoted as one strategy to prevent misuse and this area has been investigated by Dr. Fassihi (see Figure 4). In this work, matrix systems were not subjected to post manufacturing sintering step and this paradigm shift in process resulted in matrices that were crush-resistant and hard to tamper abuse. Matrices maintained their desired and sustained release properties in comparison to tampered and crush-resistant marketed products and demonstrated to be more robust and resistant to manipulations (see Figure-4). Additionally, inclusion of microchip within the system can be accomplished by multilayering, hot-melt extrusion, printing, or molding.

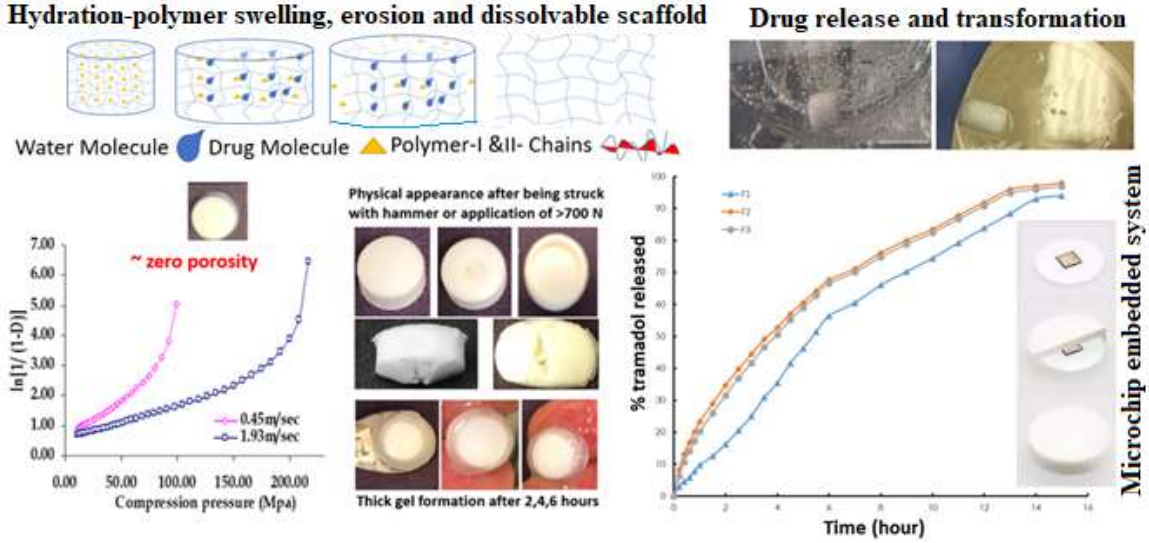

Figure 4. Heckel plots for Tramadol-PEO:P-II (4:1) matrices and changes in the physical appearances upon exposure to water, dissolution studies and hardness testing to demonstrate tamper-resistance properties. (US Patent Application Pending; Abuse deterrent delivery system - C2019-008). (C2019-008- International Publication Number- WO 2020/081762 A1).

His research explores the challenges and paradigms of advanced drug delivery systems. He has numerous book chapters, holds 10 US Patents and has over 375 abstracts and presentations. He is a member of several professional organizations including the AACP, ACS, HPA, AAPS and CRS and is a Fellow of American Association of Pharmaceutical Scientists (AAPS Fellow).

He has been an invited speaker at various professional meetings, FDA and pharmaceutical conventions and has presented seminars and workshops nationally and internationally. His research also has focused on an in-depth analysis and understanding of colloidal systems, gels, solid-state pharmaceutics, polymorphs and amorphous systems. In addition, excipient characterization, particulate systems, range of macromolecules and polymers (PEO, HPMC, HPMCAS, HPC, PVC, HEMA, PLGA, etc.), surfactants, solubilizing agents and application of biopharmaceutics in design of drug delivery systems studied. He has investigated development of amorphous solid dispersion (ASD), based on Spray Drying and Hot-Melt Extrusion (HME) techniques. He has further studied physicochemical characterization, micro-dissolution of ASDs and drug dissolution rate following various release kinetics and more importantly stability of such systems during manufacturing and postproduction, see Figure 5. Further examples in this class include production of stable amorphous system of Apremilast a BCS Class-IV drug that exists in 7 different polymorphic forms for sustained release.

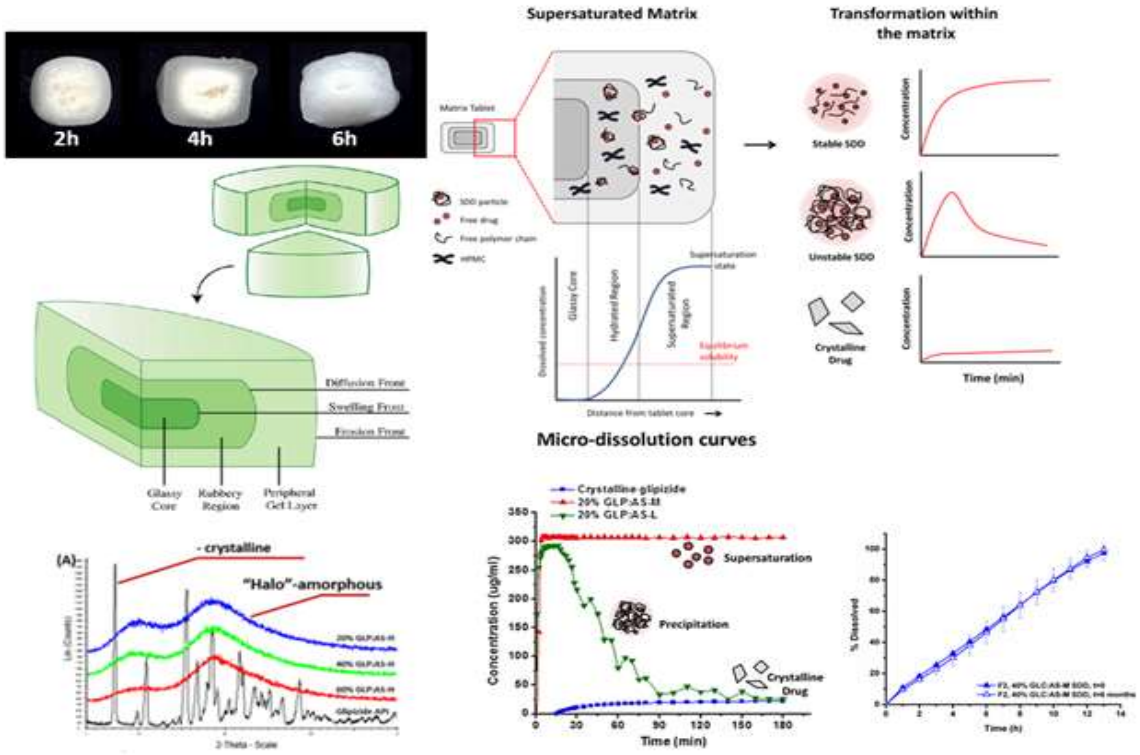

Figure 5. Use of compaction simulator to elucidate compaction effect on potential structural transformation of amorphous system (SDD) within the matrix and super-saturation state in hydrophilic SR matrix, during micro-dissolution, dissolution, and long-term stability. (Fassihi et.al. Int. Journal of Pharmaceutics 511, 957–968; 2016).

Currently he is investigating 'hot-melt extrusion (HME) technique' and developed a sustained release oral system for an insoluble API, ibrutinib (BCS-II) an inhibitor of Bruton's tyrosine kinase (BTK) over 6-8 hours to minimize GI side effects, reduce total dose and increase potential for greater bioavailability (International Journal of Pharmaceutics, August 2021; DOI: https://doi.org/10.1016/j.ijpharm.2021.120981).

Dr. Fassihi has authored or coauthored more than 145 peer-reviewed professional papers on topics related to the relationship between the physicochemical characteristics of drugs, their stability and biological effects. He has trained many professionals Pharm.D. and M.S. graduate students. He has mentored 29 Ph.D. students as well as visiting scholars and postdoctoral fellows addressing the core principles of pharmaceutics and biopharmaceutics in drug product development, drug performance, drug therapy, dissolution issues, extended-release systems and regulatory requirements etc. He currently teaches, does research, and acts as a consultant to the pharmaceutical industry and government agencies. He has served as an expert witness on issues related to drug formulations, dissolution characteristics, modified release systems, tampered resistant systems, and bioavailability and bioequivalence issues. He received the B. Pharm. (honors) (1974) Punjab University and Ph.D. (1978) from Brighton University in England, was awarded with a gold medal for his research work.