Biography (2024): Professor of Biopharmaceutics and Industrial Pharmacy

Reza Fassihi, B. Pharm., Ph.D., AAPS Fellow

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 and drug delivery design 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 September 1992 he joined Temple University, School of Pharmacy, where he has served as professor, director of graduate programs, chair of various university committees and multiple professional organizations. He has presented seminars nationally and internationally. 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 including, enteric coated, osmotic pumps, tampered resistant systems, controlled and modified release drug delivery(CR), dispersed systems, topical products, gels, parenteral, subcutaneous and advanced delivery systems. In modified release oral delivery systems, he has done extensive research in areas presented in the Figure-1.

Figure 1. Approximate size spectrum of drug carriers and drug delivery systems (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 developed and 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 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 lack of standard dissolution methods and full understanding of PLGAs degradation 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 forming implants. We developed in-situ gel depot formulations of PLGA-naltrexone and determined their drug release rate based on a novel and practical 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). 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 to detect changes in dissolution of the drug product.

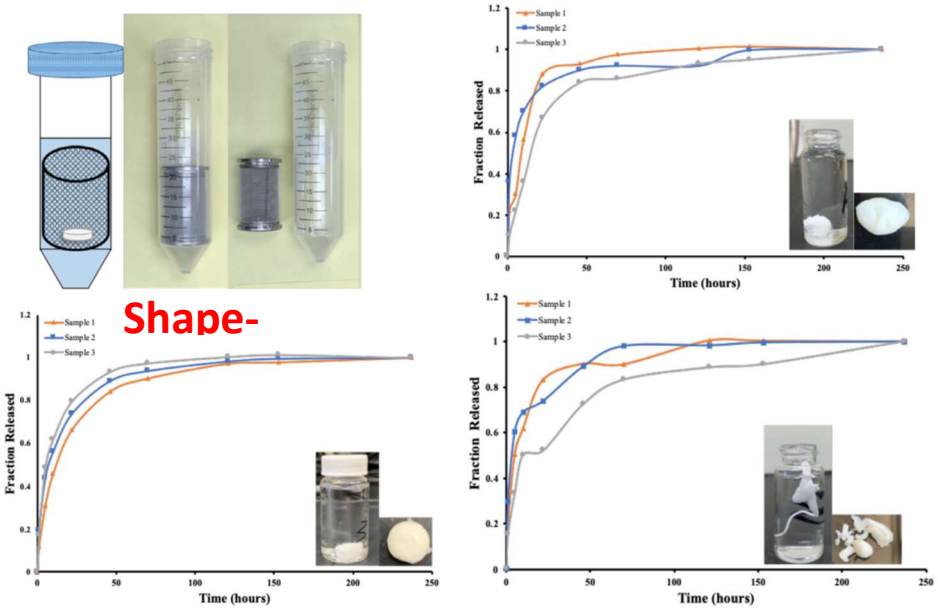

Fig.2. Schematics of the in-situ gel formation with different shapes and comparative dissolution profiles over 250 hours. (Q. Zhang and R. Fassihi, Journal of Pharmacy and Pharmacology, 72 (2020), pp. 1038–1048).

More recently we are exploring the use of thermo-responsive water-soluble polymers for advanced drug delivery design. These polymers can undergo phase transition in response to a temperature change. Currently we are investigating certain thermo-responsive in-situ gel forming formulations for potential delivery of potent drugs intravitreally, subcutaneously, and other routes. These polymers being water soluble undergo phase transition from sol to gel as temperature increases and can provide sustained drug release over a long

period of time. Delivery system composition must allow for neutralization of microenvironmental pH upon degradation of polymer over time. Typical triblock polymer and its Sol-Gel transition and drug release over time is shown in Figure 3.

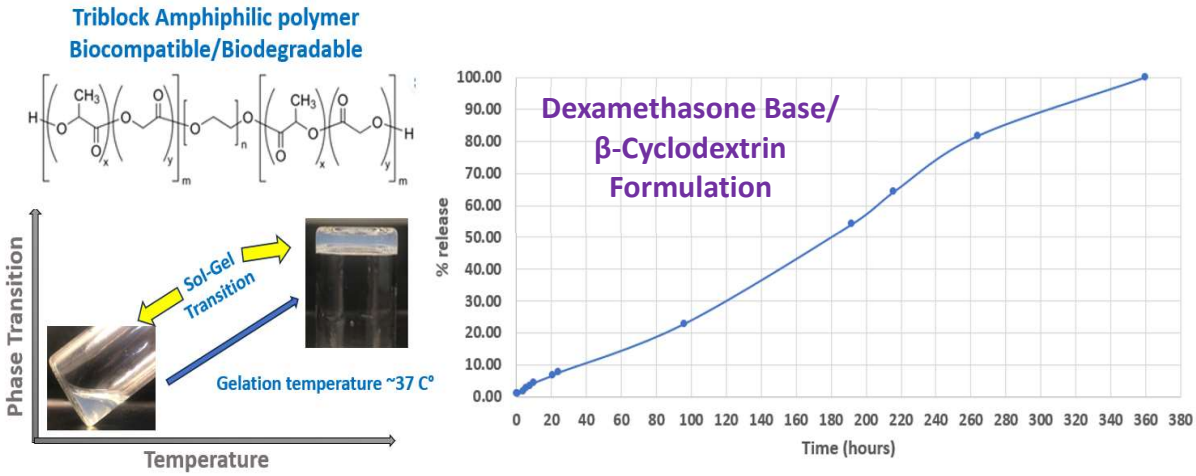

Figure 3- Typical triblock polymer and its Sol-Gel transition and drug release over time.

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 and adherence to medication regimen agreed and recommended by the health care provider, has been investigated by Dr. Fassihi. In this work, drug delivery design was based on in-process sintering of the formulation and this paradigm shift in process resulted in crush-resistant and robust delivery system. (See Figure-4). Additionally, inclusion of digestible microchip within the system can be accomplished by multilayering or 3D printing.

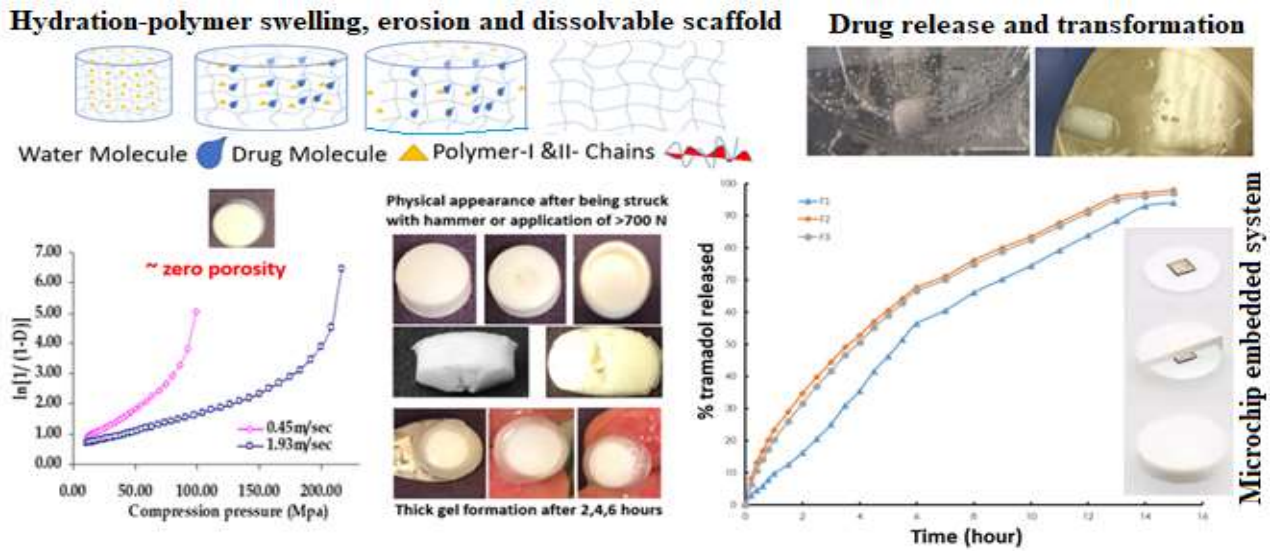

Figure 4. Heckel plots for Tramadol-PEO:P-II (4:1) matrices and changes in their physical appearances upon exposure to dissolution studies and hardness testing to demonstrate tamper-resistance properties. Schematics of digestible microchips embedment is also shown. (US Patent Application Pending; Abuse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

He has investigated development of amorphous solid dispersion (ASD), based on Spray Drying and Hot-Melt Extrusion (HME) techniques for development of sustained release delivery. In this regards, physicochemical characterization, micro-dissolution, and dissolution kinetics as well as system stability during manufacturing and postproduction was investigated (Figure 5). Selected drugs were apremilast (medication for psoriasis and psoriatic arthritis) a BCS Class-IV drug with 6 different polymorphic forms (International Journal of Pharmaceutics 615, (2022) 121516), and ibrutinib (BCS-II) an inhibitor of Bruton's tyrosine kinase (BTK) with 6 different polymorphic forms and glipizide (BCS-II) a medication for management of diabetes mellitus. Currently we are working on a novel thermos-responsive in-situ gel forming polymer for intravitreal, subcutaneous injections and inhalation delivery systems.

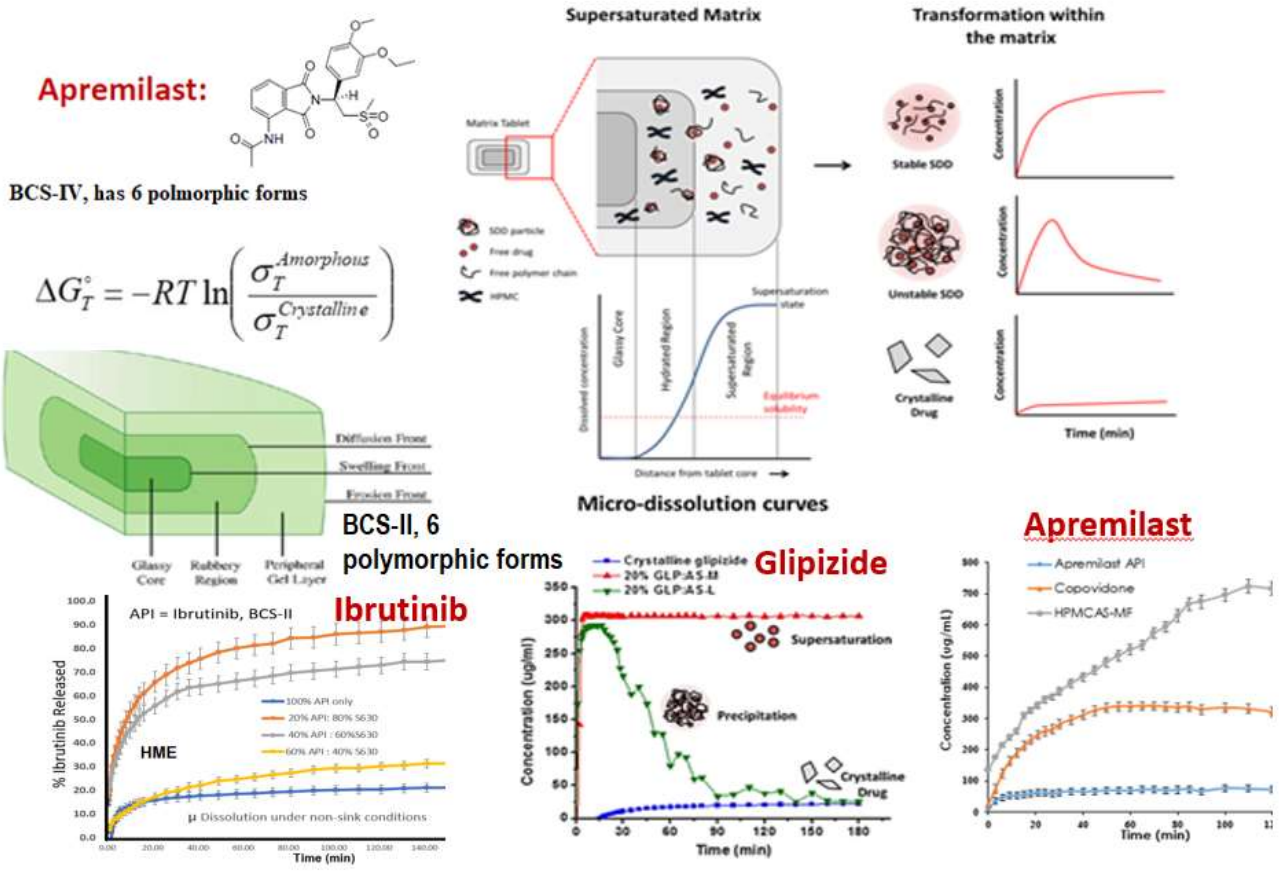

Figure 5. Development of ASD for three different drugs via spray drying and hot-melt extrusion with elucidation of potential structural transformation of amorphous system (SDD) within the matrix and super-saturation state and micro-dissolution investigation. (Lu and Fassihi et.al. Int. Journal of Pharmaceutics 511, 957–968; (2016); Alshahrouri and Fassihi et.al. Int. Journal of Pharmaceutics (2021), Zhang and Fassihi et.al (Int. Journal of Pharmaceutics 615, (2022) 121516).

Fassihi's research explores the challenges and paradigms of advanced drug delivery systems. 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, polymorphism, and amorphous systems. In addition, range of macromolecules and polymers (PEO, HPMC, HPMCAS, HPC, PVC, HEMA, PLGA, etc.), surfactants, solubilizing agents, and their biopharmaceutics application in design of drug delivery systems studied. Dr. Fassihi has authored or coauthored more than 145 peer-reviewed professional papers, 375 abstracts and presentations and holds 10 US Patents, 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 pharmaceutical sciences and biopharmaceutics in drug product development, drug performance, drug therapy, manufacturing issues, and regulatory requirements etc.

Dr. Fassihi with a few of his past and distinguished Ph.D. graduates at one of the AAPS annual meetings.

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 delivery systems, dissolution characteristics, modified release systems, tampered resistant systems, bioavailability and bioequivalence issues, patent infringements etc. He received the B. Pharm. (honors) (1974) Punjab University, India, and Ph.D. (1978) from Brighton University in England, where he was awarded with a gold medal in recognition of his outstanding research work.

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).

Dr. Fassihi with colleagues, past graduates, and friends of temple university school of pharmacy at one of the AAPS annual meetings.