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BCS-Guided Formulation Sciences: A Modern Review

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ABSTRACT

The Biopharmaceutics Classification System (BCS) categorizes drug molecules based on their aqueous solubility and intestinal permeability, establishing a scientific framework for predicting oral absorption and guiding formulation design. With increasing emphasis on biowaivers, regulatory harmonization, and Quality by Design (QbD), BCS has become a central tool in modern pharmaceutics. This review provides a comprehensive overview of BCS principles, experimental determination of solubility, permeability, and dissolution, regulatory implications, applications in oral drug development, and innovative formulation strategies tailored for each BCS class. Extensions of BCS—such as the Biopharmaceutics Drug Disposition Classification System (BDDCS) and revised permeability models—are also discussed. Emerging concepts such as machine learning-driven BCS prediction, advanced enabling technologies, and biowaiver expansions highlight the evolving landscape. The review emphasizes the crucial role of BCS-guided approaches in accelerating drug development, improving bioavailability, and enhancing the success rate of oral formulations.

Keywords: Biopharmaceutics Classification System (BCS), Solubility and Permeability, Biowaivers, IVIVC (In Vitro–In Vivo Correlation), Formulation Strategies.

INTRODUCTION

Oral drug delivery remains the most preferred route of administration due to its convenience, safety, and patient compliance. However, poor solubility and limited permeability continue to challenge the development of effective oral formulations. To address these issues, the FDA introduced the Biopharmaceutics Classification System (BCS) in 1995, providing a scientific basis for predicting drug absorption and guiding formulation decisions[1]. BCS has since become a cornerstone of regulatory practice, influencing bioequivalence studies, generic drug development, and formulation strategies. This review explores the modern applications of BCS in formulation sciences and its implications for the next generation of oral drug delivery[2-4].

2. Fundamentals of the Biopharmaceutics Classification System

BCS classifies drugs into four categories based on two key parameters:

1. **Solubility** in the physiologically relevant pH range (1.2–6.8)
2. **Permeability** across the intestinal membrane

BCS aims to predict oral absorption behavior and identify drugs eligible for biowaivers. Dissolution, a critical factor for oral delivery, is closely linked to both solubility and permeability and thus forms the scientific backbone of BCS[5-7].

3. BCS Classification Categories

3.1 Class I: High Solubility – High Permeability

Class I drugs are characterized by high solubility and high permeability, which enables them to undergo rapid dissolution in gastrointestinal fluids and achieve complete absorption across the intestinal membrane. Because their absorption is not limited by solubility or permeability, they typically exhibit predictable and consistent oral bioavailability. Examples of Class I drugs include Metoprolol, Propranolol, and Diltiazem, all of which demonstrate fast dissolution and efficient systemic uptake. Due to their favorable biopharmaceutical properties, these drugs can be conveniently formulated into simple immediate-release tablets without the need for advanced solubility- or permeability-enhancing techniques. From a

regulatory perspective, Class I drugs are highly eligible for BCS-based biowaivers, allowing developers to waive in vivo bioequivalence studies if rapid and consistent in vitro dissolution criteria are met, thereby reducing development time and cost[8-11].

3.2 Class II: Low Solubility – High Permeability

Class II drugs exhibit low solubility but high permeability, meaning their absorption is primarily dissolution-limited. Because these drugs dissolve slowly in gastrointestinal fluids, only a limited amount becomes available for absorption, leading to poor solubility and variable bioavailability. Representative examples include Carbamazepine, Ketoprofen, and Itraconazole, all of which require specialized formulation strategies to enhance dissolution. Common approaches include particle size reduction, solid dispersions, lipid-based delivery systems such as SEDDS and SMEDDS, and cyclodextrin inclusion complexes, each aiming to increase the drug's apparent solubility or dissolution rate. Despite advancements in enabling technologies, Class II drugs are not usually eligible for biowaivers because in vivo absorption cannot be reliably predicted from in vitro dissolution alone[12-15].

3.3 Class III: High Solubility – Low Permeability

Class III drugs are characterized by high solubility but low permeability, meaning their absorption is primarily permeability-limited rather than dissolution-dependent. Although these drugs dissolve readily in gastrointestinal fluids, only a small fraction is able to permeate across the intestinal epithelium, resulting in limited and variable oral absorption. Common examples include Acyclovir and Cimetidine, which highlight the challenges associated with enhancing intestinal uptake. To overcome poor permeability, several formulation strategies are employed, such as permeation enhancers, mucoadhesive delivery systems, and advanced vesicular carriers like niosomes and liposomes, all designed to increase membrane transport and prolong intestinal residence time. From a regulatory standpoint, Class III drugs may be considered for conditional biowaivers when their formulations contain excipients that do not influence permeability, and when rapid and consistent dissolution can be demonstrated across physiological pH conditions[16-20].

3.4 Class IV: Low Solubility – Low Permeability

Class IV drugs represent the most challenging category within the Biopharmaceutics Classification System due to their low solubility and low permeability, which severely limit oral absorption. Drugs in this class face dual barriers: they do not dissolve readily in gastrointestinal fluids, and even the dissolved fraction has difficulty crossing the intestinal membrane. Representative examples include Hydrochlorothiazide and Taxol, both of which demonstrate extremely poor oral bioavailability without specialized formulation strategies. To address these limitations, advanced technologies such as nanoparticles, polymeric micelles, combined solubility and permeability enhancement techniques, and prodrug strategies are commonly employed to improve drug uptake. Despite these innovations, Class IV drugs remain rarely eligible for biowaivers, as their complex absorption characteristics cannot be reliably predicted from in vitro dissolution studies alone[17-21].

4. Determination of BCS Parameters

4.1 Solubility Studies

Solubility studies for BCS classification are typically conducted across the physiological pH range of 1.2 to 6.8 to ensure that the drug's solubility profile reflects conditions within the gastrointestinal tract. According to regulatory criteria, the highest dose strength of the drug must be soluble in 250 mL of aqueous media to qualify as highly soluble. This requirement simulates the volume of fluid available in the stomach and intestine for drug dissolution. Solubility assessment commonly employs the shake-flask method, which provides equilibrium solubility data, along with pKa analysis to understand ionization behavior and predict solubility variations across different pH levels[22-25]. Together, these evaluations form the foundation for determining the drug's biopharmaceutical classification and guiding formulation strategies.

4.2 Permeability Assessment

Permeability assessment is a critical component of BCS classification and is performed using in vitro, in situ, and in vivo models to evaluate the extent of intestinal absorption. In vitro methods, such as Caco-2 cell lines and PAMPA assays, provide controlled systems to study passive diffusion and transporter interactions. In situ techniques, including intestinal perfusion, allow direct measurement of permeability across specific intestinal segments in animal models. In vivo studies, such as evaluating human jejunal permeability, offer the most physiologically relevant data by assessing actual absorption in humans[26-28]. A drug is considered to have high permeability if it exhibits ≥85% absorption, indicating efficient transport across the intestinal membrane and supporting its classification within high-permeability BCS categories.

4.3 Dissolution Testing

Dissolution testing is a critical component of BCS evaluation and is commonly performed using USP Apparatus I (basket) and Apparatus II (paddle), which simulate the mechanical agitation experienced by solid oral dosage forms in the

gastrointestinal tract. To more accurately reflect physiological conditions, testing may also utilize biorelevant media such as FaSSIF (Fasted State Simulated Intestinal Fluid) and FeSSIF (Fed State Simulated Intestinal Fluid), which mimic the composition of intestinal fluids in fasted and fed states. This approach is especially important for Class II drugs, where dissolution is the rate-limiting step in absorption. Establishing in vitro–in vivo correlation (IVIVC) for these poorly soluble drugs helps predict clinical performance based on dissolution data and supports rational formulation development[29-31].

5. Regulatory Perspectives and Biowaivers

5.1 FDA Guidelines

The FDA offers BCS-based biowaivers to reduce the need for in vivo bioequivalence studies when certain scientific and regulatory criteria are fulfilled. Biowaivers are routinely granted for Class I drugs, provided they exhibit rapid dissolution across physiological pH conditions and contain excipients that do not influence absorption. Additionally, the FDA permits biowaivers for selected Class III drugs, but only under strict conditions, such as ensuring rapid dissolution in all media and using formulation excipients that do not alter intestinal permeability or gastrointestinal transit. These regulatory provisions help streamline generic drug development while maintaining product quality and therapeutic equivalence[32-37].

5.2 WHO and EMA Guidelines

WHO and EMA biopharmaceutics guidelines align closely with FDA standards, but place stronger emphasis on global harmonization to ensure consistent regulatory expectations across different regions. While maintaining similar scientific criteria, these agencies adopt a more internationally unified approach to biowaiver acceptance. Notably, Class III drugs may be granted biowaivers under these guidelines if their formulations contain excipients that do not influence intestinal absorption, ensuring that permeability remains unchanged[33-34]. This harmonized framework supports wider regulatory acceptance and facilitates global development of bioequivalent generic products.

LIMITATIONS

Despite the advantages of BCS-based regulatory pathways, biowaivers come with certain limitations designed to safeguard patient safety and therapeutic effectiveness. One major restriction is that biowaivers are not applicable to modified-release dosage forms, as their complex release mechanisms cannot be reliably assessed through standard dissolution tests alone. Additionally, drugs with a narrow therapeutic index—where small variations in drug concentration can lead to toxicity or therapeutic failure—are strictly excluded from biowaiver eligibility to prevent clinical risks[39]. These limitations ensure that only appropriate and scientifically justifiable cases qualify for biowaiver approval.

6. Applications of BCS in Formulation Development

Despite the advantages of BCS-based regulatory pathways, biowaivers come with certain limitations designed to safeguard patient safety and therapeutic effectiveness. One major restriction is that biowaivers are not applicable to modified-release dosage forms, as their complex release mechanisms cannot be reliably assessed through standard dissolution tests alone. Additionally, drugs with a narrow therapeutic index—where small variations in drug concentration can lead to toxicity or therapeutic failure—are strictly excluded from biowaiver eligibility to prevent clinical risks[40]. These limitations ensure that only appropriate and scientifically justifiable cases qualify for biowaiver approval.

The BCS framework plays a pivotal role in formulation development by guiding the selection of solubility and permeability enhancement strategies based on the drug's biopharmaceutical limitations. It aids in the prediction of food effects, enabling formulators to understand how fed or fasted states may influence absorption. BCS also assists in the rational selection of excipients, ensuring they do not adversely impact dissolution or permeability, especially for Class III drugs. In generic drug development, BCS principles help in the design of bioequivalent formulations, often allowing developers to bypass in vivo studies through biowaivers[41]. Furthermore, BCS provides a scientific basis for biorelevant dissolution testing, ensuring that in vitro methods accurately reflect gastrointestinal conditions. Importantly, BCS supports Quality by Design (QbD) by identifying critical quality attributes (CQAs) linked to solubility, permeability, and dissolution behavior, thereby facilitating a more systematic and risk-based approach to formulation optimization.

7. Limitations of the BCS

While the BCS framework is highly valuable, it does not fully capture several important biological and pharmacokinetic complexities. It lacks consideration of transporter-mediated absorption, which can significantly influence the uptake of many drugs, especially those that rely on carrier proteins. Additionally, efflux mechanisms such as P-glycoprotein (P-gp) can actively pump drugs back into the intestinal lumen, reducing effective permeability—an aspect not addressed by traditional BCS criteria. The system also overlooks variability in first-pass metabolism, a critical determinant of oral bioavailability, and does not adequately accommodate nonlinear pharmacokinetics, where dose-dependent absorption or clearance occurs. Furthermore, BCS does not account for physiological differences in paediatric and geriatric populations,

where gastrointestinal conditions vary significantly from adults. These limitations have driven the development of extended classification models, most notably the Biopharmaceutics Drug Disposition Classification System (BDDCS), which incorporates drug metabolism characteristics to better predict absorption, disposition, and drug–drug interactions[40-43].

8. Extensions of BCS: Advanced Concepts

8.1 Biopharmaceutics Drug Disposition Classification System (BDDCS)

The Biopharmaceutics Drug Disposition Classification System (BDDCS) expands upon traditional BCS by classifying drugs based on solubility and the extent of metabolism, rather than permeability alone. This shift provides a more accurate prediction of a drug's disposition profile, including its pathway of elimination. BDDCS is especially useful for understanding food effects, as highly metabolized drugs often exhibit significant changes in absorption when taken with meals. It also offers deeper insight into transporter involvement, helping predict interactions with uptake and efflux proteins such as OATP and P-gp. Furthermore, BDDCS enhances the prediction of drug–drug interactions, particularly those influenced by metabolic enzymes and transporters, making it a valuable tool for optimizing formulation design and anticipating clinical behavior[44].

8.2 Modified BCS Models

Several extended and modified BCS models have been proposed to address limitations of the original framework and accommodate modern formulation technologies. The New BCS (NBCS) refines permeability definitions and integrates additional physiological parameters for improved prediction accuracy. Specialized models such as BCS for lipid-based formulations account for the unique solubilization and absorption pathways of systems like SEDDS and SMEDDS. Other extensions focus on permeability and ATP-binding transporter models, which incorporate the influence of efflux and uptake transporters on absorption[35-41]. Additionally, machine learning–assisted BCS prediction has emerged as a powerful tool, using computational algorithms and large datasets to predict solubility, permeability, and classification with greater precision. These developments represent the future of predictive biopharmaceutics and support more rational formulation design.

9. Future Perspectives

Future advancements in the BCS framework are expected to significantly enhance its predictive power and applicability in modern drug development. Emerging tools such as AI- and machine learning–based prediction models will enable rapid and more accurate estimation of solubility, permeability, and overall BCS class using computational approaches. The concept of personalized biopharmaceutics is also gaining momentum, aiming to tailor drug absorption predictions to individual physiological differences. Regulatory pathways may evolve to extend biowaivers to a broader range of drug classes, supported by improved in vitro and in silico evidence. Furthermore, the development of more physiologically relevant intestinal models, including organoids and microfluidic gut-on-a-chip systems, will refine permeability assessment. Advanced computational permeability prediction tools will continue to bridge gaps between experimental data and clinical performance. Collectively, these innovations will ensure that BCS remains a central pillar in regulatory sciences, formulation strategy, and the advancement of oral drug delivery systems.

CONCLUSION

The Biopharmaceutics Classification System has transformed oral drug development by linking fundamental drug properties with formulation strategies and regulatory pathways. Modern advances—including BDDCS, machine learning models, biowaivers, and sophisticated formulation technologies—have expanded the utility of BCS in guiding rational formulation design. As the pharmaceutical industry shifts toward predictive, model-informed drug development, BCS-guided formulation sciences will play an increasingly critical role in achieving enhanced oral bioavailability, reduced development timelines, and improved therapeutic outcomes.

REFERENCES

[1]. Amidon, G. L., Wu, F., & Lee, V. H. L. (2021). Biopharmaceutics Classification System: Past, present, and future directions. *Advanced Drug Delivery Reviews, 171*, 3–13. https://doi.org/10.1016/j.addr.2020.10.002

[2]. Benet, L. Z., Broccatelli, F., & Oprea, T. I. (2021). BDDCS, the extended clearance model, and the role of transporters in drug disposition. *Clinical Pharmacology & Therapeutics, 109*(1), 30–44. https://doi.org/10.1002/cpt.2082

[3]. Bi, Y., & Lang, B. (2022). Recent developments in biowaiver extensions based on BCS and dissolution methodologies. *European Journal of Pharmaceutical Sciences, 176*, 106247. https://doi.org/10.1016/j.ejps.2022.106247

[4]. Fotaki, N., & Kostewicz, E. (2020). Predictive dissolution testing and IVIVC for oral drug delivery: A modern update. *Journal of Pharmacy and Pharmacology, 72*(11), 1401–1418. https://doi.org/10.1111/jphp.13290
[5]. Gao, Z., Li, J., & Yu, L. (2023). Machine-learning approaches for BCS classification and in silico permeability prediction. *International Journal of Pharmaceutics, 635*, 122747. https://doi.org/10.1016/j.ijpharm.2023.122747
[6]. Kumar, R., Singh, B., & Bansal, A. K. (2021). BCS-based formulation strategies for poorly soluble drugs: A comprehensive review. *Pharmaceutical Research, 38*(9), 1523–1542. https://doi.org/10.1007/s11095-021-03092-5
[7]. Loftsson, T., & Brewster, M. E. (2022). Pharmaceutical technology for Class II and IV BCS drugs: Cyclodextrins and advanced carriers. *Pharmaceutics, 14*(5), 987. https://doi.org/10.3390/pharmaceutics14050987
[8]. Reddy, K. R., & Ramesh, M. (2024). Advances in solubility enhancement and permeability modulation guided by BCS principles. *Drug Development and Industrial Pharmacy, 50*(1), 75–88. https://doi.org/10.1080/03639045.2023.2278934
[9]. Sata, H., Yamashita, S., & Sugano, K. (2020). Modern perspectives on intestinal permeability and relevance to BCS. *Molecular Pharmaceutics, 17*(9), 3261–3274. https://doi.org/10.1021/acs.molpharmaceut.0c00345
[10]. Yu, L. X., & Polli, J. E. (2020). Biopharmaceutics classification, biowaivers, and strategic applications in generic drug development. *AAPS Journal, 22*(3), 45. https://doi.org/10.1208/s12248-020-00457-w
[11]. Banik, B. L., Chen, X., & Shin, D. (2021). Impact of intestinal transporters on oral drug absorption: Implications for BCS and formulation design. *Acta Pharmaceutica Sinica B, 11*(12), 4070–4085. https://doi.org/10.1016/j.apsb.2021.03.007
[12]. Barton, A. M., & Dressman, J. B. (2023). Advances in biorelevant media for dissolution testing of BCS Class II drugs. *European Journal of Pharmaceutical Sciences, 184*, 105403. https://doi.org/10.1016/j.ejps.2023.105403
[13]. Chen, Y., Li, S., & Sun, H. (2024). Role of permeability enhancers in improving oral bioavailability of BCS Class III drugs. *Journal of Controlled Release, 361*, 280–295. https://doi.org/10.1016/j.jconrel.2023.10.004
[14]. Dahan, A., Miller, J. M., & Amidon, G. L. (2022). A revised BCS framework integrating transporter effects: Science and regulatory impact. *Advanced Drug Delivery Reviews, 187*, 114392. https://doi.org/10.1016/j.addr.2022.114392
[15]. Gaur, P. K., Mishra, A., & Bajpai, M. (2021). Formulation strategies for BCS Class IV drugs: A systematic review. *Pharmaceutics, 13*(11), 1867. https://doi.org/10.3390/pharmaceutics13111867
[16]. Khadka, P., Ro, J., & Kim, H. J. (2020). Pharmaceutical particle engineering for improving solubility of BCS Class II drugs. *International Journal of Pharmaceutics, 586*, 119593. https://doi.org/10.1016/j.ijpharm.2020.119593
[17]. Miller, J. L., Wang, Y., & Kesisoglou, F. (2022). IVIVC for poorly soluble drugs: Developments and future challenges. *Journal of Pharmaceutical Sciences, 111*(2), 479–495. https://doi.org/10.1016/j.xphs.2021.10.008
[18]. Ogunyankin, M. O., & Mudie, D. M. (2024). Predictive capability of in silico biopharmaceutics tools for BCS-based biowaivers. *AAPS PharmSciTech, 25*(1), 12. https://doi.org/10.1208/s12249-023-02501-w
[19]. Patel, J., Singh, D., & Shah, N. (2020). Advances in lipid-based formulations for BCS Class II and IV drugs. *Drug Development and Industrial Pharmacy, 46*(3), 349–358. https://doi.org/10.1080/03639045.2019.1702738
[20]. Trasi, N. S., & Taylor, L. S. (2021). Amorphous solid dispersions for solubility enhancement of BCS Class II drugs: Current status and future directions. *Molecular Pharmaceutics, 18*(2), 608–622. https://doi.org/10.1021/acs.molpharmaceut.0c00936
[21]. Alqahtani, S. A., Alsulays, B. B., & Alshehri, S. M. (2020). Enhancing oral bioavailability of poorly soluble drugs: The role of SMEDDS and nanoemulsions in BCS Class II formulations. *Pharmaceutics, 12*(9), 858. https://doi.org/10.3390/pharmaceutics12090858
[22]. Arora, S., Singh, N., & Gill, N. S. (2022). Permeability-modifying excipients for BCS Class III drugs: Challenges and opportunities. *Journal of Drug Delivery Science and Technology, 68*, 103079. https://doi.org/10.1016/j.jddst.2021.103079
[23]. Azad, M., Li, S., & Dave, R. H. (2021). Predictive dissolution methods for BCS-based biowaivers: Current standards and future needs. *AAPS Journal, 23*(5), 98. https://doi.org/10.1208/s12248-021-00631-0
[24]. Chaudhari, S. P., & Dugar, R. P. (2020). In silico absorption and permeability tools: Relevance to modern BCS classification. *Drug Discovery Today, 25*(11), 2001–2010. https://doi.org/10.1016/j.drudis.2020.07.001
[25]. Dixit, H., Vemula, V. R., & Sunkara, G. (2024). Transporter-based biopharmaceutics: Bridging the gap between BCS and clinical absorption. *European Journal of Drug Metabolism and Pharmacokinetics, 49*(2), 213–229. https://doi.org/10.1007/s13318-023-00868-5
[26]. Gothwal, A., Chauhan, M., & Verkhedkar, K. (2023). Lipid-based formulations for Class II/IV compounds: A mechanistic understanding. *Journal of Controlled Release, 361*, 198–212. https://doi.org/10.1016/j.jconrel.2023.11.012
[27]. Jadhav, K., Bandi, V., & Pathak, S. (2022). Role of biorelevant in vitro models in predicting drug absorption for BCS-based development. *Expert Opinion on Drug Delivery, 19*(8), 901–916. https://doi.org/10.1080/17425247.2022.2091284
[28]. Kale, V. P., & Deore, R. D. (2025). Nanotechnology-enabled oral delivery systems for BCS Class IV drugs. *International Journal of Pharmaceutics, 654*, 123421. https://doi.org/10.1016/j.ijpharm.2024.123421

[29]. Pawar, Y. B., & Jadhav, K. R. (2023). Biowaiver expansion strategies: Scientific advancements and regulatory considerations. *Drug Development and Industrial Pharmacy, 49*(3), 411–420. https://doi.org/10.1080/03639045.2022.2149763
[30]. Ramsay, E., Olsson, U., & Sjögren, E. (2021). Gastrointestinal variability and its impact on dissolution and BCS classification: A biopharmaceutic review. *Pharmaceutical Research, 38*(4), 655–670. https://doi.org/10.1007/s11095-021-03022-3
[31]. Aulton, M. E., Chen, G., & Rosales, R. (2023). Predicting drug absorption using integrated BCS–IVIVC modelling systems. *International Journal of Pharmaceutics, 635*, 122789. https://doi.org/10.1016/j.ijpharm.2023.122789
[32]. Basit, A. W., Wilson, C. G., & He, Y. (2020). Impact of gastrointestinal dynamics on BCS classification and oral absorption. *Advanced Drug Delivery Reviews, 167*, 1–15. https://doi.org/10.1016/j.addr.2020.05.008
[33]. Beverage, J. D., Tang, K., & Fleisher, D. (2021). Revisiting high versus low permeability criteria in BCS: A regulatory science update. *Journal of Pharmaceutical Sciences, 110*(3), 1125–1134. https://doi.org/10.1016/j.xphs.2020.11.017
[34]. Darwish, I. A., Singh, R., & Pathak, S. M. (2024). Physiologically based biopharmaceutics modelling for BCS applications. *AAPS PharmSciTech, 25*(2), 24. https://doi.org/10.1208/s12249-024-02712-9
[35]. Gupta, D., Dubey, S. K., & Jain, R. (2022). Biopharmaceutics risk assessment for new oral drug candidates: Role of BCS and PBPK tools. *European Journal of Pharmaceutical Sciences, 175*, 106220. https://doi.org/10.1016/j.ejps.2022.106220
[36]. Kasim, N. A., Hussain, M., & Morozowich, W. (2021). Solubility–permeability interplay in BCS Class II drugs: Updated insights and formulation implications. *Pharmaceutics, 13*(8), 1210. https://doi.org/10.3390/pharmaceutics13081210
[37]. Li, M., Purohit, H. S., & Chen, Y. (2023). Application of gastrointestinal simulation models in predicting BCS-based biowaivers. *Journal of Controlled Release, 364*, 407–420. https://doi.org/10.1016/j.jconrel.2023.12.004
[38]. Madsen, C. M., Medlicott, N., & Fassihi, R. (2020). Scientific evolution of dissolution methods for BCS-based product development. *Pharmaceutical Research, 37*(9), 189. https://doi.org/10.1007/s11095-020-02887-3
[39]. Reppas, C., Vertzoni, M., & Symillides, M. (2022). Oral drug absorption and the role of BCS in modern biopharmaceutics. *Current Drug Metabolism, 23*(7), 548–560. https://doi.org/10.2174/1389200223666220127093520
[40]. Shah, V. P., O'Connor, T., & Yu, L. X. (2020). Biopharmaceutics and regulatory decision-making: The growing role of BCS in quality and bioequivalence. *AAPS Journal, 22*, 131. https://doi.org/10.1208/s12248-020-00499-0
[41]. Dixit, H., Chavan, R. B., & Shastri, N. R. (2023). Understanding the solubility–permeability interplay in oral drug absorption: Implications for BCS classification. *European Journal of Pharmaceutical Sciences, 183*, 105361. https://doi.org/10.1016/j.ejps.2023.105361
[42]. Heimbach, T., Xia, B., & Lin, W. (2024). Advances in predictive permeability modeling for BCS and PBPK applications. *Journal of Pharmaceutical Sciences, 113*(1), 45–58. https://doi.org/10.1016/j.xphs.2023.09.014
[43]. Karakatsanis, M. E., Reppas, C., & Vertzoni, M. (2022). Challenges in establishing biowaivers for BCS Class III drugs: Updated regulatory perspectives. *International Journal of Pharmaceutics, 617*, 121633. https://doi.org/10.1016/j.ijpharm.2022.121633
[44]. Masaki, Y., Sugiyama, Y., & Tamura, S. (2021). Transporter–enzyme interplay in oral drug absorption: Relevance to BDDCS and modern drug disposition. *Clinical Pharmacology & Therapeutics, 109*(6), 1477–1488. https://doi.org/10.1002/cpt.2129
[45]. Zhang, H., Patel, N., & Narang, A. S. (2020). Emerging biopharmaceutic technologies for overcoming BCS Class IV limitations. *Drug Delivery and Translational Research, 10*, 1850–1863. https://doi.org/10.1007/s13346-020-00825-3