Drug Development & Delivery

SPECIAL FEATURE – Solubility & Bioavailability: Difficult Beasts to Tame- March 2023

SPECIAL FEATURE - Solubility & Bioavailability: Difficult Beasts to Tame (drug-dev.com)

Solubility remains challenging as new molecules coming out of discovery are poorly soluble. Less soluble means the molecules can't be absorbed and therefore, can't be solubilized. Factors responsible for poor solubility stem from high melting (MP) and high partition coefficient (logP) of molecules. Regardless of their structures, the solubility is limited in water because most of them have a tendency to prefer organic phase over aqueous phase. "All these challenges impede drug development, which has resulted in creating the gaps for finding cures for life threatening and rare diseases, and for unmet medical needs," says Shaukat Ali, PhD, Senior Director, Scientific Affairs & Technical Marketing, Ascendia Pharma, Inc.

These challenges span across all small and large molecules, and with more than 80% of new chemical entities (NCEs) belonging to BCS II and BCS IV, many of them cannot be developed due to lack of understanding of their physicochemical properties and inability to dissolve, says Dr. Ali. Small molecules are equally challenging because of their brick dust or being hydrophobic or lipophilic in nature, as well as their inability to disperse in aqueous solutions.

Driven by the large number of BCS Class II and IV therapies in the current pipeline and growing demand for effective therapeutics, the bioavailability enhancement services market is expected to grow at a steady pace.[1] Bioavailability is a key pharmacokinetic property that affects the ability of a drug to reach systemic circulation unaltered after administration. It is dependent on multiple factors, both physiological and drug related, such as solubility, pH, absorption area, permeability, and metabolism, as well as the route of administration. "Consequently, bioavailability can play an influential role in determining whether or not an active pharmaceutical ingredient (API) will be successful or fail during the early stages of drug development," says Sundeep Sethia, PhD, Head of R&D at Pii.

More than 75 bioavailability enhancement technologies are presently available in the market. Most (55%) support solubility enhancement, and nearly 70% provide bioavailability enhancement services for solids, followed fine particles/powders.

Shifting focus of drug developers towards development of lipophilic drug compounds is anticipated to drive the demand for bioavailability enhancement technologies and services in the next 13 years. Consequently, the outsourced commercial demand for bioavailability enhancement is projected to increase.[1]

This exclusive *Drug Development & Delivery* annual report highlights the services many of these outsourced providers offer to enhance solubility and bioavailability and get their clients' projects to market faster and cost effectively – while maintaining critical quality attributes.

Ligand Pharmaceuticals: Solubility-Enhancing Excipient Opens New Routes of Administration

Ligand Pharmaceuticals has seen a steady stream of inquiries for how Captisol® (sulfobutyl ether beta cyclodextrin) can help with solubility/bioavailability and stability of active pharmaceutical ingredients. There are currently at least 60 products in development pipelines around the world using Captisol for formulation enhancement.

"Another indication that APIs continue to need assistance in solubility improvement is the increased demand for Captisol and the number of product approvals containing Captisol expected in 2023-2024," says Vince Antle, PhD, Senior Vice President of Technical Operations & Quality Assurance at Ligand. "Upcoming product approvals open the door to the use of Captisol in new routes of administration, namely oral, ocular, and subcutaneous. In addition, one of the anticipated product approvals is targeted for a pediatric demographic."

J.D. Pipkin, PhD, Vice President of New Product Development at Ligand, says that formulators know that best practices for dosage form development of poorly water-soluble compounds depend largely on the physical/chemical characteristics of the API, route of administration, indication, and whether the drug will be given on an acute or chronic regimen. "Keeping the formulation as simple as possible is usually the best strategy from both a product and regulatory standpoint," says Lian Rajewski, PhD, Senior Research Investigator at Ligand. "Typically, the fastest way to move through the development process, is to use safe, well-established, globally accepted excipients. Captisol is a solubility-enhancing excipient (derivatized cyclodextrin)."