

## Topical Drug Delivery Considerations for Biologics



According to the analyst firm Global Information, the demand for biologics and biosimilars is estimated to grow to more than \$100 billion in 2015, continuing the double-digit growth rate seen in the last decade. As the industry continues to grow, alternative delivery methods are of increasing interest—particularly the topical delivery of large molecules.

Formulation for any topical pharmaceutical is a top priority—any misstep can affect the efficacy of the molecule. Biologics also have the additional consideration of achieving the right penetration to the target. Tergus, the leader in topical pharmaceutical formulation, development, analysis and testing, works with global companies and top universities and labs to create topical formulations for biologics.

### Advantages and Issues with Topical Biologics

Biologics are playing an increasing role in treating diseases and conditions, not just as injectable dosage forms, but also as topical treatments. Large molecules, or biologics (i.e., those with a molecular weight of over 500 Dalton, such as peptides and proteins) present unique challenges in topical drug product delivery. Manufacturing also provides unique challenges.

Most therapeutic peptides and proteins cannot be delivered orally because they degrade in the gastric system. Patients often endure a series of injections with parenteral drugs due to the short half-life of these peptides/proteins. This treatment paradigm can have issues with compliance and patient satisfaction.

The advantages of topical drug delivery include:

- The avoidance of hepatic first pass metabolism
- Longer drug delivery times than oral dosage forms
- The ability to remove the delivery system to discontinue administration of the drug
- Direct administration to affected areas when the disease is localized
- The ability to modify the properties of the biological absorption barrier<sup>1</sup>

In order for any topical drug to be successful it must reach the desired target in sufficient quantity to be efficacious and the molecule must retain its potency and original therapeutic form. Topical delivery of any drug is a challenge because the skin, which is the largest organ in the human body, acts as a protective barrier. The compact structure and hydrophobic nature of the stratum corneum (SC) are the primary reasons for the barrier function of the skin. As a result, the cutaneous delivery of drugs usually requires the use of penetration enhancers or some other physical or chemical disruption of this skin layer.

Several factors influence the topical administration of drugs. These include the drug substance in question, its pharmacokinetic profile, and the desired location of action. Small molecules such as corticosteroids are more easily formulated with a variety of penetration enhancers and solvents, so they penetrate the skin and are effective at the desired location.

Biologics, on the other hand, present several unique formulation challenges. These include the selection of penetration enhancers and excipients that will perform optimally to allow the drug to maintain efficacy and reach the target area in sufficient potency.

Because of their nature, biologics require different processing to avoid damage to their structure and conformation due to degradation, aggregation, misfolding, etc. As write, "The thermodynamic stability of the native protein conformation is only about 20–80 kJ/mol in free energy more stable than unfolded, biologically inactive conformations under physiological conditions<sup>11</sup>, which is much weaker than covalent or ionic bonds."<sup>1</sup>