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The field of pharmacy has continuously embraced new challenges, bringing more and more disciplines under its umbrella. From traditional dispensing to large scale industrial production, from multiple daily doses to sustained and controlled release, the pharmaceutical technologist has sought to learn well beyond core pharmaceuticals. With the exponential growth of the biotechnology industry, the 'traditional' pharmaceutical technologist now must add a new dimension to his/her knowledge: molecular biology.

Consider the following ... a nice HPLC peak does not necessarily indicate stability of the molecule; a simple tablet compression can completely destroy the activity of a molecule; a large DNA molecule elutes with the solvent front in an HPLC analysis, irrespective of the conditions. This is the stuff of nightmares for a pharmaceutical technologist ... welcome to the new age of pharmaceuticals!

Core pharmaceuticals has always suited small molecules. With the surge in recent years in the development of large biomolecular therapeutics, such as proteins and nucleic acids, we need to improve our repertoire of manufacturing and analytical techniques. A good place to learn the ropes is with the study of molecular biology, since molecular biologists have been analysing large molecules for a long time - we need only to modify their techniques for application to pharmaceutical dosage forms.

Not only is the way we look at drugs changing, but so also is the way we view excipients. For example, we now know that many surfactants inhibit drug efflux at a molecular level, or that some polysaccharides can have an immunomodulatory effect. We have to go way beyond traditional sustained drug delivery to cell and organelle specific delivery.

The challenges extend well beyond scale-up and manufacturing, encompassing analytics, quality control guidelines, storage and transport. Where should we begin? We could delve into the weighty molecular biology books; attend workshops; we might even have to chat more often with molecular biologists! But meantime, here are some practical tips:

Lesson #1: Learn to aliquot proteins and nucleic acids into workable portions - Unlike small molecule drugs which we can store on a shelf or in a desiccator, most of the proteins/nucleic acids need to be refrigerated or frozen. They might get denatured with multiple freeze thaw cycles, hence it is important to divide them into workable portions and freeze them.

Lesson #2: Antibodies tell a better story than HPLC - While HPLC is possible for macromolecules, changes not detected by HPLC might play a big role in their activity and stability. Antibody based techniques, like western blotting and ELISA, are some of the best techniques for macromolecules; they speak to the stability of a molecule in a much better way.

Lesson #3: Use multiple techniques to draw conclusions - Macromolecules have multiple conformations and configurations and different techniques analyse different aspects of the structure. Hence it is essential to use more than one technique to analyse the molecule before jumping to rash conclusions.

Lesson # 4: Start using the 'blot' vocabulary - Western blotting analyses proteins, southern blotting analyses DNA and northern blotting analyses RNA. Learning the 'blot' lingo will help the molecular biologist feel more at home - he/she might just spill the beans to tell you about a new technique that could be very useful to you!

Lesson # 5: The master lesson - don't copy the molecular biologist blindly - Assays and techniques in molecular biology are usually most suited for use in a biological matrix which is very different both physically and chemically to a pharmaceutical matrix. We need to adapt and validate molecular biology protocols to suit the pharmaceutical matrix.

Welcome to the world of molecular bio-pharmaceuticals!

References

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