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Improving APIs & Formulation: Are You Harnessing the Power of Liquids?

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3 comments

Liquids are an essential part of our planet. Imagine our landscape and lives without them. We may take them for granted, but liquids play an important role in the reactive processes that produce small molecule active pharmaceutical ingredients (API), as well as in pharmaceutical formulation.

When we consider any chemical reaction in the laboratory, the very first thing we do is review the physical and chemical properties of each reactant. This is where our formative knowledge of the reaction begins. Some of the reactants are liquids, others are solids, and some may be gases at room temperature. A catalyst would be needed.

Proof of concept and most of the initial work is done using available labware. Liquids are the easiest to handle, and their flow can be easily controlled. Solids are typically dissolved in a solvent to facilitate handling. Gases are the most difficult to handle as a liquid in the laboratory.

Safety, conservation, and toxicity considerations also begin at this point. We should keep the related issues in mind but not dwell much on them as necessary provisions are made when the process is commercialized.

Our focus is on proving the feasibility of the reaction with the highest yield. Laboratory and scale-up experiments are done on a small scale, and may not allow use of raw materials in their actual state. If they cannot be used in their actual state, we solute them in a compatible solvent.

With process feasibility proven, our focus then shifts to marketing the product. As we progress from the lab to the pilot plant to commercial scale, we continue to use most of the methods and habits that we practiced in the lab and pilot plant.

But what happens when raw materials or conditions change in the real world?

All too often, a relentless focus on speed to market prevents us from going back to the lab, and so we fail to capitalize and/or exploit the “sociochemicological” behavior of reactants and reaction products.

Our intuitive failure to recognize and capitalize on the behavior of chemicals results in an incomplete understanding or control of the process, preventing us from developing the most innovative process. We miss out on opportunities to improve productivity and sustainability, which often translates into loss of competitive advantage via lower cost or higher profit.

Consider a raw material that is a solid but has a low melting point. In the laboratory, we dissolve it in a solvent and complete the reaction.

If the reaction products are liquid at room as well as at reaction temperature, which is above the melting point of the key raw material, we could use the liquid state of the reaction products to our advantage. We could take advantage of the formation of liquid products to lower the total solvent requirement. Solvent reduction can translate into a 10-25 percent productivity improvement. This is significant. Lower solvent requirements translate directly into lower overall investment needs.

Behaviors of chemicals are unique. Used creatively, they can help us innovate and simplify, while putting us in command of processes. However, we must first recognize the opportunities and take advantage of them.

Additional reading

Chemical Process Simplification: Improving Productivity and Sustainability, John Wiley & Sons. 2011

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