Beyond the application of RI as PAT in solid-phase synthesis

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The number of peptide drugs currently on the market as well as others in advanced studies is in increasing trend. Most of the peptides are synthesized using Solid-Phase Peptide Synthesis (SPPS) technology which the main characteristic is that skips the isolation of the synthetic intermediates. The development of a real-time monitoring method would avoid the interruption of the process to take samples and run additional testing. Here we provide the demonstration that refractive index measurements of the solutions involved in SPPS are a powerful Process Analytical Tool (PAT) for the real-time monitoring of the full process. It will be shown how this monitoring capacity helps to the determination of the endpoint of the reactions and the optimization of all synthetic steps, which would have a direct impact on the consumption of reagents, solvents, and time, thereby contributing to greener SPPS.

[1] B.G de la Torre, Shaveer Ramkisson, Fernando Albericio, John Lopez,. *Org. Process Res. Dev.,* **2021,** *25*, 1047-1053,