Introduction

Radiopharmaceuticals have played a key role in visualizing biochemical processes throughout the human body. These radiolabeled compounds utilize positron-emitting, radionuclide tracers placed on specific vehicle molecules. The vehicle molecule defines the site-specific interactions while the radionuclide provides the basis for signal detection and data interpretation. PET imaging devices such as a PET/CT scanner are able to detect and track the activity of these PET tracers.

While several PET tracers are available, physical characteristics, application, and economic restrictions must be considered when selecting a radionuclide. The short half-life of radionuclides limits applications with lengthy labeling methods and imaging procedures. Costly cyclotrons, generators, and other expensive production equipment has limited the use of several PET nuclides in clinical settings for daily use.

Medicinal radiochemistry comprises the activation of the radionuclide, the radiolabeling procedure itself, and the purification of the final product. Since most radionuclides are commercially purchased off-site in a chemical form that is not predisposed for direct labelling reactions, primary activation steps are absolutely necessary. Following the radionuclide activation, labeling and purification of the complete PET tracer must be accomplished within the short half-life of the isotope. The labeling process often requires elevated temperature or microwave assistance and is performed in dedicated synthesizers.

Microwaves have recently been utilized for this crucial process to address the need for speed and reproducibility at an affordable cost.

Microwave-Assisted Radiolabeling

Microwave reactors have made a recent appearance in the field of PET chemistry, addressing two of the field’s most critical issues: reaction rate and side-product formation. While space considerations and cost have limited widespread use of microwaves, CEM (Matthews, NC, USA) has developed a microwave reactor system (PETwave™) specifically for working with radiopharmaceutical applications. The small footprint of the cavity allows the PETwave™ to be placed in a variety of hot cells, and even utilize automation devices for post-reaction steps [see Figure 1].

Microwaves have been shown to reduce reaction times and improve yields during the radiolabeling process when compared to conventional heating1,2,3,4. In contrast to traditional synthetic chemistry, it is common to favor reduced radiochemical reaction times over reaction yield. In case of short-lived radionuclides, higher relative conversion yields are easily outbalanced by the longer reaction times. If a substrate or product is susceptible to thermal decomposition, it may be beneficial to run the reaction in a microwave reactor at a lower temperature so as to avoid excessive thermal heating without a sacrifice in yield1.

When developing a new radiosynthesis, optimizing reaction conditions can be a very time consuming and costly process. Many [18F]fluorinations are highly temperature sensitive and can only be efficiently performed within a small temperature range. Microwaves can be a useful tool to speed up the optimization process by decreasing reaction times thus allowing more runs. Belanger et al saw an increase in the range of temperatures which efficient fluorination was carried out on fatty acid esters using microwaves compared to conventional heating over a period of 15 minutes [see Figure 2]5. Microwave heating improved [18F]fluoride labeling up to 55%, while reducing reaction times to 2 min (~10-fold reduction) for bromo precursors, and temperatures to 55–60 °C (20 °C reduction). Overall decay-corrected, purified [18F]fluor fatty acid yields were higher with microwave heating (49.0±4.5%) versus conventional heating (23.6±3.5%)6.

In a similar study by Wenzel et al, the radiolabeling procedure for a small molecule targeting PETwave™ to be placed in a variety of hot cells, and even utilize automation devices for semi-automated workflows, used in hot cells, and have been shown to provide superior radiochemical yield in only minutes2,3,4,5,6. Often times, microwaves are used to optimize reaction parameters or assist in shortening reaction times in multi-step radiosyntheses.

Conclusion

Microwave synthesizers have recently become utilized as a heating tool for numerous radiopharmaceutical applications, often with impressive results over conventional heating methods. Specially designed microwave PET synthesis systems have been incorporated into semi-automated workflows, used in hot cells, and have been shown to provide superior radiochemical yield in only minutes2,3,4,5,6. Often times, microwaves are used to optimize reaction parameters or assist in shortening reaction times in multi-step radiosyntheses.

References


1CEM Corporation, Matthews, NC 28104, United States