An LC-based Determination of Palladium Residues after Digestion of Complex Organic Matrices

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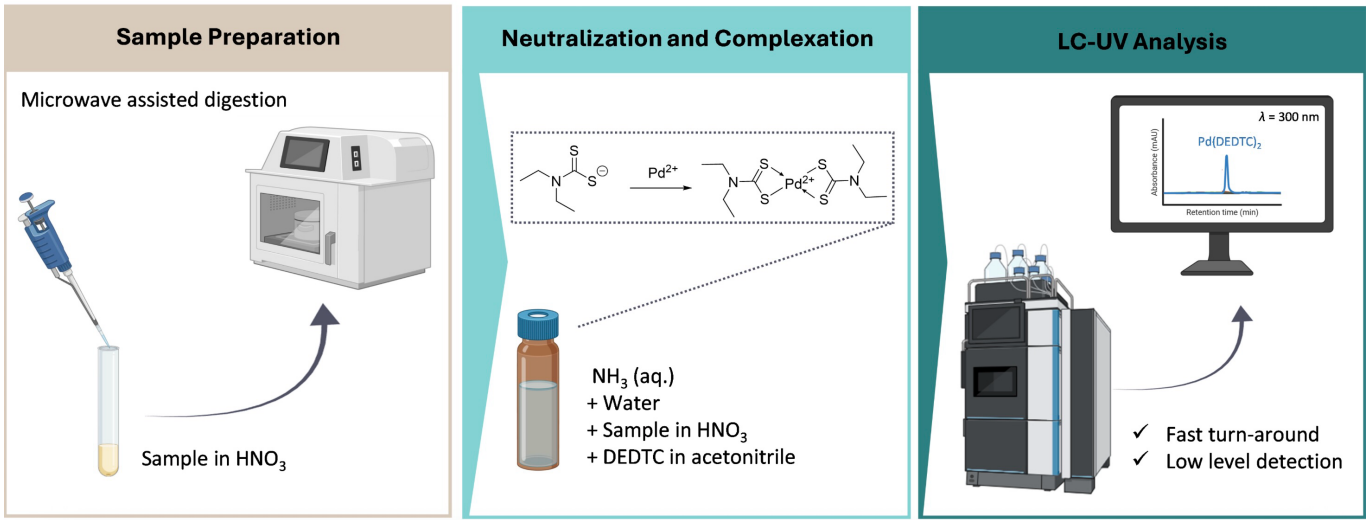
Transition-metal catalysis is a cornerstone in the synthesis of new chemical entities. Given their widespread use, especially, monitoring residual palladium after catalytic reactions is essential. For over 50 years, techniques employing inductively coupled plasma, such as ICP-OES (optical emission spectrometry) have been the gold standard, offering high sensitivity and accuracy across a broad range of elements simultaneously. However, they rely on demanding workflows, trained personnel, and daily calibration, all of which result in longer turnaround times. Furthermore, it requires a relatively large sample amount, and costs can be substantial if the instrumentation is not available in-house. In early-phase development, where rapid, single-metal analysis at ppm level is often required and material is limited, an alternative method is essential. Herein, we present an LC-based method using diethylammonium diethyldithiocarbamate (DEDTC)[1] as complexation agent for Pd^{2+}. The sample preparation includes a microwave-assisted digestion step using nitric acid to ensure oxidation of residual Pd^{0} and eliminate matrix effects of the active pharmaceutical ingredient itself, followed by sample neutralization, metal complexation, and LC-UV measurement. This method allows fast turnaround and detects palladium as low as 10 ppm, with the limit of quantification adjustable by sample size, a feature particularly valuable in early-phase development when material is scarce.

Experimental Workflow



[1] B. J. Mueller, R. J. Lovett, *Anal. Chem.*, **1985**, 57, 13, 2693–2699