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Advanced analytical workflow for investigating precipitation in cell culture medium

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Abstract

The stability of liquid cell culture media (CCM) is impacted by many different factors, including storage conditions and the formulation. Some components in liquid CCM may be subject to chemical reactions and degradation, which can lead to undesired precipitation. Due to the complexity of over 50 different components in CCM, identifying the critical ones causing the precipitation remains challenging. Therefore, this study aims to develop an analytical workflow to investigate the formation of precipitate in CCM using a combination of complementary analytical techniques adapted to the problem. First, ICP-MS was utilized to determine the concentrations of elements, since certain concentrations of metals are prone to form precipitates in CCM. The analysis pointed out that the precipitate is formed of Element A-related components. In addition, XRD confirms that the precipitate is composed of Element A and an oxalate. However, oxalate is not part of the composition of the CCM. This suggests the degradation of certain components in the CCM formulation which leads to oxalate formation. Compound A is well-known for being unstable in solution and prone to degradation into different biproducts including oxalate. A LC-MS method for the analysis of Compound A was already implemented and was utilized for the analysis of its degradation products. To gain better insights into the general stability of Compound A, the stability of a stock solution of Compound A was analyzed over a certain period. It resulted in full degradation after 4 weeks and the formation of Compound B starting after 3 weeks. By shifting the pH of the CCM, the stability of the liquid CCM could be restored. By using LC-MS, ICP-MS and XRD, Element A components and Compound A are therefore confirmed to be critical components in CCM leading to precipitation.

Keywords: CCM, LC-MS, ICP-MS, XRD, Precipitation