財団 Information ▶報告書

令和３年度「日本薬局方の試験法等に関する研究」研究報告 製剤中の元素不純物の管理に関する分析法の開発研究 ～水銀の化学形態分析～*2

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Development of Simple Speciation Analysis of Mercury as an Elemental Impurity*2

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Summary

The ICH Q3D Guideline for Elemental Impurities is now at Step 5. The final draft of Step 4 has been recommended for adoption to the regulatory bodies of the European Union, Switzerland, Japan, USA and Canada, and was published in JP18 2.66, USP<233> and EP2.4.20, and so on. In these pharmacopoeias, the analytical technique “speciation” is defined. For example, JP18 explains speciation as follows. “Speciation is defined as the distribution of elements among chemical species based on the difference of molecular structure including ionic element, molecules, or complexes, reflecting isotopic composition, electronic or oxidation state. When the toxicities of different species of the same element are known to be different, the PDE (permitted daily exposure) has been established using the toxicity information on the species expected to be in the drug product.” Although speciation is important to evaluate toxicity, no precise methods to determine it are described in the pharmacopoeia or in the ICH Q3D guideline. In this study, we focused on the speciation of mercury. Mercury is a Class 1 element, and its toxicity depends strongly on its chemical form, such as an inorganic salt or organometallic compound. We established a simple speciation technique for mercury based on cold vapor-atomic absorption spectrometry, and found that several medicines show distinctive mercury speciation. Consequently, this spectrometric technique appears to be useful for the evaluation of PDE based on mercury speciation.

Key words

Mercury, Speciation, Elemental impurities, Methylmercury, Cold vapor-atomic absorption spectrometry