報告書

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平成26年度「日本薬局方の試験法等に関する研究」研究報告*2
注射剤の不溶性微粒子試験法に関する検討
—現状と課題：Flow imaging 法について—

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Study on Insoluble Particulate Matter Test for Injections
— Current Situation and Challenges : Flow Imaging as a New Method —

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Summary

The Japanese Pharmacopoeia Insoluble Particulate Matter test for Injections (JP 16 6.07) recommends that particulate contamination of injectables should be measured using Method 1, a light obscuration particle count test. However, method 2, a microscopic particle count test, is more useful to determine the origins of particulate matter. Thus, these tests can be regarded as complementary to improve quality control procedures. On the other hand, flow imaging is a relatively new imaging-based technology that measures particle distribution and shape by capturing an image of each suspended particle in a flowing sample. This enables identification of the origins of contaminants and also detection of protein aggregates, which are not easily distinguished from other extrinsic and intrinsic contaminants by the light obscuration test. Therefore, flow imaging is considered to be a useful, orthogonal approach. Here, we discuss the current status and challenges of insoluble particulate matter testing of injections, and we compare the flow imaging and light obscuration methods. The effectiveness and adequacy of flow imaging equipment were assessed using standard polystyrene particles and model samples. We found no significant difference between the light obscuration and flow imaging methods for measuring the concentrations of 10 μm standard particles. In contrast, the particle concentration in human albumin solution measured with flow imaging was significantly higher than that measured using the light obscuration test, and many protein aggregates were observed with flow imaging. However, the size distribution of standard particles, the concentration of protein aggregates, and the quality of the captured images varied depending upon the flow imaging equipment employed. Universal application of flow imaging would require establishment of appropriate settings of multiple parameters to ensure consistency of the data.

Key words

Insoluble particulate matter test, Subvisible particles, Light obscuration, Flow imaging