How to apply the Japanese Pharmacopoeia according to the purpose〈*GZ-4-190*〉

(目的に応じた日本薬局方の適用方法)

The JP is an official document that defines the specifications, criteria and standard test methods necessary to properly assure the quality of drugs in Japan. Furthermore, it is a scientific document that publicly discloses test methods used during drug development and approval applications, at quality control sites such as pharmaceutical companies and pharmacies, at public testing institutions, and in pharmaceutical education, as well as the internationally promoted concept of quality control. In addition, it aims to include all important drugs in healthcare, and contains drugs at various stages in the drug life cycle.

Since the JP is an official document, it contains the specifications, criteria and standard test methods for assuring them. The monographs of the JP contain not only drug substances but also drug products, but the time of listing varies. Specifications and criteria are established based on the concept of quality assurance at the time of listing, as well as test methods for them. For example, specifications, criteria and test methods are specified for description, identification, purity, water content, residue on ignition, assay, storage, etc., for a drug substance, and specifications, criteria and test methods for manufacture, identification, uniformity of dosage units, dissolution, assay and storage, etc., are specified for its drug product. When a JP reference standard is not specified for a drug substance, quantitative tests for its drug product may be specified to be performed using the drug substance itself. In such cases, the drug substance that has the content of the ingredient above a certain level is specified as XX for assay in Reagents, Test Solutions <*9.41*>, and used for quantitative tests of its drug product. This provision is based on the premise that main testing sites are pharmaceutical companies that can easily obtain the drug substance meeting the specification of the JP. However, when a drug product is tested by a public testing institution, it may be difficult to obtain the drug substance meeting the specification of the JP. In this case, a commercially available reagent is used as a substitute for the drug substance, and the tests specified in the JP are performed to confirm that this reagent meets the specifications of the drug substance.

In such cases, to what extent should the reagent that replaces the drug substance be tested? In the JP, it is important to perform tests according to the fit for purpose. Therefore, for example, if a drug substance is designated as a reference material in an identification test of a drug product and a commercially available reagent replaces it, identification tests of the drug substance are performed to confirm that the reagent has certainly the same structure as the drug substance. If the identification test for the drug product is specified, for example, by thin-layer chromatography or liquid chromatography using the drug substance, it is not necessary to perform the purity tests, residue on ignition test, assay test, etc., specified for the drug substance.

Then, what if a commercially available reagent is used as a substitute for a drug substance for quantitation of its product? It is necessary to confirm that the reagent has certainly the same structure as the drug substance in some way, and then to confirm that the reagent meets requirements of XX for assay by performing the assay of the drug substance. In this case, if calculation on the anhydrous basis is necessary, the water content should also be measured. In other words, if a reagent is used instead of a drug substance to perform quantitative tests of a drug product, the tests required for the drug substance such as purity tests and residue on ignition test do not affect the quantitative value of the drug product in most cases. If this is clear, it is not necessary to perform these tests according to the fit for purpose. Similarly, when a drug substance is used in a quantitative test using liquid chromatography to confirm the system performance and is substituted by a commercially available reagent, it is only necessary to confirm that the reagent has the same structure as the drug substance, considering its purpose.

Thus, when performing the tests in the JP, it is important to consider the essential of the tests and it is considered possible to apply the necessary tests according to the purpose. If, as a result of careful consideration of the essential of tests, the application of the test method of the JP is changed, it is necessary to be able to provide a rational explanation for the appropriateness of the change. Furthermore, in the manufacture of drugs, changes should be made only within the scope that ensures the quality of drugs.