Quality Evaluation of Kampo Medical Extracts

As has been introduced in section "Manufacturing Process of Kampo Medicine", the quality of Kampo medical extracts is strictly controlled in the Kanebo factory producing these extracts. Appropriate quality assurance requires the provision of suitable analytical technologies. This section will introduce a portion of Kanebo's quality management.

I. Analytical evaluation of crude drugs

The quality of the crude drugs directly influences the final extract products. In order to verify that the delivered crude galenicals meet our company's standards, they are upon receipt subjected to rigorous examinations.

The Japanese Pharmacopoeia and the Japanese Herbal Medicine Codex, naturally provide that the material is thoroughly inspected and subjected to morphologic examinations under the microscopic. For identification and quantitative measurements of indicator substances (as outlined in the "Manufacturing Process of Kampo Medicine II") and similar physical examinations, including loss on drying, purity test, total ash, acid-insoluble ash, extract content, essential oil content etc.; applicable standards and test methods are defined. In addition to these items Kanebo performs its own unique tests like microbial tests and residual agricultural chemical examinations.

Microbial tests:

This includes testing for viable cell counts with microbial limit tests for aerobic bacteria, fungi and yeasts, as well as measurement of enteric bacteria and other Gram-negative bacteria and identification of Escherichia coli, Salmonella and Staphylococcus aureus with specific microorganism tests.

Residual agricultural chemical examinations:

These tests are performed to determine organic chlorine pesticides (Total BHC's, total DDT's etc.), organic phosphorous pesticides (Diazinon, Malathion, Parathion etc.) and pyrethroids (Cypermethrin, Fenvalerate) and similar pesticides. Organic chlorine pesticides and pyrethroids are measured using gas chromatographs equipped with electron capture detectors (ECD), whereas for the organic phosphorous pesticides, mesurements using gas chromatographs equipped with flame photometric detectors (FPD) are frequently employed. These devices are characterized by their outstanding detectability and selectivity.

II. Extract quality evaluation

In order to perform quality checks of extract powders for each lot obtained by drying the extracts after mixing the crude drugs based on individual formula compositions, the materials are subjected to identification, quantitative tests, loss on drying, purity tests, total ash, acid-insoluble ash, extract content, microbial tests and residual agricultural chemical examinations. The results of these analyses have to meet specified evaluation criteria.

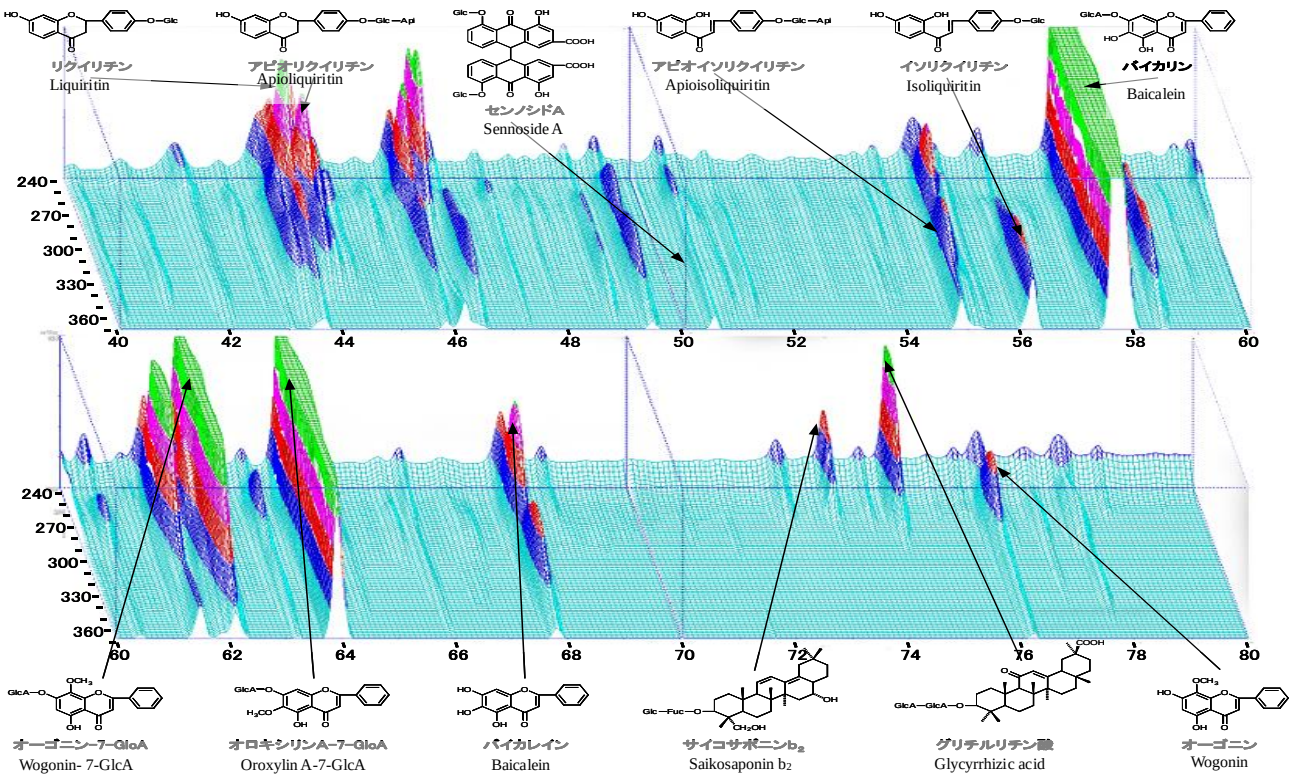
Moreover, to test whether the quality of the extract powder is constant, or if the material has been mixed with other galenicals, the gradient method chromatographs equipped with photodiode array detectors (PAD) is employed even during HPLC analysis. Sequential modification of the solvent ratio in the mobile phase results in successive elution of components with differing properties and renders visual comparison of multiple components with continuous wavelengths with a Multi-wavelength device easier. This procedure is excellent at identifying impurities.

III. Product (final products) quality evaluation

Each lot of the final products including the addition of diluting agents to the extract powders to produce the commercial products is subjected to identification, quantitative tests, loss on drying, purity tests, measurement of total ash, acid-insoluble ash, extract content, microbial tests, residual agricultural chemical examinations and additionally to product tests investigating deformations etc. i.e. particle size distribution tests for preparation disintegration tests and mass variation tests.

These test results are registered in the master computer and the system is built, so that only products confirmed to meet specific evaluation criteria will be shipped.

A 3-dimensional chromatogram of the "B"Character Decoction extract



Setting for microbial testing

Example of analyzing devices (HPLC)