



PERGAMON

Available online at www.sciencedirect.com

SCIENCE @ DIRECT®

PHYTOCHEMISTRY

Phytochemistry 64 (2003) 909–912

www.elsevier.com/locate/phytochem

Editorial Comment

Global phytochemistry: research in Japan

Japan is made up of four main islands, Hokkaido, Honshu, Shikoku and Kyushu, together with more than 4000 smaller islands. Because of the country's length of 1860 miles, the Japanese climate differs greatly from sub-frigid region to sub-tropical region. About 67% of Japan's land area is mountainous and most of this is covered with forests. Thus Japan is a rich source of all kinds of Gymnospermae and Cryptogamae. In Makino's New Illustrated Flora of Japan some 3400 species of higher plants with the representative species (504) of cryptogamae are illustrated.

Modern phytochemistry in Japan was created by Professors N. Nagai (1865–1950), T. Majima (1874–1962) and U. Suzuki (1874–1943). They found ephedrine from *Ephedra sinica*, urusols from *Rhus verniciflua* and orizantin (later named vitamin B1) from *Oriza sativa*, respectively. N. Nagai founded the Pharmaceutical Society of Japan and became the President of this Society and the Chemical Society of Japan. After their and their pupils' efforts, Japanese phytochemistry dramatically developed and many pharmacologically and medicinally important phytochemicals, such as gibberellins from *Gibberella fujikuroi*, ginkgolides from *Ginkgo biloba*, kainic acid from *Digenia simplex*, phytoecdysones from *Achyranthes fauriei* and *Podocarpis nakaii*, ginsenosides from *Gynostemma pentaphyllum*, and so on have been isolated by Japanese phytochemists and pharmacognosists.

Japanese phytochemists have studied not only medicinal and aromatic plants, fungi and microorganisms but also Wakan-yaku (Chinese and Japanese crude drugs). They have also published a tremendous number of papers on the isolation, structure determination of pharmacologically active compounds, their total synthesis and efficacy of the crude extracts and pure compounds in vitro and in vivo systems, synergetic effect, and structure–activity relationship. During the past 3 years (2000–2002), Japanese phytochemists published 82 (18.3%), 93 (20.2%) and 66 original papers (17.7%) in *Phytochemistry*. Figures 1–3 show three examples used as crude drugs in Japan and China. Zingiberis Rhizoma and Perillae Semem are also dispensed for Kampo-medicines in these countries (Namba, 1980).

I would like to introduce some Japanese symposia and journals concerning phytochemistry in order to comment on the activity of Japanese phytochemists.

Every year they have a one-day symposium on Phytochemistry. The 39th symposium (abstract pages:1–61) was held in Tokyo last year. Six lectures were presented: (1) exploration of the seed-molecules from medicinal plants and exploitation of alkaloids having biological function of lead-compounds, (2) phototropism in higher plants: a mystery revealed, (3) chirality of natural products: hyoscyamine and scopolamine, (4) diurnal and nocturnal change in floral scent emission, (5) search for inhibitors for receptor of nuclear export signal from medicinal plants and (6) scientific evaluation of Kampo medicine. This event attracts about 150–200 participants every year.

A symposium on Chemistry of Natural Products (CNP) which is sponsored by The Chemical Society of Japan (CSP) is held every year and approximately 1200 natural product chemists attend this symposium. Last year the 44th CNP (644 page abstract book) was held in Tokyo, and 44 oral and 63 poster papers were presented. Topics included the isolation, structure elucidation of biologically active compounds from medicinal plants, fungal and bacterial origin (17), and their total synthesis (35), biosynthesis (7), plant biotechnology and molecular biology (20). The 45th symposium will be held in Kyoto in 2005.

The symposium on Chemistry of Terpenes, Essential Oils and Aromatics (TEAC) is sponsored by CSP every year. The first joint symposium of 46th TEAC and the International Symposium of Essential Oils (ISEO) (446 page abstract book) was organized in Tokushima last October. It included plenary lectures (3), invited (4) and cultural lectures (1) and short oral lectures (165). The general lectures included analysis of constituents of essential oils, total synthesis of and reaction of terpenoids and aromatics, biosynthesis, biotransformation, perfumery chemistry, aromatherapy research and new separation methodology of essential oils. We attract about 500 participants to TEAC every year. The 47th TEAC will be held in Tokyo this November.

The symposium on the Development and Application of Naturally Occurring Drug Materials (209 page abstract



Activity	Active compounds	Effects
Diuretic	Quercitrin, isoquercitrin	Antipyretic, antidotal, anti-inflammatory
Anti-fungal	Decanoylacetolaldehyde	anti-constipation

Fig. 1. *Houttuynia cordata* Thunb. (Houttuyniae Herba).

book) is organized every 2 years by the Pharmaceutical Society of Japan (PSJ). In 2001, the 13th symposium was held in Osaka including topics of: Structures and bioactivities of taxoids from Japanese yew, new anti-malarial seed ingredients from natural sources, many biologically active compounds from *Evodia rutaecarpa*, *Piper methysticum*, *Eriobotrya japonica*, *Salviae reticulata*, *Echinidorus macrophyllus*, *Tripterygium wiefordii*, and *Scutellaria baicalensis* and biosynthesis of secondary metabolites in *Streptomyces* by genome analysis, molecular cloning and characterization of biosynthetic



Activity	Active compounds	Effects
Anti-microbial	Zingerones, Shogaols	Anti-emetic, anti-abominalgia, anti-cephalalgia, aromatic stomachic tonic, expectorant

Fig. 2. *Zingiber officinale* Roscoe. (Zingiberis Rhizoma).



Activity	Active compounds	Effects
Antifungal	(–)-Perillaldehyde	Diaphoresis, antidole, antitussive, analgesic, anti-bronchitis, anti-emetic

Fig. 3. *Perilla frutescens* (L.) Britton var. *crispa* (Thunb.) Decne. (Perillae Semem).

enzymes involved in triterpenoid biosynthesis in *Glycyrrhiza glabra*, molecular genetic study and post-genomic approach on secondary metabolism in plants and development of high sensitive analytical method using monoclonal antibodies to natural products etc have been reported.

The 5th symposium on Medicinal Food Pharmaceutical Sciences (84 page abstract book) was organized by the PSJ as a cosponsor in November 2000. This abstract contains the improvement of memory retention, anti-melanoma and anti-apoptosis of *Crocus sativus* constituents, soybean isoflavones as phytoestrogens, catechin oxidation and black tea polyphenol, propolis, gastroprotective substances of *Zingiber officinale*, *Laurus nobilis*, *Polygonum hydropiper* and its two varieties, *Aralia elata*, *Kochia scoparia* and *Aesulus hippocastanum*.

In addition to the above specific symposia, each society organizes an annual meeting in the spring and/or autumn. PSJ organized the annual meeting (abstract page including program: 1–1051) in Nagasaki in March 2003 which attracted about 7000 participants. It contained 24 awarded and 29 plenary lectures and 36 sym-

posia. One symposium (six papers) entitled “New trend of research for bioactive substances based on natural medicines” was organized as a phytochemistry session. 3015 Papers were presented as posters of which 345 papers on phytochemistry and pharmacognosy.

The Annual meeting (abstract pages: 1–2155) of CSJ was held in Tokyo, 2003. Papers on the total synthesis (8), the isolation, structure elucidation of bioactive compounds (12) from plants, structure–activity relationship (1) and biotransformation (4) are contained therein.

The Japan Society for Bioscience, Biotechnology, and Agrochemistry (JSBBA) organized the annual meeting (521 page abstract book including name index) in Tokyo this year. There were 16 awarded and plenary lectures and 13 symposia and 4600 oral papers. The general papers (680) on microorganisms (gene technology, biotransformation, biosynthesis), enzyme from microorganisms, fungi and higher plants (223) and structural elucidation of bioactive compounds and their efficacy (231) were presented orally.

Each society organizes the local annual meeting (Hokkaido, Tohoku, Hokuriku, Kanto, Chubu, Kinki, Chugokushikoku and Kyushu etc) for three days. Each abstract contains many Phytochemical reports.

There are four major journals concerning chemistry including phytochemistry. *Chemical Pharmaceutical Bulletin* (English) and *Journal of the Pharmaceutical Society of Japan* (Japanese) (published by PSJ, <http://cpb.pharm.or.jp>), *Bulletin of the Chemical Society of Japan* (English) and the rapid communication journal, *Chemistry Letters* (English) and *Nippon Kagaku Kaishi* (Japanese/abstract English) (published by CSJ, <http://www.chemistry.or.jp/index-e.html>), and *Biosciences, Biotechnology and Biochemistry* (English) and *Nippon Nogeikagaku Kaishi* (Japanese) (published by JSBBA, <http://www.jsbba.or.jp/>) and *Heterocycles* (published by The Japan Institute of Heterocyclic Chemistry).

In 2002, a total of 349 papers (total pages:1–1642) have been published in the *Chem. Pharm. Bull.* (Vol. 50), of which 33.2% (116 papers) were concerned with the isolation, structure elucidation of new natural products and their biological activity. The others: total synthesis of bioactive plant constituents (7 papers), biotransformation (3), biotechnology, (2) molecular biology (1), biosynthesis (2), phytochemical analysis (6).

There are many phytochemical papers in *Biosci. Biotech. Biochem.* which include analytical chemistry, organic chemistry, biochemistry, molecular biology, food and nutrition sciences, microbiology and fermentation technology.

In Vol. 66, 2002, 467 papers were published of which phytochemical papers composed of 22.7% against the total. *Bull. Chem. Soc. Jp.* (2002, Vol. 75) consists of 348 papers (total pages: 1–2750) of which two total synthesis of plant bioactive compounds and one biotechnological results have been reported.

Only one paper concerning the isolation, structure elucidation of plant biological active compound has been reported in *Chemistry Letters* (2002) (total pages: 1–1296, 613 papers). In *Heterocycles* (2000, Vol. 57, total pages: 1–2887), 22 papers concerning isolation and structure elucidation of plant components were published. This journal contains valuable tables including chemical structures of plant heterocyclic compounds in each volume.

Each Society publishes *Farumashia* (PSJ), *Chemistry and Chemical Industry* (CSJ) and *Chemistry and Biology* (JSBBA) for the members of each society to explain various points of pharmacy, chemistry and agricultural chemistry.

The Japanese Society of Pharmacognosy published *Natural Medicines* (English, Vol. 57, 2003). Each number contains about ten original papers, notes, natural medicine notes and newsletters. The Medicinal and Pharmaceutical Society for WAKAN-YAKU also published the *Journal of Traditional Medicines* (English, Vol. 20, 2003) in which 5–10 papers have been reported in each number. The papers contains the effects of oriental crude drugs, herbs, medicinal plants and the isolation and structure elucidation of the pharmacologically active substances.

There are many other journals that contain phytochemical papers and reviews including: *Biochemistry* (The Japanese Biochemical Society, Vol. 75, 2003), *The Journal of Japanese Botany* (Tsumura laboratory, Vol. 78, 2003), *Kampo Medicine* (The Japan Society for Oriental Medicine, Vol. 54, 2003), *Journal of the Japanese Society for Food Sciences* (Nippon Shokuhin Kagaku Kogyo Kai), *Protein, Nucleic Acid and Enzyme* (Kyoritsu Publisher Co. Jp, Vol. 45), *Journal of Pesticide Science* (Pesticide Science Society of Japan, <http://www.soc.nii.ac.jp/pssj2/>, Vol. 20, 2003), *Vitamins* (the Vitamin Society of Japan, Vol. 77, 2003), *Journal of Nutritional Science and Vitaminology*. *J. Hattori Bot. Lab.* (Hattori Bot. Lab., Lichenology and Bryophytes). *Foods and Food Ingredients Journal of Japan* (<http://www.saneigenffi.co.jp>, Vol. 208, 2003), *Journal of the Japan Wood Research Society* (the Japan Wood Research Society, Vol. 49, 2003, <http://www.jwrs.org>), *Food Science* (Vol. 45, Shokuhin to Kagakusha), *Cell Technology* (Vol. 22, 2003, <http://www.shujunsha.c.j>) etc. *Chemistry* (Vol. 58, <http://www.kagakudojin.co.jp>) and *Chemistry Today* (Vol. 38, 2003, <http://www.tkd-pbl.com>) have been published as monthly journals giving explanations of general chemistry, phytochemistry and biochemistry. These are generally read by undergraduate and graduate course students.

Since China, Korea and south-east Asia are geographically close to Japan, a number of foreign graduate course students and post doctoral fellows are researching about phytochemistry in Japanese national and private universities and publish many informative

papers. Some laboratories have more overseas students than Japanese students. In Japan there are 99 state, 75 public and 512 private universities. The laboratories of phytochemistry or natural product chemistry and/or pharmacognosy have been established in many universities and three to four staff members (professor, associate professor, lecturer and assistant) are allotted to each laboratory. Thus, there are approximately 2000 phytochemists in Japanese universities today.

As mentioned above, we have many annual meetings and symposia of phytochemistry in Japan and a number of interesting papers have been reported as oral and poster presentations and these scholars have published their papers in *Phytochemistry* and other phytochemical journals.

The subject of intensive investigation recently in Japan are the pharmacologically interesting secondary metabolites, possessing antitumor, anti-obesity, anti-diabetes, antiosteoporosis, anti-HIV and anti-HSV, from medicinal and aromatic plants, edible and inedible fungi and bacteria.

Dynamic phytochemical studies on plant moving factors, color formation mechanism of flowers, in vitro production of important medicinal and other pharmaceutically important compounds and essential oils in various species of lichen, bryophytes and higher plants by tissue and cell suspension culture are dramatically developed in Japan. Cell cultures are of considerable importance to phytochemists not only for commercial production of valuable compounds but also for studying biosynthetic pathway and its enzymology. One of the great successes of a commercially produced com-

pound in Japan is shikonin created from the cell culture of the root of *Lithosperma offinale*.

It is estimated that there are some 3500 species of higher plants, 370 of marine algae, 870 of fungi, 1800 of bryophytes and 630 of pteridophytes in Japan and the majority of these sources have not been examined in detail for their pharmacological activity. Many of them are still unexplored. By our leadership including plant physiologists and biochemists, clinically important natural drugs, such as taxol, artemisinin and etoposide, will be created from Japanese and other Asiatic plant flora by plant biotechnology including molecular genetics.

However, it is necessary to protect a number of rare higher and spore-forming plants and fungi and conserve their genes. Fortunately we have the UNESCO natural product network in Asia including Japan. This network cosponsors the organization of the symposium on medicinal plants and spices at which we have a good opportunity to exchange our ideas and discuss about our future phytochemical prospects.

References

- Namba, T., 1980. Coloured illustrations of Wakan-Yaku. In: The Crude Drugs in Japan, China and Neighbouring Countries, Vols. 1 & 2. Tokyo: Hoikusha Publishing Co. Ltd.

Yoshinori Asakawa
Faculty of Pharmaceutical Sciences, Tokushima Bunri
University, Yamashiro-cho, Tokushima 770-8514, Japan
E-mail address: asakawa@ph.bunri-u.ac.jp