Phytochemical and Biosynthetic Studies of Lignans, with a Focus on Indonesian Medicinal Plants

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Chapter 2

Jamu:
The Indonesian traditional herbal medicine

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Submitted

Abstract

Jamu is the Indonesian traditional herbal medicine that has been practiced for many centuries in the Indonesian community to maintain good health and to treat diseases. Although modern (western) medicine is becoming increasingly important in Indonesia, *jamu* is still very popular in rural as well as in urban areas. Based on its traditional use *jamu* is being developed to a rational form of therapy, from herbal practitioners to drugs in pharma industries. *Jamu* has acquired a potential benefit, both economically and clinically. We survey the most frequently used plants in *jamu* that in addition have been investigated as to their constituents and pharmacological effects. Many isolated compounds have potent biological activities. Examples are: curcumin (*Curcuma longa*) as anticancer, antihipertensive, antidiabetes and immunostimulating agent; andrographolide (*Andrographis paniculata*) as anticancer, antiviral and cardioprotective agent; 1'-acetoxychavicol (*Alpinia galanga*) as anticancer, antimicrobial, antifungal and gastroprotective agent; lignans (*Phyllanthus niruri*) as antiviral and hepatoprotective agent. The Indonesian government has divided the preparation of medicinal plants into three categories, i.e. *jamu*, standardized herbal medicines and *fitofarmaka*. As the biological activity ascribed to *jamu* is largely based on empirical data, more research is needed to scientifically prove efficacy and to assure safety. In the further development of *jamu*, ethical issues such as intellectual property right, benefit sharing, biodiversity and conservation should be considered. This paper aims to review the state-of-art of *jamu* and to give comprehensive views that can be used for the further improvement of the utility of *jamu* in curing illnesses and maintaining good health.

Introduction

Following the Amazon rain forests, Indonesia has the second biggest biodiversity in the world expressed by a high number of indigenous medicinal plants. Based on this rich source the use of medicinal plants is very important, and in the rural areas medicinal plants are even the first choice to treat diseases. Most of the Indonesian people have ever used traditional herbal medicines which are popularly known as *jamu*. *Jamu* is a word in Javanese tribe language, meaning the traditional medicine from plants. Today, *jamu* has been adopted into Bahasa Indonesia with the similar meaning (Riswan and Roemantyo, 2002). Nowadays *jamu* is being developed from traditional handling to industrial (larger scale) production. Worldwide however, *jamu* is less known than, e.g., Traditional Chinese Medicine (TCM), Japanese Kampo and Indian Ayuverda. *Jamu gendong* is a kind of traditional *jamu* sold without label, and freshly prepared (not preserved) from plant material in *warung,* the ubiquitous stalls along the streets in Indonesia (Limyati and Juniar, 1998, Suharmiati, 2003). *Jamu gendong* is instantly served to whom orders this *jamu*. The sellers must bring the *jamu* from door to door. The word *gendong* itself means to carry something on the back of a body. The fresh *jamu* is put inside each bottle in bamboo or rattan basket. And they use a long wide shawl called *selendang* for carrying the basket on the back (Risman and Roemantyo, 2002).

A scientific approach is essential to further develop the rational use of *jamu*. The Indonesian government, industry and academia put considerable efforts on it. Various groups of secondary metabolites are known to be active components in *jamu*, including alkaloids, flavonoids, steroids, terpenoids, coumarins, and lignans. They contribute to the therapeutic effect as single active compounds as well as in combination with others.

This article reviews the use of Indonesian medicinal plants in *jamu* including its history, current status, economical prospective, development, scientific approach, and summarizes the potential developments in the future. Both online and offline literature searches have been done to compile this review. Pubmed (Medline) and ISI Web of Science were used to retrieve any online publications. About 5,000 species of medicinal plants have been retrieved from *the Medicinal Herbs Index in Indonesia* and the plants that are most frequently used as constituents of *jamu* are discussed in this paper.

Indonesian medicinal plants

Biodiversity

Biodiversity is defined as the variety of all life forms on earth, along with the interactions between them and their physical environment. As an archipelagic state with thousands of islands, Indonesia is endowed with a rich and unique biodiversity. The area of Indonesian tropical forests covers about 143 million hectares and is inhabited by about 80% of the world's medicinal plants. It is estimated that the Indonesian tropical forests inhabit 28,000 plant species. There are various reports concerning the inventory of higher plant in Indonesia. The Indonesian Country Study on Biodiversity (ICSBD 1993) puts the number of flowering plants species in Indonesia between 25,000 and 30,000. Some 40 million Indonesians depend directly on the country's biodiversity, and the Indonesian community makes use of around 6,000 plant species. Data of the number of medicinal plants also vary. PT Eisei (1995) published the *Dictionary of Indonesian Medicinal Herbs* containing more than 2,500 plants species which potentially, while Zuhud et al. (2001) identified 1,845 species with medicinal potential in the forests of Indonesia. These numbers are potentially to be updated due to the continuing inventory and investigation of yet unidentified species. According to the National Agency of Drug and Food Control (NADFC/BPOM), 283 plant species have been officially registered for their medicinal use; the larger remaining part is used traditionally.

To facilitate the activities on the conservation and sustainable use of biodiversity, the Indonesian Government, through the National Development Planning Agency (BAPPENAS), has launched the Indonesian Biodiversity Strategy and Action Plan 2003-2020 (IBSAP). IBSAP is based on the evaluation of the previous action plan from 1993 called BAPI (Biodiversity Action Plan for Indonesia), formulated in collaboration between the Indonesian Government (BAPPENAS), the Ministry of Environment, research institutes and non-governmental stakeholders with the support of the international developments institutions.

Recent research development and research communities

Evaluation of *jamu* as a rational phytotherapy has to cover different research topics including social, cultural, economic, and ethical aspects. Phytochemical studies including extraction, isolation and characterization of secondary plant metabolites have been developed to date. Biological activity studies have been conducted *in vitro* and *in vivo*, and even a few clinical studies are available.

To coordinate and to conduct research directed to the development of medicinal plants, many institutions in Indonesia are engaged. They comprise governmental institutions such as the Ministry of Health, Ministry of Forestry, Ministry of Environment, Ministry of Agriculture, the National Development Planning Agency (BAPPENAS), the National Agency of Drug and Food Control (NADFC or BPOM). The universities are actively involved through the related faculties or departments from different areas like medicine, pharmacy, chemistry, biology, agriculture, forestry, marine, environment and engineering. National research institutions such as the Indonesian Institute of Science and the Herbarium Bogoriense, are involved as well as non-governmental institutions such as KEHATI (Indonesian Biodiversity Foundation), WALHI, SKEPHI, and various industrial companies (Bermawie et al., 2005).

Economical prospective

Since the 1980s, small size *jamu* producers have grown sufficiently to introduce larger scale and modern production methods (Beer, 2001). The *jamu* producing industry now has an annual growth of 25-30%. According to Pramono (2002) there are about 810 companies active in Indonesian traditional medicine of which 87 are classified as IOT (*Industri Obat Tradisional*, Traditional Medicine Industry) and 723 as IKOT (*Industri Kecil Obat Tradisional*, Small Industry of Traditional Medicine). In 2005, 872 companies in this field have been registered at BPOM. In addition, 462 companies from foreign countries also play a role in the production of Indonesian traditional medicine. About 20 local companies are the major players. The examples of *jamu* products from these companies are shown in Table 1. The industry revenues in 2000 was estimated to be 150 million USD. However, taking into account the possibilities on the international market and the richness of the country regarding its natural resources, this amount can potentially be increased (Pramono, 2002). In the period between January to June 2005, the export of medicinal plants such as *Amomum cardamomum*, *Cinnamomum burmani*, *Piper spp*. and many others used to make *jamu* reached an amount of 126.8 million USD (Ministry of Industry, Republic of Indonesia).

Ethical considerations in the development of medicinal plants

Intellectual property right (IPR), indigenous knowledge, benefit sharing, efficacy and safety are issues that must be considered in the further development of Indonesian medicinal plants. *Jamu* has been handed over from generation to generation based on the traditional knowledge and experience of the community. When new plant-derived therapeutics based on indigenous knowledge are being explored, it is important that the companies return benefits to the native population and the local governments from which the research material was obtained (King et al., 1996). When individuals or institutions from

biotechnologically developed countries wish to obtain indigenous raw material from a biotechnologically less developed country, an agreement for the procurement of such material may be negotiated. In article 19.2 of the Rio Convention (1992) there is an agreement about the handling of biotechnology and distribution of its benefits. It is mentioned that each contracting party shall take all practicable measures to promote and advance priority access on a fair and equitable basis by contracting parties, especially developing countries, to the results and benefits arising from biotechnologies based upon genetic resources provided by those contracting parties. Such access shall be on mutually agreed terms. Goodwill to maintain such a flow may be achieved through appropriate scientific and monetary compensation, both in real time and in long-term sharing of the benefits of discovery (Soejarto, 1996). Harvesting too much and/or cultivating too little may render medicinal plants into endangered species. It is important to take into account that the individuals or institutions exploring the medicinal plant material also have responsibilities for the conservation. Most of the current knowledge that *jamu* can maintain health and/or can cure diseases comes from the people who have experienced success in curing illness by taking *jamu*, it remains to be proved that *jamu* fulfills the generally accepted criteria of safety and efficacy in order to protect the patients.

Jamu as a way of traditional healing

Rational phytotherapy with jamu and phytomedicine

Jamu, as traditional medicine arising from experiences of the past and embedded in the culture of society cannot stand still but constantly changes and develops. Along with allopathic medicine it shares issues in appropriate and rational use. These include qualification and licensing of the provider, proper use of good quality products, good communication between traditional medicine providers and patients and provision of scientific information and guidance to the public (WHO, 2002). Although pharmacological effects of *jamu* constituents have been recorded, there is an apparent lack of records or written data reporting the effectiveness of *jamu,* especially of *jamu gendong*. To assure the proper use of such products, the Indonesian government has divided the medicinal plants in three categories based on the way they are prepared and based on their efficacy; i.e. *jamu*, standardized herbal medicines, and *fitofarmaka* (phytomedicines). All preparations have to meet basic safety criteria. The therapeutic effects of *jamu* have to be supported by empirical data. The efficacy of standardized herbal medicines has to be proved in pre-clinical trials and standardization on active ingredients is required. For *fitofarmaka* clinical trials have to be available. The Indonesian government has launched the Centre for Development and Application of Traditional Treatment (Sentra P3T) in 1995. The Centre's activities include research, testing, education, training and service of traditional treatment. Other programmes include selecting, testing, certifying, registration/licensing, inventory, screening, clinical testing, utilization and evaluation of traditional medicine, and compilation of laws applicable to traditional treatment.

Preparation of jamu

Original *jamu* (*jamu gendong*) exists in the form of a decoction and is sold by ladies carrying *jamu* on their back. *Jamu gendong* is produced by household scale industries in a simple and traditional way. Traditional *jamu* makers also care about hygiene, sanitation and chemical contaminations from biological or non-biological sources. They try to protect raw materials and products from contamination, although this is far from international industrial standards. The way of preparation is often different from producer to producer, and production steps like selection of raw materials, sorting, grating, scraping, crushing, mixing and cooking, followed by boiling of the plant material in a hygienic way can differ significantly. From this background professional training was necessary to introduce certain standards like standardization of the raw materials used in *jamu* according to the *Materia Medika Indonesia* (MMI). *Jamu* makers have to be trained on hygienic production methods and for semi-modern

technologies. The most important aspect of the training is the introduction of scientific aspects of *jamu*. From household scale industries *jamu* has been developed and is now produced by the industries called IKOT and IOT. To prepare *jamu*, IKOT and IOT use the modern technologies and their activities are based on a scientific approach. They have to follow the directions for good manufacturing production (GMP). Today *jamu* made by the industry is not anymore only in the form of a decoction but also in the form of a tablet, pill, powder, pastille, capsule, extract, cream, and ointment.

Legislative aspects of jamu and phytomedicines in Indonesia

The Indonesian government, through the Ministry of Health and BPOM, has regulated *jamu* and phytomedicines (*fitofarmaka*). The regulations are aimed to develop herbal medicinal products, to protect the people from unwanted (adverse) effects, and to watch over the quality including efficacy and efficiency. Three types of Indonesian medicinal plants that mentioned before have been regulated by BPOM through a regulation nr. HK.00.05.4.2411, 2004.

For the production of traditional medicine in Indonesia, the industries have to refer to good manufacturing practice guidelines for traditional medicine, called CPOTB (*Cara Pembuatan Obat Tradisional yang Baik*). CPOTB is regulated by the Ministry of Health (regulation nr. 659/MENKES/SK/X/1991). This regulation has been renewed by BPOM in 2005 with regulation nr. HK.00.05.4.1380. CPOTB includes all aspects of production such as raw material, production process, quality control, factory building, workers, management, instrument, sanitation, etc. CPOTB is also to be applied in the industries to produce standardized herbal medicines and phytomedicine.

The traditional medicine industry (IOT and IKOT) as well as the products have to be registered in the BPOM (246/MENKES/Per/V/90 and HK.00.05.41.1384, 2005). Using this regulation, the production and distribution of traditional medicine could be controlled to fulfill the requirements according CPOTB. There are several forms of traditional medicine such as powders, pills, capsules, crude extracts, tablets, liquids. These products have to be produced according to the description published in regulation number 661/MENKES/SK/VII/1994. To develop the traditional medicines, the Indonesian government has established the Centre for Development of Traditional Medicine (Sentra P3T). The Centre is supported by regulation number 0584/MENKES/SK/VI/1995.

Table 1. Examples of *jamu* products from the big *jamu* companies in Indonesia.

Industry name	Jamu name	Plant used	Indications / use
Sariayu Martha Tilaar	Post Partum Herbs	*Calami* rhizome, *Zingiberis purpurei* rhizome, *Ligusticae acutilobumae* radix, *Baeckeae* folium, *Curcumae domesticae* rhizome, *Parkiae* semen, *Isorae* fructus, *Sappan* lignum, *Curcumae* rhizome, *Andrographidis* herba, *Caryophylli* flos	Relieves stomach pain after giving birth, eases excrements. Vaginal inflammations, stimulates blood circulation and improves appetite and digestion as well as strengthening and promoting health
PT. Phapros	Menstralax	*Ligustici* rhizome, *Paeomiae alba* radix, *Polygalae tenuifolia* radix, *Rehmanniae preparata* radix, *Carthami tinctorius* flos, *Leonuri heterophyclus* herba, *Angelicae sinensis* radix, *Concha ostrea gigas*, *Albizziae julibrissin* cortex, *Moutan radicis* cortex	Regulates endocrine gland secretion and period, promotes ovulation, reduces menstrual clot
PT. Sido Muncul	Sakit kencing	*Orthosiphonis* folium, *Ligustrinae* lignum, *Blumeae* folium, *Curcumae* rhizome, *Imperatae* rhizome	Disorders of the urinary tract
	Beras kencur	*Tamarindi pulpa* extract, *Zingiberis* rhizome extract, *Cinamomi* cortex, *Kaempferiae* rhizome extract, *Oryza sativa*	It reduces fatigue, refreshes the body, prevents hemorrhoids and cold, raises stamina and immunity
	Kuku Bima	*Ginseng* radix extract, *Eurycomae* radix extract, *Kaempferiae* rhizome extract, *Zingeberis* rhizome extract, *Zingeberis aromaticae* rhizome extract, *Phyllanti* herba extract	It raises men's stamina, libido, and makes them look young, blood circulation, discharging feces, reduce the possibility of atherosclerosis and diabetes
PT. Kimia Farma	Fitogas	*Hypericum* extract, *Centellae* folium extract, *Curcumae domesticae* rhizome pulveratum, *Curcumae xanthorrhizae* rhizome extract.	Relieves digestive disorder symptoms
	New Padibu	*Trigonella foenum graecum*, *Tribulus terrestris*, *Yohimbee* extract, *Talinum paniculatum*, *Plantago mayor* extract	Liver and kidney disturbance
	Fitolac	*Sauropus* folium extract	Increases and accelerates breast milk production
PT.Deltomed Laboratories	Srongpas Ginseng	*Retofracti* fructus, *Zingiberis zerumbeti* rhizome, *Elephantopi* radix, *Eurycoma* radix, *Panax ginseng* radix extract	Increases vitality, relieves backache, sore muscle, fatigue, and general debility, improves appetite, and nourishes the kidneys
	Antangin JRG	*Zingiberis* rhizome, *Panax ginseng* extract, *Blumeae* folia, *Menthae* folia, *Alstoniae* cortex, *Myristicae* semen	Effectively combats cold and alleviates its symptoms such as fever, nausea, bloating, cold sweat, dizziness, and fatigue
PT. Jamu Iboe Jaya	Hiperten	*Orthosiphonis* folium, *Phyllanthi* herba, *Plantaginis* folium, *Blumeae* folium, *Centellae* herba, *Morindae* fructus, *Alstoniae* cortex, *Andrographidis* herba, *Apii* herba	Reduces symptoms of mild hypertension
	Diabetin	*Tinosporae* caulis, *Andrographidis* herba, *Curcumae* rhizome, *Syzigii* semen	Diabetes mellitus
PT. Mustika Ratu	Tonic tea plus daun dewa dan ginseng	*Zingiberis aromaticae* rhizome, *Zingiberis* rhizome, *Panax ginseng* radix, *Retrofracti* fructus, *Theae* folium, *Colae* semen, *Gynurae* folium	Effective for general health maintenance of men and women, good for improvement of stamina vitality and body immunity so that will make the body fresh, fit and energetic
	Jamu godog bugar ayu	*Usneae thalus*, *Zingiberis purpurei* rhizome, *Retrofracti* fructus, *Santali* lignum, *Sappan* lignum, *Illicium verum*, *Kaempferiae* rhizome, *Curcumae* rhizome, *Foenigraeci* semen, *Andrographidis* herba, *Centellae* herba, *Curcumae* domesticae rhizome	Slowing the ageing process, improving the blood circulation, adding more energy and strengthen
Jamu Jago	Encok	*Orthosiphonis* folia, *Zingiberis zerumbeti* rhizome, *Zingiberis* rhizome	Rheumatism

	Sirnakarang	*Boesenbergiae* rhizome, *Curcumae domestica* rhizome, *Curcumae* rhizome, *Orthosiphonis* folia, *Serycocalycis* folia	Dissolves kidney stone
	Pegal linu	*Curcumae* rhizome, *Eucalipty* fructus, *Retrofracti* fructus, *Zingiberis zerumbeti* rhizome, *Zingiberis* rhizome	To get rid of muscle pains, to improve their stamina and to avoid lethargy or insomnia
	Esha	*Eurycomae longifoliae* radix, *Retrofracti* fructus, *Piperis nigri* fructus, *Phyllanthi* herba, *Zingiberis* rhizome	Immunostimulating
PT. Jamu Borobudur	Allus	*Piperis* folium, *Centella* herba, *Curcumae* domesticae rhizome, *Languatis* rhizome	
Nyonya Meneer	Jamu sakit Maag	*Euphorbiae thymifoliae* herba, *Kaempferia* rhizome, *Caricae* folium, *Blumeae* folium	Peptic ulcer
	Jamu Akas Jantung	*Coriandri* fructus, *Parameriae* cortex, *Baeckeae* folium, *Foeniculi* fructus, *Curcuma* rhizome	Various coronary problems
	Singkir angin	*Foeniculi* fructus, *Paederiae* folium, *Menthae arvensis*, *Zingiberis* rhizome	Common cold
PT. Air Mancur	Jaket pegal linu	*Zingiberis purpurei* rhizome, *Zingiberis* rhizome, *Piperis nigri* fructus, *Saccharum* album, *Zingiberis aromaticae* rhizome, *Languatis* rhizome, *Peppermint* powder, *Foeniculi* fructus, *Glycyrrhizae* radix, *Curcumae domesticae* rhizome, *Curcumae* rhizome, *Coptici* fructus, *Alyxiae* cortex, *Boesenbergiae* rhizome	Eliminates fatique, reliefs painful stiffness of the muscles and joints after hard work, to freshen up and strengthen body stamina
PT. Martha Tilaar	Jamu postnatal Innoshape	*Sauropi* folium, *Zingiberis zerumbeti* rhizome, *Curcumae* rhizome, *Elephantopi* folium	Slims down and firms up the body, reducing cellulite, while rejuvenating natural beauty
PT. Soho Farmasi	Diapet NR	*Curcumae domesticae* rhizome, *Granati pericarpium* extract, *Psidii folium* extract, *Coicis* semen, *Chebulae* fructus extract	Anti diarrhea
PT. Bintang Toedjoe	Encok	*Siler* radix, *Zingiberis rhizome*, *Anemarrhena* rhizome, *Notopterigium* rhizome, *Pterospermum* lignum	To get rid of muscle pains
	Irex Max	*Yohimbe* bark extract, *peppermint* oil, *Retrofracti* fructus, *Eurycoma longifolia* extract, *Ginseng* extract	Improves vitality and sexual power
	Diami	*Sausurea* radix, *Curcumae domesticae* rhizome, *Kaempferiae* rhizome, *Agastachis* herba, *Amomi* fructus, *Atractylodes* rhizome	Anti-diarrhoea
PT. Konimex	Sentia	*Coptidis* rhizhoma, *Curcuma domesticate* rhizome	Stomach pain, diarrhoea
PT. Tenaga Tani farma	Pil Binari	*Catechu*, *Gallae*, *Jatrophae curcas* folium	Inner care for woman's health
PT. Puspo Internusa	Pacekap diabest	*Morindae fructus* extract, *Orthosiphonis* folium extract, *Syzygii polyanthi* extract, *Andrographidis* herba extract, *Centellae* herba extract, *Curcumae* rhizome extract	Diabetes mellitus
Perusahaan jamu Sido Jodo	Diamanis	*Plantaginis* folium, *Swieteniae macrothyllae* semen, *Syzygii jambolani* cortex, *Momordicae* fructus, *Murrayae* folium, *Ocimi bacillici* folium, *Curcumae* rhizome, *Kaempferiae* rhizome, *Melaleucae* fructus, *Blumeae* folium, *Caryophylli* flos, *Catharanthi* radix, *Alii cepae* bulbus, *Alstoniae* cortex, *Andrographidis* herba	Diabetes mellitus

Biological activity of the most common plants in *jamu*

Biological activities of the most common plants in *jamu* as reported in the literature are summarized in Table 2. In the following sections in more details are discussed.

Anticancer

Plants from the family *Zingiberaceae* are the most often used ingredient of *jamu*. Eleven *Curcuma* species (*Curcuma aeruginosa, C. aurantiaca, C. colorata, C. domestica* (synonym: *C. longa*), *C. euchroma, C. mangga, C. petiolata, C. purpurascens, C. soloensis, C. xanthorrhizae, and C. zedoria*) have been used traditionally as a spice and to treat several illness such as appendicitis, asthma, itch, rheumatism, abdominalgia, anemia, hypertension, diarrhea, and dysentery. Curcumin is a main phenolic constituent of the genus especially in the rhizome of tumeric (*Curcuma domestica*). Although *C. domestica*, that is also called *C. longa*, has not been used traditionally for anticancer purposes, recent investigations show that this plant has promising effects in this area, mainly to be ascribed to curcumin (Fig. 1). The mechanism of action of curcumin has been partly elucidated. Inducing apoptosis plays an important role. Furthermore, it reduces the cell cycle progression thereby preventing cancerous cell growth (Chattopadhay et al., 2004, Karunagaran et al., 2005). *In vitro* and *in vivo*, it suppressed carcinogenesis of the liver, kidney, colon, and breast (Okazaki et al., 2005, Kirana et al., 2003). Preclinical and clinical studies with curcumin in relation to its anticancer potential have been reviewed. Human clinical trials indicated no dose-limiting toxicity up to 10 g/day taken orally. These studies carried out so far suggest that curcumin has potential in the prevention and therapy of cancer (Aggarwal et al., 2003, Sharma et al., 2005). For *C. xanthorrhiza* that is used traditionally as antibacterial, anticancer and anti-inflammatory agent scientific proof has been given for its antiproliferative and anticancer activities. These activities are largely attributed to the sesquiterpene compound xanthorrhizol isolated from this plant. It significantly increased apoptosis in HeLa cells (Ismail et al., 2005).

Ginger (*Zingiber officinale* Rose) that contains the phenolic ketones gingerol and paradol has been launched in Indonesia as *fitofarmaka* (phytomedicine) for malignancies (antineoplasma). Anticancer activity of the ginger extract has been reported *in vitro* and *in vivo*. The strongest anticancer activity has been shown for another *Zingiberaceae* species, *Zingiber aromaticum* (Kirana et al., 2003, Manju and Nalini, 2005). It has been suggested that *Z. aromaticum* containing the sesquiterpene zerumbone, also has the potential to be developed as *fitofarmaka* with anticancer properties. Panduratin, a chalcone derivative isolated from *Kaemferia pandurata* rhizome has been reported to suppress carcinogenesis in human colon cancer cell lines (Kirana et al., 2003, Yun et al., 2005). Pinostrobin, a flavonoid from this plant showed cytotoxic activity against human mammary carcinoma cells (Sukardiman et al., 2000). Ethyl *trans*-cinnamate and ethyl 4-methoxy-*trans*-cinnamate from galanga root oil (*Alpinia galanga*) induced the activity of the detoxifying enzyme, glutathione S-transferase (GST), a major mechanism for chemical carcinogen detoxification (Zheng et al., 1993). Another isolated compound from this plant, l'-acetoxychavicol acetate has been found to suppress chemical- and virus-induced tumor initiation and promotion. Although the mechanism is not fully understood, this compound inhibits activation of NF-κB and NF-κB-regulated gene expression. This may explain its ability to enhance apoptosis and to inhibit invasion (Ichikawa et al., 2005).

Isolated compounds from *jamu* showed antioxidative activity *in vitro* using H4IIE rat hepatoma cells. Kaempferol and luteolin protected these cells against oxidative stress. The ability of kaempferol and luteolin to inhibit oxidative DNA strand breaks supports their suggested role as protective agents against diseases such as cancer (Steffan et al., 2005). Three anthraquinone glycosides (pulmatin, chrysophanein and physcionin) isolated from *Rheum palmatum* roots exhibited moderate cytotoxic activity against HeLa epitheloid cells and inhibited the growth of BT-20 human breast carcinoma cells (Kubo et al., 1992). The *in vitro* cytotoxicity of the plumieride, an iridoid compound which was isolated

from methanol extract of the bark of *Plumeria bicolor* and several analogues was determined in radiation-induced fibrosarcoma (RIF) tumor cells. The analogues gave stronger activity than plumieride itself (Dobhal et al., 2004). An ethanol extract of the bark of *Alstonia scholaris* enhanced the anticancer activity of berberine in the Ehrlich ascites carcinoma-bearing mice. This extract also showed cytotoxic activity to HeLa cells. Compared to the active principle echitamine, present in *Alstonia scholaris,* the extract was more powerful to kill HeLa cells. The cytotoxic activity of the extract depends on the season of collection of the plant bark. The extract of bark collected in the summer season has the highest activity (Jagetia and Baliga, 2004, 2005). Usually this plant to be used in *jamu*, is collected during the dry season (also considered as the summer season). *Andrographis paniculata* that is called *sambiloto* by local people in Indonesia has been intensively investigated for its anticancer activity. The diterpenoid compounds 14-deoxyandrographolide and 14-deoxy-11,12-didehydroandrographolide isolated from aerial parts of this plant showed marked activity against a human breast carcinoma cell lines (Tan et al., 2005). The consumption of *Ardisia compressa* tea (aqueous extract) resulted in complete inhibition of the chemically-induced hepatocarcinogenesis in Wistar rats (De Mejia and Ramirez, 2004). *Catharanthus roseus* that has been used to treat cancer (Eisei, 1995) contains the clinically used anticancer drugs vincristine, vinblastin and other vinca alkaloids (Cragg and Newman, 2005). A water extract of *Centella asiatica* significantly reduced the multiplicity of neoplasms in the small intestine. This result suggests that *C. asiatica* has a chemopreventive effect on colon tumorigenesis in male F344 rats (Bunpo et al., 2004). 2'-Hydroxycinnamaldehyde isolated from *Cinnamomum cassia* bark, strongly inhibited the *in vitro* growth of a broad panel human cancer cells and the *in vivo* growth of the SW-620 human tumor xenograft (Lee et al., 1999). *Coriandrum sativum* was shown to act protectively against the deleterious effects in lipid metabolism in experimental colon cancer (Chithra and Leelamma, 2000).

Ganopoly, an aqueous polysaccharide fraction extracted from the fruiting bodies of *Ganoderma lucidum* has antitumor activity combined with immunomodulating activity. Ganopoly significantly reduced the tumor weight in a dose-dependent manner, with inhibition rates of 32.3, 48.2, and 84.9% at doses of 20, 50, and 100 mg/kg, respectively in mice. It may represent a novel promising immunotherapeutic agent or a lead for cancer treatment (Gao et al., 2005). Immunomodulating effects that may be useful in the treatment of cancer have been reported for ethanolic extracts of aerial parts of *Phyllanthus niruri* (Ma'at, 2002). Combination of anticancer drugs such as paclitaxel with the herbal extracts e.g. from *Glycyrrhizae radix, Rhei rhizome, Scutellariae radix, Zizyphi fructus* and *Zingiberis rhizome* enhanced the paclitaxel sensitivity in HeLa cells via the inhibition of multidrug resistance. These extract suppressed the growth of HeLa cells concentration dependently. The results concluded that the combination of anticancer drugs with some herbal extracts contributes to the improvement of clinical outcomes in cancer chemotherapy (Takara et al., 2005). Alkaloids and quassinoids from *Eurycoma longifolia*, iridoids and lignans from *Plumeira rubra* showed cytotoxic activity to human breast, colon, fibrosarcoma, lung, melanoma, KB, KB-V1 cancer cell lines and in murine lymphocytic leukemia (Kardono et al., 1990, 1991).

Antiviral

Hundreds of medicinal plants used in *jamu* have been tested for antiviral activity *in vitro* and *in vivo*. But the antiviral efficacy of such herbal medicine has seldom been tested in rigorous clinical trial. The methanol extracts of plants used in *jamu* e.g *Andrographis paniculata*, *Swietinia mahagoni* and *Curcuma aeruginosa* showed anti-HIV activity using HIV-I-infected MT-4 cells. With the dose range of 4.2 to 175 $\mu g\ mL^{-1}$ they inhibited the HIV-protease (Otaka et al., 1995). Methanol extracts of *Melaleuca leucadendron* fruit and *Annona muricata* stembark collected in Indonesia have been reported to be active against herpes simplex virus-1 *in vitro. M. leucadendron* significantly prolonged the development of skin lesions and reduced the mortality (Padma et al., 1998, Nawawi et al., 1999). Aqueous extracts, tannin, lignan and other isolated compounds from *Phyllanthus* species have been tested for their anti-

HIV activity *in vitro* and *in vivo*. They inhibited the HIV-key enzymes e.g. integrase, reverse transcriptase and protease (Calixto et al., 1998, Notka et al., 2004). The genus *Phyllanthus* has been intensively studied clinically for its antiviral effects. A systematic review of 22 randomized clinical trial showed that *Phyllanthus* species have positive effect on antiviral activity and show positive effects on liver biochemistry in chronic hepatitis B virus infection (Liu et al., 2001, Calixto et al., 1998). *Andrographis paniculata* was also clinically tested for its antiviral activity. A phase I clinical trial of andrographolide from *A. paniculata* was conducted in 13 HIV positive patients and five HIV uninfected, healthy volunteers. This trial concluded that andrographolide may inhibit HIV induced cell cycle deregulation, leading to a rise in CD4 (+) lymphocyte levels in HIV-1 infected individuals (Calabrese et al., 2000). Helicterins A-F (Fig. 1), dimeric (7.5',8.2')-neolignans with a bicyclo[2.2.2]octene C-framework isolated from *Helicteres isora* showed a mild inhibitory activity against reverse transcriptase from avian myeloblastosis virus (Tezuka et al., 2000).

Antimalaria and antiparasitic

Most of the plants mentioned here have been traditionally used as antimalarial agent in Indonesia. Methanol extracts prepared from stem bark of *Alstonia scholaris*, *A. macrophylla* and *A. glaucescense* have been assessed for antiplasmodial activity against multidrug-resistant K1 strain of *Plasmodium falciparum* cultured in human erythrocytes. The active indole alkaloids from these extracts, in contrast to chloroquine, had a significantly higher affinity to the K1 strain than to the T9-96 strain (Keawpradub et al., 1999). 1,2-Dihydroxy-6,8-dimethoxy-xanthone, isolated from *Andrographis paniculata* possessed *in vitro* activity against *P. falciparum*. *In vivo* it gave a reduction (62%) in parasitemia after treating the Swiss Albino mice with *P. berghei* (Dua et al., 2004). The petroleum ether extracts of the rind of *Carica papaya* and *Citrus sinensis* also showed antimalarial activity against strain *P. falciparum* FCK 2 *in vitro* (Bhat and Surolia, 2001). Screening of plant extracts that are traditionally used for the treatment of malaria on Java showed strong antimalarial and antibabesial activitiy. They include *Achillea millefolium*, *Baeckea frutenscens*, *Brucea javanica*, *Curcuma xanthorrhiza*, *Strychnos lucida, Swietenia macrophylla* and *Phyllantus niruri* (Trimurningsih et al., 2005, Subeki et al., 2005). Antibabesial activity was also found for protoberberine alkaloids and 20-hydroxyecdysone from *Arcangelisia flava* against *Babesia gibsoni* (Subeki et al., 2005). An *in vitro* study on traditionally used malaria remedies in the Kenyah of the Apo Kayan, East Kalimantan (Indonesian Borneo) concluded that plants such as *Lansium domesticum* and *Carica papaya* are more likely to be effective antimalarials. These herbal remedies were found to have activity against chloroquine-resistant *P. falciparum* (Leaman et al., 1995). Eurycomanone and 7-methoxy-β-carboline-1-propionic acid from *Eurycoma longifolia*, triterpenoid lansioides from *Lansium domesticum*, and *Azadirachta indica* collected from Kalimantan demonstrated significant antimalarial activity (Kardono et al., 1991, Omar et al., 2003).

Anti-inflammatory, antirheumatic, antipyretic and analgesic

The anti-inflammatory effects of extract of *Morinda officinalis* (*noni* or *mengkudu*) in *vitro* and *in vivo* have been shown by inhibition of the production of nitric oxide, prostaglandin E-2 and tumor necrosis factor-alpha in lipopolysaccharide-stimulated RAW 264.7 macrophages (Kim et al., 2005). The inhibition of the prostaglandin E2 production has been also shown by *Aloe vera* gel. Another effect of *A. vera* was the inhibition on reactive oxygen metabolites in the human colorectal mucosa. This finding may have a therapeutic relevance in inflammatory bowel disease (Langmead et al., 2004)**.** The aqueous extract of *tempe* (fermented soja-beans) which is a popular food in Indonesia have been reported to have anti-inflammatory, antioxidant and antithrombotic activity in an experimental photochemical thrombogenesis model using rat femoral artery (Rilantono et al., 2000). *Cinnamomom cortex* that was collected in Indonesia inhibited the rise in vascular permeability and edema induced by acetic acid,

carrageenin, serotonin and arachidonic acid. The effect was also shown on secondary lesions in the development of adjuvant-induced arthritis (Kubo et al., 1996). Hydroxypanduratin A and panduratin A isolated from *Kaempferia pandurata* rhizome showed significant topical anti-inflammatory activity in the assay of TPA-induced ear edema in rats. The presence of these compounds may very well be related to the uses of this plant in traditional medicine (Tuchinda et al., 2002). The lignans niranthin, phyltetralin and nirtetralin isolated from aerial parts of *Phyllanthus amarus* exhibited marked anti-inflammatory properties and suggest that these lignans are the main active principles responsible for the traditional application of this plant for anti-inflammatory properties (Kassuya et al., 2005). Screening of 75 medicinal plants collected in Indonesia showed that many of them had the inhibitory effects on the nitric oxide (NO) production in lipopolysaccharide-stimulated RAW264.7 macrophages as well as antioxidant activity through the evaluation of free radical scavenging effect and reducing power (Choi and Hwang, 2005). NO is widely recognized as an important messenger and effective molecule in a variety of biological system. The NO production is inhibited by the nitric oxidase inhibitors that can be used as therapeutic agents for inflammatory diseases (Tinker and Wallace, 2006). Chrubasik et al. (2005) comprehensively reviewed on the effects of an ethanol extract of ginger (*Zingiber officinale* rhizome) and its efficacy profiles *in vitro*, *in vivo* and in clinical studies. The ginger extracts showed a pain relieving effects in which up to 0.3 g ginger/day for musculoskeletal pain in human were administered. This review, however, suggested the further studies to prove the efficacy and to find an optimum dosage of ginger preparations in the treatment of osteoarthritic pain. The ethanol extract of ginger (*Z. officinale*) together with *Alpinia galanga*, *Curcuma longa*, *Camellia sinensis* and *Uncaria tomentosa* had also a statistically significant effect on reducing symptoms of osteoarthritis of the knee of patients (Altman and Marcussen, 2001, Ahmed et al., 2005).

Hepatoprotective

Herbal preparations containing *Andrographis panuculata* and *Phyllanthus amarus* for various liver disorders have been proved to have antihepatotoxic activity (Ram, 2001). The ethanol extract and isolated diterpenes andrographolide and neoandrographolide from the aerial parts of *Andrographis paniculata* showed significant antihepatotoxic action in *Plasmodium berghei* K173-induced hepatic damage in *Mastomys natalensis* (Chander et al., 1995). The ethanol extract of *Carica papaya* seeds caused elevation of rat serum levels of acid phosphatase (ACP), alkaline phosphatase (ALP), and aspartate amino transferase (AST). Also mild to severe metaplasia of hepatocytes was revealed in a dose-related manner as well as proliferation of Kupfer cells and hepatic cells cirrhosis. These biochemical and pathological changes indicated liver cell damage and malfunction (Udoh and Udoh, 2005). A hepatoprotective effect of ethanol extracts of turmeric together with sesquiterpenes and curcuminoid containing fractions has been shown to be related to the suppression of alanin and aspartate aminotransferase and lactate dehydrogenase level on D-galactosamin induced liver injury in rats (Miyakoshi et al., 2004). The hepatoprotective effect of *Alstonia scholaris* bark on liver injuries induced by the carbon tetrachloride (CCl_4), β-D-galactosamine, acetaminophen and ethanol were investigated by means of serum-biochemical and histopathological examinations. Ethanol extracts of *A. scholaris* bark significantly lowered β-D-galactosamine induced serum transaminases elevation in the serum-biochemical analysis in rats (Lin et al., 1996). (CCl_4)-induced hepatotoxicity in the liver of rats, as judged by the raised serum enzymes, glutamate oxaloacetate transaminase and glutamate pyruvate transaminase, was prevented by pretreatment with the extracts of *Phyllanthus niruri*, demonstrating its hepatoprotective action (Harish and Shivanandappa, 2006).

Antidiabetic

Diabetes mellitus is recognized by chronic elevation of the glucose level in the blood and often accompanied by symptoms of severe thirst, profuse urination, polyuria, weigh loss, and stupor. Medicinal plants that are used clinically to treat diabetes have shown their antidiabetes activity *in vitro*, *in vivo* and in clinical studies. The methanol and aqueous extracts derived from *Alpinia galanga* caused highly significant reduction in the blood glucose levels of normal rabbits (Akhtar et al., 2002). The glucosidic compounds 4'-O-methylpiceid and rhapontin, isolated from *kelembak* (*Rheum palmatum*) roots that were collected from the market in Indonesia exhibited moderate α-glucosidase inhibitory activity in *vitro*. The inhibition of α-glucosidase activity may be effective in controlling abnormal levels of blood glucose in metabolic diseases such as diabetes (Kubo et al., 1991). Hypolipidemic effects have been shown for aqueous extracts of cumin seeds (*Cuminum cyminum*) on alloxan-induced diabetic, triton and cholesterol fed hyperlipemic rats. Hyperlipidemia is an associated complication of diabetes mellitus. In this study, administering cumin extract to diabetic rats significantly reduced the blood glucose level. The mechanism may be by potentiating the insulin effect or by increasing the pancreatic secretion of insulin from the cells (Dhandapani et al., 2002). *Guazuma ulmifolia* leaves and *Trigonella fonum graceum* seeds that are used clinically against diabetes mellitus have been studied for their antihyperglycemic effect. Aqueous extract of these plants reduced hyperglycemic peak in the rabbits (Alarcon-Aguilara et al., 1998). *Ganoderma lucidum*, the water and ethanol extracts of *Piper betle* and dianex, a polyherbal formulation consisting of the aqueous extracts of *Gymnema sylvestre* leaves, *Eugenia jambolana* seeds, *Momordica charantia* fruits, *Azadirachta indica* leaves, *Cassia auriculata* flowers, *Aegle marmelose* fruits, *Withania somnifera* roots, and *Curcuma longa* rhizome had hypoglycemic activity in normal and streptozotocin induced diabetic mice and rats (Yang et al. 2004, Mutalik et al., 2005, Arambewela et al., 2005). Most of those plants are used in *jamu*. Preclinical evaluation consisting of animal studies, acute and subacute toxicity testing and evaluation of the antidiabetic effect of *Eugenia jambolana* seed powder in streptozotocin-diabetic rats was adequate for approval to start phase 2 clinical trials to evaluate this seed powder as complementary therapy in type 2 diabetes. The study showed that *E. jambolana* possibly acts as a hypoglycemic agent by increasing insulin levels. Toxicity studies showed no evidence of mortality or abnormality (Sridhar et al., 2005). The total triterpenoid fraction from aerial parts of *Centella asiatica*, has been studied in the patients with diabetic microangiopathy. It was shown that this fraction is useful in diabetic microangiopathy by improving microcirculation and decreasing capillary permeability and protects against the deterioration of microcirculation due to diabetic microangiopathy (Cesarone et al., 2001).

Antimicrobial and antifungal

Antibacterial and antifungal activities have been shown by aqueous extracts, andrographolide and arabinogalactan proteins isolated from *Andrographis paniculata* and are comparable (in term of growth inhibition of *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Candida albicans*) to some known antibiotics, streptomycin, gentamycin and nystatin (Singha et al., 2003). Extracts of *Alstonia scholaris*, *Anacardium occidentale* (hexane), *and Carica papaya* seeds (methanol and buthanol) have been reported to possess a broad spectrum of antibacterial activity (Bouttier et al., 2002, Khan et al., 2003, Dawkins et al., 2003). The growth-inhibiting activity of cinnamaldehyde isolated from *Cinnamomum cassia* toward human intestinal bacteria (*Clostridium perfringens, Bacteroides fragilis* and *Bifidobacterium bifidum)* was shown using an impregnated paper disk method and compared with that of tetracycline and chloramphenicol (Lee and Ahn, 1998). The essential oils of *Coriandrum sativum* and *Foeniculum vulgare* were reported to possess antibacterial activity to *Escherichia coli* and *Bacillus megaterium in vitro* (Lo Cantore et al., 2004). The essential oil from *Cuminum cyminum* and the isolated compounds, p-mentha-1,4-dien-7-al, cumin aldehyde, γ-terpinene, and β-pinene, showed antibacterial

activity against the genera *Clavibacter*, *Curtobacterium*, *Rhodococcus*, *Erwinia*, *Xanthomonas*, *Ralstonia*, and *Agrobacterium* (Iacobellis et al., 2005). The essential oils from *Cymbopogon citratus*, *C. nardus*, and *C. schoenanthus* showed a fungistatic effect against superficial mycosis (Koba et al., 2003). The essential oil of *Cinnamomum burmanni* (bark and leaves) and *Tagetes erecta* (leaves) that were collected in Indonesia have been reported to exhibit antimicrobial activity against *Bacillus subtilis* and *Salmonella typhimurium* and antifungal activity against *Candida albicans in vitro* (Sukandar et al., 1999, Hartati et al., 1999). An ethyl acetate extract of *Curcuma longa* has been reported to have antibacterial activity and the potential to restore the effectiveness of β-lactams against methicillin-resistant *Staphylococcus aureus* (MRSA), and inhibit the MRSA invasion of human mucosal fibroblasts (Kim et al., 2005). A study of Indonesian plants with ethnomedical uses showed that the methylene chloride and methanol extracts of *Terminalia catappa*, *Swietenia mahagoni*, *Phyllanthus acuminatus*, *Ipomoea spp*., *Tylophora asthmatica* and *Hyptis brevipes* have the antibacterial activities against *Eschericia coli*, *Staphylococcus aureus*, *Xanthomonas campestris* and *Bacillus subtilis* and the antifungal activities against *C. albicans*, *Pythium ultimum*, *Rhizoctonia solani* and *Sclerotium rolfsii* (Goun et al., 2003). The ethanol extracts from several plant species belonging to the *Zingiberaceae* family used in Kenyah (Indonesian Borneo), especially *Alpinia galanga*, *Curcuma zedoaria* and *Zingiberis purpureum*, were found to have pronounced inhibitory activities against a wide variety of human pathogenic fungi, including strains resistant to the common antifungals amphotericin B and ketoconazole. As members of the *Zingiberaceae* are generally regarded as safe for human consumption, these species are excellent candidates for development as novel therapeutic (Ficker et al., 2003). 1'-Acetoxychavicol acetate, an active compound from *Alpinia galanga* has antifungal activity against *Trichophyton mentagrophytes*, *T. rubrum*, *T. concentricum*, *Rhizopus stolonifer* and *Aspergillus niger* with a concentration 14 mg mL^{-1} (Janssen and Scheffer, 1985)

Gastroprotective

1S-1'-Acetoxychavicol acetate and 1S-1'-acetoxyeugenol acetate, isolated from *Alpinia galanga* markedly inhibited the ethanol-induced gastric mucosal lesions in rats. The action of 1S-1'-acetoxychavicol was attenuated by pretreatment with indomethacin and N-ethylmalcimide and significantly increased the glutathione (GSH) levels of gastric mucosa in rats. GSH acts as antioxidant and is important for maintaining the mucosal integrity in the stomach (Matsuda et al., 2003). A different mechanism of hepatoprotective activity was shown by asiaticoside, an active triterpenoid constituent of *Centella asiatica* and its extract. They were found to promote angiogenesis and stimulate blood vessel formation and mucosal cell regeneration during the gastric ulcer healing stage that are important parts of the wound healing. Angiogenesis in granulation tissues improves circulation to the wound site thus providing oxygen and nutrients are essential for the healing process (Cheng et al., 2004). The effect of an ethanolic extract of *Aloe vera* on acute gastric mucosal lesions induced by 0.6 M HCl and acid output was studied in pylorus ligated and lumen perfused rats, respectively. *Aloe vera* is endowed with gastric acid anti-secretory activity and could protect the gastric mucosa at low concentrations against injurious agents (Yusuf et al., 2004). *Morinda citrifolia* (noni) inhibits gastric emptying in male rats via a mechanism involving stimulation of cholecystokinin and its receptor activation. Cholecystokinin is a peptide hormone of the gastrointestinal system responsible for stimulating the digestion of fat and protein. It delays gastric emptying and inhibits gastric acid and plasma gastrin responses (Konturek et al., 1994, Pu et al., 2004). Ethanol and water extract of *Abrus cantoniensis*, *Saussurea lappa*, *Eugenia caryophyllata*, *Magnolia officinalis* and *Ligusticum* species strongly inhibited the growth of *Helicobacter pylori* which is an important etiologic impetus leading usually to chronic active gastritis and gastric ulcer (Li et al., 2005).

Cardioprotective

A study on the edible plants common in Asian diets such as *Ipomoea batatas*, *Piper betle*, *Anacardium occidentale*, *Gynandropsis gynandra*, *Carica papaya*, and *Mentha arvensis* extracts showed that they exhibited more than 50% relaxing effect on aortic ring preparations. *Piper betle* and *Cymbopogon citratus* showed comparable vasorelaxation on isolated perfuse mesenteric artery preparation (Runnie et al., 2004). 14-deoxy-11,12-didehydroandrographolide from *Andrographis paniculata* was shown to have bradycardia-inducing and β-adrenoceptor antagonistic properties *in vivo* using anesthetized Sprague-Dawley rats (Zhang et al., 1998). A cardioprotective effect of *Centella asiatica* on the antioxidant tissue defense system during doxorubicin induced cardiac damage in rats has been reported. The water extracts of this plant resulted in significant reduction in the levels of lactate dehydrogenase, creatine phosphokinase, glutamate oxaloacetate transaminase and glutamate pyruvate transaminase. Increased activity in serum of these enzymes is a well-known diagnostic marker of myocardial function. As active ingredients triterpenes (asiatic acid and asiaticoside) may be responsible for the cardioprotective effect of *C. asiatica* extracts (Gnanapragasam et al., 2004). The cardioprotection provided by ligustrazine is related to a reduction of TNF-alpha content by inhibition of free radical production in isolated rat hearts. It was known that TNF-alpha can contribute to myocardial damage during ischemia-reperfusion (Zhou et al., 2004). The studies of the antioxidative and cytoprotective effects using H9c2 cardiac myoblasts showed that *Phyllanthus urinaria* have a protective activity against doxorubicin cardiotoxicity. This protection was mediated through multiple pathways such as enhancement of survival factor through elevation of glutathione, activation of catalase/superoxide dismutase activity and inhibition of lipid peroxidation. This plant may serve as an alternative source of antioxidants for prevention of doxorubicin cardiotoxicity (Chularojmontri et al., 2005).

Antihypertensive

The ethanol extracts of fresh matured fruits of *Carica papaya* markedly depressed the blood pressure and heart rate in mineralocorticoid salt and in renal hypertensive rats when compared with the normotensive controls. The extracts (20 mg/kg i.v.) decreased the blood pressure by about 20.1%, 50.7% and 54.5% in normotensive, renal and deoxycortocosterone acetate-salts hypertensive rats, respectively. The extract appeared to be more potent than hydrallazine (200µg/kg i.v.), a well known antihypertensive (vasodilator) agent that decreased the blood pressure by about 10.7%, 22.8% and 26.4% in those three types of hypertension (Eno et al., 2000). The total triterpenoid fraction of *Centella asiatica*, a venoactive drug acting on the microcirculation and on capillary permeability, has been tested in three groups of patients with venous hypertension. The improvement of signs and symptoms by extracts observed in venous hypertensive patients correlated well with the improvement of the variation of capillary filtration rate and ankle edema (De Sanctis et al., 2001). The vasodilatory effect of *Curcuma herbs* has been studied. *C. longa* induced endothelium-independent vasodilatation. It was concluded that *Curcuma* herbs have hypotensive and protective effects on the endothelium in spontaneously hypertensive rats, and its mechanism is thought to be related to a radical scavenging effect and improvement of hemorheology (Goto et al., 2005). A major constituent in the water decoction of *Orthosiphon aristatus* leaves, methylripariochromene A (a benzochromene), exhibited a continuous decrease in systolic blood pressure after subcutaneous administration in conscious stroke-prone spontaneously hypertensive rats. This plant is popular as *kumis kucing* in Indonesia. Javanese people prescribe the leaves in their *jamu*, mainly for treatment of hypertension (Matsubara et al., 1999).

Anti-asthma, antitussive and anti-allergic

A study of selected medicinal folklore plants that are traditionally used for asthma treatment in Indonesia indicated that alcoholic extracts, from *Plantago major* leaves, from *Eucalyptus globulus*

leaves and fruits, from *Cinnamomum massoiae* cortex and from *Vitex trifolia* leaves and two hexane extracts -*Eucalyptus globulus* leaves and *Vitex trifolia* leaves- inhibited IgE-dependent histamine release from RBL-2H3 cells. This suggested that extracts contain active compounds which inhibit mast cell degranulation, and may be used in the development of new drugs for treating asthma and/or allergic disease (Ikawati et al., 2001). An ethanol extract of *Alstonia scholaris* leaves induced pronounced bronchodilatory activity in anaesthetized rats with the probable involvement of prostaglandins (Channa et al., 2005). Clinical studies with *Andrographis paniculata* suggested that this plant may be effective as an early treatment of uncomplicated acute upper respiratory tract infection on the patients tested. The ethanol extract of *A. paniculata* alone or in combination with the ethanol extract of *A. senticocus* appear to be more effective than placebo (Poolsup et al., 2004). The active constituents of *A. paniculata*, andrographolide and neoandrographolide, have been reported to have anti-allergic effect. This effect is due to its mast cell stabilizing activity, the same as for the antiallergic drug, disodium cromoglycate. Neoandrographolide was more potent than andrographolide in this study. All three compounds demonstrated significant inhibition of passive cutaneous anaphylaxis (Gupta et al., 1998). An antitussive effect of liquiritin apioside, liquritin and liquiritigenin, isolated from *Glychirrhiza radix* (licorice) has been reported. The effect of liquiritin apioside may depend on both peripheral (modulation of ATP-sensitive K^+ channels) and a central mechanism (modulation of serotonergic system) (Kamei et al., 2005). An aqueous extract of *Alpinia galanga* rhizome was found to inhibit the release of β-hexosaminidase, a marker of antigen-IgE-mediated degranulation in RBL-2H3 cells. Isolated compounds, 1'S-1'-acetoxychavicol acetate and 1'S-1'-acetoxyeugenol acetate inhibited β-hexosaminidase and a passive coetaneous anaphylaxis reactions in mice and the antigen-IgE-mediated TNF-alpha and IL-4 production, both of which participate in the late phase of type I allergic reactions (Matsuda et al., 2003).

Immunostimulating

An immunostimulating effect has been reported from *pule* (*Alstonia scholaris*) that is used in South East Asia mainly as antimalarial and antidysentery agents, in BALB/c mice. The bark aqueous extract stimulated non specific immune response, restored the reduction of phagocytic action induced by prednisolone and protected the body from the opportunistic infection caused by *Escherichia coli* (Iwo et al., 2000). This effect was also shown by curcumin from *Curcuma longa* in BALB/c mice (Antony et al., 1999). A polysaccharide extract of *Alpinia galanga* rhizome showed a marked stimulating effect on the reticulo-endothelial system (RES) and increased the number of peritoneal exudate cells, and spleen cells of mice (Bendjeddou et al., 2003). Immunomodulating effects were also shown by a methanol extract, andrographolide, 14-deoxyandrographolide and 14-deoxy-11,12-didehydroandrographolide isolated from *Andrograpis paniculata*. They enhanced the proliferation and interleukin-2 (IL-2) induction in human peripheral blood lymphocytes (Kumar et al., 2004). The different mechanism of immunostimulating effect was shown by the hexane and aqueous extract of *Carica papaya* seeds and its bioactive fractions. They significantly enhanced the phytohemagglutinin responsiveness of lymphocytes and inhibited the classical complement-mediated hemolytic pathway (Mojica-Henshaw et al., 2003).

Central nervous system (CNS) activity

The essential oil from the fruits of *Cuminum cyminum*, that is used traditionally as a stimulant exhibited anticonvulsant activity. This effect was shown in both pentylenetrazole- and maximal electroshock-induced seizures in male NMRI mice (Sayyah et al., 2002). Recently, also antidepressant effects have been reported for curcumin. This effect may be mediated by actions in the central monoaminergic neurotransmitter systems (Xu et al., 2005). *Glycyrrhizae radix*, together with other medicinal plants has been tested to the patients who were exhibiting tremor, a symptom of

antipsychotic-induced parkinsonism. The results concluded that the combination of those plants was effective against tremor from parkinsonism (Ishikawa et al., 2000). *Alstonia macrophylla* has been reported to have a CNS depressant activity. It caused a significant reduction in spontaneous activity, a remarkable decrease in exploratory behavioral pattern, a reduction in muscle relaxant activity and also significantly potentiated phenobarbital sodium-induced sleeping time (Chattopadhyay et al., 2004).

Other activities

Various other activities have been reported from the medicinal plants which are used in *jamu*. Grosvenor et al. (1995) surveyed the medicinal plants in Riau Province, Indonesia. Out of one hundred and fourteen species of flowering plants belonging to 51 families, and claimed to have medicinal uses, 50% were recorded to be used to combat fever, 33% for diarrhea and 31% for other gastrointestinal problems. Unny et al. (2003) reviewed about 161 medicinal plants which are a potential source of new contraceptive principles. The review contains the isolated compounds and the mechanism of actions. Some of them are used in *jamu*, e.g, *Foeniculum vulgare, Abrus precatorius*, *Muraya paniculata, Punica granatum, Curcuma longa,* and *C. zedoria*. They inhibited implantation and increased fetal loss in mice and reduced secretory activity and weight of accessory sex glands. The aqueous extracts of *Carica papaya* and *Ananas comosus* have been reported to possess diuretic activity. Both plant extracts gave similar profiles of urinary electrolyte excretion to that of the hydrochlorothiazide. The analysis of the urinary osmolality and electrolyte excretion per unit time, together with the plant salt contents, may help to differentiate the mechanism by which these plants acts as diuretic. The results indicated that the diuretic activity of *Ananas comosus* was intrinsic and not a result of the salt loading effect, whereas *C. papaya* extracts may have resulted from a high salt content of this extracts. This activity correlated well with the maximum volume, the highest osmolality, and the amount of electrolytes excreted during urine collection (Sripanidkulchai et al., 2001). The methanol extracts of *Areca catechu*, *Brucea sumatrana*, *Allamanda cathartica*, collected in Sumateran rainforests showed strong antinematodal activity against *Bursaphelenchus xylophilus* (Alen et al., 2000).

Known risks and side effects of medicinal plants used in *jamu*

It is generally assumed by the public, and also even by some medical practitioners, that plant drugs are harmless and therefore are preferable. Put in such general terms this clearly is not always true. In fact various medicinal plants also induce side effects. Powerful herbal drugs like *Digitalis*, *Strychnos*, *Belladonna* and *Colchicum* can even be highly dangerous. Between 1988 and 2002, 70 patients with a diagnosis of digoxin intoxication at the National Cheng Kung Hospital, Hongkong have been studied. The symptoms that were caused by digoxin overdose included nausea, vomiting, anorexia, weakness, syncope, dizziness and a change in consciousness (Chen et al., 2004). Digitalis may induce the toxicity of licorice (the root of *Glycyrrhiza glabra*) by drug interaction via licorice-associated electrolyte imbalance, particularly in elderly. Licorice itself may be a cause for exogenously induced hypertension, hypokalemia, hypernatremia, or suppression of the renin-aldosterone system (Harada et al., 2002). Deadly nightshade (*Atropa belladonna*) intoxication has been infrequently reported in both children and adults. Caksen et al. (2003) showed that meaningless speech, lethargy, coma, and absence of tachycardia were ominous signs in deadly nightshade intoxication in childhood. Huntley et al. (2005) have reviewed the adverse effect of *Echinacea* species reported between 1950 an 2002. Some adverse effects such as headache, dizziness, tiredness, occasional nausea and abdominal pain have been suffered by people after taking *Echinacea*.

Data from clinical trials suggest that the most commonly experienced adverse effects of *Panax ginseng* are headache, sleep and gastrointestinal disorder. The possibility of more serious adverse effects even was found in combination products containing ginseng as one of the constituents (Coon and Ernst,

2002). Kava-kava (*Piper methysticum*) may cause tiredness, low energy, headache, gastrointestinal symptoms. A 50-year-old woman was seen with papules and plaques on the face and later on her dorsal and ventral thorax and arms after taking a kava product for 3 weeks (Stevinson et al., 2002). Although ginger (*Zingiberis officinale*) shows a very broad range pharmacological effect, there are still undesirable effects such as causing heartburn. In the quantities exceeding 6 g dried ginger may act as a gastric irritant. Inhalation of dust from ginger may produce IGE-mediated allergy (Chrubasik et al., 2005).

The risk of herbal medicines producing an adverse reaction depends not only on the medicine and its dosage but also on consumer-related parameters, such as age, genetics, concomitant diseases and co-medication (herb-herb and herb-drug interactions). Reports of herbal medicinal products affected by contamination, adulteration or substitution of botanical material have repeatedly caused concern. Asian herbal medicinal products including *jamu* are most often implicated (Ernst and Pittler, 2002). One report was found that mentioned the microbial contamination of raw material and end product of *jamu gendong* (Limyati and Juniar, 1998). Agranulocytosis and citrobacterial infection have been found after using *jamu* containing phenylbutazone (Paul et al., 2005). A study of 23 commercial *jamu* showed the occurrence natural aflatoxins that exhibit carcinogenic, teratogenic and mutagenic properties (Ali et al., 2005). A side effect of *Morinda citrifolia* in a 45-year-old patient who has highly elevated transaminases and lactate dehydrogenase has been reported. This gave rise to the suspicion of herbal toxicity, which was confirmed by taking a liver biopsy (Millonig et al., 2005).

Conclusion

The *in vitro*, *in vivo* and clinical studies on medicinal plants that are used in *jamu* have scientifically proved their claimed biological activities in part. Species belonging to the family *Zingiberaceae* such as *Curcuma, Zingiber, Kaempferia*, are the most frequently used plants in *jamu*. These species have also been studied intensively for their secondary metabolites and biological activity. Curcumin and panduratin are typical examples of bioactive secondary metabolites from these plants. As members of the Zingiberaceae are generally regarded as safe for human consumption, these species are excellent candidates for development as novel therapeutic. BPOM has done systematic and comprehensive research on 9 priority medicinal plants in Indonesia, i.e. ginger (*Zingiber officinale*) and king of bitter (*Andrographis paniculata*) as antineoplasma; turmeric (*Curcuma domestica*), Java turmeric (*C. xanthorrhiza*) and *Guazuma ulmifolia*, as antihyperlipidemic, Java noni (*Morinda citrifolia*) and *Syzygium polyanthum*, as antidiabetic and *Piper retrofractum* as androgenic. Other medicinal plants have been launched as *fitofarmaka* such as *Phyllanthus niruri* as immunostimulating, *C. xanthorrhiza* as antirheumatic, *Psidium guajava* and *C. domestica* as antidiarrhea (Bermawie et al., 2005). Based on the literature search, we conclude that there are many more medicinal plants that have potential to be developed as *fitofarmaka* or as sources of new therapeutic agents. Although the commonly used plants in *jamu* have been investigated scientifically for their biological activities, the *jamu* makers or the industries still have to standardize the formulae of *jamu* in order to assure the efficacy and safety.

Jamu has the potential to develop because it is economically prospective and used to maintain the health and to cure diseases. Compared to Traditional Chinese Medicine (TCM), *jamu* still needs considerable efforts to reach optimum beneficiary. The scientific study of the common plants should be continued. Exploration of medicinal plants which are the indigenous knowledge of the Indonesian community should also consider ethical issues, such as efficacy, safety, IPR, benefit sharing and biodiversity conservation.

Table 2. Survey of studies of medicinal plants used in *jamu*.

Plant name	Plant part	Extracts or products	Compound(s) or group of compounds	Test system (and dose)	Results	Traditional use of plant
Curcuma domestica	rhizome	Ethanol	Curcumin	Clinical (180 mg per day)	Inhibition of DNA polymerase II and induction apoptosis (Sharma et al., 2005)	Appendicitis, metritis, tonsillitis, asthma, chancre, rheumatism, anemia, diarrhea, hypertension, scabies, dysentry, hemorrhoid, Anorexia, malaria, gastritic, anthelmenthic
				Clinical (120 mg per day)	Improvement of the morning stiffness and joint swelling in arthritis patiens (Chattopaday et al., 2004)	
Curcuma xanthorrhiza	rhizome	Ethanol	Xanthorrhizol	*In vitro* IC_{50} = 40 µM	Inhibition of HIV-I integrase (De Clercq, 2000)	
				In vitro and *in vivo* EC_{50} = 6.16 µg/ml	Induction apoptosis (Ismail et al., 2005)	
Zingiber officinalle	rhizome	Ethanol	Gingerol, paradol	*In vitro*, *in vivo*, IC_{50} = 40.6 µg/ml	Induction of apoptosis (Kirana et al., 2003)	Headache, rheumatism, anorexia, cholera, antiemeti, anorexia, influenza, anemia, malaria, anthelmentic, cough, vertigo
Zingiber aromatica		Ethanol	Zerumbone	*In vitro*, *in vivo*, IC_{50} = 20.2 µg/ml	Induction of apoptosis (Kirana et al., 2003)	
Kaemferia pandurata	rhizome	Hexane	Pinostrobin	*In vitro* 10-100 µg/ml	Inhibition of DNA topoisomerase I in human tumour cell (Sukardiman et al., 2000)	Dry cough, fungi, diphtheria, gonorrhoea, spice
		Chloroform	Hidroxypanduratin A, panduratin A	*In vitro*, topical, IC_{50} = 84 and 12 µg/ear	Inhibition of TPA induced ear edema formation (Tuchinda et al., 2002)	
				In vitro IC_{50} = 5.6 µM and 18.7 µM	Inhibition of HIV-1 protease activity (Cheenpracha et al., 2006)	
				In vitro MIC = 2-4 µg/ml	Antibacterial activity against *Prevotella intermedia*, *P. loescheii*, *Streptococcus matans* (Park. Et al., 2005)	
Alpinia galanga	rhizome	Oil	Ethyl- and ethyl 4-methoxy-trans-cinnamate	*In vitro* 20 mg per 2 days	Induction of glutatione S-transferase (GST) (Zheng et al., 1993)	Stomatic, anorexia, dermatosis, anaesthetic, malaria, gastritis
		Aqueous acetone	l'-Acetoxychavicol and 1S-1'-acetoxyeugenol acetate	*In vivo* 2 mg/kg BW	Induction of apoptosis (Ichikawa et al., 2005)	
				In vitro IC_{50} = 15 and 19 µM	Increase of the glutathione (GSH) levels of gastric mucosa in rats (Matsuda et al., 2003)	
					Inhibition of β-hexosaminidase, as a marker of antigen-IgE-mediated degranulation (Matsuda et al. 2003)	
Rheum palmatum	root	Methanol	Pulmatin and chrysophanein physcionin	*In vitro* IC_{50} = 1.5 µg/ml 2.5 µg/ml	Inhibition of the growth HeLa epithelioid and BT-20 human breast carcinoma cells (Kubo et al., 1992)	Astringent, stomach-ache, tonic
			4'-O-methylpiceid and rhapontin	*In vitro* IC_{50} = 280 µg/ml and 600 µg/ml	Inhibition of α-glucosidase activity (Kubo et al., 1991)	

Cymbopogon citratus	leaves	Oil	d-Limonene, geraniol	*In vitro* 20 mg per 2 days	Induction of glutatione S-transferase (GST) (Zheng et al., 1993)	Dysuria, diaphoretic, edeme, cold, rheumatism, gastritis, enteritis
			Geranial, neral, myrcene, β-pinene	*In vivo* 500 mg/kg BW	Suppression of parasitemia till 86.6% (Tchoumbougnang et al., 2005)	
Plumeria bicolor	bark	Methanol	Plumieride	*In vitro*, IC_{50} = 49.5 µg/ml	Inhibition of the growth RIF tumor cell lines (Dobhal et al., 2004)	Dysuria, malaria, syphilis, purgative, fever, edema
Alstonia scholaris	stem bark	Ethanol	Echitamine	*In vivo* 180 mg/kg body weight	Increase of the killing effect of berberine against tumour (Jagetia and Baliga, 2004)	Fever, dermatosis, anorexia, nephritis, malaria, hypertensive, depurative
				In vitro, ED_{50}=2.5 µg/ml	Cytotoxic effect in HeLa cell (Jagetia and Baliga, 2005)	
		Aqueous, ethanol	Alkaloid	*In vivo* 50 - 100 mg/kg BW	Stimulation of non specific immune respone (Iwo et al., 2000)	
Cuminum cyminum	seed	Ethanol		*In vivo*, 160 mg/g diet	Increase of GST activity, inhibit hepatocarcinogenesis (Aruna and Sivaramakrishnan, 1998)	Stimulant, stomachic, gastric ulcer
			Essential oil			
	fruit	--		*In vivo* ED_{50} = 0.12 ml/kg	Exhibition of anticonvulsant activity in both PTZ- and MES-induced seizures (Sayyah et al., 2002)	
Andrographis paniculata	aerial part	Ethanol	14-Deoxyandrographolide	*In vitro* ED_{50}= 2.8 µg/ml	Exhibition of the cytotoxic activity against human T-47D cell line (Tan et al., 2005)	Tonsillitis, chancre, antidote for poisoning, typhus, fever, diabetes, tonic, dysentery, ear diseases, eczema, appendicitis, cold, diphtheria, depurative, epilepsy, gonorrhoea, syphilis, dandruff
			14-Deoxy-11,12-didehydroandrographolide	1.5 µg/ml		
			Andrographolide	Clinical 5 mg/kg bodyweight (BW)	Inhibition of HIV induced cell cycle dysregulation (Calabrese et al., 2000)	
				In vivo 1.5 mg/kg BW	Reduction of the plasma glucose level in streptozotocin-induced diabetic rats (Yu et al., 2003)	
	roots	Chloroform Ethanol	Xanthone	*In vitro* IC_{50} = 4µg/ml	Antiplasmodial activity against *Plasmodium falciparum* (Dua et al., 2004)	
				In vivo 30 mg/kg		
	leaves		Andrograpanin	*In vitro* 3 µM	Enhancement of chemokine stromal cell-derived factor-1 alpha (SDF-1 alpha) induced chemotaxis (Ji at al., 2005)	
Arcangelisia flava	whole part		Berberine	*In vitro,* 25 µM	Inhibition of the growth of human HepG2 cells (Chi et al., 1994)	Jaundice, stomachic, anthelmentic
Ardisia compressa	leaves	Aqueous	Phenolic compounds	*In vivo*, IC_{50} = 47 µg/ml	Inhibition of hepatocarcinogenesis (De Mejia et al., 2004)	Fever, diarrhoea, cough
Phyllanthus species	whole plant	Aqueous	Alkaloids, flavonoids, lignans and terpenoids, tanins	Clinical 1.5 g per day	Antihepatitis B virus (Liu et al., 2000)	Wound, asthma, epilepsy, malaria, constipation, hypertensive, menstrual disorder, tetanus, diarrhoea, convulsant
					Anti-HIV activity (Notka et al., 2004)	
			Elargic acid, lignans, quercetin, lupeol	*In vitro* and *in vivo* IC_{50} = 1.3 µg/ml	Antiplasmodial activity against *P. falciparum* (Tona et al., 2004)	

Piper sarmentosum	berries	Methanol	Sarmentine, 1-piperettyl pyrrolidine	*In vitro* IC_{50} =18.9 µg/ml 6.5 µg/ml	Antiplasmodial activity against *P. falciparum* (Rukachaisirikul et al., 2004)	Cough, asthma
Piper caba		Aqueous acetone	Piperine, piperanine, pipernonaline	*In vivo* 25 mg/kg BW	Inhibition of ethanol- and indomethacin-induced gastric lesions (Morikawa et al., 2004)	
Piper longum		Ethanol	Alkaloid piperine	*In vitro* IC_{50} = 7.0 µM	Inhibition of monoamine oxidase and antidepressant like activity (Lee et al., 2005)	Diaphoretic, edema
Piper nigrum			Isobutyleicosatrienamide, trachyone, pergumidiene	*In vitro* MIC = 70, 60, 58 µM	Inhibition of the growth of *B. subtilis*, *B. sphaericus*, *S. aureus* *Klebsiella aerogenes* and *Chromobacterium violaceum* (Reddy et al., 2004)	Hypertensive, diaphoretic, dyspnea
Glycyrrhiza glabra	root	Ethanol	Isoliquiritigenin	*In vitro* 1 µg/ml	Inhibition of reductase activity and platelet aggregation (Tawata et al., 1992)	Rheumatic
			Liquiritin apioside, liquritin and liquiritigenin	*In vivo* 30 mg/kg BW	Antitussive (Kamei et al., 2005)	
Eurycoma lancifolia	root	Methanol	Eurycomanone 7-methoxy-β-carboline-1-propionic acid	*In vitro* IC_{50} =1.9 µg/ml IC_{50} =2.1 µg/ml	Antiplasmodial activity (Kardono et al., 1991)	Fever, depurative, dysentery, aphtha, tonic, anorexia
Anacardium occidentale	stem bark	Aqueous	--	*In vivo* 800 mg/kg BW	Inhibition of the fresh egg albumin-induced acute inflammation (Ojewole et al., 2004)	Purgative, aphtha, dermatosis
		Hexane	Stigmast-4-en-3-ol and stigmast-4-en-3-one	I*n vivo* 1.5mg/kg BW	Hypoglycaemic activity in normal, healty dogs (Alexander-Lindo et al., 2004)	
			Anacardic acid	*In vitro* MIC = 6.25 µg/ml	Inhibition of β-lactamase (Bouttier et al., 2002)	
Abelmoschus moschatus	aerial parts	Buthanol	Flavonoid myricetin	*In vivo* EC_{50} = 0.1 µM	Reduction of the plasma glucose level in streptozotocin-induced diabetic rats (Liu et al., 2005)	Convulsant, stomachic, aphrodisiac, itch
Aloe vera	leaves	Ethanol	--	*In vivo* 200 mg/kg BW	Reduction the plasma glucose level in streptozotocin-induced diabetic rats (Rajasekaran et al., 2004)	Hemorrhoid, anthelmentic, diabetes, cough, gonorrhea, tuberculosis
Centella asiatica	aerial part	Aqueous	Asiaticoside Polysacharide	*In vivo* 10 mg/kg BW *In vitro* 100 µg/ml	Enhancement of gastric ulcer healing (Cheng et al., 2004) Enhancement of proliferation on T and B lymphocytes (Wang et al., 2005)	Stomachic, anorexia, wound, chancre, bronchitis, dysentery, cough
Orthoshipon aristatus	leaves	Aqueous	Pimarane-type diterpenes, neoorthosiphols A and B	*In vitro* IC_{50} 15.2 and 60.1 nmol/ml	Inhibition of the contractile respons in rat thoracic aorta smooth muscle (Ohashi et al., 2000)	Laxative, hemorrhoid, dysentery, diarrhea, colitis
			Methylripariochromene A	*In vivo* IC_{50} = 23.8 µg/ml	Decrease of systolic blood pressure in conscious stroke-prone spontaneously hypertensive rats (Ohashi et al., 2000)	Menstrual disorder, stomachic, cholecystopathy
Coriandrum sativum	fruit	Essential oil	Terpenoids	*In vitro* MIC 0.87 mg/ml	Inhibition of the growth of *Escherichia coli*, *Bacillus megaterium*, *Pseudomonas*, *Erwinia, Xanthomonas*, *Agrobacterium* (Lo Cantore et al., 2004)	Stomach-ache, vertigo, emetic, stomachic, aphtha, menstrual disorder

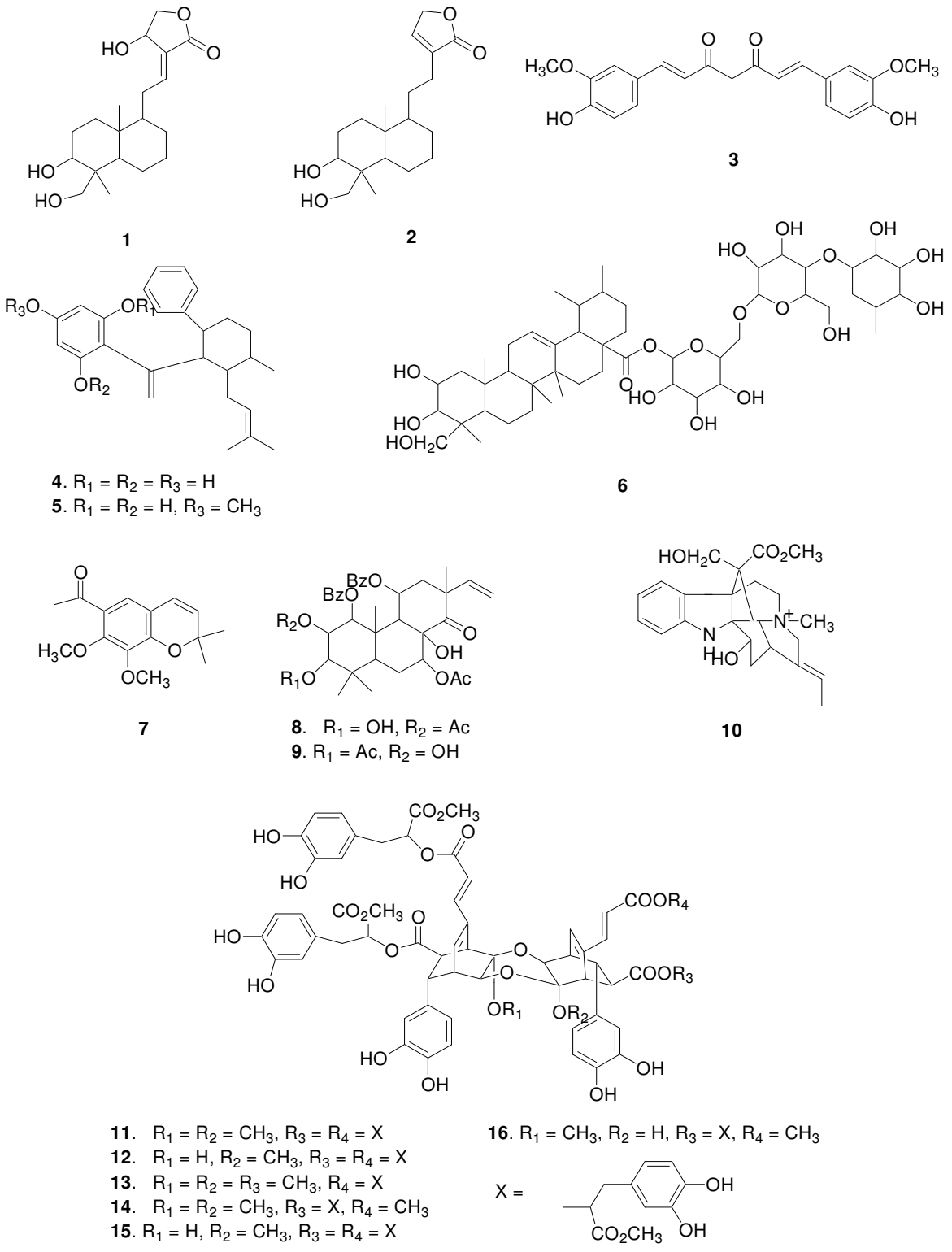

Fig. 1. Chemical structure of several active compounds from plants used in *jamu*; andrographolide (**1**), 14-deoxyandrographolide (**2**) (*Andrographiis paniculata*), curcumin (**3**) (*Curcuma domestica*), hydroxypanduratin A (**4**), panduratin A (**5**) (*Kaempferia pandurata*), asiaticoside (**6**) (*Centela asiatica*), methylripariochromene A (**7**), orthosiphol A and B (**8** and **9**) (*Orthoshipon aristatus*), echitamine (**10**) (*Alstonia scholaris*), helicterins A-F (**11-16**) (*Helicteres isora*).