Medicinal Plants and Phytomedicines. Linking Plant Biochemistry and Physiology to Human Health

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The past decade has witnessed a tremendous resurgence in the interest and use of medicinal plant products, especially in North America. Surveys of plant medicinal usage by the American public have shown an increase from just about 3% of the population in 1991 to over 37% in 1998 (Brevoort, 1998). The North American market for sales of plant medicinals has climbed to about $3 billion/year (Glaser, 1999). Once the domain of health-food and specialty stores, phytomedicines have clearly re-emerged into the mainstream as evidenced by their availability for sale at a wide range of retail outlets, the extent of their advertisement in the popular media, and the recent entrance of several major pharmaceutical companies into the business of producing phytomedicinal products (Brevoort, 1998; Glaser, 1999). No doubt a major contributing factor to this great increase in phytomedicinal use in the United States has been the passing of federal legislation in 1994 (Dietary Supplement Health and Education Act or "DSHEA") that facilitated the production and marketing of phytomedicinal products (Brevoort, 1998).

The past decade has also witnessed intense interest in "nutraceuticals" (or "functional foods") in which phytochemical constituents can have long-term health promoting or medicinal qualities. Although the distinction between medicinal plants and nutraceuticals can sometimes be vague, a primary characteristic of the latter is that nutraceuticals have a nutritional role in the diet and the benefits to health may arise from long-term use as foods (i.e. chemoprevention) (Korver, 1998). In contrast, many medicinal plants exert specific medicinal actions without serving a nutritional role in the human diet and may be used in response to specific health problems over short- or long-term intervals.

For many of the medicinal plants of current interest, a primary focus of research to date has been in the areas of phytochemistry, pharmacognosy, and horticulture. In the area of phytochemistry, medicinal plants have been characterized for their possible bioactive compounds, which have been separated and subjected to detailed structural analysis. Research in the pharmacognosy of medicinal plants has also involved assays of bio-activity, identification of potential modes of action, and target sites for active phytomedicinal compounds. Horticultural research on medicinal plants has focused on developing the capacity for optimal growth in cultivation. This has been especially pertinent as many medicinal plants are still harvested in the wild, and conditions for growth in cultivation have not been optimized. Wild harvesting of medicinal plants can be problematic in terms of biodiversity loss, potential variation in medicinal plant quality, and occasionally, improper plant identification with potential tragic consequences.

From the perspective of plant physiology, extensive opportunities exist for basic research on medicinal plants and the study of their phytomedicinal chemical production. This review presents a discussion on some fundamental aspects of phytomedicinal chemical production by plant cells with an overview of several medicinal plants that have received considerable use and attention over the past decade.

PHYTOMEDICINAL ACTIONS OFTEN RESULT FROM SECONDARY PRODUCTS INVOLVED IN PLANT ECOPHYSIOLOGY

The beneficial medicinal effects of plant materials typically result from the combinations of secondary products present in the plant. That the medicinal actions of plants are unique to particular plant species or groups is consistent with this concept as the combinations of secondary products in a particular plant are often taxonomically distinct (Wink, 1999). This is in contrast to primary products, such as carbohydrates, lipids, proteins, heme, chlorophyll, and nucleic acids, which are common to all plants and are involved in the primary metabolic processes of building and maintaining plant cells (Kaufman et al., 1999; Wink, 1999). Although plant secondary products have historically been defined as chemicals that do not appear to have a vital biochemical role in the process of building and maintaining plant cells, recent research has shown a pivotal role of these chemicals in the ecophysiology of plants. Accordingly, secondary products have both a defensive role against herbivory, pathogen attack, and inter-plant competition and an attractant role toward beneficial organisms such as pollinators or symbionts (Kaufman et al., 1999; Wink and Schimmer, 1999). Plant secondary products also have protective actions in relation to abiotic stresses such as those associated

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with changes in temperature, water status, light levels, UV exposure, and mineral nutrients (Kaufman et al., 1999). Furthermore, recent work has indicated potential roles of secondary products at the cellular level as plant growth regulators, modulators of gene expression, and in signal transduction (Kaufman et al., 1999).

Although secondary products can have a variety of functions in plants, it is likely that their ecological function may have some bearing on potential medicinal effects for humans. For example, secondary products involved in plant defense through cytotoxicity toward microbial pathogens could prove useful as antimicrobial medicines in humans, if not too toxic. Likewise, secondary products involved in defense against herbivores through neurotoxin activity could have beneficial effects in humans (i.e. as antidepressants, sedatives, muscle relaxants, or anesthetics) through their action on the central nervous system. To promote the ecological survival of plants, structures of secondary products have evolved to interact with molecular targets affecting the cells, tissues, and physiological functions in competing microorganisms, plants, and animals (for discussion, see Wink and Schimmer, 1999). In this respect, some plant secondary products may exert their action by resembling endogenous metabolites, ligands, hormones, signal transduction molecules, or neurotransmitters and thus have beneficial medicinal effects on humans due to similarities in their potential target sites (e.g. central nervous system, endocrine system, etc.) (Kaufman et al., 1999). As noted by Wink (1999), the development of structural similarity between plant secondary products and the endogenous substances of other organisms could be termed "evolutionary molecular modeling."

THE BENEFITS OF PHYTOMEDICINES OFTEN RESULT FROM SYNERGISTIC ACTIONS OF MULTIPLE ACTIVE CHEMICALS

In contrast to synthetic pharmaceuticals based upon single chemicals, many phytomedicines exert their beneficial effects through the additive or synergistic action of several chemical compounds acting at single or multiple target sites associated with a physiological process. As pointed out by Tyler (1999), this synergistic or additive pharmacological effect can be beneficial by eliminating the problematic side effects associated with the predominance of a single xenobiotic compound in the body. In this respect, Kaufman et al. (1999) extensively documented how synergistic interactions underlie the effectiveness of a number of phytomedicines. This theme of multiple chemicals acting in an additive or synergistic manner likely has its origin in the functional role of secondary products in promoting plant survival. For example, in the role of secondary products as defense chemicals, a mixture of chemicals having additive or synergistic effects at multiple target sites would not only ensure effectiveness against a wide range of herbivores or pathogens but would also decrease the chances of these organisms developing resistance or adaptive responses (Kaufman et al., 1999; Wink, 1999).

A PERSPECTIVE ON FIVE MEDICINAL PLANTS RECEIVING WIDESPREAD USE AND CURRENT INTEREST

Of the vast number of medicinal plants used in Western and non-Western medical approaches, a small number have received considerable interest and use in North America over the past few years. What follows is an overview of five medicinal plants of current interest focusing on their biochemical characteristics and pharmacological actions of their plant secondary product chemicals.

Ginseng

The name "ginseng" often leads to some confusion due to its use for different plants with different phytochemical constituents. True ginsengs are plants in the genus *Panax* from which Asian ginseng (*Panax ginseng*) and American ginseng (*Panax quinquefolium*) have received the most interest for phytomedicinal use (Bruneton, 1995; Schulz et al., 1998; Attele et al., 1999). These plants are low-growing perennial shade plants that generate a bulky storage root that is used medicinally. However, *Eleutherococcus senticosis*, a completely different plant not even in the genus *Panax*, is sometimes referred to as Russian or Siberian "ginseng." Roots from this shrubby tree, native to regions of Siberia and Northern China, were studied in the former Soviet Union as a substitute for Asian ginseng (Bruneton, 1995; Schulz et al., 1998).

Interest in the use of ginseng and *Eleutherococcus* sp. comes from their purported "adaptogen" or "tonic" activities. Such activities are thought to increase the body's capacity to tolerate external stresses, leading to increased physical or mental performance (Schulz et al., 1998). Although an extensive literature documenting adaptogenic effects in laboratory animal systems exists, results from human clinical studies are conflicting and variable (Schulz et al., 1998; Attele et al., 1999; Huang, 1999; World Health Organization, 1999). However, there is evidence that extracts of ginseng and *Eleutherococcus* sp. can have an immunostimulatory effect in humans, and this may contribute to the adaptogen or tonic effects of these plants (Schulz et al., 1998; World Health Organization, 1999; Blumenthal et al., 2000).

The major secondary products present in ginseng roots are an array of triterpene saponins, collectively called ginsenosides (Dewick, 1997; Huang, 1999). The ginsenosides are glycosylated derivatives of two major aglycones, panaxadiol and panaxatriol (Bruneton,

1995; Dewick, 1997). At present, 30 ginsenosides have been identified of which the ginsenosides, Rb1, Rb2, Rc, Rd, Re, Rf, Rg1, and Rg2 (Fig. 1) are considered to be the most relevant for pharmacological activity (Bruneton, 1995; Dewick, 1997; World Health Organization, 1999). Different ginseng species have different proportions of ginsenosides in root tissue, and this may relate to reported differences in the pharmacological properties of these plant materials (Attele et al., 1999). Moreover, within a particular ginseng species, levels of particular ginsenosides can also be affected by environmental factors such as soil mineral nutrient supply (Li and Mazza, 1999). From laboratory studies, it has been suggested that the pharmacological target sites for these compounds involve the hypothalamus-pituitary-adrenal axis due to the observed effects upon serum levels of adrenocorticotropic hormone and corticosterone (Huang, 1999). However, it should also be noted that the overall effects of the ginsenosides can be quite complex due to their potential for multiple actions even within a single tissue (Attele et al., 1999).

Although extracts of *Eleutherococcus* sp. roots have been reported to have similar effects as the ginsenosides in animal systems, the active constituents may be quite different (Dewick, 1997). In *Eleutherococcus* sp., the active constituents are thought to be lignan-glycosides (eleutheroside E) or phenylpropane glycosides (eleutheroside B) (Bruneton, 1995; Dewick, 1997). However, the pharmacological action of these compounds remains unclear, and little information is available on their biosynthetic pathway (Dewick, 1997 and refs. therein).

St. John's Wort

The use of St. John's wort (*Hypericum perforatum*) for depression has its origins in the medical traditions of Europe well before the 1600s (Upton, 1998). In Germany, St. John's wort is currently one of the most widely used prescription medications for depression and is also extensively used in the United States as a non-prescription botanical supplement (Schulz et al., 1998; Upton, 1998). For the botanical medicine, the aerial portion of the plant is harvested and dried just after flowering, and then an alcohol/water extract is produced (Schulz et al., 1998; Upton, 1998 and refs. therein; Blumenthal et al., 2000).

Naphthodianthrones such as hypericin and pseudohypericin (Fig. 2) are predominant components in St. John's wort extracts, and most St. John's wort phytomedicines are currently standardized according to their hypericin content (Schulz et al., 1998; Upton, 1998). These chemicals are localized in dark glandular structures mainly located on the margins of St. John's wort leaves and flower petals and appear to serve in the defense against insect herbivory (Fornasiero et al., 1998). Although there is some evidence that biosynthesis of St. John's wort naphthodianthrones involves the polyketide pathway, few details are known (Dewick, 1997; Nahrstedt and Butterwick, 1997 and refs. therein). The production of napthodianthrones in St. John's wort can be influenced by environmental factors such as light and soil mineral nutrients (Upton, 1998). There is strong evidence that hypericin and pseudohypericin contribute to the antidepressant action of St. John's wort, but it is unclear if this is associated with its activity as a monoamine oxidase inhibitor (Nahrstedt and Butterwick, 1997; Upton, 1998). Inhibition of monoamine oxidase is one mechanism by which some antidepressants operate to increase levels of neurotransmitters such as serotonin, norepinephrine, or dopamine (Schulz et al., 1998).

The prenylated phloroglucinol derivative, hyperforin (Fig. 2), can also be a predominant component in extracts of the flowers and leaves of St. John's wort, and there is recent evidence that this phytochemical contributes to the plant's antidepressant action (Schulz et al., 1998). In human clinical studies, the hyperforin content in St. John's wort extracts

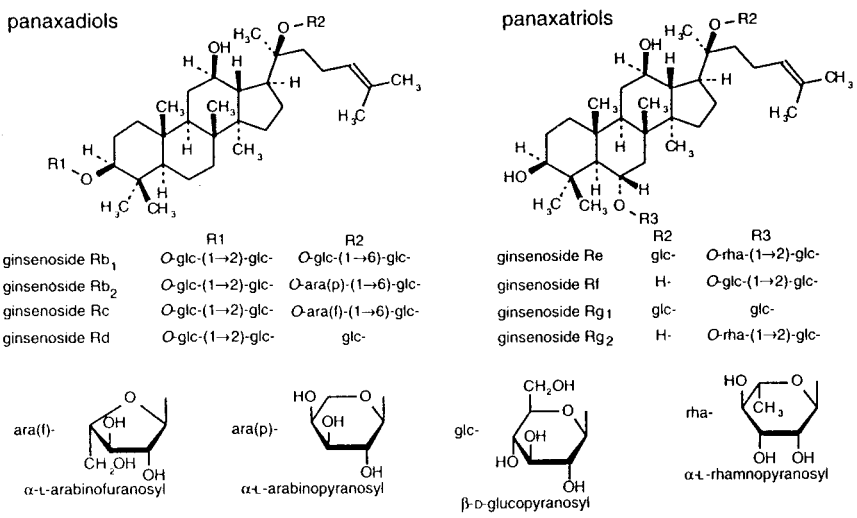


Figure 1. The ginsenosides from ginseng (*Panax* sp.) as panaxadiol and panaxatriol derivatives (adapted from World Health Organization, 1999).

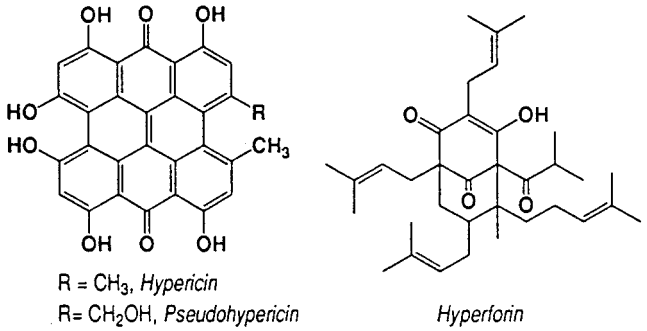


Figure 2. Hypericin, pseudohypericin, and hyperforin from St. John's wort (*H. perforatum*; adapted from Bruneton, 1995).

correlated with the level of antidepressant action (Laakman et al., 1998). This chemical appears to block synaptic re-uptake of serotonin, dopamine, and norepinephrine (Chatterjee et al., 1998). Blocking neurotransmitter re-uptake elevates their synaptic concentration. This represents another mechanism by which synthetic antidepressants may operate (Schulz et al., 1998). Whereas hyperforin also has antibacterial activity (Upton, 1998), it is uncertain as to whether or not this compound is effective in defense functions for the plant.

Ginkgo (*Ginkgo biloba*)

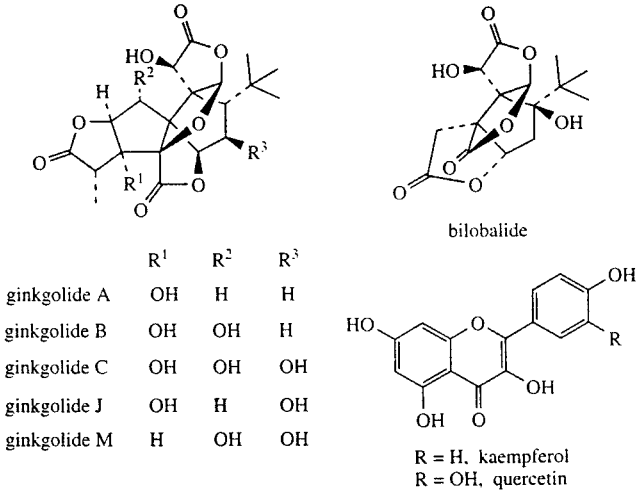
Ginkgo is the last living relative of a primitive family of gymnosperms (Ginkgoaceae); all other species exist only as fossils (Bruneton, 1995). Ginkgo trees are used as ornamentals worldwide due to their hardiness and appearance. Although the therapeutic use of ginkgo dates back about 2,000 years in traditional Chinese medicine, most medical applications only involved use of the seeds (Huang, 1999). However, the phytomedicine used today is based upon acetone extraction of the fan-shaped leaves and a further purification of active constituents (Schulz et al., 1998). Clinical studies have supported the effectiveness of ginkgo in improving peripheral and cerebrovascular circulation (Dewick, 1997; Schulz et al., 1998; Huang, 1999; Blumenthal et al., 2000). A major use of ginkgo is in the management of cognitive decline associated with disturbances in brain blood circulation (i.e. vascular insufficiency dementia) that can occur in the elderly (Schulz et al., 1998 and refs. therein; Blumenthal et al., 2000). In addition, ginkgo extracts are useful in the treatment of tinnitus, vertigo, and for improving circulation in the legs (Schulz et al., 1998 and refs. therein). However, it should be noted that the effectiveness of ginkgo extracts in improving the cognitive performance of young healthy individuals is less certain.

The active constituents present in extracts of ginkgo leaves have been shown to be a mixture of terpene lactones and flavonoids (Bruneton, 1995; Dewick, 1997). Most commercial preparations of ginkgo are leaf extracts standardized to approximately 5% to 7% terpene lactones and 22% to 27% flavonoids (Dewick, 1997; World Health Organization, 1999; Blumenthal et al., 2000). The prominent terpene lactones in ginkgo extracts are ginkgolides A, B, C, J, M, and bilobalide (Fig. 3). Although the ginkgolides are considered to be diterpenes, and bilobalide is considered to be a sesquiterpene, the latter compound most likely represents a product of ginkgolide metabolism (Dewick, 1997). Studies by Cartayrade et al. (1997) have shown that although ginkgo leaves represent sites of ginkgolide (and bilobalide) accumulation, biosynthesis of these compounds takes place in the roots. Moreover, these authors demonstrated that for ginkgolides A to C, biosynthesis occurs in a sequential manner (ginkgolide A → ginkgolide B → ginkgolide C) through successive addition of hydroxyl groups (Cartayrade et al., 1997).

Pharmacological studies have demonstrated that the ginkgolides (especially ginkgolide B) represent potent antagonists of platelet activating factor, a bioregulatory molecule involved in blood platelet activation and inflammatory processes (Dewick, 1997; Schulz et al., 1998; Huang, 1999). The flavonoids present in ginkgo extracts exist primarily as glycosylated derivatives of kaempferol and quercetin (Bruneton, 1995; Dewick, 1997; World Health Organization, 1999; Blumenthal et al., 2000) (Fig. 3). These flavonoid glycosides have been shown to be extremely effective free-radical scavengers (Dewick, 1997; Schulz et al., 1998; Huang, 1999). It is believed that the collective action of these components leads to a reduction in damage and improved functioning of the blood vessels (Schulz et al., 1998; Huang, 1999; World Health Organization, 1999).

Kava

The use of Kava originated in the "Oceana" island communities encompassed by Polynesia, Melanesia,



	R^1	R^2	R^3
ginkgolide A	OH	H	H
ginkgolide B	OH	OH	H
ginkgolide C	OH	OH	OH
ginkgolide J	OH	H	OH
ginkgolide M	H	OH	OH

Figure 3. Ginkgolides and flavonoids present in ginkgo (adapted from Dewick, 1997).

and Micronesia (Singh and Blumenthal, 1997). In these cultures "Kava" (also known as "Kava-Kava," "Ava," and "Awa") refers to an intoxicating beverage used in rituals and ceremonies, which is produced from the mashed rhizome and roots of the woody shrub, *Piper methysticum*. However, Kava is now used as the common name for *P. methysticum* as well as the phytomedicine produced from root/rhizome extracts. Worldwide, Kava is receiving considerable attention for its use as a treatment for anxiety, nervous tension, agitation, and/or insomnia. Clinical studies have shown an effectiveness of Kava that is comparable with sedatives such as benzodiazapines but without the development of either physical or psychological dependency (Singh and Blumenthal, 1997; Schulz et al., 1998).

From intensive chemical and pharmacological studies conducted on Kava root/rhizome extracts over the past century, several key active constituents have been identified (Bruneton, 1995; Singh and Blumenthal, 1997). The pharmacological activity of this plant appears to be associated with a family of styrylpyrones called "kavapyrones" (or "kavalactones") that have effects on several neurotransmitter systems including those involving Gln, GABA, dopamine, and serotonin (Schulz et al., 1998). Whereas the kavapyrones shown in Figure 4 represent the predominant pharmacologically active components in Kava root extracts, a total of 18 have been identified at present (He et al., 1997). These remaining kavapyrones appear to be derivatives of either kawain, yangonin, or dihydromethysticin (Bruneton, 1995; He et al., 1997). Although details regarding kavapyrone biosynthesis are still lacking, evidence from other systems such as *Equisetum arvense* gametophytes suggest that styrylpyrones may arise from a triketide produced by successive condensation of two malonyl-coenzyme A (CoA) molecules with a phenylpropanoid CoA-ester (Schröder, 1997 and references therein). This is similar to reactions catalyzed by chalcone synthase except that two, rather than three, successive condensations involving malonyl CoA are involved. Recent studies have shown that kavapyrone levels in Kava roots are influenced by environmental factors. In cultivated Kava plants, kavapyrone levels appear to increase with irrigation and mineral nutrient supplementation and decrease with shading (Lebot et al., 1999). Moreover, varietal differences in Kava also appear to have a role in determining the overall level of kavapyrone production (Lebot et al., 1999).

It is quite interesting that Kava plants are sterile and plantation production involves propagation from stem cuttings (Singh and Blumenthal, 1997). From genetic studies, it has been suggested that Kava likely represents a sterile relative of *Piper wichmannii* (native to New Guinea), which became distributed across the South Pacific islands with human migration and through somatic mutation became sterile (Lebot et al., 1999 and references therein). Kava's sterility combined with its limited growth habitat range (South Pacific Tropics), time required for growth before root harvest (approximately 8 years), and high world demand have raised concerns about potential over harvesting. Although attempts have been made to grow Kava in tissue culture for propagation and possible in vitro phytochemical production, little success has been achieved (Taylor and Taufa, 1998).

Echinacea sp.

Although there are 11 species in the genus *Echinacea*, this term is typically used to describe a phytomedicine produced from the aerial portion of *Echinacea purpurea* cv Purple Coneflower, roots of *Echinacea pallida* cv Pale-Purple Coneflower, roots of *Echinacea angustifolia* cv Narrow-Leaf Coneflower, or a combination of these materials (World Health Organization, 1999; Blumenthal et al., 2000). These plants are herbaceous perennials native to North America, and were originally used in Native American herbal traditions for wound healing, infections, and rattlesnake bite (Bruneton, 1995). Use of this phytomedicine was subsequently introduced to Europe in the early 1900s, and current interest lies in its use for colds, flu-like infections, and upper-respiratory infections (Schulz et al., 1998; World Health Organization, 1999). The most well-studied and effective versions of this phytomedicine involve the expressed juice of the aerial portion of *E. purpurea* and an alcohol extract of *E. angustifolia* roots (World Health Organization, 1999). A number of studies suggest that *Echinacea* sp.-based phytomedicines may be beneficial in reducing the symptoms and perhaps duration of upper-respiratory infections (Schulz et al., 1998 and references therein; World Health Organization, 1999). Pharmacological studies (>350 to date) have provided strong evidence for effects of *Echinacea* sp. extracts in modulating immune system capacity including stimulation of the phagocytic activity of hu-

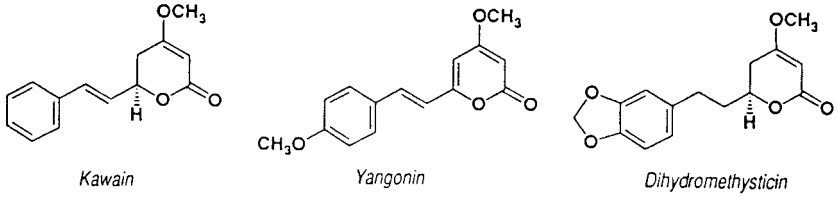


Figure 4. Examples of kavapyrones from *P. methysticum* (Kava) (adapted from Bruneton, 1995).

man lymphocytes, stimulation of fibroblasts for new tissue production, increased respiration, and elevated mobility of leukocytes (Schulz et al., 1998; World Health Organization, 1999). Extracts of *Echinacea* sp. also appear to inhibit both tissue and bacterial hyaluronidase, and this action is thought to aid in localization of infection, preventing its spread to other regions of the body (World Health Organization, 1999 and refs. therein).

The immunostimulatory activity of *Echinacea* sp. preparations appears to result from the combined effects of a complex array of constituents (Fig. 5): (a) a series of alkylamides as isobutylamides; (b) caffeic acid derivatives (cichoric acid, cynarin, echinacoside); (c) a series of polyalkynes (polyacetylenes); (d) a series of polyalkenes; and (e) high-M_r polysaccharides including heteroxylans (35,000 approximate M_r) and arabinorhamnogalactans (45,000 approximate M_r) (Bruneton, 1995; Schulz et al., 1998; World Health Organization, 1999). Pharmacological studies have shown effects of the alkylamides, polyalkynes, and caffeic acid derivatives in stimulating white blood cell phagocytosis (World Health Organization, 1999 and refs. therein; Blumenthal et al., 2000). The high-M_r polysaccharide components also appear active in stimulating phagocytosis as well as promoting production of interferon (World Health Organization, 1999 and references therein). Furthermore, through their inhibitory effect on 5-lipoxygenase, the alkylamide constituents may provide anti-inflammatory activity. Although details regarding the biosynthetic pathways of these active constituents are unknown, the hydrocarbon portion of alkylamides and polyalkynes most likely represent desaturation products of long-chain fatty acids (e.g. oleic acid) shortened through β-oxidation (for discussion of these processes, see Dewick, 1997). Chicoric acid, cynarin, and echinacoside most likely arise as conjugated products of caffeic acid generated through the shikimic acid pathway. Although factors influencing the biosynthetic pathways of these chemicals are unknown, it has been shown that the phytomedicinal content of *Echinacea* sp. can be affected by environmental conditions (soil nitrogen and potassium) and the developmental state of the plant (El-Gengaihi et al., 1998).

Currently, many *Echinacea* sp. phytomedicines are standardized according to their echinacoside content because this caffeic acid derivative is a marker chemical unique to *Echinacea* sp. However, such standardization does not consider the complex chemical interactions and possible synergistic effects necessary for the beneficial affects of this phytomedicine on humans.

CONCLUSIONS AND OUTLOOK

For the plant physiologist, work on medicinal plants opens up a wide range of research possibilities, and plant physiological studies would indeed have a major role to play in this burgeoning field. With only a few exceptions, many widely used medicinal plants have not received the extensive plant physiological characterization received by food crops or model plant systems. Although active phytochemicals may have been identified, in general, many pathways for the biosynthesis of specific me-

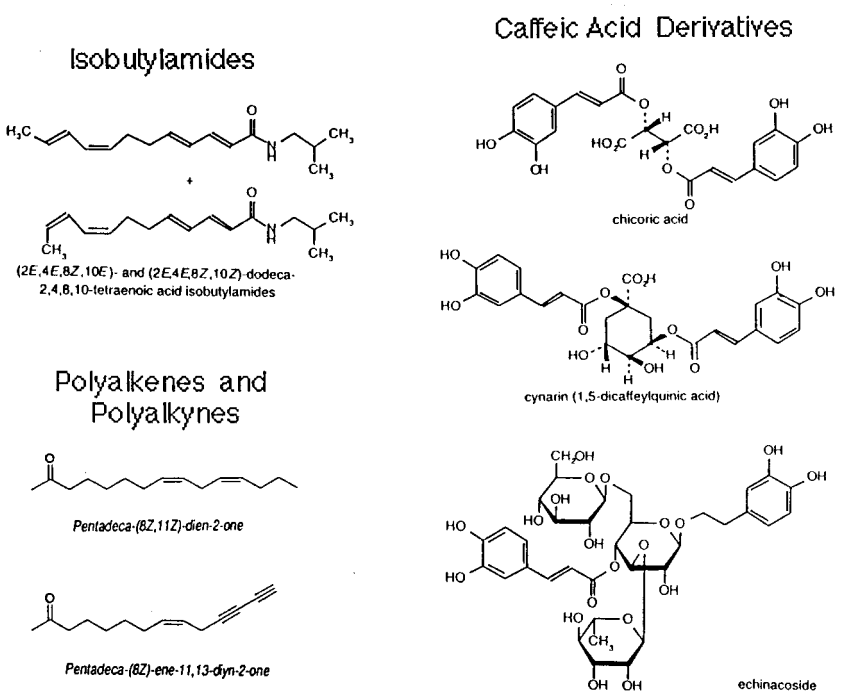


Figure 5. Examples of immunostimulating phytochemicals present in *Echinacea* sp. extracts (adapted from Bruneton, 1995; World Health Organization, 1999).

dicinal compounds and the factors (biotic and abiotic) regulating their production remain unclear. At present, a major concern with the use of phytomedicines regards the maintenance of consistent medicinal quality in botanical medicines (Matthews et al., 1999). Whereas the focus has tended to be on quality control in herbal manufacturing practices, variation in phytomedicinal content due to environmental effects upon secondary plant metabolism in the plant material could represent a significant factor. It is clear that understanding how environmental factors affect phytomedicinal production will be of great importance toward optimizing field growth conditions for maximal recovery of phytomedicinal chemicals.

In most cases, it is also unknown as to the extent to which levels of phytomedicinal chemical production by medicinal plants are determined by genetic potential versus environmental modulation. Here, the use of molecular markers (i.e. RFLP, random-amplified polymorphic DNA, and amplified fragment length polymorphism) in the characterization of medicinal plant populations for levels of phytomedicinal chemical production could prove useful for the analysis of traits and in selective breeding. The use of molecular approaches and biotechnology could also have wide application and promise especially with regard to such topics as the modification of phytomedicinal chemical pathways. Production of medicinal chemicals in plants may be modified by overexpression, antisense expression, or cosupression of biosynthetic genes. Transgenic genes could also be introduced to modify existing pathways. Mutational alterations and analysis could also be performed to dissect out basic components of metabolic pathways. The application of molecular approaches with medicinal plants would also benefit from the development of cell, tissue, and organ culture systems for in vitro growth and regeneration of medicinal plants. In addition, such tissue culture systems could also prove useful for large-scale biotechnological production of medicinal plant phytochemicals.

Overall, metabolic engineering could be useful for modifying or enhancing synthesis of valuable therapeutic agents present in medicinal plants. However, as the beneficial actions of medicinal plants can be related to combinations of phytochemicals acting collectively or synergistically, alteration of single phytochemical components could potentially affect the efficacy of a phytomedicine. In this respect, any work on modification of the phytomedicinal chemical composition of a medicinal plant through molecular methods would need to be conducted in conjunction with pharmacological studies on drug effectiveness.

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