Production of Medicinal Compounds in Plants

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Abstract

Once plants anchor its root into the soil, they stay in the place forever albeit various environmental conditions are exposed to them. The ability of plants to solve environmental conditions is amazing and rise question of how the plants regulate physiological mechanism under the environmental stress. Base on the fact that plants are autotrophic, it is very likely that plants produce specific compound to alleviate stress. It is also hypothesized that candidate for these compounds are originated from primary metabolites synthesized by plants in chloroplast. So, specific compounds produced by plants to alleviate stress conditions are commonly known as secondary metabolites. Diversities of these specific compounds are enormous, thousands of it has been found. Those various compounds are then grouped into terpenoids, alkaloids and phenolics compounds. Some of the compounds have been successfully used to alleviate human diseases. More importantly, Indonesia as a tropical country is reported to have a half of world plants species. If those specific compounds are produced by specific plants species, Indonesia is therefore has a tremendous source of secondary metabolites which could be use to ease medicinal problems. However, only some plants are already known as medicinal plants, so, further comprehensive study is still required to ease medicinal problems.

Key words: Biosynthesis, environment, medicinal plants, secondary metabolites.

Introduction

Human survival depends on the sustainability of organic compounds synthesized by plants. This is because food as a source of energy for humans being can only be produced by plants. The study of the biosynthesis of organic compounds in plants has been done for centuries and continues to this day. Unlike animals and human being, plants are able to produce organic material because they have organelles known as chloroplast. This organelle is the sites where plants synthesize organic compounds using energy from sun light. The main products of this process are carbohydrates, fats, proteins and nucleic acids. This compound is mainly used by plants for growth and reproduction. Therefore they are classified as primary metabolites. The same compounds are also used by animals and humans for growth and energy sources, but because they do not have chloroplast, animals and humans depend on plants for their food.

In addition to primary metabolites, plants also produce a variety of compounds that are not directly related to growth and reproduction. These compounds are then classified as secondary metabolites. This secondary metabolite is also an interesting subject for a long time, especially in medicine (Pavarini et al. 2012). Some argue that secondary metabolites are produced by plants to overcome the disturbance of their environment or as a tool that can help species preservation. For plants, this material is very important because since the plant stuck his roots on the ground, it will remain in that place forever. The environment, where the plant is located, can turn out to be very dangerous for its growth, both in terms of biotic and abiotic stress. Without the ability to cope with the dangerous situation, the existence of plants in the place will be threatened with extinction. Therefore plants also produce compounds that are not directly related to growth and reproduction called secondary metabolites.

Unlike plants, humans and animals can move to avoid dangerous environments, but they can also experience dangerous situations, both biotic and abiotic. Bacteria or viruses, which can cause disease in humans, can be anywhere. Likewise, weather and chemical changes can threaten human health. However, humans and animal could not synthesize their own secondary metabolites, as the plants do. Therefore, humans depend on plants not only for energy and growth, but also for medicine.

It has now been recorded that thousands of secondary metabolite compounds produced by plants. For humans and animals, these secondary metabolites have varying effect. Some plants produce secondary metabolites that can be toxic to humans. These compounds belong to the group of alkaloids, such as nicotine, caffeine, morphine and cocaine produced by tobacco plants, coffee, cannabis and coca. Other compounds produced by plants have a bitter taste. These compounds belong to terpenoid groups, such as mint, taxol, rubber and resins. Compounds that also belong to terpenoid groups are cyanogenic glycosides and cardiac glycosides. If cyanogenic glycosides which produced by Passiflora plant are consumed by animals or humans then these compounds will turn into cyanide in the body and will endanger the safety of humans and animals. Cardiac glycosides produced by Digitalis plants. This compound is very famous because it can affect the work of the heart. Plants also produce secondary metabolites that produce attractive colors for animals and humans. The purpose of plants to produce this compound is to attract animals and humans to help pollination or disperse seeds so that the sustainability of the plant species is preserved. These compounds are classified in Phenolic

groups. Examples of compounds belonging to this group are flavonoids (coloring grapes), tannins and lignins. The compound which also includes phenolic is salicylic acid which is the main component of painkillers aspirin. This salicylic acid is produced by willow plants.

Discussion

Biosynthesis of secondary metabolites in plants

Secondary metabolites in plants are produced from primary metabolites synthesized primarily in chloroplasts from inorganic compounds using energy from sunlight. The metabolic pathway to produce secondary metabolites begins with the main route: (1) glycolysis producing pyruvic acid, (2) conversion of pyruvic acid to acetyl-koa and (3) the Kreb cycle.

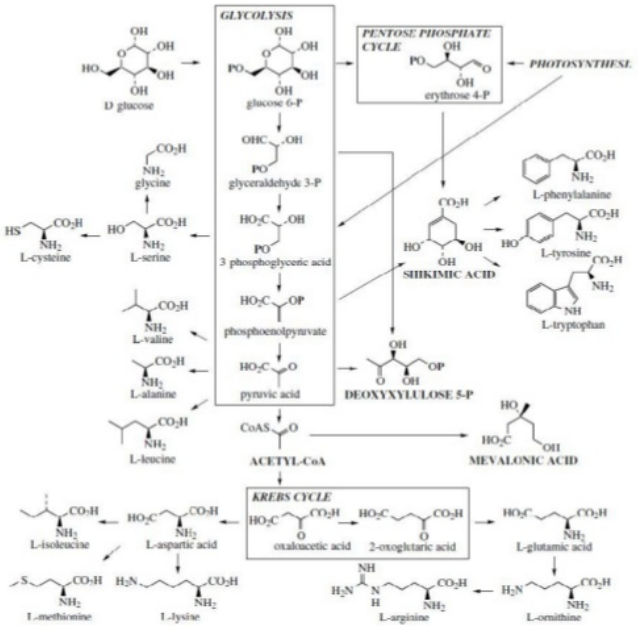

Figure 1. Amino acids as the precursor for secondary metabolite are produced from the primary metabolite, glucose (Kabera et al 2014).

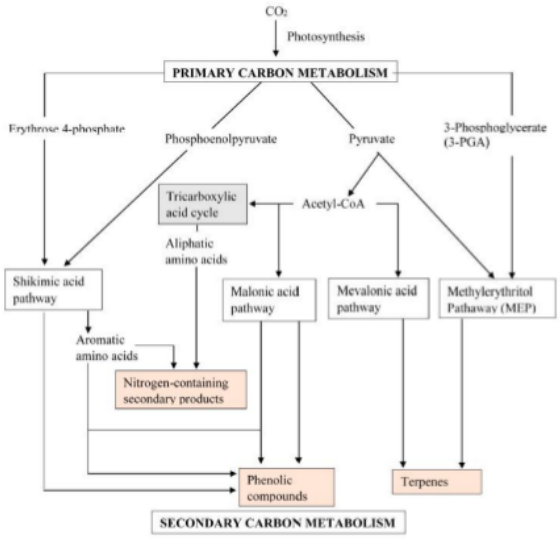

Figure 2. The synthesis of alkaloid, terpene and phenolic compounds (Ncube and Van Staden 2015).

At each stage of this glucose metabolism, different amino acids are produced which become the precursor for secondary metabolites. From stage 1 (glycolysis), produce Shikimic acid, which is then converted to amino acid phenylalanine, tyrosine and triptopan. From stage 2, mevalonic acid is produced. Secondary compounds originated from stage 3 (Kreb cycle) includes: methionine, lysine, arginine. Secondary metabolites produced from shikimic acid are phenol, tannin and aromatic alkaloid. From mevalonic acid, plant then produced terpene, steroid and alkaloids. The amino acids produced from primary metabolism is presented in Figure 1 (Kabera et al 2014) and the secondary metabolite synthesizes are presented in figure 2 (Ncube and Van Staden 2015).

Secondary metabolites as medicine

Secondary metabolites are essential for plant growth because they are useful for overcoming unfavorable environments and as a means of self-defense. Secondary metabolites are also very important for human health because it could determines the quality of food, color, flavor, aroma,

anti-oxidants, anti-cancer, tension reduction, anti-swelling, anti-microbial, triggers the body's defense system, lowers cholesterol etc. (Irchhaiya et al. 2014). According to Wink (2015), secondary metabolites produced by plants are well known for their toxic properties usually contain alkaloid or terpene. Some of these compounds has been extracted and used in modern medicines. This author also indicated that secondary metabolite of this kind has specific target on human (Wink 2015, Tab. 1).

Table 1. Use and bioactivity of a few selective secondary metabolites which are applied as isolated compounds in medicine [12]; alkaloid (A), terpenoids (T) [11–14].

Plant Species	Substance (Class)	Mode of Action	Properties/Applications
Aconitum napellus	aconitine (A)	activates Na^+ channels	analgesic
Atropa belladonna	L-hyoscyamine (A)	antagonist of mAChR	parasympathomimetic
Camptotheca acuminate	camptothecin (A)	inhibitor of DNA topoisomerase	tumour therapy
Cannabis sativa	tetrahydrocannabinol (T)	activates THC receptor	analgesic
Catharanthus roseus	dimeric Vinca alkaloids (A)	inhibit microtubule assembly	tumor therapy
Chondrodendron tomentosum	tubocurarine (A)	inhibits nAChR	muscle relaxant
Cinchona pubescens	quinidine (A)	inhibits Na^+ channels	antiarrhythmic
Coffea arabica	caffeine (A)	inhibits phosphodiesterase and adenosine receptors	stimulant
Colchicum autumnale	colchicine (A)	inhibits microtubule assembly	gout treatment

Table 1. *Cont.*

Plant Species	Substance (Class)	Mode of Action	Properties/Applications
Cytisus scoparius	sparteine (A)	inhibits Na^+ channels	antiarrhythmic
Digitalis lanata	digitoxin, digoxin (T)	inhibits Na^+,K^+-ATPase	heart insufficiency
Erythroxylum coca	cocaine (A)	inhibits Na^+ channels and reuptake of noradrenaline and dopamine	analgesic; stimulant
Galanthus woronowii	galanthamine (A)	inhibits AChE	Alzheimer treatment
Lycopodium clavatum	huperzine A (A)	inhibits AChE	Alzheimer treatment
Papaver somniferum	morphine (A)	agonist of endorphine receptors	analgesic, hallucinogen
Physostigma venenosum	physostigmine (A)	inhibits AChE	Alzheimer treatment
Pilocarpus joborandi	pilocarpine (A)	agonist of mAChR	glaucoma treatment
Psychotria ipecacuanha	emetine (A)	protein biosynthesis inhibitor	treatment of amebae infections; emetic
Rauvolfia reserpina	reserpine (A)	inhibits the uptake of noradrenalin into postsynaptic vesicles	hypertonia treatment
Sanguinaria canadensis	sanguinarine (A)	DNA intercalator	antibacterial, antiviral
Strophantus gratus	ouabain (T)	inhibits Na^+, K^+-ATPase	heart insufficiency
Taxus brevifolia	paclitaxel (taxol) (A)	inhibits microtubule disassembly	tumour therapy

In traditional medicine those compounds are rarely found and because extract is usually applied, it bioactivity is almost not known. This particularly because extract contain various form of compounds, so it is almost impossible to find it bioactivity (Wink 2015, Tab. 2).

Table 2. Composition of extracts from medicinal plants used in traditional phytotherapy and their putative interactions [10–12].

Medicinal Plant/Drug	Phenolics *	Terpenoids *	Saponins *	Polysaccharides *	Covalent Interactions **
Actaea (syn. Cimicifuga) racemosa	++	++			
Aesculus hippocastanum	++		++		
Allium sativum	+				++
Althaea officinalis	+			++	
Andrographis paniculata	+	++			
Arctostaphylos uva-ursi	++				++
Arnica montana	++	++	+	+	+
Boswellia sacra		++	++	+	
Calendula officinalis	++	++	++	+	
Centella asiatica		+	++		
Cistus creticus	++	+			
Crataegus monogyna	++		+		
Curcuma longa	++	++		+	
Cynara cardunculus	++	++			+
Echinacea purpurea	++			++	
Eleutherococcus senticosus	++	++	++	+	

Factors affected the biosynthesis of medicinal compounds in plants

In plants, production of secondary metabolites is used for a defense system and adaptation to the environment. The production is affected by various factors such as; biotic, abiotic and plant growth factors. Biotic factors can be herbivores, bacteria or viruses that cause disease in plants. Abiotic factors can be light, dryness, temperature, height of place etc. While the development of plants is an internal factor associated with the growth phase.

Biotic factors

Several types of secondary metabolite compounds include diterpines and sesquiterpines produced by plants as a direct defense against herbivore and microbial pathogens. Because it can be toxic or has a very unpleasant taste, then the animal will not consume it so that the plant is free from herbivore attack. In the event of a bacterial or herbivorous attack, the plant will increase the production of this compound so that its accumulation will increase in the plant (Cheng et al., 2007).

Altitude.

Flavonoids are a very obvious example showing that the production of secondary metabolites is affected by the altitude of the site. Compounds belonging to this flavonoid group include: Carotene, vitamin C, anthocyanin. These compounds were found higher in the northern regions compared to the southern regions (Jaakola and Mohtola 2010). The increase in flavonoid levels is attributed by the responds of plants to cold environmental conditions.

Light, temperature and drought

Under serious conditions, such as high light intensity, high temperature and draught the plant cannot continue its growth unless it could produce compounds to alleviate the condition. These environmental factors can lead to production of excess energy in plants that resulted in the formation of reactive oxygen. These reactive compounds can adversely affect physiological processes in plants. Therefore under condition of these environment, the plant will increase the production of anti-oxidants i.e. flavonoids and phenolic acid (Ramakrishna et al. 2011). Abiotic factor that may affect secondary metabolite production in plant is presented in Fig. 3.

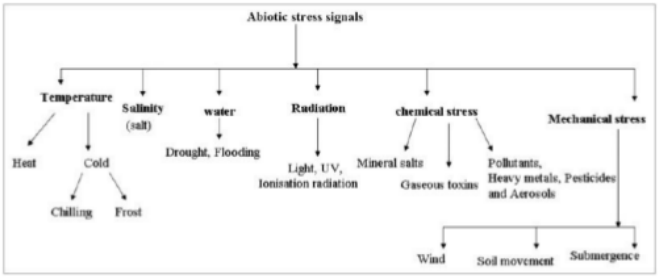

Fig. 3. Abiotic factors affected the production of secondary metabolites.

It is believed that plants have been used for medicine since human civilization. Plant part that is used for traditional medicine may be root, flower, leaf or fruit. In the "Usada of Bali", the number of recorded species used as medicinal materials and has been known scientifically is only about 60 species (Adiputra 2008). This amount is very small when it is compared with the existing plant species in Indonesia which accounted for about 170000 (one hundred and seventy thousand) types of plants (Tjitrosoepomo 2004).

Conclusion

Plants appear to have a philosophy similar to humans, i.e. taking drugs when there is a health problem. However, whereas humans look for drugs to alleviate diseases because they could not produce it, plants will make their own materials to alleviate health problems. Since secondary metabolite in plants is species specific, potentially Indonesia has various kinds of medicinal plants. So, in order to ease medicinal problem, Indonesia should promote more researcher to identify and subsequently conserve medicinal plants.

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