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Chapter 4
Scientific Study of *Wedang Secang* as Indonesian Traditional Drink

Dinia Rizqi DWIJAYANTI

1. A Short History of *Wedang Secang*

Secang (sappan wood; *Caesalpinia sappan* L.) is a native plant of China, India, Malaysia, Myanmar, and Thailand (the green area in Figure 1), while it is an exotic plant in Indonesia, Papua New Guinea, the Philippines, the Solomon Islands, Sri Lanka, Taiwan, and the US. Initially, the red coloring of sappan wood was widely used as a natural dye. Then sappan wood is believed to have been used as a traditional medicine to increase stamina, to warm the body during cold weather, and sometimes to prevent colds. With these benefits, it is not surprising that since the seventeenth century, sappan wood was included among the popular spice commodities exported from Southeast Asian nations (especially Thailand) aboard by *Shuinsen* (trading ships licensed by the shogunate) to Japan.

Figure 1. The distribution of sappan wood worldwide
Source: [Orwa et al., 2009]

In Indonesia, sappan wood has been used as the main ingredient of *wedang secang* (Figure 2). *Wedang secang* is a traditional red drink that comes from the natural dye of sappan wood and has a fresh aroma. *Wedang secang* consists not only of sappan wood but also other herbal plants such as small ginger (*Zingiber officinale* var.), cinnamon (*Cinnamomum verum* J. Persl), and lemongrass (*Cymbopogon flexuosus*). *Wedang secang* is a typical drink from Trowulan, Mojokerto, East-Java, Indonesia. *Wedang secang* also became the favorite drink of the kings in the Majapahit Kingdom.

Figure 2. *Wedang secang*
Source: Shutterstock.com/Ariyani Tedjo

2. *Wedang Secang*, Local Wisdom and the Problem

Indonesia is rich not only in biodiversity but also in local wisdom. One such traditional custom is the consumption of *wedang secang* in local communities. *Wedang secang* can be served hot or cold as needed. In the rainy season, *wedang secang* is delicious when served as a hot drink that makes the body feel fresh and warm. *Wedang secang* can

also be served cold during the day in the hot season. In the midst of the dominance of drinks with various types and brands, this traditional drink is still very much in demand, because apart from being a traditional heritage, *wedang secang* is believed to be highly beneficial for health. This drink is traditionally used to warm the body, relieve a sore throat, treat diarrhea, and enhance the immune system. Recently, this drink has also been one of the drinks chosen to enhance the immune system during the COVID-19 pandemic in Indonesia.

Uniquely, in the past, this drink was said to only have been enjoyed by relatives of the royal family. However today, *wedang secang* can be enjoyed by all levels of society and is even served to teenagers in modern cafes. It can be bought very easily and is widely traded in an instant tea-bag form. While such products are distributed from large factories, there is also a growing home industry. Nowadays, everyone is free to mix their own *wedang secang* using the ingredients that are widely available in the traditional market. The type and amount of the ingredients used to make *wedang secang* also vary from region to region, even among the sellers of the *wedang secang* concoctions. *Wedang secang* can be made by simply washing all the ingredients needed until clean, and then boiling them over a low flame so that the substances contained can be completely extracted. After the mixture becomes brown and smells good, sappan wood is added and the pot is covered until the water boils and turns reddish. As a sweetener, sugar or honey can be added according to taste.

Unfortunately, the widespread production of *wedang secang* by a large number of undocumented sources has become a big problem in this modern era. Many people are starting to doubt its efficacy, and are worried about its possible toxicity because, as explained above, there is no standard recipe, and its composition, and dosage have not been measured accurately.

3. Scientific View of Crude Drugs

Besides synthetic drugs, the use of crude drugs has long been popular in the community. Based on a scientific view, before use, crude drugs have to pass several tests. The first is the efficacy test which can later be used to determine indications or claims of their benefits. The second is the study or isolation of the active compounds, which is not only to know what active compounds are responsible for the healing mechanisms, but also to find out the contraindications of the compounds contained in them. The third is the toxicity test which is very important to determine the right dosage because the use of crude drugs with an incorrect dosage can be toxic and damage our organs such as the liver and kidneys which function to filtrate toxins in the body. These three tests are important to do as a preliminary study before making an efficacy claim for some crude drugs.

Figure 3. The classification symbols in the packaging of the crude drugs in Indonesia
Source: [BPOM, 2004]

In Indonesia, three different levels of crude drugs have been announced by the Food and Drug Monitoring Agency (*Badan Pengawasan Obat dan Makanan*; BPOM), namely (Figure 3): traditional medicines (including *jamu*), standardized herbal medicines (*obat herbal terstandar*;

OHT) and phyto-pharmaceuticals (*fitofarmaka*). We will discuss their criteria in the following parts.

(1) Traditional Medicines (*Jamu*)

Traditional medicine is derived from plants, animal materials, and mineral materials, or preparations of extracts or mixtures of these materials, which have been used for generations for treatment. *Jamu* is one example of a form of traditional medicine. *Jamu* must meet the following criteria:

1. It is safe in accordance with the requirements set.
2. Claims of efficacy are proven based on **empirical data**.
3. It meets the applicable quality requirements.
4. The type of claim of use must begin with the words: "**Traditionally used for …**"

   In *jamu* there should be no claims of efficacy using pharmacological/medical terms such as *jamu* for hypertension, *jamu* for diabetes, *jamu* for hyperlipidemia, *jamu* for tuberculosis etc.

(2) Standardized Herbal Medicines (*OHT*)

Standardized Herbal Medicines (*OHT*) are crude drugs that have been scientifically proven to be safe and effective by preclinical testing (on experimental animals) and the raw materials have been standardized. *OHT* must meet the following criteria:

1. It is safe in accordance with the requirements set.
2. Claims of efficacy are scientifically proven / preclinical (**in experimental animals**).
3. **Standardization of raw materials** used in finished products has been carried out.
4. It meets the applicable quality requirements.

(3) Phyto-pharmaceuticals (*fitofarmaka*)

Phyto-pharmaceuticals are natural medicines that have been scientifically proven to be safe and effective by means of pre-clinical tests (on experimental animals) and clinical trials (on humans), standardized raw materials and finished products. Phytopharmaceuticals meet the following criteria:

1. They are safe in accordance with the requirements set.
2. Claims of efficacy have been proven scientifically/pre-clinical (**in animals**) and clinically (**in humans**). Indeed, phyto-pharmaceuticals are crude drugs that are prescribed by doctors considering that they have been tested on both animals and humans.
3. **Standardization of raw materials** used in finished products has been carried out.
4. They meet the applicable quality requirements.
5. The type of claim for use is in accordance with a medium to high level of evidence.

Based on these classifications, currently research on the certification of *jamu* is aimed at bringing the level of *jamu* to OHT (as minimum target) or phyto-*pharmaceuticals* (in long term) so that it can be used safely. Unfortunately, this classification is not widely known by the public, especially in traditional communities, even though it is very important to understand before using the crude drug itself, and this includes the use of *wedang secang* which is under the traditional medicine classification (*jamu*) and has also been one of the local wisdoms in Indonesia since the seventeenth century. Scientific studies are not intended to abolish local wisdom, rather, the scientific study of *wedang secang* is actually important for the preservation of local wisdom. It is hoped that in the future people can continue to enjoy *wedang secang* safely.

4. Scientific Study of *Wedang Secang*

As I have explained, *wedang secang* is a kind of *jamu* which consists of several herbal compositions, namely: sappan wood (*Caesalpinia sappan* L.), small ginger (*Zingiber officinale* var.), cinnamon (*Cinnamomum verum* J. Persl), and lemongrass (*Cymbopogon flexuosus*). Therefore, each of these plants is thought to provide efficacy that may work synergistically to provide the efficacy of *wedang secang* as claimed empirically by the traditional community. Here we will discuss the efficacy of each plant and its popular active compounds to elucidate the possible mechanism of action of *wedang secang* according to the scientific view.

(1) Sappan Wood (*Secang*; *C. sappan* L.)

Pharmacological researches have revealed that sappan wood has many bioactivities, such as the inhibition of melanin production, anti-inflammation, antioxidant and antibacterial effects, and immune regulation. In addition, the ethyl acetate, methanol, and water extracts of sappan wood exhibit strong antioxidant activity by the method of DPPH and nitric oxide. It has also been reported that the extract of sappan wood inhibits cancer cells in vitro and in vivo. It has also been found that methanolic and 50% ethanolic extracts of sappan wood showed inhibitory effects on Propionibacterium acnes and lipase activity. Chemical constituents and pharmacological investigations of sappan wood showed that the main bioactive components of sappan wood were phenolic compounds such as brazilin and sappanchalcone (Figure 4).

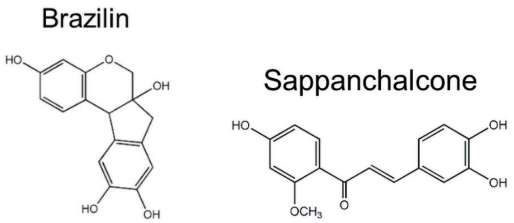

Figure 4. The chemical structure of Brazilin and Sappanchalcone

Brazilin has potential pharmacological properties such as anti-tumor, anti-cancer, anti-inflammatory, anti-diabetic, and immunostimulant effects. Brazilin, the principle component of sappan lignum has been found to exhibit hypoglycemic properties and to increase glucose metabolism in diabetics rats. It improved glucose metabolism in cultured rat hepatocytes, and also increased basal glucose transport in 3T 3L1 fibroblasts and adipocytes, but insulin stimulated glucose transport was not influenced. It was also found that brazilin possessed a stronger anti-inflammatory effect than hematoxylin and berberine hydrochloride. Brazilin also exhibited hypoglycemic effect in diabetic animals through amelioration of glucose metabolisms in insulin-responsive tissues. Another study also found that brazilin could reduce the BrCCl3-induced toxicities on hepatocytes and depress BrCCl3-induced microsomal calcium sequestration.

Not only brazilin, but also sappanchalcone contained in sappan wood is responsible for its anti-inflammatory properties. In the rheumatoid arthritis mice model, the levels of pro-inflammatory cytokines (TNF-α, IL-6, and 1L-1β) were significantly lower in the serum of sappanchalcone-treated mice as compared with the control group and suggest that sappanchalcone could be used as an anti-inflammatory and bone-protective agent. Another research showed the anti-cancer properties of sappanchalcone isolated from sappan wood.

Based on that data, sappanchalcone treatment decreased the proliferation and further promoted apoptosis in HCT116 cells compared with the findings in SW480 cells. Sappanchalcone triggered phosphorylation of p53, which is involved in the activation of caspases and increased expression of Bax in HCT116 cells.

(2) Small Ginger (*Jahe emprit*; *Z. officinale* var.)

In recent years, ginger has been found to possess biological activities, such as antioxidant, anti-inflammatory, antimicrobial, and anti-cancer activities. In addition, accumulating studies have demonstrated that ginger possesses the potential to prevent and manage several diseases, including neurodegenerative diseases, cardiovascular diseases, obesity, diabetes mellitus, chemotherapy-induced nausea and emesis, and respiratory disorders. As grounds for these efficacies, many bioactive compounds in ginger have been identified, such as phenolic and terpene compounds. The phenolic compounds are mainly Gingerenone-A, gingerols, shogaols, quercetin, zingerone, 6-dehydrogingerdione and paradols which have the responsibility for the various bioactivities of ginger.

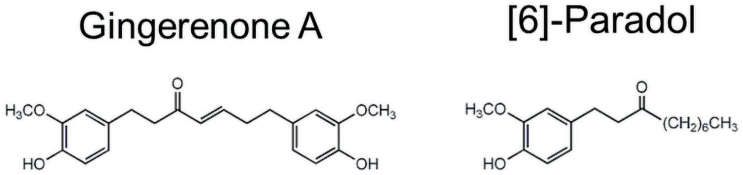

Figure 5. The chemical structure of Gingerenone-A and [6]-Paradol

Photographic and quantitative assessments of intracellular lipid content by Oil red O staining revealed that Gingerenone-A (Figure 5) had the most potent anti-adipogenic effect of the tested ginger compounds at the same concentration without affecting cell viability. The

treatment was with non-toxic concentrations of Gingerenone-A reduced lipid accumulation in a dose-dependent fashion. Consistent with these results, protein expression levels of adipogenic transcription factors such as PPARγ and C/EBPα, and lipogenic protein FAS in cells treated with Gingerenone A were lower than those in MDI only differentiated cells. Moreover, Gingerenone-A also possesses the anti-inflammatory properties by inhibiting the expression of CCL-2 and TNF in co-cultures of differentiated 3T3-L1 adipocytes and Raw264.7 macrophages in the contact system. Those studies showed that Gingerenone-A suppressed the development of obesity and adipose tissue inflammation by reducing adipocyte hypertrophy and inhibiting macrophage infiltration.

Furthermore, another study showed the anti-inflammatory, anti-diabetic, and anti-cancer effects of [6]-paradol (Figure 5) isolated from ginger. When [6]-paradol was added to cultures of BV2 microglia after they were exposed to LPS for 24 h, [6]-paradol reduced NO production and increased cell viability. The reduced NO production by [6]-paradol was mediated by the attenuation of LPS-induced iNOS upregulation. [6]-paradol blocked the secretion of cytokines TNF-α and IL-6 in a concentration-dependent manner in stimulated microglia. In addition, [6]-paradol also significantly reduced blood glucose, cholesterol and body weight in high-fat diet-fed mice. In another study, they proved that [6]-paradol suppressed the proliferation and metastases of pancreatic cancer by decreasing EGFR and inactivating PI3K/AKT signaling.

(3) Cinnamon (*C. verum* J. Persl)

Cinnamon has been reported to have many different health properties, such as its antioxidant content and its effect on diabetes and neurological, microbial, and cardiovascular diseases due to the properties of bioactive components. Cinnamon was reported to upregulate anti-autoimmune Tregs and Th2, suppress autoimmune Th17

and Th1, inhibit inflammatory infiltration, and reduce the expression of pro-inflammatory molecules. Furthermore, cinnamon extract exhibits hypolipidemic activity in hypercholesterolemic albino rats. Daily administration of the extract reduced serum levels of total cholesterol, triglycerides, and low-density lipoprotein cholesterol. Numerous studies have shown the presence of biologically active compounds in cinnamon, mainly cinnamaldehyde and eugenol (Figure 6). However, the efficiency of the compounds in the extracted cinnamon oil depends on the separation methods, solvents, and all the parameters related to the extraction/separation process, such as time, temperature, and pressure.

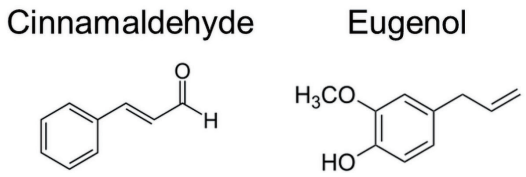

Figure 6. The chemical structure of Cinnamaldehyde and Eugenol

Looking further at the benefits of cinnamon, cinnamaldehyde and eugenol have been reported to play a role in protecting the gut from injury from conditions of inflammation, infections, and oxidative stress. In addition, cinnamaldehyde has been reported as a factor that decreases the production and expression of nitric oxide (NO), IL-1β, IL-6, and TNF-α in LPS-activated BV2 microglia and is therefore thus indicating that it has an anti-neuroinflammatory effect. Moreover, it has been reported to aid in neuroprotection due to its potential to inhibit tau protein aggregation, the hallmark of Alzheimer's disease. Cinnamaldehyde also has the potential to control harmful fungal and mycotoxin contamination of agricultural commodities. Cinnamaldehyde is a predominant compound in the bark oil extracted from Cinnamon. It

seems to reduce plasma glucose levels more effectively than metformin, which is commonly used in traditional medicine. The bioactive compounds of cinnamon oil enhance the expression of proteins that play key roles in glucose transport, insulin signaling, and the regulation of dyslipidemia. More to the point, cinnamaldehyde and eugenol have also shown positive results in the treatment of leukemia and lymphoma. These compounds have also been used as nutraceuticals in fighting colon and liver cancer cells.

(4) Lemongrass (*C. flexuosus*)

The plant is used as a fragrance and flavoring agent and in folk medicine as an antispasmodic, hypotensive, anticonvulsant, analgesic, antiemetic, antitussive, anti-rheumatic, antiseptic and as a treatment for nervous and gastrointestinal disorders and fevers. The plant is also used as an antibacterial, antidiarrheal, antioxidant and anti-inflammatory. Methanol or water extracts, infusion and decoction of lemongrass were shown to have free radical scavenging effects by measuring the bleaching of the DPPH radical, scavenging of the superoxide anion and inhibition of the enzyme xanthine oxidase and lipid peroxidation in human erythrocytes. The hot water extract of the dried leaves administered intragastrically to rats was active when compared with carrageenin-induced pedal edema, as an inflammatory model. A fresh leaf aqueous extract of lemongrass administered in normal rats lowered the fasting plasma glucose, total cholesterol, and triglycerides.

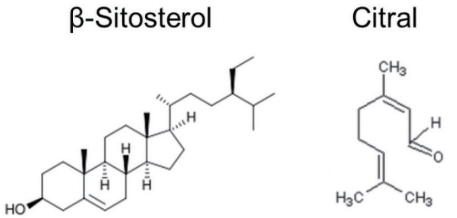

Figure 7. The chemical structure of β-sitosterol and citral

Lemongrass contains various constituents such as flavonoids and phenolic compounds, terpenoids and essential oils, which may be responsible for the different biological activities, but the mode of action for the different bioactivities has not been studied in detail. β-Sitosterol (Figure 7) is one of the compounds contained in lemongrass. Several studies have shown that β-sitosterol has a wide range of anti-inflammatory effects in peripheral tissues. More specifically, it has a certain role in inflammation models such as chronic obesity-related inflammation, ovalbumin-induced lung inflammation, TNBS-induced colitis, and rheumatoid inflammation in mice.

Furthermore, Citral (Figure 7) is an essential oil from lemongrass that possesses anti-inflammatory properties, since it enhances TNF-α as a target for the prevention of inflammatory events induced by chemicals. Citral oil inhibits an increase in TNF-α levels in RAW 264.7 cells that are stimulated with lipopolysaccharide (LPS). In the same way, it was observed in the literature that citral oil reduced the TNF-α relative expression compared to treatment with LPS. Another study showed that treatment with citral oil in mice with lung injury induced by LPS inhibited TNF-α, IL-1β, and IL-6 levels both in vivo and in vitro, demonstrating that the citral oil can inhibit a possible inflammatory response.

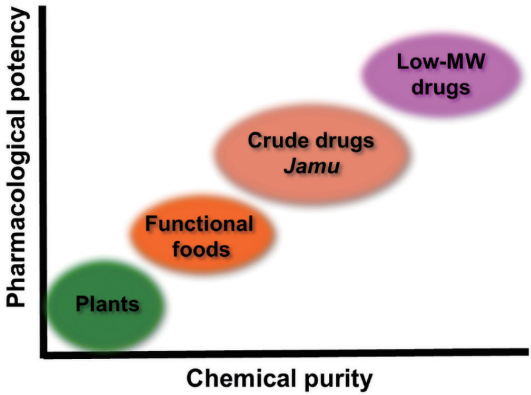

Figure 8. The relationship between chemical purity of the crude drugs and their pharmacological potency. Source: Author

Based on the scientific study explained before, the bioactive compounds isolated from the herbs contained in wedang secang have been proven to have several efficacies especially for anti-oxidant, anti-inflammation, anti-diabetes, anti-obesity and anti-cancer treatments. However, it should be emphasized that these studies were conducted mainly by using pure compounds. Figure 8 shows the relationship between the chemical purity of the crude drugs and their pharmacological potency. It means that, even though there is a high possibility that wedang secang has several efficacies as an anti-oxidant, anti-inflammation, anti-diabetes, anti-obesity and anti-cancer treatment, an experiment on whole wedang secang using experimental animals is still needed to show its potency and toxicity when it is consumed in a whole form as a decoction.

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Chapter 4: Scientific Study of *Wedang Secang* as Indonesian Traditional Drink

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