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The Potential Utilization of Young Teak Leaves (*Tectona grandis Linn.f.*) as Basic Ingredients on Producing Anti-cancer Herbal Tea

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Abstract

Gunungkidul Regency is the main teak tree (*Tectona grandis* Linn.f.) producing area in Special Region of Yogyakarta, Indonesia. Their trunks are commonly used for furniture and buildings, while leaves are still less of use. Teak leaves contain antioxidant compounds in form of flavonoids that play important role in protecting the body against damaging free radicals in cancer sufferers. The number of cancer sufferers in Indonesia is still high, but cancer problem not yet be handled optimally because cannot be fully reached by the community. The aims of this review are studying the production process of herbal tea from young teak leaf and mechanism of flavonoids as an anticancer. This review was conducted by literature study. The writing source is then analyzed and synthesized to draw conclusions. The results obtained production process of young teak leaf herbal tea through several stages, picking, washing, withering, cutting, fermentation, drying, and packaging. The anticancer activity in young teak leaf herbal tea is influenced by the content of flavonoids as antioxidants that can neutralize free radicals and prevent cancer. The conclusion of this review are young teak leaves (*T. grandis*) can be used as basic ingredient in herbal teas that are good for health, and flavonoids in young teak leaves are antioxidants that potential as anticancer substances.

Keywords: *Tectona grandis*; anticancer; flavonoids; herbal tea; young teak leaves

Abstrak

Kabupaten Gunungkidul merupakan daerah utama penghasil pohon jati (*Tectona grandis* Linn.f.) di Daerah Istimewa Yogyakarta. Pohon jati biasa dimanfaatkan batangnya untuk furnitur dan bangunan, sementara daunnya masih sedikit dimanfaatkan. Daun jati mengandung senyawa antioksidan berupa flavonoid yang berperan melindungi tubuh terhadap serangan radikal bebas pada penderita kanker. Angka penderita kanker di Indoneisa tergolong tinggi, namun permasalahan kanker belum bisa tertangani dengan maksimal karena belum bisa dijangkau secara menyeluruh oleh masyarakat. Review ini bertujuan untuk mempelajari proses produksi teh herbal berbahan dasar daun jati muda dan mekanisme flavonoid sebagai antikanker. Metode penulisan yang digunakan adalah studi pustaka. Sumber penulisan tersebut dianalisis dan disintesis untuk mengambil kesimpulan. Hasil yang diperoleh adalah proses pengolahan teh herbal daun jati muda melalui beberapa tahapan, yaitu pemetikan, pencucian, pelayuan, pemotongan, fermentasi, pengeringan, dan pengemasan.Aktivitas antikanker pada teh herbal daun jati muda dipengaruhi kandungan flavonoid sebagai antioksidan yang mampu menetralisir radikal bebas dan mencegah kanker. Kesimpulan dari review ini adalah daun jati muda (*T. grandis*) dapat dimanfaatkan sebagai bahan dasar pembuatan teh herbal yang baik bagi kesehatan, dan flavonoid pada daun jati muda merupakan antioksidan yang berperan sebagai zat antikanker.

Kata-kata kunci: *Tectona grandis*; antikancer; daun jati muda; flavonoid; teh herbal

Introduction

Gunungkidul Regency is the main teak tree producing area (*Tectona grandis* Linn.f.) in Special Region of Yogyakarta. In 2007, 70% of teak wood production in Yogyakarta was supplied from Gunungkidul (Marsoem, 2013). Teak trunks are used for furniture and building materials. Until now, the utilization of teak trees is still focused on trunk and has not yet penetrated other parts of the tree. To obtain good quality of wood, farmers cutting the branch of teak and grows upright without any branches. One part of teak tree that has not been used optimally is the leaves. Teak leaves contain antioxidant that play a role in protecting the body against damaging free radicals. The antioxidant compounds contained in teak leaves are flavonoids (Lismawenning *et al.*, 2013). Flavonoids can act as a source of natural antioxidants that are able to neutralize free radicals and prevent cancer (Toripah *et al.*, 2014).

In Indonesia, the number of cancer sufferers is still high. The prevalence of cancer of all ages population in 2013 was 1.4% or estimated to be around 347,792 people. Meanwhile, Yogyakarta has the highest prevalence of cancer with 4.1%. The handling of cancer in Indonesia has been carried out by government through the Ministry of Health, BKKBN, as well as non-governmental organizations both cancer care organizations and professional organizations, but these efforts are still not comprehensive. Therefore, cancer problems in Indonesia still cannot be handled optimally (Kementrian Kesehatan RI, 2015). Cancer treatment has not been fully reached by the community. Early cancer prevention is important to decrease number of cancer sufferers each year. One of the efforts to prevent cancer is by updating the diet, by eating functional foods that contain antioxidants.

Teak leaves contain antioxidant in form of flavonoids that have potential to prevent cancer. The use of teak as an anticancer is carried out by producing functional food in the form of herbal teas. The level of Indonesian people's tea consumption is high. The highest tea consumption was achieved in 2014 with 0.61 kg/capita/year (Kementrian Pertanian RI, 2015). This review aims to determine the made processing of herbal teas from young teak leaves, and the mechanism of flavonoids in young teak leaf herbal teas as anticancer agents.

Method

Data Sources

The data used in this review comes from various literatures related to issues discussed. Some of the main types of references used are textbooks, scholarly articles, and

other relevant sources. The types of data obtained were varied, both qualitative and quantitative.

Data Collection

Data and information that supports writing are collected by conducting literature searches, relevant sources and data via the internet. The writing is attempted to be related one another and in accordance with the topics discussed. The data collection technique used is literature study which is taken into consideration and additional insight for author regarding the scope of activities and concepts covered in writing. To discuss the analysis and synthesis of data, reference data is needed to be used as a reference, where the data can be developed to be able find unity of the material in order to obtain a solution and conclusion.

Data analysis

Some of data and information obtained at the data collection stage are then processed with descriptive analysis based on secondary data. The collected data are selected and sorted according to the topic of study. Then a review is made based on data that has been prepared logically and systematically. Data analysis techniques are descriptive argumentative. Conclusions are obtained after referring back to the purpose of writing and discussion. The conclusions drawn present the subject of review.

Result and Discussion

Young Teak Leaves

The leaves of *T. grandis* have chloroform and butanol fractions which contain anthraquinone called tectone. Teak leaf extract also contains terpenoids, flavonoids, flavone glycosides, and phenol glycosides (Sukhla *et al.*, 2010). Apart from these secondary metabolites, teak leaves have also been shown to contain oils which have antioxidant activity because they contain many phenolic compounds. *T. grandis* oil is pale yellow in color which contains up to 20.5% terpenoids such as monoterpenes and sesquiterpenes. *T. grandis* leaf oil has been shown to have antimicrobial activity (Aboaba *et al.*, 2013). Nayeem & Karvekar (2010) reported that the phenolic acid content of young leaf extracts was higher than adult leaf extracts. The flavonoid content was determined spectrophotometrically by the aluminum chloride method, which also showed that young leaves had higher levels of flavonoids than adult leaves. These flavonoids are responsible for the antioxidant activity of plant extract.

T. grandis leaves can be used as hemostatic, anti-inflammatory and treatment of skin diseases (Neha & Bhargava, 2013). The ethanolic extract of *T. grandis* leaves has antibacterial activity against *Salmonella typhi*, *Klebsiella pneumoniae*, *Escherichia coli*,

Streptococcus pyogenes and *Enterococcus* spp. (Sukhla *et al.*, 2010). Phytochemical examination of the ethanol extract of *T. grandis* leaves showed the presence of flavonoid compounds, saponins, gallat tannins, katekat tannins, quinones, and steroids/triterpenoids (Hartati *et al.*, 2005). Phytochemical compounds that have been isolated from *T. grandis* leaves are acetovanillone, e-isofuraldehyde, evofolin, syringaresinol, medioresinol, balaphonin, lariciresinol, zhebeiresinol, 1- hydroxypinoresinol, and two new ingredients, namely tectonoelin A and tectonoelin B (Lacret *et al.*, 2012). *T. grandis* leaves can be used as natural dyes because contain anthocyanin pigments (Ati *et al.*, 2006). Anthocyanins are pigments that can give blue, purple, violet, magenta, red, and orange colors to plant parts such as fruits, vegetables, flowers, leaves, roots, tubers, legumes, and cereals. This pigment is non-toxic and safe for consumption.

The methanolic extract of *T. grandis* leaves also contains flavonoid compounds which have pharmacological activities as antioxidants and anticancer (Ghareeb *et al.*, 2014). Flavonoids have polar properties and extracted using solvents such as ethanol and water which have hydroxyl groups (Astina, 2010; Safithri & Fahma, 2008). *T. grandis* has pharmacological effects as anti-ulcer, anti-anemia, antibacterial and heals wounds (Goswami *et al.*, 2009). Other studies have also reported that teak has benefits in treating colds, headaches, laxatives, sedatives, bronchitis, diuretics, anti-diabetes, scabies, analgesics, and anti-inflammatory (Diallo *et al.*, 2008; Ghaisas *et al.*, 2009; Nayeem & Karvekar, 2010; Singh *et al.*, 1996). Test of cytotoxic activity with the Brine Shrimp Lethality Bioassay Method from teak root petrol extract showed high cytotoxicity activity with LC_{50} 5 ppm (Sandermann & Simatupang, 1966).

Herbal Tea

Herbal tea is a tea beverage product, in the form of single or mixture herbal. Apart from being consumed as a regular drink, herbal tea is also consumed as drink that is nutritious for improving health. The properties of each herbal tea vary, depending on the raw material. The mixture of raw materials used are herbs or medicinal plants that naturally have properties to help treat certain types of diseases. Herbal teas are usually served in dry form like a tea made from the tea plant. Medicinal plants in dry form formulated as herbal tea can be used for daily consumption by households and industries. The process of making dried herbs includes washing, slicing, drying, size reduction, and packaging. The conditions of the process must be considered in order to avoid the loss of important nutritious substances from fresh ingredients. Various herbs or medicinal plants can actually be processed into dry herbs. Basically, the processing of all types of medicinal plants is almost the same. The difference

lies in the drying time and temperature because it is adjusted to the characteristics of fresh ingredients. The dried herbs are then mixed with certain composition according to type of herbal tea (Hambali *et al.*, 2005).

The production process of young teak leaf herbal tea is done by picking fresh and healthy leaves that are not eaten by caterpillars, then washing, so any dirt or fine hairs disappear. After washing, withering in dry conditions for 5 - 6 hours, cutting, fermentation, then drying until the water content is not there, then stored in a dry place and packaging (Sudarmanto, 2015). Enzymatic fermentation or oxidation, is the process of oxidizing polyphenol compounds with help of polyphenol oxidase enzymes that produce theaflavins and thearubigins. This substance will determine the properties of strength, color, quality, and briskness in the steeping water (Setyamidjaja, 2000). The tea fermentation process results in oxidation process by changing catechins into simpler compounds, flavonoid polyphenols (Siringoringo, 2012). In accordance with Arpah (1993), teaflavin compound gives a yellowish red color, is bright and affects the clarity of the brew. Drying aims to reduce the water content in the leaves up to 3 - 4% (Ajisaka, 2012). The main factor influencing the leaf drying process is temperature. Too low temperature causes the drying process run slowly so the leaves are prone to mold. Meanwhile, if the temperature is too high it will cause outside of the leaves to dry faster but the inside is still wet. To avoid this, it is sufficient to warm up at 60 °C (Ibrahim, 2008).

According to Rahmawati (2015), variations in fermentation time and drying methods have an effect on antioxidant activity. The results of research on water henna leaf tea products showed the highest antioxidant content in long treatment of fermentation and roast drying method for 60 minutes. The longer fermentation give lower antioxidant activity. According to Lai *et al.* (2001), fermentation time affects antioxidant activity because it results in the loss of several antioxidant components due to enzymatic oxidation reactions. Roasted drying method produced the highest antioxidant activity compared to other methods. This is because drying in the sun and oven requires a long time for the leaves to dry completely, with this time lag it is possible to fermentation again so that the active compounds contained therein are oxidized. Meanwhile, in roasting method the antioxidant activity is high because drying process is not too long so the fermentation process is completely stopped (Rahmawati, 2015).

Meanwhile, according to Anggorowati *et al.* (2016) the highest antioxidant content of avocado leaf tea drinks is at temperature of 40 °C with drying time of 30 minutes. This test is carried out to determine antioxidant activity found in avocado leaves after experiencing

drying process. The results of antioxidant activity analysis showed that the lower temperature and drying time give greater antioxidant activity. This condition is caused by decrease in active substance contained in the tea leaves during drying process (Kahkonen *et al.*, 2001). The lower antioxidant activity create less water content in the sample. Tea produced at 50 °C has good texture, color and aroma. Drying also affects water content in the leaves, because water is one of the best media for microbial growth, so it also affects the shelf life of avocado leaf tea from microbial growth. The temperature is 50 °C and the optimum time is 50 minutes for making avocado leaf tea. Because at this temperature it has a fairly high reduction in water content, there is no *E. coli* contained in sample (Anggorowati *et al.*, 2016).

The drying process on tea leaves can cause changes in pectic acid. Where the pectic acid will dry out and form a kind of varnish so that the surface of tea becomes dry and rough. According to Nasution & Tjiptadi (1975) the compounds that form aroma of tea mainly consist of volatile and reduced volatile oils so can produce a fragrant aroma in tea. Good tea texture is coarse (Lee *et al.*, 2001). Apart from affecting the antioxidant activity, high time and temperature can also affect the color and aroma of avocado leaf tea when it's been brewed. Tea contains components other than polyphenols such as organic materials, carbohydrates, pigments, enzymes, and vitamins. This vitamin component can act as an antioxidant and affects the measurement of antioxidant capacity (Nasution & Tjiptadi, 1975). According with Rohdiana (2015), tea is a drink containing tannins, an infusion made by brewing leaves, leaf shoots, or dried leaf stalks from the *Camellia sinensis* plant with hot water.

Anticancer Mechanism of Flavonoid

Ethanol extract of *T. grandis* leaf contains antioxidant compounds with the phytochemical content of flavonoids, saponins, galat tannins, katekat tannins, quinones, and steroids/niterpenoid (Fathinatullabibah *et al.*, 2014). Flavonoids are plant pigments that can play a role in protecting body against damaging free radicals (Manthey & Guthrie, 2002). Flavonoid compounds are reported to have a role as antioxidants (Adom & Liu, 2002). According to Delgado *et al.* (2003), flavonoids are phenolic compounds that have potential for bioactivity as medicine. Antioxidant compounds are able to counteract negative effects of oxidants in the body. The way antioxidant compounds work is by donating one electron to compounds that are oxidant and activity can be inhibited (Winarsi, 2007). Flavonoids are polar compounds that dissolve in polar solvents such as ethanol (EtOH), methanol (MeOH), butanol (BuOH), acetone, dimethylsulfoxide (DMSO), dimethyl formamide (DMF), and water (Laleh *et al.*, 2006).

There are many flavonoids in vegetables and fruits. Flavonoids have shown their role as antioxidant, antimutagenic, antineoplastic and vasodilatory activity (Yanislieva *et al.*, 2001). According to Lamson & Brignall (2000), flavonoids (3,3', 4', 5,7-pentahydroxyflavone) including molecules that are found in nature. Flavonoid is an aglycone which bound to the glycon will become a glycoside. This compound can act as an anticancer in cell cycle regulation, interact with type II estrogen receptors (ER) and inhibit the tyrosine kinase enzyme. Flavonoids also have antioxidant activity by highly reactive phenolic components. Flavonoids will bind free radical species and reduce the reactivity of these free radicals (Pietta, 2000).

Antioxidants work through several mechanisms. First, antioxidants suppress the formation of reactive oxygen species by inhibiting enzymes and binding to trace metals involved in free radical production. Second, antioxidants work by extinguishing reactive oxygen species. And third, by protecting the body's antioxidants. Flavonoids meet the first two criteria. Thus, its antioxidant activity is doubled. The action mechanism of flavonoids is to inhibit enzymes involved in the production of superoxide anions, such as xanthine oxidase and protein kinase. Flavonoids also inhibit the action of cyclooxygenase, lipoxygenase, microsomal monoxygenase, glutathione-S-transferase, mitochondrial succinoxidase, and NADH oxidase (Narayana *et al.*, 2001). A number of flavonoid compounds are efficient in chelating trace metals. Trace metals such as free iron ions and copper increase the formation of reactive oxygen species as shown in the formation of OH radicals.

$H_2O_2 + Fe^{2+} (Cu^{2+}) \rightarrow \bullet OH + OH^- + Fe^{3+}(Cu^{2+})$

Or via the copper-mediated LDL oxidation reaction:

$LH \rightarrow L\bullet \rightarrow LOO\bullet$ (LH represents LDL)

Its ability to chelate trace metals can have negative impact because basically metal ions have various physiological functions. One of them is an enzyme cofactor, including enzymes for defense antioxidants such as iron ions in catalase, copper in ceruloplasmin, and Cu, zinc superoxide dismutase. The binding side of the trace element to flavonoids is catechol group in B ring, 3-OH-4-Oxo- groups in heterocyclic ring, and 4-oxo- and 5-OH in heterocyclic ring and A ring (He & Liu, 2007). Flavonoids (Fl-OH) have a low reduction potential value (0.23 - 0.75 V) so they can easily reduce superoxide, peroxyl, alkoxyl, and hydroxyl radicals (2.13 - 1.0 V). The mechanism is executed through the donation of H atoms (Figure 1).

Fl-OH + R• → Fl-O• + RH

The aroxyl radical (Fl-O•) can react with the second radical to produce a stable quinone structure. However, aroxyl radicals can also react with oxygen to produce quinones and superoxide anions. The final reaction will occur when a large number of transition metal ions are available. Through this mechanism, flavonoids act as prooxidants. The capacity of flavonoids as antioxidants does not only depend on the reduction potential of Fl-O•/Fl-OH, but also the possibility of side reactions to aroxyl radicals. In addition to extinguishing radicals, flavonoids can stabilize free radicals involved in the oxidation process by complex binding with these compounds sluiss (Van der Sluis *et al.*, 2002).

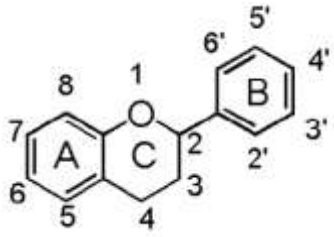

Figure 1. The basic structure of flavonoids (Pietta, 2000)

The antioxidant and prooxidant properties depend on OH group in the basic skeleton. The more OH create more antioxidant and prooxidant properties. Flavonoids that contain a lot of OH show anti-peroxyl radical activity several times stronger than trolox (α –tocopherol analogue). Substitution at -OH positions 3' and 4' is important for scavenging activity of peroxyl radicals from flavonoids. Conversely, methylation of OH will inactivate antioxidant activity and prooxidant flavonoids. Most phenolics display prooxidant activity at low concentrations. Compounds with similar structures show trends in antioxidant activity. Antioxidant activity increases with presence hydroxyl groups and decreases in the presence of glycosylation (Cao *et al.*, 1997).

The activity of radical extinguishing depends on structure and substituents of heterocyclic ring and ring B. The ability of radical extinguishing is determined by the presence of catechol groups on ring B (Figure 1). Catechol groups can be radical targets for bonding because better electron donors. A2,3- conjugated double bond with 4-oxo group increases stability of the radical produced by delocalizing electrons. Anti-radical activity is determined by the presence of orthohydroxylation B ring in flavonoid molecule, number of free OH groups, C2-C3 double bonds on the C ring, and presence of 3-OH group (OH at position 3). In contrast, the addition of OH and methoxyl groups at positions 3,5, and 7 in

rings A and C does not have much effect (Fukumoto & Mazza, 2000). The addition of 3-OH to heterocyclic ring increases stability of the aroxyl radical, or antioxidant capacity of parent flavonoids.

Flavonols and flavones which contain catechol groups in ring B are active antioxidants. Flavonols contain 3-OH groups and more potent than flavones. Glycosylation largely determines the antioxidant properties of flavonoids. The addition of OH group (pyrogallol group) on B ring will increase antioxidant activity as shown by myricetin. Only one OH in ring B will eliminate antioxidant activity of flavonoids. Flavonols and flavonones are weak antioxidants, because there is no electron conjugation in their structure as occurs when there are 2-3 double bonds and 4-oxo groups. Flavone monomers have antioxidant activity similar to flavonols. If there is addition of pyrogallol groups in ring B (as in epigalocatekin) or galoylation in 3-OH (as in epigalocatekin errors), its antioxidant properties will increase (Burda & Oleszek, 2001).

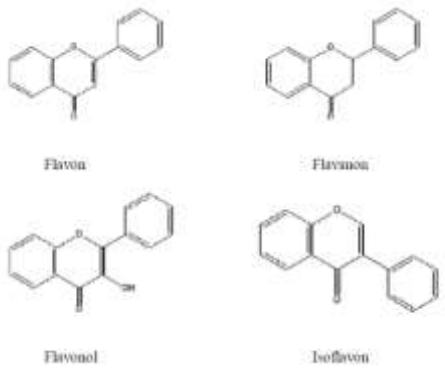

Figure 2. The main classifications of flavonoids (Pietta, 2000)

Anthocyanidins and their glycosides (anthocyanins) have the same antioxidant activity as quercetin and error catechins, as long as there are catechol groups in ring B. If 3-OH is removed from ring B (in kaempferol), antioxidant activity will decrease. This indicates that the catechol group on ring B is the main determinant from radical suppression capacity of flavonoid compounds. The antioxidant activity increases with amount of OH in B ring anthocyanidins. The substitution at position 3 on ring C plays an important role in determining the antioxidant activity of this class of compounds. Anthocyanidins that have OH at position 3 indicate potential antioxidant activity. For cyanidine, the higher number of glycosyl units will create lower antioxidant activity. Likewise, the substitution of position 3 with galoyl group on catechins (Seeram & Muraleedharan, 2002).

Table 1. Constituents in flavonoid classification (Hartati *et al.*, 2005)

Nomor Atom C	5	7	3'	4'	5'
Flavon					
Luteolin	OH	OH	OH	OH	
Apigenin	OH	OH		OH	
Chrysin	OH	OH			
Flavanon					
Hesperetin	OH	OH	OH	OCH_3	
Naringenin	OH	OH		OH	
Flavonol					
Quersetin	OH	OH	OH	OH	
Kaemferol	OH	OH		OH	
Galangin	OH	OH			
Fisetin		OH	OH	OH	
Myricetin	OH	OH	OH	OH	OH
Flavanonol					
Taksifolin	OH	OH	OH	OH	
Isoflavon					
Genistein	OH	OH		OH	
Genistin	OH	Oglk		OH	
Daidzein		OH		OH	
Daidzin		Oglk		OH	
Biochanin A	OH	OH		OCH_3	
Formononetin		OH		OCH_3	

OH : Hidroksi, Oglk: O-Glikosilat, OCH_3 : Metoksi

The antioxidant properties of flavonoid compounds are able to inhibit carcinogenesis process. Carcinogens are able to oxidize DNA, causing mutations. Flavonoids as antioxidants can prevent oxidation in the initiation and propagation phases. In the initiation stage, flavonoids are able to stabilize free radicals formed by carcinogens such as oxygen, peroxide and superoxide radicals (Gordon, 1990). Flavonoids stabilize these compounds through hydrogenation reactions and complex formation (Yang *et al.*, 2011). Through this reaction, free radicals are converted into more stable form and unable to oxidize DNA. In addition, it was found that the antioxidant radical derivatives were relatively more stable than free radicals formed by the carcinogenic compounds earlier (Gordon, 1990). Even so, flavonoid radicals have the energy to react with other antioxidant radicals. The antioxidant radicals from flavonoids can react with each other to form non-radical products (Hamilton, 1983). In the propagation stage flavonoids prevent autoxidation, which is to prevent the formation of peroxide radicals through fast binding of radical compounds and do not bind to oxygen. With the presence of flavonoids, the oxygenation reaction that runs rapidly and the formation of peroxide radicals can be prevented. Flavonoids also bind to peroxide radicals that have been formed and stabilize them so that the rapid and chain autoxidation reaction can be inhibited (Ikawati *et al.*, 2015).

Flavonoids also play a role in suppressing the expression of mutant protein p53. In wild type conditions, this protein is important in cell cycle control by spurring cells to arrest or apoptosis. If mutation occurs, this protein becomes a marker of abnormality with cycle spurring the cell into G2-M phase (cell multiplication) and if the cell continues in this phase there will be proliferation (uncontrolled division). Flavonoids in a serum concentration of 248 μM can suppress expression of the mutant protein p53 formed by breast cancer cells until

they are not detected in these cells (Lamson & Brignall, 2000). Flavonoids are the first compounds capable of inhibiting tyrosine kinase in stage one preclinical tests. With inhibition of tyrosine kinase expression, the ability of cells to oncogenesis through the ability to regulate growth outside of normal can be inhibited. In addition, drugs that work with tyrosine kinase targets when viewed in conventional chemotherapy have possibility of being antitumor agents without cytotoxic side effects on normal cells (Klohs *et al.*, 1997).

Flavonoids are able to inhibit the production of heat shock protein (HSP) in many malignant cancer cells, including breast cancer (Hansen *et al.*, 1997), leukemia (Elia *et al.*, 1996) and colon cancer (Koishi *et al.*, 1992). The heat shock protein itself is formed through complex bonds with the p53 mutant. HSP inhibition induces tumor cells that were initially able to pass through normal mechanism of the resting cell cycle (Go) to become unable pass through. In addition, HSP which causes cancer cells able to develop and live in different conditions (low circulation, fever) and associate with other diseases to survive can be stopped (Ciocca *et al.*, 1993). Heat shock protein in breast cancer causes chemotherapy drugs to become resistant (Oesterreich *et al.*, 1993). With the presence of flavonoids, resistance of cancer cells to chemotherapy agents can be inhibited so that flavonoids are suitable for use as a chemotherapy companion in cancer therapy.

Conclusion

The production process of young teak leaf herbal tea (*Tectona grandis*) is done by picking, washing, withering, cutting, fermentation, drying, and packaging. Young teak leaves can be used as basic ingredient in herbal teas that are good for health. Flavonoids in young teak leaves are antioxidants that potential as anticancer substances. The mechanism of flavonoids as anticancer is stabilize free radicals formed by carcinogens at the initiation stage through hydrogenation reactions and complex formation, also prevent autoxidation so that mutations do not occur, suppress the expression of mutant protein p53 which triggers cell multiplication, inhibits tyrosine kinase so that the ability of cells to oncogenesis is through growth regulation outside of normal can be inhibited, and inhibits the production of HSP in malignant cancer cells so that cancer cells are unable to develop.

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