Industrial Development of Indonesian Natural Medicine

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1. Introduction

Indonesian natural medicine, traditionally known as jamu is all medicine of Indonesian natural resources including plants, animals, and minerals. In reality, jamu is a term used originally for Javanese traditional medicine, but now becomes popular as general term of Indonesian traditional medicine. Indonesia consists of different islands in which their specific traditional medicine can be found. The main part of Indonesian traditional medicines is Javanese traditional medicine (*Jamu Jawa*). Other specific and known Indonesian traditional medicine can be found at Bali, Madura, Sumatra, Borneo, Celebes, and Papua. Further it must be noted that the term of Indonesian traditional medicine is also used for the methods traditionally used by Indonesian people to treat their health problems. According to the regulatory of Indonesian Department of Health, Indonesian traditional medicine is divided into 4 categories: those based on skill, supernatural, religion, and herbs. The first category includes massage, acupressure, fracture treatment, and other specific skills for treatment. The supernatural consists of different magic and mystic powers, while the healing process based on the third category depends on the religion. Moslems use *ruqyah,* Hindus from Bali use *mantra.* Therefore the term of jamu is more appropriate to Indonesian traditional medicine in the fourth category and it is named Indonesian herbal medicine. It should be noted that this term is not completely correct due to the reality that herbal medicine does not cover medicines of animal and mineral origin. The correct term is Indonesian natural medicine and it is now officially adopted by Indonesian National Agency for Drug and Food Control (NA-DFC).[1] Even though the term of Indonesian herbal medicine is still widely used in Indonesia because the most part of Indonesian traditional medicine consist of plant materials. The use of animal materials is very limited because of the rule of Islamic religion which screens in consuming certain animals such as pork, dog, snake, scorpion, etc. World Health Organization uses also term of herbal medicine officially in the guidelines, documents, and different books for medicines of natural resources and term of traditional medicine for all methods traditionally used in treating diseases.[2]

In Indonesia, each jamu may be used in different application, depends on the aim of usage. It may be pills to treat chronic illness or an herbal tea to promote health or to prevent illness, or paste to maintain beauty. According to this reality, the scope of jamu includes three categories: jamu as medicine, jamu as health promoter or freshener, and jamu as cosmetic. The important aim of consuming jamu is to cure diseases such as cough, rheumatoid, hypertension, or malaria. It must be noted that at the ancient time, Indonesian people did not know exactly some diseases such as hypertension, diabetic, lipid disorder, gouts, cancer, and different infectious diseases, but they know the symptoms and according to their experiences they cure not only the symptoms but also the

causative of diseases. They know hypertension by pain symptom on backside of head; tired and sweetness of urine for diabetic; pain on internodes of fingers for gouts; and fever for infectious diseases. There is also a term namely *sawan tahun* which is known as a dangerous disease but until now it has not been clarified what kind of disease is, perhaps it is cancer or other infectious disease. These notes are important to some one who wants to understand the formulation of jamu medicine, to search biological activities of certain medicinal plants, or to read a book of Indonesian herbal medicine. Since 2005 all product of natural medicine sold in Indonesia have been divided into 3 levels. They are Empirical Traditional Medicines, Standardized Herbal Medicines, and Phytopharmaceuticals.[1] Each category of Indonesian natural medicine has logo and the explanation such as follow.

The logo is in a cyrcle. It indicates that all product of natural medicine are safe product.

Green leaves picture on yellow backround indicate biodiversity of Indonesian plant resources

Simple leaves style indicates that Empirical Traditional Medicine (ETM) are simple in ensuring the quality, efficacy, and safety

Three radial leaves style indicates that Standardized Herbal Medicine (SHM) are rather complicated in ensuring quality (proven by standardization of plant raw materials), efficacy (proven on animals by pharmacological effect) and safety (proven by toxicological data on animals).

Star form of radial leaves style indicates that Phytopharmaceuticals are complicated in ensuring quality (proven by standardization of plant raw materials and also product preparations), efficacy (proven on animals by pharmacological effect), safety (proven by toxicological data on animals), clinical trial in patients.

The regulation could hopefully increase jamu industries in establishing scientific base of jamu especially by carrying out research programs.

2. Industrial aspect of medicinal plant raw materials

There are more than 20 relatively big jamu companies located in Central Java and Yogyakarta Province that each of them uses more than 1 tons plant materials every week. They use approximately 200 plant materials for their jamu products while Javanese people use commonly more than 700 plant materials in the preparation of Javanese traditional medicine. Fortunately this big amount of materials are dominated by ginger family (Zingiberaceae) that regularly cultivated in Java and some places in other islands such as at Southern Sumatra and Madura. Besides Zingiberaceae, some Umbelliferae species are intensively cultivated at Boyolali located in east side of mount Merapi in Central Java. The medicinal plants are usually intercropped with beans. *Orthosiphon*, *Piper retrofractum*, *Sonchus arvensis*, and some plants containing essential oils are also intensively cultivated. However warning sign should be emphasized to some endangered plants such as *pulosari* (*Alyxia reinwardtii*), *masoyi* (*Cryptocarya massoy*), *kayu angin* (*Usnea barbata*). Program of conservation is urgently needed because the exploration is continuously carried out without sufficient cultivation especially *Usnea dasypoga, U. barbata,* and other *Usnea spp*. This lichen grows as saprophyte in trees and some impatient collectors cut the trees in order to obtain easily the lichen. It cause environmental damage and any organ of lichen

left. Besides improving cultivation method to increase active chemical content, sustainability of plant material resources must be programmed seriously. The first attention in the collection of raw material from medicinal plants is about harvesting. The content of active chemical constituents of raw material depend on plant organ used, plant age at harvesting time, time of harvesting, and habitat of the plant. Active chemical constituents are optimally formed in certain organ at certain age. Tropane alkaloid in *Atropa belladonna* is firstly formed in roots, while at the first year of growth, formation of alkaloid move to green stem. During second year the stem begins to be lignified and its alkaloid content decreases but in the leaves it increases significantly. The highest alkaloid content occurs in the leaves when the flowers are blooming and it decreases during and after fruit season. Menthol content of leaves of *Mentha piperita* achieve maximum level in the beginning of flowering, whilst maximum camphor content of *Cinnamomum camphora* can be obtained in old bark. Flavonoids of celery, *Sonchus*, *Orthosiphon*, and other medicinal plants achieve maximum level when the flowers are blooming where metabolism is going on intensively.[3]

When an organ is harvested there is no substrate to be catalyzed by enzyme because there is no supply from photosynthesis. In more than 10% of water content, an enzyme is still active and due to absent of usual substrate it will catalyze available substance that may be an active chemical constituent to form other substance that may be inactive. This phenomenon would not occur if the plant organs are dried soon after harvesting and have less than 10% of water content. Several enzymes as destroyer some active chemical constituents are hydrolases, oxidases, peroxidases, isomerases and polymerases. Hydrolases catalyze ester to form alcohol and organic acid, glycoside to form sugar and non-sugar or aglycone, polysaccharide to form monosaccharides. Numbers of Indonesian plants contain components of essential oil in form of ester such as methyl salicylate in leaves of *Gaultheria fragantissima.*, ethyl *p*-methoxycinnamate in rhizomes of *Kaempferia galanga*, linalyl acetate in leaves of *Ocimum basilicum*, and benzyl acetate in flowers of *Jasminum officinale*. The first two mentioned compounds are counterirritant and analgesic, while the two last ones are used in aromatherapy and perfumery. Methyl salicylate gives methanol and salicylic acid as product of hydrolysis and the last mentioned substance has effect of irritation on the skin. Benzyl acetate is hydrolyzed to benzyl alcohol and acetic acid which have no good odor. [4, 5]

Apiin or apigenin-7-*O*-apiosylglucoside of celery (*Apium graveolens*) having vasodilator effect. It gives an aglycone and two molecules of sugar as product of hydrolysis. They are apigenin, apiose and glucose. Apigenin, as aglycone of apiin, has also vasodilator effect and can reduce blood pressure, but the problem comes to the extraction process in industry. Celery leaves is usually extracted by digestion process using water as solvent or by maceration using ethanol 30 % based on the fact that the main vasodilator compound in celery leaves is apiin glycoside, a hydrophilic substance. If the harvested celery leaves are not dried soon, the glycoside might be hydrolyzed enzymatically to form apigenin which is significantly less polar and less soluble in water or ethanol 30%. The extraction process becomes ineffective. Activity of hydrolase is sometimes followed by polymerase such as in leaves of *Aucuba japonica*. The leaves become rapidly blackish because of hydrolysis of aucuboside and then followed by polymerization of the aglycone.

Besides ester and glycoside, activity of hydrolases may occur on polysaccharides. Mucilage in leaves of *Guazuma ulmifolia* decreases appetite and always found

in Javanese herbal medicine for body slimmer. If the substance is enzymatically hydrolyzed, it will produce monosaccharide that would not have slimming effect but contrary it gives calories and causes obesity. [6]

Harvested plant organs with high water content give also risk of degradation of chemical constituents due to microbial contamination. Less than 10% water content might inhibit growth of microbes.[5] The case of Javanese pepper *(Piper retrofractum)* is exceptional. The fruits and also their extract are resistant to microbial contamination even with more than 15% of water content.

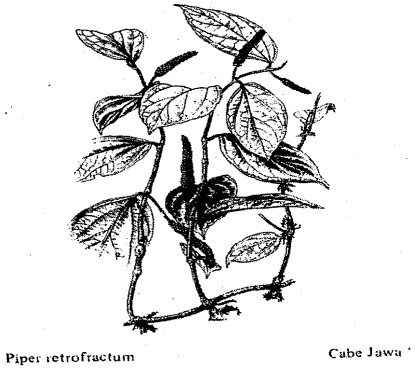

Fig.1 Javanese pepper, a widely used Piperaceae plant in jamu industry

Since a plant organ is harvested, different steps of production process are required to obtain good quality of raw materials and ready to be proceeded for herbal medicine preparations. Some factories receive fresh plant raw materials especially Zingiberaceae*e* rhizomes such as ginger and different curcuma. The process of sorting, washing, slicing, drying, and packing steps must be done correctly and efficiently in order to obtain economically accepted raw materials in good quality. Sorting process of fresh raw materials is aimed to throw away all impurities and other materials. In case of rhizomes, sorting process is emphasized for separating soil, gravel, grass, stem, leaves, damaged rhizomes, and other impurities including other rhizomes.

The next step is washing fresh raw materials in order to clean up from impurities especially soil as source of microbial contamination. The rhizome surface usually has much wrinkle with soil attached on it and only by using brush followed by shaking the rhizomes in water the clean up can be well carried out. Washing process of fresh rhizomes must be carried out soon after harvesting. It could reduce microbial contamination significantly in comparison to washing process that was carried out 2 days after harvesting with the same method of washing. Even though it is not easy to carry out washing process soon after harvesting because the rhizomes are cultivated and harvested in villages and the farmers use water from river to carrying out washing process. Microbial content of water from river is questionable. *Pseudomonas, Proteus, Micrococcus, Bacillus, Streptococcus, Enterobacter,* and *Escherichia* is generally found in water of river. Due to this reality, some big factories take part in the collaboration with the farmers in controlling and assisting not only washing process but almost all steps of raw material production. The clean fresh rhizomes are then sliced resulting 3 to 5 mm of thick. Less than 3 mm gives risk of lost of essential oils that are generally the important constituent of Zingiberaceae rhizomes. Contrary, more than 5 mm of thick will make longer time of drying and give risk of microbial contamination.

Next step after slicing is drying process in order to reduce water content as much as possible without degradation of active chemical constituents. Drying process of fresh rhizomes is usually carried out on racks under sunlight, but some chemical constituents can be decomposed by ultra violet part of sunlight. Black curcuma or *C. aeruginosa* contains azulene derived substance located in endodermis cells outside piths and it gives specific drawn of the rhizome as blue blackish circle. When the rhizomes are dried directly under

sunlight the color will disappear due to the degradation of compound by ultra violet light. When black tissue or black plastic was put on the rack, ultra violet exposure would be inhibited and the degradation of substance would not occur without make longer time of drying. It is proven by the existence of blue blackish circle of the rhizomes after drying process. Similar phenomenon was observed on drying process of *Sonchus arvensis* leaves. Covered rack with black tissue produced bright green dried leaves, while direct exposure of sunlight gave dull grey color of leaves after drying process.[6] Curcuminoids are also sensitive to ultra violet light and give brownish color to the surface of rhizomes after drying process. Other method of drying in the production of plant raw materials can be carried out by using oven, with or without vacuum system. Temperature of oven depends on sort of plant materials, usually from 30 °C to 90 °C, but preferable less than 60 °C. High temperature gives risk to occurrence of face hardening, decomposition of thermo labile substances, and lost of essential oil components. Due to high temperature, time of drying is reduced but the surface of rhizomes will dry faster than the inner part. When the surface becomes hard and the drying process is stopped the inner part of rhizomes still contain high quantity of water and give risk to instability of plant material. Such above phenomenon is named face hardening and happens frequently in some Indonesian jamu factories especially during wet season where the rhizomes are directly dried in oven. High temperature can also decompose thermo labile substances such as curcuminoid in curcuma rhizomes, coumarins in *Alyxia* barks and *Morinda* fruits, while unoxygenated terpenoids of essential oil will evaporate due to the relatively low of boiling point. In this case, the optimum temperature of drying process will be better about 30 °C to 45 °C. All steps of production have to be done correctly because starting material dominantly influence product quality.

3. Industrial aspect of extract production

Among more than 1000 jamu factories approximately 100 of them use extract as starting materials for different preparations of jamu product and among them only 6 big factories have modern machine for extract production. Others have simple extractors or take toll manufacturing. In reality, simple extractors do not cause problem of efficiency and quality of extract, but the problem is on evaporator used for concentrating solution obtained from extractor. Evaporators in medium capacity are urgently needed with relatively low price. Other industrial problem of extract production comes from necessity of increasing product efficacy. Most of jamu factories use crude extract as starting materials in producing different preparations. Efficacy of crude extract can be said more than plant raw materials, nevertheless concentration of active chemical constituents in crude extract are still relatively small in comparison to that of other chemical constituents namely ballast substances. Aqueous extract contains carbohydrate, protein, saponin, tannin and other polar substances, while ethanolic extract contains chlorophyll, resin, and other non polar substances. The concentration of active chemical constituents becomes smaller when certain amount of powder such as amylum, avicel, or aerosyl must be added in preparing capsules, tablets, or other pharmaceutical preparations. Some factories have initiated to use purified extract in increasing product efficacy. Elimination of lipid, chlorophyll, resin, carbohydrate, protein, saponin, tannin, and other ballast substances have been developed in order to increase concentration of active chemical constituents. The use of solvents outside water and ethanol will be developed in condition that they can be accepted in

industry. Product preparation of purified extract is easier than that of crude extract due to decreasing problem of voluminous, hygroscopic, and interaction between chemical constituents.

In jamu factories, maceration is more frequently used as method of extraction in comparison to percolation due to the less quantity of solvent needed for extraction. It should be evaluated whether the disadvantages of maceration influence significantly effectiveness of extraction and consequently decrease quality of extract. In percolation, diffusion can occur continuously without concentration equilibrium because the solvent is always renewed so that the concentration difference between inside and outside cells always occurs. Of course it needs more quantity of solvent in comparison to maceration, but the extraction is more effective. Besides, renewing solvent in percolation process can inhibit saturation of solvent by chemical constituents, while in maceration solvent saturation can occur and consequently dissolution of chemical constituents will be stopped. Most jamu factories try to reduce such disadvantage of maceration by pressing the mixture strongly so that almost total liquid can be separated and the residue contains only insoluble fiber. Exhausted extraction occurs but the macerate also contains insoluble substances such as lipid, protein, carbohydrate and other ballast substances and the difficulty in clarifying occurs because the macerate forms stable suspension.

Effectiveness of extraction has close relation to the similarity in polarity of solvent and active chemical constituents. Curcumin is an active constituent of some Zingiberaceae rhizomes. It has relatively high lipophilicity so that extraction of the rhizomes by water is not effective. Contrary leaves of *Sonchus arvensis* contains a polar active substance namely luteolin-7-*O*-glucoside. Aqueous extraction of the leaves is more effective than extraction by ethanol. When a single plant material contains homogenous active chemical constituents in polarity, the extraction can be carried out with appropriate solvent. Javanese turmeric (*Curcuma xanthorrhiza*) contains curcuminoid and essential oil. These two active chemical constituents are relatively non polar and are soluble in ethanol or less polar solvents. More complex constituents are found in *Orthosiphon stamineus* containing 3 groups of active chemical constituents for diuretic effect. Sinensetin and other methylated flavones are non polar, while potassium salt and saponin are polar substances. It is not practical to do two extraction steps. A mixture of water and ethanol is chosen as solvent of extraction. Further more complexity of extraction is found in most jamu factories due to the system of extraction. More than 10 plant materials are grinded together and then the obtained powder is extracted. There are many active chemical constituents with different polarities and also a lot of ballast substances present. The last mentioned constituents can saturate solvent so that dissolution of active chemical constituent decreases and consequently the concentration of each active chemical constituent become very low. Fortunately some jamu factories have planed to change the extraction system due to the trend of standardized herbal medicine production where one of product requirements is standardization of extract as starting material. [6]

4. Industrial problem of jamu preparation

Traditionally Javanese people sell jamu in form of suspension of fresh medicinal plant materials in bottles placed in a basket made from bamboo namely jamu *gendong*. It has some disadvantages especially easy to be contaminated by microbes and voluminous. In industrial development the simplest product is powder dosage form.

Most jamu factories produce powder form packed in sachets of paper or aluminum foil. In small scale, powder form can be made by grinding dried plant raw materials, sieving, and weighing. In industrial scale, some aspects have to be managed rigorously in order to obtain dried, homogenous, and free flowing powder. The first problem comes from high moisture content of air in Indonesia which can make dried plant raw materials absorb moisture and difficult to be grinded. Reheating process of dried raw material often has to be done just before grinding process.

Fig.2 Jamu *gendong* as initial industry of Indonesian natural medicine

Before 1990, jamu powder and pills dominated jamu products in Indonesia and after that some relatively big jamu factories started to produce capsules and tablets. Modern image of capsules and tablets results in increasing their market demand and consequently decrease popularity of pills. Even thought many jamu factories still produce pills and part of people still prefer traditional style of jamu product. According to NA-DFC regulation, starting material of pills can be plant extract or plant powder. In case of powder as starting material, due to friability of plant powder it needs more binding agent in production process and it results in bigger of obtained pills. The use of hot steams for finishing process before drying increase hardness of pills due to tannin content of plant materials. It results in very long disintegration time of pills. Therapeutic dose and long disintegration time are questionable so that many jamu factories change starting material from plant powder to extract or purified extract if the crude extract still contains high amount of tannin.

According to NA-DFC regulation, starting material of jamu product in form of capsules can not be powder plant material but extract. Usual therapeutic dose of powder plant is about 7 g, while 1 capsule can be filled maximum 0.7 g of powder. It means that the consumer must take 3 times 10 capsules daily. In case of extract as material, the problem is on hygroscopic property so that drying agent needed is often too much. Another problem comes from formula containing high quantity of essential oils that it can attack gelatin capsule. Some pharmaceutical industries have used soft capsule for it but there is still problem especially if the formula also contains very polar substances that are difficult to mix with essential oils even it has been converted into suspension with lipophilic dispersants. Most jamu factories prefer change the preparation into syrup form Similar to problems in capsule form, hygroscopic property of extract and essential oil are two dominant problems in tablet production. The use of granulation method and fluidized bed dryer often gives inconsistent results and the most important problem is the concentration of active chemical constituent. When good tablet performance is obtained by certain method, the amount of drying agent is usually very high so that concentration of active chemical constituents become very low and their therapeutic effect is questionable.

Problem of syrup dosage form are often found in precipitation of insoluble substances, separation of oily liquid, microbial contamination, decomposition of active chemical constituents, and unpleasant taste. All mentioned problems are not specifically found in

Indonesia but generally found in syrup preparation. Discussion here will be emphasized on problem of some plant raw materials or extracts frequently used in Indonesian herbal medicine in form of syrup. Among plant raw materials, Zingiberaceae rhizomes and plant materials containing essential oils are the most frequently used in syrup preparations. The first main active constituents of Zingiberaceae rhizomes are non polar substances namely curcuminoids. Their lipophilicity needs suspending agent to inhibit precipitation in liquid dosage forms while their sensitivity to alkalis pH needs acidic condition. The second active constituents of Zingiberaceae rhizomes are essential oils and usually they can be managed by addition of emulsifying agent to make homogenous. The difficulty comes from the presence of resinous material that is insoluble and has unpleasant taste. It produces brown blackish oily liquid on surface of syrup that can only be managed by addition of surfactants, but in certain concentration of surfactant the syrup becomes very sticky with unpleasant taste.

Fig. 3 Javanese turmeric, a Zingiberaceae plant containing curcuminoid, essential oil, and resin

Another trouble maker substance in syrup preparation is chlorophyll that dominates ethanolic extract of leaves and herbs. There are some kinds of chlorophyll but generally they are insoluble in water and cause non homogeneity of syrup preparation. The use of purified extract is recommended to solve the problem.

5. Good Manufacturing Practice to Assure Jamu Quality

Herbal medicines consist of materials of natural origin that their chemical constituents have big variation both in chemical and physical properties. In order to assure the quality, efforts have to be emphasized in handling of raw materials and process of production. It depends on quality of raw materials, method of production, quality control, facilities used in the production, and personnel working on it. Application of Good Manufacturing Practice is basic proper of requirement in quality assurance of herbal medicine product admitted internationally. The NA-DFC have declared the guidelines of GMP for herbal medicine in 2005

The aims of the application of GMP on herbal medicine especially in Indonesia are as follow.

1. Protect people from under standard product concerning quality, safety, and efficacy
2. Increase level of value and competitiveness of Indonesian herbal medicine in global market.

GMP may be regarded as guideline that has to be followed by all personnel of factory. It must be clear, correct, and realistic which means that the procedures do not make confusion, can be carried out exactly such as mentioned in each established procedure, and can be carried out in available standard condition in Indonesia.

6. Standardization

Efficacy of herbal medicine depends on concentration of active chemical constituents, amount of ballast substances, interactive between chemical constituents, and quality of preparation, while safety

depends on the presence of hazardous substances originally from the plant material, artifact, or added from out side plant material. In plant material level, the quality related to efficacy can be assured by determining specificity and measuring percentage of active chemical constituent. Determination of specificity consists of organoleptic, macroscopic, microscopic, chromatographic profile or detection of marker substance if needed, and then followed by determination of foreign inorganic and organic matter. All mentioned procedures are carried out to convince that the used plant material is true and with high level of purity. Specificity determination is first step of quality assurance while the second step consists of determination of percentage of active chemical constituents, or determination of extractable components if active chemical constituent is not known but the last mentioned procedure is rarely recommended. The quality related to safety can be assured by measuring moisture content, total ash, acid insoluble ash, microbial contamination, heavy metals content, and pesticide residue. If all above mentioned procedures have been carried out on a plant material and the obtained data are in range of standard values established in pharmacopoeias or other recognized references, quality of the plant material has been assured and ready to be used for jamu production with good efficacy and safety. This plant material can also be classified as standardized plant material. Even thought it must be noted that the term of standardization is often only used for determination of percentage of active chemical constituent. It will be better if each country has own herbal pharmacopoeia emphasizing on percentage of active chemical constituent and other relevant parameters carefully determined. In Indonesia the herbal pharmacopoeia has been planned in 2006 and hopefully will be published in near future. The official reference used before publication of Indonesian herbal pharmacopoeia is *Materia Medika Indonesia* containing monographs of Indonesian medicinal plants.[8]

Active chemical constituents should be used as parameter of standardization both for starting materials and products. If active chemical constituent is not known the percentage of marker substances are used as parameter completed with chromatographic profile of extract. In line with progress in science and research on medicinal plants in the world, only relatively small part of frequently used Indonesian medicinal plants are not known their active chemical constituents so that program on marker substances is not attractive. Marker substances will be more appropriate for qualitative identification if there is confusion of plant materials. In the level of jamu product term of quality control much more appropriate to be used and besides the dose of active chemical constituents, the physical properties of preparation have to be in the range of required values. Standardization using active chemical constituent as parameter is very important in the evaluation of interactive components in jamu formula including complementary interactive, combination with similar effect, and contraindication, both pharmacologically or via cytochrome P450 and glutathione S-transferase.[6,9,10] In case of jamu preparation containing different curcuma or other Zingiberaceae rhizomes, determination of curcumin can be carried out by high performance liquid chromatography or thin layer chromatography-densitometry while if the essay is not emphasized on curcumin but curcuminoid, spectrophotometry ultra violet/visible will be appropriate and by using curcumin as standard substance. Many indications referred curcumin or curcuminoid as active substances such as anti inflammatory,[11] anti oxidant,[12] anti hypercholesterolemia,[13] and anti cancer.[14]

In point view of program priority in Indonesia, it will be better that all efforts can be focused in establishing

range content of active chemical constituents even only in groups such as total alkaloid, steroid, tannin, essential oil, because it has direct correlation to efficacy of product. In case of single active chemical constituent the essay methods should be densitometry-thin layer chromatography or high performance liquid chromatography compared with ultraviolet-visible spectrophotometry because instrument of the last mentioned method is usually available in many jamu factories. Of course due to lack of selectivity, spectroscopic essay usually gives bigger value. Comparison data with 2 other above mentioned methods can be used to make correction. It will be a big plan of Indonesian government but it will be very useful for more than 100 medium to big jamu factories in Indonesia. Other problem of standardization is lack of standard substances. Some Indonesian medicinal plants contain enough quantity of active chemical constituent to be isolated but the others contain only small amount so that isolation process is not easy to be carried out.

7. Conclusion

Industrial development of jamu in Indonesia should be carried out systematically including application of Good Agriculture Practice, program of sustainable resources, application of Good Collecting Practice, Good Manufacturing Practice, standardization of starting materials, and evaluation of jamu formula.

Bibliography

1. National Agency for Drug and Food Control, 2005, *Peraturan Perundangan-undangan di bidang Obat Tradisional, Obat Herbal Terstandar, dan Fitofarmaka*, Badan POM, Jakarta.
2. World Health Organization, 1999, *WHO Monograph on Selected Medicinal Plants*, Vol. I, WHO, Geneva.
3. Evans WC, 1989, *Trease and Evans' Pharmacognosy*, 13th Edition, ELBS, Balliere Tindale, London.
4. Bruneton J, 1997, *Pharmacognosie, Phytochimie, Plantes Medicinales*, TDn Lavoisier, Paris.
5. List PH and Schmidt PC, 1989, *Phytopharmaceutical Technology*, CRC] Press, Boston.
6. Pramono S, 2007, *Jamu, In Indonesian daily life and industry,* Institute of Natural Medicine, University of Toyama, Toyama.
7. Tonnesen HH and Karlsen J, 1985, 1985, Studies on curcumin and curcuminoids, V, Alkaline degradation of curcumin, *Z. Lebenson-Unters Forsch, 180*: 132.
8. Department of Health Republic of Indonesia, 1977, *Materia Medika*, Jilid I, Ditjen POM, Jakarta.
9. Subehan, Usua T, Kadota S, Tezuka Y, 2005, Constituents of *Zingiber aromaticum* and their CYP3A4 and CYP2D6 inhibitory activity, *Chem. Pharm. Bull., 53*:333-335 .
10. Commandeur JNM and Vermulen NPE, 1996, Cytotoxicity and cytoprotective activities of natural compounds. The case of curcumin. *Xenobiotica, 26*: 667-680.
11. Wichtl M, 1994, *Herbal Drug and Phytopharmaceuticals*, CRC Press, Boca Raton.
12. Jitoe A, Masuda T, Tengah IGP, Suprapto DN, Gara IW, Nakatani N, 1992, Antioxidant activity of tropical ginger extracts and analysis of contained curcuminoids, *J. Agric. Food Chem. 40(8)*: 1337-1340.
13. Pramono S, Purnomo FX, Sugiarto, 2005, Development of Javanese turmeric as phytopharmaceutical for anti hyperlipidemia, *Research Report*, National Agency for Drug and Food Control, Jakarta.
14. Reddy S, Rishi AK, Sarkar FH. Majumdar APM, 2006, Mechanism of curcumin- and EGF- receptor

related protein (ERRP)-dependent growth inhibition of colon cancer cells, *The International Symposium on Recent Progress in Curcumin Research*, Gadjah Mada University, Yogya