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Analysis of acetaminophen, mefenamic acid, sibutramine hydrochloride, and sildenafil citrate

Eva Susanty Simaremare*, Rizka Agustine Susilowati, Yeyen Dwi Astuti, Rusadi Hermawan, Elsye Gunawan, Rani Dewi Pratiwi, Rusnaeni

Department of Pharmacy, Universitas Cenderawasih, Jayapura 99358, Indonesia.

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ABSTRACT

Jamu, Indonesia herbal medicine, has long been used for helping to heal many diseases. But nowadays, many of *jamu* were adulterated with chemical drugs that are harmful to consumers. Adulterations were analyzed in several places except in Papua Jayapura. We conducted an analysis of *jamu* which containing acetaminophen (ACE), mefenamic acid (MEFA), sibutramine hydrochloride (SH), and sildenafil citrate (SILC). Samples were taken by representing herbal that predicted containing chemicals. Thin-layer chromatography and UV-Vis spectrophotometry methods were used for quantitative analysis while the determination of concentration was used by titration and UV-Vis spectrophotometry methods. In this study, we reported that there was one sample in herbal medicines containing ACE, three samples containing MEFA, two samples of slimming herbal contained SH, and three samples of aphrodisiac herbal contained SILCs.

INTRODUCTION

Herbal medicines (HMs) are widely used by consumers in the world for treatment because of cheaper, minor side effect, and harmless (Haneef *et al*., 2013; WHO, 2012, 2014; Kartal, 2007; Hayun *et al*., 2016). Several countries use HMs, such as Ayurveda and Unani (India and Bangladesh), Sowa (Nepal and Sri Lanka), Rigpa (Bhutan), Koryo (Korea), Dhiveshbeys (Maldives), Myanmar TM, Thai TM (WHO, 2014), Kompa, as well as *Jamu* (Indonesia).

Jamu, Indonesia herbal medicines (IHMs), have long been used for healing diseases (Gitawati, 2013; Septiani and Damayanti, 2015; Mustarichie *et al*., 2017). IHMs are used for analgesic, diet, sex medicine (aphrodisiac), supplement immunity, gout, skin, cough, erectile dysfunction (ED), cancer, lung, antirheumatic, and diabetic (Nuryunarsih, 2017). However, at this moment, various IHMs were contaminated with chemical drugs that pose danger for consumers (BPOM, 2008, 2010, 2014). Regulation of Ministry of Health Indonesia No. 007 2012 and The National Agency for Drugs and Food Control said that IHMs are prohibited for chemical adulteration, including isolate from natural product, chemical substances, and ethanol (>1.0%) (Depkes RI, 1985, 1990; Tilaar and Widjaja, 2015). The addition of chemicals into IHMs to obtain instant effect nevertheless will be very harmful to consumers if it is continuously used over a long period with uncontrolled dosage (Krivohlavek *et al*., 2016). Fifty-one IHMs samples were containing 16 dangerous adulterants which are dominated by pain relievers, slimming, aphrodisiac HMs; acetaminophen (ACE), mefenamic acid (MEFA), sildenafil citrate (SILC), phenylbutazone, caffeine, and sibutramine hydrochloride (SH) (BPOM, 2014). The purpose of this research was to perform analysis of the chemical drugs on HMs: ACE and MEFA in pain relief menstuation (analgesic) *jamu*; SH in slimming *jamu*; and SILC in ED/aphrodisiac IHMs.

Paracetamol (PCM) or ACE with molecular structure $C_8H_9NO_2$ has chemical name 4-hydroxyacetanilide (Fig. 1)

*Corresponding Author
Eva Susanty Simaremare, Department of Pharmacy, Universitas Cenderawasih, Jayapura 99358, Indonesia.
E-mail: eva_smare @ yahoo.com

(Bebenista and Nowak, 2014; Florey, 1974). ACE is identified as white crystalline powder, odorless, slightly bitter, and used for analgesic. The solubility is freely soluble in alcohol, soluble in boiling water and NaOH 1N (USP, 2012).

MEFA, $C_{15}H_{15}NO_2$, was known as 2-(2, 3-dimethyl-phenyl) amino (Fig. 1). MEFA is identified as white crystalline powder, melting point 230°C, with decomposition. MEFA is soluble in alkali hydroxide solution, sparingly soluble in chloroform, slightly soluble in alcohol and methanol, and moreover practically insoluble in water (USP, 2012; Florey, 1986).

SH, with structure molecule $C_{17}H_{29}Cl_2NO$, is an orally administered agent for the treatment of obesity (Hunsel *et al*., 2015; Krivohlavek *et al*., 2016; Maryam, 2016) that was usually adulterated in HMs (Fig. 1). The active ingredient is a racemic mixture of the (+) and (−) enantiomers of cyclobutanemethanamine, 1-(4-chlorophenyl)-N,N-dimethyl-α (2-methylpropyl)-, hydrochloride, and monohydrate. SH monohydrate is a white to cream crystalline powder with a solubility of 2.9 mg/ml in pH 5.2 water. SH is soluble in water partition coefficient is 30.9 at pH 5.0 (FDA, 2004; Calahan *et al*., 2016).

SILC is a therapy used for ED that was usually added in HM (Blok-Tip *et al*., 2004; Podder *et al*., 2014). The other name is 5-[2-ethoxy-5-(4-methylpiperazin-1-yl)sulfonylphenyl]-1-methyl-3-propyl-4H-pyrazolo[4,3-d]pyrimidin-7-one;2-hydroxypropane-1,2,3-tricarboxylic acid (Fig. 4) (PubChem, 2018). It gives action by inhibiting cGMP-specific phosphodiesterase type-5, an enzyme that causes degradation of cGMP, which controls blood flow in the penis (Saeed *et al*., 2015; Daraghmeh *et al*., 2001).

MATERIALS AND METHODS

Materials

Reference standards were used ACE, MEFA, SH, and SILC. All reagents, IHMs analysis was performed on precoated TLC plates with Silica Gel F_{254} (Merck). Sample used are HMs that were not included into the list of public warning National Agency for Drugs and Food Control in Jayapura Indonesia. Sample HM as analgesic for menstruation *jamu* were coded as *jamu* A, B, C, D, E, and F (Fig. 2). Slimming *jamu* were coded as *jamu* G, H, I, J, and K (Fig. 2). Aphrodisiac samples were coded as jamu L, M, N, and O. (Fig. 2). All jamu were collected from existing pharmacies in Jayapura city on January 2016.

Research tools: Spectrophotometer UV-Vis 1601 (Shimadzu, Japan) and pH meter (Shimadzu, Japan).

Organoleptic test

These observations included the dosage form, color, taste, and smell of HMs (Depkes RI, 1995).

Qualitative identification of ACE and MEFA on relieving menstrual pain IHMs

Sample that indicated consist of ACE was weighed approximately 100 mg by testing with an analytical balance. Then, it was shaked for 30 minutes with 50 ml CH_3OH and filtered

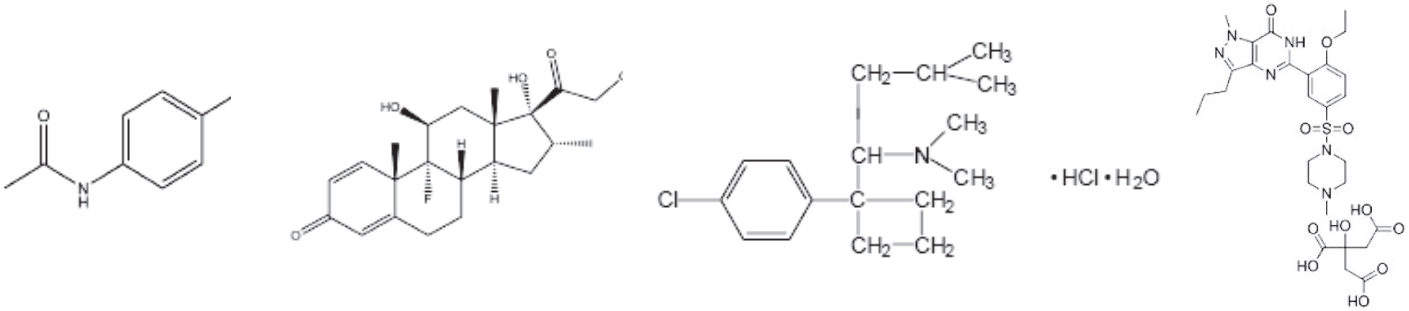

Figure 1. The chemical structures of compounds: ACE (1), MEFA (2), sibutramine hydrochloride (3), and SILC (4)

Figure 2. Back cover sample of HM: relieving menstrual pain *jamu* (1), slimming *jamu* (2), and aphrodisiac *jamu* (3).

through Whatman filter. (1) The filtrate was ready for application on TLC plate with mobile phase CH_2Cl_2-CH_3OH (9:1). (2) Next filtrate also was scanned using Spectrophotometer in 243 together with 250 nm (Mustarichie *et al*., 2017; International Conference on Harmonization, 1995).

For identification of MEFA, (1) Samples 250 mg was dissolved to CH_2Cl_2-CH_3OH (3:1) and filtered. The filtrate was dotted in TLC plate by capillary pipe used mobile phase toluene-1,4 dioxane-ammonia 13M (95:25:1). (2) The other method, 100 mg sample was dissloved to 100 ml NaOH consequence scanned using Spectrophotometer with 285 nm (Gitawati, 2013; Depkes RI, 2015).

Sibutramine hydrochloride on slimming IHMs

(1) Samples were weighed approximately 1 g, shaked to 5 ml CH_3OH for 30 minutes, and later filtered. The filtrate was spotted in TLC plate with two types of eluent $CHCl_3$-acetone (8:2) together with acetone-$CHCl_3$-hexane (5:3:2). (2) 200 mg sample was dissolved to 25 ml aqua bidestillate soon after filtered. 250 µl of the filtrate was transferred to 10 ml volumetric flask using Eppendorf pipette. After aqua bidestillate was added, shaked, and 5 ml scanned to spectrophotometer in wavelength 224 nm (Depkes RI, 2015; Hayun *et al*., 2016).

Sildenafil citrate aphrodisiac of IHMs

(1) Aphrodisiac samples were put on scales 1 g, shaked to 5 ml acetonitrile-water (3:1), and filtered. The filtrate was spotted in TLC plate with mobile phase phosphate buffer pH 2.0—acetonitrile (1:3). The filtrate likewise was skimmed using Spectrophotometer in 269.5 nm (Saeed *et al*., 2015). (2) Color test: Sample was weighed 0.5 mg dissolved with NaOH 10% 2 ml and heated. Then, the solution was cooled and added with $PbSO_4$ 1 ml. The other test color, filtrate was added to $AgNO_3$ and heated. The change in color was observed (Depkes RI, 2015).

Quantitative identification of chemical drugs in IHMs

IHMs adulterated with ACE were weighed 250 mg shaked to 20 ml HCl dissolute 39%—distilled water (1:2). This mixture was warmed up to 85°C for 30 minutes then next added with 5 mg KBr. Mixture was titrated by 0.1N $NaNO_2$ in 15°C using blue timol with blue methylene indicator. IHMs were adulterated with MEFA, 100 mg sample was dissolved in 100 ml of ethanol then titrated with 0.1N NaOH with indicator phenolphthalein. IHMs were adulterated with SH, 200 mg sample was dissolved to 5 ml water then added with KNO3 1.2M. Solution was titrated with 0.1 M KOH (Depkes RI, 2015).

Quantitative analysis for SILC adulterant was preparated the standard preparation of calibration curve and determination of the concentration. Standard of SILC was dissolved with phosphate-acetonitrile buffer (1:3) with a variation of concentrations 40, 90, 120, 170, 190, 200, and 250 ppm. Each concentration measured absorbance with UV-Vis spectrophotometer at a wavelength of 269.5 nm. The curve of calibration was obtained by linear regression equation from the curve. Sample test was prepared by 500 µl filtrate which was dissolved with phosphate-acetonitrile (1:3) phosphate buffer in 10 ml volumetric flask. The absorbance was obtained and applied to the curve in the linear regression equation formerly the sample concentration would be obtained (Depkes RI, 2015).

RESULTS AND DISCUSSION

Organoleptic

Organoleptic test from three types of herbs stated; (1) Menstrual pain relievers *jamu* (A–F) had the form of *jamu* was a powder with various colors ranging such as green, yellow, and brown; Some *jamu* are tasteless, bitter, and spicy which were dominated by the smell of herbs. (2) Slimming *jamu* (G–K) had the form were powder and capsules with various colors ranging from white, yellow, green, and brown. All of *Jamu* were tasteless and odorless. (3) Aphrodisiac *jamu* (L–O) had the form were powder and granule; with white, yellow, and brown. *Jamu* is tasteless and bitter with smell herb (Table 1).

Table 1. The organoleptic observation of each IHMs.

Type of *jamu*	Sample *jamu*	Shape	Color	Sense	Odor
Menstrual pain relievers	A	Powder	Green	Bitter	Typical herbs
	B	Powder	Yellow	Tasteless	Mint and turmeric
	C	Powder	Brownish yellow	Bitter mildly spicy	Typical herbs
	D	Powder	Brownish yellow	Bitter mildly spicy	Typical herbs
	E	Powder	Brownish yellow	Tasteless	Turmeric
	F	Powder	Brown	Bitter	Ginger
Slimming	G	Powder	Yellowish brown	Tasteless	No smell
	H	Powder	Greenish yellow	Tasteless	No smell
	I	Powder	Greenish yellow	Tasteless	No smell
	J	Capsule	White	Tasteless	No smell
	K	Capsule	Brown	Tasteless	No smell
Aphrodisiac	L	Fine powder	White	Bitter	No smell
	M	Powder	Yellowish white	Bitter	Typical herbs
	N	Granule	Yellowish white	Tasteless	Typical herbs
	O	Powder	Light brown	Tasteless	Typical herbs

Color reaction of SILC in aphrodisiac jamu

The presence of synthetic compounds SILC in aphrodisiac *jamu* can be identified by the use of reagents that can react with the compound being analyzed and will cause a reaction which we can observe that coloration, precipitation, and formation of gases or odors. Sulfur test is a technique for identifying the presence of SO_2 compounds. The results obtained from sulfur testing found a black spot on the solution until the A, B, and D. Spot tests formed were derived from formation salt with Pb^{2+} metal ions, which indicated the presence of SO_2 compounds in the test sample herbal solution. Identification test of carboxylic function groups was carried out with the addition of $AgNO_3$. The addition of silver nitrate forms a bond between ions acetate (CH_3COO^-) with silver ions (Ag^-). Test samples A, B, and D occur color change from the color of the initial solution to cloudy brown. Change of this color identifies the presence of carboxylic groups from deep citric salts herbal preparations test.

Qualitative and quantitative identification of chemical drugs on commercial traditional medicine

ACE and MEFA on relieving menstrual pain IHMs

Relieving menstrual pain *jamu* is usually combined with chemicals drug in IHMs which as potential analgesics to reduce pain, especially for instance tablet and bulk (Ogunjimi and Alebiowu, 2016; Thippeswamy *et al*., 2015). Some drugs like ACE, MEFA, ibuprofen, ketoprofen, and aspirin have analgesic therapy (Fowler, 1987; Smith, 1971). Usually, ACE/PCM and MEFA are added to this IHMs for reducing pain during menstruation. PCM, fascinetic metabolite, has antipyretic effects that were caused by aminobenzene groups (Moertei *et al*., 1972). MEFA is a nonsteroid anti-inflammatory drug class that also used for painkiller such as in rheumatism (Zhang and Wang, 1998; Ottani *et al*., 2006). Six relieving menstrual pain IHMs samples as shown in Table 1 had been analyzed with organoleptic (Fig. 2) and containing medicinal adulteration (Fig. 3).

The chemical analysis of ACE and MEFA of menstrual pain relieving traditional *jamu* in Jayapura used the TLC method and UV/Vis spectrophotometer. The sample can be separated based on the components of the compound by selecting the appropriate mobile phase, $CHCl_3$–CH_3OH (9:1) for ACE and toluene-1,4 dioxan-13M ammonia (95:25:1) for MEFA. The maximum separation in the R_f solute is between 0.2 and 0.8 (Gandjar and Rohman, 2007) while the UV/Vis spectrophotometer can be identified qualitatively based on the wavelength of the active compound. F has been evaluated as blended with the ACE drug (Table 2). As same as a standard reference, F sample had R_f value which was 0.6. In the other hands, MEFA drug was founded in D, E, and F samples in which R_f value was same as reference standard 0.8 (Fig. 3).

ACE was analyzed using UV-Vis spectrophotometry because ACE has a chromophore (benzene) and ausochrome (NH) group in the form of benzene hydroxide in the range of 200–400 nm UV wavelength. The maximum wavelength of ACE in several references is 200–400 nm, 243 nm, and 250 nm (Gandjar and Rohman, 2007). While the results were obtained that ACE was 219 nm with an absorbance of 0.79. This was different with references because of the sample of herbs containing various kinds of compounds that could reduce the intensity and wavelength of ACE.

MEFA has a chromophore group (benzene at 255 nm and benzoate acid at 273 nm) and ausochrome (–NH) which results in a shift in the absorption band to a larger (bathochromic) wavelength and hyperchromic effect. From several references, the maximum wavelength of MEFA was 285 nm UV-Vis spectrophotometry (Jain *et al*., 2016) and 200–400 nm (Naveed and Qamar, 2014; Chen *et al*., 2015). The results showed that samples D had a maximum wavelength of 222 nm and the absorbance of 0.3. For sample E with a maximum wavelength of 216 nm with an absorbance of 0.29 and for sample F with a maximum wavelength of 220 nm and an absorbance of 0.68. Therefore, F sample was adulterated with ACE while D, E, and F samples were MEFA drugs.

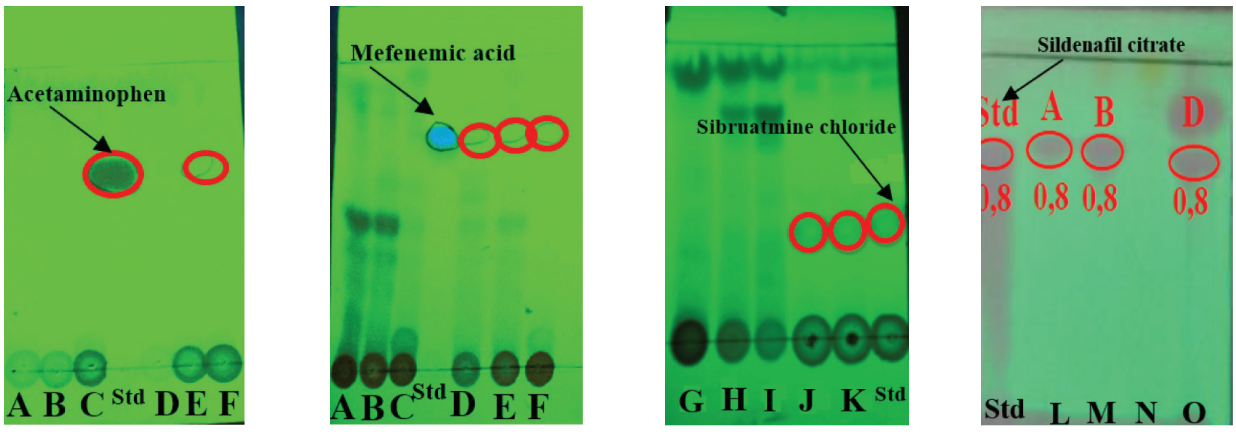

Figure 3. Thin Layer chromatogram of sample relieving menstrual pain *jamu* and standard mixture: identification of ACE on sample with mobile phase dichloromethane-methanol (9:1) (1), identification of MEFA with eluent toluene-1,4 dioxane-ammonia 13 M (95:25:1) (2), identification of SH on sample with eluent acetone-$CHCl_3$-hexane (5:3:2) (3), and identification of SIL with eluent phosphate buffer pH 2.0—acetonitrile (1:3) (4).

Nitrimetry was used for the determination of ACE in the sample. The sample was dissolved with hydrochloric acid-water (1:2) to form an acidic pH and make a secondary amine hydrolyzing that changing to a primary amine. It is not stable because the formation of diazonium salts is easy to be formed in the phenol compounds and nitrogen gas. Therefore, the reaction is carried out at a low temperature. The ACE nitrimetrically in sample D was 12.82% (Table 1). Reaction mechanism HCl and $NaNO_2$:

$$NaNO_2 + HCl \rightarrow NaCl + HNO_2$$

$$Ar\text{-}NH_2 + HNO_2 + HCl \rightarrow Ar\text{-}N{=}N^+Cl^- + H_2O$$

The determination of MEFA was used by alkalimetry titration method. MEFA is one of the nonsteroidal anti-inflammatory drugs of carboxylic acid derivatives whatever is insoluble in water (Smith, 1971; Fowler, 1987). Because MEFA is a weak acid with pKa 4.2, the concentration was determined with titration in non-aqueous solvent (Cakrer *et al*., 1999). MEFA has a carboxylic acid functional group. The –COOH compound can be titrated as one valence so that NaOH is selected as a standard solution (Cakrer *et al*., 1999; Glomme *et al*., 2005). The result showed that sample D obtained adulteration MEFA was 13.10%; E was 12.69%; and F was 36.43% (Table 2).

Sibutramine hydrochloride on slimming IHMs

SH has a sign as an appetite retention and fat content into energy in the body (Kohler *et al*., 2016; Muller *et al*., 2009; Suthar *et al*., 2009). Two from five samples of slimming herbs had the same R_f value as the reference standard (Fig. 3) with mobile phase chloroform-acetone (8:2) was 0.37 and also R_f in acetone-chloroform-hexane (5:3:2) eluent was 0.6 (Table 3).

SH can be analyzed using UV-Vis spectrophotometry method because it has a chromophore group in the form of benzene chloride (200–400 nm). Benzene groups are usually at 200 nm but SH in 224 nm because the benzene chloride group experiences a bathochromic shift so that the maximum wavelength shifts to the right or greater.

The maximum wavelength was obtained by the J sample at 224 nm, while for the K sample was 221.5 nm. In sample K, the wavelength obtained was different with 224 nm because there were many compounds in herbs that causing the maximum wavelength to shift to the left or smaller. From several studies that have been conducted, the maximum λ ever obtained is 223.5 nm (Pundra, 2013), 225 nm (Suthar *et al*., 2009), 224 nm, and 224.9 nm (Kuo-Chih, 2007). Thus, J and K samples were adulterated with SH. SH is good at daily doses but should not present in slimming herbs (Maulana, 2016).

Because SH is a weak acid with pH value 5.2 (2.9 mg/ml water), determination of SH used acid-base titration, the mechanism reaction in Figure 4. The pH was obtained by scanning the change of pH value of the solution using pH meter. In this reaction, KNO_3 was used to the standard solution to keep ionic strength in solution. KNO_3 is a strong electrolyte in solution (water) will dissociate into K^+ and NO_3^-. The K^+ ion will react at the first time then H^+ ion. As a result, the concentration of H^+ ions in the solution will be more stable.

Table 2. The results of analysis ACE and MEFA in relieving menstrual pain *jamu.*

Sample	Code	Rf of mobile phase (MB)		Scan λ max		Result	Amount (% bb)	
		MB 1	MB 2	219 nm	216–222 nm		ACE	MEFA
Standard	ACE	0.65	–	+	–			
	MEFA	–	0.87	–	222			
Menstrual relief pain *jamu*	A	0.82	0.65	–	–	–	–	
	B	0.82	0.65	–	–	–	–	
	C	0.05	0.65	–	–	–	–	
	D	0.82	0.87	–	222	+ MEFA	–	13.11
	E	0.05	0.87	–	216	+ MEFA	–	12.69
	F	0.65	0.87	+	220	+ ACE and MEFA	12.82	36.43

Information:
MB 1: CHCl3-CH3OH (9:1)
MB 2: Toluene-1,4 dioxan-ammonia 13M (95:25:1)

Table 3. The results of analysis sibutramine HCl in slimming *jamu*.

Sample	Code	Rf of mobile phase (MB)		Scan λ max	Result	Amount SH (% b/b)
		MB 3	MB 4	221–224 nm		
Standard	SH	0.37	0.62	224		
Sliming *Jamu*	G	0.9	0.8	–	–	–
	H	0.7	0.7	–	–	–
	I	0.7	0.7	–	–	–
	J	0.37	0.62	221.5	+	3.67
	K	0.37	0.62	224	+	1.17

Information:
MB 3: CHCl3-acetone (8:2)
MB 4: Acetone-CHCl3-hexane (5:3:2)

The curve that estimates the concentration SH used acid-base titration. Figure 5 explained that pH changed was titrated with the standard solution. The J sample contains adulteration was 3.67% and K was 1.17% (Table 3).

Sildenafil citrate on aphrodisiac IHMs

Sildenafil is the first oral drug used in the treatment of ED, with the highest frequency of use in cardiovascular patients (Pharmaceutical Forum, 1998; Podder *et al*., 2014; Lee *et al*., 2016). The price of a blue pill unit is expensive that certainly not reachable by consumers from middle and lower society. Aphrodisiac often contains SILC and also many illegal products finally used to HM as a substitute therapy. Many studies had researched SH with several different methods (Sakur and Affas, 2017). Two from four of aphrodisiac HM samples L and M (Table 4) had the same R_f value with reference standard was 0.8 (Fig. 3).

SILC has conjugated carbon double bond (C = C), carbonyl group (C = O), and ausochrome were hydroxyl groups (−OH) and amides (NH2) (200–400 nm). Susilowati (2013) reported that the maximum wavelength of the standard SILC was at 292 nm. While the maximum absorption in this study was 269.5 nm. The difference was due to the low purity of the isolate and the influence of other complex compounds in the HM. By using a spectrophotometer test obtained the maximum wavelength of samples L with M which is equal to the standard is 269.5 nm. Thus, L and M samples were adulterated with SILC. From calibration curve was found the regression linear $y = 0.0006x + 0.1749$. Consequently, samples L, M, and O were 0.106%, 0.104%, and 0.020%, respectively.

Impact by adulteration of herbal medicines

Self-medication for minor ailments and complaints by consuming traditional HM (*jamu*) should be done rationally and safely. With a number of herbal products containing drugs (adulterated *jamu*) still existed in various markets in Indonesia, people still exposed to the possibility of taking *jamu* products which are dangerous and can be harmful to health. Beside manufactured *jamu* (branded *jamu*) found adulterated with medicinal, presumably, there are also "ready-to-consume" herbals which are taken directly by consumers, that purposely mixed with medicinal by the seller (Gitawati, 2013). The use of jamu is usually recommended three times a day with brewed with 250 ml of water each sachet, meaning if a pack of the herbal weight of 7 g of the HM contains approximately 450 mg of chemical medicine. This is likely to cause the user or customer to think that she was taking the herbs that are effective with not aware of any additional substances into it (Mustarichie *et al*., 2017).

ACE is an analgesic-antipyretic drug relatively safe if it is used in a therapeutic dose. This is an OTC drug which can be sold directly to the consumer without a prescription. Although it is relatively safe, the addition to the herbal product is illegal, especially because the dosage used might be uncontrolled and overdosed. Prolonged use and high dosage of PCM may cause liver damage (Gitawati, 2013). PCM becomes a dangerous and life-threatening drug because a highly reactive (N-acetyl-p-benzoquinone imine) is a metabolite of acetaminophen metabolite covalently binds to hepatocyte macromolecules leading to the impoverishment of enzymatic systems and structural and metabolic damage to the liver (potential lethal hepatic necrosis) (Anderson, 2008). In the later stage of poisoning, renal tubular necrosis and hypoglycemic

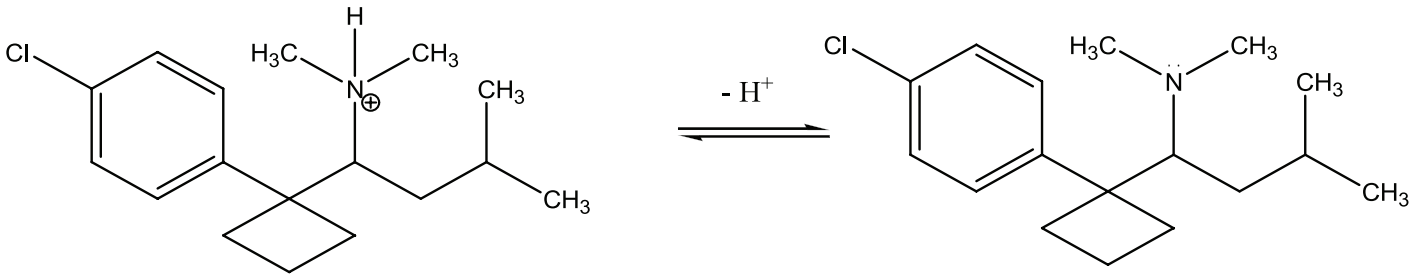

Figure 4. Reaction of Sildenafil hydrochloride in the titration process.

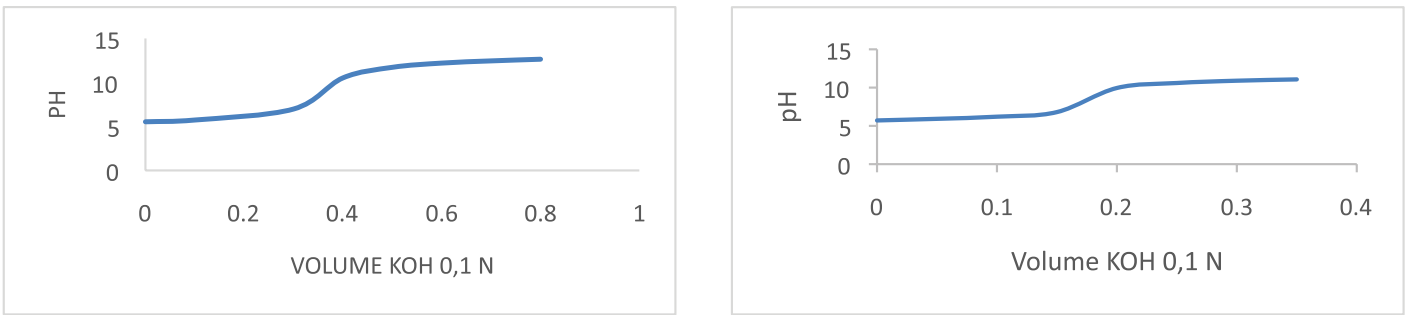

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Figure 5. Determination the end volume titration: sample J, B (1) and sample K (2).

Table 4. The results of analysis SILC in aphrodisiac *jamu*.

Sample	Code	Color reaction		Rf	Result	Amount (% b/b)
		$PbSO_4$	Fungsional group test	MB 5		
Standard	SILC	Black	Brown	0.8		
Aphrodiac *jamu*	L	Black	Brown	0.8	+	0.11
	M	Black	Brown	0.8	+	0.10
	N	–	–	–	–	–
	O	Black	Brown	0.8	+	0.02

Information:
MB 5: Phosphate buffer pH 2.0 – acetonitrile (1:3)

coma may appear (Bebenista and Nowak, 2014). MEFA has several adverse reactions, the most common is gastrointestinal effects (included abdominal pain, gastric/duodenal ulcers, gross bleeding/ perforation, dyspepsia, constipation, diarrhea, flatulence, heartburn, nausea, and vomiting). Hematological adverse reactions have also reported included anemia, increased bleeding time, ecchymosis, eosinophilia, leucopenia, purpura, and thrombocytopenia. Respiratory side effects have included asthma and dyspnea; while renal adverse effects include the abnormal renal function and renal failure. MEFA is contraindicated for patients with GI ulcers, asthma, and renal dysfunction (Gitawati, 2013).

Side effects that can be caused from the overdose use of SH making increased heart rate, palpitations, increased blood pressure, headaches, anxiety, loss of appetite, constipation, dry mouth, irritation, vasodilation, insomnia, dizziness, and sweating (BPOM, 2008). SILC has proven to be an effective treatment for ED. However, after SILC was approved by the Food and Drug Administration (FDA) in 1998, several deaths were reported in patients taking SILC. It is assumed that the patient is associated with a history of the underlying disease (for example, ischemia), not because of the specific effects of a particular drug (Shakir, 2001). SILC can potentiate the hypotensive effect due to contraindications to all forms of inhalation of nitrates, such as amyl nitrate or nitrite, also known as poppers. Poppers act by dilating blood vessels and concomitant use of popper and SILC can cause sudden blood pressure reduction which can be potentially serious or even fatal.

The presence of adulterations in HMs is very dangerous because hazard drugs must be prescribed by doctors. By reason of, there will be dangerous effects due to side effects and contraindications. If herbs are consumed regularly, it will be very dangerous to consumers (Nuryunarsih, 2017). Government should take necessary steps to make people aware about these falsified products and formulate appropriate regulations to stop this type of unethical use of Import identification number (BPOM, 2015) All the dietary supplements should be brought under the regulation of Drugs Administration and any kind of unjustified advertisements of traditional medicines and dietary supplements in mass media (newspaper, TV) should be brought under regulation like prescriptional drugs. All these measures are to be taken immediately to save public health because these falsifications and hiding of facts are dangerous for the consumers due to the inherent serious adverse effects of the undisclosed ingredients used in these products.

The analysis of adulteration in this study was first conducted in Jayapura with a simple, inexpensive, and precise used qualitative test with TLC method and functional group analysis with UV/Vis spectrophotometer. This method is relatively fast for testing adulteration in the market and field by carrying a portable instrument spectrophotometer kit. In the future, it is necessary to develop methods to obtain a more certain recovery value.

CONCLUSION

There were adulterations in 15 HMs. Six samples of relieving menstrual pain HMs, one sample was found to contain the addition of ACE and three samples of MEFA. From five samples of slimming herbs, two samples were found to be with the addition of SH. From four samples of aphrodisiac herbs, three samples were found with the addition of SILC.

CONFLICT OF INTEREST

Declared None.

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