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Searching the chemical content of drug sibutramine hydrochloride in herbal slimming products

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ABSTRACT

Sibutramine hydrochloride as an additive in herbal slimming products is prohibited by the Ministry of Health by the Regulation of the Minister of Health of the Republic of Indonesia number 007 of 2012 concerning the Registration of Traditional Medicines. The purpose of this review is to determine the content, the highest concentration value, the identification method, and the distribution area of herbal slimming products containing sibutramine hydrochloride. The method used is a traditional systematic review with inclusion criteria in the form of the year of publication of the journal with a period of the last 10 years, which uses both English and Indonesian, full text, articles that contain methods and methods of identifying sibutramine hydrochloride, and articles that list the number of positive samples. contains sibutramine hydrochloride and contains levels of sibutramine hydrochloride in herbal slimming products, the article lists the research location or the location of the herbal product sampling. The presentation of data from the results of the review in the descriptive form includes the percentage of products containing sibutramine hydrochloride and the highest content of sibutramine hydrochloride. The results of the article review, herbal slimming products from different research locations contain sibutramine hydrochloride by 52.17% (36). Sibutramine hydrochloride analysis methods include TLC- Densitometry, UV-Vis Spectrophotometry, HPLC, and GC-MS. The herbal slimming product with the highest concentration comes from the city of Depok with a concentration of 26.24 mg/pill, China with a concentration of 78 mg/capsule.

Keywords: Obesity, Herbal Slimming, Sibutramine Hydrochloride, *Review*, Article

INTRODUCTION

Obesity is a very serious problem where the World Health Organization (WHO) states that cases of overweight and obesity are considered a problem that occurs in developed or high-income countries, not only that obesity rates have also increased in developing or low- and middle-income countries, which dominated by people who live in urban areas (World Health Organization, 2000). Basic health research (Riskesdas) in 2018 showed data from research conducted by the Ministry of Health (Kemenkes) found that the obesity rate in adults in Indonesia increased to 21,8% from previous research which experienced an increase in prevalence from 14,8% (Kementerian Kesehatan Republik Indonesia, 2018). One of the therapies that can be used to reduce obesity is traditional medicine. The use of traditional medicines made from herbs for obesity is considered safe because it has fewer side effects for the body compared to synthetic drugs (Wisnu et al., 2017)

According to the regulation of the Minister of Health, number 007 of 2012 article 7 concerning the Registration of Traditional Medicines states that in the preparation of traditional medicines there should be no medicinal chemicals (Peraturan Menteri Kesehatan RI, 2012). Referring to the ministerial regulation, the Food and Drug Supervisory Agency (BPOM) inspected the trade in herbal medicines suspected of

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containing medicinal chemicals and determined Sibutramine HCl as a medicinal chemical that is often added in herbal slimming products where in 2010, sibutramine HCl was withdrawn from the market. global market because it has been proven to have dangerous side effects such as psychosis, hepatitis, arrhythmias, and other side effects that are quite dangerous (Oberholzer et al., 2014). The widespread mixing of sibutramine HCl makes it necessary to conduct further studies to know the content of sibutramine hydrochloride in herbal slimming products in circulation and know the analytical method used to identify sibutramine hydrochloride in herbal slimming products. In addition, knowing the areas where herbal slimming products are distributed and knowing the highest levels of sibutramine hydrochloride in herbal slimming products.

The study of the distribution and content of sibutramine HCl in herbal slimming was carried out through a review of previous articles in which the article contained sibutramine HCl content in several slimming products that were circulating in the area. The review is carried out by taking samples of articles from several regions in Indonesia and other countries and processing the data obtained so that they are easier to understand and compare with each other. Further assessment of the content of sibutramine HCl is something to consider considering the side effects that can occur such as excitation of the central nervous system: nervousness, xerostomia, headache, numbness, and paresthesias, cardiovascular events, increased blood pressure, pulse, increased risk of a heart attack. and stroke (Ariburnu et al., 2012).

Sibutramine HCl or 1-(1-(4-Chlorophenyl) cyclobutyl)-3-methyl butyl-N, N-dimethylamine HCl H_2O is an antiobesity drug with efficacy as an anorexiant that has properties in suppressing or eliminating appetite. This class of drugs is used to support the diet process in treating obesity (Petkova-Gueorguieva et al., 2018). Sibutramine HCl is white in the form of a crystalline powder. In addition, Sibutramine HCl also has a BM of 334.3 g mol^{-1} and a melting point of 191.0192 °C. It is soluble in methanol and water (2.9 mg L1 at a pH of 5.2) (Sylvia et al., 2018). Barriers to the reuptake of noradrenaline and serotonin cause a feeling of fullness in patients who consume and reduce the desire to eat. The circulating herbal products with similar therapeutic effects to sibutramine HCl need to be studied further regarding the addition of medicinal chemicals into it. There are still a lot of traditional medicines that have been mixed with synthetic drugs and are not included in the packaging. There are still many herbal products added with medicinal chemicals, including herbal slimming products, this needs to be watched out for considering the practice of mixing medicinal chemicals into herbal medicines is an activity that violates the law (Khazan et al., 2014).

MATERIALS AND METHOD

The research design is the traditional literature review or literature review. The literature review is a research method by reviewing certain topics and emphasizing single questions that have been systematically identified, assessed, selected, and concluded according to predetermined criteria based on high-quality research evidence relevant to the research question. Traditional literature review studies are steps to collect data or sources related to certain topics and can be obtained from various sources such as journals, books, the internet, and other libraries.

The references used in this article review are based on previous studies. The articles used are published in journals in Indonesian or English. The article used is also related to the content of the Medicinal Chemical (BKO) Sibutramine HCl in herbal slimming products. Literature searches were carried out in PubMed, PubMed Central, Science Direct, Medigraphic, and the Google Scholar database. The literature search was carried out using the following keywords and strategies: "*analysis*" OR "*determination*" OR "*diagnosis*" OR "*screening*" AND "*sibutramine*" AND "*herbal*" AND "*slimming*" AND "*dietary*" AND "*supplements*" OR "*dietary supplements*" OR "*supplements*".

The literature used was selected with inclusion criteria (1) the year of publication of the journal within the last 10 years; (2) articles using both English and Indonesian, full text (3) articles containing methods and methods of identifying sibutramine HCl in herbal slimming products (4) articles used stating the number of positive samples containing sibutramine HCl (5) articles containing sibutramine HCl levels

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in herbal slimming products (6) articles that include research locations or herbal product sampling locations. The exclusion criteria for this review are (1) studies that describe cases of side effects of sibutramine HCl and (2) studies that only discuss the description of sibutramine HCl. The articles used to refer to the following criteria: (1) the clarity of the results obtained by the objectives to be achieved, (2) the accuracy of the author's results in reviewing the sources to be used, (3) the suitability of the studies listed in the article and have important meanings. , (4) the articles used have a decent quality as a source of study, (5) the results of the study can be accepted after merging with other articles. The study of the criteria of the article was carried out by two researchers.

The review articles reviewed include the author, year of publication, region, country of study, and the content of the article. The research design used in this article is non-experimental to determine the levels of Sibutramine HCl from samples of herbal slimming products sampled in each region. Other data needed from the article are the identification method used by the researcher in the article and the content of the levels in each preparation analyzed by the researcher. The data presentation of Sibutramine HCl levels in the description includes the percentage of products containing Sibutramine HCl and the highest levels of Sibutramine HCl.

RESULT AND DISCUSSION

Article Characteristics

The characteristics of the reviewed articles include the year and place of research. An article discusses the addition of sibutramine hydrochloride in herbal slimming products and the side effects of sibutramine hydrochloride. In addition, there are articles on analytical methods that can be used to detect the content of sibutramine hydrochloride. Several articles, articles were selected that discussed the acquisition of sibutramine hydrochloride levels in the herbal products reviewed. In addition, articles were seen from research that had been carried out in several countries such as China, Thailand, Turkey, and Indonesia. Weight loss products have side effects that occur differently for each person. According to research conducted in several countries, there are still some herbal slimming products mixed with sibutramine hydrochloride (Khazan et al., 2014; Phattanawasin et al., 2012). Countries and regions that research the content of sibutramine hydrochloride in herbal slimming products can be seen in the description of Table I.

Table I. Location and Form of Herbal Product Sample

Authors (Years)	Article Titles	Research Locations	Preparation Forms
(Wisnu et al., 2017)	Analysis of Sibutramine Hydrochloride Drug Chemicals in Slimming Herbs Circulating in Manado City	Manado	pills (made into powder)
(Petkova-Gueorguieva et al., 2018)	Detection of sibutramine in herbal food supplements by UHPLC/HRMS and UHPLC/MS-MS.	Tidak ada laporan	Capsules, tablets or pills
(Hayun et al., 2016)	Determination of Sibutramine Adulterated In Herbal Slimming Products Using TLC Densitometric Method	Depok City	Capsules and pills
(Khazan et al., 2014)	“Identification and Determination of Synthetic Pharmaceuticals as Adulterants in Eight Common Herbal Weight Loss Supplements”	China	Capsules and pills

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(Susila et al., 2013) (2013)	Identification and Quantification of the Medicinal Chemical Sibutramine in Slimming Herbs Circulating Surakarta Using the Uv-Vis Spectrophotometric Method	Surakarta	Capsules
(Sylvia et al., 2018)	Analysis of Sibutramine Hydrochloride in Slimming Herbal Medicine in Curug District Using UV Spectrophotometry	Kecamatan Curug	powders
(Phattanawasin et al., 2012)	Quantitative determination of sibutramine in adulterated herbal slimming formulations by TLC-image analysis method	Thailand	Coffee, slimming drink capsules

The dosage forms of slimming products that are suspected to contain sibutramine hydrochloride are different. Most of them are in pill and capsule form. Not a few are in the form of tablets and drinks such as coffee and slimming drinks. The literature listed in Table I shows that the mixing of sibutramine hydrochloride in herbal slimming products does not only occur in Indonesia but also occurs in China and Turkey. China itself is a country with fairly good use of herbs, but there is still the addition of medicinal chemicals to herbal slimming products. Besides China, several regions in Indonesia are also rife with mixing sibutramine hydrochloride with herbal or herbal slimming products which are sold in different dosage forms.

Identification Method of Sibutramine Hydrochloride

Determination of the content of Sibutramine hydrochloride can be used by several methods such as HPLC (Kanan *et al.*, 2009; Ancuceanu *et al.*, 2013; Khazan *et al.*, 2014), LC-MS / MS and TLC / HPTLC - densitometry (Phattanawasin *et al.*, 2012; Mathon *et al.*, 2014). Some of the articles reviewed used different methods which can be seen in Table II.

Table II. Sibutramine Hydrochloride Compound Analysis Method

Authors (Years)	Methods	How to Identify
(Wisnu et al., 2017)	UV-Vis Spectrofotometry	Identification was conducted using UV-Vis spectrophotometry. Quantitative analysis is done by first reading the maximum wavelength. After obtaining the wavelength, the standard curve series was read with concentrations of 5 µg/mL, 7.5 µg/mL, 10 µg/mL, 12.5 µg/mL, and 15 µg/mL prepared from a standard solution of sibutramine hydrochloride. After reading the standard curve series then proceed with the sample reading at the maximum lambda (266 nm).
(Petkova-Gueorguieva et al., 2018)	HPLC UHPLC	Identification was conducted using UHPLC / HRMS and UHPLC / MS-MS. Samples that had been prepared using 15 ml polypropylene and 80% Acetonitrile were then read using the mobile phase, namely Mobile phase A: 95% air / 5% acetonitrile (pH = 4.3; 10 mm ammonium formate), Mobile phase B: 95% acetonitrile / 5% air (pH = 4.3; 10 mm ammonium formate), Gradient: 50% cellular phase A / 50% cellular phase B.

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(Hayun et al., 2016)	TLC-Densitometry	Identification was conducted using TLC- Densitometry. The analysis was carried out by comparing the Rf value, UV spectrum, and color (after spraying with Dragendorff reagent). Samples and standards were spotted on the stationary phase (silica gel 60 F254) then eluted with toluene-diethylamine mobile phase (10: 0.3v/v) and then read with a densitometry instrument at 277 nm lambda
(Khazan et al., 2014)	GC-MS	Identification was conducted using GC-MS (Agilent 7000, Triple Quaed, GC7890A). with a capillary column [HP-5ms, 30 m (length), 0.25 mm (diameter), 0.25 μm (film)] used as the stationary phase. The initial temperature of the column was 50°C for 2 minutes, then increased to 290°C (5°C/min increase) for a total time of 36 minutes. The injector and detection temperatures are set at 250° and 300°C. The carrier gas phase used is helium, with a working flow rate of 1mL/min, and an injection volume of 1 μL.
(Susila et al., 2013)	UV-Vis Spectrofotometry	Identification was conducted using UV-Vis spectrophotometry by first reading the maximum wavelength. After obtaining the wavelength, the standard curve series was read with concentrations of 50, 75, 100, 125, and 150 μL prepared from a standard solution of sibutramine hydrochloride. After reading the standard curve series then proceed with the sample reading at the maximum lambda (223.5 nm).
(Sylvia et al., 2018)	UV Spectrophotometry	Identification was carried out using UV spectrophotometry. Quantitative analysis was carried out by first reading the maximum wavelength on the UV spectrophotometric instrument. After obtaining the wavelength, then reading the standard curve series with concentrations of 30, 40, 50, 60, and 70 ppm prepared from a standard solution of sibutramine hydrochloride. Furthermore, the prepared sample was then read at the maximum lambda (225 nm).
(Phattanawasin et al., 2012)	TLC-Densitometry	Identification was conducted using TLC-Densitometry. The analysis was conducted by comparing the Rf values, and UV spectrum. Samples and standards were spotted on the stationary phase (silica gel 60 F 254) and then eluted with toluene: hexane: diethylamine (9: 1: 0.3 v/v/v) mobile phase. The elution results were viewed at 254 nm UV light and read with a densitometry instrument.

The description of Table II shows that various methods can be used to identify the content of sibutramine hydrochloride in herbal slimming products. The identification used in each article shows that sibutramine hydrochloride can be identified by Thin Layer Chromatography (TLC). The polar nature of sibutramine hydrochloride allows sibutramine hydrochloride to be eluted together with a mobile phase having the same polarity. The mobile phase used must be optimized before use to obtain a truly maximal mobile phase in the elution of sibutramine hydrochloride. Another method that can be used is UV spectrophotometry because sibutramine hydrochloride has alternating double bonds or chromophore groups that make sibutramine hydrochloride have a wavelength of 200 – 400 nm. The HPLC method can also be used by utilizing the same polarity difference as TLC but the stationary phase used is in liquid form.

The method used in this article shows the advantages and disadvantages of each method. Articles that use the TLC-Densitometry method have a weakness in the elution results when viewed with 254 nm and 366 nm UV light. The spot elution results are not very visible so it is necessary to spray with

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Dragendroff's reagent besides the difference in the mobile phase also affects the resulting Rf value. As for the UV spectrophotometry method, it shows a difference in the maximum lambda obtained. The temperature difference may be due to the standard used being impure or having been contaminated by either the excipient or other substances. For the mobile phase HPLC method used, more attention must be paid to the preparation of the sample to be injected into the instrument so as not to affect the results obtained. As for the GC-MS method, it is necessary to pay attention to the temperature used so that the results obtained are more optimal where the temperature used for sibutramine hydrochloride is 290 °C for approximately 36 minutes.

Results of identification/analysis of Sibutramine

In addition to differences in the identification process, dosage form, the number of samples used, and trademarks are also the causes of differences in the levels obtained in each article. Of the 7 articles reviewed, several articles present the levels of sibutramine hydrochloride with very large values found in herbal products that are considered safe and fast in losing weight as listed in Table III.

Table III. Rate of Sibutramine Hydrochloride

Authors (Years)	Result
(Wisnu et al., 2017)	The results obtained from the 10 samples identified showed that all samples contained sibutramine hydrochloride with units of mg/mL in 200 mg samples: Sample A = 0.008124; Sample B = 0.003543; Sample C = 0.006732; Sample D = 0.012790; Sample E = 0.009479; Sample F = 0.019520; Sample G = 0.010613; Sample H = 0.015461; Sample I = 0.018444; Sample J = 0.009265
(Petkova-Gueorguieva et al., 2018)	The results of the 10 samples identified showed that 2 of them contained sibutramine hydrochloride with different levels, namely: Sample 5 of 0.005 mg/ 1 capsule and Sample 8 of > 20 mg/tablet;
(Hayun et al., 2016)	The results obtained from 7 samples identified 6 of which contained sibutramine as follows which were contained in mg/single dose units: AR (capsules) = 9.83 ±0.03; SU (capsule)= 2.45 ±0.01; DI (capsule) = 26.24 ±0.01; PL (pill) = NR; SL (capsule) = 20.47 ±0.19; LK (capsule) =15.97 ±0.11; LM (capsule) = 3.43 ±0.01
(Khazan et al., 2014)	The results obtained from 8 samples, 6 of which contain sibutramine as follows, are contained in units of mg/capsule or mg/pill: Original Super Slim = 78; Magic Slim = 6; Green Lean Super Slim = 15; Shangaya HG = NR; Herbaceous Essence = 30; Fast Slim = 57; Fat loss = 48; Mobic = NR
(Susila et al., 2013)	The results obtained from the 10 samples identified were 2 that were positive for sibutramine with units of mg/capsule: Sample A = 24; Sample F = 19
(Sylvia et al., 2018)	The identification results of the 4 samples of herbal medicine used showed that all samples contained sibutramine hydrochloride with levels in mg/mL in 200 mg samples: Sample 1 = 0.0030078; Sample 2 = 0.0050039; Sample 3 = 0.0037369; Sample 4 = 0.0020060
(Phattanawasin et al., 2012)	The results of the 20 samples identified were 6 samples containing sibutramine with units of mg/unit from two different methods (TLC-Image Analysis (a) and TLC-Densitometry (b)): S2 (slimming coffee (a) 11.85 (b) 12.27); S6 (slimming gel (a) 16.64 (b) 17.07); S7 (slimming coffee plus green tea (a) 6.75 (b) 6.82);

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S9 (slimming coffee (a) 16.36 (b) 16.36); S10 (slimming capsule (a) 19.98 (b) 20.63); S19 (slimming capsule (a) 23.57 (b) 24.16)

Research conducted by (Wisnu et al., 2017) used the UV-Vis spectrophotometry method as a quantitative analysis. Before conducting quantitative analysis, qualitative analysis was carried out using the Thin Layer Chromatography method. The stationary phase used is silica gel GF254 with an elution distance of 8 cm. In carrying out the analysis, samples and standards were spotted on the TLC plate and then eluted with ethyl acetate: n-hexane (7:3), acetone: chloroform (7:3), acetone: chloroform: n-hexane (5: 3:2). The number of mobile phase comparisons used aims to optimize the mobile phase so that it can be seen which mobile phase is the best in elution of sibutramine hydrochloride. The results of the elution of the three mobile phases used in the study showed that there was no similarity between the eluted samples and the resulting spots varied when read at 254 nm and 366 nm UV light. Readings on UV light can be done because sibutramine hydrochloride has a chromophore group (conjugated double bond) where the chromophore group can absorb electromagnetic radiation from UV light. The data obtained from the qualitative analysis is in the form of the Rf value that is the same or almost close to the standard Rf value. Samples that have the same Rf value as the standard will be further identified with UV-Vis spectrophotometric instruments. The absorbance results from the identified samples were then calculated using the linear regression equation $y = 0.0438x – 0.0532$ and the correlation coefficient $r = 0.9935$. This equation is obtained from the value of the calibration curve equation. The advantage of this article is the accuracy of the researchers from the results of qualitative analysis obtained one positive sample containing sibutramine hydrochloride then analyzed using UV spectrophotometry with the results showing all samples identified as containing sibutramine hydrochloride.

Research conducted by (Phattanawasin et al., 2012) used the TLC-Densitometry method as a qualitative and quantitative analysis where the method used was to compare two TLC methods, namely TLC-Image analysis and TLC-Densitometry. To sharpen the appearance of the band on the TLC plate, the plate was dipped in Dragendroff's reagent and produced an orange color indicating the presence of sibutramine hydrochloride. For the application of TLC-Image analysis, the plate that has been dipped in Dragendroff's reagent is then dried for 10 minutes for later digital scanning. The TLC-Image analysis is reading through a plate image scanned using a Hewlett Packard SCAN Jet 3500C at a resolution of 200 dpi. The photo of the plate that has been made has the correct size as the original (20 cm x 10 cm) with a resolution of 40 pixels and then reads with the Sorbfil TLC Video densitometer software. The results obtained from these two different TLC methods indicate that there is a not-too-significant difference, which is approximately 0.36 mg of the 6 samples that were positive for sibutramine hydrochloride. The advantage of this article is the application of the TLC-image analysis method where this method has similarities with the use of a densitometry instrument in the form of a photo scan so that the instrument used is simpler. However, the weakness of this method is that it requires special skills and more accuracy in adjusting the photo taken to the original size on the plate.

Research conducted by (Susila et al., 2013) also used TLC for qualitative analysis in which the mobile phase used was ethyl acetate: n-hexane (7:3), acetone: chloroform (7:3), acetone: chloroform: N-hexane (5:3:2). The elution results obtained were different which were influenced by the elution strength with the order of the elution strength values from the largest being acetone: chloroform (7:3), ethyl acetate: n-hexane (7:3), and acetone: chloroform: N- hexane (5:3:2). However, the Rf value shown by acetone: chloroform: N-hexane (5:3:2) is greater because the system is more polar than ethyl acetate: n-hexane (7:3) which has a smaller Rf value because it is not too polar. The advantage of this article is the use of three mobile phase comparisons. The three mobile phases showed different Rf values when irradiated with UV

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light of 254 nm and 366 nm. However, at 366 nm UV light, the elution spot of sibutramine hydrochloride is not visible, so accuracy is needed in determining the Rf value.

Research conducted by (Sylvia et al., 2018) used UV spectrophotometry as a qualitative and quantitative analysis in which samples that had been analyzed qualitatively and had the same absorption as the standard were then identified further to determine the levels of sibutramine hydrochloride in the sample. Sibutramine hydrochloride can be analyzed by the UV spectrophotometry method because it has a chromophore group (conjugated double bond) in the form of benzene chloride. The benzene group has a maximum lambda of about 200 nm when read using UV spectrophotometry, but sibutramine hydrochloride which has a benzene chloride group makes a shift in absorption towards bathochromic and makes sibutramine hydrochloride shift towards a larger value with a maximum shift value not exceeding 3% so that the obtained lambda of 230 nm. The shift that occurs can be caused because the standard used is not a pure standard but a standard that still contains excipients. After all, it is taken from sibutramine hydrochloride tablets. The excipients contained in this sibutramine tablet can affect the content of the active substance. The weakness of this article is that the standard used is derived from sibutramine hydrochloride tablets which still contain excipients so the maximum lambda obtained is not very precise and the number of samples identified is too small so it is feared that it will not meet the entire circulating sample.

Research conducted by (Petkova-Gueorguieva et al., 2018) to identify the presence of sibutramine hydrochloride in slimming products can also use the HPLC/UHPLC method where 2 samples containing sibutramine hydrochloride were obtained. Sample 5 was taken from 1 g of extract where the detector of the mass spectrometry scan ranged from 279.68 to 280.68 m/z and the mass spectrum peaked with a retention time of 1.48 minutes. As for the other samples using a combination of ion chromatography in the scanning range of 200 – 300 m/z. the analyte from the extracted chromatogram emits an electronic signal of 125 m/z and 139 m/z greater than 280 m/z, the characteristics of the analyte and the ESI mass spectrum include the reference solution which is to the left of the reference solution for the standard and is to the right of the reference solution. right for sample analysis. The weakness in this article is the use of units that are not the same between one sample and another, besides that the range of scans carried out on two samples that are positive for sibutramine hydrochloride has different values. The advantage of this article is the use of ultra HPLC so that it can detect small amounts of sibutramine hydrochloride.

The research of (Khazan et al., 2014) research was conducted to detect many types of slimming drugs that are commonly used as mixtures so two methods were used, namely GC-MS and LC-MS, while for detecting sibutramine hydrochloride the GC-MS method was used. This method can be used in identifying sibutramine because of the nature of sibutramine which easily melts at a temperature of 191.019 degrees Celsius so the application of this method using high temperatures is gradually expanded from 50 degrees Celsius to 290 degrees Celsius. The time used in the overall sample reading is 36 minutes, determined at a temperature of 250 and 300 degrees Celsius. MS detector conditions with ionization energy of 70 eV, in the mass range of 25 - 1000 amu. Identification of the number of constituent cations in the sample is carried out by comparing the mass variation and sample retention time and standard comparison data can be seen in the Wiley 275 and NIST libraries which are then connected to GC-MS. The advantages of this article are the use of two methods, namely GC-MS to identify the presence of sibutramine hydrochloride, phenolphthalein, bumetanide, and phenytoin and LC-MS to identify the presence of bumetadine in each herbal slimming preparation where in each preparation it is identified that it contains five synthetic slimming agents.

The articles reviewed show that there are still many herbal slimming preparations containing sibutramine hydrochloride where the methods used for identification include UV Spectrophotometry, TLC-Densitometry, HPLC, and GC-MS. The articles reviewed were carried out in several regions in Indonesia such as Depok, Tangerang, Surakarta, and Manado, and other countries such as China and Thailand. The highest levels of content in each article are as follows: 0.019520 mg/mL; > 20 mg/tablet; 26.24 mg/ single dose; 78 mg/capsule; 24 mg/capsule; 0.0050039 mg/mL; 24.16 mg/unit; 12mg/1.76 grams. Of the seven

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articles reviewed, there were two articles whose levels of sibutramine hydrochloride in each sample contained less than 10 mg of sibutramine hydrochloride or it could be said that it did not exceed the minimum dose of sibutramine hydrochloride. However, there should be no medicinal chemicals in herbal preparations so the presence of sibutramine hydrochloride in herbal slimming products is not allowed.

CONCLUSION

The seven articles reviewed showed that herbal slimming products were identified as containing 52, 17% Sibutramine hydrochloride out of a total of 69 samples analyzed using the Sibutramine hydrochloride content analysis method including TLC- Densitometry, HPLC/UHPLC, GC-MS, UV-Vis Spectrophotometry. Herbal slimming products containing sibutramine hydrochloride are circulating in Indonesia in Manado, Depok City, Surakarta, Curug District (Tanggerang City), China, and Thailand with the highest levels of sibutramine hydrochloride at 26.24 mg/capsule in Depok and 78 mg/pill in China.

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