Evaluation of Indonesian Anti-obesity Traditional Medicinal Plants: A Systematic Review and Meta-analysis on Pancreatic Lipase Inhibition Activity

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Research

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Research

Evaluation of Indonesian Anti-obesity Traditional Medicinal Plants: A Systematic Review and Meta-analysis on Pancreatic Lipase Inhibition Activity

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Abstract

Background: Researches and publication discussing performance of medicinal plants as anti-obesity have proliferated in recent years. In the view of ethnopharmacology, empiric evidence of Indonesian medicinal plants in management of obesity is widely accepted. In attempt to find anti-obesity agent, it is evidenced that the disorder can be resolved through inhibition of pancreatic lipase since the mechanism allowed to retard absorption of fat into cells. This current work aimed to screen Indonesian medicinal plants by using ethnopharmacology and meta-analysis approaches, emphasizing their ability to deal with obesity via pancreatic lipase inhibition.

Methods: The study followed two stages, i.e. systematic review and meta-analysis. Data from 6 scientific (Scopus, Science Direct, Proquest, Ebsco, Cengage Library and Emerald) were collected, screened according to inclusion and exclusion criteria. The eligibility of the trials was determined according to criteria as follows: (1) design for lipase inhibition experiments; (2) population in all researches using in vitro protocols for antiobesity in last 10 years; (3) intervention for comparison between lipase inhibition IC50 properties of selected medicinal plants and orlistat; and (4) data adequacy enabling to estimate the standardized mean difference (SMD) and the corresponding 95% confidence interval (CI). Further, all published papers we reviewed were written in English. Furthermore, steps of meta-analysis were performed on the selected data. Extraction of data in these articles collected number of

samples, average values and standard deviation of IC50. The values focused on IC50 of samples in inhibiting lipase activities performed by plant extracts and orlistat as control.

Result: A total 10 selected data meet the inclusion criteria. Morever these plant can be found and common as traditional medicine plant in Indonesia

Conclusion: As the results, there were top 10 anti-obesity medicinal plants as follows: i.e. *kelor* (*Moringa oleifera*) leaves, *kemangi* (*Ocimum basilicum*) leaves, *asam jawa* (*Tamarindus indica*) leaves, *asam gelugur* (*Garcinia atroviridis*) fruit, *lengkuas* (*Alpinia galanga*) rhizome, and *kencur* (*Kaempferia galanga*) rhizome, *kumis kucing* (*Orthosipon aristatus*) leaves, *jambu biji* leaves (*Psidium guajava* leavaes), *serai wangi* (*Cymbopogon nardus*) and *kayu secang* (*Caesalpinia sappan*).

Keywords: antiobesity; ethnopharmacology; Indonesian medicinal plants; lipase pancreas inhibition; meta-analysis

1. Introduction

Obesity is medically characterized as excess adiposity in tissues as a result of disparity between energy intake and energy expenditure [1]. Currently, the prevalence is rising at alarming rate reaching approximately three times within 1975 – 2016, and therefore becomes health issues worldwide [2]. In 2016, WHO reported that more than 1.9 billion adults were overweight, while 650 million of them were obese. [2]. Furthermore, obesity prevalence continues to rise, not only in adults, but also in children and teenagers [3]. With a rapid growing prevalence, obesity receives serious concern since it is associated with degenerative diseases such as diabetes, heart and liver disease, stroke, hypertension, hypercholesterolemia, kidney failure and osteoarthritis [3].

In Indonesia, obesity has become foremost nutrition concern besides stunting [4]. The case in this country markedly increased in 2007-2018. Obesity proportion of Indonesian adults with body mass index (BMI) of ≥27 in 2007, 2013, and 2018 reaches 10.5, 14.8, and 21.8, respectively, while the average proportion of obesity is 21.8. Specifically, the highest proportion is found in Province of Sulawesi Utara (30.2); in contrast, the lowest one is attributed to Province of Nusa Tenggara Timur (10.3) [4]. Regarding the current obese cases, there is a need to treat obesity using therapy and medical approaches.

Medical treatments for obesity can be performed through orlistat and sibutramine [5]. Orlistat induces weight loss by alleviating intestinal fat absorption via inhibition of pancreatic lipase [6] [7]. Sibutramine (reductil) is an anorexic drug widely accepted for anti-obesity treatment, and able to reduce palatable food intake [7]. However, both drugs are then associated with deleterious side effects such as rising blood pressure, headache, insomnia, constipation and dry mouth [7]. Alternatives to these drugs are often applied to treat obesity, such as radafaxine and

oleoyl-estrone, which modulates peripheral episodic satiety signals, i.e. rimonabant and APD356, while other drugs such as cetilistat and AOD9604 inhibit fat absorption [8, 9]. The side effects of using these anti-obesity drugs are main reason for searching safe treatments of obesity, including herbal medicines [7].

Studies on the use of herbal plants for management of anti-obesity have been carried out, as attempt to find safe and healthier drugs [10]. Indonesian indigenous herbal plants vary greatly, and among them, 76 of the plants are evidenced to exert anti-obesity properties [11]. Previous researches reported performance of anti-obesity treatments using some herbal plants such as jati belanda (*Guazuma ulmifolia*), kemuning (*Murraya paniculata*) leaves, kelembak (*Rheum officinale*) roots, tempuyung (*Sonchus arvensis*) leaves [12,13]; sirih merah (*Piper crocatum*) [14]; asam gelugur *(Garcinia atroviridis)*, kunci pepet, (*Kaempferia rotunda),* lengkuas *(Alpinia galanga)*, daun asam Jawa *(Tamarindus indica* leaves*)*, kencur (*Kaempferia galanga*) [15,16]; and teh hitam (*Camelia sinensis*)[17]. The herbs for obesity treatment registered in Permenkes No. 6 Year 2016 about Indonesian indigenous herbs-based drugs included jati belanda and kemuning.

Attempts to find the efficacy of some potential plants for anti-obesity treatment still continue, emphasizing the roles of phytochemical bioactivities. Some of the bioactive compounds were reported capable of reducing obesity, including polyphenols, saponin, alkaloid, flavonoid, and saponin [18]. How these chemicals work is intriguing, since they display different mechanisms, i.e. satiety modulation, inhibition of adipogenesis and fat absorption, as well as retardation of pancreatic lipase [19]. With the growing researches discussing the topic, some evidences elucidated how the phytochemicals work for anti-obesity treatments, grouped into 5 basic mechanisms: (1) lowering lipid absorption, (2) decreasing energy intake, (3) rising energy expenditure, (4) suppressing differentiation and proliferation of preadipocyte and (5) declining lipogenesis while enhancing lipolisis [10]. Pancreatic lipase constitutes a pivotal enzyme responsible for fat absorption into cells, and this enzymatic activity can be hindered by tetrahydroplistatin (orlistat) [10]. In this regard, inhibiting pancreatic lipase is one the key mechanism in dealing with obesity. The inhibition of lipase can be expressed as IC50 or % inhibition.

Studies pertaining to inhibition of pancreatic lipase for anti-obesity have increased markedly worldwide. However, meta-analysis on anti-obesity treatments via pancreatic lipase restriction induced by Indonesian plant chemicals is not available. This present work aimed to screen medicinal plants originating from Indonesia that possesses anti-obesity properties based on their ability inhibit pancreatic lipase. Main data included inhibition of lipase (IC50 value) with orlistat as control.

2. Materials and Methods

2.1. Literature Search

This research referred to the guidelines of a meta-analysis handbook [20]. Relevant studies published in various electronic databases such as Proquest, Science Direct, Ebsco, Cengage Library, and Emerald for inhibitory lipase pancreatic were identified (up to May 2021). The four studies that we used in this research can also be found in the PubMed and Embase database.

Keywords used in the search strategy included "antiobesity", "medicinal plants", "lipase inhibition", and "antihiperlipidemia". After reading the titles and abstracts, we excluded irrelevant studies using Collandrapp. Subsequently, we examined the full text of all remaining articles to determine eligibility. The discrepancies were verified by discussion and consensus. We also reviewed the identified trials and review articles in reference lists to find any other potential proper articles.

2.2. Eligibility Criteria

The eligibility of the trials was determined according to criteria as follows: (1) design for lipase inhibition experiments; (2) population in all researches using *in vitro* protocols for antiobesity in last 10 years; (3) intervention for comparison between lipase inhibition IC50 properties of selected medicinal plants and orlistat; and (4) data adequacy enabling to estimate the standardized mean difference (SMD) and the corresponding 95% confidence interval (CI). Further, all published papers we reviewed were written in English.

2.3. Data Extraction

Data from each included study were extracted and integrated into the database. The following information was collected: first author, year of publication, country of origin, number of experiments, intervention, control, solvent, method, and outcomes data (IC50 lipase inhibition).

2.4. Statistical Analysis

Calculation in meta-analysis was carried out using Hedge's method [21]. Data processing employed open source software OpenMEE. Because all the observation indexes are continuous, and the measurement time of out-

come is inconsistent across studies, we pooled the SMD with a corresponding 95% CI using the random-effects model. The variable used for subgroup analysis was Indonesian name of traditional medicine.

3. Results

3.1 Systematic Review Diagram

A total of 326 articles (from 810 articles) was selected for full-text review, resulting in four articles that best fit inclusion criteria. Four hundred eighty four of them were rejected due to irrelevant content. Nine additional articles from reference lists of identified trials were included in the study because they met the inclusion criteria. Then, 331 articles were excluded because they did not meet the criteria (8 review articles, 31 articles not discussing Indonesian medicinal plants, and 291 articles with no available data for analysis). In total, the meta-analysis involved four articles included ten Data, as exhibited in Figure 1.

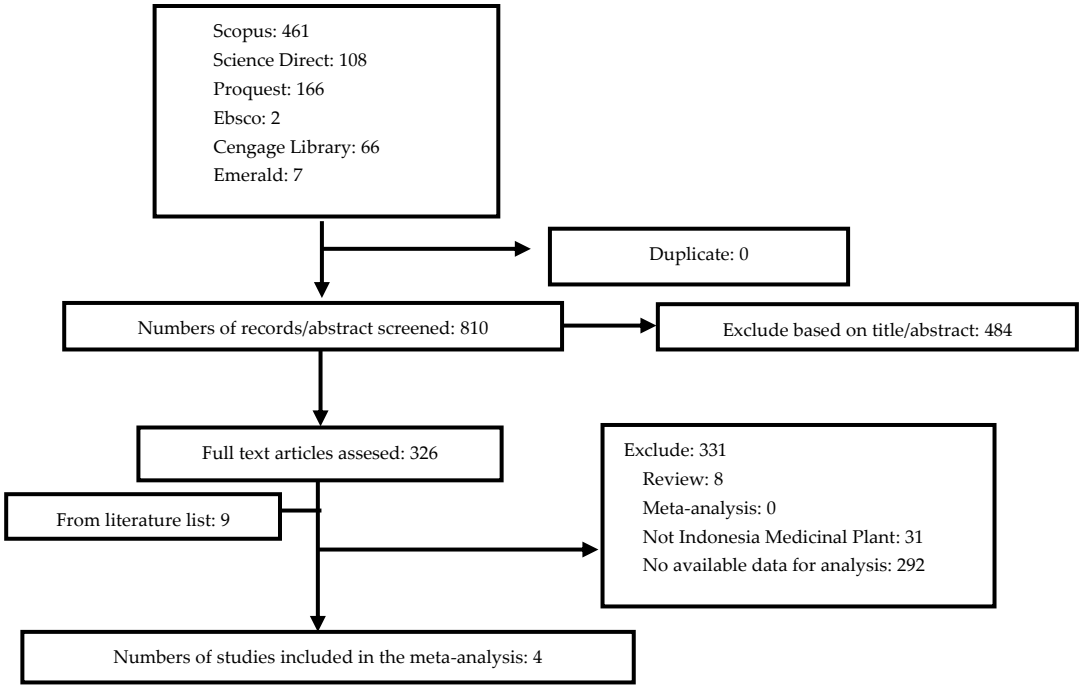

Figure 1. The PRISMA flow chart of the literature review process

3.2. Characteristics of Articles

Ten studies involving 30 experiments were published from 2012 to 2021. The PICO of this research is defined as Participants, Interventions, Comparisons, Outcomes, and Study Design. Participants in in vitro experiment were IC50 lipase inhibition. Interventions were Indonesian medicinal plants, while anti-obesity

medicine, i.e. orlistat was used as comparison. Outcome of this research was the best potential lipase inhibition activity by Indonesian medicinal plant. The study design used in this research was the randomized control.

3.3 Profile of pancreatic lipase inhibition by Indonesian medicinal plants.

In this work, IC50 value represents the inhibitory activity against pancreatic lipase, meaning the concentration of a drug that gives a half-maximum response. Lower value of IC50 denotes that the drug shows more powerful inhibition. As a consequence, in this work, we searched for medicinal plants with lowest value of IC50. To select the potential plants, we discarded rare or not popular plants such as johar, ginko biloba, daun seribu, delima, jeruk bali, and kapulaga sabrang. Additionally, the exclusion also referred to their IC50 close to selected medicinal plants.

Forest plot (Figure 2) exhibits average and CI 98% of Indonesian medicinal plants displaying anti-obesity properties, i.e. 13.42 [-0.05, 26,89] with I^2= 89.98% and P<0.001. In this regard, we found kelor (*Moringa oleifera*) possessing value lower than the average, i.e. 3.61 [1.70, 5.52]. Kemangi (*Ocimum basillicum*) also shows a relatively low IC50 in comparison with other studied plants. Therefore, referring to IC50, two Indonesian medicinal plants showing the best inhibition against pancreatic lipase were kelor and kemangi.

Kelor leaves showed a considerable inhibition of pancreatic lipase, while also significantly reducing body mass index of obese rats [22]. Using in vivo experiment, it was evidenced able to improve lipid profiles, i.e. reducing total cholesterol, triglycerides, low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), increasing high-density lipoprotein (HDL), modulating fat deposition through down-regulating the expression of adipogenesis-associated proteins peroxisome proliferator-activated receptor gamma (PPARγ) and fatty acid synthase (FAS), up-regulating expression of lipolytic protein (adipose triglyceride lipase (ATGL), as well as reducing leptin concentration [23]. An A previous study using 3T3-L1 cells revealed that kelor leaves could diminish expression of protein accounting for adipogenesis and lipogenesis [24]. In case of Indonesian medicinal plants, the studies discussing anti-obesity treatments worked with adiposity test under in vitro experiment (evaluation based on % lipid accumulation and % glycerol release) involving 76 plants, as the results, red ginger (Zingiber officinale var. rubrum) showed the most effective drug on treatment of obesity. Meanwhile, kelor was also included in top 5 plants [11]. Intriguingly, kelor has been accepted as one of the top 50 future foods since it is rich in health-improving bioactivities [25].

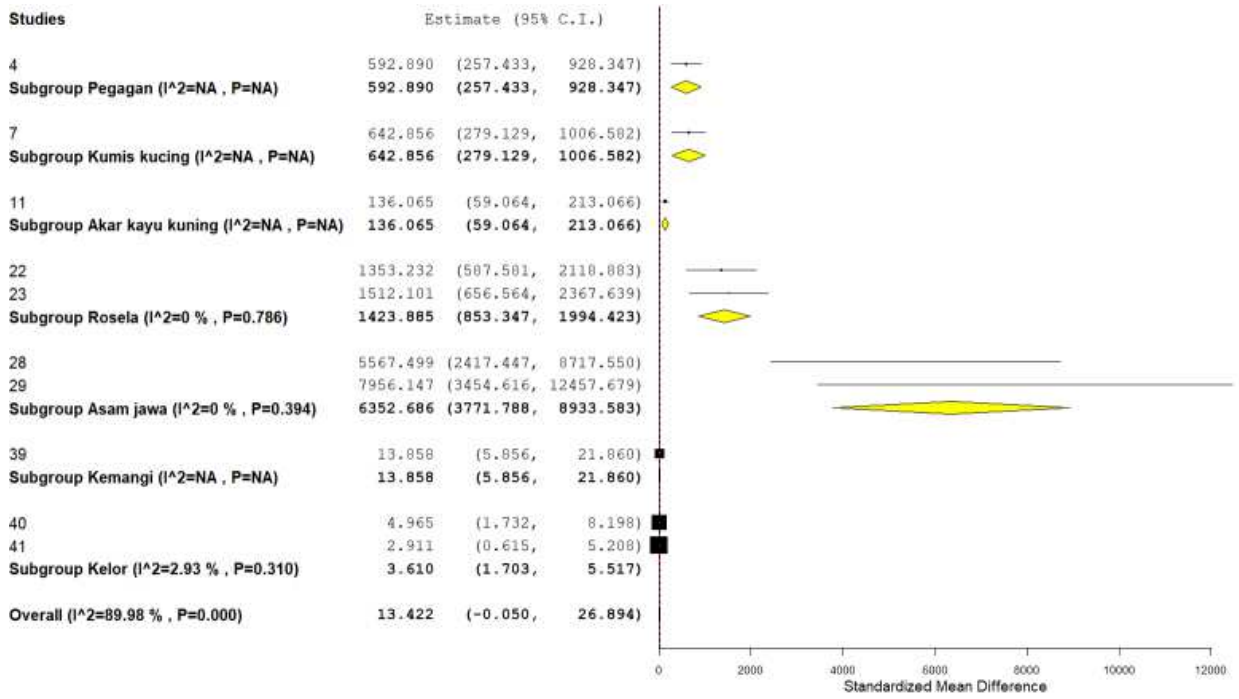

Figure 2. Forest Plot of IC50 Lipase pancreas

Note: Subgroup analysis of the lipase pancreatic inhibition capacity in Indonesian medicinal plants. Standardized mean difference (SMD), confidence interval (CI), and point represent the estimated overall effect size (with 95% CIs) for each study. Positive values indicate relatively higher IC50 pancreatic lipase inhibition in Indonesian medicinal plant. Negative values indicate relatively lower IC50 pancreatic lipase inhibition in Indonesian medicinal plant.

4. Discussion

In this work, we reported phytochemicals in Indonesian medicinal plants that are able to serve as anti-lipase, including phenolic, flavonoid, polyphenol and niazirin (Figure 3). Based on forest plot, the overall score reached 3.6 [1.7, 5.5], while specifically, score for phenolic and flavonoid was 13.86 [5.86, 21.86] and niazirin reached 3.610 [-0.1, 26.9].

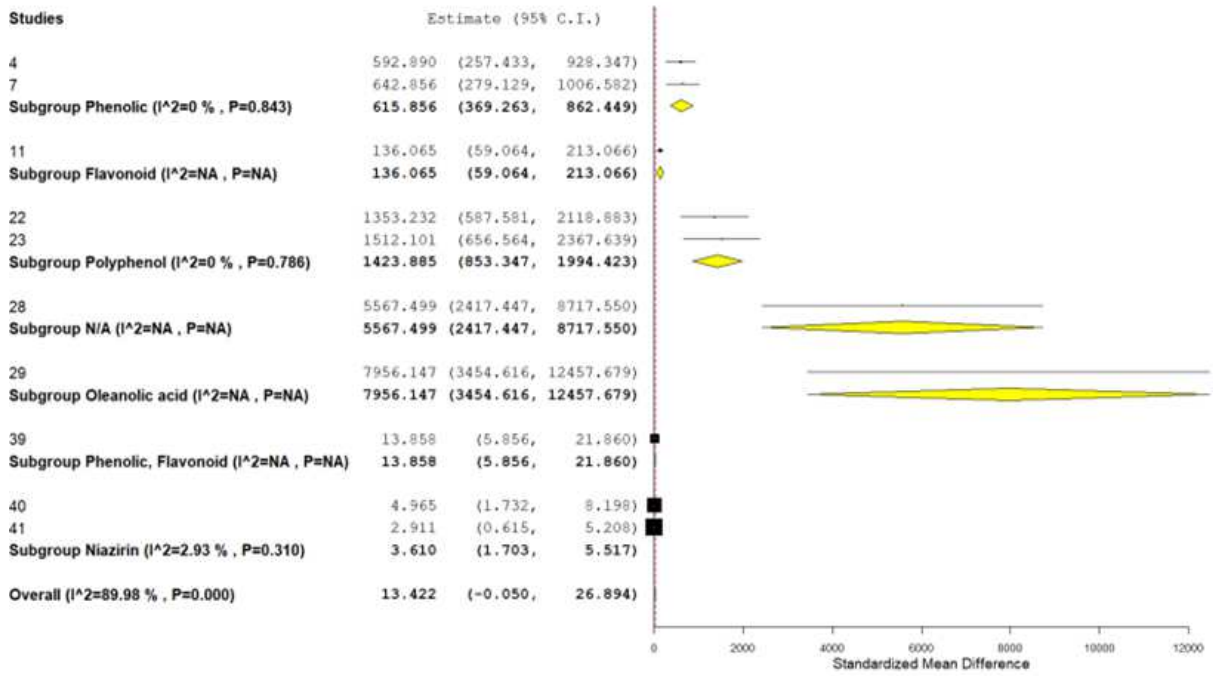

Figure 3. Forest plot of bioactive compounds from Indonesian medicinal plants.

Four main classes of phytochemicals showing anti-obesity effects are alkaloid, phytosterol, polyphenol and terpenoid [26]. Rajan *et al.* (2020) [27] reported 5 bioactive compounds that exert lipase inhibitory effects; and they included phenolic, flavonoid, saponin, alkaloid and terpenoid. To evaluate their inhibition capacity, IC50 value of lipase inhibition can be a proper indicator, resulting that flavonoid possesses low value, meanwhile the other groups (saponin, terpenoid and flavonoid) show a high value of IC50. Regarding their mode of action, anti-obesity effect by flavonoid relates with its ability to reduce lipid accumulation, total cholesterol and pancreatic lipase activity [28,29]. Meanwhile, saponin acts as anti-obesity agent through regulation of thermogenesis, lipogenesis and lipolysis [30].

4.2 Proper solvent for bioactive compound extraction

Phytochemicals responsible for anti-obesity can be extracted using various solvents. As depicted in Figure 4, meta-analysis revealed that methanol showed the most proper solvent in the extraction of anti-obesity phytochemicals in Indonesian medicinal plants, with score of 4.18 [-5.3, 13.7], while the overall average reaching up to 13.4 [-0.05, 26.9].

Besides methanol, phytochemicals showing pancreatic lipase inhibition can be isolated by water and ethanol. However, each solvent shows dissimilar performance on how they extract anti-pancreatic lipase phytochemicals, with a following sequence: ethanol> methanol>water [31, 32].

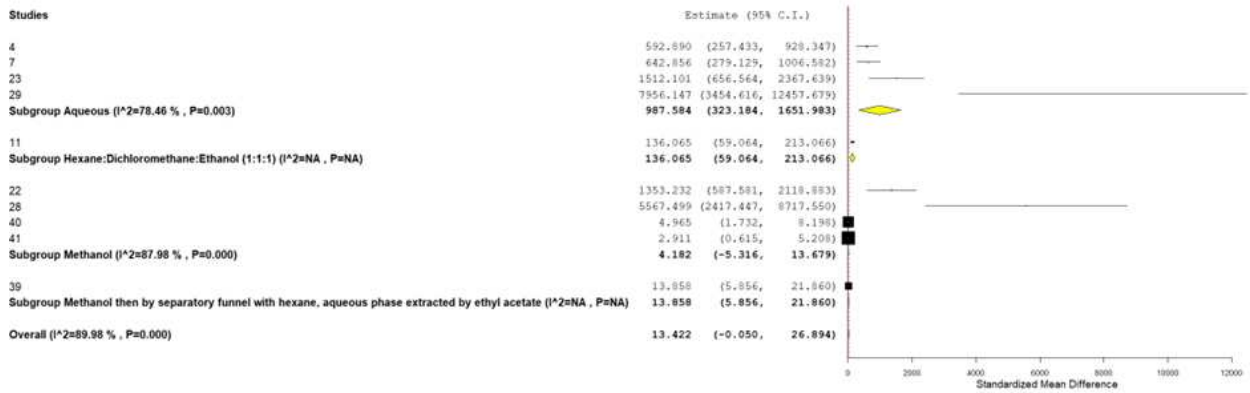

Figure 4. Forest plot of solvents applied to extract phytochemicals in Indonesian medicinal plants

4.3 Anti-obesity performed by Indonesian medicinal plants

We collected research data related to anti-obesity effects by Indonesian medicinal plants as well as by orlistat as control, covering IC50 value, average and standard deviation. Regarding incompletion of data, we summarized other indicators that support the analysis. Summary of data collected from various references was presented in Table 1. The extract of medicinal plants can be a potential candidate of anti-obesity when its lipase inhibition capacity ranged 75-100%. In addition, the extract with the inhibition capacity of 50-70% and 25-50% was grouped as moderate and low, respectively, and no anti-lipase activity occurred when the capacity was <25% [33]. After comparing the capacity for each plant, we found some plants that show high lipase pancreas inhibition capacity, including *kemuning, meniran, daun kumis kucing, serai wangi, kayu secang, daun murbei, jahe, daun alpukat, jambu biji* leaves, and *jambu air* leaves [Table 1].

Bibliometric data in Scopus database processed by VoS Viewer indicates 4 research clusters focusing on the use of medicinal plants for treatment of obesity. Each cluster color occurs differently. Studies on obesity consider experimental animal, diet, body weight, review articles and medicinal plant used. Meanwhile, studies on the effect of anti-obesity are restricted to some aspects such as inhibitory activity, high-fat diet, evaluation of anti-obesity, pancreatic lipase and medicinal plants linked to their phytochemical profiles (Figure 5).

Investigation of anti-obesity treatments was carried out within 2011-2013, while numerous researches on pancreatic lipase, medicinal plants and obesity were reported within 2013-2015. Studies discussing phytochemicals were reported in 2016. It is noteworthy that studies discovering inhibition, effects of anti-obesity and pancreatic lipase are rather scarce as indicated by dark green color. Sweileh *et al*. (2017) [44] reported bibliometric analysis of obesity focusing on its relation to other topics, involved countries and authors. penulis referensi. In this regard, the

obesity-related topics covered weight reduction and physical activities, while countries dominantly contributing to the topic were USA, UK and Canada. Additionally, the foremost author in this research topic was Whittaker R.

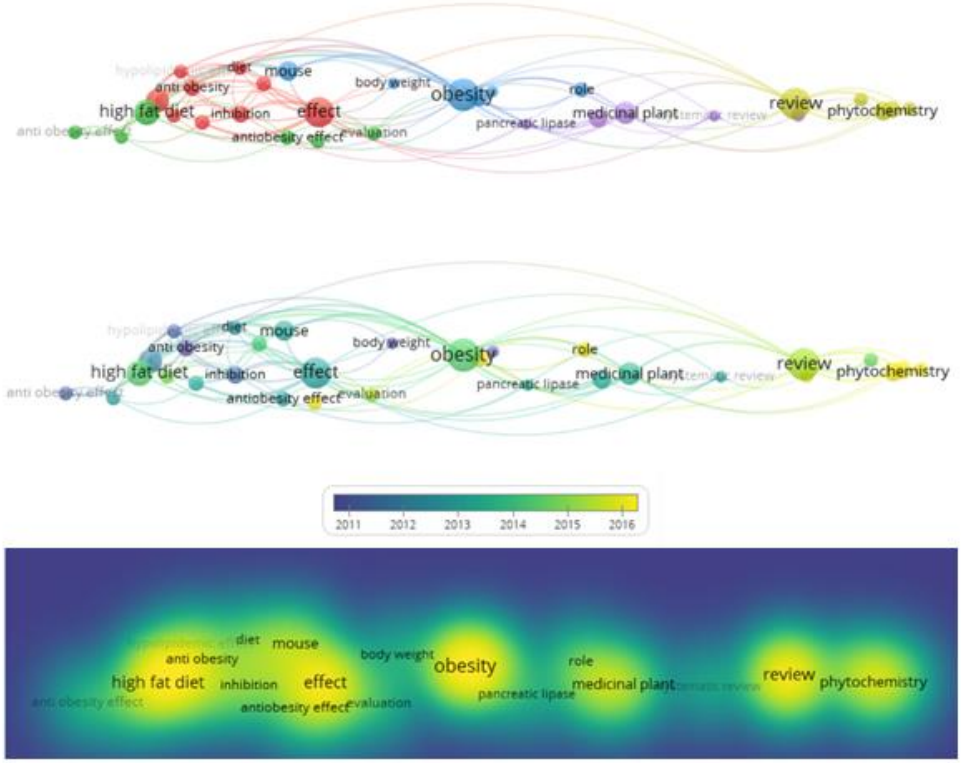

Figure 5. Distribution of medicinal plants and anti-obesity referring to Scopus database.

4.4 Anti-obesity capacity of Indonesian medicinal plants based on inhibition and sample number

Scientific data of some Indonesian medicinal plants are unavailable. In several cases, the paper only reported average values and number of samples, but did not inform standard deviation. To deal with this incompletion, effect size was calculated according to logarithmic natural response ratio (lnR), while the variation was determined using non-parametric variance (V_{lnR}) [45]. Considering % inhibition used as indicator, the best data located on the right of vertical line (Figure 6). Using the results of meta-analysis, Indonesian medicinal plants that showed anti-obesity properties included leaves and fruit of asam jawa (*Tamarindus indica*), asam gelugur (*Garcinia atroviridis*), *Garcinia atroviridis* fruit (*asam gelugur*), lengkuas (*Alpinia galanga)* rhizome, and kencur (*Kaempferia galanga)* rhizome.

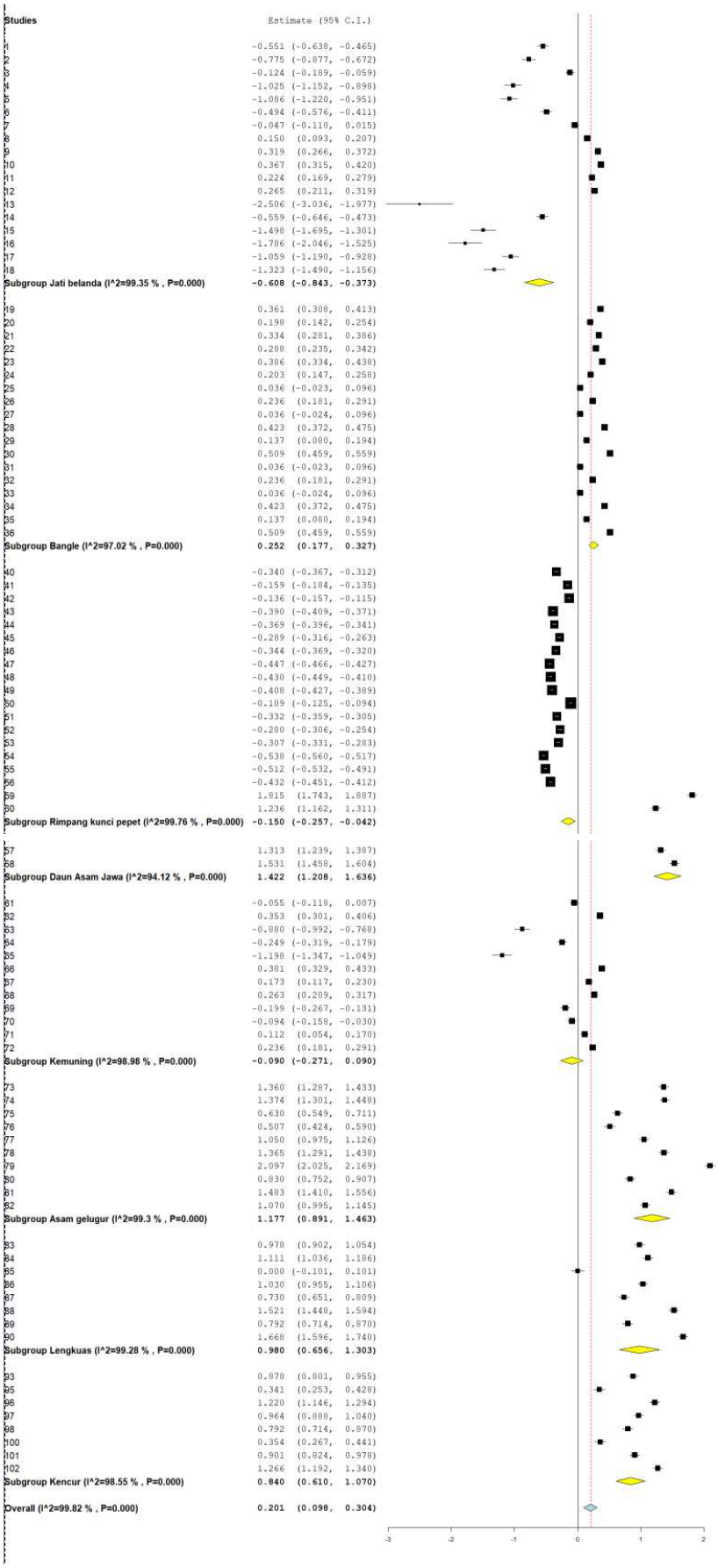
Studies
Estimate (95% C.I.)
1 -0.551 (-0.638, -0.465)
2 -0.775 (-0.877, -0.672)
3 -0.124 (-0.189, -0.059)
4 -1.025 (-1.152, -0.898)
5 -1.086 (-1.220, -0.951)
6 -0.494 (-0.576, -0.411)
7 -0.047 (-0.110, 0.015)
8 0.150 (0.093, 0.207)
9 0.319 (0.266, 0.372)
10 0.367 (0.315, 0.420)
11 0.224 (0.169, 0.279)
12 0.265 (0.211, 0.319)
13 -2.506 (-3.036, -1.977)
14 -0.559 (-0.646, -0.473)
15 -1.498 (-1.695, -1.301)
16 -1.786 (-2.046, -1.525)
17 -1.059 (-1.190, -0.928)
18 -1.323 (-1.490, -1.156)
Subgroup Jati belanda (I^2=99.35 % , P=0.000) -0.608 (-0.843, -0.373)
19 0.361 (0.308, 0.413)
20 0.198 (0.142, 0.254)
21 0.334 (0.281, 0.386)
22 0.288 (0.235, 0.342)
23 0.386 (0.334, 0.438)
24 0.203 (0.147, 0.258)
25 0.036 (-0.023, 0.096)
26 0.236 (0.181, 0.291)
27 0.036 (-0.024, 0.096)
28 0.423 (0.372, 0.475)
29 0.137 (0.080, 0.194)
30 0.509 (0.459, 0.559)
31 0.036 (-0.023, 0.096)
32 0.236 (0.181, 0.291)
33 0.036 (-0.024, 0.096)
34 0.423 (0.372, 0.475)
35 0.137 (0.080, 0.194)
36 0.509 (0.459, 0.559)
Subgroup Bangle (I^2=97.02 % , P=0.000) 0.252 (0.177, 0.327)
40 -0.340 (-0.367, -0.312)
41 -0.159 (-0.184, -0.135)
42 -0.136 (-0.157, -0.115)
43 -0.390 (-0.409, -0.371)
44 -0.369 (-0.396, -0.341)
45 -0.289 (-0.316, -0.263)
46 -0.344 (-0.369, -0.320)
47 -0.447 (-0.466, -0.427)
48 -0.430 (-0.449, -0.410)
49 -0.408 (-0.427, -0.389)
50 -0.109 (-0.125, -0.094)
51 -0.332 (-0.359, -0.305)
52 -0.280 (-0.306, -0.254)
53 -0.307 (-0.331, -0.283)
54 -0.538 (-0.560, -0.517)
55 -0.512 (-0.532, -0.491)
56 -0.432 (-0.451, -0.412)
59 1.815 (1.743, 1.887)
60 1.236 (1.162, 1.311)
Subgroup Rimpang kunci pepet (I^2=99.76 % , P=0.000) -0.150 (-0.257, -0.042)
57 1.313 (1.239, 1.387)
58 1.531 (1.458, 1.604)
Subgroup Daun Asam Jawa (I^2=94.12 % , P=0.000) 1.422 (1.208, 1.636)
61 -0.055 (-0.118, 0.007)
62 0.353 (0.301, 0.406)
63 -0.880 (-0.992, -0.768)
64 -0.249 (-0.319, -0.179)
65 -1.198 (-1.347, -1.049)
66 0.381 (0.329, 0.433)
67 0.173 (0.117, 0.230)
68 0.263 (0.209, 0.317)
69 -0.199 (-0.267, -0.131)
70 -0.094 (-0.158, -0.030)
71 0.112 (0.054, 0.170)
72 0.236 (0.181, 0.291)
Subgroup Kemuning (I^2=98.98 % , P=0.000) -0.090 (-0.271, 0.090)
73 1.360 (1.287, 1.433)
74 1.374 (1.301, 1.448)
75 0.630 (0.549, 0.711)
76 0.507 (0.424, 0.590)
77 1.050 (0.975, 1.126)
78 1.365 (1.291, 1.438)
79 2.097 (2.025, 2.169)
80 0.830 (0.752, 0.907)
81 1.483 (1.410, 1.556)
82 1.070 (0.995, 1.145)
Subgroup Asam gelugur (I^2=99.3 % , P=0.000) 1.177 (0.891, 1.463)
83 0.978 (0.902, 1.054)
84 1.111 (1.036, 1.186)
85 0.000 (-0.101, 0.101)
86 1.030 (0.955, 1.106)
87 0.730 (0.651, 0.809)
88 1.521 (1.448, 1.594)
89 0.792 (0.714, 0.870)
90 1.668 (1.596, 1.740)
Subgroup Lengkuas (I^2=99.28 % , P=0.000) 0.980 (0.656, 1.303)
93 0.878 (0.801, 0.955)
95 0.341 (0.253, 0.428)
96 1.220 (1.146, 1.294)
97 0.964 (0.888, 1.040)
98 0.792 (0.714, 0.870)
100 0.354 (0.267, 0.441)
101 0.901 (0.824, 0.978)
102 1.266 (1.192, 1.340)
Subgroup Kencur (I^2=98.55 % , P=0.000) 0.840 (0.610, 1.070)
Overall (I^2=99.82 % , P=0.000) 0.201 (0.098, 0.304)
-3
-2
-1
0
1
2

Figure 6. Meta-analysis of Indonesia medicinal plants with anti-obesity properties estimated by their inhibition of pancreatic lipase.

5. Conclusions

In general, this present work reported that *Moringa oleifera* leaves demonstrated the most potential anti-obesity in comparison with other Indonesian medicinal plants. This finding referred to the result of meta-analysis covering 810 articles from 6 scientific databases. In addition, based on evaluation of lipase inhibition by medicinal plants, we presented 10 potential plants for management of obesity, i.e. *Moringa oleifera* leaves, *Ocimum basilicum* leaves, *Tamarindus indica* leaves, *Garcinia atroviridis* fruit, *Alpinia galanga* rhizome, and *Kaempferia galanga* rhizome, *Orthosipon aristatus* leaves, *Psidium guajava* leavaes, *Cymbopogon nardus* and *Caesalpinia sappan*. The evaluation of their anti-obesity effects conformed to inhibition of pancreatic lipase activity expressed as IC50.

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Author Contributions

All authors' responsibilities were as follows: designed the subject and revised the article, H., DNF; developed inclusion and exclusion criteria, developed and performed the search strategy, conducted the statistical analysis and wrote the article FAA, ENQ, H, DNF; screened relevant literature, made decisions according to inclusion and exclusion criteria FAA, ENQ.

Availability of data and materials

All data are available in the corresponding author email: hasim@apps.ipb.ac.id

Ethics approval and consent to participate

All the authors agree with the manuscript and consent to participate in it.

Consent for publication

The authors give their consent for publication of this manuscript

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Conflicts of Interest

The authors declare no conflict of interest

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TABLE 378

Table 1. List of Indonesian medicinal plants showing anti-obesity effects 379

No.	Plant source Indonesian name	Species name (latin name)	IC_{50}	Orlistat (%)	Lipase inhibition (%)	n	Concentration (mg/mL)
1.	Angkak [34]	Red yeast rice	61.2 ± 5.1	-	-	3	-
2.	Kunci Pepet [35]	*Kaempferia rotunda*	-	10.6	5.8	3	0.10
3.	Daun asam Jawa [35]	*Tamarindus Indica* leaves	-	10.6	10.8	3	0.10
4.	Asam gelugur [15]	*Garcinia atroviridis*	-	10.6	41.3	3	0.10
5.	Lengkuas [15]	*Alpinia galanga*	-	10.6	28.2	3	0.10
6.	Kencur [15]	*Kaempferia galanga*	-	10.6	25.5	3	0.10
7.	Bangle [32]	*Zingiber cassumunar* Roxb.	-	17.53	21.47	3	0.10
8.	Jati Belanda [32]	*Guazuma ulmifolia*	-	17.53	10.70	3	0.10
9.	Kemuning [36] (IC50 Orlistat: 1.71 µg/mL) [37]	*Murraya paniculata*	55.18 µg/mL	17.53 99.6 ± 0.3	25.66 75.6 ± 5.4	3	0.10
10.	Pegagan [38]	*Centella asiatica*	-	21.0 ± 0.4*	25.3 ± 0.4*	3	0.25
11.	Mengkudu [38]	*Morinda citrifolia*	-	21.0 ± 0.4*	25.8 ± 0.1*	3	0.25
12.	Pare [38]	*Momordica charantia* L.	-	21.0 ± 0.4*	21.0 ± 1.3*	3	0.25
13.	Meniran (IC_{50} Orlistat: 1.71 µg/mL) [37]	*Phyllanthus niruri* L.	27.65 µg/mL	99.6 ± 0.3	76.7 ± 0.4	3	0.50
14.	Daun belimbing wuluh [37]	*Averrhoa bilimbi* L. Leaves	41.45 µg/mL	99.6 ± 0.3	73.9 ± 2.0	3	0.50
15.	Daun kumis kucing [37]	*Orthosipon aristatus* leaves	34.74 µg/mL	99.6 ± 0.3	95.3 ± 2.0	3	0.50
16.	Sambiloto [37]	*Andrographis paniculata*	-	99.6 ± 0.3	0	3	0.50
17.	Daun salam [37]	*Syzygium polyanthum* leaves	-	99.6 ± 0.3	38.2 ± 6.5	3	0.50
18.	Temu ireng [37]	*Curcuma aeruginosa* Roxb.	-	99.6 ± 0.3	38.2 ± 6.5	3	0.50
19.	Daun temulawak [39]	*Curcuma zanthorriza* leaves	-	-	16.9	3	100
20.	Kunyit [33]	*Curcuma longa*	-	-	70.4 ± 3.4	3	0.25
21.	Kayu secang [40]	*Caesalpinia sappan*	-	Cetilistat: 55	90	3	0.50
22.	Serai wangi [40]	*Cymbopogon nardus*	-	Cetilistat: 55	91 ± 1.5	3	1.0
23.	Daun murbei [40]	*Morus alba* leaves	-	Cetilistat: 55	90 ± 20.6	3	1.0
24.	Kayu manis [41]	*Cinnamomum verum*	-	46.79	16.23	-	10
25.	Teh hijau [41]	*Camellia sinensis*	-	46.79	47.82	-	10

26.	Jahe [42]	*Zingiber officinale*	-	68.90	87.30	3	0.1
27.	Daun alpukat [39]	*Percea americana* leaves	-	-	92.8	3	-
28.	Sirih [39]	*Piper betle*	-	-	9.9	3	-
29.	Lada putih [39]	*Piper nigrum*	-	-	24.1	3	-
30.	Daun jambu biji [39]	*Psidium guajava* leaves	-	-	99.0	3	-
31.	Daun jambu air) [39]	*Syzygium samarangense* leaves	-	-	85.6	3	-
32.	Buah asam Jawa [39]	*Tamarindus indica* fruit	-	-	68.0	3	-
33.	Daun katuk [39]	*Sauropus androgynus* leaves	-	-	9.9	3	-
34.	Jeruk purut [43]	*Citrus hystrix*	-	100	58.0	3	0.01
35.	Jintan hitam [39]	*Nigella sativa*	-	-	37.1	3	-

n= replication