Bioprospecting medicinal plants of Centhini: Javanese ancient manuscript

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Research

Abstract

Background: The inhabitants of Java-Indonesia have been developing a distinct culture for thousands of years. The resulting principles were depicted in Serat Centhini, a literary treasure of Javanese culture comprising values from spirituality to medicine centuries ago. There has been no comprehensive study regarding the potency of medicinal plants listed in this ancient book.

Methods: Information was gathered from medicinal plants and diseases that were reported in the book. These were categorized by indications/traditional uses of the plants, and then the literature was reviewed for scientifically based evidence for their biological activities.

Results: A total of 82 medicinal plants were described to treat twelve diseases, in which 32 species were previously reported to possess pharmacological potency relevant to their traditional claims. For example, 6-gingerol and zingerone from *Z. officinale* were demonstrated as erectile agents by testing in animals. Constituents of *B. rotunda* and *Z. montanum* (pinostrobin, boesenbergin A, zerumbone) indicated strong anti-ulcer activity based on an *in vivo* model. Cubebin from *P. cubeba* reduced AChE activity, with it's potency being related to its use in Alzheimer therapy. Despite these reports, there are large research gaps, with reported activities based on crude extracts rather than single compounds. This requires extensive additional research to establish the active constituents and to clarify their mechanism of action.

Conclusions: Serat Centhini reports medicinal plants with high potency, with the traditional knowledge of the Javanese people surviving the history of Indonesia. This knowledge can be used to expand the local pharmacopeia.

Keywords: Serat Centhini; Javanese; Medicinal plants; Bioprospecting.

Background

Serat Centhini, a literary treasure of Javanese Culture, traces its origins to the early 19th century (Inandiak 2019; Sukenti *et al.* 2004). The manuscript was written on the initiative of Kanjeng Gusti Pangeran Adipati Anom Amêngkunagara III or Ingkang Sinuhun Pakubuwana V from the Surakarta Sultanate, with the assistance of Radèn Ngabèi Yasadipura II and Radèn Ngabèi Sastradipura. As the ruler, Pakubuwana V made great efforts to revitalize Javanese literary tradition when the political power of the Surakarta Sultanate was in decline. He was the initiator of the writing of Serat Centhini (1814–1823). Raden Ngabei Yasadipura II (1760-1844) was a court poet (pujangga), combining Arabic-Islamic literature with Javanese traditions. In his writings, Yasadipura II interpreted moral-spiritual aspects based on Javanese Islam (Naif, 2016). Raden Ngabehi Sastradipura was an Islamic scholar and Arabic linguist. Later known as Kyai Haji Muhammad Ilhar, Raden Ngabehi Sastradipura played a crucial role in enriching the Serat Centhini with the spiritual framework of Javanese Islam. He was seen as an intellectual bridge between aspects of Islamic law (sharia) and Javanese mysticism (tasawuf). With his expertise, Sastradipura was a central figure in cross-cultural studies and classical Javanese literature (Naif 2007).

The original book of Centhini is in Javanese letters, divided into 12 volumes and 3500 pages (Fig. 1). This work has often been described as a Javanese-language encyclopedic work, consisting of 722 cantos and 247,766 lines of poetry (Day 2021). Serat Centhini synthesized Islamic teachings, Javanese mysticism, natural sciences, arts, and customs. The manuscripts were translated into Latin letters and published by the Centhini Foundation, Yogyakarta in 1985 (Kamajaya 1985). Serat Centhini offers a comprehensive exploration of Javanese spirituality, ethics, and daily life (Figure 1). It serves as a testament to the richness and depth of Javanese cultural heritage, providing valuable insights into the beliefs and customs of the region (Figure 2). The manuscripts recorded 331 plant species, including staple foods, wood, cosmetics, rituals, and medicines. According to their function, the plant species recorded in the Serat Centhini can be classified further: 158 for food, 82 for medicine, 84 for rituals, 46 for tools, and the rest for construction, cosmetics, and natural dyes (Sukenti *et al.* 2004). In addition, the manuscript describes essential medicinal plants, valuable plant species among the Javanese community in dealing with health promotion and ailments treatment.

Figure 1. (A) Borobudur relief depicting drinking traditional medicine in the 8th Century in Java Island, (B) Current practice of drinking traditional medicine among the Indigenous people of Java Island, (C) and (D) Serat Centhini the old manuscript of Javanese culture written in 12 volumes.

The rich content of Serat Centhini was hidden for almost 200 years and was rarely accessible as it was written in Javanese script. To tackle the language barrier and preserve and expand access to Javanese literary heritage, the Serat Centhini transliteration project was an enormous effort initiated by the Indonesian authorities. This project involved linguists and humanists who transformed the original Serat Centhini text into the Latin alphabet, making it vastly more accessible to readers. This allowed the broader dissemination of the work and permitted new generations to understand and appreciate the richness of Javanese culture. Thus, this transliteration project was a practical effort to preserve Javanese literary heritage and an important step in strengthening Javanese cultural identity.

The significance of Serat Centhini is shown by its detailed portrayal of Javanese society and the complex intertwining of mystical and worldly elements. The manuscript delves into mystical traditions, rituals, and beliefs, revealing a glimpse into

the mystical underpinnings of Javanese society (Geertz 1976). According to Naif (2007), Javanese society in the Serat Centhini is neither unthinkingly religious nor merely mystical without rules (Naif 2007). They are an example of a wise religious society, capable of bridging Islamic law and Sufism, a concept of harmony highly relevant in contemporary Islamic-Javanese discourse. A similar view is put forward by Wibawa (2014), suggesting the picture of Javanese society in the Serat Centhini as an ideal community, internalizing high moral values through the figure of Seh Amongraga (Wibawa 2014). This society is presented as a circle of interactions prioritizing virtues: gender equality, social justice, spiritual piety, and humility. The daily interactions between Seh Amongraga and his wife, Niken Tambangraras, are shown through in-depth dialogues that build a family structure (the rights and obligations of members) and serve as a vehicle for moral education (Wibawa 2014). Through allegorical tales and philosophical reflections, various aspects of life, from romance and courtship to religious practices and social norms are presented.

The manuscript stands as a testament to the enduring legacy of Javanese wisdom and tradition, providing valuable insights into the beliefs and customs of the region. Serat Centhini also offers valuable insights into ethnomedicine, reflecting the traditional healing practices prevalent in Javanese society. Within its extensive volumes, Serat Centhini contains numerous references to medicinal plants and healing rituals, providing a comprehensive understanding of indigenous medical knowledge (Wijaya 2015). Scholars have meticulously analyzed these references, uncovering the intricate relationship between cultural beliefs, natural remedies, and healthcare practices in Java (Wijaya 2018). The study of Serat Centhini within the context of ethnomedicine not only enriches the understanding of traditional healing methods but also highlights the profound connection between culture, nature, and well-being in Javanese culture.

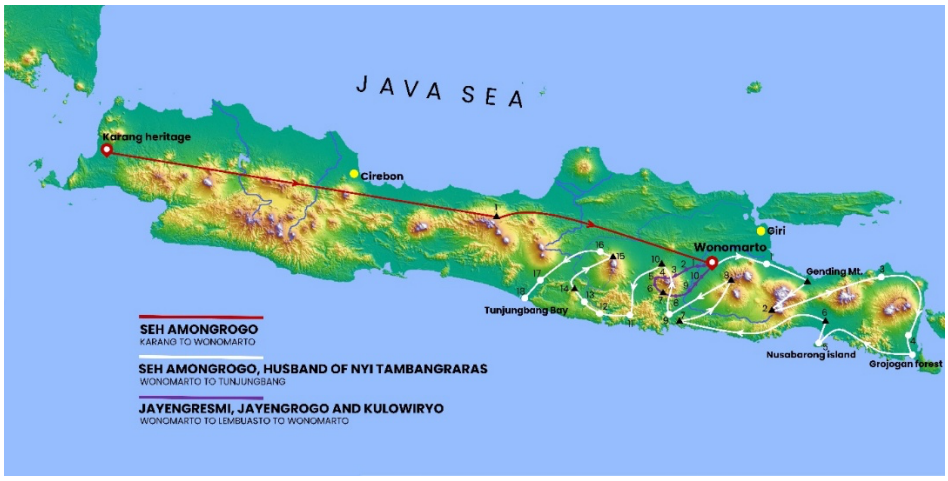


Figure 2. Map of Java Island that indicated journeys described in the Serat Centhini aspiring the culture of Javanese by Seh Amongrogo (From Karang to Wonomarto *via* 1. Sindoro mountain 2. Wonomarto), by Seh Amogrogo, Husband of Nyi Tambangraras (From Wonomarto to Tanjungbang *via* 1. Sirupan cave, 2. Semeru Mountain, 3. Muncar Lake, 4. Bidadari Cave, 5. Nusabarong Island, 6. Kilang mountain, 7. Indrokilo mountain, 8. Kelud mountain, 9. Wajak Watu-urip pool, 10. the Lake of Ngebel, 11. Srobojo cave, 12. Kabaretan, 13. Probodalem cave, 14. Dlepih mountain, 15. Lawu mountain, 16. Village of lemah abang, 17. Celor and Manganticave, 18. the Grand Mosque of Kanigoro), by Jayengresmi, Jayengrogo and Kulowiro (From Wonomarto to Lembuasto to Wonomarto *via* 1. Kepleng adventure, 2. Selomangleng Cave, 3. Seh Rogoyuni, 4. Pulung, 5. the enchanted banyan tree, 6. Ki Sindurogo, 7. Bajangkaki Mountain, 8. Lembuasto, 9. Widuri wrath, 10. Ki Seh Ekawerdi).

Materials and Methods

The historical ethnobotany study followed a notable approach in reconstructing cultural identities based on a retrospective review of historical plant uses in medicinal applications (Silva *et al.* 2014). Traditional medical knowledge (medicaments) contained within the Centhini manuscript were extracted, focusing on medicinal plants-based medicaments. The medicaments and indications were grouped based on Staub's use category using the protocols described previously (Staub *et al.* 2015). The medicinal plants listed were determined for their scientific names. Previous publications were retrieved from Scifinder and Pubmed database by applying Boolean operator "species name" AND "Staub's use category". Collected references from primary research data were screened for duplication. Eligibility criteria involved full text article written in English, those with bioassays that was accompanied with a positive control and the single plant use data. This type of research was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) (Figure 3). Published scientific literature was sourced from reputable databases, PubMed and SciFinder with the uses of

Boolean operators, "Species name" AND (Sub-category use by Staub). The resulting manuscript hits were screened for duplication, followed by inclusive and exclusive evaluation to produce relevant data involving type of sub-category of use, plant part used, sample type, solvent used, secondary metabolites in plants, isolates produced, type of test, test parameters, and test results.

The extracted data were summarized and processed in a Google spreadsheet, followed by data analysis to produce diagram visualizations and quantitative descriptive analysis. The number of research article publications by year and the number of articles in each plant species are depicted by a bar chart. The testing method is depicted by a pie chart, and the type of sample and plant part used in the study are depicted by a bar chart. The types of Indonesian plant species in Serat Centhini that have been studied are depicted by a Sankey diagram visualization. Finally, a scientific approach was used to provide a comprehensive discussion on individual medicinal plant species in which were grouped based on Staub's use category using the protocols described previously (Staub *et al.* 2015).

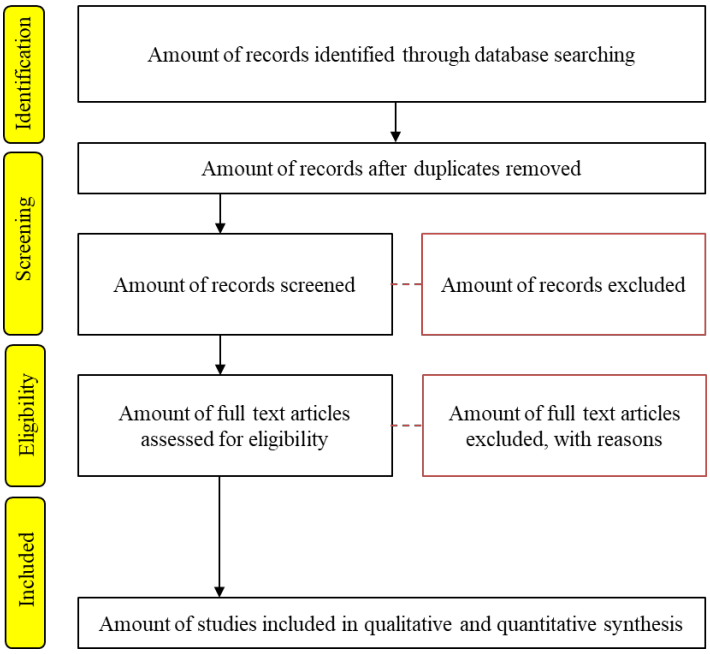


Figure 3. Systematic Reviews and Meta-Analysis Protocols (PRISMA-P)

Results and Discussion

Overview of studies of medicinal plants listed in *Serat Centhini*

A total of 37 formula of traditional medicaments were extracted from *Serat Centhini* comprised of a total of 82 medicinal plant species which were successfully identified and categorized into eleven use categories (Table 1).

Table 1. Staub's use category and species name in Serat Centhini.

Use Category	Species Name
AND	*Zingiber officinale* Roscoe
CAR	*Tamarindus indica* L
DER	*Acorus calamus* L, *Cinnamomum verum* J.Presl
EYE	*Sesbania grandiflora* L.
FOO	*Zingiber zerumbet* (L.) Sm.
GAS	*Acorus calamus* L, *Alpinia galanga* (L.) Willd., *Averrhoa bilimbi* L, *Boesenbergia rotunda* (L.) Mansf., *Curcuma longa* L, *Foeniculum vulgare* Mill, *Nigella sativa* L, *Oryza sativa* L, *Tamarindus indica* L, *Tectona grandis* L.f, *Zingiber montanum* (J.Koenig) A. Dietr, *Zingiber officinale* Roscoe
INF	*Allium cepa* L, *Allium sativum* L, *Areca catechu* L, *Caesalpinia pulcherrima* (L.) Sw, *Cassia occidentalis* L, *Cocos nucifera* L, *Curcuma longa* L, *Foeniculum vulgare* Mill, *Moringa oleifera* Lam, *Piper nigrum* L, *Portulaca oleracea* L, *Psophocarpus tetragonolobus* (L.) DC, *Quercus infectoria* Oliv, *Sesbania grandiflora* L, *Syzygium aromaticum* (L.) Merr. & L.M.Perry, *Tamarindus indica* L, *Tectona grandis* L.f, *Zingiber zerumbet* (L.) Sm

MET	*Allium cepa* L, *Alpinia galanga* L, *Morinda citrifolia* L, *Moringa oleifera* Lam, *Piper nigrum* L, *Zingiber officinale* Roscoe, *Zingiber zerumbet* (L.) Sm.
NER	*Acorus calamus* L, *Allium sativum* L, *Alpinia galanga* L, *Foeniculum vulgare* Mill, *Limonia acidissima* Houtt, *Moringa oleifera* Lam, *Piper betle* L, *Piper cubeba* Bajoer, *Piper nigrum* L, *Portulaca oleracea* L, *Sesbania grandiflora* L, *Tamarindus indica* L
RES	*Foeniculum vulgare* Mill
SKE	*Acorus calamus* L
URO	*Coriandrum sativum* L

AND: andrology; CAR: cardiovascular disease; DER: dermatologic disorders; EYE: ophthalmic problems; FOO: food; GAS: gastrointestinal problem; INF: infections; MET: metabolic syndrome; NER: nervous system; RES: respiratory complaints; SKE: skeleton-muscular system; and URO: urology.

Through a literature search, a total of 6,868 publications were obtained, of which 4,917 were identified as duplicates. Further filtrating based on predetermined inclusion and exclusion criteria produced 434 manuscripts in which only 137 were relevant to the traditional claims (Figure 4).

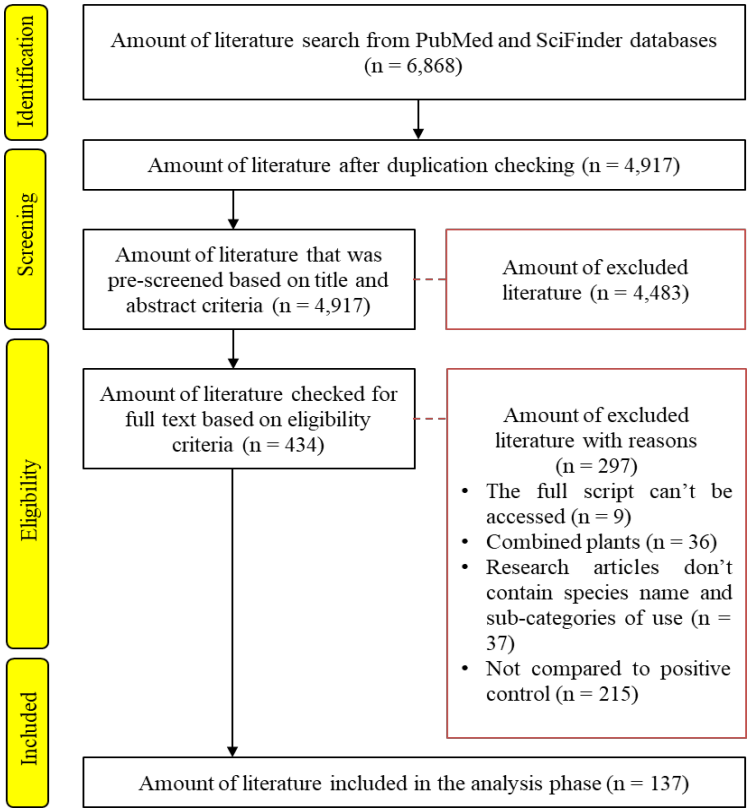


Figure 4. PRISMA Flow diagram indicating the selected scientific manuscripts for the Serat Centhini review study.

In the *Serat Centhini*, a total of 82 medicinal plant species has been used to treat various types of diseases, however only 32 species were studied against intended pharmacological claims (Figure 5). For example, *M. oleifera* was the most researched species due to its highly nutritious value and potential as a nutraceutical food ingredient across the globe (Winarno 2018).

The pharmacological claims of medicinal plants listed in the Serat Centhini were evaluated by *in vitro* studies (90 articles), but only limited *in vivo* experiments were reported (47 articles). Most studies were conducted on crude leaf extracts and essential oils (Figure 6a and 6b). Interestingly, leaves have been commonly used in traditional medicament preparation in the Java Island-Indonesia.

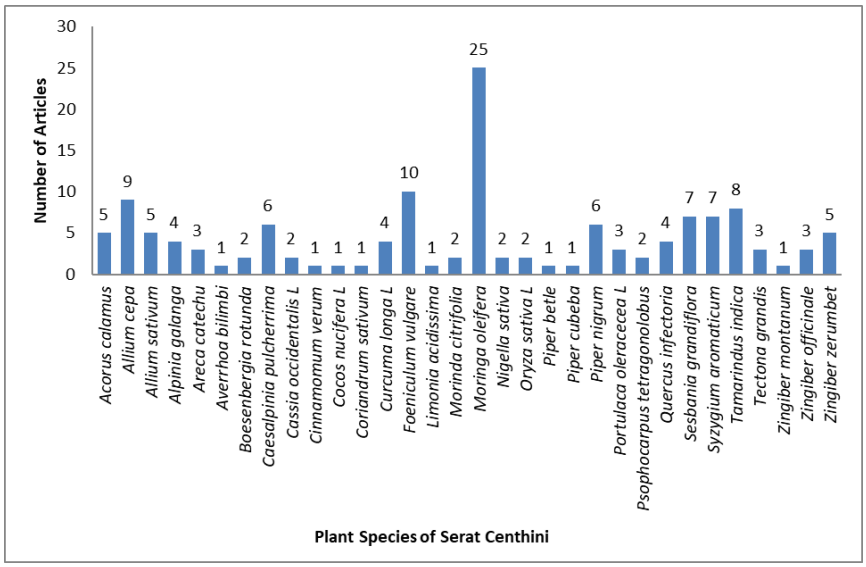


Figure 5. The number of publications (Y-axis) and medicinal plants listed in the *Serat Centhini* (X-axis).

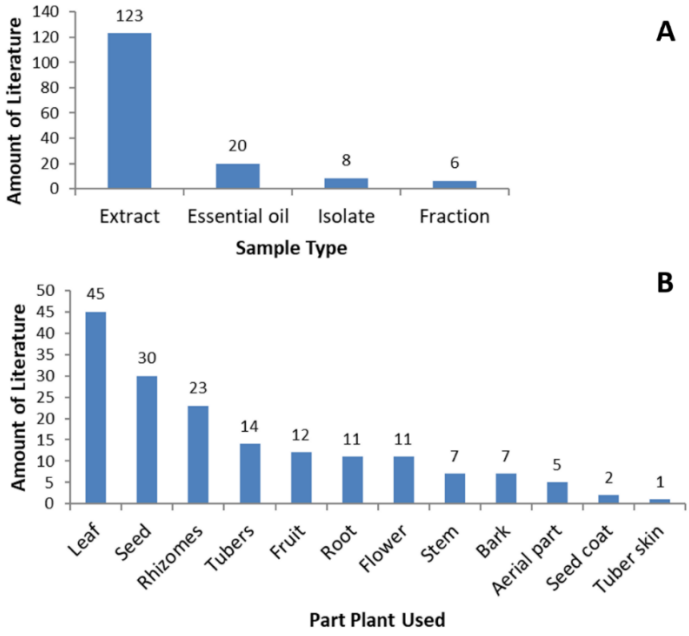


Figure 6. (a) Sample type, (b) Plant parts used in plant research in *Serat Centhini*

Confirmed pharmacological claims of medicinal plants in *Serat Centhini*.

There were 32 plant species whose activities had been studied in different use categories (Figure 7). Traditional knowledge for treating infectious diseases has been depicted in Serat Centhini - INF with 99 tests, GAS and NER each with 17 tests, MET with 10 tests, DER with two tests, and CAR, URO, SKE, RES, EYE, FOO, and AND each tested one time. The plant species in Centhini fiber that have been researched are based on their use categories for further discussion.

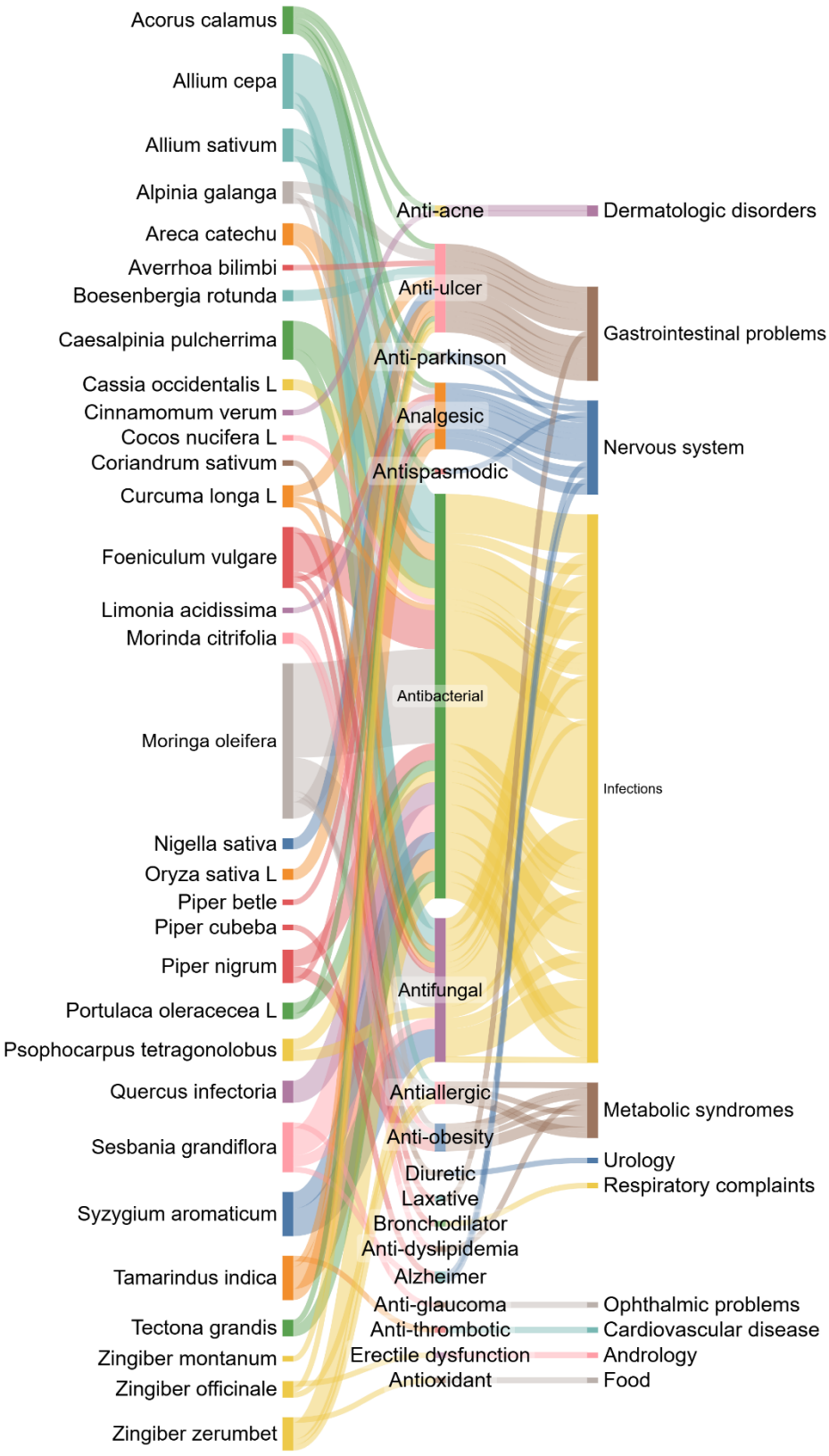


Figure 7. Sankey diagram indicating correlation among plant species data, pharmacological uses and Staub's use categories.

Andrology (AND)

The Serat Centhini describe treatments for erectile dysfunction with the use of medicinal plants including *Momordica charantia* L*, Zingiber montanum, Alpinia galanga* (L.) Willd*, Boesenbergia rotunda* (L.) Mansf*, Zingiber officinale* Roscoe and *Cinnamomum verum* J. Presl, which are prepared as topical and oral dosage forms by mean a decoction. Among these medicinal plants, only *Zingiber officinale* Roscoe has been tested for efficacy using its chloroform extract and hexane fraction which revealed their potency as sexual stimulants based on *in vivo* experiments using male and female Wistar albino rats. The positive control was injected with sildenafil (50 mg/kg BW). The 6-gingerol (1) and Zingerone (2) (Figure 8) content in *Zingiber officinale* Roscoe is thought to help combat the accumulation of free oxygen radicals and lipid peroxides, which constrict blood vessels, so that blood flow to the penis can increase and result in an erection. These results could be used as a reference with the *Zingiber officinale* Roscoe hexane fraction deconvoluted with individual molecules isolated and clinically tested. Further, the effectiveness of 6-gingerol (1) and zingerone (2) as erection agents also needs further evidence. The results of this research are in accordance with the efficacy claims and categorization of ingredients in Serat Centhini, indicating that *Zingiber officinale* Roscoe can be used as an erectile agent. In addition, research needs to be conducted on the potential of the plants *Momordica charantia* L*, Zingiber montanum, Alpinia galanga* (L.) Willd*, Boesenbergia rotunda* (L.) Mansf*,* and *Cinnamomum verum* J. Presl as erectile agents.

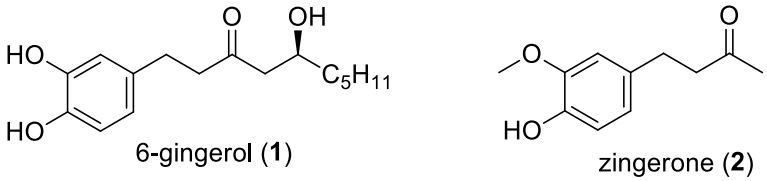


Figure 8. Isolates that have been tested as erectile agents.

Cardiovascular disease (CAR)

In Serat Centhini, cardiovascular disease covers all disorders of the heart and blood vessels. Based on Staub's classification, cardiovascular disease has sub-categories of use, namely anti-arrhythmic, antihypertensive, antithrombotic, capillary fragility, hemostatic, hypertension, and vasodilator. The Serat Centhini described the use of several medicinal plants including *A. cepa, Alyxia stellate, A. catechu, F. vulgare, S. aromaticum,* and *T. indica* which are prepared in oral dosage form. Among these medicinal plants, only *T. indica* has been studied as anti-thrombotic agent.

Antithrombotic research with the ethanol extract of *T. indica* fruit was tested *in vivo* on male Mus musculus mice to determine the bleeding time (Saputri *et al.* 2018). The negative control, CMC 0.5% (0.3 mL/20 g) showed a bleeding time of 7.32 minutes whereas the positive control, aspirin (0.208 mg/20 g), showed a bleeding time of 16.5 minutes. The ethanol extract of *T. indica* fruit was tested using three concentrations, namely 14 mg/20 g, 28 mg/20 g, and 56 mg/20 g and the results showed a bleeding time of 14.56 minutes, 15.92 minutes, and 16.68 minutes, respectively. Based on these results, the ethanol extract of *T. indica* fruit 56 mg/20 g caused significant bleeding compared to the positive control aspirin (0.208 mg/20 g). The flavonoid content in *T. indica* is thought to be able to inhibit platelet aggregation with the same mechanism of action as aspirin, namely blocking the cyclooxygenase pathway through the mechanism of inhibiting arachidonic acid so that the amount of prostaglandin, prostacyclin, and thromboxane A2 decreases and platelet aggregation is inhibited (Magdalena *et al.* 2015). The flavonoid compounds in *T. indica* extract have the potential to be studied as anti-thrombotic isolates.

Another study tested Okanin, a member of the flavonoid family of compounds (Liu *et al.* 2022). *In vivo* testing on Kunming mice showed high activity as an anti-thrombotic agent, with activity equivalent to the positive control used, aspirin. This result can be a reference for future research, where the ethanol extract of *T. indica* fruit, which is known to have potential as an anti-thrombotic agent, can be continued to the isolate stage. The results of this study are also in accordance with the efficacy claims and categorization of the ingredients in Serat Centhini, indicating that *T. indica* can be used as an anti-thrombotic in the cardiovascular disease category. In addition, further research is needed on the potential of the plants *A. cepa, A. stellate, A. catechu, F. vulgare,* and *S. aromaticum* as therapies for cardiovascular disease.

Dermatologic disorders (DER)

The Serat Centhini described the use of several medicinal plants for treatment of dermatological disorders including *A. calamus, A. galanga, Alyxia oliviformis* Roem. & Schult*, A. stellate, Artemisia vulgaris* L, *B. rotunda, Caladium bicolor* (Aiton) Vent*, Capsicum frutescens* L*, Carthamus tinctorius* L*, C. verum, C. sativum, Cryptocarya massoia, Ficus benjamina* L*, F. vulgare,*

Kaempferia galanga L*, Musa acuminata* Colla*, Myristica fragrans* Houtt*, Ocimum Sanctum* L, *Oryza sativa* L, *Pandanus amaryllifolius* Roxb*, P. betle, P. nigrum, P. oleracea*, *Q. infectoria, Syzygium myrtifolium* Walp*, T. indica, Z. officinale,* and *Z. zerumbet* which are prepared in a topical dosage form. Among these medicinal plants, Nevertheless, only *A. calamus* and *C. verum* have been scientifically evaluated as cures in the dermatologic disorders category. Based on Staub's classification, the use category for dermatologic disorders has sub-categories including anti-acne, antipsoriatic, leukoderma, rubefacient, skin photodamage, vitiligo, and vulnerary. Acne can be caused by the bacteria *Propionibacterium acnes*, *Staphylococcus aureus*, and *Staphylococcus epidermidis*, which can secrete hydrolytic enzymes that cause damage to the pilosebaceous follicles, thereby triggering inflammation.

The study of the methanol extract of *C. verum* tree bark (5 mg/mL) against *P. acnes* and *S. epidermidis in vitro* showed an inhibition zone diameter of 13 mm (Madhubala *et al.* 2018), while testing of a 10% ethanol extract of *A. calamus* showed a 0 mm zone against *P. acnes* (Chaiwaree *et al.* 2021). The results can be used as a reference for future studies, where the methanol extract from *C. verum* tree bark, which has been tested *in vitro*, can continue to be isolated and tested *in vivo*. These results are also in accordance with the efficacy claims and categorization of ingredients in Serat Centhini; *C. verum* can be used as an anti-acne treatment in the skin disease category, while the anti-acne activity of the *A. calamus* plant species requires further research. Nevertheless, studies on *A. galanga, A. oliviformis, A. stellate, A.vulgaris*, *B. rotunda, C. bicolor, C. frutescens, C. tinctorius, C. sativum, C. massoia, F. benjamina, F. vulgare, K. galanga, M. acuminata, M. fragrans, O. Sanctum*, *O. sativa*, *P. amaryllifolius, P. betle, P. nigrum, P. oleracea*, *Q. infectoria, S. myrtifolium, T. indica, Z. officinale,* and *Z. zerumbet* are necessary to unravel their therapeutic potency in dermatology.

Ophthalmic problems (EYE)

The Serat Centhini also described the use of several medicinal plants to treat eye disorders including *A. oliviformis, A. catechu, C. longa*, *F. vulgare, P. tetragonolobus, Sapindus rarak* DCU*, S. grandiflora, T. indica,* and *T. grandis* which were prepared as topical agents. Among these medicinal plants, only *S. grandiflora* has been subsequently studied as eye disorders category including antiglaucoma. Glaucoma is an eye disease caused by increased intraocular pressure, resulting in damage to the optic nerve and loss of vision, as well as permanent blindness if undiagnosed and untreated (Lee and Higginbotham 2005).

The study of the water extract from *S. grandiflora* leaves (200 mg/kgBW and 400 mg/kgBW) as an antiglaucoma agent was conducted *in vivo* using male and female rabbits (Lakshmi *et al.* 2019). On the 6th day after induction of intraocular pressure, the control group (no treatment), the intraocular pressure of the left eye was 18.24 and the right eye was 38.35. The group with the positive control (0.1% brinzolamide) showed the intraocular pressure of the left eye as 19.39 and the right eye was 20.39. The test group with 200 mg/kgBW extract showed the intraocular pressure of the left eye as 18.22 and the right eye was 21.82, and the test group with 400 mg/kgBW extract showed the intraocular pressure of the left eye as 20.58 and the right eye was 20.12. Based on these results, 400 mg/kgBW water extract from *S. grandiflora* leaves has great potential as an antiglaucoma agent. In addition, 400 mg/kgBW of extract was also able to reduce intraocular pressure almost to the same extent as the positive control. The water extract from *S. grandiflora* leaves has the same mechanism of action as the positive control brinzolamide, inhibiting carbonic anhydrase II and suppressing the formation of aqueous humor in the eye, thus reducing intraocular pressure. These results can be a reference for subsequent studies, where these *S. grandiflora* leaf extracts can be tested *in vivo*, and for the extracts deconvoluted to isolate and identify the active constituent. This could also lead to clinical testing. The results of this research are also in accordance with the efficacy claims and categorization of ingredients in Serat Centhini, indicating that *S. grandiflora* can be used as an anti-glaucoma in the eye disease category. Further research also needs to be conducted on the potential of the plants *A. oliviformis, A. catechu, C. longa*, *F. vulgare, P. tetragonolobus, S. rarak, T. indica,* and *T. grandis* as therapies for ophthalmic problems.

Food (FOO)

In Serat Centhini, stomachache caused by food is included in the use category of food by staub. The Serat Centhini also described the use of several medicinal plants including *Curcuma xanthorrhiza* D.Dietr*, Tetrastigma glabratum* (Roxb.) Planch*, Z. montanum,* and *Z. zerumbet* which are prepared as an oral dose form by means of decoction. Among these medicinal plants, only *Z. zerumbet* has been subsequently reported. The use category for food has sub-categories, namely antioxidants, flavorings and sweeteners. Antioxidant activity can be defined as 'very strong' (IC_{50} <50 µg/mL); 'strong' (50-100 µg/mL) moderate (100-250 µg/mL); 'weak' (250-500 µg/mL); and 'inactive' (>500 µg/mL) (Rahmi 2017).

The methanol extract of the *Z. zerumbet* rhizome was tested as an antioxidant using the DPPH and ABTS test methods (Kothandaraman and Shanmugam 2018). The extract showed an IC_{50} value of 179 and 77 g/mL, respectively. In addition, positive control L-ascorbic acid and BHT indicated respected IC_{50} values of 33 g/mL and 36 g/mL against ABTS. This *Z.*

zerumbet rhizome extract showed strong antioxidant activity using the ABTS method whereas the DPPH method showed the activity to be moderate. The flavonoid content in *Z. zerumbet* rhizomes is thought to be relevant to its activity through the capture of free radicals protecting cells from oxidative stress, thereby preventing various diseases such as cardiovascular disease, cancer, inflammation, and Alzheimer's. The results of this research are in accordance with the efficacy claims and categorization of ingredients in Serat Centhini, indicating that *Z. zerumbet* can be used as an antioxidant in the food category. In addition, further studies are neededon the potential of the plants *C. xanthorrhiza, T. glabratum,* and *Z. montanum* as antioxidants.

Gastrointestinal problems (GAS)

In Serat Centhini, gastrointestinal problems include stomach pain that can cause nausea and vomiting, diarrhea, and constipation. The Serat Centhini also described the use of several medicinal plants including *A. calamus, Allium ascalonium* L, *A. cepa, A. sativum, A. galanga*, *A. vulgaris*, *Artocarpus elasticus* Reinw, *A. bilimbi, B. rotunda, C. frutescens, Citrus aurantiifolia* (Christm.) Swingle, *Citrus hystrix* DC, *Cocos nucifera* L, *C. sativum, Curcuma aeruginosa* Roxb, *C. longa*, *C. xanthorrhiza, Eleutherine bulbosa* (Mill.) Urb, *F. benjamina, F. vulgare, K. galanga*, *M. acuminata, N. sativa, Ocimum Sanctum* L, *Oryza sativa* L, *P. betle, P. nigrum, Q. infectoria, T. indica, T. grandis, Tetrastigma glabratum* (Roxb.) Planch, *Z. montanum, Z. officinale,* and *Z. zerumbet* which are prepared in oral and topical dosage forms. Among these medicinal plants, *A. calamus, A. galanga, A. bilimbi, B. rotunda, C. longa*, *F. vulgare, N. sativa, O. sativa*, *T. indica, T. grandis, Z. montanum*, and *Z. officinale* have been studied as antiulcers and laxatives. Based on Staub's classification, the use category for gastrointestinal problems has sub-categories of anti-hepatotoxic, antiulcer, choleretic, chronic idiopathic constipation, and laxative. Peptic ulcer disease is a digestive tract disorder occurring in the stomach and duodenum and has a high level of morbidity and mortality. It is characterized by damage to the mucosa due to the secretion of pepsin and gastric acid (Malfertheiner *et al.* 2009; Ramakrishnan and Salinas 2007). Constipation is a common intestinal problem in which laxatives agents are used to alleviate the problem (Krisnani *et al.* 2017). Several previous studies on medicinal plants listed in the *Serat Centhini* with laxative properties are summarized in Table 2. The *in vivo* studies show that plants from the Zingiberaceae family have strong potential as antiulcers. and these results can be used as a basis for further research, *e.g.* in clinical trials. Isolates from the Zingiberaceae family of plants have been identified and tested as antiulcer agents and include pinostrobin (3), boesenbergin A (4), zerumbone (5), 6-gingerol (1), 6-shagaol (6), and 6-gingesulfonic acid (7) (Figure 9). Strong antiulcer activity was demonstrated by isolates of pinostrobin (3), boesenbergin A (4), zerumbone (5), and 6-gingesulfonic acid (7).

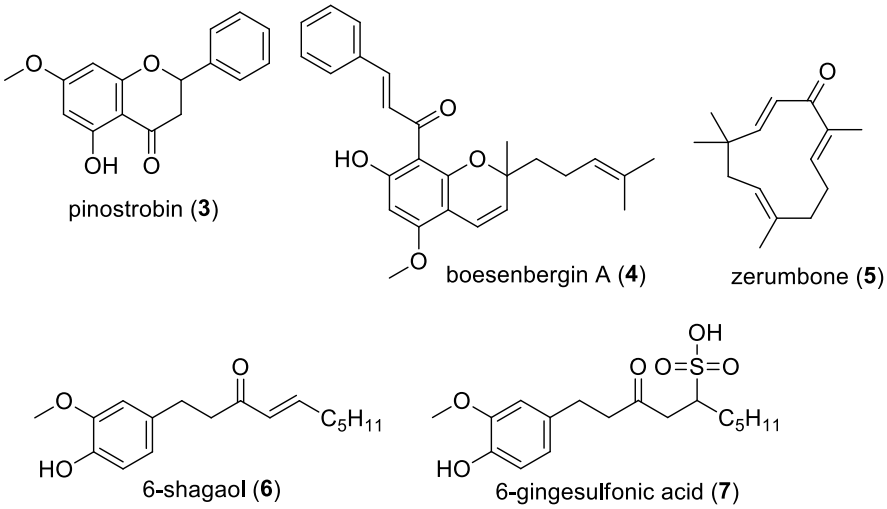


Figure 9. Isolates that have been tested as antiulcer agents.

The alkaloid content in *A. calamus, C. longa, N. sativa*, and *T. grandis* is thought to accelerate wound healing and increase gastric mucus production after injury due to an inducing agent. The flavonoid content in *A. galanga* and *B. rotunda* is thought to trigger tissue repair through antioxidant activity. The tannin content in *C. longa* and *T. grandis* can be expected to inhibit gastric secretion and protect the gastric mucosa. The phenolic compound content in *Z. officinale* works by triggering tissue repair through antioxidant activity (Saptarini *et al.* 2011). These activities are summarised in Table 2.Research needs to be conducted on the potential of other plants reported in the *Serat Centhini* including *A. ascalonium*, *A. cepa, A. sativum, A. vulgaris*, *A. elasticus, C. frutescens, C. aurantiifolia, C. hystrix, C. nucifera*, *C. sativum, C. aeruginosa, C. xanthorrhiza, E. bulbosa, F. benjamina, K. galanga*, *M. acuminata, O. Sanctum*, *P. betle, P. nigrum, Q. infectoria, T. glabratum,* and *Z. zerumbet* as therapies for gastrointestinal problems.

Table 2. Plant activity in Serat Centhini reported as an anti-ulcer or laxative for the treatment of gastrointestinal problems.

Plant Species	Function	Test Method	Sample Type	Activity	Reference
Acorus calamus L	Antiulcer	*In vivo*	Ethanol extract	Antiulcer activity was significant with a % gastric swelling value of 0% (extract 1 mL/kgBW) compared to the positive control (ranitidine 20 mg/kgBW) swelling of 33.3%.	(Dababneh et al.2021)
Foeniculum vulgare Mill	Laxative	*In vivo*	Ethanol extract	The weight of the stool 4 g, after administration of the extract (300 mg/kgBW) was smaller than the 5.7 g positive control (bisacodyl 3.3 mg/kgBW)	(Jang and Yang 2018)
Tamarindus indica L	Antiulcer	*In vivo*	Methanol extract	Extract (200 mg/kgBW) showed an ulcer index of 18.67, compared to 15 for the positive control (ranitidine 50 mg/kgBW)	(Kumar *et al.* 2011)
Tectona grandis L.f	Antiulcer	*In vivo*	Ethanol extract	Extract (200 mg/kgBW) showed ulcer index of 1.25, compared to 0.916 for the positive control (omeprazole 10 mg/kgBW)	(Singh *et al.* 2017)
Oryza sativa L	Antiulcer	*In vivo*	*n*-Hexane + $NaNO_3$ extract	Extract (400 mg/kgBW) showed ulcer index of 1.33, compared to 0.67 for the positive control (omeprazole 36 mg/kgBW)	(Trinovita *et al.* 2018)
	Antiulcer	*In vivo*	Ethanol extract	Extract (800 mg/kgBW) showed diameter ulcer of 2.36, compared to 1.45 for the positive control (omeprazole 10 mg/kgBW)	(Tonchaiyaphum *et al.* 2021)
Nigella sativa L	Antiulcer	*In vivo*	Alcohol extract	Antiulcer activity was significant with an ulcer index of 1 (extract 150 mg/kgBW) compared to the positive control (ranitidine 20 mg/kgBW) with an ulcer index of 1.6.	(Rajkapoor *et al.* 2002)
	Antiulcer	*In vivo*	Water extract	Antiulcer activity was significant with an ulcer index of 4.05 (extract 500 mg/kgBW) compared to the positive control (famotidine 3 mg/kgBW) with an ulcer index of 4.66.	(Bruce *et al.* 2021)
	Antiulcer	*In vivo*	Essential oil	Antiulcer activity was significant with an ulcer index of 4.62 (essential oil 1.5 mL) compared to the positive control (famotidine 3 mg/kgBW) value of 4.66.	(Bruce *et al.* 2021)
Alpinia galanga (L.) Willd	Antiulcer	*In vivo*	Water extract	Extract (200 mg/kgBW) showed ulcer index of 2.33, compared to 1.66 for the positive control (ranitidine 20 mg/kgBW)	(Johnley *et al.* 2020)
	Antiulcer	*In vivo*	Ethanol extract	Extract (200 mg/kgBW) showed ulcer index of 3.02, compared to 2.5 for the positive control (ranitidine 50 mg/kgBW)	(Nagpure *et al.* 2022)
Boesenbergia rotunda (L.) Mansf	Antiulcer	*In vivo*	Methanol extract	Antiulcer activity was significant with an ulcer index of 135.8 (dose 200 mg/kgBW) and 43.2 (dose 400 mg/kgBW) compared to the positive control (omeprazole 20 mg/kgBW) with an ulcer index of 210.	(Abdelwahab *et al.* 2011)

Plant Species	Function	Test Method	Sample Type	Activity	Reference
	Antiulcer	*In vivo*	Pinostrobin (3) isolate	Antiulcer activity was significant with an ulcer index of 150 (dose 20 mg/kgBW) and 7.2 (dose 40 mg/kgBW) compared to the positive control (omeprazole 20 mg/kgBW) with an ulcer index of 210.	(Abdelwahab *et al.* 2011)
	Antiulcer	*In vivo*	Boesenbergin A (4) isolate	Isolate (20 mg/kgBW showed ulcer area of 90 mm, compared to 70 mm for the positive control (omeprazole 20 mg/kgBW)	(Mohan *et al.* 2020)
Curcuma longa L	Antiulcer	*In vivo*	Ethanol extract	Extract (1000 mg/kgBW) showed ulcer index of 0.92, compared to 0.75 for the positive control (ranitidine 50 mg/kgBW)	(Savaringal and Sanalkumar 2018)
	Antiulcer	*In vivo*	Methanol extract	Extract (50 mg/kgBW) showed ulcer index of 19, compared to 9 for the positive control (ranitidine 2 mg/kgBW)	(Sujane *et al.* 2018)
Zingiber montanum (J.Koenig) A. Dietr	Antiulcer	*In vivo*	Zerumbone (5) isolate	Antiulcer activity was significant with % ulcer inhibition of 29.07% (isolate 20 mg/kgBW) compared to positive control (lansoprazole 30 mg/kgBW) value of 37.21%.	(Al-Amin *et al.* 2012)
Zingiber officinale Roscoe	Antiulcer	*In vivo*	6-Gingerol (1) isolate	Isolate (150 mg/kgBW) showed % ulcer inhibition of 57.5%, compared to positive control (cetraxate 300 mg/kgBW) with % ulcer inhibition of 98.5%.	(Yoshikawa *et al.* 1994)
	Antiulcer	*In vivo*	6-Shagaol (6) isolate	Isolate (150 mg/kgBW) showed % ulcer inhibition of 70.2% compared to positive control (cetraxate 300 mg/kgBW) with % ulcer inhibition of 98.5%.	(Yoshikawa *et al.* 1994)
	Antiulcer	*In vivo*	6-Gingesulfonic acid (7) isolate	Isolate (300 mg/kgBW) showed % ulcer inhibition of 99.6% compared to positive control (cetraxate 300 mg/kgBW) with % ulcer inhibition of 98.5%.	(Yoshikawa *et al.* 1994)

Infections (INF)

In Serat Centhini, infection is all diseases characterized by the presence of abscesses and blood coming out of the body. It also described the use of several medicinal plants as anti-infectives including *A. cepa, A. sativum, A. oliviformis, A. catechu, Caesalpinia pulcherrima, Cassia occidentalis* L, *Cocos nucifera* L, *C. longa*, *F. vulgare, K. galanga*, *M. oleifera, M. acuminata, P. nigrum, P. oleracea*, *P. tetragonolobus, Q. infectoria, Saccharum spontaneum* L*, S. grandiflora, S. aromaticum, T. indica, T. grandis,* and *Z. zerumbet* which prepared as oral and topical dosage form. Among these medicinal plants, *A. cepa, A. sativum, A. catechu, C. pulcherrima, C. occidentalis, C. nucifera*, *C. longa, F. vulgare, M. oleifera, P. nigrum, P. oleracea*, *P. tetragonolobus, Q. infectoria, S. grandiflora, S. aromaticum, T. indica, T. grandis*, and *Z. zerumbet.* Based on Staub's classification, the use category for infection problems has sub-categories of use, namely antibacterial, antifungal, antiplasmodial, and antiviral.

Table 3 summarises the plant activity,efficacy claims and categorization of ingredients as reported in Serat Centhini - these plants are defined in the antibacterial and antifungal infection category. The results of searches on these plants showed that most antibacterial tests were carried out on *Staphylococcus aureus* (gram positive) and *Escherichia coli* (gram negative), and most antifungal tests were carried out on *Candida albicans*.

Very strong inhibitory potential on *S. aureus* was demonstrated by extracts of *A. catechu*, *F. vulgare, T. indica*, and an *Emodin* isolate. In *E. coli*, very strong inhibitory potential was demonstrated by the extracts of *A. catechu, F. vulgare, Q. infectoria*, and *T. grandis*. In antifungal testing, the *F. vulgare* essential oil had very strong inhibitory potential against *C. albicans.* The method used in all antibacterial and antifungal testing was *in vitro*, and can therefore be used as a reference for *in vivo* testing and clinical trials. Isolates that have been tested for antibacterial and antifungal properties include quercetin (8), lunarin (9), 4'-*O*-methylquercetin (10), phloroglucinoyl-3,4-dihydroxybenzoate (11), catechin (12), epicatechin (13), EGCG (14), [(3*E*)-3- (1,3-benzodioxol-5-ylmethylene)-2,3-dihydro-7-hydroxy-4*H*-1-benzopyran-4-one] (15), [(3*E*)-2,3-dihydro-3-[(3,4-dimethoxyphenyl)methylene]-7-methoxy-4*H*-1-benzopyran-4-one] (16), sappanone A (17), emodin (18), demethoxycurcumin (19), *n*-isobutyleicosatrienamide (20), pellitorine (21), trachyone (22), isopiperolein (23), pergumidiene (24), and apigenin (25) (Figure 10).

The flavonoid content in *A. cepa, A. sativum, A. catechu, C. pulcherrima, C. longa, F. vulgare, M. oleifera,* and *P. oleracea* works by damaging the lipid layer on the bacterial cell membrane so that it can cause membrane leakage and cell lysis, whereas antifungals work by damaging the permeability of cell wall membranes and extracellular proteins. The tannin content in *C. pulcherrima, Q. infectoria*, and *T. indica* works by coagulating the protoplasm of bacterial cells whose cell walls have been lysed by saponin and flavonoid compounds, as well as inhibiting the synthesis of fungal cell chitin. The anthraquinone content in *C. occidentalis* interferes with bacterial growth by inhibiting bacterial protein synthesis. The alkaloid content in *P. nigrum, Q. infectoria, T. indica*, and *Z. zerumbet* works by interfering with the components that make up peptidoglycan in bacterial cells. Research needs to be conducted on the potential of the plants *A. oliviformis, C. nucifera*, *K. galanga*, *M. acuminata,* and *S. spontaneum* as therapies for infections.

Metabolic syndromes (MET)

In Serat Centhini, metabolic syndrome is reported as acollection of metabolic disorders that can cause various degenerative diseases such as cardiovascular disease, stroke, and diabetes mellitus. The Serat Centhini also described the use of several medicinal plants including *Aleurites moluccana, A. cepa, A. sativum, A. galanga*, *A. oliviformis, C. pulcherrima, C. verum, C. hystrix, C. aeruginosa, C. longa*, *C. xanthorrhiza, Elettaria cardamomum, Ficus amelas, F. benjamina, F. vulgare, Morinda citrifolia* L*, M. oleifera, M. acuminata, Piper cubeba, P. nigrum, S. spontaneum, S. aromaticum, T. indica, Wrightia javanica* A.DC*, Z. officinale,* and *Z. zerumbet* which are prepared in oral and topical dosage form. Among these medicinal plants, *A. cepa, A. galanga, M. citrifolia, M. oleifera, P. nigrum, Z. officinale,* and *Z. zerumbet* have been studied to treat metabolic syndrome. Based on Staub's classification, the use category for metabolic syndromes have sub-categories of use, namely addison, anti-allergic, anti-hyperprolactinemia, anti-obesity, anti-tyrosinemia, homocystinuria, immunological-inflammatory and related diseases, as well as lipoprotein disorders.

Allergy is a hypersensitivity reaction caused by the presence of allergens (compounds that can cause allergies). Obesity is the main component of metabolic syndrome, which is followed by increased fat metabolism, namely the production of reactive oxygen species (ROS) in the circulation and in adipose cells. Increased ROS in adipose cells can disrupt the balance of reduction and oxidation reactions, so that antioxidant enzymes decrease (called oxidative stress) and can cause type 2 diabetes mellitus.

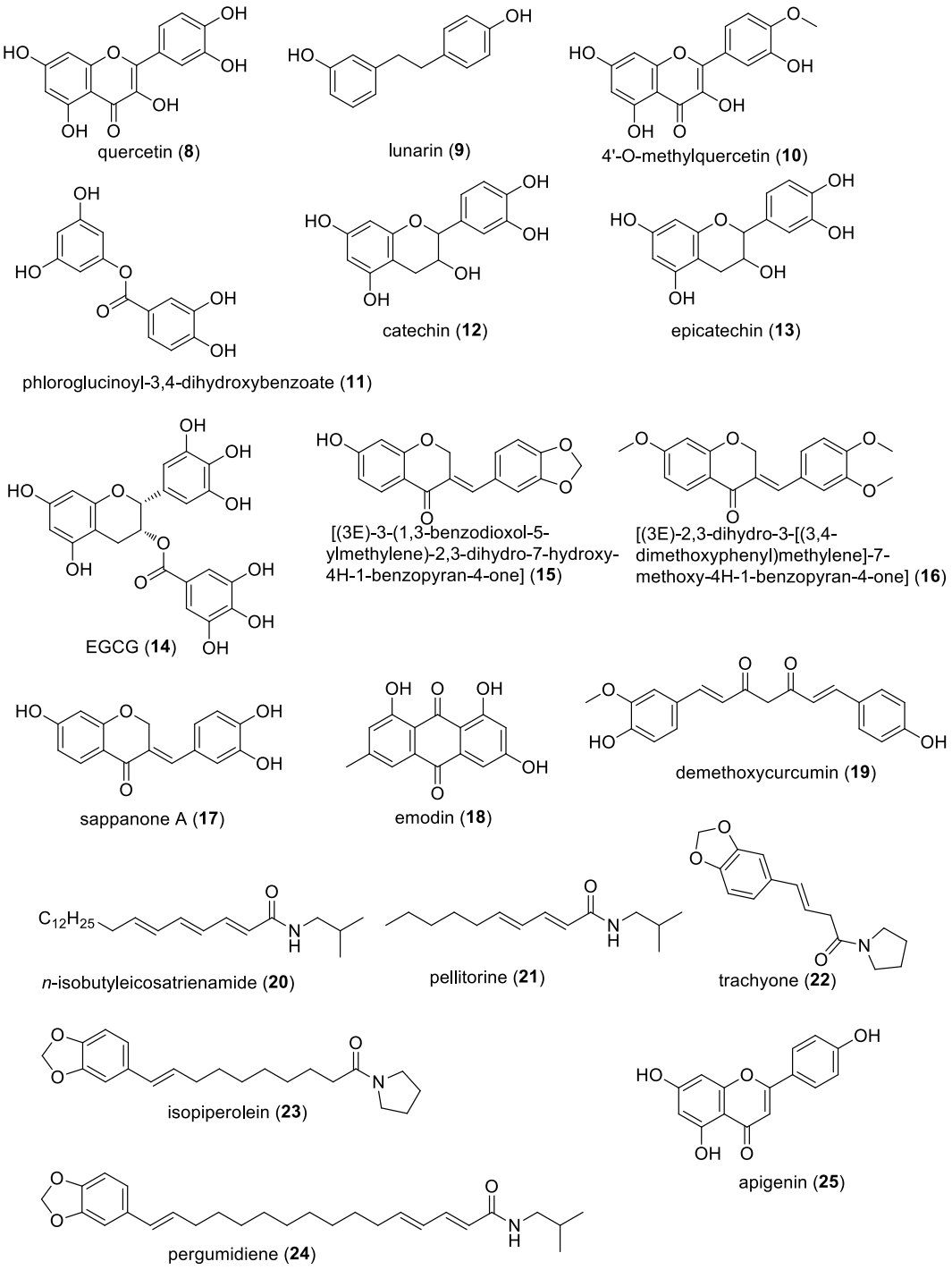


Figure 10. Isolates that have been tested for antibacterial and antifungal

Table 3. Plant activity in Serat Centhini as antibacterials and antifungals for infection categories that have been subsequently published.

Plant Species	Bacteria / Fungi	Activity
Allium cepa L	*Listeria monocytogene*	The diameter of the inhibition zone for the air extract is 27.5 mm, and that of the ethanol extract is 20.5 mm (Tetracycline, 10 µg/disc, 40 mm) (Nnamchi *et al.* 2021).
	Escherichia coli	The diameter of the ethanol extract inhibition zone is 30.1 mm (Nnamchi *et al.* 2021), methanol extract is 23 mm, acetone extract is 10 mm, ethyl acetate extract is 12 mm, and chloroform extract is 10 mm (Streptomycin 10 µg/mL, 8 mm) (Sharma *et al.* 2018; Sikandri *et al.* 2020) The diameter of the inhibition zone of quercetin (8) isolate is 13 mm (Streptomycin 10 µg/mL, 8 mm)
	Pseudomonas aeruginosa	The diameter of the inhibition zone for the water extract is 17.5 mm, ethanol extract 17 mm (Nnamchi *et al.* 2021), methanol extract 20 mm, acetone extract 15 mm, ethyl acetate extract 10 mm, chloroform extract 12 mm (Sharma *et al.* 2018), and 15 mm for the n-hexane extract (Imipenem + Cilastatin, 5 mg/mL, 25 mm) (Penecilla and Magno 2011). The diameter of the inhibition zone of quercetin (8) isolate is 16 mm (Streptomycin 10 µg/mL, 8 mm) (Sharma *et al.* 2019)
	Klebsiella pneumonia	The diameter of the inhibition zone for the ethanol extract is 28.5 mm, hexane extract is 20.5 mm (Nnamchi *et al.* 2021), methanol extract is 26 mm, acetone extract is 10 mm, ethyl acetate extract is 17 mm, and petroleum ether extract is 10 mm (Streptomycin 10 µg/mL, 8 mm) (Sharma *et al.* 2018) The diameter of the inhibition zone of quercetin (8) isolate is 15 mm (Streptomycin 10 µg/mL, 8 mm) (Sharma *et al.* 2019)
	Shigella flexneri	The diameter of the inhibition zone for the methanol extract is 20 mm, acetone extract is 17 mm, ethyl acetate extract is 10 mm, and petroleum ether extract is 14 mm (Streptomycin 10 µg/mL, 8 mm) (Sharma *et al.* 2018).
	Enterococcus faecalis	The diameter of the inhibition zone for the methanol extract is 14 mm, acetone extract is 13 mm, ethyl acetate extract is 10 mm, chloroform extract is 11 mm, petroleum ether extract is 14 mm, and benzene extract is 11 mm (Streptomycin 10 µg/mL, 8 mm) (Sharma *et al.* 2018).
	Staphylococus aureus	The diameter of the inhibition zone for the methanol extract is 16 mm, ethyl acetate extract is 12 mm, petroleum ether extract is 12 mm (Sharma *et al.* 2018), n-hexane extract is 16 mm, and acetone extract is 10 mm (Imipenem + Cilastatin, 5 mg/mL, 25 mm) (Penecilla and Magno 2011).
	Proteus mirabilis	The diameter of the inhibition zone for the methanol extract is 20 mm, chloroform extract is 11 mm, and benzene extract is 11 mm (Streptomycin 10 µg/mL, 8 mm) (Sharma *et al.* 2018).
	Salmonella typhi	The diameter of the inhibition zone for the methanol extract is 15 mm, and that for acetone extract is 12 mm (Streptomycin 10 µg/mL, 8 mm) (Sharma *et al.* 2018).
	Serratia marcescens	The diameter of the inhibition zone for the methanol extract is 26 mm, acetone extract is 11 mm, ethyl acetate extract is 10 mm, chloroform extract is 12 mm, petroleum ether extract is 10 mm, and benzene extract is 12 mm (Streptomycin 10 µg/mL, 8 mm) (Sharma *et al.* 2018).
	Bacillus subtilis	The diameter of the inhibition zone for the n-hexane extract is 15 mm, and the acetone extract is 10 mm (Imipenem + Cilastatin, 5 mg/mL, 25 mm) (Penecilla and Magno 2011).
	Multidrug-Resistant Staphylococcus aureus	The diameter of the inhibition zone for quercetin (8) is 10 mm, and the lunarin (9) is 11 mm (amoxicillin, 25 ng/mL, 18 mm) (Ramos *et al.* 2006).

Plant Species	Bacteria / Fungi	Activity
	Helicobacter pylori	The diameter of the inhibition zone for quercetin (8) is 13 mm, *4'-O-methylquercetin* (10) 11 mm, and phloroglucinoyl-3,4-dihydroxybenzoate (11) 13 mm (amoxicillin, 25 ng/mL, 18 mm) (Ramos *et al.* 2006).
	Malassezia furfur	MIC of the ethanol extract > 100 µg/mL (Ketoconazole, 10 µg/mL, 0.251-4.522 10 µg/mL) (Shams-Ghahfarokhi *et al.* 2006)
	Candida albicans	
	Candida glabrata	
	Candida tropicalis	
	Candida parapsilosis	
	Trichophyton mentagrophytes	
	Trichophyton rubrum	
	Microsporum canis	
	Microsporum gypseum	
	Epidermophyton floccosum	
Allium sativum L	*Shigella* sp	The diameter of the water extract inhibition zone is 13–15 mm (Ciprofloxacin, 0.1 mL, 10-15 mm) (Bamal and Sharma 2021; Chaimanee *et al.* 2017; Eja *et al.* 2007; Shams-Ghahfarokhi *et al.* 2006).
	Salmonella sp	
	Escherichia coli	
	Proteus mirabilis	
	Candida albicans	The diameter of the inhibition zone for 20 mg/mL water extract is 30 mm (Clotrimazole, 20 mg/mL, 28 mm) (Singh *et al.* 2022).
Areca catechu L	*Pseudomonas aeruginosa*	The diameter of the inhibition zone for 100 µL of acetone extract is 15.5 mm, and for 100 µL of ethanol extract is 18.17 mm (Ciprofloxacin, 15 µL/well, 30 mm) (Ambika and Rajagopal 2017; Khan and Akhter 2020).
	Salmonella paratyphi	The diameter of the inhibition zone for 100 µL of acetone extract is 18.17 mm, and for 100 µL of ethanol extract is 17.67 mm (Ciprofloxacin, 15 µL/well, 18 mm) (Khan and Akhter 2020).
	Micrococcus sp	The diameter of the inhibition zone for 100 µL of acetone extract is 17.3 mm, and for 100 µL of ethanol extract is 19 mm (Ciprofloxacin, 15 µL/well, 30 mm) (Khan and Akhter 2020).
	Staphylococus aureus	The diameter of the inhibition zone of 50 µL of acetone extract from seeds is 17.17 mm, 100 µL of acetone extract is 20.17 mm, and 100 µL of ethanol extract from seeds is 15.5 mm (Ciprofloxacin, 15 µL/well, 30.67 mm) (Khan and Akhter 2020).
	Salmonella typhi	The diameter of the inhibition zone of 50 µL of acetone extract from seeds is 16.17 mm, 100 µL of acetone extract is 20.17 mm, and 100 µL of ethanol extract from seeds is 16.83 mm (Ciprofloxacin, 15 µL/well, 31.5 mm) (Khan and Akhter 2020).
	Escherichia coli	The diameter of the inhibition zone of 50 µL of acetone extract from seeds is 17.5 mm, 100 µL of acetone extract is 20.83 mm, and 100 µL of ethanol extract from seeds is 16.17 mm (Ciprofloxacin, 15 µL/well, 29.5 mm) (Khan and Akhter 2020).
	Vibrio cholera	The diameter of the inhibition zone for 100 µL of acetone extract is 18 mm, and for 100 µL of seed ethanol extract is 16.67 mm (Ciprofloxacin, 15 µL/well, 32 mm) (Khan and Akhter 2020).

Plant Species	Bacteria / Fungi	Activity
	Mycobacterium tuberculosis	MIC of methanol extract from endosperm is 0.975 µg/mL; MIC of ethanol fraction is 0.91 µg/mL. MIC of catechin (12) isolate from endosperm is 3.906 µg/mL; MIC of epicatechin (13) isolate from endosperm is 3.906 µg/mL; MIC of epigallocatechin gallate *(EGCG)* (14) is 1.05 µg/mL (Ethambutol, 4 µg/mL) (Raju *et al.* 2021).
Caesalpinia pulcherrima (L.) Sw	*Staphylococcus aureus*	The diameter of the inhibition zone is 75 µg/mL methanol extract from roots 19 mm, 150 µg/mL methanol extract from roots 22 mm, and 225 µg/mL methanol extract from roots 23 mm (Piperacillin, 100 µg/disc, 28 mm) (Prakash *et al.* 2009). The diameter of the inhibition zone for 100 µg/mL isolate [(*3E*)-3- (1,3-benzodioxol-5-ylmethylene)-2,3-dihydro-7-hydroxy-4*H*-1-benzopyran-4-one] (15) and sappanone A (17) 11–15 mm (Penicillin G 30 µg/ml, 21-25 mm) (Asati and Yadava 2018).
	Staphylococcus epidermidis	Inhibition zone diameter 75 µg/mL methanol extract from roots is 18 mm, 150 µg/mL methanol extract from roots is 21 mm, 225 µg/mL methanol extract from roots is 22 mm (Piperacillin, 100 µg/disc, 18 mm) (Prakash *et al.* 2009).
	Pseudomonas aeruginosa	The diameter of the inhibition zone of 75 µg/mL methanol extract fromroots is 20 mm, 150 µg/mL methanol extract from roots is 21 mm, and 225 µg/mL methanol extract from roots is 25 mm (Piperacillin, 100 µg/disc, 18 mm) (Prakash *et al.* 2009).
	Klebsiella pneumoniae	Inhibition zone diameter from 75 µg/mL methanol extract from roots is 19 mm, 150 µg/mL methanol extract from roots is 20 mm, 225 µg/mL methanol extract from seeds is 27 mm (Prakash *et al.* 2009), and aerial part water extract is 13 mm (Piperacillin, 100 µg/disc, 25 mm) (Parekh and Chanda 2007).
	Bacillus cereus	The diameter of the inhibition zone for the aerial part of the water extract is 12 mm, and the methanol extract is 20 mm (Piperacillin, 100 µg/disc, 18 mm) (Parekh and Chanda 2007).
	Enterobacter aerogenes	The diameter of the inhibition zone of the methanol extract aerial part is 15 mm (Piperacillin, 100 µg/disc, 12 mm) (Parekh and Chanda 2007). Inhibition zone diameter: 100 µg/mL of isolates [(*3E*)-3- (1,3-benzodioxol-5-ylmethylene)-2,3-dihydro-7-hydroxy-4*H*-1-benzopyran-4-one] (15) and [(*3E*)-2,3-dihydro-3-[(3,4-dimethoxyphenyl)methylene] -7-methoxy-4H-1-benzopyran-4-one] (16) is 11–15 mm (Penicillin G 30 µg/ml, 21-25 mm) (Das *et al.* 2009).
	Escherichia coli	The diameter of the inhibition zone of the methanol aerial part extract is 14 mm (Penicillin G 30 µg/ml, 21-25 mm) (Parekh and Chanda 2007).
	Chromobacterium violaceum	Inhibition zone diameter: 100 µg/mL isolate [(3*E*)-3- (1,3-benzodioxol-5-ylmethylene)-2,3-dihydro-7-hydroxy-4*H*-1-benzopyran-4-one] (Clotrimazole, 100 µg/ml, 21-25 mm) (15) is 11–15 mm (Das *et al.* 2009).
	Candida parapsilosis *Candida krusei* *Candida guilliermondii* *Candida albicans* *Aspergillus flavus* *Aspergillus furmigatus* *Cryptococcus neoformans*	The MIC of the leaf acid-base fraction is 31.25 µg/mL (Clotrimazole, 100 µg/ml, 21-25 mm) (de Melo *et al.* 2020).

Plant Species	Bacteria / Fungi	Activity
Cassia occidentalis L	*Bacillus subtilis*	The diameter of the inhibition zone for the hexane, dichloromethane, ethylacetate, diethylether, and methanol extracts from leaves is 10–20 mm (Samy and Ignacimuthu 2000).The MIC of emodin (18) isolate is 7.8 µg/mL, equivalent to 28.86 µM (Cloramphenicol, 30 µg/disc, 21-23 mm) (Chukwujekwu *et al.* 2006).
	Escherichia coli	The diameter of the inhibition zone for the hexane, dichloromethane, ethylacetate, diethylether, and methanol extracts from leaves is 10–20 mm (Cloramphenicol, 30 µg/disc, 21-23 mm) (Samy and Ignacimuthu 2000). The MIC of emodin (18) isolate at 3.9 µg/mL is equivalent to 14.42 µM (Cloramphenicol, 30 µg/disc, 21-23 mm) (Chukwujekwu *et al.* 2006).
	Klebsiella aerogenes *Pseudomonas aeruginosa* *Proteus vulgaris* *Staphylococcus aureus*	The diameter of the inhibition zone for the hexane, dichloromethane, ethyl acetate, diethyl ether, and methanol extracts from leaves is 10–20 mm (Cloramphenicol, 30 µg/disc, 21-23 mm) (Samy and Ignacimuthu 2000).
Curcuma longa L	*Colletotrichum coccodes*	Methanol extract at 3000 µg/mL and 1000 µg/mLwere able to inhibit *C. coccodes* by 88% and 50%, respectively. In addition, 2000 µg/mL ethyl acetate and butanol fractions had inhibition values of 92% and 50%, respectively. Tests were also carried out on 500 µg/mL and 250 µg/mL demethoxycurcumin isolates, which were able to inhibit 97% and 92%, respectively (Ciprofloxacin, 5 µg, 23-33 mm) (Cho *et al.* 2006).
Foeniculum vulgare Mill	*Escherichia coli*	The diameter of the inhibitory zone for essential oil seeds is 24.63 mm, and the MIC of essential oil seeds is 6 µg/mL (Upadhyay 2015). The diameter of the inhibitory zone for the hexane extract from seeds is 22 mm, ethyl acetate extract is 18 mm, acetone extract is 22 mm, ethanol extract is 15 mm (Kaur and Arora 2009; Rezende *et al.* 2017), and the diameter of the inhibition zone of 50 mg/mL water extract from leaves is 15.22 mm (Amoxicillin, 30 µg, 18-22 mm) (Shahmokhtar and Armand 2017).
	Bacillus cereus	The diameter of the inhibition zone for essential oil seeds is 26.5 mm, and the MIC of essential oil seeds is 12 µg/mL (Ampicillin, 24 µg/disc, 15.1-18.8 mm) (Upadhyay 2015).
	Lactobacillus acidophilus	The diameter of the inhibition zone for essential oil seeds is 25.9 mm, and the MIC of essential oil seeds is 24 µg/mL (Ampicillin, 24 µg/disc, 15.1-18.8 mm) (Upadhyay 2015).
	Micrococcus luteus	The diameter of the inhibitory zone for essential oil seeds is 24.1 mm, and the MIC of essential oil seeds is 48 µg/mL (Ampicillin, 24 µg/disc, 15.1-18.8 mm) (Upadhyay 2015).
	Staphylococcus aureus	The diameter of the inhibitory zone for essential oil seeds is 21.6 mm, the MIC of essential oil seeds is 48 µg/mL (Ampicillin, 24 µg/disc, 15.1-18.8 mm) (Akeel *et al.* 2017; Upadhyay 2015), the diameter of the inhibitory zone for the hexane extract from seeds is 29 mm, ethyl acetate extract is 23 mm, acetone extract is 28 mm, ethanol extract is 21 mm (Kaur and Arora 2009), and the MIC of the seed methanol extract was 8.33 µg/ml (Ampicillin, 25 µg/ml, MIC 0.5 µg/ml) (Dua *et al.* 2013).
	Klebsiella pneumoniae	The diameter of the inhibition zone for essential oil seeds is 23.2 mm, and the MIC of the essential oil seeds is 48 µg/mL (Ampicillin, 24 µg/disc, 15.1-18.8 mm) (Beyazen *et al.* 2017; Upadhyay 2015).
	Streptococcus pneumoniae	The diameter of the inhibition zone for the essential oil seeds is 20.2 mm, and the MIC of the essential oil seeds is 24 µg/mL (Ampicillin, 24 µg/disc, 15.1-18.8 mm) (Upadhyay 2015).

Plant Species	Bacteria / Fungi	Activity
	Enterococcus faecalis	The diameter of the inhibition zone of the hexane extract from seeds is 28 mm, ethyl acetate extract is 26 mm, acetone extract is 29 mm, and ethanol extract is 21 mm (Chloramphenicol, 30µg/disc, 23 mm) (Kaur and Arora 2009).
	Salmonella typhimurium	The diameter of the inhibition zone of the hexane extract from seeds is 13 mm, ethyl acetate extract is 12 mm, acetone extract is 13 mm, and ethanol extract is 10 mm (Chloramphenicol, 30µg/disc, 32 mm) (Kaur and Arora 2009).
	Shigella flexneri	The diameter of the inhibition zone of the hexane extract from seeds is 26 mm, ethyl acetate extract is 23 mm, acetone extract is 26 mm, and ethanol extract is 19 mm (Chloramphenicol, 30µg/disc, 25 mm) (Kaur and Arora 2009).
	Pseudomonas aeruginosa	The diameter of the inhibition zone for the 50 mg/mL water extract from leaves is 18.74 mm, and for 25 mg/mL water extract, it is 16.42 mm (Amoxicillin, 100 µg/mL, 19.36 mm) (Shahmokhtar and Armand 2017).
	Bacillus subtilis	The diameter of the inhibition zone of the 50 mg/mL water extract from leaves is 14.27 mm, and that of 25 mg/mL water extract is 12.20 mm (Amoxicillin, 100 µg/mL, 14.89 mm) (Shahmokhtar and Armand 2017).
	Bacillus pumilis	The diameter of the inhibition zone of the methanol extract from seeds is 11.27 mm, and the MIC of methanol extract from seeds was 8.33 µg/ml (Ampicillin, 25 µg/ml, MIC 0.5 µg/ml) (Dua *et al.* 2013).
Moringa oleifera Lam	*Pseudomonas aeruginosa*	Inhibitory zone diameter of the leaf methanol extract is 21 mm, leaf ethanol extract is 22 mm, root methanol extract is 22 mm, root ethanol extract is 20 mm, root ethyl extract is 24 mm, flower methanol extract is 25 mm, flower ethanol extract is 22 mm, flower ethyl extract is 20 mm, stem methanol extract is 26 mm, stem ethanol extract is 20 mm, stem ethyl extract is 22 mm, seed methanol extract is 23 mm, seed ethanol extract is 20 mm (thymol, 100 µL, 30 mm) (Amabye and Tadesse 2016; Goswami and Singhai 2015; Prabakaran *et al.* 2018).
	Erwinia carotovora	Inhibitory zone diameter of the leaf methanol extract is 20 mm, leaf ethanol extract is 21 mm, root methanol extract is 20 mm, root ethyl extract is 22 mm, flower ethyl extract is 22 mm, stem methanol extract is 21 mm, stem ethyl extract is 21 mm, seed methanol extract is 22 mm, ethanol extract of seeds is 20 mm, and ethyl extract of seeds is 21 mm (thymol, 100 µL, 28 mm) (Genemo 2021; Prabakaran *et al.* 2018).
	MRSA	The diameter of the inhibition zone of the 40% leaf ethanol extract is 15.5 mm (linezolid 30 µg/disc, 20 mm) (Sinaga *et al.* 2021).
	Bacillus subtilis	The diameter of the inhibition zone is 20 mm (methanol extract of leaves); methanol extract of stem bark is 22 mm; benzene extract of seeds is 22 mm; and water extract of seeds is 20 mm (chlorampenicol, 15 µL, 22 mm) (Haseeb *et al.* 2019; Priya *et al.* 2011).
	Escherichia coli	The diameter of the inhibition zone for the leaf water extract is 20 mm, and for the fruit water extract, is 20 mm (chlorampenicol, 15 µL, 19 mm) (Mensah *et al.* 2012; Priya *et al.* 2011).
	Klebsiella pneumoniae	The diameter of the inhibition zone of the methanol extract of stem bark is 20 mm, petroleum ether extract of seeds is 20 mm, methanol extract of seeds is 21 mm, and water extract of seeds is 22 mm (chlorampenicol, 15 µL, 22 mm) (M *et al.* 2021; Priya *et al.* 2011).
	Shigella dysentriae	The diameter of the inhibition zone of the methanol leaf extract is 21 mm, leaf water extract is 22 mm, stem bark methanol extract is 20 mm, fruit benzene extract is 21 mm, and fruit water extract is 20 mm (chlorampenicol, 15 µL, 20 mm) (Priya *et al.* 2011; Sanusi *et al.* 2017).
	Staphylococcus aureus	The diameter of the inhibition zone of the leaf methanol extract is 20 mm, the leaf water extract is 21 mm, and the seed methanol extract is 21 mm (chlorampenicol, 15 µL, 23 mm) (Nishu *et al.* 2020; Priya *et al.* 2011).

Plant Species	Bacteria / Fungi	Activity
	Salmonella sp	The diameter of the inhibition zone of the leaf ethanol extract is 23 mm (tetracyclin, 30 µg/disc, 22 mm) (Rahman *et al.* 2010; Zaffer *et al.* 2001).
	Enterobacter sp	The diameter of the inhibition zone of the leaf ethanol extract is 19 mm (tetracyclin, 30 µg/disc, 19 mm) (Rahman *et al.* 2010).
	Serratia marcescens	The diameter of the inhibition zone of the leaf ethanol extract is 17 mm (tetracyclin, 30 µg/disc, 11 mm) (Rahman *et al.* 2010).
	Corynebacterium pseudotuberculosis,	The diameter of the inhibition zone of the leaf water extract is 22.5 mm, and the leaf ethanol extract is 25.65 mm (tetracyclin, 30 µg/disc, 18 mm) (Fouad *et al.* 2019).
	Corynebacterium ulcerans	The diameter of the inhibitory zone of the leaf water extract is 25.5 mm, and theleaf ethanol extract is 30.5 mm (tetracyclin, 30 µg/disc, 20 mm) (Fouad *et al.* 2019).
	Proteus vulgaris	The diameter of the inhibition zone of the leaf water extract is 14.75 mm, and the leaf ethanol extract is 24.75 mm (tetracyclin, 30 µg/disc, 19 mm) (Fouad *et al.* 2019; Shailemo *et al.* 2016).
	Citrobacter sp	The diameter of the inhibition zone of the leaf water extract is 20.65 mm, and the leaf ethanol extract is 19.5 mm (tetracyclin, 30 µg/disc, 22 mm) (Fouad *et al.* 2019; Shukla and Tripathi 2015).
	Proteus mirabilis	Inhibition zone diameters of the 500 mg/mL leaf ethanol extract is 12.1 mm and the 250 mg/mL leaf ethanol extract is 11.1 mm (ciprofloxacin disc, 5 µg/disc, 38 mm) (Bunza *et al.* 2019; Jha *et al.* 2009).
Piper nigrum L	*Streptococcus mutans*	The diameter of the inhibition zone for the 5% ethanol extract from seeds is 29 mm, and the 2.5% ethanol extract from seeds is 24 mm (ampicillin, 0.32 µg/mL, 5 mm) (Kaho *et al.* 2019)
	Escherichia coli	The diameter of the inhibition zone of the 5% ethanol extract from seeds is 14 mm (ampicillin, 0.32 µg/mL, 4 mm) (Kaho *et al.* 2019; Okmen *et al.* 2017).
	Bacillus subtilis	Inhibition zone diameter: 100 µg/mL *n*-isobutyleicosatrienamide (20) isolate 10 mm, 100 µg/mL trachyone (22) isolate 11 mm, 30 µg/mL, and 100 µg/mL isopiperolein (23) isolate 16 mm and 21 mm, respectively; and 30 µg/mL and 100 µg/mL,isolate zpergumidiene (24) 12 mm and 14 mm, respectively (streptomycin, 30 µg/mL, 15 mm) (Reddy *et al.* 2004).
	Staphylococcus aureus	Inhibition zone diameter: 30 µg/mL and 100 µg/mL *n*-isobutyleicosatrienamide (20) isolate: 18 mm and 23 mm respectively; 100 µg/mL pellitorine (21) isolate: 11 mm; 30 µg/mL, and 100 µg/mL trachyone (22) isolate 14 mm and 20 mm, respectively; 30 µg/mL and 100 µg/mL of 17 mm and 21 mm isopiperolein (23) isolate, respectively; , and 100 µg/mL of 13 mm pergumidiene (24) isolate (streptomycin, 30 µg/mL, 12 mm) (Reddy *et al.* 2004).
	Bacillus sphaericus	Inhibition zone diameter: 100 µg/mL *n*-isobutyleicosatrienamide (20) isolate 10 mm; 30 µg/mL, and 100 µg/mL pellitorine (21) isolate 10 mm and 12 mm, respectively; 100 µg/mL trachyone (22) isolate 13 mm; 30 µg/mL, and 100 µg/mL isopiperolein (23) isolate 15 mm and 19 mm, respectively; 30 µg/mL, and 100 µg/mL pergumidiene (24) isolate 12 mm and 14 mm, respectively (streptomycin, 30 µg/mL, 14 mm) (Reddy *et al.* 2004).
	Klebsiella aerogenes	Inhibition zone diameter: 30 µg/mL and 100 µg/mL n-isobutyleicosatrienamide (20) isolate 19 mm and 28 mm, respectively; 30 µg/mL and 100 µg/mL trachyone (22) isolate 16 mm and 22 mm, respectively; 30 µg/mL and 100 µg/mL isopiperolein (23) isolate 18 mm and 23 mm respectively, 30 µg/mL and 100 µg/mL pergumidiene (24) isolate 10 mm and 12 mm, respectively (streptomycin, 30 µg/mL, 30 mm) (Reddy *et al.* 2004).

Plant Species	Bacteria / Fungi	Activity
	Chromobacterium violaceum	Inhibition zone diameter: 30 µg/mL and 100 µg/mL *n*-isobutyleicosatrienamide (20) isolate 18 mm and 24 mm, respectively; 30 µg/mL and 100 µg/mL trachyone (22) isolate 14 mm and 19 mm, respectively; 30 µg/mL, and 100 µg/mL, and isopiperolein (23) isolate 17 mm and 21 mm, respectively (streptomycin, 30 µg/mL, 28 mm) (Reddy *et al.* 2004).
Portulaca oleracea L	*Pseudomonas aeruginosa* *Klebsiella pneumoniae* *Salmonella typhimurium* *Proteus mirabilis* *Enterobacter aerogenes*	The diameter of the inhibition zone of 10 μL apigenin (25) isolate from aerial parts is 10–20 mm (streptomycin, 10 μL, 11-19 mm) (Lei *et al.* 2015; Nayaka *et al.* 2014).
Psophocarpus tetragonolobus (L.) DC	*Bacillus subtilis* *Bacillus cereus* *Bacillus licheniformis* *Staphylococcus aureus* *Agrobacterium tumefacien* *Micrococcus luteus* *Escherichia coli* *Salmonella typhimurium* *Salmonella typhi* *Klebsiella pneumoniae* *Pseudomonas aeruginosa*	The diameter of the inhibition zone of 10 mg/mL chloroform, ethanol, and ethylacetate extracts from roots, stems, leaves, and seeds ranges from 10 to 20 mm (ampicilin, 50 mg/mL, 12-32 mm) (Nazri *et al.* 2011; Sasidharan *et al.* 2008).
Quercus infectoria Oliv	*Micobacterium tuberculosis* *Pseudomonas aeruginosa* *Staphylococcus aureus* *Vibriyo harveyi*	The diameter of the inhibition zone of the seed methanol extract at 0.5 mg/mL is 26–28 mm (streptomycin, 0.5 mg/mL, 25-40 mm) (Baharuddin *et al.* 2015; Faki *et al.* 2018; Mohammadzadeh *et al.* 2021; Sheeba *et al.* 2015)
Sesbania grandiflora L	*Klebsiella pneumoniae*	The diameter of the inhibition zone for petroleum ether, chloroform, methanol, and water extracts from the roots at 100 µg/mL was 20 to 22 mm (ciprofloxacin, 100 µg/mL, 25 mm) (Anantaworasakul *et al.* 2011; Kumar 2016; Noviany *et al.* 2020; Packiyalakshmi *et al.* 2016; Subramanian *et al.* 2003).
Syzygium aromaticum (L.) Merr. & L.M.Perry	*Bacillus cereus* *Staphylococcus saprophyticus*	The diameter of the inhibition zone of 500 mg/mL methanol extract of flower buds is 10 to 20 mm (chlorampehnicol, 2.5 mg/disc, 25-35 mm) (Abdallah 2020).

Plant Species	Bacteria / Fungi	Activity
	Enterococcus faecalis	
	Staphylococcus epidermidis	
	Proteus vulgaris	
	Klebsiella pneumoniae	
	Staphylococcus typhimurium	
	Staphylococcus flexneri	
	Escherichia coli	
Tamarindus indica L	*Staphylococcus aureus*	The diameter of the inhibition zone of the dichloromethane flower extract is 25 mm, methanol extract is 28 mm, and water extract is 20 mm (ampicillin, 10 µg/disc, 26 mm) (Al-Fatimi *et al.* 2007).
	Bacillus subtilis	The diameter of the inhibition zone of the flower dichloromethane extract is 15 mm, methanol extract is 20 mm, and water extract is 20 mm (ampicillin, 10 µg/disc, 28 mm) (Al-Fatimi *et al.* 2007).
	Micrococcus flavus	The diameter of the inhibition zone of water extracts from flowers is 15 mm (ampicillin, 10 µg/disc, 31 mm) (Al-Fatimi *et al.* 2007).
	Escherichia coli	The diameter of the inhibition zone of the methanol extract of flowers is 18 mm, water extract is 20 mm (gentamicin, 10 mg/disc, 15 mm) (Al-Fatimi *et al.* 2007), and 250 µg/mL ethanol extract of leaves is 12.7 mm (Chigurupati *et al.* 2018).
	Pseudomonas aeruginosa	The diameter of the inhibition zone of the flower methanol extract is 20 mm, and the water extract is 20 mm (gentamicin, 10 mg/disc, 18 mm) (Al-Fatimi *et al.* 2007).
	Salmonella paratyphi	The diameter of the inhibition zone of the methanol seed extract is 15 mm, and that of the water extract is 16 mm (ofloxacin, 5 µg/disc, 31 mm) (Kothari and Seshadri 2010).
	Staphylococcus epidermidis	The diameter of the inhibition zone of the methanol seed extract is 10 mm, and that of the water extract is 12 mm (streptomycin, 10 µg/disc, 20 mm) (Kothari and Seshadri 2010).
	Neisseria gonorrhoeae	The diameter of the inhibition zone is 10 mm from the 250 µg/mL leaf ethanol extract (Gentamicin, 14 mm, 250 µg/mL) (Chigurupati *et al.* 2018).
Tectona grandis L.f	*Escherichia coli*	The MIC of the fruit ethanol extract is 64 µg/mL (positive control, ciprofloxacine MIC 5 µg/mL) (Bitchagno *et al.* 2015).
	Enterobacter aerogenes	The MIC of the fruit ethanol extract is 64 µg/mL (positive control, ciprofloxacine MIC 25 µg/mL) (Bitchagno *et al.* 2015).
Zingiber zerumbet (L.) Sm	*Mycoplasma gallisepticum*	The diameter of the inhibition zone of the 500 mg/mL, 250 mg/mL, 125 mg/mL, and 62.5 mg/mL rhizome ethanol extract is 10–20 mm (oxytetracyclin, 28 mm, 30 µg/mL) (Sutardi *et al.* 2015).

Table 4 summarizes the plant species with the efficacy claims and categorization of ingredients in Serat Centhini, which have been further investigated and can be used as anti-allergies and anti-obesity agents in the metabolic syndrome category. Based on the results of research on these plants, *A. cepa* and *M. oleifera* have strong potential as anti-allergenic agents, while *A. galanga* has strong potential as an anti-obesity agent. Extraction and fractionation of several plants have isolated some molecules which have been subjected to biological testing for their anti-allergy and anti-obesity properties. These include kaempferol (26), ethyl- (*E*)–undec-6-enoate (27), 3,5,6-trihydroxy-2- (2,3,4,5,6-pentahydroxyphenyl)-4*H*-chromen-4-one (28), *β*-sitosterol-3-*O*-glucoside (29), stigmasterol (30), oleic acid (31), glucomoringin (32), galangin (33), and piperine (34) (Figure 11). Isolates with stronger activity than positive controls were galangin (33) and kaempferol (26).

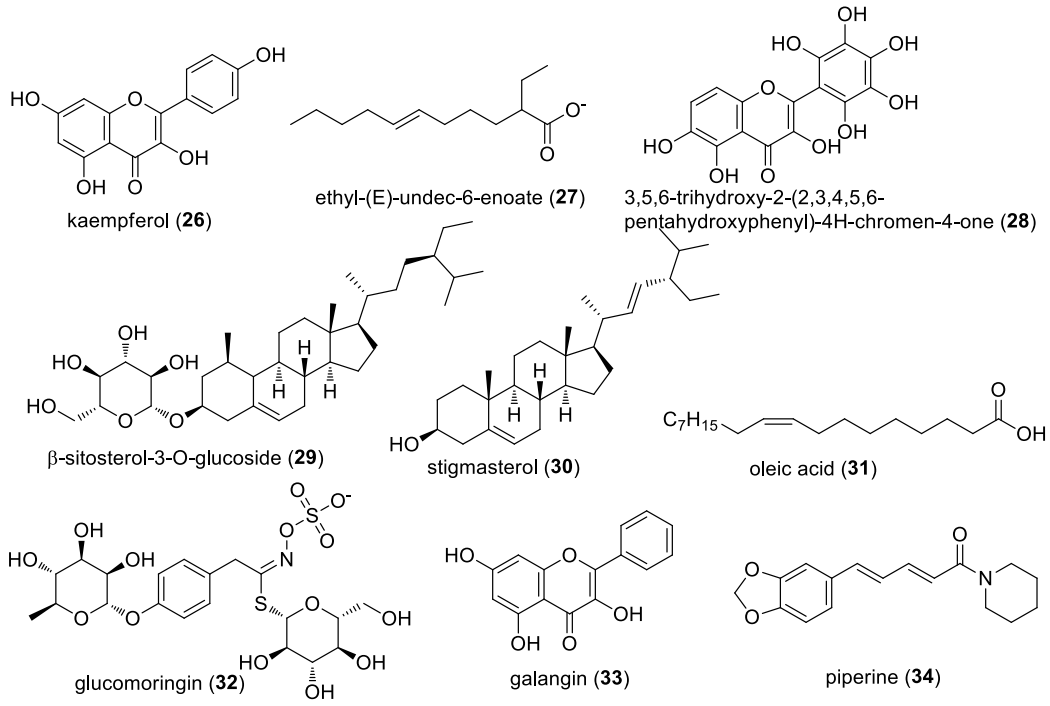


Figure 11. Isolates that have been tested for anti-allergy and anti-obesity

The flavonoid content in *A. cepa, Z. officinale*, and *Z. zerumbet* is thought to inhibit the release of histamine, which is a chemical mediator that causes allergies (Kawai *et al.* 2007). For anti-obesity activity, the flavonoid content (in *A. galanga*) and alkaloids (in *P. nigrum*) work by inhibiting the activity of the lipase enzyme, which hydrolyzes fat into monoglycerides and fatty acids, thereby reducing free fatty acids and reducing obesity. This research can be a reference for future research. Further research needs to be conducted on the potential of the plants *A. moluccana, A. oliviformis, C. pulcherrima, C. verum, C. hystrix, C. aeruginosa, C. xanthorrhiza, E. cardamomum, F. amelas, F. benjamina, F. vulgare, M. acuminata Varr balbisiana, P. cubeba, S. spontaneum, S. aromaticum, T. indica,* and *W. javanica* as therapies for metabolic syndrome.

Nervous system (NER)

The Serat Centhini reports the nervous system category as diseases that can cause disorders of the nerves, such as pain and inflammation. The Serat Centhini also described the use of several medicinal plants including *A. calamus, A. sativum, A. galanga*, *A. oliviformis, B. rotunda, C. pulcherrima, C. frutescens, Cassia occidentalis* L, *Citrus aurantiifolia* (Christm.) Swingle*, C. aeruginosa, C. longa*, *Elettaria cardamomum* (L.) Maton*, F. benjamina, F. vulgare, Limonia acidissima* Houtt*, M. oleifera, M. acuminata, O. sativa*, *P. betle, P. cubeba, P. nigrum, P. oleracea*, *P. tetragonolobus, S. spontaneum, S. grandiflora, T. indica, Z. montanum,* and *Z. zerumbet* which were prepared in oral and topical dosage form. Among these medicinal plants, *A. calamus, A. sativum, A. galanga, F. vulgare, L. acidissima, M. oleifera, P. betle, P. cubeba, P. nigrum, P. oleracea, S. grandiflora*, and *T. indica* have been subsequently studied and based on Staub's classification, the nervous system use category uses the sub-categories Attention Deficit Hyperactivity Disorder (ADHD), analeptic, Alzheimer's disease, analgesic, anticholinergics, Parkinson's disease, anxiety and psychosis, cerebral stimulants, major depression, narcolepsy, neuropathic pain, and vascular dementia.

Table 4. Plant activity in Serat Centhini as an anti-allergic and anti-obesity for metabolic syndrome categories has been studied.

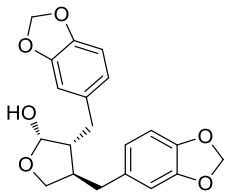
Plant Species	Function	Test Method	Sample Type	Activity	Reference
Allium cepa L	Anti-allergic	*In vivo*	Ethyl alcohol extract	Extract (concentration 400 µg/assay) showed anti-allergic activity with a histamine release amount of 148 µg compared to the positive control (ketotifen 4 µg/assay) with a histamine release amount of 133.7 µg.	(Kaiser *et al.* 2009)
	Anti-allergic	*In vivo*	Chloroform fraction	Fraction (concentration 4 µg/assay) showed anti-allergic activity with a histamine release amount of 199 µg compared to the positive control (ketotifen 4 µg/assay) with a histamine release amount of 133.7 µg.	(Kaiser *et al.* 2009)
	Anti-allergic	*In vivo*	Butanol fraction	Fraction (concentration 2.5 µg/mL) showed significant anti-allergic activity with a histamine release amount of 67 µg/mL compared to the positive control (ketotifen 4 µg/assay) with a histamine release amount of 133.7 µg.	(Kaiser *et al.* 2009)
	Anti-allergic	*In vivo*	Water fraction	Fraction (concentration 370 µg/assay) showed anti-allergic activity with a histamine release amount of 192 µg compared to the positive control (ketotifen 4 µg/assay) with a histamine release amount of 133.7 µg.	(Kaiser *et al.* 2009)
Alpinia galanga (L.) Willd	Anti-obesity	*In vivo*	Galangin (32)	Isolate (50 mg/kgBW) showed significant anti-obesity activity with % weight loss was 52.58% compared to positive control (sibutramine 2 mg/kgBW) with % weight loss 40.02%.	(Kumar and Alagawadi 2013)
Morinda citrifolia L	Anti-obesity	*In vitro*	Water extract	0.1 mg/mL and 0.5 mg/mL extract showed the inhibition of lipid accumulation 14.43% and 26.91%. It was smaller than 62.86% positive control (0.1 µg/mL cafein)	(Saraphanchotiwitthaya and Sripalakit 2016)
Moringa oleifera Lam	Anti-allergic	*In vitro*	Leaf ethanol extract	Extract (20 µL) showed anti-allergic activity with histamine inhibition IC_{50} 11.66 µg/mL compared to positive control (ketotifen fumarate 20 µL) with IC_{50} 6.97 µg/mL	(Rani *et al.* 2019)
	Anti-allergic	*In vitro*	Seed ethanol extract	Extract (20 µL) showed significant anti-allergic activity with histamine inhibition IC_{50} 5.97 µg/mL compared to positive control (ketotifen fumarate 20 µL) with IC_{50} 6.97 µg/mL.	(Rani *et al.* 2019)
	Anti-allergic	*In vitro*	Fruit ethanol extract	Extract (20 µL) showed anti-allergic activity with histamine inhibition IC_{50} 7.43 µg/mL compared to positive control (ketotifen fumarate 20 µL) with IC_{50} 6.97 µg/mL	(Rani *et al.* 2019)

Plant Species	Function	Test Method	Sample Type	Activity	Reference
	Anti-allergic	*In vitro*	Quercetin (8)	Isolate (20 µL) showed anti-allergic activity with histamine inhibition IC_{50} 44.87 µM compared to positive control (ketotifen fumarate 20 µL) with IC_{50} 6.97 µg/mL	(Rani *et al.* 2019)
	Anti-allergic	*In vitro*	Kaempferol (26)	Isolate (20 µL) showed significant activity with histamine inhibition IC_{50} of 7.77 µM equivalent to 2.224 µg/mL compared to positive control (ketotifen fumarate 20 µL) with IC_{50} of 6.97 µg/mL.	(Rani *et al.* 2019)
	Anti-allergic	*In vitro*	Ethyl- (*E*)–undec-6-enoate (27)	Isolate (20 µL) showed anti-allergic activity with histamine inhibition IC_{50} 82.07 µM compared to positive (ketotifen fumarate 20 µL) control with IC_{50} 6.97 µg/mL	(Rani *et al.* 2019)
	Anti-allergic	*In vitro*	3,5,6-Trihydroxy-2-(2,3,4,5,6-pentahydroxyphenyl)-4*H*-chromen-4-one (28)	Isolate (20 µL) showed anti-allergic activity with histamine inhibition IC_{50} 46.94 µM compared to positive (ketotifen fumarate 20 µL) control with IC_{50} 6.97 µg/mL	(Rani *et al.* 2019)
	Anti-allergic	*In vitro*	*β*-Sitosterol-3-O-glucoside (29)	Isolate (20 µL) showed anti-allergic activity with histamine inhibition IC_{50} 46.94 µM compared to positive (ketotifen fumarate 20 µL) control with IC_{50} 6.97 µg/mL	(Rani *et al.* 2019)
	Anti-allergic	*In vitro*	Stigmasterol (30)	Isolate (20 µL) showed anti-allergic activity with histamine inhibition IC_{50} 56.05 µM compared to positive (ketotifen fumarate 20 µL) control with IC_{50} 6.97 µg/mL	(Rani *et al.* 2019)
	Anti-allergic	*In vitro*	Oleic acid (31)	Isolate (20 µL) showed anti-allergic activity with histamine inhibition IC_{50} 27.22 µM compared to positive (ketotifen fumarate 20 µL) control with IC_{50} 6.97 µg/mL	(Rani *et al.* 2019)
	Anti-allergic	*In vitro*	Glucomoringin (32)	Isolate (20 µL) showed anti-allergic activity with histamine inhibition IC_{50} 38.27 µM compared to positive (ketotifen fumarate 20 µL) control with IC_{50} 6.97 µg/mL	(Rani *et al.* 2019)
	Anti-obesity	*In vivo*	Ethyl alcohol extract	Extract (300 mg/kgBW) showed rat body weight 24.9 g, compared to positive control (simvastatin 40 mg/kgBW) with 23.8 g rat body weight.	(Othman *et al.* 2019)
Piper nigrum L	Anti-obesity	*In vivo*	Water extract	Extract (20 g/rats) showed rat body weight 114 g, compared to positive control (orlistat 5 mg/kgBW) with 91.5 g rat body weight.	(Nazish *et al.* 2020)

Plant Species	Function	Test Method	Sample Type	Activity	Reference
	Anti-obesity	*In vivo*	Piperine (34)	Isolate (40 mg/kgBW) showed rat body weight 369.2 g, compared to positive control (orlistat 5 mg/kgBW) with 344.3 g rat body weight.	(Brahmanaidu *et al.* 2014)
Zingiber officinale Roscoe	Anti-allergic	*In vitro*	Ethanol extract	Extract (10.4 % w/w) showed the IC_{50} value is 40.3 µg/mL, compared with IC_{50} of positive vontrol (ketotifen fumarate) 20.2 µg/mL.	(Tewtrakul and Subhadhirasakul 2007)
	Anti-allergic	*In vitro*	Water extract	Extract (10.4 % w/w) showed the IC_{50} value is 62.6 µg/mL, compared with IC_{50} of positive vontrol (ketotifen fumarate) 20.2 µg/mL.	(Tewtrakul and Subhadhirasakul 2007)
	Anti-allergic	*In vitro*	Essential oil	Essential oil (0.7 % v/w) showed the IC_{50} value is >100 µg/mL, compared with IC_{50} of positive vontrol (ketotifen fumarate) 20.2 µg/mL.	(Tewtrakul and Subhadhirasakul 2007)
Zingiber zerumbet (L.) Sm	Anti-allergic	*In vitro*	Ethanol extract	Extract (24.6 % w/w) showed the IC_{50} value is 91 µg/mL, compared with IC_{50} of positive vontrol (ketotifen fumarate) 20.2 µg/mL.	(Tewtrakul and Subhadhirasakul 2007)
	Anti-allergic	*In vitro*	Water extract	Extract (24.6 % w/w) showed the IC_{50} value is 68.2 µg/mL, compared with IC_{50} of positive vontrol (ketotifen fumarate) 20.2 µg/mL.	(Tewtrakul and Subhadhirasakul 2007)
	Anti-allergic	*In vitro*	Essential oil	Essential oil (3 % v/w) showed the IC_{50} value is >100 µg/mL, compared with IC_{50} of positive vontrol (ketotifen fumarate) 20.2 µg/mL.	(Tewtrakul and Subhadhirasakul 2007)

Pain is an unpleasant sensory and emotional experience due to tissue damage that is subjective and related to the avoidance reflex (Bahrudin 2017). Analgesics are drugs to reduce or eliminate pain. Alzheimer's is a type of dementia characterized by a progressive decline in cognitive function, including all intellectual functions, in the form of a decrease in the ability to think, speak, and remember, as well as changes in behavior (Purba 2020). Parkinson's disease is a chronic neurodegenerative disorder caused by the loss of dopaminergic neurons in the substantia nigra pars compacta basal ganglia, which is characterized by movement disorders such as bradykinesia, or slow movements, muscle rigidity or stiffness, and tremors (Istarini *et al.* 2020).

Table 5 summarises the activities of plant extracts and isolates that have been reported in accordance with the efficacy claims and categorization of ingredients in Serat Centhini. These plants can be used as an analgesic, anti-alzheimer's, and anti-parkinson in the nervous system category. Based on the results of research on these plants, *A. calamus, A. galanga, F. vulgare, M. oleifera, P. nigrum*, and *P. oleracea* have strong potential as analgesic agents. *P. cubeba* and *S. grandiflora* have strong anti-alzheimer potential. Isolates with stronger activity than the positive control were piperine (34) and cubebin (35) (Figure 12). All results arise from *in vivo* testing.



cubebin (**35**)

Figure 12. Structure of the cubebin (35) compound isolated from *P. cubeba* fruit.

The flavonoid and alkaloid content in *A. calamus, L. acidissima, M. oleifera, P. nigrum,* and *T. indica* works by inhibiting cyclooxygenase resulting in the synthesis of prostaglandins, which are pain mediators, is also being inhibited (Debeturu *et al.* 2022). The alkaloid content in *P. cubeba* can reduce AChE activity, which is the cause of Alzheimer's (Acqua 2013). The content of phenolic compounds (in *A. sativum*) and flavonoids (in *A. calamus*) can prevent damage to dopaminergic nerve cells, which invokes Parkinson's disease. Research needs to be conducted on the potential of the plants *A. oliviformis, B. rotunda, C. pulcherrima, C. frutescens, C. occidentalis*, *C. aurantiifolia, E. cardamomum, F. benjamina, M. acuminata Varr balbisiana, O. sativa*, *S. spontaneum, Z. montanum,* and *Z. zerumbet* as therapies for disorders of the nerves.

Respiratory complaints (RES)

The Serat Centhini reports diseases related to the respiratory system and has described the use of several medicinal plants to treat these complaints including *A. cepa, A. stellate, A. catechu, B. rotunda, C. frutescens, C. aurantiifolia, C. hystrix, C. longa*, *F. vulgare, Justicia gendarussa* Burm.f.*, T. indica,* and *Z. officinale,* which prepared in oral dosage form by means of a decoction. Only *F. vulgare* has been laboratory studied to treat respiratory complaints. Based on Staub's classification, the sub-categories of use are antitussives, bronchodilators, and expectorants. Chronic Obstructive Pulmonary Disease (COPD) is a common disease caused by significant exposure to harmful particles or gases and is characterized by persistent respiratory symptoms and limited airflow in the respiratory tract. Bronchodilators are a class of drugs for COPD that work by relieving symptoms due to a narrowing of the respiratory tract.

The study of water, ethanol, and essential oil extracts from *F. vulgare* herbarium as bronchodilators has been tested *in vivo* on the trachea of male guinea pigs (Boskabady and Khatami 2003). In the positive control test, 1 mM anhydrous theophylline showed a relaxation value of 56.8%, and the negative control of 0.8 mL normal saline was 0.13%. The test results for 0.8 mL water extract were 20.9%; essential oil 0.06 mL of 20.9%; and 0.15 mL ethanol extract of 67.8%. These results indicate that 0.15 mL of *F. vulgare* herbarium ethanol extract can significantly relax compared to the positive control of 1 mM anhydrous theophylline. The results of this research are in accordance with the efficacy claims and categorization of ingredients in Serat Centhini, which show that *F. vulgare* can be used as a bronchodilator in the category of respiratory problems. Research needs to be conducted on the potential of the plants *A. cepa, A. stellate, A. catechu, B. rotunda, C. frutescens, C. aurantiifolia, C. hystrix, C. longa*, *J. gendarussa, T. indica,* and *Z. Officinale* to treat respiratory complaints.

Table 5. Reporting in Serat Centhini of plants with analgesic, anti-parkinson, and anti-alzheimer's for nervous system activities and with the subsequent studies.

Plant Species	Function	Test Method	Sample Type	Activity	Reference
Acorus calamus L	Analgesic	*In vivo*	Ethanol extract	Extract (500 mg/kgBW) showed significant analgesic activity with writhing of 45.49% compared to positive control (diclofenac sodium 25 mg/kgBW) with writhing of 48.92%	(Khan and Islam 2012)
	Anti-parkinson	*In vivo*	Methanol extract	Extract (400 mg/kgBW) activity showed the catalepsy time 55.37 second, compared with positive control (levodopa 30 mg/kgBW) 27.16 ssecond	(Raut *et al.* 2021)
Allium sativum L	Anti-parkinson	*In vivo*	Ethanol extract	Extract (400 mg/kgBW) activity showed the catalepsy time 78.33 second, compared with positive control (levodopa + carbidopa 10 mg/kgBW) 70.83 ssecond	(Banu *et al.* 2016)
Alpinia galanga (L.) Willd	Analgesic	*In vivo*	Ethanol extract	Significant analgesic activity with writhing inhibition of 80.17% (extract 800 mg/kgBW) compared to positive control (aspirine 100 mg/kgBW) with writhing inhibition of 64.33%.	(Acharya *et al.* 2011)
Foeniculum vulgare Mill	Analgesic	*In vivo*	Methanol extract	Significant analgesic activity with writhing inhibition reaching 44.4% (extract 400 mg/kgBW) compared to positive control (aspirin 200 mg/kgBW) with writhing inhibition of 33.3%.	(Monalisa and Rahmatullah 2015)
Limonia acidissima Houtt	Analgesic	*In vivo*	Methanol extract	Extract (500 mg/kgBW) showed % pain 60.53%, weaker than positive control (diclofenac sodium 10 mg/kgBW) with pain inhibition of 78.07%.	(Islam *et al.* 2020)
	Analgesic	*In vivo*	Acetone extract	Extract (500 mg/kgBW) showed % pain 59.65%, weaker than positive control (diclofenac sodium 10 mg/kgBW) with pain inhibition of 78.07%.	(Islam *et al.* 2020)
Moringa oleifera Lam	Analgesic	*In vivo*	Methanol extract	Significant analgesic activity with a pain inhibition of 83.3% (dose 100 mg/kg) and 90.3% (dose 200 mg/kg) compared to the positive control (diclofenac sodium) with a pain inhibition of 82.2%.	(Adedapo *et al.* 2015)
Piper betle L	Analgesic	*In vivo*	Methanol extract	Extract showed % pain 64.53%, weaker than positive control (diclofenac sodium 5 mg/kgBW) with pain inhibition of 68.19%.	(Alam *et al.* 2013)
Piper cubeba Bajoer	Anti-alzheimer's	*In vivo*	cubebine (35) isolate	The anti-alzheimer effect of isolate (cubebin 50 mg/kg) showed escape latency 22.8 second, compared with positive control (donepezile 1 mg/kg) 12.5 second	(Somani *et al.* 2017)
Piper nigrum L	Analgesic	*In vivo*	Hexane extract	Significant analgesic activity with pain inhibition reaching 99.71% (extract 15 mg/kgBW) compared to positive control (aspirin 10 mg/kgBW) with pain inhibition reaching 54.9%.	(Tasleem *et al.* 2014)

Plant Species	Function	Test Method	Sample Type	Activity	Reference
	Analgesic	*In vivo*	Ethanol extract	Significant analgesic activity with pain inhibition reaching 100% (extract 15 mg/kgBW) compared to positive control (aspirin 10 mg/kgBW) with pain inhibition reaching 54.9%.	(Tasleem *et al.* 2014)
	Analgesic	*In vivo*	Piperine (34)	Significant analgesic activity with pain inhibition reaching 100% (isolate 15 mg/kgBW) compared to positive control (aspirin 10 mg/kgBW) with pain inhibition reaching 54.9%.	(Tasleem *et al.* 2014)
Portulaca oleracea L	Analgesic	*In vivo*	Ethanol extract	Significant activity was observed with a pain inhibition of 249.7% (dose 200 mg/kgBW) and 187.2% (dose 400 mg/kgBW) compared to the positive control (diclofenac sodium 4 mg/kgBW) with a pain inhibition of 157.3%.	(Chan *et al.* 2000)
Sesbania grandiflora L	Anti-alzheimer's	*In vivo*	Methanol extract	The anti-alzheimer effect of 400 mg/kgBW extract showed escape latency 111.3 second, compared with positive control (donepezile 5 mg/kgBW) 108.1 second	(Av *et al.* 2020)
Tamarindus indica L	Analgesic	*In vivo*	Water extract	Extract (600 mg/kgBW) showed % pain 73.33%, weaker than positive control (aspirin 100 mg/kgBW) with pain inhibition of 78.07% and (morphine 5 mg/kgBW) with pain inhibiton 84.94%	(Khalid *et al.* 2010)

Skeleton-muscular system (SKE)

In Serat Centhini, all diseases that attack the skeleton, joints, and muscles are included in the category of the skeleton-muscular system. The Serat Centhini also described the use of several medicinal plants including *A. calamus, A. cepa, A. sativum, A. galanga*, *A. stellate, Amomum cardamomum* L, *Artocarpus elasticus* Reinw*, A. bilimbi, Avicennia marina* (Forssk.) Vierh*, C. frutescens, C. verum, C. aurantiifolia, C. nucifera*, *C. sativum, C. massoia, C. longa*, *Eleutherine bulbosa* (Mill.) Urb*, F. vulgare, K. galanga*, *Myristica fragrans* Houtt*, N. sativa, Parkia timoriana* (DC.) Merr*, P. cubeba, Plantago major* L*, P. tetragonolobus, Q. infectoria, Ruta graveolens* L*, S. aromaticum, T. indica, T. grandis, Tetrastigma glabratum* (Roxb.) Planch*, Z. montanum,* and *Z. zerumbet* which are prepared in oral dosage form by mean a decoction. Only *A. calamus* has been further studied to treat skeleton-muscular disorders. Based on Staub's classification, in the skeletal and muscular system use category, there are sub-categories of use, namely antispasmodics, muscle relaxants, and skeletal-muscle relaxants. Antispasmodics (spasmolytics) are drugs commonly used to reduce excessive smooth muscle contractions (Heghes *et al.* 2019).

The study of methanol extract of *A. calamus* rhizome as an antispasmodic has been conducted by testing in vivo on rabbit jejunum (Gilani *et al.* 2006). The test was conducted using the positive control verapamil and extracts with concentrations of 0.03 mg/mL, 0.1 mg/mL, 0.3 mg/mL, 1 mg/mL, and 3 mg/mL. The results showed that the % inhibition of contractions in verapamil 0.03 mg/mL was 1.34% and extract 0.03 mg/mL was 0%. In verapamil 0.1 mg/mL it was 16.46%, and extract 0.1 mg/mL was 10.87%. In verapamil 0.3 mg/mL, it was 57%, and extract 0.3 mg/mL was 29.13%. In verapamil 1 mg/mL, it was 73.46%, and extract 1 mg/mL was 91.63%. Last, verapamil 3 mg/mL and extract 3 mg/mL by 100%. This value shows that methanol extract of *A. calamus* rhizome concentrations of 1 mg/mL and 3 mg/mL can significantly inhibit contractions compared to the positive control verapamil. The presence of the alkaloids, saponins, and tannins in *A. calamus* is thought to have the same mechanism of action as verapamil.

The results of this research are also in accordance with the efficacy claims and categorization of ingredients in Serat Centhini that *A. calamus* can be used as an antispasmodic in the skeletal and muscular system categories. Research needs to be conducted on the potential of the plants *A. cepa, A. sativum, A. galanga*, *A. stellate, A. cardamomum*, *A. elasticus, A. bilimbi, A. marina, C. frutescens, C. verum, C. aurantiifolia, C. nucifera*, *C. sativum, C. massoia, C. longa*, *E. bulbosa, F. vulgare, K. galanga*, *M. fragrans, N. sativa, P. timoriana, P. cubeba, P. major, P. tetragonolobus, Q. infectoria, R. graveolens, S. aromaticum, T. indica, T. grandis, T. glabratum, Z. montanum,* and *Z. zerumbet* to treat skeleton-muscular disorders.

Urology (URO)

In Serat Centhini, all diseases related to male and female urinary tract disorders are included in the urology category. The Serat Centhini also described the use of several medicinal plants including *A. galanga*, *A. vulgaris*, *C. sativum,* and *Z. zerumbet* which are prepared in oral dosage form by mean a decoction. Among these medicinal plants only *C. sativum* has been studied as a diuretic agent. Based on Staub's classification, the urology use category has a sub-category of use, namely diuretics. Diuretics are substances that can increase the volume and speed up the flow of urine.

The study of methanol extract and water fraction of *C. sativum* fruit as diuretic agents has been tested *in vivo* on Wistar rats (Jabeen *et al.* 2009). In the methanol extract, the results showed that the urine volume of the negative control group of normal saline 50 mL/kg was 4.4 mL, the positive control of furosemide 10 mg/kg was 8.3 mL, the methanol extract 30 mg/kg was 5 mL, and the methanol extract 100 mg/kg was 6.5 mL. In the water fraction, the results showed that the urine volume of the negative control group of normal saline 50 mL/kg was 4 mL, the positive control of furosemide 10 mg/kg was 8 mL, the water fraction 30 mg/kg was 5.7 mL, and the water fraction 100 mg/kg was 6.5 mL. These results indicate that the methanol extract and the water fraction 100 mg/kg have diuretic activity that is close to the positive control of furosemide. The mechanism of action of furosemide as a diuretic is to increase the levels of sodium and potassium ions in the ascending segment of the henle loop. The flavonoid content in *C. sativum* fruit has a diuretic mechanism of action, namely inhibiting the reabsorption of sodium, potassium, and chloride ions, resulting in an increase of electrolytes in the tubules, resulting in diuresis (Maryam *et al.* 2020).

The results of this research are also in accordance with the efficacy claims and categorization of ingredients in Serat Centhini, indicating that *C. sativum* can be used as a diuretic agent in the urology category. Research needs to be conducted on the potential of the plants *A. galanga*, *A. vulgaris,* and *Z. zerumbet* asdiuretic agents.

Serat Centhini Bioprospecting Potential and Strategy

The existence of traditional knowledge in the uses of medicinal plants among the indigenous people of Java can be observed in current daily life (Figure 13). The traditional medicine has been categorized by the Government of the Republic of Indonesia into three sections; *Jamu (empirical-based herbal medicine), Herbal Terstandard* (OHT, *preclinical-based herbal medicine)*) and *Fitorfarmaka (clinical-based herbal medicine)* (Rani *et al.* 2023). The first refers to traditional medicine which merely relies on empirical knowledge inherited through generations with no pre-clinical and clinical experimental data. This practice has contributed to Indonesian health with the largest product reaching more than 12,000 *jamu* in the market. The second, a development of Jamu with pre-clinical supporting data in which more than 86 OHT available in the market. The most developed, *Fitofarmaka*, requires pre-clinical and clinical data to comply with the regulation under The Indonesian Food and Drug Authority (Asri and Octasari 2024). Currently the Government provides several incentives including research funding for cooperative projects between research laboratories and an industry focusing on developing the Jamu or OHT into fitofarmaka. This program aims to ensure an increasing number of herbal based medicines to possess high efficacy and safety which will be available in the formal healthcare services throughout the archipelago (Figure 14) (Rani *et al.* 2023). The government through the Ministry of Health has established a herbal medicine center for research and service at Karanganyar-Java Island. This will be an acceleration in the developing of Indonesian medicinal plants including plant listed in Centhini manuscript to be prospected for the most benefit to the Society in Java Island and other Islands in the republic.

Figure 13. Indonesian traditional medicine, *Jamu*, sold in the Beringhardjo Market, Yogyakarta, Java Island, Indonesia. The figure depicting famous *jamu godhog* (traditional herbal medicine prepared through decoction) to alleviate metabolic disorders as described in the Centhini manuscript.

A review of the literature shows four medicinal plants, *A. calamus, S. grandiflora, M. oleifira, M. citrifolia, L. acidissima* with full information on pharmacological claims described in the Centhini manuscript based on previous studies (Figure 15). Our study reveals the medicinal plants listed in the Centhini manuscript that are confirmed, partly confirmed and unconfirmed (Figure 16).

Despite medicinal plants listed in Centhini manuscript still being practiced among the indigenous people of Java Island, a total of 32 medicinal plants remain under studied for their potency to support their traditional claims. These plants, including *M. charantia* as an erectile agent. *Z. montanum* as an antioxidant and a therapeutic agent for skeleton-muscular disorders; *A. oliviformis* as a therapeutic agent for ophthalmic problems, infections, metabolic syndrome and nerve discorder; *A. vulgaris* as a therapeutic agent for dermatologic disorders, gastrointestinal problems and as diuretic agents; *C. bicolor* as a therapeutic agent for dermatologic disorders; *C. frutescens* as a therapeutic agent for dermatologic disorders,

gastrointestinal problems, nerve disorder, respiratory complaints and skeleton-muscular disorders; *C. tinctorius* as a therapeutic agent for dermatologic disorders.;*C. massoia* as a therapeutic agent for dermatologic disorders and skeleton-muscular disorders; *F. benjamina* as a therapeutic agent for dermatologic disorders, gastrointestinal problems, metabolic syndrome and disorders of the nerves; *K. galanga* as a therapeutic agent for dermatologic disorders, gastrointestinal problems, infections, skeleton-muscular disorders and as diuretic agents; *M. acuminata* as a therapeutic agent for dermatologic disorders, gastrointestinal problems, infections, metabolic syndrome and disorders of the nerves; *M. fragrans* as a therapeutic agent for dermatologic disorders, skeleton-muscular disorders; *O. Sanctum* as a therapeutic agent for dermatologic disorders, gastrointestinal problems; *P. amaryllifolius* as a therapeutic agent for dermatologic disorders; *S. myrtifolium* as a therapy for dermatologic disorders; *S. rarak* as a therapeutic agent for ophthalmic problems; *C. xanthorrhiza* as an antioxidant, and as a therapeutic agent for gastrointestinal problems and metabolic syndrome; *T. glabratum* as an antioxidant, and as a therapeutic agent for gastrointestinal problems, and skeleton-muscular disorders; *A. ascalonium*, as a therapy for gastrointestinal problems; *A. elasticus* as a therapeutic agent for gastrointestinal problems andskeleton-muscular disorders; *C. aurantiifolia* as a therapeutic agent for gastrointestinal problems, disorders of the nerves, respiratory complaints, and skeleton-muscular disorders. *C. hystrix* as a therapy for gastrointestinal problems, metabolic syndrome, and respiratory complaints; *C. aeruginosa* as a therapy for gastrointestinal problems and metabolic syndrome; *E. bulbosa* as a therapy for gastrointestinal problems and skeleton-muscular disorders; *S. spontaneum* as a therapeutic agent for infections, metabolic syndrome, and disorders of the nerves; *C. verum* as an erectile agent, as a therapeutic agent for metabolic syndrome and skeleton-muscular disorders; *W. javanica* as a therapeutic agent for metabolic syndrome; *E. cardamomum* as a therapy for metabolic syndrome, disorders of the nerves, and skeleton-muscular disorders; *J. gendarussa* as a therapeutic agent for respiratory complaints; *P. major* as a therapeutic agent to treat skeleton-muscular disorders; *R. graveolens* as a therapeutic agent to treat skeleton-muscular disorders.

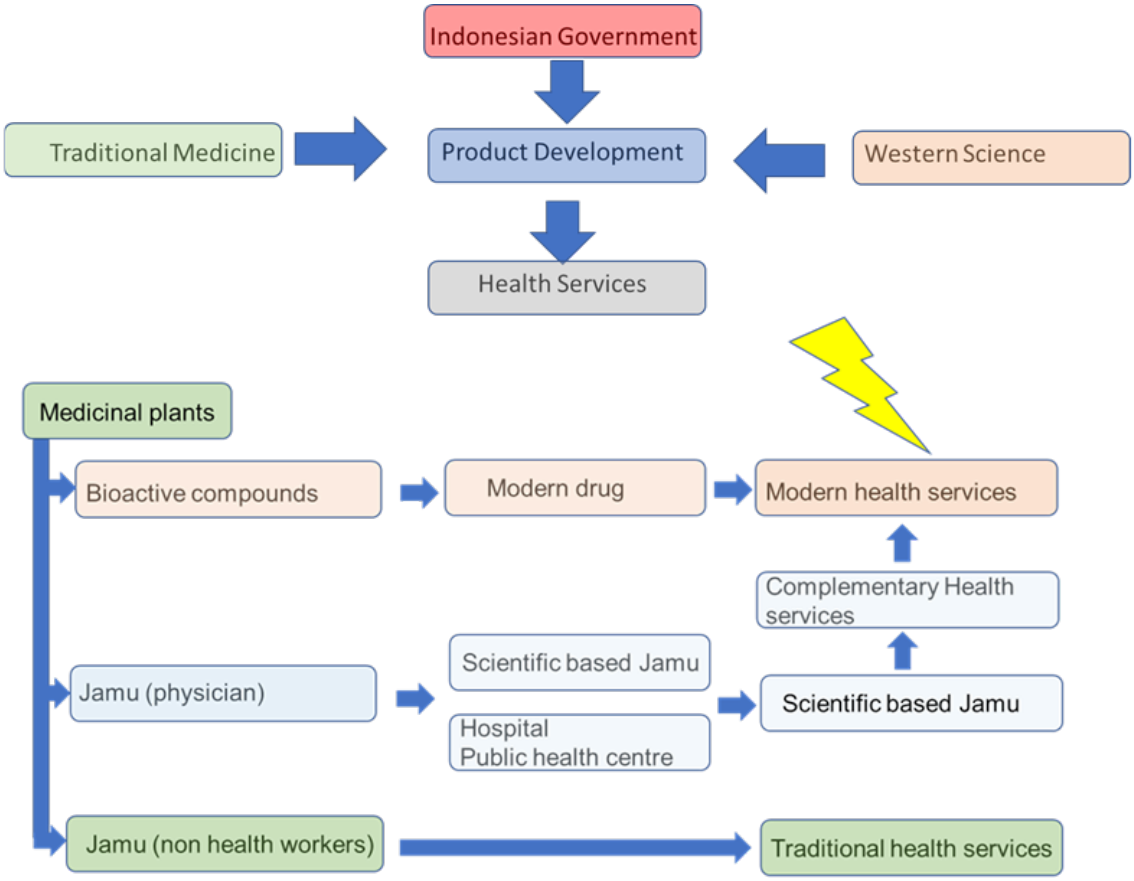


Figure 14. Indonesian Government's strategy in developing modern medicine sourced from Indonesian medicinal plants.

The challenges in bioprospecting are evolving by finding targeted biomarkers within large numbers of secondary metabolite possibilities against protein targets and can be assisted with current techniques including a metabolomic approach to provide large coverage on compounds annotated in large samples without isolation. In the case of compound identification with unknown molecules, the use of molecular networking has become a helpful assistant in compound grouping. All together

with advanced virtual screening, discovering of medicinal plants potency of medicinal plant listed in the Centhini manuscript will become more feasible.

Figure 15. Medicinal plants (A) *A. calamus,* (B) *S. grandiflora,* (C) *M. citrifolia,* (D) *L. acidissima* (E)*M. oleifira,* with full information on pharmacological claims described in the Centhini manuscript based on previous studies

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Conclusion

This review successfully revealed the potency of 32 medicinal plant species listed in the Serat Centhini from a total of 82 medicinal plants. Notable findings, including the discovery of 6-gingerol and zingerone from *Z. officinale* as an erectile agent based on *in vivo* experiments. The potency of *B. rotunda* and *Z. montanum* as an anti-ulcer agent was confirmed through animal model evaluation in which correlated with phytoconstituent, pinostrobin, boesenbergin A, zerumbone. Cubebin from *P. cubeba* indicated significant inhibitory activity against AChE, supporting the traditional use in Alzheimer's therapy. Despite these successes, scientific investigations are still required to test the claims of some of the most potent treatments from the medicinal plant listed in the Centhini manuscript. This will bring the practice of existing traditional practices into modern life by developing the medicinal plants into modern and scientifically proven according to the regulations. Overall, the most benefit of this heritage will go to the current people of Java and also to the Indonesian and global community.

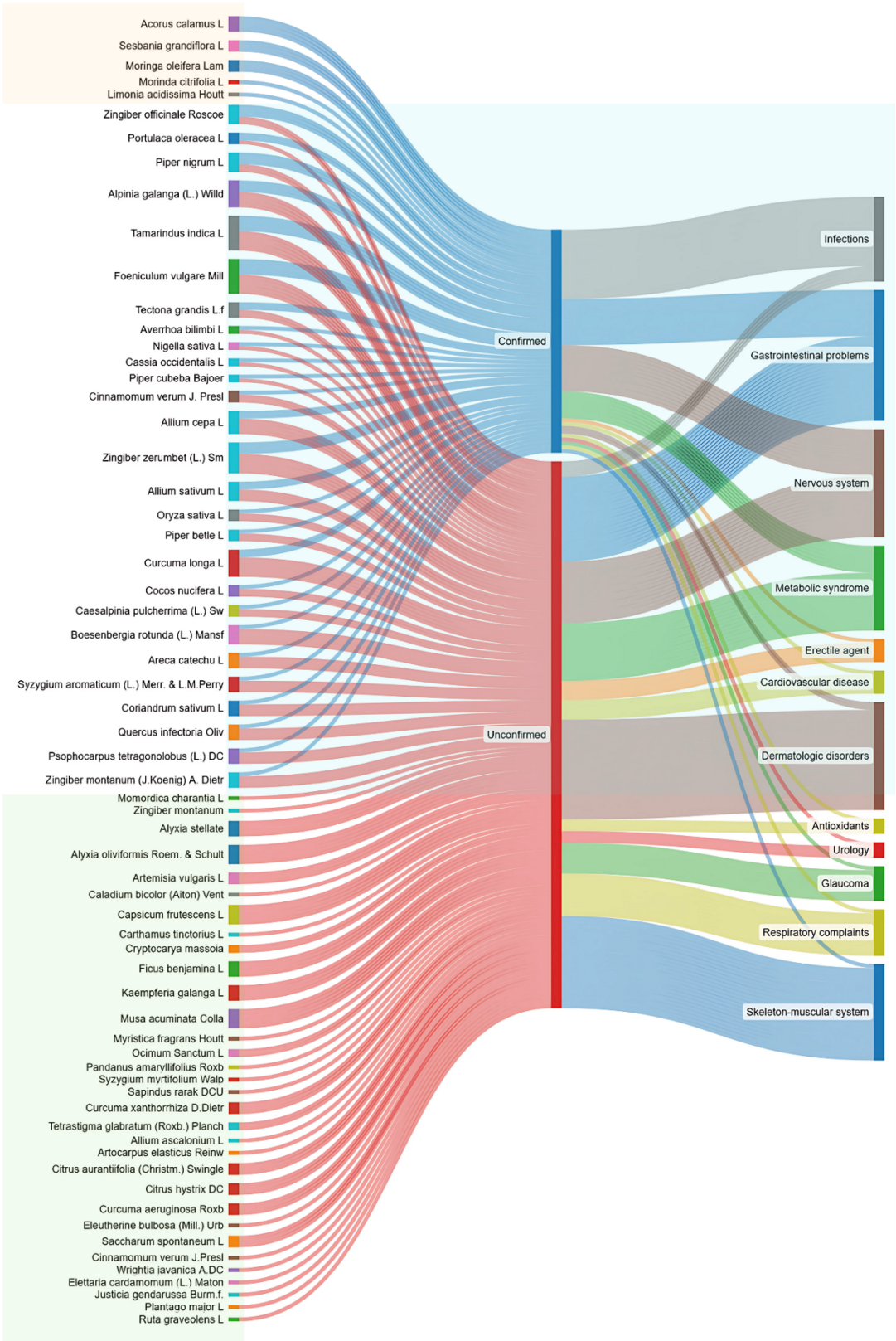

Figure 16. Sankey diagram indicating medicinal plants listed in the Centhini manuscript with their confirmed and unconfirmed pharmacological claims. This provides direction for future Serat Centhini Bioprospecting

Declarations

Ethics approval and consent to participate: Not applicable.

Consent for publication: Not applicable.

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