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Benefits of Fatimah grass for women's health

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Abstract---Introduction: Traditionally, fatimah grass water bath is consumed to help induce labor, but until now there is not enough scientific evidence regarding its safety. Although there are many studies that explain the benefits of Fatimah grass for the female life cycle. For this reason, understanding the benefits of Fatimah grass scientifically for women's life cycles is very important. Methods: The author searches for articles from the databases: PubMed, Scient Direct, MDPI, Google Scholar, Research Gate, and Semantic Scholar published from January 2007 to May 2021 to find out potential studies that are appropriate and meet the inclusion criteria requirements. From the six electronic databases, 47 articles were identified and reduced to 27 relevant articles. The authors summarize the sample size, study design, research results, conclusions, and recommendations. The keywords used are: 'Fatimah grass' or 'kacip Fatimah' or 'Labisia pumila' or 'Benefits of Labisia Pumila For Women' or 'fatimah grass and its benefits' Results: The authors identified 27 relevant articles that were significantly related to the content of phytochemicals that are beneficial to health, such as the content of

flavonoid compounds, saponins, phenolics, phytoestrogens or natural estrogen benzoquinones, alkenyls. In vitro studies show that Fatimah grass extract with ethanol can increase the hormone oxytocin and alkaline phosphatase secretion. Conclusion : The many phytochemical benefits of the Fatimah Grass plant include antioxidant, anti-inflammatory, antimicrobial, and produce the hormone estrogen which can be used as hormone replacement therapy (HRT), estrogen replacement therapy (ERT) for postmenopausal women.

Keywords--Fatimah Grass, review, Fatimah Grass, Women's Health.

Introduction

Indonesia is a country rich in biodiversity. There are about 30,000 plant species (species) that have been identified and 950 plants are known to have biopharmacological functions or benefits, which have potential as food and medicine. Some tribes in Indonesia still entrust their health naturally by utilizing existing plants. Of the many plants, the most frequently used by Indonesian women is Fatimah grass (*labisia pumila/ kacip fatimah*) *Anastatica Hierochuntica*, a plant from the Myrsinacea family ¹. Traditionally, Fatimah grass soaks from the dried roots, stems and leaves are consumed by women to assist in labor induction, however, until now there is not enough scientific evidence regarding its safety, the mechanism that forms the basis for facilitating labor induction and the dose of use. safety. So that medical personnel forbid its use for fear of causing uterine atony and uterine rupture.

Previous research has proven the effects of fatimah grass water immersion, including increasing the hormone oxytocin, antioxidant, anti-inflammatory, reducing the risk of dyslipidemia, phytoestrogens, skin collagen synthesis, playing a role in the process of estrogen hormone therapy in menopause, improving lipid profiles, therapy for dysentery, dysmenorrhea^{2,3,4,5}. Therefore, the use of Fatimah grass soaking water is still used today because it is considered to have great benefits, especially for women who are more interested in herbal or natural medicines. So understanding the benefits of consuming fatimah grass scientifically is very important.

Apart from the various benefits of fatimah grass that have been known in the health sciences, there are only a few studies that systematically examine the prevalence and biological activities of Fatimah grass in the health sector, especially for women's health. The research questions that guide this review are: "What are the benefits of Fatimah Grass in the female life cycle, what chemical classification and biological activities does Fatimah Grass have?".

Method

The author obtained articles from the PubMed, Scient Direct, MDPI, Google Scholar, Research Gate, and Semantic scholar databases to find out which potential studies were appropriate and met the requirements as inclusion criteria.

This review discusses articles published starting from 2007 to May 2021, articles published in English and Indonesian. The keywords used are: 'Fatimah grass' or 'kacip Fatimah' or 'Labisia pumila' or 'Benefits of Labisia Pumila For Women' or 'fatimah grass and its benefits' The search was conducted from April to June 2021.

The authors adopted the scoping review methodology by Arksey and O'Malley. Scoping review is a descriptive literature review by mapping key concepts in a particular literature area. Therefore, the authors use a five-step approach to conducting a scoping review: 1) Identify the research question (see Introduction); 2) Identify relevant studies; 3) Select relevant studies; 4) Mapping data; and 5) Compile, summarize, and report the results.

Identify relevant studies

Several electronic databases were searched to identify studies relevant to June 2021: PubMed, Scient Direct, MDPI, Google Scholar, Research Gate, and Semantic Scholar. The keyword selected in the search is 'fatimah grass' (and its variations, for example, labisia pumila, fatimah grass benefits, fatimah grass phytochemicals). The search strategy is customized for each database and title. A total of 47 articles were identified as PubMed: 5, Scient Direct: 10, MDPI:2, Google Scholar:16, Research Gate:4, and Semantic scholar: 10. Removing articles deemed irrelevant reduces the number of articles to 36 eligible for title and abstract review. Articles were evaluated with the following inclusion criteria: 1) Articles must discuss the fatimah grass (eg studies involving the phytochemicals of fatimah grass, labisia pumila, but articles on the toxicity of Fatimah grass were excluded). 2) Articles must report specific results about the benefits of Fatimah grass that can be taken; and 3) Articles are available in full-text. A total of 27 articles met these criteria (figure 1).

Mapping data

The author extensively went through the spreadsheet to identify inclusion criteria and select articles. A review was carried out on several articles that had met the inclusion criteria and data were extracted and mapped related to chemical classification, research design, interventions provided, research results, and biological activities. The authors reviewed all the data reported in Tables 1 and 2.

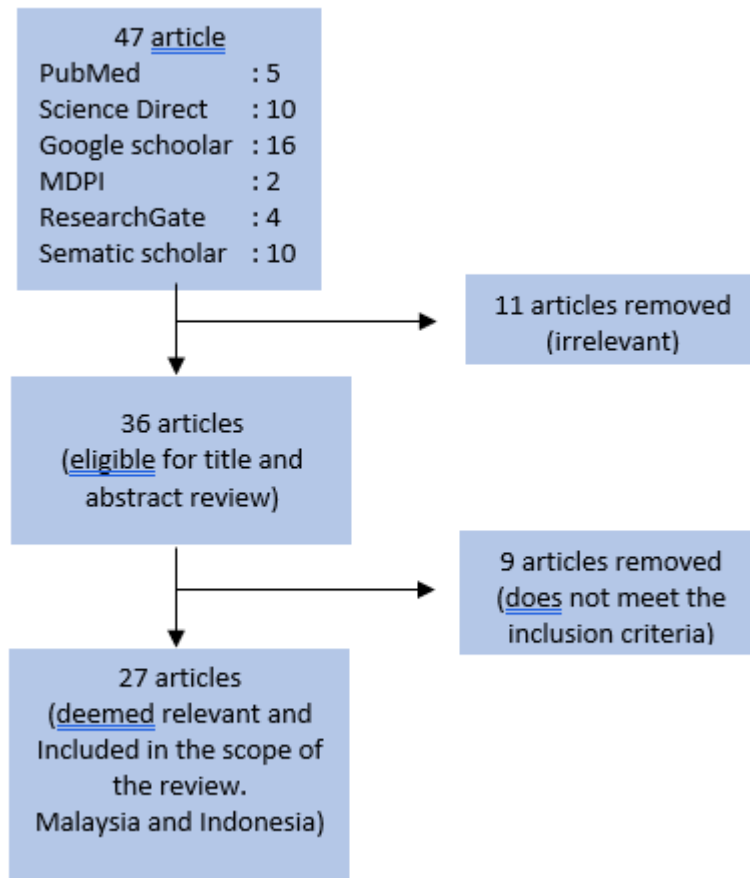
Result

The final result of the review where the identification process has been carried out, there are 27 review articles that are included. Several electronic databases were searched and relevant studies were identified until June 2021: PubMed, Science Direct, Google Scoolar, MDPI, Research Gate, Semantic scholar. This article reports the results of laboratory analysis and discusses the benefits of Fatimah grass.

Regarding the research location, 27 studies were spread over 2 countries. The studies were from each of the following countries: Twenty-one studies were conducted in Malaysia 1, 5, 6, 7, 8, 10, 11, 12, 13, 15, 16, 17, 18, 21, 22, 23, 24,

25, 26, 27, 28, and Indonesia 3, 4, 9, 14, 19, 20. See Figure 1 for details on study settings.

Figure 1. Search strategy flowchart



After searching for journals in PubMed, Science Direct, Google Scolar, MDPI, Research Gate, Semantic scholar, several journals were screened according to inclusion and exclusion criteria. So there are 27 research articles that are relevant to the research objectives. The 27 research articles are reviewed in table 1.

Author (Country and Year) Article title	Chemical Classification	Research design and samples	Interventions	Research Measurement Tools	Research result	Biological Activity
Azrie, et al Effect of solvents on the extraction of Kacip Fatimah (Labisia pumila) leaves. (Malaysia, 2014) ⁵	Gallic acid	Sample Experimental Design: dry leaves of Labisia pumila	Four types of solvents were used in the experiment including water (H ₂ O), ethanol (EtOH), ethyl acetate (EA) and hexane (Hex). 10:1 (v/v). Four hours long. Low temperature 40 °C. 10 grams of dry leaves of Labisia pumila were added to a round bottom flask (500 ml). Extract filtered.	Lab Observation ANOVA	1. The main phytochemicals of Labisia Pumilala are high polarity and soluble in H ₂ O. 2. Labisia pumila is a polar compound, which is easier to extract compared to non-polar compounds.	Gallic acid is a compound that has beneficial activities including antioxidant and anti-inflammatory
Nazrun A., et al. The effects of Labisia pumila var. alata on bone markers and bone calcium in a rat model of post-menopausal osteoporosis (Malaysia, 2011) ⁶	Estrogen	Experimental Design Sample: 32 female wistar rats aged 3 months were divided into 4 groups, each group consisted of 8 tails.	32 female wistar rats aged 3 months were divided into 4 groups. the first group had fake surgery (Sham). second group ovariectomized (OVX), third group (LPva) the fourth group (ERT) was also ovariectomized and given LPva 17.5 mg/kg and Premarin 64.5 g/kg.	ELISA Kit Power Lab recording system	Osteocalcin levels were significantly higher in the LPva and ERT groups compared to the OVX group. CTX levels were significantly lower in the LPva and ERT groups compared to the OVX group.	Anti-inflammatory prevent changes in bone biochemical markers, prevent bone calcium loss caused by ovariectomy
George A., et al. Safety and efficacy of a Labisia pumila var alata water extract on sexual well being and lipid profile of pre- and postmenopausal women. (Malaysia, 2014) ⁷	Lipid Profile	Design Double-blind, placebo-controlled randomized study. Sample: 36 healthy pre- and postmenopausal North American women between the ages of 18 and 70	36 healthy pre- and postmenopausal North American women. Participants were randomized to Labisia Pumila (LP) (200 mg) or placebo for 12 weeks. The female sexual function index (FSFI) and 36th brief health survey (SF-36) were completed, and lipid profiles, anti-inflammatory markers, urinary antioxidants and safety parameters were assessed.	Laboratory analysis with ethylenediaminetetraacetic acid (EDTA) 4 mL ELISA Kit	participants who received LP had significantly lower body weight (p=0.019) and body mass index (BMI) (p=0.04) also had lower mean fasting glucose levels (p=0.026) than those who received placebo although the values remained within the normal clinical range.	anti-inflammatory, urine antioxidant
Abdul Kadir et al The Effect of Labisia pumila var. alata on Postmenopausal Women. (Malaysia, 2012) ⁷	Benzoquinoid	Randomized, double-blind, placebo-controlled study design Sample: postmenopausal Malay women.	29 patients treated with Labisia pumila and 34 patients in the placebo group. Menopausal symptoms were assessed at baseline and at 6 months. during visits every two months.	ANCOVA analysis	there was a significant main effect of treatment on <u>Triglyceride</u> (TG) level [F(1,63) = 4.309, P = 0.042, ANCOVA] where the mean adjusted TG in LP subjects was significantly lower than placebo (1.4 versus 1.9 mmol/L) difference 0.5, 95% CI: 0.02, 0.89).	reduce triglycerides (TG). Maintain cardiovascular health in postmenopausal women. anti-inflammatory, antioxidant.
Chua, L. S. et al Labisia pumila (Kacip Fatimah): Bioactive phytochemicals and skin collagen synthesis promoting herb', Fitoterapia (Malaysia, 2012) ⁸	Favonols Phenolic acids (benzoic acid cinnamic acid)	Experimental Design Sample: dried leaves of labisia pumila	Pumila Labisia Extract	ELISA Laboratory observations	The extract has been shown for its growth-promoting efficiency in human skin fibroblasts and keratinocytes.	antioxidant, anti-estrogenic and immune deficiency. skin collagen synthesis. anti-aging/anti-aging
Rimawati <u>D. et al</u> The Histological Differences of Balb/c Mice Uterine Glands in Gestation Period Which Given Kacip Fatimah (Labisia Pumila) Exposure With Graded Dose. (Semarang Indonesia, 2015) ⁹	pure estrogen	experiment with Post Only Control Group Test. The sample was 20 pregnant Balb/c mice which were randomly divided into 4 groups (group control, P1, P2, P3, and P4)	P1 was administered on day 18 ± 20 of gestation, P2 was administered on day 16 ± 20 of gestation, and P3 was administered on day 14 ± 20 of gestation. On day 20 the mice were <u>terminated</u> , the uterus was taken and histology slides were made (stained with HE) and read in 5 fields of view.	Laboratory histological observations ANOVA	Compared with the control, P1 showed a non-significant difference of uterine gland damage (p=0.213). P2 showed no significant difference in uterine gland damage (p=0.050). P3 showed a non-significant difference in uterine gland damage (p=0.070)	na
Karimi <u>E. et al.</u> , Chemical composition, antioxidant and anticancer potential of Labisia pumila variety alata under CO2 enrichment NIAS. (Malaysia, 2016) ¹⁰	phenolic flavonoids saponins Gallic Acid pyrogallol epicatechin look up diadzein, quercetin myricetin	Experimental design	Seedlings that are healthy and the same in terms of the number of leaves are selected, cleaned, separated, dried and stored for further analysis. The experiment lasted for 15 weeks.	ELISA Kit Laboratory histological observations	Phenolic content increased in leaves and stems of Betula pendula growing below 700 mol mol-1CO2.	Antioxidants and Anti cancer
Karimi <u>E. et al.</u> Phenolics and flavonoids profiling and antioxidant activity of three varieties of Malaysian indigenous medicinal herb Labisia pumila Benth. (Malaysia, 2011) ¹¹	Phenolic Flavonoid	Experimental Design Sample: Labisia Pumila	The leaves, stems and roots of L. pumila Benth were cleaned, separated, and freeze-dried for further analysis. Extract preparation <u>The</u> dry crude extract was weighed and dissolved in methanol and stored at -20°C for further experiments.	ANOVA	Leaves of L. pumila var. Alata contains higher total phenolics (2.65 mg gallic acid equivalent/g DW) of var. pumila (2.56 mg gallic acid equivalent/g DW) and var. lancet (2.44 mg gallic acid equivalent/g DW).	Antioxidants
Astutik H. et al The Effect of Anastatica hierochuntica L. Extract on the Histology of Myometrial Cells and Prostaglandin Levels (PGE2, PGF2α) in Pregnant Mice. (Surabaya Indonesia, 2020) ⁴	Estrogen Flavonoid	Experimental Designs, samples; Test animal mice	pregnant mice were divided into three groups: (1) control group, treated with 0.5% CMC solution 10 ml/kg bw/day; (2) two treatment groups were given extracts of A. hierochuntica L. at a dose of 100 mg/kg bw/day each. Uterine tissue	ELISA Kit ANOVA Analysis	Doses of 100 mg/kg bw/day had a greater effect on myometrial hypertrophy than 150 mg/kg bw/day, resulting in higher levels of PGE2 and PGF2α	increased levels of Prostaglandin

				was collected for histological analysis and blood serum was collected to check PGE2 and PGF2 α levels.			
Norhayati MN. et al Efficacy and Safety of Labisia pumila var. alata Water Extract Among Pre- and Postmenopausal Women. (Malaysia, 2014) ¹²	Pure estrogen	double-blind, placebo-controlled, parallel group. Sample: pre and postmenopausal healthy women aged 40-60 years A total of 197 subjects	16 weeks in healthy pre and postmenopausal women aged 40-60 years. randomized to 400mg of L. pumila extract or placebo. The Women's Health Questionnaire was used to assess the quality of life. Repeated measure of variance analysis.	Questionnaire		A total of 197 subjects were analyzed (L. pumila, 102; placebo, 95). showing the baseline demographic characteristics of L. pumila and placebo groups, there was no significant difference between two groups	anti-inflammatory
L. Mannerås, et al Beneficial metabolic effects of the Malaysian herb Labisia pumila var. alata in a rat model of polycystic ovary syndrome. (Malaysia, 2009) ¹³	estrogen	Design: true experimental, post test only control group design Sample: Rat test animals with PCOS	At 9 weeks of age, PCOS mice were randomly divided into two groups; PCOS Control Labisia Pumila Var. alata (LPva) and PCOS. PCOS LPva mice received daily oral doses of LPva (50 mg/kg body weight), for 4-5 weeks.	ELISA Kit		LPva increased uterine weight (27%) and insulin sensitivity (36%). Plasma resistin levels increased and lipid profile improved in LPva mice.	antiestrogenic
Mariati, N. Effects of Giving Fatimah Grass Extract (Labisia Pumila) on Serum Osteocalcin and Urine Deoxyripyridine in Post Ovariectomy Rats. (2016) ¹⁴	Fitoestrogen	True experimental design, post test only control group design Sample: Female rats and divided into 5 groups	female rats and divided into 5 groups Fatimah grass extract was given for 8 weeks and administered using a probe with different doses, namely 10 mg/KgBW/day, 20 mg/KgBW/day and 40 mg/KgBW/day.	ELISA Kit ANOVA Analysis		The average deoxyripyridinolin expression was highest in the group given fatimah grass extract with a concentration of 40 mg/KgBW/day. The lowest average expression of osteocalcin was given fatimah grass extract with a concentration of 20 mg/KgBW/day.	Reducing serum osteocalcin levels
M. Yunus. et al Shoot Multiplication and Callus Induction of Labisia pumila var. alata as Influenced by Different Plant Growth Regulators Treatments and Its Polyphenolic Activities Compared with the Wild Plant (Malaysia, 2021) ¹⁵	fenolik flavonoid	In vitro Experimental Design Sample: labis pumila for 8 weeks and subcultured at 4-week intervals before the next experiment.	8 weeks old L. pumila var. alata were cultured on Murashige and Skoog (MS) media for shoot multiplication and auxin (2,4-dichlorophenoxyacetic acid (2,4-D) and picloram) for callus induction, respectively.	ANOVA		biochemical properties of LP plants grown in vitro, and callus L. pumila var. Alata, is the best source of antioxidants.	antioxidant
<u>Mitayani et al</u> Kacip Fatimah Extract as a Postpartum Uterine Recovery Material. (2019) ¹	Phytoestrogen	Laboratory experimental design randomized post test only control group design. Samples of 28 female "mus musculus" mice were obtained using the Abo Crombi formula.	Drying fatimah grass material, making ethanol extract, chemical content analysis and treatment by giving Fatimah grass extract orally to post partum female white mice with doses of 250, 350, 500, 750, 1000, and 1500 mg/kg/bb.	ANOVA statistical test followed by Multiple Comparison (Posthoc Test Bonferoni type).		The average weight loss of female white mice after treatment was 4.06mg/kg/BW.	increase uterine contractions
Effendy NM., et al Time and Dose-Dependent Effects of Labisia pumila on Bone Oxidative Status of Postmenopausal Osteoporosis Rat Model. (Malaysia, 2014) ¹⁶	Pure estrogen Glutathione Peroxidase (GPx)	Experimental Design Sample: Ninety-six female Sprague-Dawley rats aged 3-5 months weighing between 200 and 250 g	Ninety-six female Sprague-Dawley rats were randomly assigned into six groups; ovariectomized (OVX) and given 64.5 g/kg Premarin (ERT), ovariectomized and given 20 mg/kg LP (LP20) and ovariectomized and given 100 mg/kg LP (LP100).	ANOVA		LP administration had significantly lower MDA levels than the ERT group.	anti-oxidative
Hussain NHN. et al. Potential Role of Labisia pumila in the Prevention and Treatment of Chronic Diseases. (Malaysia, 2013) ¹⁷	Fenolik Flavonoid Fitoestrogen	In vitro experimental design Sample: Labisia Pumila (LP)	LP herbal plants that have been studied extensively. Support for the efficacy of plant products can be obtained from animal experiments.	Laboratory observations	histological	Labisia pumila is an alternative to be used as a phytoestrogen, prevention and treatment of cardiovascular disease and osteoporosis	antioxidant anti-inflammatory bronchodilator
Abdullah N., et al Labisia pumila :A Review on its Traditional, Phytochemical and Biological Uses. (Malaysia, 2013) ¹⁸	Phenolics Gallic acid Flavonoids Quercetin Beta carotene	Experimental Design in vivo Sample using test animal	Making labisia pumila ekstrak Solvent extraction using methanol, ethanol and hexane is also applied	Laboratory observations ANOVA	histological	Labisia pumila is indicated Phytoestrogenic effects that can be used in the treatment of conditions associated with an imbalance of the hormone estrogen in women.	antioxidant , antibacterial , antimicrobial , anti-inflammatory , anticancer activities , Antitumor , Anti thrombogenic , antiosteoporotic , Antibacterial , antifungi .
Herman RB. et al Effect of Giving Water of Fatimah Grass (Anastatica hierochuntica) Toward The Level of Estrogen Hormone in Pregnant Albino Rats (Rattus Norvegicus). (Aceh, 2017) ¹⁹	Flafonoid Estrogen	Experimental design with the Post-Test Only Control Group design. The sample consisted of 24 pregnant white rats	24 pregnant white rats were divided into 4 groups, namely the control group and 3 treatments P1, P2 and P3 which were each given 10gr, 20gr and 40gr fatimah grass.	ELISA. One Way ANOVA Test Multiple Comparison (post hoc test) type Bonferoni		showed that there was a significant difference (p<0.05) Estrogen levels between the control group (55.51 \pm 7.60) and the P2 (67.37 \pm 7.14) and P3 (68.13 \pm 7.33) groups with doses of 20 g and 40 g.	increase uterine sensitivity after binding to estrogen

Nurdiana, et al Effects of Labisia pumila on bone turnover markers and OPG/ RANKL system in a rat model of post-menopausal osteoporosis. (Malang Indonesia, 2018) ¹⁰	estrogen	Experimental Design Samples total of 25 female wistar rats were acclimatized and randomized	25 female Wistar rats were divided into five groups (n 5), treated with L. pumila extract at various doses (10 mg/kg; 20 mg/kg and 40 mg/kg). L. pumila extract was administered daily for 8 weeks	ELISA ANOVA analysis	All doses of L. pumila given significantly reduced serum osteocalcin levels compared to the post-menopausal osteoporosis rat model group (p < 0.05).	normalize osteoblastic bone formation in a mouse model of post-menopausal osteoporosis
Maizan N.et al Vasorelaxant effect of water fraction of Labisia Pumila and its mechanisms in spontaneously hypertensive rats aortic ring preparation. (Malaysia, 2020) ²¹	Galic acid	Experimental Design Samples were rats with spontaneous hypertension (SHR, 250-300 g)	The aqueous extract of Labisia pumila was carried out by liquid extraction to obtain ethyl acetate, n-butanol and water fraction. In SHR aortic ring preparation, the water fraction (WF-LPWE) was determined as the most potent fraction for vasorelaxation.	ANOVA with Bonferroni's post hoc test.	WF-LPWE significantly reduces the release of intracellular calcium ions (Ca ²⁺) from intracellular stores and suppresses calcium chloride (CaCl ₂)-induced contractions.	vasorelaxant effect
Fatein W., et al. Marantodes pumilum (Blume) Kuntze (Kacip Fatimah) stimulates uterine contraction in rats in post-partum periode. (Malaysia,2019) ²²	Estrogen	Experimental Design The sample is female rats after giving birth on day 1	Postpartum female rats on day 1 were given MPE (100, 250 and 500 mg/kg/day) orally for seven consecutive days. The day after the last treatment (8th day), mice were sacrificed and uteri harvested and subjected to ex-vivo contraction studies.	ELISA	Serum analysis showed that estradiol levels decreased while progesterone levels remained low on day 8 post-partum in rats receiving MPE 250 and 500 mg/kg/day.	uterotonic agent
Fathilah SN., et al Labisia pumila Prevents Complications of Osteoporosis by Increasing Bone Strength in a Rat Model of Postmenopausal Osteoporosis. (Malaysia,2012) ²³	estrogen	Experimental design Post-Test Only Control Group. Samples were 32 female Wistar rats, with a mean age of three months and weight between 200 to 250 g	Rats were housed per cage, at normal room temperature for 12 hours. The treatment group was given Labisia pumila var. Alata at 17.5 mg/kg/day (LPva) and Premarin at 64.5 g/kg/day (ERT) daily for 8 weeks. After 8 weeks of treatment, mice were euthanized.	ANOVA	LPva in ovariectomized mice increases femoral strength. LPva (Labisia pumila <u>var alata</u> 17.5 mg/kg/day), and ERT (Premarin 64.5 g/kg/day). Values are expressed as mean \pm SEM; P<0.05 is considered significant	Anti-inflammatory
Ibrahim MH., et al. Primary, Secondary Metabolites, Photosynthetic Capacity and Antioxidant Activity of the Malaysian Herb Kacip Fatimah (Labisia Pumila Benth) Exposed to Potassium	Fenolat Flavonoid Asorbid acid	Random complete block experimental design Labisia pumila samples were divided into four levels of treatment.	Labisia pumila Benth var. Alata below four levels of potassium Fertilization experiments (0, 90, 180 and 270 kg K/ha) were carried out for 12 weeks	Analysis laboratory	Ditemukan bahwa produksi total fenolat, flavonoid dan asam askorbat lebih tinggi di bawah 270 kg K/ha dibandingkan menjadi 180, 90 dan 0 kg K/ha. kalium tinggi (270 kg K/ha) dan memiliki a korelasi negatif yang signifikan	Antioxidant
Fertilization under Greenhouse Conditions. (Malaysia,2012) ²⁴					dengan total fenolat dan produksi flavonoid	
Dianita R., et al. Protective Effects of Labisia pumila var. alata on Biochemical and Histopathological Alterations of Cardiac Muscle Cells in Isoproterenol-Induced Myocardial Infarction Rats. (Malaysia, 2015) ²⁵	gallic acid, alkylresorcinol flavonoids	Experimental in vivo design waster rat sample	The extract LP was administered to Wistar rats orally for 28 days at three doses (100, 200 and 400 mg/kg body weight) before ISO-induced MI (85 mg/kg) in two doses on days 29 and 30.	ANOVA	The extract showed a significant protective effect as pretreated mice showed a significant dose-dependent decrease (p < 0.05)	cardioprotective effect
Aladdin NA., et al. Xanthine oxidase inhibitory activity of a new isocoumarin obtained from Marantodes pumilum var. pumila leaves. (Malaysia, 2020) ²⁶	fitoestrogen	In vitro Experimental Design Sample: Labisia pumila extract	M. pumilum var. pumila, and M. pumilum var. lanceolata was tested using xanthine oxidase inhibition assay in vitro. The structure of isolated compounds was determined using spectroscopic techniques.	Laboratory Observation ANOVA with post-hoc Tukey multiple comparison test	the most active xanthine oxidase inhibitor with IC ₅₀ value of 0.66 \pm 0.01 g/mL, which was not significantly different (p > 0.05) from the positive control, allopurinol (IC ₅₀ = 0.24 \pm 0.00 g/mL)	xanthine oxidase inhibitor
Hairi HA., et al. Demethylbelamcandaquinone B Isolated from Labisia Pumila Enhanced Proliferation and Differentiation of Osteoblast Cells. (Malaysia,2018) ²⁷	Demethylbelamcandaquinone B	Experimental design Sample: Animal test mice (MC3T3-E1)	The crude aqueous extract of Labisia Pumila var alata (LPva) was fractionated into solvents of hexane (Hex), dichloromethane (DCM) and methanol (Met) and their proliferative effect on the mouse osteoblastic cell line (MC3T3-E1) evaluated by MTS bioassay.	ANOVA	Based on mass spectrometry analysis and NMR spectrum, the compound was determined as demethylbelamcandaquinone B with the molecular formula C ₄₃ H ₆₆ O ₅	anti osteoporosis
Dianita R., et al Effects of Labisia pumila var alata extracts on the lipid profile, serum antioxidant status and abdominal aorta of high-cholesterol diet rats. (Malaysia,2016) ²⁸	gallic acid flavonoids alkyl resorcinol	Validated reverse phase HPLC Experimental Design. Sample: Rat test animal	Rats were induced Three different doses (10 0, 20 0 and 400 mg/kg) of extract were administered daily at week 4, Mice were sacrificed and blood was collected through the abdominal aorta and serum was separated by centrifugation for biochemical analysis.	ANOVA	The serum of LPva-treated mice showed a decrease in serum aspartate aminotransferase (AST) levels, the abdominal aorta showed a significant reduction of atheroma lesions in the treated mice.	lowers the risk of dyslipidemia by improving serum lipid profiles and modulating serum antioxidants

Scientific research on Fatimah Grass or Labisia Pumila was conducted to identify bioactive phytochemicals that contribute to its pharmacological properties. The

chemical classification study identified flavonoids, isoflavonoids, estrogens, galic acid, benzoquinoids and phenolic compounds as bioactive ingredients in the plant extracts of Grass Fatimah or *Labisia Pumila*. Phytochemical assessment was carried out using in vivo rodent tests, with different doses at mg/kg body weight, fatimah grass extract showed potential bioactive phytochemicals. Clinical trials in humans have also been carried out, although still limited, to show that this plant extract is safe from a hematological and biochemical profile. Long-term studies are needed to assess the safety of consuming Fatimah grass plant extracts (Table 1).

Table 2. Biological Activity of Fatimah Grass

Biological Activity	Supporting Studies
Anti-Oxidant	1, 5, 7, 8, 10, 11, 15, 16, 17, 18, 24, 26, 28
Anti Inflammation	1, 5, 6, 7, 12, 17, 18, 23
Uterotonic Agent	3, 19, 22
Anti Osteoporosis	20, 27
Anti-estrogenic	8, 13
Anti-Cancer, Anti-Tumor	10, 18
Anti Aging	8
Anti-Microbial, Anti-Fungal	18
Bronchodilators	17
Vasorelaxant Effect	21
Cardioprotective Effect	25
Lowering osteocalcin levels	14
Increase Prostaglandin levels	4

Assessment of biological activity was carried out in 27 studies using in vivo rodent tests and clinical trials in humans, although still limited. There are 13 biological activities that have been identified, including anti-oxidant, anti-inflammatory, uterotonic agent, anti-estrogen, anti-cancer, anti-osteoporosis, anti-aging, anti-microbial, anti-fungal, anti-tumor, bronchodilator, vasorelaxant effect, cardioprotective effect, and increased oteocalcin levels. The most widely reported biological activities were: Anti-oxidant 1, 5, 7, 8, 10, 11, 15, 16, 17, 18, 24, 26, 28; anti-inflammatory agents 1, 5, 6, 7, 12, 17, 18, 23 and uterotonic agents 3, 19, 22. (Table 2).

Phytochemicals, Teratogenicity

In vitro and in vivo studies report the content of bioactive phytochemicals consisting of phenolic compounds, flavonoids, saponins, alkenyls and benzoquinones, research conducted by Abdullah et al., (2013) which functions as follows ¹⁸

1. Antioxidant and anti-inflammatory

There are phenol levels ranging from 2.53 to 2.55 mg/g in various types of fatimah grass¹⁸. Flavonoids or polyphenols, have potential as anti-allergic, anti-viral, anti-platelet, anti-diarrheal, anti-inflammatory and anti-tumor properties. Phenolics are compounds that have antioxidant potential, phenolic acids are easily absorbed by the digestive system and are useful as anti-aging compounds⁸.

Based on Karimi, Jaafar and Ahmad (2011) reported that saponins have medicinal properties including anticarcinogenic, hypocholesterolemic, anti-inflammatory, antioxidant and antimicrobial activity. In the roots, stems and leaves of Fatimah grass has one of the saponin compounds, namely triterpenoids, Ardisicrenoside B and ardisiacrispin A, 3-O- which have functions as anti-cancer, anti-bacterial, and anti-neoplastic^{29,5}.

Antimicrobial

Alkenyl resorcinol which in fatimah grass includes groups (Z) -5- (pentadec-4-enyl) -resorcinol, (Z) -5- (pentadec-8'-enyl) -resorcinol and (Z) -5 - (pentadec10 '-enyl)-resorcinol based on an epidemiological study conducted by Al-Wahabi., et al., was reported to be useful in the treatment of gastrointestinal cancer as well as cardiovascular disease³⁰. Meanwhile, Karimi E et al., (2011) reported that benzoquinone derivatives in the leaves and roots of fatimah grass have anti-bacterial benefits³¹.

to assess the dose range by assessing the teratogenic potential of the fatimah grass water immersion extract administered to pregnant rats Sprague Dawley, with doses of 0 in the control group, and 2, 20, 200, 400, 1000 mg/kg/day in the treatment group. Administration started on day 6 to day 16 of pregnancy and was started to be given or sacrificed on day 21 of pregnancy. The results of the study said that there was no significant effect except in the administration of low-dose extract (2 mg/kg/day) there was a change in body weight in pregnant rats Sprague Dawley³².

Statistically, uterine weight in pregnant rats tested, number of live fetuses, number of implantation sites, percentage of fetal resorption, number of corpora lutea, fetal weight and fetal sex ratio did not show any significant differences. The conclusion is that the water extract of fatimah grass soaked statistically up to 1000 mg/kg/day did not show any significant toxic or teratogenic effect.³

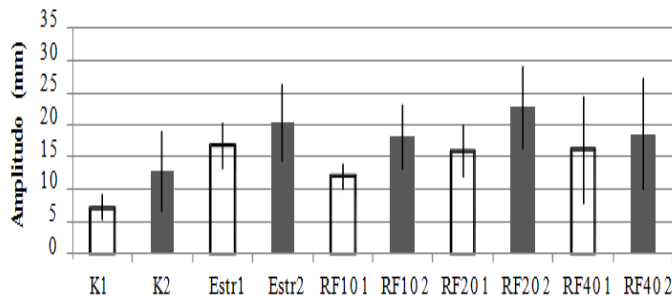
Benefits and Effects of Fatimah Grass in the Life Cycle of Women

Changes in the Amplitude of Uterine Contractions

Fatimah grass is a natural ingredient that contains natural estrogen or is called phytoestrogenic which has natural estrogen-containing activity, Fatimah grass has a Calcium membrane that is able to increase the synthesis of connexin 43 and form gap junctions in the myometrium which is much needed. In intracellular communication, it can also stimulate the production of prostaglandins F2 E and E2 which can function as stimulants for uterine contractions²².

In previous studies conducted on experimental animals, namely female Sprague Dawley rats, weighing 150-250 grams, aged 10-14 weeks in the estrus phase (the physiological state of female animals ready to accept mating with male animals), subjects were divided into 5 groups given orally using a pipette, among others, in group 1, namely the control group (given water solvent), group 2 (given estradiol), group 3 (given 10 grams of fatimah grass root decoction (*labisia pumila*), group 4 (given 20 grams of fatima grass soaking water).) and group 5 (given 40 grams of fatima grass soaking water) as shown in Figure 2³³.

Figure 2. Changes in the amplitude of uterine contractions



Information:

K = Control group

Estr = estradiol group

RF = Fatima grass

Nani (2009) found that the fatimah grass group was given a concentration of 20 grams of grass water that had been soaked in 350 cc of water at an initial temperature of 70°C. The results showed an increase in the response of the uterine muscles to oxytocin stimulation. Fatimah grass increases the number of oxytocin receptors and -adrenergic agents that modulate calcium membrane channels. Fatimah grass is a natural ingredient that contains phytoestrogens or natural estrogens³³.

Fatimah Grass Extract As A Postpartum Uterus Recovery Material

The main function of estrogen is to cause cell proliferation and tissue growth in the sex organs and other tissues related to the reproductive system. Estrogen (17 α -estradiol) is a steroid hormone in women which functions for the development of the mammary ducts together with oxytocin and PGF 2 α which can increase the frequency of uterine contractions. Estrogen with oxytocin has an effect on uterine contractions so that it is useful in accelerating the recovery of the postpartum uterus. Based on the results of studies that reported a positive correlation between the number of uterine oxytocin receptors and the concentration of estradiol³.

Mitayani,(2019) reported that the average uterine weight loss of female white mice after the different treatments was 4.06 mg/kg/BW. Based on the statistical tests performed, it can be seen that the comparison of the control group with the treatment group at doses of 250mg/kg/BW and 500mg/kg/BW did not show any significant difference, where $p>0.05$. The difference will be seen significantly in the treatment group given a dose of 1000 mg/kg/BW and 1500 mg/kg/BW where $p<0.05$ ³.

Treatment Effects of Serum Osteocalcin and Deoxyiridinolin Urine on Post

Ovariectomy Rats

The study used ovariectomized rats, conducted at the Pharmacology and Physiology Laboratory, Faculty of Medicine, Universitas Brawijaya Malang, East Java. Reported the results that there was an increase in urinary deoxyiridinolin and a decrease in serum osteocalcin in post-ovariectomized rats. Giving fatimah grass affects the expression of deoxyiridinolin about 53.46% and osteocalcin expression about 66.97%³⁴.

The Effect of Fatimah Grass on Menopausal Women (Before And After)

Hussain., et al (2013) reported that a study was conducted on 63 pre and postmenopausal healthy women, the results showed that subjects given fatimah grass experienced an increase in concentration or memory. Indicates that the safety profile is normal and improvements are seen in cardiovascular parameters¹⁷. Postmenopausal women who consumed fatimah grass did not show changes in gynecologically relevant hormones, folliculating hormone (FSH), luteinizing hormone (LH), and 17 β -Estradiol. Water extract of fatimah grass is proven safe and very effective to improve quality of life parameters and lower risk factors for cardiovascular events (total cholesterol [TC] and density lipoprotein cholesterol [LDL-C])⁷.

Phytoestrogenic effects: fatimah grass is believed to have phytoestrogens that function as the main producer of sex hormones in women, especially the hormone estrogen. Phytoestrogens can be either isoflavones, or flavonoids and coumestans. An in vitro study conducted by Nor-Ashila Aladdin., et, al (2020) reported that the ethanolic extract of Fatimah grass root in estrogen-free basal media was able to increase the secretion of alkaline phosphatase in endometrial adenocarcinoma cells in humans. Several researchers also reported the results that fatimah grass plant extract has estrogenic properties that act as an estrogen receptor modulator²⁶.

Fatimah grass has the ability of extracts to modulate postmenopausal adiposity. This finding is based on the results of the observations of Ehsan Karimi.et, al (2016) who conducted in vivo research on ovariectomized rats. It was found that aqueous extract of fatimah grass (10-50 mg/kg/day) can modulate postmenopausal adiposity similar to the outcome of ERT treatment by initiating lipolysis in adipose tissue, thereby reducing symptoms of obesity or overweight. Plasma leptin from fatimah grass water extract was comparable in ovarian frequency that had received ERT . treatment¹⁰.

Manneras et al., (2009) reported the results of research that there is a promising effect of Fatimah grass. This has been proven from the body composition and metabolic picture of test rats that have been given dihydrotestosterone to be used as an induction of polycystic ovary syndrome (PCOS). It was reported that 50 mg/kg/day of water extract of fatimah grass increased insulin sensitivity by 36%, increased uterine weight by 27%, and increased lipid profile in PCOS without affecting body composition in mice ¹³.

Effendy et al., (2014) also report that giving Fatimah grass soaked water as much as 17.5 mg/kg/day can prevent osteoporosis after menopause. In addition, menopause always causes the aortic wall to become stiff. This stiffness of the aorta leads to the risk of cardiovascular disease ¹⁶.

Nadia Mohd Effendy et al., (2012) This study has confirmed that *Labisia Pumila* or Fatimah grass has the potential to reduce oxidative stress in postmenopausal rat models that lack estrogen and can increase anti-oxidative enzymes. Because the effect is comparable to that of ERT and the presence of a good safety profile, *Labisia Pumila* or Fatimah grass is reported to have the potential to be used as an alternative treatment for the prevention of postmenopausal osteoporosis. This is because the mechanism may be contributed by the anti-oxidative properties of *Labisia Pumila* or Fatimah grass. Dianita et al., (2016) also reported that the phytoestrogenic properties of fatimah grass can maintain the elasticity of the aortic architecture in ovariectomized mice^{35,28}

Discussion

Based on reviews from several articles, it is known that Fatimah grass or *Labisia Pumila* has many bioactive phytochemicals that are beneficial to human health, especially for women's health, as reported by Ehsan Karimi et al (2016) in the article Chemical composition, antioxidant and anticancer potential. of *Labisia pumila* variety *alata* under CO₂ enrichment that the benefits of Fatimah grass are very potential for cancer therapy and estrogen replacement therapy (ERT) which was carried out in an in vivo study on ovariectomized rats that had been given water extract of fatimah grass 17.5 mg/kg/day orally and 120 mg/kg/day as estrogen replacement therapy (ERT) as a positive control. It was found that aqueous extract of fatimah grass (10-50 mg/kg/day) can modulate postmenopausal adiposity similar to the outcome of ERT treatment by initiating lipolysis in adipose tissue, thereby reducing symptoms of obesity or overweight. Plasma leptin from fatimah grass water extract was comparable in ovarian frequency that had received ERT treatment ¹⁰.

In postmenopausal women are also very susceptible to osteoporosis, which results in discomfort in the body. Nurdiana, et al (2018) reported the Biological Activity of Fatimah grass that post-menopausal women can use to reduce serum osteocalcin levels so as to prevent osteoporosis. This was proven by the treatment of 25 female Wistar rats divided into five groups (n 5), treated with *L. pumila* extract of various doses (10 mg/kg; 20 mg/kg and 40 mg/kg) given every day for 8 weeks, proven with results to normalize osteoblastic bone formation in a mouse model of post-menopausal osteoporosis ²⁰.

In terms of beauty, Fatimah grass extract also plays a very important role. It is interesting to know that aging can be slowed down only by consuming Fatimah grass extract. Meanwhile, by definition, aging is a time-dependent stage of progressive, intrinsic, cumulative, destructive functional and structural changes that usually begin at reproductive maturity or aging and eventually lead to death. The fact is that aging is a natural biological process, due to chronological genetic changes in the body. Endocrine is a system of organisms that will gradually degrade and change so that they reflect endogenous aging. Aging is also caused by environmental factors such as pollution, climate, disease, emotional stress, and ultraviolet radiation (UVA AND UVB) is a major factor in contributing to the onset of premature aging. Excessive exposure to ultraviolet radiation is very worrying living in the tropics. One of the most well-known methods to delay slow down the aging process of the skin is to improve the condition of the collagen in the skin layers. In a study reported by Chua, L. S. et al (2012), that extract of Labisia Pumila or Grass Fatimah can be a promoter of collagen synthesis that can restore pro-collagen skin that has been destroyed by ultraviolet radiation. In addition, the content of Phytotherapy Extract of Fatimah grass or labisia pumila allows it to reduce the secretion of inflammatory pro-cytokines. The biological activity of Fatimah grass as an anti-aging agent provides a protective effect and dermatological benefits, so that the appearance of aging can be slowed down. Thus, Fatimah Grass extract is very suitable for cosmetic purposes ⁸.

With modern management systems and the dissemination of correct information related to products, the dose of use and how to use fatimah grass extract can be the basis for changing the behavior of people who often use fatimah grass extract as a natural or traditional therapy for the birth process, even though scientific evidence applied to all biological activities is only studied in vitro using in vivo and cell lines in laboratory test animals and not yet in humans, it was proven in a study by Dianita, et al., 2016 reported that the serum of mice treated with LPva showed a significant reduction in serum aspartate aminotransferase (AST) levels. , and abdominal aorta showed a significant reduction of atheroma lesions in treated rats, but this still requires further research in humans, so that the pharmacological potential of Fatimah grass can be utilized or used to its full potential. Although from several research results it has been reported very clearly that fatimah grass has many benefits and holds extraordinary potential for humans, especially for the life cycle of women for the future that needs to be discovered. ²⁸.

Conclusion

Fatimah grass or Labisia Pumila based on research results have proven to have many phytochemical benefits which have been identified to date and most of the researchers have reported or demonstrated beneficial biological activities of Fatimah grass plants such as antimicrobial, anti-inflammatory, antioxidant compounds, to maintain the reproductive system. and women's health. Therefore, fatimah grass extract has great potential to be used as the main ingredient in the cosmetic and pharmacology industry.

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