https://doi.org/10.20473/mgi.v19i1.57–72

A NARRATIVE REVIEW OF KNOWN PLANTS WHICH HAVE POTENTIAL BENEFITS AS NATURAL GALACTAGOGUES IN INDONESIA

Grace Marlina Winata[1], Hardinsyah Hardinsyah[2*], Sri Anna Marliyati[2], Rimbawan Rimbawan[2], and Dimas Andrianto[3]

[1]Program of Nutrition Science, Graduate School, IPB University, Bogor, 16680, Indonesia

[2]Department of Community Nutrition, Faculty of Human Ecology, IPB University, Bogor, 16680, Indonesia

[3]Department of Biochemistry, Faculty of Mathematics and Natural Science, IPB University, Bogor, 16680, Indonesia

*E-mail: hardinsyah@apps.ipb.ac.id

ABSTRACT

Human milk is the gold standard for infant nutrition during the first six months of life. According to Indonesia Demographic and Health Survey in 2017, about 45% of mothers in Indonesia provided pre-lacteal feeding within three days postpartum. Low or no milk production and perceived insufficient milk for the infants need were common reasons for pre-lacteal feeding. Galactagogues are believed to help augment human milk production. Therefore, galactagogue consumption is highly recommended, especially natural galactagogue, to help overcome low milk production problem. Most natural galactagogues are used as a local tradition only. Scientific studies regarding the phytochemical compounds and the mechanisms involved are still very limited. This narrative review aimed to describe selected research articles reporting the potency of torbangun, katuk, kelor, and papaya leaves as known plants acting as natural galactagogues in Indonesia. A total of 22 original research articles from Indonesia written in Indonesian or English over a 20 years period were included in this review. Studies were selected if selected natural galactagogues were evaluated at least for the proposed mechanism of action and effects. The data have shown strong evidence about the positive effect of torbangun, katuk, kelor, and papaya leaves as natural galactagogues on increasing human milk production. The five leaves contain different phytoestrogens that have an estrogen effect to stimulate prolactin production and increase milk production. Further studies at the molecular level are needed to identify underlying mechanisms contributing to the effectiveness and safety of the five leaves as natural galactagogues to make it easier to extend into generalizable findings. Individual variability must also be concerned because it may cause different responses to the galactagogues given.

Keywords: natural galactagogue, torbangun, katuk, kelor, papaya, milk production

INTRODUCTION

Good nutrition is essential for the survival, physical growth, mental development, productivity, health, and well-being of infants (WHO, 2000). Optimal nutrition during the first 1000 days of life will provide short and long-term health outcomes, including lowering morbidity and mortality, reducing the risk of chronic diseases, and enhancing better development (WHO, 2020). Breastfeeding has an important role, at least through exclusive breastfeeding, in providing 100% of the nutrition the infants need before six months.

Human milk is the gold standard for infant nutrition during the first six months of life. It contains all macronutrients (carbohydrate, fat, and protein) and micronutrients (vitamins and minerals) the newborns need. It also contains bioactive molecules (immunoglobulin, growth factor, hormone) that are important for the immune system, organ development, microbial colonization in the digestive tract, and protecting infants from infection and inflammation (Ballard and Morrow, 2013).

Human milk compositions depend on maternal diet and body stores (Valentine and Wagner, 2013). Lactating mothers should maintain human milk quality and quantity to meet the balanced nutrition the infants need. Lactation, the process of human milk production and secretion, is affected by two lactogenic hormones, prolactin and oxytocin. They work independently at different cell receptors, but the combination of both is very important for successful lactation (Johnston and Amico, 1986). So, human milk production is a complex process involving physical and psychological factors and hormone interactions (Brodribb, 2018).

 Received 04-09-2023, Accepted 04-12-2023, Published online 30-01-2024.

https://doi.org/10.20473/mgi.v19i1.57–72

Galactagogues are believed to help initiate, maintain, and augment human milk production (Brodribb, 2018). Galactagogue can be synthetically made or naturally derived from plants. Synthetic galactagogues, such as chlorpromazine, sulpiride, metoclopramide, and domperidone, are commonly used but may cause side effects to mothers such as dry mouth, indigestion, insomnia, irregular heart rhythm, hypertension, tremors, sudden death, and to infants such as indigestion and loss of consciousness (Zuppa and Sindico, 2010). Therefore, using natural galactagogue is highly recommended.

Most of the natural galactagogues are used as a local tradition only. The effects have been studied in animals and humans, but scientific studies regarding the phytochemical compounds and the mechanisms involved are still very limited (Tabares et al., 2014). Some studies mentioned that natural galactagogues contain various phytochemical components, such as alkaloids, isoflavones, polyphenols, tannins, and saponins, that may act as phytoestrogens with estrogen effect to stimulate prolactin production and increase milk production (Mohanty et al., 2014).

Only 44% of infants worldwide were exclusively breastfed (WHO, 2020). Meanwhile, in the Sustainable Development Goals agenda, World Health Organization and United Nations International Children's Emergency Fund target exclusive breastfeeding coverage to reach a minimum of 50% by 2025 (Davidove and Dorsey, 2019). In 2020, exclusive breastfeeding coverage in Indonesia was 66.06% (Kemenkes, 2021), exceeding the Strategic Plan target of 60% by 2024 (Kemenkes, 2020). However, Indonesia Demographic and Health Survey in 2017 showed that 45% of mothers in Indonesia provided pre-lacteal feeding (Rahmartani et al., 2020). Prelacteal feeds are any foods or drinks other than human milk given to newborns before breastfeeding initiation or milk comes in, usually within three days postpartum (Chea and Asefa, 2018). It turned out that low or no milk production and perceived insufficient milk have become common reasons for pre-lacteal feeding (Nandini et al., 2017; Odom et al., 2013; Robert et al., 2014). To help overcome this problem, besides nonpharmacological interventions, natural galactagogue consumption is highly recommended (Brodribb, 2018) to improve milk production.

According to Widayanti (2015), katuk (*Sauropus androgynous* (L). Merr), torbangun (*Coleus amboinicus* Lour.), papaya (*Carica papaya* Linn.), kelor (*Moringa oleifera* Lam.), bitter gourd (*Momordica charantia*), and mungbean (*Vigna radiate*), are some plants that are commonly used in Indonesia as natural galactagogues. Three plants listed as natural galactagogues in the Regulation of the Minister of Health of the Republic of Indonesia no. 6/2016 regarding Indonesian native drug formulary are torbangun, katuk, and fenugreek (Kemenkes, 2016). This literature review aimed to describe selected research articles reporting the potency and efficacy of selected known plant leaves which believed to have potential benefits as natural galactagogues in Indonesia.

METHODS

A literature review was conducted by searching published and gray literature related to known plants traditionally used as natural galactagogues in Indonesia. The online search from IPB University Scientific Repository, Google Scholar, and Google Website was conducted using the following keywords either in solo or in combination: galactagogue, natural galactagogue, Indonesia, human milk, breast milk, phytochemical, phytoestrogen, phytosteroid, torbangun, katuk, kelor, moringa, papaya, and leaves, within the articles. Original research articles from Indonesia that were published in Science and Technology Index- and Scopus-indexed journals, nonindexed journals, and gray literature which are published informally, non-commercially published, or unpublished, including theses, dissertations, and unpublished articles, were included in this review. The review was limited to articles in English and Indonesian languages with lactating mice, rats, and humans as research subjects. All types of in vivo study were included in this review to get an in-depth understanding of the efficacy of selected known natural galactagogues commonly used in Indonesia. Studies were selected if natural galactagogues were evaluated, at least for the proposed mechanism of action and effects. With the consideration of language, in vivo study types, and details of the study result required for this review, articles written over a 20 years period were included.

RESULTS AND DISCUSSION

Table 1 summarized several studies about the potency of torbangun (Damanik et al., 2017), katuk (Handayani et al., 2020; Soka et al., 2011; Subekti, 2007; Suprayogi et al., 2015), fenugreek (Bumrungpert et al., 2018; Gabay, 2002; Turkyilmaz et al., 2011), kelor (K et al., 2013; King et al., 2013; Setiasih et al., 2019; Utary et al., 2019), and papaya (Canini et al., 2007; Ikhlasiah et al., 2020; Setyono et al., 2016; Sugiyanto et al., 2012) as five known natural galactagogues in Indonesia. The part used as a galactagogue for fenugreek is the seeds, while torbangun, katuk, kelor, and papaya are the leaves. Based on previous studies, these parts have an estrogen effect to help increase milk production. Torbangun, katuk, kelor, and papaya were selected for this review as they use the leaves as natural galactagogues. A total of 22 articles representing in vivo studies of these plants as natural galactagogues were included in this review. Three studies were using lactating mice, nine studies were using lactating rats, and 10 studies were using lactating mothers.

Table 1. Some of the known plants that are believed as natural galactagogues in Indonesia

Plant name	Picture	Part	Proposed effect/mechanism	Phytochemical components and active compounds predicted to act as a galactagogue	Reference
Torbangun (*Coleus amboinicus* Lour.)		Leaf	Estrogen effect (increase proliferation in mammary epithelial cells, induce prolactin receptor expression (PRLR), increase casein production, and increase lactose synthetase activity in mammary epithelial cells to increase milk production)	Phenol (digiprolactone, kaempferol-3,7-O-di-ramnopyranoside (kaempferitin))	Damanik et al., 2017
Katuk (*Sauropus androgynus* (L). Merr)		Leaf	Estrogen effect, vasodilator	Sterol (stigmasterol, sitosterol, fucosterol, androstan-17-one, 3-ethyl-3-hydroxy-5-alpha), alkaloid (papaverine)	Handayani et al., 2020; Soka et al., 2011; Subekti, 2007; Suprayogi et al., 2015
Fenugreek (*Trigonella foenum-graecum* Linn.)		Seed	Estrogen effect, increase sweat production so that it is predicted to increase milk production because mammary glands are modified sweat glands	Sapogenin steroid (diosgenin), flavon (apigenin, luteolin)	Bumrungpert et al., 2018; Gabay, 2002; Turkyilmaz et al., 2011
Kelor (*Moringa oleifera* Lam.)		Leaf	Estrogen effect	Sterol (campesterol, stigmasterol, β-sitosterol), isoflavone (daidzein, biochanin A, glycitein)	K et al., 2013; King et al.; 2013; Setiasih et al., 2019; Utary et al., 2019
Papaya (*Carica papaya* Linn.)		Leaf	Estrogen effect	Flavonol (kaempferol, quercetin)	Canini et al., 2007; Ikhlasiah et al., 2020; Setyono et al., 2016; Sugiyanto et al., 2012

https://doi.org/10.20473/mgi.v19i1.57–72

Table 2 summarized the characteristics of torbangun, katuk, kelor, and papaya leaves in the edible part of fresh, simplicia, and extract. The comparison of the four fresh leaves is as follows (Mahmud et al., 2018). Kelor leaves have the highest energy, carbohydrates, fiber, ash, vitamin

Table 2. Characteristics of torbangun, katuk, kelor, and papaya leaves

Parameter	Torbangun leaves	Katuk leaves	Kelor leaves	Papaya leaves
	Content in 100 g edible part of fresh leaves (Mahmud et al., 2018) / dry leaves (Iwansyah, 2018)			
Protein (g)	1.3 / 17.36	6.4 / 29.46	5.1 / 25.22	8 / 30.85
Fat (g)	0.6 / 5.87	1 / 6.73	1.6 / 5.67	2 / 5.46
Carbohydrate (g)	4 / 52.18	9.9 / 45.09	14.3 / 48.91	11.9 / 45.77
Fiber (g)	1 / 11.13	1.5 / 9.86	8.2 / 9.34	1.5 / 10.62
Water (g)	92.5 / 10.33	81 / 9.03	75.5 / 9.24	75.4 / 7.70
Ash (g)	1.6 / 14.26	1.7 / 9.71	3.5 / 10.97	2.7 / 10.28
	Content in 100 g edible part of fresh leaves (Mahmud et al., 2018)			
Vitamin				
β-carotene (μg)	1,489	9,152	3,266	5,409
Total carotene (μg)	13,288	10,020	NA	18,250
Thiamine (vitamin B1) (mg)	0.16	0	0.3	0.15
Riboflavin (vitamin B2) (mg)	0.1	0.31	0.1	0.5
Niacin (vitamin B3) (mg)	0	2.3	4.2	1.9
Vitamin C (mg)	5	164	22	140
Mineral				
Calcium (mg)	279	233	1,077	353
Phosphor (mg)	40	98	76	63
Iron(mg)	13.6	3.5	6	0.8
Zinc (mg)	NA	1.3	0.6	1.5
Kalium (mg)	144	478.8	298	926.6
Sodium (mg)	4	21	61	4
Copper (mg)	NA	0.3	0.1	0.2
	Simplicia (Iwansyah, 2018)			
pH	7.05	6.46	5.74	6.05
Aw	0.67	0.44	0.47	0.51
Color	dark, slightly reddish, slightly yellow	dark, slightly greenish, more yellow	dark, slightly greenish, more yellow	dark, slightly greenish, more yellow
L (lightness)	33.67	42.06	35.73	34.33
a (redness)	4.58	-4.51	-4.81	-3.04
b (yellowness)	10.81	23.37	22.58	20.88
	95% ethanol extract (Iwansyah, 2018)			
Yield (%)	0.85	2	0.95	1.25
Phytochemical component				
Total phenol (mg GAE/g)	49.98	27.49	53.89	47,78
Total flavonoid (mg QE/g)	14.49	43.63	36.60	21,73
	NA	**70% ethanol extract (Subekti, 2007)**	**Extract (Kristina and Syahid, 2014)**	**NA**
Total sterol (%)	NA	1.1 (stigmasterol), 0.69 (sitosterol), 0.64 (fukosterol)	1.15 (sitosterol), 1.52 (stigmasterol)	NA

NA = not available; GAE = mg equivalent gallic acid; QE = mg equivalent quercetin

B1, vitamin B3, mineral Ca, and Na content. Papaya leaves have the highest protein, fat, total carotene, vitamin B2, mineral Zn and K content. Katuk leaves have the highest β-carotene, vitamin C, mineral P, and Cu content. Torbangun leaves have the highest mineral Fe content. Consecutively, kelor and katuk leaves 95% ethanol extracts have the highest total phenolic and flavonoid content compared to others (Iwansyah, 2018). Sterol content is found in katuk (Subekti, 2007) and kelor leaf extracts (Kristina and Syahid, 2014).

Torbangun leaf

Torbangun leaves contain phenol components (digiprolactone and kaempferol-3,7-O-di-ramnopyranosida (kaempferitin)) in torbangun leaves ethyl acetate fraction. They work synergistically and are predicted to play a role in stimulating and increasing milk production (Damanik et al., 2017). Torbangun leaves also contain alkaloid, flavonoid, and tannin and are listed as a grade C natural galactagogue in the Regulation of the Minister of Health of the Republic of Indonesia no. 6/2016 regarding Indonesian native drug formulary based on previous preclinical studies to goats and cows and clinical study to lactating mothers aged 20 to 40 years old, who gave normal birth to babies with minimum birth weight 2.5 kg and gave exclusive breastfeeding for a minimum of four months. The suggested dosage for lactating mothers was 3x50 g torbangun simplicia per day, and the LD_{50} (50% lethal dose) was more than 5000 mg/kg of body weight in the rat (Kemenkes, 2016). Table 3 summarized selected in vivo studies of torbangun leaves as a galactagogue using lactating rats (Damanik et al., 2017; Hasianna et al., 2021; Hutajulu and Junaidi 2013; Iwansyah et al., 2017) and humans (Herlina, 2018; Santosa, 2001).

Hasianna et al. (2021) showed that 432 mg of dried torbangun leaves had the most significant effect on increasing prolactin level compared to the negative control, 108 mg, and 216 mg of dried torbangun leaves. There was no significant difference in the weight gain of the pups. Consecutively, the weight gain of the pups from the highest to the lowest was in 432 mg, 216 mg, 108 mg of dried torbangun leaves, positive control (1 mg of domperidone), and negative control treatment. Damanik et al. (2017) showed that milk production from the highest to the lowest was in 50 mg/kg of kaempferol, 50 mg/kg of commercial human milk booster (containing 114 mg of katuk leaves extract, 20 µg of vitamin B12, 25 mg of vitamin B2, 10 mg of vitamin B1), 30 mg/kg torbangun leaves ethyl acetate fraction, control, and 80 mg/kg torbangun leaves aqueous extract treatment. Iwansyah et al. (2017) also showed that the weight gain of the pups in torbangun leaves ethyl acetate fraction treatment was significantly different from the control, and the average weight gain of the pups in torbangun leaves ethyl acetate fraction treatment was higher compared to the commercial booster and control. In addition, there was no significant difference in the weight gain of the lactating rats. Hutajulu and Junaidi (2013) also showed that torbangun leaves extract could increase milk production as indicated by the higher weight gain of the pups compared to the control.

Herlina et al. (2018) showed that consumption of 500 mg of torbangun leaves extract three times a day in lactating mothers could significantly increase the prolactin level of the mothers, weight of the babies, urination and defecation frequency of the babies, sleep duration of mothers and babies, and frequency of the mothers to breastfeed, compared to control. Santosa (2001) showed the consumption of 150 g of fresh torbangun leaves every two days could significantly increase milk production, the weight of the babies, and the iron content in human milk. In addition, there was also a significant increase in the potassium content of human milk compared to the commercial human milk booster (Lancar ASI and Moloco) and in the zinc content of human milk compared to the commercial human milk booster (Moloco). Although not significantly different, there was also an increase in the protein, calcium, and magnesium content of human milk and the prolactin level of the mothers.

Katuk leaf

Katuk leaves contain sterol components (stigmasterol, sitosterol, fucosterol (Subekti, 2007), androstane-17-one, 3-ethyl-3-hydroxy-5-alpha (Suprayogi et al., 2015)) and alkaloid component (papaverine) (Soka et al., 2010). Both have a positive effect as phytoestrogens to

https://doi.org/10.20473/mgi.v19i1.57–72

Table 3. Several studies about the efficacy of torbangun leaves as a natural galactagogue in Indonesia

Subject and period	Dosage	Result	Reference
15 Sprague-dawley rats, weight range between 250 to 300 g, for 13 days (from day two to day 14 after delivery)	Once every two days: 30 mg/kg of torbangun leaves ethyl acetate fraction 50 mg/kg of commercial human milk booster (containing 114 mg of katuk leaves extract, 20 µg of vitamin B12, 25 mg of vitamin B2, 10 mg of vitamin B1 Control (aquadest)	Semipolar compounds group in torbangun leaves ethyl acetate fraction can be considered as a trigger for milk production as indicated by a significantly higher total milk production yield in torbangun leaves ethyl acetate fraction compared to the control. There was no significant difference in the weight gain of the lactating rats. The weight gain of the pups treated with torbangun leaves ethyl acetate fraction was significantly higher compared to the control.	Iwansyah et al., 2017
Rats, for 14 days (from 7 days before delivery to 7 days after delivery)	-Fresh torbangun leaves extract (25 kg of fresh leaves in 500 ml hot water) -Dry torbangun leaves extract (3%, 5%, 7% of dry leaves in 500 ml hot water) -Control	-Torbangun leaves extract consumption can increase milk production as indicated by a weight gain of the mother and pups in fresh torbangun leaves extract treatment. Meanwhile, in other treatment, there was a decrease in the weight of lactating rats, with the highest reduction in the control and the lowest reduction in the dry torbangun leaves extract treatment. -The highest weight gain of the pups was in 5% dry torbangun leaves extract treatment compared to the other extracts. The lowest weight gain of the pups was in the control.	Hutajulu and Junaidi, 2013

Subject and period	Dosage	Result	Reference
16 lactating Batak women, for 21 days (from day 4 to day 24 after delivery)	-150 g of fresh torbangun leaves every two days (in the form of a food menu) -“Kaptab” “Lancar ASI” three times a day (containing 25% of katuk leaves extract) Moloco + vitamin B12 pills three times a day (containing 15 mg of placenta extract and 20 mg of vitamin B12) -Control (only daily food menu)	The effect of torbangun leaves treatment compared to the control and other treatments: -Significant increase in milk production. -Significant increase in weight of the babies but no significant difference in the body length and head circumference of the babies. -Significant increase in the iron content of human milk. -An increase in the potassium content of human milk with a significant difference only with the “Lancar ASI” and Moloco Pills treatment only. -Increased zinc content of human milk with a significant difference only with (Moloco + vitamin B12) treatment. -Increased level of protein, calcium and magnesium although there was no significant difference. Higher level of prolactin although there was no significant difference.	Santosa,2001
30 lactating Wistar rats, for 14 days	Three times a day: 108 mg of dry torbangun leaves 216 mg of dry torbangun leaves 432 mg of dry torbangun leaves Positive control (1 mg of domperidone) Negative control (10% of CMC)	-All dried torbangun leaves treatments gave the effect to increase prolactin level compared to the negative control. -Treatment of 432 mg of dried torbangun leaves gave the most significant effect to increase prolactin level compared to the negative control, 108 mg, and 216 mg of dried torbangun leaves. -No significant difference in prolactin level of 108 mg and 216 mg of dried torbangun leaves compared to the negative control. -No significant difference in the weight gain of the pups between treatments.	Hasianna et al., 2021

Subject and period	Dosage	Result	Reference
32 lactating mothers after delivery, for 14 days	500 mg of torbangun leaves extract, three times a day Control	The effect of torbangun leaves extract treatment compared to control: -Significant increase in the prolactin level of the mothers, weight, urination dan defecation frequency of the babies. -Significant increase in the duration of sleep of the mothers and babies. -Significant increase in the frequency to breastfeed.	Herlina et al., 2018
25 lactating rats, weight range between 250 to 300 g, for 27 days (from day two to day 28 after delivery	Once every two days: -30 mg/kg of torbangun leaves ethyl acetate fraction -80 mg/kg of torbangun leaves water extract -60 mg/kg of kaempferol -50 mg/kg of commercial human milk booster (containing 114 mg of katuk leaves extract, 20 µg of vitamin B12, 25 mg of vitamin B2, 10 mg of vitamin B1) -Control	-Consecutively, the increase in milk production from the highest to the lowest was in kaempferol, commercial human milk booster, torbangun leaves ethyl acetate fraction, control, and torbangun leaves aqueous extract treatment. -Torbangun leaves ethyl acetate fraction treatment did not show any toxicity symptoms in mammary the gland, liver, intestines, and kidney. -The content of digiprolactone and kaempferol derivatives in ethyl acetate fraction is predicted to play a role in stimulating and increasing milk production.	Damanik et al., 2017

induce prolactin and oxytocin gene expression. Papaverine is a vasodilator that may increase blood vessel dilation to facilitate prolactin and oxytocin circulation through blood vessels (Handayani et al., 2020). The hexane extract contains an aliphatic compound. The ether extract contains monomethyl succinate benzoic acid, and 2-phenylmalonic acid as major compounds, and terbutol, 2-propagytoxane, 4H-pyran-4-one, 2-methoxy-6-methyl-, 3-penten-2-one, 3-(2-furanyl)-, and palmitic acid as minor compounds. The ethyl acetate extract contains cis-2-methyl-cyclopentanol acetate, 2-pyrrolidinone, and methyl pyroglutamate as the major compounds and p-dodecyl phenol (Agustal et al., 1997), protein, fat, calcium, phosphorus, iron, vitamins A, B, and C as the minor compounds (Kemenkes, 2016). Katuk leaves are listed as a natural galactagogue in the Regulation of the Minister of Health of the Republic of Indonesia no. 6/2016 regarding Indonesian native drug formulary based on previous preclinical studies to rats and lambs and clinical study to lactating mothers. The suggested dosage for lactating mothers was 3x300 mg extract daily, and the LD_{50} in rats was more than 5000 mg/kg of body weight. 20%, 40%, and 80% of leaves infusion to mice during organogenesis didn't show any teratogenic signs (Kemenkes, 2016). Table 4 summarized selected in vivo studies of katuk leaves as a galactagogue using lactating rats (Miharti et al., 2018; Suprayogi, 2015), mice (Darsono et al., 2014; Soka et al., 2010; Soka et al., 2011) and humans (Nasution, 2018; Sa'roni et al., 2004; Situmorang and Singarimbun, 2019).

Miharti et al. (2018) showed that 72 mg of katuk extract effectively increased prolactin level in lactating rats because it could stimulate prolactin receptors in lactotroph cells to trigger neurohormones in stimulating the release of Prolactin Releasing Factor. Suprayogi et al. (2015) showed that katuk leaves hexane fraction contains sterol components (androstane-17-one, 3-ethyl-3-hydroxy-5-alpha) which can increase milk production by stimulating estrogen. It was demonstrated that milk production in lactating rats treated with 57.5 mg/day of hexane fraction increased compared to the control. Milk production in lactating rats treated with 40 mg/day of ethyl acetate fraction and 297.5 mg/day of crude ethanol extract was lower, while 209 mg/day of aqueous fraction gave the same milk production compared to the control. In addition, the average weight gain of the pups in lactating rats treated with hexane fraction significantly increased compared to the control.

Darsono et al. (2014) showed that consecutively, the most effective treatment to increase the number of mammary alveoli in

Table 4. Several studies about the efficacy of *katuk* leaves as a natural galactagogue in Indonesia

Subject and period	Dosage	Result	Reference
80 pregnant rats, for 24 days (from day 8 to day 21 of pregnancy, and the treatment was continued after delivery until day 10 of lactation)	-57.5 mg/day of hexane fraction of katuk leaves extract (19.3% of crude ethanol extract) -40 mg/day of ethyl acetate fraction of katuk leaves extract (13.4% of crude ethanol extract) -209 mg/day of water fraction of katuk leaves extract (70% of crude ethanol extract) -297.5 mg/day of katuk leaves crude ethanol extract -Control	-Hexane fraction treatment showed an increase in milk production as indicated by a significant increase in the average weight gain of the pups, compared to the control. The hexane fraction contains sterol components (androstan-17-one and 3-ethyl-3-hydroxy-5-alpha) which can increase milk production by stimulating estrogen. -Milk production in ethyl acetate fraction and crude ethanol extract treatment was lower while water fraction treatment gave the same milk production compared to the control.	Suprayogi et al., 2015
30 female mice after delivery, for 12 days	-173.6 mg/kg/day of katuk leaves extract -868 mg/kg/day of katuk leaves extract -Mixture of 173.6 mg/kg/day of katuk leaves extract and 0.078 mg/day of domperidone -Positive control (Moloco) -Negative control	-Consecutively, the most effective treatment in increasing the number of mammary alveoli was the positive control, 173.6 mg/kg of the extract, and a mixture of katuk leaves extract and domperidone. -There was a significant difference between the negative control and positive control, 173.6 mg/kg of extract, and the mixture of katuk leaves extract and domperidone treatment.	Darsono et al., 2014
24 lactating BALB/C mice, for 12 days	Two times a day: -173.6 mg/kg/day of mature katuk leaves extract -868 mg/kg/day of mature katuk leaves extract -Control	-There was a decrease in prolactin gene expression in higher concentration of katuk leaves extract treatment compared to negative control because prolactin secretion will increase dopamine secretion which can inhibit prolactin secretion (mechanism of short-loop feedback). -There was an increase in oxytocin gene expression in higher concentration of katuk leaves extract treatment because papaverine content in katuk leaves which acts as a vasodilator to facilitate oxytocin circulation through blood vessels.	Soka et al., 2011

Subject and period	Dosage	Result	Reference
24 lactating BALB/C mice, for 12 days	-173.6 mg/kg/day of young katuk leaves extract -173.6 mg/kg/day of mature katuk leaves extract -Control	The content of papaverine in mature katuk leaves (0.38 ± 0.04 µg/ml) induced prolactin and oxytocin gene expression as indicated by the increase in prolactin and oxytocin gene expression in mature leaves extract (consecutively 15.75 and 25.77 times) was higher than in the young leaves extract (consecutively 9.04 and 2.25 times).	Soka et al., 2010
96 lactating mothers, for 15 days	Three times a day: -300 mg of katuk leaves extract -Control	-Katuk leaves extract treatment gave a significant effect on increasing human milk production by up to 50.7%.	Sa'roni et al., 2004
32 lactating mothers, for 10 days	Three times a day: -150 ml of boiled katuk leaves (300 g of katuk leaves boiled with 1.5 L of water) -Control	There was a significant increase in milk production of boiled katuk leaves treatment compared to the control.	Situmorang and Singarimbun, 2018
24 lactating Wistar rats, weight range between 150 to 200 g, for 8 days	-24 mg/day of katuk leaves ethanol extract -48 mg/day of katuk leaves ethanol extract -72 mg/day of katuk leaves ethanol extract -Control	-The higher the ethanol extract, the higher increase in prolactin production of lactating rats because it could stimulate prolactin receptors in lactotropic cells as prolactin producers to trigger neuro hormone which will stimulate the release of Prolactin Releasing Factor (PRF). -There was a significant difference in the increase in prolactin production between the control and 72 mg extract treatment, and between 24 mg and 72 mg extract treatment.	Miharti et al., 2018
24 mothers after delivery, for 2 weeks	Two times a day: -2 g of dried katuk leaves tea -Control	There was a weight gain of the babies and significant increase in milk production of katuk leaves tea treatment compared to the control.	Nasution, 2018

lactating mice was in commercial human milk booster (Moloco), 173.6 mg/kg of katuk leaves extract, and a mixture of 173.6 mg/kg/day of katuk leaves extract and 0.078 mg/day of domperidone. Soka et al. (2011) showed that lactating mice treated with 173.6 mg/kg of mature katuk leaves extract had the most effective effect on prolactin and oxytocin gene expression, followed by 868 mg/kg of extract compared to the control. Prolactin secretion may increase dopamine secretion, inhibiting prolactin secretion, the so-called short-loop feedback mechanism. In higher katuk leaves extract treatment, prolactin gene expression decreased.

On the other hand, papaverine content in katuk leaves may inhibit dopamine receptors so that it may restimulate prolactin secretion. The increase in oxytocin gene expression occurred due to papaverine content in katuk leaves which acts as a vasodilator. Soka et al. (2010) showed that the increase in prolactin and oxytocin gene expression in lactating mice occurred in mature katuk leaves extract higher than in young katuk leaves extract treatment.

Situmorang and Singarimbun (2019) showed that milk production and defecation, urination, and weight of the babies of lactating mothers treated with water-boiled katuk leaves significantly increased compared to the control. Nasution (2018) also showed that the milk production and weight of the babies of lactating mothers treated with katuk leaves tea significantly increased compared to the control. Sa'roni et al. (2004) showed that milk production of lactating mothers treated with 300 mg of katuk leaves extracts three times a day significantly increased by up to 50.7% compared to the control.

Kelor leaf

Kelor leaves contain sterol components (campesterol, stigmasterol, β-sitosterol (K et al., 2013)) and isoflavone components (daidzein, biochanin A, glycitein (Setiasih et al., 2019)) which have a positive effect as phytoestrogens.

Table 5 summarized selected in vivo studies of kelor leaves as a galactagogue using lactating rats (K et al., 2013; Utary et al., 2019) and humans (Renityas, 2018; Sulistiawati et al., 2017).

Utary et al. (2019) showed that kelor leaves ethanol extract positively affected the alveoli growth of lactating rats, depending on the given dosage. Treatment of 168 mg/kg of extract gave a better effect than 42 mg/kg. Although not significantly different, the weight gain of the pups in ethanol extract treatment was higher than in the control. K et al. (2013) showed that the birth weight of the pups and after 15 days after birth was highest in lactating rats treated with 168 mg/kg dried steam-blanched kelor leaves treatment and lowest in the control. Phytosteroids in kelor leaves act as precursors of steroid hormones like estrogen. Renityas (2018) showed that 800 mg of kelor leaf extract capsules treatment significantly increased the milk production of lactating mothers. Sulistiawati et al. (2017) showed that 250 mg kelor leaves capsules treatment significantly increased the prolactin level of the mothers and sleep duration of the babies. Although not significantly different, the weight gain of the babies was higher in 250 mg kelor leaves capsules treatment than in the control.

Papaya leaf

Scientific research using animals and humans regarding the efficacy of papaya leaves as a galactagogue has not been carried out much compared to the three leaves above. However,

Table 5. Several studies about the efficacy of kelor leaves as a natural galactagogue in Indonesia

Subject and period	Dosage	Result	Reference
24 pregnant female rats, aged between 8 to 10 weeks, weight between 150 to 210 g, from day 14 of pregnancy to day 7 after delivery	-42 mg/kg of dried kelor leaves ethanol extract -168 mg/kg of dried kelor leaves ethanol extract -13 mg/kg of positive control (Moloco) -Negative control (aquadest)	-Higher ethanol extract of kelor leaves gave a greater effect on the growth of mammary gland alveoli, -Higher increase in the weight of the pups in the ethanol extract compared to the control treatment. When given to pregnant woman, it is expected that kelor leaves can prevent low birth weight.	Utary et al., 2019
20 lactating mothers, for 1 month	800 mg of kelor leaves ethanol extract in capsule (leaves extract: dried leaves = 1:4)	Consumption of kelor leaves ethanol extract in the capsule was effective to significantly increase milk production of lactating mothers.	Renityas, 2018
30 mothers who were willing to give exclusive breastfeeding, for 14 days (from day 1 to day 14 after delivery)	Two times a day: -250 g of dried kelor leaves capsule -Control	The effect of kelor leaves capsule treatment compared to the control: -Significant increase in prolactin level. -Increase in weight gain of the babies. -Increase in sleep duration of the babies. Kelor leaves contain phytosteroids that have a galactagogue effect.	Sulistiawati et al., 2017
Pregnant Wistar white rats, from the beginning of pregnancy until day 14 of lactation	-42 mg/kg of dried kelor leaves -84 mg/kg of dried kelor leaves -168 mg/kg of dried kelor leaves Kelor leaves were given three treatments as follows: non-blanched, steam-blanched, boil-blanched, boiled with Na_2CO_3 -Control	Dried kelor leaves treatment effect: -The highest birth weight of the pups was in the rat treated with 168 mg/kg of dried steam-blanched kelor leaves and the lowest was in the control. -After 15 days of treatment, the highest weight of the pups was in the lactating rats treated with 168 mg/kg of dried steam-blanched kelor leaves and the lowest was in the control. Estrogen potency of kelor leaves comes from phytosteroid content such as stigmasterol, sitosterol, and kaempferol which can function as a precursor of steroid hormone like estrogen.	K et al., 2013

Table 6. Several studies about the efficacy of papaya leaves as a natural galactagogue in Indonesia

Subject and period	Dosage	Result	Reference
36 mothers after delivery, for 7 days	-458 mg/day of papaya leaves nano particle in capsule -Control	-Papaya leaves capsule treatment showed a significant increase in the weight of the babies compared to the control. -Nano particles have a very small size so that the body could absorb them easily.	Khasanah et al., 2021
24 Wistar female rats, aged between 12 to 14 weeks, weight between 200 to 225 g, for 14 days (from day 1 to day 14 after delivery)	-0.95 mg/200 g body weight/day of papaya leaves ethanol extract -1.9 mg/200 g body weight/day of papaya leaves ethanol extract -3.8 mg/200 g body weight/day of papaya leaves ethanol extract -Control (only standard meal)	-All papaya leaves ethanol extract treatments showed a significant increase in prolactin level, prolactin receptor gene expression, breast alveoli, and breast lobules compared to the control. -1.9 mg/200 mg body weight/day extract was the most effective dosage because it gave the highest increase.	Herawati et al., 2021
10 lactating mothers with babies from 0 to 6 months of age, for 7 days	Papaya leaves juice, two times a day	Papaya leaves juice treatment showed a significant increase in the weight of the babies and prolactin level of the lactating mothers compared to before treatment was given.	Ikhlasiah et al., 2020
48 mothers after delivery, for 7 days	Two times a day: -400 mg/day of papaya leaves ethanol extract powder -300 mg/day of papaya leaves ethanol extract powder -Control (only standard meal)	2x400 mg/day of extract treatment was significantly effective in increasing prolactin level and human milk production. As an indicator of human milk production, the weight of the babies was measured.	Pratiwi, 2018

papaya leaves contain flavonol components (kaempferol and quercetin), which positively affect phytoestrogens because they can activate prolactin receptors to increase milk production (Setyono et al., 2016). Table 6 summarized selected in vivo studies of papaya leaves as a galactagogue using lactating rats (Herawati et al., 2021) and humans (Ikhlasiah et al., 2020; Khasanah et al., 2021; Pratiwi, 2018).

Herawati et al. (2021) showed that papaya leaves ethanol extract significantly increased prolactin level, prolactin receptors gene expression, and the number of breast alveoli and lobules in lactating rats compared to the control. A dosage of 1.9 mg/200 g body weight/day of papaya leaves ethanol extract was the most effective treatment since it gave the highest increase. Khasanah et al. (2021) showed that 458 mg/day of papaya leaves nanoparticles in the capsule treatment significantly increased the weight of the babies compared to the control. Nanoparticles have a very small particle size and can easily be absorbed by the body. Ikhlasiah et al. (2020) showed that after lactating mothers were treated with papaya leaves juice, there was a significant increase in the prolactin level and weight of the babies. Pratiwi (2018) showed that the consumption of 400 mg of papaya leaves ethanol extract powder twice a day significantly increased prolactin level and human milk production. The babies were weighted as the indicator of milk production.

CONCLUSION

Five plant leaves (torbangun, katuk, kelor, and papaya leaves) that have potential benefits as natural galactagogues were reviewed and showed a positive effect on increasing human milk production. Current research on natural galactagogues is relatively inadequate to guide clinical recommendations regarding the concentration of the natural galactagogues content in each various formats of the products. Further studies at the molecular level are needed to identify underlying mechanisms contributing to the effectiveness of natural galactagogues towards the development of lactation insufficiency to make it easier to extend into generalizable findings. Evaluating the cause of low milk production, toxicity level, contradictions, warnings, side effects, and medicine interactions must also be considered before giving natural galactagogues. The evidence above is needed to facilitate the appropriate development and evaluation of novel natural galactagogues products due to individual variability that may cause different responses.

ACKNOWLEDGMENTS

This work was supported and funded by PT. Indofood Sukses Makmur Tbk through 2021/2022 Indofood Riset Nugraha Program.

REFERENCE

[Kemenkes] Kementerian Kesehatan RI. *Peraturan Menteri Kesehatan Republik Indonesia Nomor 6 Tahun 2016 tentang Formularium Obat Herbal Asli Indonesia*. , (2016).

[Kemenkes] Kementerian Kesehatan RI. (2020). *Peraturan Menteri Kesehatan Republik Indonesia Nomor 21 Tahun 2020 tentang Rencana Strategis Kementerian Kesehatan tahun 2020 - 2024*. Jakarta: Kementerian Kesehatan Republik Indonesia.

[Kemenkes] Kementerian Kesehatan RI. (2021). *Profil kesehatan Indonesia tahun 2020* (B. Hardhana, F. Sibuea, & W. Widiantini, Eds.). Jakarta: Kementerian Kesehatan Republik Indonesia. https://doi.org/10.1524/itit.2006.48.1.6

[WHO] World Health Organization. (2000). *Nutrition for Health and Development : Progress Report. A global agenda for combating malnutrition*.

[WHO] World Health Organization. (2020). Infant and young child feeding. Retrieved from https://www.who.int/news-room/fact-sheets/detail/infant-and-young-child-feeding

Agustal, A., Harapini, M., & Chairul, C. (1997). Analisis kandungan kimia ekstrak daun katuk (Sauropus androgynus L. Merr) dengan GCMS. *Warta Tumbuhan Obat Indonesia*, *3*(3), 31–33.

Ballard, O., & Morrow, A. L. (2013). Human Milk Composition : Nutrients and Bioactive Factors. *Pediatr Clin North Am.*, *60*(1), 49–74. https://doi.org/10.1016/j.pcl.2012.10.002.

Brodribb, W. (2018). ABM clinical protocol #9 : Use of galactogogues in initiating or augmenting maternal milk production, second revision 2018. *Breastfeeding Medicine*, *13*(5), 307–314. https://doi.org/10.1089/bfm.2018.29092.wjb

Bumrungpert, A., Somboonpanyakul, P., Pavadhgul, P., & Thaninthranon, S. (2018). Effects of fenugreek, ginger, and turmeric supplementation on human milk volume and nutrient content in breastfeeding mothers: A randomized double-blind controlled trial. *Breastfeeding Medicine*, *13*(10), 645–650. https://doi.org/10.1089/bfm.2018.0159

Canini, A., Alesiani, D., D'Arcangelo, G., & Tagliatesta, P. (2007). Gas chromatography-mass spectrometry analysis of phenolic compounds from Carica papaya L. leaf. *Journal of Food Composition and Analysis*, *20*(7), 584–590. https://doi.org/10.1016/j.jfca.2007.03.009

Chea, N., & Asefa, A. (2018). Prelacteal feeding and associated factors among newborns in rural Sidama, south Ethiopia: A community based cross-sectional survey. *International Breastfeeding Journal*, *13*(7). https://doi.org/10.1186/s13006-018-0149-x

Damanik, R. M., Kustiyah, L., Hanafi, M., & Iwansyah, A. C. (2017). Evaluation lactogenic activity of ethyl acetate fraction of torbangun (Coleus amboinicus L.) leaves. *IOP Conference Series : Earth and Environmental Science*, *101*(1). https://doi.org/10.1088/1755-1315/101/1/012007

Davidove, M. E., & Dorsey, J. W. (2019). Breastfeeding: A cornerstone of healthy sustainable diets. *Sustainability*, *11*(18), 4958. https://doi.org/10.3390/su11184958

Gabay, M. P. (2002). Galactogogues : Medications that induce lactation. *Journal of Human Lactation*, *18*(3), 274–279. https://doi.org/10.1177/089033440201800311

Handayani, S., Setyawati, I., Ariendha, D. S. R., Pratiwi, Y. S., Idyawati, S., & Fatmawati, N. (2020). The effect of katuk leaf (Sauropus androgynus L. Merr.) biscuit consumption toward increasing breastmilk volume on the

10th day. *Journal of Physics : Conference Series*, *1594*. https://doi.org/10.1088/1742-6596/1594/1/012051

Hasianna, S. T., Ivone, J., Shinta, S. D., & Nadhira, R. Z. (2021). The use of torbangun leaf powder (Coleus amboinicus L) in increasing prolactin in breastfeedings Wistar rats and bodyweight of the litters. *Journal of Medicine and Health*, *3*(1), 26–33. https://doi.org/10.28932/jmh.v3i1.3145

Herawati, Y., Kalsum, U., Wiyasa, I. W. A., Yuniarti, L., & Sardjono, T. W. (2021). Ethanol extract of Carica papaya leaf can increase breast milk in lactating rat. *Open Access Macedonian Journal of Medical Sciences*, *9 (A)*, 520–526. https://doi.org/10.3889/oamjms.2021.6529

Herlina, Hadisaputro, S., & S, K. A. (2018). Torbangun (Coleus Amboinicus L) leaves extract as an alternative to increase breast milk production and prolactin hormone level among normal postpartum women (study in the work area of bergas community health center Semarang district). *International Journal of Allied Medical Sciences and Clinical Research (IJAMSCR)*, *6*(3), 684–697.

Hutajulu, T. F., & Junaidi, L. (2013). Manfaat ekstrak daun bangun-bangun (Coleus amboinicus L.) untuk meningkatkan produksi air susu induk tikus. *Jurnal Riset Industri*, *7*(1), 15–24.

Ikhlasiah, M., Winarni, L. M., Poddar, S., & Bhaumik, A. (2020). The effects of papaya leaf juice for breastfeeding and working mothers on increasing prolactin hormone levels and infant's weight in Tangerang. *Enfermeria Clinica*, *30*(S5), 202–205. https://doi.org/10.1016/j.enfcli.2019.11.054

Iwansyah, A. C. (2018). *Efek komponen bioaktif ekstrak daun torbangun (Coleus amboinicus L) terhadap kadar dan ekspresi gen-gen reseptor hormon laktogenik pada tikus laktasi [Disertasi]*. Institut Pertanian Bogor.

Iwansyah, A. C., Damanik, M. R. M., Kustiyah, L., & Hanafi, M. (2017). Potensi fraksi etil asetat daun torbangun (Coleus amboinicus L.) dalam meningkatkan produksi susu, bobot badan induk, dan anak tikus. *Jurnal Gizi Pangan*, *12*(1), 61–68. https://doi.org/10.25182/jgp.2017.12.1.61-68

Johnston, J. M., & Amico, J. A. (1986). A prospective longitudinal study of the release of oxytocin and prolactin in response to infant suckling in long term lactation. *Journal of Clinical Endocrinology and Metabolism*, *62*(4), 653–657. https://doi.org/10.1210/jcem-62-4-653

K, T. M., Harijono, Estiasih, T., & W, E. S. (2013). Effect lactagogue moringa leaves (Moringa oleifera Lam) powder in rats white female Wistar. *Journal of Basic and Applied Scientific Research*, *3*(4), 430–434.

Khasanah, U., Anwar, C., & Fatmasari, D. (2021). The effectiveness of nanoparticle supplementation from papaya leaves (Carica Papaya L) to increase weights of babies. *International Journal of Innovative Science and Research Technology*, *6*(11), 795–797.

King, J. S., Raguindin, P. F. N., & Dans, L. F. (2013). Moringa oleifera (Malunggay) as a galactagogue for breastfeeding mothers : A systematic review and meta-analysis of randomized controlled trials. *The Philippine Journal of Pediatrics*, *61*(2), 34–42.

Kristina, N. N., & Syahid, S. F. (2014). Pemanfaatan tanaman kelor (Moringa oleifera) untuk meningkatkan produksi air susu ibu. *Warta Penelitian Dan Pengembangan Tanaman Industri*, *20*(3), 26–29.

Lusiana Darsono, Khie Khiong, J. F. (2014). *Pengaruh kombinasi ekstrak daun katuk (Sauropus androgynus (L.) Merr) dan domperidon terhadap perkembangan alveoli mencit menyusui tahun 2014*.

Mahmud, M. K., Hermana, Nazarina, S, M., Zulfianto, N. A., Muhayatun, … Marlina, L. (2018). *Tabel Komposisi Pangan Indonesia 2017*. Jakarta: Kementerian Kesehatan Republik Indonesia. Retrieved from panganku.org

Miharti, S. I., Oenzil, F., & Syarif, I. (2018). Pengaruh ekstrak etanol daun katuk terhadap kadar hormon prolaktin tikus putih menyusui. *Jurmal Iptek Terapan*, *12.i*, 202–211.

Mohanty, I., Senapati, M. R., Jena, D., & Behera, P. C. (2014). Ethnoveterinary importance of herbal galactogogues - a review. *Veterinary World*, *7*(5), 325–330. https://doi.org/10.14202/vetworld.2014.

Nandini, N., Chalidyanto, D., Pudjirahardjo, W. J., & Putri, N. K. (2017). Breastfeeding among First Time Mothers. *Proceedings of the 2nd International Symposium of Public Health (ISOPH 2017) - Achieving SDGs in South East Asia : Challenging and Tackling of Tropical Health Problems*, (December), 286–289. https://doi.org/10.5220/0007513002860289

Nasution, A. N. (2018). *Efektivitas pemberian simplisia daun katuk terhadap produksi ASI pada ibu pospartum di praktik mandiri Bidan Afriana, Am. Keb. tahun 2018 [Skripsi]*.

Odom, E. C., Li, R., Scanlon, K. S., Perrine, C. G., & Grummer-Strawn, L. (2013). Reasons for earlier than desired cessation of breastfeeding. *Pediatrics*, *131*(3). https://doi.org/10.1542/peds.2012-1295

Pratiwi, T. E. (2018). *Peningkatan program ASI eksklusif dengan pemberian kapsul daun pepaya (Carica papaya L.) pada kunjungan nifas terhadap peningkatan hormon prolaktin dan produksi ASI [Tesis]*.

Rahmartani, L. D., Carson, C., & Quigley, M. A. (2020). Prevalence of prelacteal feeding and associated risk factors in Indonesia: Evidence from the 2017 Indonesia Demographic Health Survey. *PLoS ONE*, *15*(12 December), 1–19. https://doi.org/10.1371/journal.pone.0243097

Renityas, N. N. (2018). The effectiveness of moringa leaves extract and cancunpoint massage towards breast milk volume on breastfeeding mothers. *Jurnal Ners Dan Kebidanan*, *5*(2), 150–153. https://doi.org/10.26699/jnk.v5i2.art.p150-153

Robert, E., Coppieters, Y., Swennen, B., & Dramaix, M. (2014). The Reasons for early weaning, perceived insufficient breast milk, and maternal dissatisfaction: Comparative studies in two belgian regions. *ISRN Obstetrics and Gynecology*. https://doi.org/10.1155/2014/678564

Sa'roni, Sadjimin, T., Sja'bani, M., & Zulaela. (2004). Effectiveness of the Sauropus androgynus (L.) Merr leaf extract in increasing mother's breast milk production. *Media Litbang Kesehatan*, *14*(3), 20–24. Retrieved from https://www.creightonmodel.com/effectiveness.htm

Santosa, C. M. (2001). *Khasiat konsumsi daun bangun-bangun sebagai pelancar sekresi air susu ibu dan pemacu pertumbuhan bayi [Tesis]*. Institut Pertanian Bogor.

Setiasih, Sri, W., Sri, W., & Hendrawan, S. (2019). The effect of adding Moringa Oleifera leaves extract on rabbit does' milk production and mammary gland histology. *Russian Journal of Agricultural and Socio-Economic Sciences*, *8*(92), 296–304. https://doi.org/10.18551/rjoas.2019-08.34

Setiasih, Wahjuningsih, S., Winarsih, S., & Soetanto, H. (2019). The effects of adding Moringa Oleifera leaves extract on rabbit does' milk production and mammary gland histology. *Russian Journal of Agricultural and Socio-Economic Sciences*, *92*(8), 296–304. https://doi.org/10.18551/rjoas.2019-08.34

Setyono, F. S., Adi, A. C., & Ismawati, R. (2016). Galactogogue instant powder combination of papaya leaves and red ginger for breastfeeding mother. *International Journal of Preventive and Public Health Sciences*, *2*(4), 32–36. https://doi.org/10.17354/ijpphs/2016/44

Situmorang, T. S., & Singarimbun, A. P. B. (2019). Pengaruh konsumsi air rebusan daun katuk terhadap pengeluaran produksi ASI pada ibu nifas di bidan praktek Mandiri Manurung Medan tahun 2018. *Indonesian Trust Health Journal*, *1*(2), 55–60. https://doi.org/10.37104/ithj.v1i2.13

Soka, S., Alam, H., Boenjamin, N., Agustina, T. W., & Suhartono, M. T. (2010). Effect of Sauropus androgynus leaf extracts on the expression of prolactin and oxytocin genes in lactating BALB/C Mice. *Journal of Nutrigenetics and Nutrigenomics*, *3*(1), 31–36. https://doi.org/10.1159/000319710

Soka, S., Wiludjaja, J., & Marcella. (2011). The expression of prolactin and oxytocin genes in lactating BALB / C mice supplemented with mature Sauropus androgynus leaf extracts. *International Proceedings of Chemical, Biological and Environmental Engineering*, *9*, 291–295.

Subekti, S. (2007). *Komponen sterol dalam ekstrak daun katuk (Sauropus androgynus L. Merr) dan hubungannya dengan sistem reproduksi puyuh [Disertasi]*.

Sugiyanto, R. N., Khamsita, R., Lambertus, M., Utomo, R. Y., & Susidarti, R. A. (2012). Ethanolic extract of papaya (Carica papaya) leaf exhibits estrogenic effects in vivo and in silico. *Indonesian Journal of Cancer Chemoprevention*, *3*(2), 384–390. https://doi.org/10.14499/indonesianjcanchemoprev3iss2pp384-390

Sulistiawati, Y., Suwondo, A., Hardjanti, T. S., Soejoenoes, A., Anwar, M. C., & Susiloretni, K. A. (2017). Effect of Moringa Oleifera on level of prolactin and breast milk production in postpartum mothers. *Belitung Nursing Journal*, *3*(2), 126–133. https://doi.org/10.33546/bnj.75

Suprayogi, A., Kusumorini, N., & Arita, S. E. D. (2015). Fraksi heksan daun katuk sebagai obat untuk memperbaiki produksi susu, penampilan induk, dan anak tikus. *Jurnal Veteriner*, *16*(1), 88–95. Retrieved from https://ojs.unud.ac.id/index.php/jvet/article/view/13326

Tabares, F. P., Jaramillo, J. V. B., & Ruiz-

https://doi.org/10.20473/mgi.v19i1.57–72

Cortés, Z. T. (2014). Pharmacological overview of galactogogues. *Veterinary Medicine International*. https://doi.org/10.1155/2014/602894

Turkyilmaz, C., Onal, E., Hirfanoglu, I. M., Turan, O., Koç, E., Ergenekon, E., & Atalay, Y. (2011). The effect of galactagogue herbal tea on breast milk production and short-term catch-up of birth weight in the first week of life. *The Journal of Alternative and Complementary Medicine*, *17*(2), 139–142. https://doi.org/10.1089/acm.2010.0090

Utary, N., Murti, K., & Septadina, I. S. (2019). Effects of Moringa (Moringa oleifera) leaf extract on alveolar diameter of breastfeeding and weight of infant Wistar rats. *Journal of Physics : Conference Series*, *1246*(012067). https://doi.org/10.1088/1742-6596/1246/1/012067

Valentine, C. J., & Wagner, C. L. (2013). Nutritional management of the breastfeeding dyad. *Pediatric Clinics of North America*, *60*(1), 261–274. https://doi.org/10.1016/j.pcl.2012.10.008

Widayanti, E. (2015). *Tanaman untuk pelancar ASI di sekitar kita* (I. Y. Prapti, Y. Widiyastuti, S. Wahyono, & H. Widodo, Eds.). Tawangmangu: Balai Besar Penelitian dan Pengembangan Tanaman Obat dan Obat Tradisional.

Zuppa, A. A., & Sindico, P. (2010). Safety and efficacy of galactogogues : Substances that induce , maintain and increase breast milk production. *Journal of Pharmacy and Pharmaceutical Sciences*, *13*(2), 162–174. https://doi.org/10.18433/J3DS3R