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(54) Title: MODIFIED NUTRACEUTICAL COMPOSITION

(57) Abstract: A nutraceutical composition for the treatment of lactating females, including humans, including a lactagogue com-
ponent derived from, or present in the *Coleus amboinicus* plant, or an isolate therefrom or fraction thereof; and optionally a nutraceu-
tically acceptable carrier therefor.



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MODIFIED NUTRACEUTICAL COMPOSITION

The present invention relates to a method for improving lactation in female animals including humans and to a nutraceutical composition for use therein.

5 WHO recommends exclusive breastfeeding for at least the first four and if possible the first six months of an infant's life, and continued breastfeeding with adequate complementary food for up to two years of age or more. Yet many infants stop breastfeeding in the first few weeks or months and, as a result, are at increased risk of illness, malnutrition and death.

10 In the past relactation and induced lactation were considered exceptional experiences and were not well researched. However, there are now sufficient reports to show that most women can relactate if they are motivated.

In a number of societies, there are traditions in which post-partum females are treated with various foods thought to improve health and assist in lactation.

15 For example, in certain traditional societies, moloco (moloko) is used as a food additive. Moloco has been found to include vitamin B-12, but is generally seen as otherwise having only a placebo effect.

20 In Europe, a herbal remedy, including fenugreek seeds (*Trigonella foenum-graecum*) is used as a treatment for lactating females, Katuk leaves (*Sauropus androgynus*) and Indian borage (*Coleus amboinicus* Lour) are also used in other societies.

25 In relation to Katuk plants, Supravogi *et al.* [Suprayogi A, N Kusumorini, P Achmadi & DA Astuti. Effects of Katuk's leaves (*Sauropus androgynus*) on the metabolism, milk yield and milk composition in the mammary gland of lactating goats, Grant of Research Institute, Bogor Agricultural University 1991/1992], were able to identify seven compounds present in the leaves. Five of these compounds were C17, C18 and C20 polyunsaturated fatty acids and their derivatives. The remaining two compounds identified were 3-ethyl-3-hydroxy-5-

alpha androstan-17-one (a 17-ketosteroid) and 3,4-dimethyl-2-oxocyclopent-3-enylacetic acid.

Another study of Katuk leaves by Agusta *et al.* [J Indonesian Med Plants, 1997, 3, 31-34] identified a number of organic acids in the leaves, namely monomethyl succinate; phenylmalonic acid; cyclopentanol, 2-methylacetate and methylpyroglutamate.

While these studies were able to identify various compounds present in the Katuk leaves, there were no investigations as to the effect of these compounds on lactating women. Thus, the component(s) of the leaves responsible for the effect attributed to the leaves by some traditional societies is unknown.

"Bangun-bangun" is the name given by *Bataknese* people in the Lake Toba region (Toba Batak), for the *Coleus amboinicus* Lour plant. The Bataknese people in Simalungun region (or Karo Batak) called the *Coleus amboinicus* plant 'torbangun' or 'tarbangun'. The Bataknese people in these two regions share the belief that *Coleus amboinicus* leaves boost breast milk production. Traditionally, women who have just given birth are given the *Coleus amboinicus* plant in order to recover. It is believed that delivery upsets the balance achieved during pregnancy and brings about weakness. A special diet of *Coleus amboinicus* soup, considered nourishing, is given to the mother "in order to return her to a state of balance". The Simalungun people believe *Coleus amboinicus* serves several purposes in a new mother, namely, stimulating and enhancing breast milk production, decreasing the risk of placental retention (ie, a uterine cleansing agent) and restoring energy and strength lost during parturition. The consumption of the *Coleus amboinicus* plant by lactating women in Simalungun has been practiced for hundreds of years.

Heretofore, no attempt has been made to conduct quantitative studies into the various traditional remedies, or to identify the active principle(s), if any, contained in the products.

It would be a significant advance in the art if improvements could be made in the volume and/or quality of breast milk produced by animals, including humans.

Accordingly, it is an object of the present invention to overcome, or at least alleviate, one or more of the problems or deficiencies in the prior art.

Summary of the invention

In a first aspect of the present invention there is provided
a nutraceutical composition for the treatment of lactating females,
including humans, including a lactagogue component derived from, or present in
the *Coleus amboinicus* plant, or an isolate therefrom or fraction thereof; and
optionally
a nutraceutically acceptable carrier therefor.

It has surprisingly been found that administration of the nutraceutical composition according to this aspect of the present invention, preferably orally, may significantly increase the quantity and/or quality of milk produced by lactating females.

The term lactagogue (or galactagogue), as used herein, refers to any compound or groups of compounds that stimulate the production of breast milk in lactating females, including humans.

The lactagogue components derived from the *Coleus amboinicus* plant may include a compound selected from the group consisting of sterols, fatty acids, steroids, organic acids and derivatives thereof, or a combination thereof.

Preferably the lactagogue component includes a combination of a sterol and a fatty acid.

Preferably, the sterol is a phytosterol.

Preferably, the fatty acid is a mono- or poly-unsaturated fatty acid, most

preferably a C17, C18 or C20 unsaturated fatty acid, or a derivative thereof.

Preferred lactagogue components include one or more of 3-ethyl-3-hydroxy-5- α andostran-17-one; 3,4-dimethyl-2-oxocyclopent-3-enylacetic acid; monomethyl succinate; phenylmalonic acid; cyclopentanol, 2-methylacetate and methylpyroglutamate.

The term nutraceutical (or nutriceutical), as used herein, refers to any food or food ingredient considered to provide medical or health benefits, including the prevention and treatment of disease. Food and food substances may qualify for health claims only if they meet FDA requirements, which require that the claims be supported by sufficient scientific evidence. However, nutraceuticals are not regulated as strictly as drugs.

Preferably, the lactagogue component of the present invention is present in an amount of approximately 5 to 75% by weight, preferably approximately 10 to 50% by weight, based on the total weight of the composition.

The lactagogue component of the present invention may be derived from the *Coleus amboinicus* plant in any suitable manner. Leaves from the *Coleus amboinicus* plant may be used. An extract, preferably an aqueous extract, may be utilised.

The nutraceutical composition according to this aspect of the present invention may further include one or more secondary nutraceutical components active nutritionally and/or therapeutically in the treatment of lactating females. The secondary nutraceutical component may be selected from one or more of vitamins, minerals, other nutritional supplements, hormones including prolactin, and pharmaceuticals active in increasing milk supply, including metoclopramide.

The secondary nutraceutical component, when present, may comprise from approximately 0.05% to 50% by weight, preferably approximately 1% to 40% by weight, more preferably 5% to 25% by weight, based on the total weight of the pharmaceutical composition.

As stated above, the nutraceutical composition according to this aspect of the present invention may further include a pharmaceutically acceptable carrier or excipient.

5 The nutraceutical composition may be formulated for administration utilising a suitable route. The nutraceutical composition may be formulated for oral, intravenous, intramuscular, intrarectal, transdermal, sublingual or subcutaneous administration. An oral route is preferred.

10 When an oral route is chosen, the nutraceutical composition may be formulated as a food additive, tablet, capsule, caplet, lozenge, syrup, suspension, emulsion or the like.

The pharmaceutical carrier may constitute from approximately 1% to 50% by weight, preferably approximately 10% to 30% by weight, based on the total weight of the pharmaceutically active composition.

15 The pharmaceutically acceptable composition may include additional carriers or excipients, lubricants, fillers, buffers, antibacterials, bulking agents, plasticisers, binding agents, colourants, anti-oxidants and stabilising agents.

Suitable fillers or excipients may be selected from the group consisting of talc, titanium dioxide, starch, cornstarch, modified cornstarch, kaolin, cellulose (microcrystalline or powdered) and mixtures thereof.

20 Suitable binding agents include polyvinyl pyrrolidone, hydroxypropyl cellulose and hydroxypropyl methyl cellulose and mixtures thereof.

Suitable solution vehicles include, but are not limited to, ethanol, water, propylene glycol, butylene glycol, acetone, or other pharmaceutically acceptable vehicle.

25 In a further aspect of the present invention there is provided a food additive composition for the treatment of lactating females,

including humans, including a lactagogue component derived from, or present in the *Coleus amboinicus* plant, or an isolate therefrom or fraction thereof; and optionally

a nutraceutically acceptable carrier therefor.

5 The lactagogue components derived from the *Coleus amboinicus* plant may include a compound selected from the group consisting of sterols, fatty acids, steroids, organic acids and derivatives thereof, or a combination thereof.

10 Preferred lactagogue components include one or more of 3-ethyl-3-hydroxy-5-alpha andostran-17-one; 3,4-dimethyl-2-oxocyclopent-3-enylacetic acid; monomethyl succinate; phenylmalonic acid; cyclopentanol, 2-methylacetate and methylpyroglutamate.

15 In a still further aspect of the present invention there is provided a food composition including the food additive composition. The food composition may be of any type, for example, a soup, condiment, seasoning, or food drink composition.

20 In another aspect of the present invention there is provided a method for improving lactation in female animals, including humans, which method includes administering to the female subject an effective amount of a nutraceutical composition for the treatment of lactating females, including humans, including a lactagogue component derived from, or present in the *Coleus amboinicus* plant, or an isolate therefrom or fraction thereof; and optionally
a nutraceutically acceptable carrier therefor.

25 The lactagogue components derived from the *Coleus amboinicus* plant may include a compound selected from the group consisting of sterols, fatty acids, steroids, organic acids and derivatives thereof, or a combination thereof.

Preferred lactagogue components include one or more of 3-ethyl-3-hydroxy-5-alpha andostran-17-one; 3,4-dimethyl-2-oxocyclopent-3-enylacetic acid; monomethyl succinate; phenylmalonic acid; cyclopentanol, 2-methylacetate

and methylpyroglutamate.

The dosage regimen of nutraceutical composition to be administered will vary with the age, weight and condition of the subject. The nutraceutical composition may be administered in an amount of approximately 0.25 to 10 g/kg/day, preferably approximately 1 to 5 g/kg/day.

The nutraceutical composition may be administered orally.

In a preferred embodiment of this aspect of the present invention there is provided a method for modifying milk production in lactating animals, which method includes improving lactation in the female animal by a method including administering to the animal an effective amount of a food additive composition for the treatment of lactating females, including humans, including a lactagogue component derived from, or present in the *Coleus amboinicus* plant, or an isolate therefrom or fraction thereof; and optionally a nutraceutical carrier therefor.

It has surprisingly been found that administration of the nutraceutical composition according to this aspect of the present invention, preferably orally, may significantly increase the quantity and/or quality of milk produced by lactating females.

The female animal may be selected from the group consisting of sheep, cows, goats, and the like.

In a further aspect of the present invention there is provided a dairy product produced by the method as described.

The dairy product may be selected from the group consisting of, but not limited to, milk, milk extracts including whey, yoghurt, cream, cheese, butter, and ice-cream.

Preferably, as discussed above, the lactagogue component of the

nutraceutical composition may be derived from the leaves of the *Coleus amboinicus* plant.

More preferably, as also discussed above the nutraceutical composition includes a secondary nutraceutical component.

5 The dosage regimen of nutraceutical composition to be administered will vary with the age, weight and condition of the subject. The nutraceutical composition may be administered in an amount of approximately 0.25 to 10 g/kg/day, preferably approximately 1 to 5 g/kg/day.

The nutraceutical composition may be administered orally and/or topically.

10 In a still further aspect of the present invention there is provided a cosmetic composition including

a lactagogue component derived from, or present in the *Coleus amboinicus* plant, or an isolate therefrom or a fraction thereof; and optionally an acceptable carrier therefore.

15 The lactagogue components derived from the *Coleus amboinicus* plant may include a compound selected from the group consisting of sterols, fatty acids, steroids, organic acids and derivatives thereof, or a combination thereof.

20 Preferred lactagogue components include one or more of 3-ethyl-3-hydroxy-5- α -androstan-17-one; 3,4-dimethyl-2-oxocyclopent-3-enylacetic acid; monomethyl succinate; phenylmalonic acid; cyclopentanol, 2-methylacetate and methylpyroglutamate.

The present invention will now be more fully described with reference to the accompanying examples. It should be understood, however, that the description following is illustrative only and should not be taken in any way as a restriction on the
25 generality of the invention described above.

Example 1

Phase 1: Focus Group Discussion

Study subjects and methods

5 The Focus Group Discussions took place in three villages in Simalungun Regency from June to August 2001. Two discussions, one involved 10-12 recent mothers (aged 35-51 years) and the other elderly mothers (aged 51-91 years) took place in each village. Participants were purposively selected so that the majority were mothers with more than three children.

10 The discussions focused on cultural perceptions of the *Coleus amboinicus* plant on breastfeeding. The following issues were explored: (a) the breastfeeding practice among Bataknese women, (b) the history of and the knowledge about the *Coleus amboinicus* plant, and (c) the experience in using *Coleus amboinicus* leaves during the lactating period. The discussions were conducted either in the local language (Batak Simalungun) or in Indonesian
15 language, and moderated by an assigned midwife who was given a semi-structured question guide. Each discussion session lasted about 60-90 minutes and was recorded audio-visually.

20 The data on the videotapes were first transcribed by a bilingual research assistant and then by the researcher independently. The transcribed data were then reviewed for accuracy and contexts were analysed. Basic content analysis was used to identify, code, count and group ideas and themes, within and across the conversations. Attention was paid to the words, contexts, frequency
25 extensiveness and specificity of responses. Content analysis was then combined with an ethnographic approach to presenting the data, and quotations from participants that were thought to best express the main ideas and significant themes were taken into the narrative.

Preliminary results

- 5 • Traditionally, women who have just given birth are given the *Coleus amboinicus* plant in order to recover. It is believed that delivery upsets the balance achieved during pregnancy and brings about weakness. A special diet of *Coleus amboinicus* soup, considered nourishing, is given to the mother 'in order to return her to a state of balance'. The diet is also intended to ensure that the mother can take care of the newborn properly, especially by breastfeeding.
- 10 • In general, the women felt fit (not tired but, rather, fresh) and healthy after consuming *Coleus amboinicus* leaves. They felt their breasts become full with breast milk. Moreover, most participants found that consuming *Coleus amboinicus* leaves helped control postpartum bleeding and 'acted as a uterine cleansing agent'.
- 15 • All participants started to consume *Coleus amboinicus* leaves on the second day after giving birth, and most of them consumed a bowl of *Coleus amboinicus* soup three times a day for 30-40 days, whilst others did so for only 14-21 days.
- 20 • To make the soup more delicious, slices of chicken meat or fish are added. The husband or the mother or mother-in-law usually cooks the soup at home. They obtain the *Coleus amboinicus* leaves from their home garden or the local market.
- 25 • According to the elderly mothers, there was no restriction to or required frequency with which to consume this soup.
- All participants considered the effects of consuming *Coleus amboinicus* soup during their nursing period to be beneficial.

Phase 2: Intervention Study

A group of 45 pregnant women participated in a randomised, placebo-

controlled intervention study, which took place in Simalungun district of North Sumatra Province, Indonesia, where *Coleus amboinicus* leaves are commonly consumed by nursing mothers. Recruitment was made through local community health centres (Puskesmas) and midwives' offices.

5 The inclusion criteria included prospective mothers who:

- 1 were in their last trimester of pregnancy, aged 20-40 years.
- 2 had a plan to exclusively breastfeed their babies for at least four months without using any other lactagogue plants or agents, apart from what was assigned by the research team.
- 10 3 were apparently healthy, having no symptoms of infection and/or malnutrition, and who had no medical conditions or complications during previous pregnancies or deliveries.

15 However, if the infant was not delivered at term (gestation of 37-43 weeks) or the infant's weight was less than 2.5 kg, the mother was deemed not eligible for this study. Pregnant women having a chronic disease or who regularly took medication were excluded from the study. Regular smokers or alcohol drinkers were also excluded.

Study design

Subjects were randomly assigned into one of the following two groups.

- 20 • *Coleus amboinicus* Group – to consume *Coleus amboinicus* soup containing 150 g *Coleus amboinicus* leaves each day as part of their diet on Mondays to Saturdays (23 subjects);
- Reference Group – to take a vitamin supplement, Moloco+B12™ sugar coated tablets three times a day (22 subjects).

25 All subjects started taking assigned food or tablets on Day 2 after delivery,

and were instructed to maintain their usual food intake during the intervention period of two months.

Measurements

1 Questionnaires:

- 5 • Information on demography and general health status was obtained using a questionnaire.
- A food frequency questionnaire was used to gather information on usual food intake of the mother, before, during and after pregnancy.

2 Anthropometric measurements made every two weeks, starting on Day 2 after delivery.

- Measurements of stature, body weight and skinfold thickness at biceps, triceps, subscapular and suprailiac sites, performed on the mother.
- Measurements of weight and length of the infant.

3 Biochemical measurements

- 15 • Fasting blood samples were collected from the mother for the measurements of prolactin and oxytocin hormones, and immunoglobulin A.
- The volumes of the 24-hour breast milk intake were recorded on Days 14, 28, 42 and 56 after parturition, and the milk samples were collected from the subjects for nutrient analysis on Days 8, 33 and 60. The effects of *Coleus*
20 *amboinicus* were examined by comparing the percentage changes in the volume and nutritional quality of breast milk (using the values of the first measurements as the baseline, i.e. Day 14 for milk volume and Day 8 for milk nutrient contents) with those of the Reference Group.

Results

The 24-hour breast milk intakes were recorded every 2 weeks over the 2-month period, and the results are shown in Table 1.

Table 1

5. The breast milk intake during the 2-month post partum period (mL)

Parameters	Reference Group		<i>Coleus amboinicus</i> Group	
	n	Mean \pm SD	n	Mean \pm SD
Day 14 (baseline)	22	453.8 \pm 192.6	23	361.1 \pm 201.1
Day 28	22	385.1 \pm 201.9	23	478.7 \pm 157.0 *
Day 42	22	387.4 \pm 188.3	23	439.8 \pm 196.7
Day 56	22	385.5 \pm 170.5	23	478.3 \pm 265.0

No significant differences from the Reference Group (Moloco+B12™) were observed at Day 14 (ANOVA).

Significant differences from Day 14 within the same Group (paired t-test): *, $P < 0.05$.

10 The information on 24-hr breast milk intake was collected for the first time on Day 14 post-partum, and was used as the baseline for comparison with the information subsequently collected on Days 28, 42 and 56. Table 1 shows that although the mean milk volume at Day 14 of the *Coleus amboinicus* Group was 361 mL, and about 100 mL less than that of the Reference Group (454 mL), statistical analysis showed that there were no significant differences amongst
15 these two groups.

It was observed that during the last two weeks of *Coleus amboinicus* supplementation (from Day 14 to Day 28), the 24-hr breast milk intake significantly increased from 361 to 479 mL ($P < 0.05$), an average increase of 65% (Table 2). Additionally, it was found that, even after the completion of
20 supplementation, the increase in breast milk intake of the *Coleus amboinicus* Group still remained higher than that of the Reference Group (Table 2).

Table 2

% Change in breast milk intake during the 2-month post partum period

Parameters	Reference Group		<i>Coleus amboinicus</i> Group	
	n	Mean \pm SD	n	Mean \pm SD
% Changes from Day 14 to				
Day 28	22	9.7 \pm 97.7	23	65.2 \pm 83.8
Day 42	22	-1.2 \pm 56.1	23	53.5 \pm 95.2 *
Day 56	22	-4.2 \pm 44.1	23	68.4 \pm 139.1 *

Significant difference from the Reference Group (Moloco+B12™) (ANOVA): *, $P < 0.05$.

5 Changes in nutrient contents in the breast milk samples during the first two-month lactation period are presented in Tables 3-6.

Table 3

% Change in milk proximate analysis results during 2 months of lactation

Parameters	Reference Group		<i>Coleus amboinicus</i> Group	
	N	Mean \pm SD	N	Mean \pm SD
% Changes from Day 8 to Day 33				
Fat	22	24.0 \pm 48.2	23	32.1 \pm 86.0
Protein	22	3.4 \pm 3.3	23	-1.2 \pm 5.3 §
Lactose	22	1.6 \pm 1.9	23	0.6 \pm 4.8
Water	22	0.2 \pm 0.6	23	-0.3 \pm 0.5 ¶
Ash	22	3.1 \pm 3.9	23	0.5 \pm 3.7 *
%Changes from Day 8 to Day 60				
Fat	22	11.6 \pm 41.5	23	18.4 \pm 68.7
Protein	22	0.5 \pm 3.6	23	-1.4 \pm 5.0
Lactose	22	1.1 \pm 2.4	23	-0.1 \pm 3.8
Water	22	0.0 \pm 0.7	23	0.0 \pm 0.5
Ash	22	1.8 \pm 2.1	23	-2.6 \pm 3.5 ¶¶

Significant difference from the Reference Group (Moloco+B12™) (ANOVA): *, $P < 0.05$; ¶, $P < 0.01$; §, $P < 0.001$; ¶¶, $P < 0.0001$.

Table 4

% Change in mineral content of breast milk during 2 months post partum

Parameters	Reference Group		<i>Coleus amboinicus</i> Group	
	n	Mean \pm SD	n	Mean \pm SD
<u>% Change from Day 8 to Day 33</u>				
Iron	22	68.4 \pm 148.3	23	24.3 \pm 138.7
Zinc	22	-34.0 \pm 44.0	23	-34.4 \pm 25.9
Calcium	22	0.7 \pm 18.6	23	-0.5 \pm 20.3
Potassium	22	-16.8 \pm 15.3	23	-20.5 \pm 22.4
Magnesium	22	-2.3 \pm 16.4	23	9.0 \pm 92.9
<u>% Change from Day 8 to Day 60</u>				
Iron	22	16.2 \pm 132.6	22	1.2 \pm 73.7
Zinc	22	-56.5 \pm 21.9	23	-55.3 \pm 22.4
Calcium	22	3.2 \pm 21.8	23	8.7 \pm 20.3
Potassium	22	-22.4 \pm 15.2	23	-23.7 \pm 18.4
Magnesium	22	1.4 \pm 19.5	23	-9.0 \pm 18.8

No significant differences from the Reference Group (Moloco+B12™) were observed (ANOVA).

Table 5**%Change in saturated fatty acids content during 2 months post partum**

Parameters	Reference Group		<i>Coleus amboinicus</i> Group	
	n	Mean \pm SD	n	Mean \pm SD
% Change from Day 8 to Day 33				
Decanoic (C10:0)	22	50.1 \pm 55.5	23	172.9 \pm 267.3 *
Lauric acid (C12:0)	22	27.4 \pm 54.4	23	48.1 \pm 120.6
Myristic acid (C14:0)	22	4.0 \pm 41.6	23	-18.8 \pm 31.7 *
Palmitic acid (C16:0)	22	-1.3 \pm 8.0	23	-13.0 \pm 11.8 §
Stearic acid (C18:0)	22	4.3 \pm 14.1	23	6.3 \pm 26.4
% Change from Day 8 to Day 60				
Decanoic (C10:0)	22	64.0 \pm 62.2	23	76.6 \pm 148.2
Lauric acid (C12:0)	22	44.2 \pm 76.6	23	-10.4 \pm 65.5 *
Myristic acid (C14:0)	22	13.0 \pm 58.4	23	-30.7 \pm 36.2 †
Palmitic acid (C16:0)	22	-1.7 \pm 9.2	23	-16.0 \pm 13.6 §
Stearic acid (C18:0)	22	8.0 \pm 19.8	23	5.1 \pm 24.6

Significant difference from the Reference Group (Moloco+B12™) (ANOVA): *, $P < 0.05$; †, $P < 0.01$; §, $P < 0.001$.

Table 6**5 % Change in unsaturated fatty acids content during 2 months post partum**

Parameters	Reference Group		<i>Coleus amboinicus</i> Group	
	n	Mean \pm SD	n	Mean \pm SD
% Change from Day 8 to Day 33				
Palmitoleic (C16:1)	22	-3.0 \pm 24.0	23	94.4 \pm 140.6 †
Oleic (C18:1)	22	1.8 \pm 10.1	23	9.7 \pm 27.7
Linoleic (C18:2)	22	10.7 \pm 30.7	23	26.9 \pm 34.5
% Change from Day 8 to Day 60				
Palmitoleic (C16:1)	22	-9.5 \pm 20.2	23	83.9 \pm 111.8 §
Oleic (C18:1)	22	1.0 \pm 14.5	23	13.7 \pm 32.2
Linoleic (C18:2)	22	10.2 \pm 28.9	23	36.1 \pm 43.6 *

Significant difference from the Reference Group (Moloco+B12™) (ANOVA): *, $P < 0.05$; †, $P < 0.01$; §, $P < 0.001$.

Note: Most of Linolenic (C18:3) values are zero, and % change values are not calculated.

The observations in the present study of the increase in milk production without compromising the nutritional quality of the breast milk in the *Coleus amboinicus* Group has confirmed the belief amongst Batakese people that *Coleus amboinicus* can be used as a lactagogue in humans. The residual effect of *Coleus amboinicus* supplementation during the first month of lactation can be seen even after the supplementation was ended for one month. Over the study period of two months, the *Coleus amboinicus* Group had a smaller decline in prolactin in the mother's serum, compared to the Reference Group (see Table 7). It is likely that the higher milk production in the *Coleus amboinicus* Group was partially due to the greater prolactin hormone concentrations.

Table 7

% Change in serum hormone concentrations during the first 2 months lactation

Parameters	Reference Group		<i>Coleus amboinicus</i> Group	
	n	Mean \pm SD	n	Mean \pm SD
% Change from Day 8 to Day 34				
Prolactin	22	-45.6 \pm 34.4	23	-14.8 \pm 77.1
Oxytocin	22	27.5 \pm 30.7	23	21.3 \pm 24.3
% Change from Day 8 to Day 61				
Prolactin	22	-61.3 \pm 19.1	23	-36.7 \pm 52.4 ^a
Oxytocin	22	33.3 \pm 63.8	23	36.8 \pm 43.3 ^a

Significant difference from the Reference Group (Moloco+B12™) (ANOVA): ^a, $P < 0.05$.

The results observed in this study indicated that *Coleus amboinicus* improved the quantity of breast milk produced by the lactating women by about 10%, when measured against the milk production of the women in the Reference Group. The consumption of *Coleus amboinicus* also resulted in the retention of the quality of breast milk (in terms of macro- and micronutrient composition).

It will be understood that the invention disclosed and defined in this specification extends to all alternative combinations of two or more of the

individual features mentioned or evident from the text or drawings. All of these different combinations constitute various alternative aspects of the invention.

It will also be understood that the term "comprises" (or its grammatical variants) as used in this specification is equivalent to the term "includes" and should not be taken as excluding the presence of other elements or features.

Claims

1. A nutraceutical composition for the treatment of lactating females, including humans, including

a lactagogue component derived from, or present in the *Coleus amboinicus* plant, or an isolate therefrom or fraction thereof; and optionally

a nutraceutically acceptable carrier therefor.

2. A nutraceutical composition according to claim 1 wherein the lactagogue component includes one or more compounds selected from the group consisting of sterols, fatty acids, steroids, organic acids, and derivatives thereof.

3. A nutraceutical composition according to claim 2 wherein the lactagogue component includes a combination of a sterol and a fatty acid.

4. A nutraceutical composition according to claim 2 or claim 3 wherein the sterol is a phytosterol.

5. A nutraceutical composition according to any one of claims 2 to 4 wherein the fatty acid is a mono- or poly-unsaturated fatty acid.

6. A nutraceutical composition according to claim 5 wherein the fatty acid is a C17, C18 or C20 unsaturated fatty acid, or a derivative thereof.

7. A nutraceutical composition according to any one of the preceding claims wherein the lactagogue component includes one or more of

3-ethyl-3-hydroxy-5-alpha androstan-17-one;
3,4-dimethyl-2-oxocyclopent-3-enylacetic acid;
monomethylsuccinate;
phenylmalonic acid;
cyclopentanol, 2-methylacetate; and
methylpyroglutamate.

8. A nutraceutical composition according to any one of the preceding claims wherein the lactagogue component is present in an amount of approximately 5% to 75% by weight, based on the weight of the composition.

5 9. A nutraceutical composition according to any one of the preceding claims wherein the lactagogue component is derived from the leaves of the *Coleus amboinicus* plant.

10 10. A nutraceutical composition according to any one of the preceding claims wherein the lactagogue component is an aqueous extract of the *Coleus amboinicus* plant.

10 11. A nutraceutical composition according to any one of the preceding claims further including one or more secondary nutraceutical components, wherein the secondary nutraceutical component is active nutritionally or therapeutically in the treatment of lactating females and is selected from one or more of the group consisting of nutritional supplements, hormones and
15 pharmaceuticals active in increasing milk supply.

12. A nutraceutical composition according to claim 11 wherein the nutritional supplement is a vitamin or a mineral.

13. A nutraceutical composition according to claim 11 wherein the hormone is prolactin.

20 14. A nutraceutical composition according to claim 11 wherein the pharmaceutical is metoclopramide.

25 15. A nutraceutical composition according to any one of claims 11 to 14 wherein the secondary nutraceutical composition is present in an amount of approximately 5% to 25% by weight, based on the total weight of the composition.

16. A nutraceutical composition according to any one of the preceding

claims wherein the composition is formulated as a food additive, tablet, capsule, caplet, lozenge, syrup, suspension or emulsion.

17. A nutraceutical composition according to any one of the preceding claims wherein the nutraceutically acceptable carrier is present in an amount of approximately 10% to 30% by weight, based on the total weight of the composition.

18. A nutraceutical composition according to any one of the preceding claims wherein the nutraceutically acceptable carrier is selected from one or more of the group consisting of talc, titanium dioxide, starch, cornstarch, modified cornstarch, kaolin, microcrystalline cellulose or powdered cellulose.

19. A food additive composition for the treatment of lactating females, including humans, including

a lactagogue component derived from, or present in the *Coleus amboinicus* plant, or an isolate therefrom or fraction thereof; and optionally

a nutraceutically acceptable carrier therefor.

20. A food additive composition according to claim 19 wherein the lactagogue component includes one or more compounds selected from the group consisting of sterols, fatty acids, steroids, organic acids, and derivatives thereof.

21. A food additive composition according to any one of claims 19 to 20 wherein the lactagogue component includes one or more of

3-ethyl-3-hydroxy-5-alpha androstan-17-one;

3,4-dimethyl-2-oxocyclopent-3-enylacetic acid;

monomethylsuccinate;

phenylmalonic acid;

cyclopentanol, 2-methylacetate; and

methylpyroglutamate.

22. A food additive composition according to any one of claims 19 to 21 wherein the lactagogue component is present in an amount of approximately 5% to 75% by weight, based on the weight of the composition.

23. A food additive composition according to any one of claims 19 to 22 wherein the lactagogue component is derived from the leaves of the *Coleus amboinicus* plant.

24. A food additive composition according to any one of claims 19 to 23 wherein the lactagogue component is an aqueous extract of the *Coleus amboinicus* plant.

25. A food additive composition according to any one of claims 19 to 24 further including one or more secondary nutraceutical components, wherein the secondary nutraceutical component is active nutritionally or therapeutically in the treatment of lactating females and is selected from one or more of the group consisting of nutritional supplements, hormones and pharmaceuticals active in increasing milk supply.

26. A food additive composition according to claim 25 wherein the secondary nutraceutical composition is present in an amount of approximately 5% to 25% by weight, based on the total weight of the composition.

27. A food additive composition according to any one of claims 19 to 26 wherein the composition is in the form of a soup, condiment, seasoning or food drink composition.

28. A food composition including a food additive composition according to any one of claims 19 to 27.

29. A method for improving lactation in female animals, including humans, which method includes

administering to the female subject an effective amount of a nutraceutical composition including a lactagogue component derived from, or present in the

Coleus amboinicus plant, or an isolate therefrom or fraction thereof; and optionally

a nutraceutically acceptable carrier therefor.

30. A method according to claim 29 wherein the lactagogue component includes one or more compounds selected from the group consisting of sterols, fatty acids, steroids, organic acids, and derivatives thereof.

31. A method according to any one of claims 29 to 30 wherein the lactagogue component includes one or more of

3-ethyl-3-hydroxy-5- α androstran-17-one;

3,4-dimethyl-2-oxocyclopent-3-enylacetic acid;

monomethylsuccinate;

phenylmalonic acid;

cyclopentanol, 2-methylacetate; and

methylpyroglutamate.

32. A method according to any one of claims 29 to 31 wherein the lactagogue component is present in an amount of approximately 5% to 75% by weight, based on the weight of the composition.

33. A method according to any one of claims 29 to 32 wherein the lactagogue component is derived from the leaves of the *Coleus amboinicus* plant.

34. A method according to any one of claims 29 to 33 wherein the lactagogue component is an aqueous extract of the *Coleus amboinicus* plant.

35. A method according to any one of claims 29 to 34 further including one or more secondary nutraceutical components, wherein the secondary nutraceutical component is active nutritionally or therapeutically in the treatment of lactating females and is selected from one or more of the group consisting of nutritional supplements, hormones and pharmaceuticals active in increasing milk supply.

36. A method according to claim 35 wherein the secondary nutraceutical composition is present in an amount of approximately 0.05% to 50% by weight, based on the total weight of the composition.

5 37. A method according to any one of claims 29 to 36 wherein the nutraceutical composition is administered in an amount of approximately 0.25 g/kg/day to 10 g/kg/day.

10 38. A method according to any one of claims 29 to 37 wherein the nutraceutical composition is administered by a method selected from the group consisting of oral, intravenous, intramuscular, intrarectal, transdermal, sublingual and subcutaneous.

39. A method according to any one of claims 29 to 38 wherein the animal is selected from the group consisting of humans, sheep, cows and goats.

40. A method according to any one of claims 29 to 39 further including collecting the milk produced by the female animal.

15 41. A dairy product produced from milk obtained by a method according to claim 40.

42. A dairy product according to claim 41 wherein the product is selected from the group consisting of milk, milk extracts, whey, yoghurt, cream, cheese, butter and ice-cream.

20 43. A cosmetic composition including

a lactagogue component derived from, or present in the *Coleus amboinicus* plant, or an isolate therefrom or a fraction thereof; and optionally

an acceptable carrier therefore.

44. A cosmetic composition according to claim 43 wherein the lactagogue component includes one or more compounds selected from the group consisting of sterols, fatty acids, steroids, organic acids, and derivatives thereof.

5 45. A cosmetic composition according to claim 43 or claim 44 wherein the lactagogue component includes one or more of

3-ethyl-3-hydroxy-5-alpha androstran-17-one;
3,4-dimethyl-2-oxocyclopent-3-enylacetic acid;
monomethylsuccinate;
phenylmalonic acid;
10 cyclopentanol, 2-methylacetate; and
methylpyroglutamate.

46. A cosmetic composition according to any one of claims 43 to 45 wherein the lactagogue component is derived from the leaves of the *Coleus amboinicus* plant.

15 47. A cosmetic composition according to any one of claims 43 to 46 wherein the lactagogue component is an aqueous extract of the *Coleus amboinicus* plant.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU2005/000459

A. CLASSIFICATION OF SUBJECT MATTER		
Int. Cl. ⁷ : A61K 35/78, A61P 15/14		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols)		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) T.E.K. P.A.D., DWPI, Medline; Keywords; coleus amboinicus, indian borage, spanish thyme, cuban oregano, plectranthus amboinicus, coleus aromaticus, torbangun, bangun bangun, broadleaf thyme, tarbangun		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Damanik R et al, "The use of putative lactagogue plant on breast milk production in Simalungun, North Sumatra, Indonesia", Asia Pacific Journal of Clinical Nutrition, 2004, Vol. 13 (Suppl), page S118. Abstract	1-47
X	Damanik R et al, "Consumption of bangun-bangun leaves (Coleus amboinicus Lour) to increase breast milk production among Batakneese women in North Sumatra Island, Indonesia", Proceedings of the Nutritional Society of Australia, 2001, Vol. 25, page S67. Abstract	1-47
X	Brieskorn CH and Riedel W, "Triterpenic acids from Coleus amboinicus Loureiro", Arch Pharm (Weinheim), Nov 1977, Vol. 310(11), pages 910-6. Abstract, Table 1	1-28, 43-47
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C <input checked="" type="checkbox"/> See patent family annex		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 19 April 2005		Date of mailing of the international search report 26 APR 2005
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaaustralia.gov.au Facsimile No. (02) 6285 3929		Authorized officer ANTHONY MURFETT Telephone No : (02) 6283 2243

INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU2005/000459

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Castillo RA and Gonzalez VP, "Plecthranthus amboinicus (Lour.) spreng", Rev Cubana Plant Medicine, 1999, Vol. 3(3), pages 110-115. Summary, Table on page 111-112	1-28, 43-47
X	Derwent Abstract Accession Number 1987-112958; JP62059218 A (Tsuru Yakuhin Kogy KK), 14 March 1987. Abstract	1-28, 43-47

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/AU2005/000459

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Member
JP	62059218	NONE
Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.		
END OF ANNEX		