ORIGINAL RESEARCH ARTICLE

The use of Thai herbal galactogogue, 'Plook-Fire-Thatu', for postpartum heat re-balancing

DOI: 10.29063/ajrh2023/v27i7.9

Kitti Krungkraipetch[1] and Chuleekorn Kwanchainon[2]

Medical Faculty, Burapha University, 169 Bangsaen rd. Sansuk, Distr. Maung, Chonburi, Thailand 20131[1]; Thai Traditional Medicine department, Allied Health Science Faculty, Burapha University, 169 Bangsaen rd. Sansuk, Distr. Maung, Chonburi, Thailand 20131[2]

***For Correspondence:** Email: *kitti@go.buu.ac.th*; Phone: +6638386554

Abstract

Plook-Fire-Thatu is a traditional Thai medication designed to assist breastfeeding moms. However, no documented clinical research on its efficacy exists. Therefore, the authors recruited women who had a singleton baby vaginally between June 2019 and July 2020 and randomly allocated them to one of three groups: Plook-Fire-Thatu, Domperidone, or Placebo. The test-weight method was used to compare breastmilk amounts. During the hospital stay, all volunteers and newborns were followed for adverse effects. There were three groups of participants: Plook-Fire-Thatu 78, Domperidone 74, and Placebo 76. On the third postpartum day, the Plook-Fire-Thatu group exhibited a statistically significant increase in breastmilk quantity (F=15.11, $p \leq 0.01$). The mean body temperature of postpartum women in the Plook-Fire-Thatu group on the third day was significantly higher than in the placebo group. (F=4.22, p=0.016). Participants and infants in the intervention groups experienced a few adverse effects. In comparison to domperidone, Plook-Fire-Thatu has been discovered to be a natural way to increase postpartum breastmilk supply. *(Afr J Reprod Health 2023; 27 [7]: 85-98).*

Keywords: Breastmilk, domperidone, galactogogues, herbal medicine, Plook fire thau, tradition

Résumé

Plook-Fire-Thatu est un médicament thaïlandais traditionnel conçu pour aider les mères qui allaitent. Cependant, aucune recherche clinique documentée sur son efficacité n'existe. Par conséquent, les auteurs recruté des femmes qui ont eu un bébé unique par voie vaginale entre juin 2019 et juillet 2020 et les avons réparties au hasard dans l'un des trois groupes : Plook-Fire-Thatu, Domperidone ou Placebo. La méthode du poids spécifique a été utilisée pour comparer les quantités de lait maternel. Pendant le séjour à l'hôpital, tous les volontaires et les nouveau-nés ont été suivis pour les effets indésirables. Il y avait trois groupes de participants : Plook-Fire-Thatu 78, Domperidone 74 et Placebo 76. Le troisième jour post-partum, le groupe Plook-Fire-Thatu a présenté une augmentation statistiquement significative de la quantité de lait maternel (F=15,11, $p \leq 0.01$). La température corporelle moyenne des femmes post-partum du groupe Plook-Fire-Thatu le troisième jour était significativement plus élevée que dans le groupe placebo. (F=4,22, p=0,016). Les participants et les nourrissons des groupes d'intervention ont subi quelques effets indésirables. Par rapport à la dompéridone, Plook-Fire-Thatu s'est avéré être un moyen naturel d'augmenter la production de lait maternel après l'accouchement. *(Afr J Reprod Health 2023; 27 [7]: 85-98).*

Mots-clés: Lait maternel, dompéridone, galactogogues, phytothérapie, Plook fire thau, tradition

Introduction

According to the recommendations of the World Health Organization, optimal baby nutrition and well-being are the goals for child health; therefore, exclusive breastfeeding has become the strategic method for achieving these results[1]. However, the overall breastfeeding rate remained low. Less than forty percent of infants younger than six months are exclusively breastfed in low- and middle-income countries[2]. Aside from returning to work and breast nipple issues, the most prevalent cause for moms terminating exclusive nursing was a noticeable decrease in breastmilk output[3]. In the cases of low breastmilk adequacy, the sense of insufficient quantity has been a common issue for these women, particularly new mothers[4]. Therefore, there were two decision options: transitioning to infant formula or using a galactogogue. Some mothers may prefer to utilize them both.

Galactogogues have been known for assisting postpartum women in obtaining exclusive breastfeeding success. In the pharmaceutical sector, there are modern pharmaceuticals as well as numerous herbal medications. Domperidone (DD) and metoclopramide are two well-known contemporary medications that have been used as galactogogues. Many studies have shown that both items are effective in increasing breastmilk production[5,6]. On the other hand, these contemporary pharmaceuticals were used off-label because the US Food and Drug Administration had yet to approve them for galactogogue use[7,8]. However, there were a few adverse effects among mothers who had ever used it as galactogogue[5,8].

Herbal galactogues, on the other hand, have been used regularly and modestly in postnatal care in several communities around the world, particularly in Southeast Asian and African countries[9-11]. Due to comparable climatic conditions in the vicinity of the equator, both regions are habitat to countless plant species. In addition, the majority of the region's inhabitants believe in traditional medicine, which consists of folk remedies based on ancestral culture, rituals, and traditions[10-12]. Consequently, the use of herbs for postpartum care is analogous. However, there was limited clinical evidence for these herbal remedies or recipes[9,11,13].

Herbal galactogogues is a term that encompasses more than just a type of medicine. On the inside, they carry the history and wisdom of communities. As a result, many postpartum women still preferred to use them as a common practice without hesitation, regardless of their safety or efficacy. A similar picture of postpartum care has emerged in Thailand, as it has in many other Asian countries. Through folk healers, traditional medical scripture and norms have continued to play an important role in a number of Thai communities. All traditional medical formulations in the scripture were developed through centuries of trial and error in human subjects and are now waiting to be discovered using modern scientific methods. Plook-Fire-Thatu (PFT) is a sample from a historic Thai medicinal scripture called "Mahachotirat". It has been on the Thai National Drug Information's herbal drug lists since 2016[14]. However, it has been used infrequently since most healthcare providers are unfamiliar with it and lack confidence in using it.

This research focused on the clinical effectiveness of PFT on breastmilk production compared to domperidone (DD) and placebo. The study procedures were used as an augmentation approach in order to fulfill the WHO and UNICEF recommendations for exclusive breastfeeding in the first hour after birth[1,15]. In terms of theoretical contribution, this study opted to present a medical concept in the re-balancing of the heat element in postpartum women, which is commonly lost following childbirth. This care concept derived from integration of humoral theory and traditional Chinese medicine that use the correction of imbalance of four body elements (earth, fire, air, and water)[16]. Childbirth causes the body to lose heat through blood and amniotic loss, making some mothers ill and affecting their breastmilk production. Therefore, traditional medicine in non-western countries has adopted the practice of warming the body[17]. Plook-Fire-Thatu refers to the enhancement of heat element in the mother's body through the use of fiery herbs. From the standpoint of clinical management, this research will provide clinical information in a scientific manner, enhancing healthcare practitioners' confidence in the use of PFT in clinical practices.

The purpose of this study was to compare the lactogenic effect and adverse effects of PFT, DD, and placebo (PB) in postpartum women who delivered vaginally. We hypothesized that the PFT group would have a greater positive effect on breastmilk production than the DD and PB groups, as well as increase postpartum women's core body temperature.

Methods

Trial design

A randomized controlled trial with a single blind.

Participants

Postpartum women who delivered between June 2019 and July 2020 at three general hospitals in Chonburi province were the population in this study. The following criteria were used to determine eligibility: postpartum women aged 18 to 45, singleton vaginal birth, good health with no underlying illness, and no history of allergy to phenytoin, propranolol, theophylline, or rifampicin.

In order to respond to the questions, they needed to be alert and understand Thai. Her baby's birth weight had to be greater than 2499 grams, and there was no illness that would interfere with breastfeeding. All participants had normal electrocardiography results, which a cardiologist validated. Exclusion criteria included a newborn's postnatal complications requiring intensive care, a drug allergy, and the use of infant formula milk.

Intervention

There were three trial groups: PFT and DD were the intervention groups, while the placebo group was the third. Plook-Fire-Thatu was a herbal medicine formula recorded in the Thai medical scripture "Mahachotirat" more than a century ago[18]. It was made up of 11 plants that had been mixed together. Each 100 gram contained 50 grams of Piper nigrum L and five grams of the following: Zingiber officinale Roscoe, Piper sarmentosum Roxb, Piper retrofractum Vahl, Arnebia euchroma (Royle) I. Johst, Ardisia elliptica Thunb, Citrus hystrix DC., Oenanthe javanica (Blume) DC., Acorus calamus L., Piper wallichii (Miq.) Hand.-Mazz, and Cyperus rotundus L[19]. According to the "Mahachotirat" scripture, every postpartum mother lost their heat balance to varying degrees while giving birth, so each mother experienced different postpartum symptoms. Someone reported feeling cold and/or body chills quickly after labor, whereas another reported malaise, lethargy, or sleepiness on another day. As a result, warm keeping and re-heat balancing became necessary practices in postnatal care for both the mother and the newborn as a result. However, there was no scientific evidence of this traditional formula's mechanism of action.

According to Thailand's National List of Essential Medicines (NLEM), the maximum PFT dosage during the postpartum period was 90 mg three times per day for three days in a row. Prior to the start of the PFT intervention, samples of PFT from the factory and raw materials used in this recipe were sent to the pharmacological laboratory at Mahidol University for Thin Layer Chromatography (TLC) analysis. Piperine and beta-pinine were the standard agents. Image analysis was performed using the ultraviolet light wave lengths of 254 and 366 nanometers. The analysis discovered that the standard agents from the image analysis and densitometer were present in both commercial drugs and raw materials. PFT medication has also been inspected and determined to fulfill the Ministry of Health's department of Medical Sciences criteria for heavy metal, microbe, and contaminant levels.

Domperidone is a dopamine receptor (D2) antagonist used to control emesis, regulate body temperature, and increase prolactin release. It has the same clinical uses as metoclopramide, but it does not cross the blood-brain barrier. As a result, it has no extrapyramidal side effects [20]. Because the drug has never been approved by the FDA in the United States, prescribing domperidone should be done with caution[8,21]. Prior research, however, found that it had a positive effect on breastmilk production. The recommended dosage was 10 mg three times per day. It had fewer negative effects on mothers and babies at this dosage[22,23]. As a result, this dosage was employed in this study to compare to PFT over the course of three postnatal days.

In the placebo group, they received one starch capsule three times per day before meals, following the same postpartum care protocol as the PFT and DD groups. For concealment, the placebo medicine was packaged in a foil pouch. The augmentation approach was used in this study to prevent breastfeeding failure. Despite the fact that all moms were advised and taught proper breastfeeding techniques by healthcare practitioners, if they felt their breastmilk was insufficient, they might choose infant formula instead. Another factor was a limitation of beds in general hospitals, which meant that postpartum women could only stay in the hospital for two or three days unless they were in a life-threatening situation.

To prevent confounding variables from interfering with our research, we recruited a sample consisting only of specific participants and managed them under identical conditions according to the same protocol, with the exception of the independent variables. We also randomly assigned sufficient numbers of participants to the treatment and control groups. All of the researcher assistants received training on the research methodology, and regular site visits were used to oversee its execution. The funding representative and our

institution's ethical committee also oversaw this study through random site visits and the review of the progress report on the research.

Outcome

A notable finding of this study was the volume of breastmilk produced. The possible value of this study will be solid evidence for clinical practice and support for the herbal medication business. Furthermore, the efficacy of Thai herbal galactogogue will be scientifically confirmed in this investigation.

Sample size

The sample size was calculated using the G-Power program version 3.1.9.2 and the following statistics were used: one-way ANOVA, effect size = 0.25, alpha error = 0.05, and power of test = 0.80. The sample size was determined to be 159 females. To account for inadvertent withdrawal, the authors increased the sample size by 10%, resulting in a sample size of 174.9. At this point, our sample size was set at 180 women. These women were selected using simple randomization and divided into three groups: PFT, DD, and PB. The sample size was distributed equally among the three study sites.

Randomization and allocation

Every study site utilized the same procedure to randomize participants and assign them to one of three study groups. For group classification, each participant had to open one of 60 envelopes containing colored paper. The colorful paper indicated which group she belonged to. For instance, if she received red paper, she belonged to the PFT group. The yellow and green papers, likewise, indicated that she was in DD and PB, respectively. The authors changed the color coding every week for sample concealment and forwarded it to the study site coordinator on the weekend. The enrolled data and the allocation number were illustrated in Figure 1.

Concealment mechanism and blinding

All participants had no idea which group they were in; only the registered nurses were aware of this. During each work shift, the operation nurses were assigned to dispensing drugs, monitoring clinical outcomes, and documenting research data. They had no notion which individuals in this investigation belonged to which group. However, the authors and research assistance knew this information. All testing drugs were filled in foil sachets by assistant researchers at the faculty research center and mailed to studying sites once a week. The registered nurses were able to identify which group was which based on the color paper coding that the research teams had provided each week until the experiment was completed. Even though they were not study participants, all postpartum women on the hospital unit received the identical breastfeeding practice care approach.

Implementation

At the study sites, registered nurses on the work shift enrolled participants who met the inclusion criteria and randomly allocated them to distinct groups using simple randomization. Each hospital's pharmacist dispenses intervention drugs in accordance with the doctor's prescription. Operation nurses were in charge of data collection.

Measurements and statistical methods

The amount of breastmilk was collected three times per day: 06.00-8.00, 12.00-14.00, and 18.00-20.00 o'clock, using the "Test weight" method, which used the difference in weight between before and after breastfeeding without removing the newborn's diaper[24-26]. The frequency, color, and content of the baby's urine and stool were all recorded. All participants and their babies were observed and assessed for adverse effects of trial medication during hospitalization, as well. All operation nurses who collected and recorded data were instructed on how to collect data in accordance with research requirements.

The frequency, intensity, and burden of side effects rating (FIBSER) scale was used to assess the adverse effects of the intervention drug and placebo[27]. This scale consisted of three items: frequency, severity, and day-to-day function interference. Participants had to rate their own frequency, intensity, and level of impairment for each item. In addition, the authors assigned that

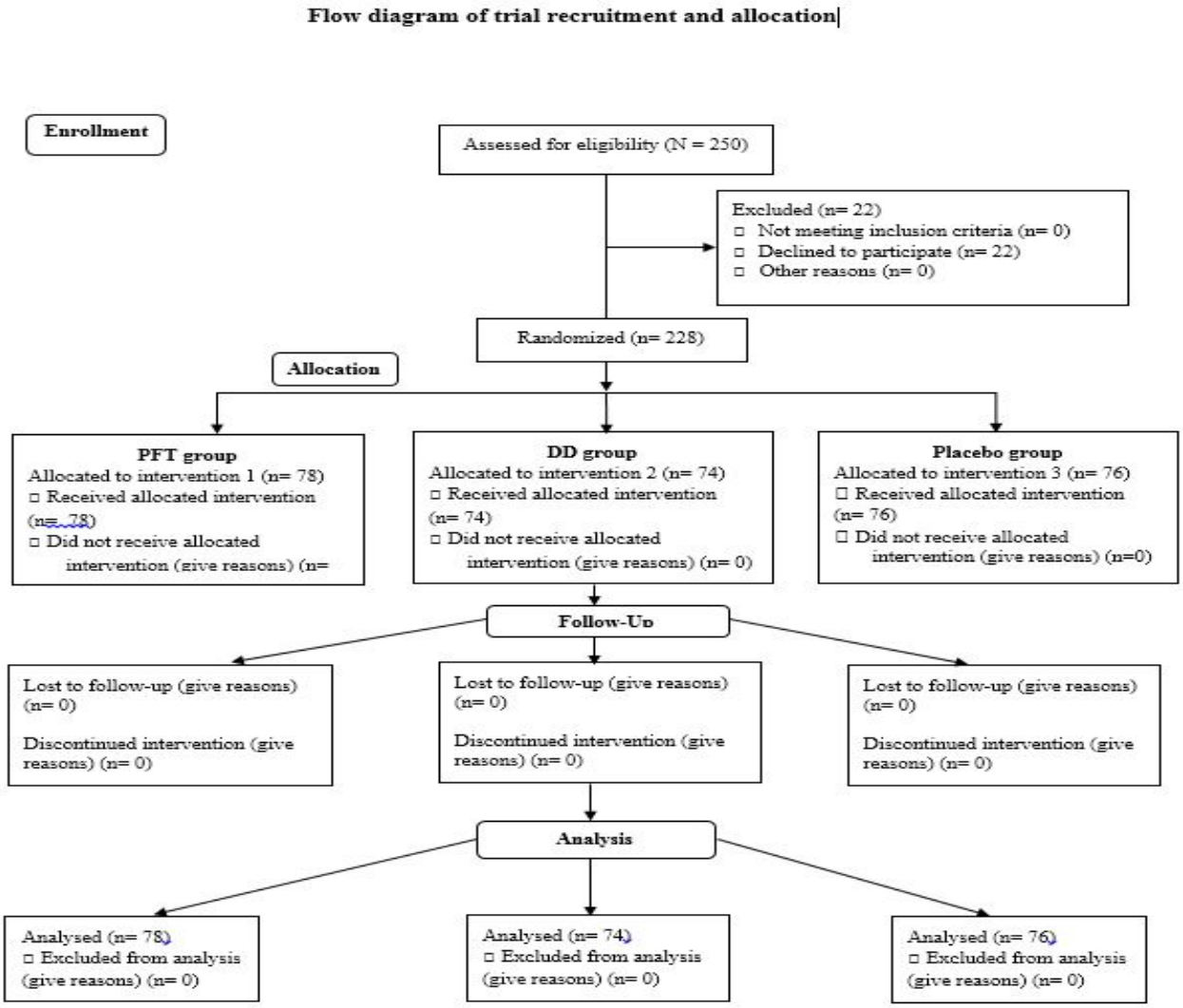

Figure 1: According to the study flow, 228 participants were enrolled and divided into three groups: PFT=78, DD=74, and Placebo =76. In this investigation, there were no discontinuities or withdrawals

pharmacists at all trial sites had to apply the Thai Algorithm for adverse drug reaction monitoring[28]. This scale was adapted from Naranjo scores, which consisted of ten questions with Yes, No, or Do Not Know answers. Different point values start from -1 to +2 for each question. The total scores range from -4 to +13. There are four levels of score for interpretation: ≥ 9; definite, 5-8; probable, 1-4; possible, and ≤ 0; doubtful[29,30]. For assessment in daily practice, the Thai algorithm and Naranjo's scale demonstrated similar sensitivity and specificity[28]. General data was analyzed by frequency, mean, standard deviation, and chi-square. One-way ANOVA was used to analyze the comparison of breastmilk quantity.

Ethical concerns

This study protocol has been authorized by the Burapha University ethics committee since March 7, 2020, with permission number 34/2562.

Results

There were 250 postpartum women who met the eligibility criteria, with 22 women being denied participation for personal reasons. As a result, 228

Table 1: Demographic data of participants with information of age, monthly family income, gestational age, birth weight, BMI, graduation status, occupation, and parity

Items	**PFT (n=74)**		**DD (n=78)**		**PB (n=76)**		**ANOVA**	
	Mean	**SD.**	**Mean**	**SD.**	**Mean**	**SD.**	**F**	**Sig**
Age (year)	27.01	4.84	25.76	4.45	26.66	5.66	1.58	0.207
Monthly family income (Baht)	17405.41	9008.24	17141.03	7620.42	16717.11	9115.68	0.12	0.885
Gestational age (week)	38.84	1.30	36.68	1.33	38.62	1.10	0.68	0.541
Birth weight (gram)	3165.46	366.49	3141.32	362.20	3203.01	348.68	0.58	0.563
BMI (kg/m^2)	25.43	2.10	26.23	2.10	25.42	1.64	1.28	0.094
	No.	**%**	**No.**	**%**	**No.**	**%**	**X^2**	**p- value**
Education							3.09	0.929
- Never learned	5	6.76	10	12.82	9	11.84		
- primary	15	20.27	13	16.67	15	19.74		
- Junior high school	27	36.49	27	34.62	30	39.47		
- High school	23	31.08	25	32.05	19	25.00		
- Bachelor degree	4	5.41	3	3.85	3	3.95		
total	74	100	78	100	76	100		
Occupation							6.88	0.332
- Trading	9	12.16	15	19.23	8	10.53		
- Employment	27	36.49	32	41.03	39	51.32		
- Civil Service/State Enterprise	3	4.05	1	1.28	2	2.63		
- Home Maid	35	47.30	30	38.46	27	35.53		
Total	74	100	78	100	76	100		
Parity							0.06	0.970
- Nulliparity	20	27.40	20	25.64	20	26.32		
- Multiparity	53	72.60	58	74.36	56	73.68		
Total	74	100	78	100	76	100		

Note. PFT = Plook-Fire-Thatu, DD = Domperidone, PB = Placebo, Alpha level = .05

Table 2: Comparative results of breast milk quantity during consecutive three days postpartum period between PFT, DD, and PB groups

Groups	**Average production of breast milk (gram) during the postpartum period in which it was collected three times/day (mean ± sd.)**		
	1st day	**2nd day**	**3rd day**
PFT (N = 74)	15.80 ± 8.61	22.31 ± 12.42	24.61 ± 7.98
DD (N = 78)	16.99 ± 8.92	19.20 ± 11.35	19.52 ± 5.30
PB (N = 76)	14.70 ± 7.52	19.21 ± 12.68	18.22 ± 8.87
Total (N = 228)	15.84 ± 8.39	20.18 ± 12.19	20.74 ± 7.97

Average breast milk production at postpartum period	**Levene statistic**	**df1**	**df2**	**Sig.**
1st day	1.38	2	225	0.254
2nd day	1.46	2	225	0.234
3rd day	1.64	2	225	0.197

ANOVA

Average production of breast milk supply by postpartum date		**Sum of Square**	**df**	**Mean Square**	**F**	**Sig**
1st day	Between Groups	202.02	2	101.01	1.44	0.239
	Within Groups	15786.08	225	70.16		
	Total	15988.10	227			
2nd day	Between Groups	497.07	2	248.53	1.68	0.188
	Within Groups	33257.66	225	147.81		
	Total	33754.73	227			
3rd day	Between Groups	1706.75	2	853.38	15.11	≤0.01*
	Within Groups	12710.12	225	56.4		
	Total	14416,88	227			

PFT = Plook-Fire-Thatu, DD = Domperidone, PB = Placebo, Alpha level = .05

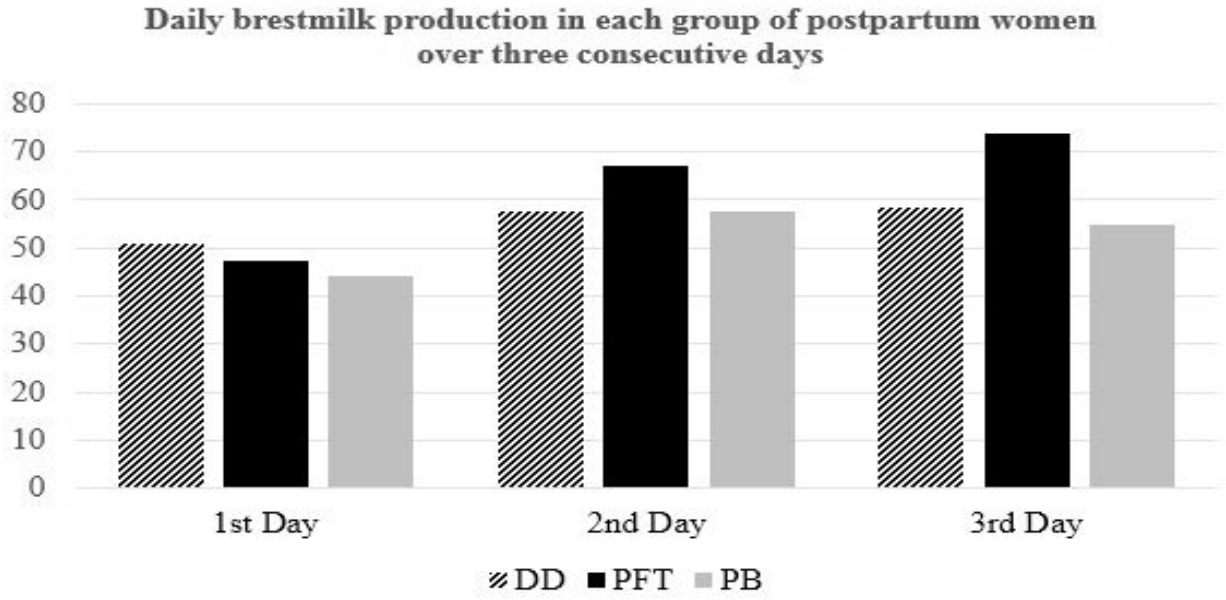

Figure 2: A comparison of breastmilk production on the third consecutive day following delivery. The PFT group had a statistically significant increase in breastmilk on the third day compared to the other groups

Table 3: Multivariate comparison test of the average breast milk production at third day postpartum among three groups by Tukey HSD technique

	Group No. (I)	Group No (J)	Mean Difference (I-J)	SE.	Sig.	95% Confidence Interval	
						Lower	Upper
Tukey HSD	DD	PFT	-5.09	1.22	≤.01*	-7.97	-2.21
		Placebo	1.30	1.21	0.533	-1.56	4.16
	PFT	DD	5.09	1.22	≤.01*	2.21	7.97
		Placebo	6.39	1.23	≤.01*	3.49	9.28
	Placebo	DD	-1.30	1.21	0.533	-4.16	1.56
		PFT	-6.39	1.23	≤.01*	-9.28	-3.49

PFT = Plook-Fire-Thatu, DD = Domperidone, PB = Placebo, Alpha level = .05

women participated in this trial as research subjects: 78 for PFT, 74 for DD, and 76 for the placebo. There was no participant withdrawal during the trial. The authors changed their plan to include more people in this study since one hospital site's desktop personal computer, which was used for data collection, was in disarray. As a result, the study samples exceeded the target numbers. Because of the COVID-19 pandemic, the recruiting and follow-up periods began in June 2019 and were extended until September 2020.

There was no statistically significant difference in age (F=1.58, p=0.207), monthly family income (F=0.12, *p*=0.885), gestational age (F=0.68, *p*=0.541), or birth weight (F=0.58, *p*=0.563) between the three groups based on the baseline demographic data. There also was no statistically significant difference in the studied groups' educational level (X^2 = 3.09, *p*=0.929), occupation (X^2 = 6.88, *p*=0.332), or parity type (X^2 = 0.06, *p*=0.970). (Table 1)

The amount of breastmilk increased in proportion to the number of days after childbirth. When comparing average breastmilk production by postpartum date, there was no statistically significant difference on the first two days, but there was a significant difference on the third postpartum day. (F=15.11, *p*≤0.01) (Table 2 and Figure 2). The Tukey HSD of multivariate comparisons between three groups discovered a statistically significant difference between PFT and DD (95% CI = 2.21 to 7.97, *p*≤0.01) and PFT against Placebo group (95% CI = 3.49 to 9.28, *p*≤0.01) (Table 3). The comparison weights of infants during the three days

Table 4: Comparative results of infantile weight between three groups on three consecutive days during postpartum period

Groups	**Average infantile weight (gram) at postpartum period (mean ± sd.)**		
	1st day	**2nd day**	**3rd day**
PFT (N = 74)	3206.11 ± 355.81	3097.03 ± 364.96	3143.26 ± 359.45
DD (N = 78)	3156.41 ± 395.51	3074.04 ± 404.04	3080.42 ± 361.67
PB (N = 76)	3201.72 ± 373.42	3098.45 ± 383.06	3139.06 ± 334.82
Total (N = 228)	3187.64 ± 374.65	3089.64 ± 383.17	3120.36 ± 351.85

Average infantile weight at postpartum period	**Levene statistic**	**df1**	**df2**	**Sig.**
1st day	0.11	2	225	0.894
2nd day	0.49	2	225	0.614
3rd day	0.44	2	225	0.645

ANOVA

Average infantile weight in three consecutive day of postpartum period		**Sum of Square**	**df**	**Mean Square**	**F**	**Sig**
1st day	Between Groups	116387.02	2	58193.51	0.41	0.663
	Within Groups	31745249.20	225	141090.44		
	Total	31831736.22	227			
2nd day	Between Groups	28919.17	2	14459.58	0.10	0.907
	Within Groups	33298435.62	225	147993.05		
	Total	33327354.79	227			
3rd day	Between Groups	189851.56	2	94925.78	0.77	0.466
	Within Groups	27911680.87	225	124051.91		
	Total	28101532.43	227			

PFT = Plook-Fire-Thatu, DD = Domperidone, PB = Placebo, Alpha level = .05

Table 5: Interaction of parity and protocol grouping effect to breast milk production at the third day of postpartum period

Source	**Type III Sum of Square**	**df**	**Mean Square**	**F**	**Sig.**
Corrected Model Intercept	1350.87	5	270.17	12.53	≤.01
Group	1287.34	2	643.67	29.85	≤.01
Parity	54.85	1	54.85	2.54	0.114
Group*Parity	21.69	2	10.84	0.50	0.606
Error	2005.59	93	21.57		
Total	38792.11	99			
Corrected Total	3356.46	98			

of all groups showed no statistically significant difference (Table 4). The analysis of the parity on breastmilk quantity of study groups found no statistically significant difference (F=0.50, *p*= 0.606) (Table 5)

There was nausea or vomiting in three, four, and three cases of PFT, DD, and placebo, respectively. Their symptoms appeared about 10% of the time with minor intensity but no interference with daily activities (FISBER score = 2). Two patients in the DD group complained of dry mouth (FISBER score = 2). One patient in the PFT group experienced heartburn, but she recovered after taking antacids (FISBER score = 2). One case in the PFT group and one case in the placebo group developed a maculopapular rash, but it was only temporary and went away within 24 hours. (FISBER score = 2). During hospitalization, there were no adverse reactions in the infants. They also had normal urination and defecation.

According to the Thai algorithm, adverse effect scores, nausea and vomiting symptoms of intervention drugs were possible in both groups. The symptoms of dry mouth in the DD group and heartburn in the PFT group were both probable. The appearance of a skin rash in one PFT participant seemed questionable. The redness on her chest vanished within two to three minutes. At that moment, the operating nurse did not see her skin lesion.

The data from all study sites' postpartum clinics revealed that 115 participants came for follow-up, allowing the researchers to collect additional data on the first week of postpartum. There were 35 in the PFT group, 40 in the DD group, and 40 in the placebo group, and no

Table 6: Comparison body temperature of mothers during three consecutive days in postpartum period

Groups		**Average body temperature (℃) during three postpartum day which dividing by groups (mean ± sd.)**				
		1st day		**2nd day**	**3rd day**	
PFT (N = 74)		36.17 ± 0.28		36.38 ± 0.24	36.64 ± 0.24	
DD (N = 78)		36.14 ± 0.26		36.33 ± 0.26	36.57 ± 0.28	
Placebo (N = 76)		36.23 ± 0.27		36.28 ± 0.28	36.51 ± 0.24	
ANOVA						
Average production of breast milk supply by postpartum date		**Sum of Square**	**df**	**Mean Square**	**F**	**Sig**
1st day	Between Groups	0.3222	2	0.1611	2.21	0.113
	Within Groups	16.4391	225	0.0731		
	Total	16.7613	227			
2nd day	Between Groups	0.3750	2	0.1875	2.76	0.065
	Within Groups	15.2900	225	0.0680		
	Total	15.6650	227			
3rd day	Between Groups	0.6345	2	0.3173	4.22	0.016*
	Within Groups	16.9268	225	73.09		
	Total	17.5613	227			
Tukey HSD Post-hoc test of 3rd day postpartum maternal temperature						
Group matching	**difference**	**95% CI**				**Sig**
PFT vs DD	0.07	-0.17		0.03		0.209
PFT vs Placebo	0.13	-0.24		-0.03		≤0.01*
DD vs Placebo	0.06	-0.16		0.04		0.311

PFT = Plook-Fire-Thatu, DD = Domperidone, PB = Placebo, Alpha level = .05

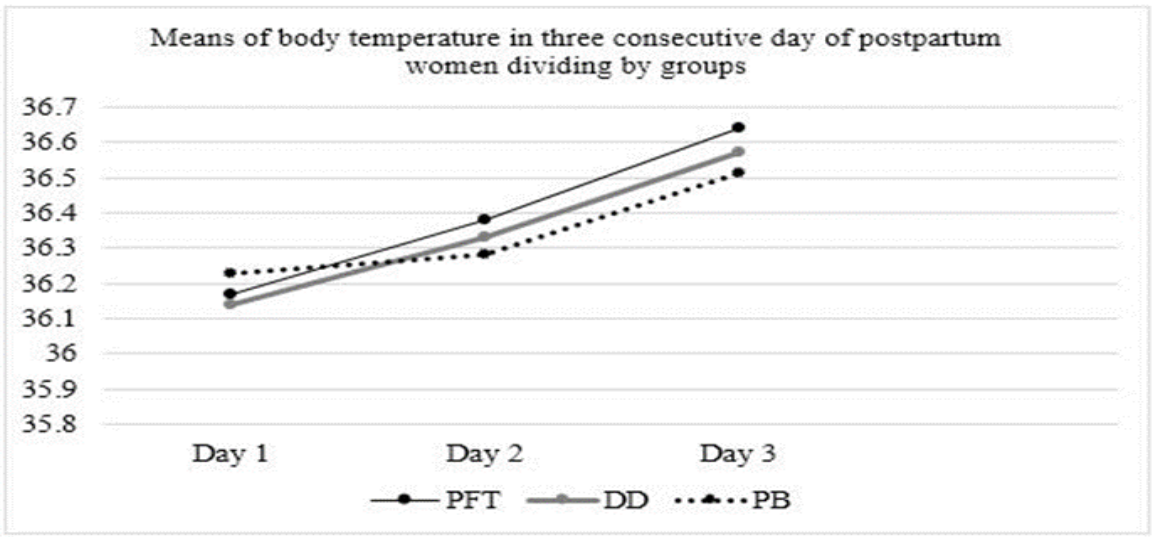

Figure 3: During the early postpartum period, the average temperature of all groups rose. However, the temperature in the PFT group was statistically significant higher than in the other group

statistically significant difference in baby weight was found using the tested weight method. This result, however, was tested only once at an outpatient clinic and without randomization.

The authors examined additional data on body temperature of participants during their three-day hospital stay and discovered a trend of rising temperature during the hospital stay. There was no statistically significant difference in the first two days of postpartum. However, the average temperatures for PFT, DD, and PB on the third day were 36.64 ± 0.24, 36.57 ± 0.28 and 36.51 ± 0.24 ℃, respectively. The analysis showed a statistically significant difference of body temperature (F =4.22, *p*= 0.016). Following that, a multivariate comparison was performed, which revealed that the

temperature in the PFT group was higher than in the PB group. (Difference = - 0.13, 95% CI =0.24 to -0.0243, $p \leq 0.01$) (Table 6, Figure 3).

Discussion

To increase the internal validity of this study, we blinded all participants such that they were ignorant of the intervention they were receiving. The selection and assignment were conducted at random. Moreover, we closely controlled the research process at each study site. There was no participant attrition or diffusion during the experiment. To enhance external validity, we chose two local government hospitals rather than a university hospital whose participants mirrored the broader population. In addition, we established the inclusion and exclusion criteria to guarantee that the study participants represent the intended population for this drug. Nevertheless, our study was done in a hospital, where participants were subject to study protocol, hospital regulation, and hospital environment restrictions. Consequently, interpretation of the results after their hospital discharge may be limited.

This study was designed to prove the efficacy of PFT in the role of galactogogue among postpartum women compared to DD and PB. The results supported the traditional evidence that was recorded in Thai medical scripture. There were no significant differences in demographic data among the participants, such as age, gestational age, birth weight, parity, and BMI. As a consequence, there were few confounding factors in this trial.

According to the results, the efficacy of galactogogues was expressed on the 3rd day of postpartum. It meant that there was a duration of action for PFT. Therefore, the healthcare providers should explain this information to the mothers in order to relieve their expectations. Some might argue that this was a result of physiologic changes in human lactation. Because antenatal corticosteroids and sex hormones, particularly progesterone, suppress prolactin hormone for a few days after delivery, human lactogenesis might be delayed[31]. In order to reduce this bias, the PB group was included in this study. According to our results, the PFT group also gained more from increased breastmilk than the PB group, and it outperformed DD in terms of efficacy.

What were the possible explanations for PFT's stronger galactogogue effect than DD? The PFT formula contains many herbal plants that may have synergistic effects, particularly Piper nigrum, Piper retrofractum Vahl, Piper sarmentosum Roxb, Piper interruptum Opiz, and Piper wallichii (Miq.) Hand-Mazz. Because white pepper make up 50% of this formula, piperine is the main active agent in PFT. Piperine has numerous properties, such as anti-inflammation, antioxidant, and vasomotor effects[32]. Despite the fact that there was no scientific evidence on piperine's effect on human lactogenesis, an animal study discovered that piperine might indeed act as a calcium channel blocker, resulting in vasodilatation and lowering blood pressure in rats[33]. In addition, the previous study discovered piperine's vasomoderator[34]. These facts imply that PFT would possibly has an impact on thermoregulation. As a result, this herbal medicine was developed to be used as a heat booster in postpartum women for an extended period of time.

Piperine may be beneficial for breastfed mothers who have a problem with mastitis. This complication interferes with breastmilk production and can cause breastfeeding failure [35]. There was a study in mouse model and demonstrated that piperine inhibited lipopolysaccharide (LPS) induced inflammatory cytokines such as TNF-alpha and interleukin-1 beta[36]. LPS is a major virulence factor found in gram-negative bacteria that can activate the TLR4 signaling pathway, resulting in the release of inflammatory cytokines. However, this research was carried out on animals[37]. This is one of the great properties that DD lacks.

PFT also contains ginger root, or zingiber officinale, Ginger, like pepper, has a variety of pharmacological characteristics and can help postpartum moms produce more breastmilk[38,39]. A previous study in Thai patients indicated that ginger powder boosted breastmilk output within three days, despite the experimental and control groups' prolactin levels remaining unchanged[40]. This inferred that, other than prolactin hormone, extra components controlling human lactogenesis seem to exist, such as the adjusting of human body elements, which has long been recognized in Asian therapeutic conventions.

According to Thai traditional medicine, the harmony of these four body components was vital

for maximum health. Instead of referring to physical objects, "essential body elements" refers to attributes. The element of fire or heat fosters metamorphosis and maturation in the human body. The fire element is the catalyst for change. The element of fire creates emotion and fever and provides bodily warmth. It also causes physical decay and aging[41]. As a result, understanding and recognizing the reactions of the four elements is critical in Thai traditional medicine medical treatments.

According to the ancient scriptures, all women who gave birth had lost their fire element balance. Body warming has become an essential thing for all mothers to accomplish. Therefore, "Plook-Fire-Thatu," which translates as "heat element booster action," was created with the notion of re-balancing the fire element based on Thai traditional care philosophy.

Most folk healers/community leaders believed that if a postpartum woman's heat balance was not corrected, it would have a negative impact on her health later on. According to traditional medicine, all postpartum mothers' bodily elements, particularly the fire element, are impaired, and their external and internal organs should be recovered.[42]. However, there was no known physiologic study to confirm these disorder. Previously, the number of maternal morbidities was obtained entirely through observation, with no use of the research process to assess. The majority of herbal galactogogue formulas have a strong and spicy flavor that can warm the body. Recent studies in Thai postpartum mothers demonstrated that supplementation with this type of herbal medication can boost breastmilk volume[43,44]. In the Thai traditional practice known as "You Fire," there were numerous ways to keep the mother's body warm, such as lying on a bamboo bed with burning coal underneath, hot herbal compresses, bathing with herbal water, eating herbal cuisine, and taking herbal medicine[45]. These traditional practices were also common in other Southeast Asian countries, such as Cambodia, Malaysia, and Brunei[46-48]. These rituals all served the same purpose of maintaining the body's fire element, i.e., taboo foods, hot herbal massages, and behavioral taboos for protection against heat loss: bathing or hair washing, especially with cold water, was rigorously forbidden for varying days after birth. It was believed that these practices would prevent blood clots, aching bones, and generally speed up body temperature restoration[10]. Due to additional data, the authors determined that the average maternal temperature in the PFT group was higher than in the PB group on the third day. It is possible that PFT could help postpartum mothers modify their fire element more successfully than conventional postpartum care.

Further data from the study sites' postpartum clinics shows that approximately half of the participants returned within one week as a routine follow-up in every hospital. There was no problem with insufficient breastmilk among them, despite the lack of galactogogue supplement. This information could indicate that galactogogues' role in augmentation was able to serve exclusive breastfeeding in postpartum women. However, the data on breastfeeding practices after they stayed home was limited, so it was only an expectation.

Similar to traditional herbal galactogogue in different continents, the main concept of non-western postpartum care is speculated in hot and cold balancing[10,17]. In African countries, similar to Asian countries, the majority of women feel comfortable discussing their women's problems with female traditional healers and following the folk healers' self-care practices despite the unreasonableness of some rituals[11]. However, the herbal plants that are used during pregnancy and postpartum in Asia are similar in Africa, for instance, ginger, licorice, pumpkin, peppermint, lemon grass[49]. Some herbal plants are included in the PFT formula; therefore, we can learn and share our knowledge of various herbal galactogogues across communities and countries.

From study results, domperidone had a beneficial influence on the production of breastmilk. This result was consistent with prior findings in Thai women, which indicated the use of domperidone as a galactogogue in the augmentation procedure. Those investigations found no negative effects in volunteers, but the sample size was small[50,51]. In this trial, there were a few adverse effects on all participants. Although PFT and DD have been deemed safe for use in clinical practice, clinicians must closely monitor adverse effects.

This research provided a recommendation for the use of PFT as a galactogogue in postpartum women as early as possible. It not only helped them to initiate breastfeeding but also maintained their balanced fire element.

Limitation and recommendation of future research

This study was only a clinical study by picking up the ready-made formula for study. Therefore, some users might be doubtful about the mechanism of action because there are many herbal plants in this formula. So, the pharmacologic properties of PFT needed to be explored. In this study was time limited only in three day postpartum, so the study's result was limited for interpretation if use duration was changed. Furthermore, what are the negative impacts on mothers and infants if the length of drug usage is extended? These would be the questions that have been awaiting solutions.

In study design, it might be best if a double-blind study could be applied. But there was a limit to the number of healthcare workers, so it was not easy for establishing this concealment. On other hand, the participants might talk together about the process in the protocol and compare each other. Additionally, all study sites might have different breastfeeding practices for participants. The authors provided training to all research assistants at all study sites prior to the start of the experiment to address these issues. The authors visited the study sites once a month for supervision and issue solving during the experiment.

Conclusions

This study concluded that the supplement 'Plook-Fire-Thatu' aided breastfeeding practices. It was equally effective as domperidone and had little side effects in mothers and infants.

References

1. Infant and young child feeding. *Newsrooom* [Monograph on the internet]. 2021; https://www.who.int/news-room/fact-sheets/detail/infant-and-young-child-feeding. Accessed Oct, 19, 2021.
2. Victora CG, Bahl R, Barros AJ, França GV, Horton S, Krasevec J, Murch S, Sankar MJ, Walker N, Rollins NC and Lancet Breastfeeding Series Group. Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. *The Lancet.* 2016;387(10017):475-490.
3. Gianni ML, Bettinelli ME, Manfra P, Sorrentino G, Bezze E, Plevani L, Cavallaro G, Raffaeli G, Crippa BL, Colombo L, Morniroli D, Liotto N, Roggero P, Villamor E, Marchisio P and Mosca F. Breastfeeding Difficulties and Risk for Early Breastfeeding Cessation. *Nutrients.* 2019;11(10):2266.
4. Mortel M and Mehta SD. Systematic review of the efficacy of herbal galactogogues. *Journal of human lactation : official journal of International Lactation Consultant Association.* 2013;29(2):154-162.
5. Bazzano AN, Hofer R, Thibeau S, Gillispie V, Jacobs M and Theall KP. A Review of Herbal and Pharmaceutical Galactagogues for Breast-Feeding. *The Ochsner journal.* 2016;16(4):511-524.
6. Shen Q, Khan KS, Du M-C, Du W-W and Ouyang Y-Q. Efficacy and Safety of Domperidone and Metoclopramide in Breastfeeding: A Systematic Review and Meta-Analysis. *Breastfeeding Medicine.* 2021;16(7):516-529.
7. Sewell CA, Chang CY, Chehab MM and Nguyen CP. Domperidone for Lactation: What Health Care Providers Need to Know. *Obstetrics & Gynecology.* 2017;129(6).
8. Hale TW, Kendall-Tackett K and Cong Z. Domperidone Versus Metoclopramide: Self-Reported Side Effects in a Large Sample of Breastfeeding Mothers Who Used These Medications to Increase Milk Production. *Clin Lactation.* 2018(1):10-17.
9. Budzynska K, Gardner ZE, Low Dog T and Gardiner P. Complementary, holistic, and integrative medicine: advice for clinicians on herbs and breastfeeding. *Pediatr Rev.* 2013;34(8):343-352; quiz 352-343.
10. Withers M, Kharazmi N and Lim E. Traditional beliefs and practices in pregnancy, childbirth and postpartum: A review of the evidence from Asian countries. *Midwifery.* 2018;56:158-170.
11. Okaiyeto K and Oguntibeju OO. African Herbal Medicines: Adverse Effects and Cytotoxic Potentials with Different Therapeutic Applications. *International journal of environmental research and public health.* 2021;18(11).
12. Micozzi MS. *Fundamentals of complementary and alternative medicine-E-book.* Elsevier Health Sciences; 2014.
13. Kamsu-Foguem B and Foguem C. Adverse drug reactions in some African herbal medicine: literature review and stakeholders' interview. *Integrative medicine research.* 2014;3(3):126-132.
14. Thai traditional medicine. *Thai traditional medicine* [Monograph on the internet]. 2018; https://be7herb.wordpress.com/. Accessed November, 8, ~~2018~~, 2018.
15. Wallingford J. Breastfeeding in the 21st century. *The Lancet.* 2016;387(10033):2087.
16. Elter PT, Kennedy HP, Chesla CA and Yimyam S. Spiritual Healing Practices Among Rural Postpartum Thai Women. *Journal of transcultural nursing : official journal of the Transcultural Nursing Society.* 2016;27(3):249-255.
17. Kim-Godwin YS. Postpartum Beliefs and Practices Among Non-Western Cultures. *MCN: The American Journal of Maternal/Child Nursing.* 2003;28(2):74-78.
18. Wirasombat N, Amattrawong D, Prakobkij W, Tunthaworn T, Sawatsri O, Maneeratanapun C, Jantarawivatn S, Poltue P, Chueadet A, Satia W, Rakchantuek K, Narpasawad K, Seesaard T, Sintupattanapun U and Saramunee K. Efficacy and safety of Plook-fai-tat Formula to increase milk volume in post-partum

women with lactation insufficiency. *Journal of Thai Traditional & Alternative Medicine.* 2020;18(2):11.
19. List of herbal medicine. In: information ND, ed. Bangkok: Thai Food and Drug Administration; 2018.
20. Sharkey KA and MacNaughton WK. Gastrointestinal Motility and Water Flux, Emesis, and Biliary and Pancreatic Disease. In: Brunton LL, Hilal-Dandan R, Knollmann BC, eds. *Goodman & Amp; Gilman's: The Pharmacological Basis of Therapeutics, 13e.* New York, NY: McGraw-Hill Education; 2017.
21. Finnikin S and Finnikin L. Viewpoint: Domperidone and breastfeeding. *The British journal of general practice : the journal of the Royal College of General Practitioners.* 2017;67(662):408-408.
22. Haase B, Taylor SN, Mauldin J, Johnson TS and Wagner CL. Domperidone for Treatment of Low Milk Supply in Breast Pump-Dependent Mothers of Hospitalized Premature Infants: A Clinical Protocol. *Journal of human lactation Consultant Association.* 2016;32(2):373-381.
23. Khorana M, Wongsin P, Torbunsupachai R and Kanjanapattanakul W. Effect of Domperidone on Breast Milk Production in Mothers of Sick Neonates: A Randomized, Double-Blinded, Placebo-Controlled Trial. *Breastfeeding Medicine.* 2020;16(3):245-250.
24. Rankin MW, Jimenez EY, Caraco M, Collinson M, Lostetter L and DuPont TL. Validation of Test Weighing Protocol to Estimate Enteral Feeding Volumes in Preterm Infants. *J Pediatr.* 2016;178:108-112.
25. Funkquist EL, Tuvemo T, Jonsson B, Serenius F and Nyqvist KH. Influence of test weighing before/after nursing on breastfeeding in preterm infants. *Adv Neonatal Care.* 2010;10(1):33-39.
26. Hill PD and Johnson TS. Assessment of Breastfeeding and Infant Growth. *Journal of midwifery & women's health.* 2007;52(6):571-578.
27. Wisniewski SR, Rush AJ, Balasubramani GK, Trivedi MH and Nierenberg AA. Self-rated global measure of the frequency, intensity, and burden of side effects. *J Psychiatr Pract.* 2006;12(2):71-79.
28. Suwankesawong W, Sriphiromyam P, Tragulpiankit P, Phetcharat C and Sornsrivichai V. Evaluation of Thai Algorithm Usage for Adverse Drug Reaction Monitoring. *Journal of Health Science.* 2016;25(4):10.
29. Murali M, Suppes SL, Feldman K and Goldman JL. Utilization of the Naranjo scale to evaluate adverse drug reactions at a free-standing children's hospital. *PloS one.* 2021;16(1):e0245368.
30. Adverse Drug Reaction Probability Scale (Naranjo) in Drug Induced Liver Injury. In: *LiverTox: Clinical and Research Information on Drug-Induced Liver Injury.* Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012.
31. McGuire TM. Drugs affecting milk supply during lactation. *Australian Prescriber.* 2018;41(1):7-9.
32. Haq I-U, Imran M, Nadeem M, Tufail T, Gondal TA and Mubarak MS. Piperine: A review of its biological effects. *Phytotherapy Research.* 2021;35(2):680-700.
33. Hlavackova L, Urbanova A, Ulicna O, Janega P, Cerna A and Babal P. Piperine, active substance of black pepper, alleviates hypertension induced by NO synthase inhibition. *Bratislavske lekarske listy.* 2010;111(8):426-431.
34. cTaqvi SIH, Shah AJ and Gilani AH. Blood Pressure Lowering and Vasomodulator Effects of Piperine. *Journal of cardiovascular pharmacology.* 2008;52(5):452-458.
35. Pevzner M and Dahan A. Mastitis While Breastfeeding: Prevention, the Importance of Proper Treatment, and Potential Complications. *Journal of clinical medicine.* 2020;9(8).
36. Yu S, Liu X, Yu D, Changyong E and Yang JH. Piperine protects LPS-induced mastitis by inhibiting inflammatory response. *International Immunopharmacology.* 2020;87.
37. Park BS and Lee JO. Recognition of lipopolysaccharide pattern by TLR4 complexes. *Experimental & molecular medicine.* 2013;45(12):e66.
38. Kausar T, Anwar S, Hanan E, Yaseen M, Aboelnaga S and Azad ZRAA. Therapeutic Role of Ginger (Zingiber officinale) - A Review. *Journal of Pharmaceutical Research International.* 2021:9-16.
39. Dilokthornsakul W, Rinta A, Dhippayom T and Dilokthornsakul P. Efficacy and Safety of Ginger regarding Human Milk Volume and Related Clinical Outcomes: A Systematic Review of Randomized Controlled Trials. *Complementary medicine research.* 2021:1-7.
40. Paritakul P, Ruangrongmorakot K, Laosooksathit W, Suksamarnwong M and Puapornpong P. The Effect of Ginger on Breast Milk Volume in the Early Postpartum Period: A Randomized, Double-Blind Controlled Trial. *Breastfeeding medicine : the official journal of the Academy of Breastfeeding Medicine.* 2016;11:361-365.
41. Jacobsen N and Salguero CP. *Thai Herbal Medicine: Traditional Recipes for Health and Harmony.* Inner Traditions/Bear; 2014.
42. Kruekaew J and Kritcharoen S. Thai Traditional Midwifery Care. *Songklanagarind Journal of Nursing.* 2018;38(1):103-110.
43. Bumrungpert A, Somboonpanyakul P, Pavadhgul P and Thaninthranon S. 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.* 2018;13(10):645-650.
44. Saejueng K, Nopsopon T, Wuttikonsammakit P, Khumbun W and Pongpirul K. Efficacy of Wang Nam Yen herbal tea on human milk production: A randomized controlled trial. *PloS one.* 2022;17(1):e0247637.
45. Jamjan L, Khantarakwong S, Hongthong S and Jampates N. Thai Traditional Medicine for Postnatal Motherin the Community of Central Region. *Journal of The Royal Thai Army Nurses.* 2014;15(2):7.
46. Muhammad Wafiuddin Wa'ie IR, Koh Soo Quee D, H Sharbini S, Mohd Noor SH, Kisut R, Tuah NA, Abdul Rahman H, Kifli N, H Abdul Hamid MRW and Abdul-Mumin KH. Practice of Postpartum Warming Among Mothers in Brunei. *Journal of*

transcultural nursing : official journal of the Transcultural Nursing Society. 2020;31(6):576-581.
47. Bazzano AN, Stolow JA, Duggal R, Oberhelman RA and Var C. Warming the postpartum body as a form of postnatal care: An ethnographic study of medical injections and traditional health practices in Cambodia. *PloS one*. 2020;15(2):e0228529.
48. Fadzil F, Shamsuddin K and Wan Puteh SE. Traditional Postpartum Practices Among Malaysian Mothers: A Review. *Journal of alternative and complementary medicine (New York, NY)*. 2016;22(7):503-508
49. El Hajj M and Holst L. Herbal Medicine Use During Pregnancy: A Review of the Literature With a Special Focus on Sub-Saharan Africa. *Frontiers in pharmacology*. 2020;11:866-866.
50. Jantarasaengaram S and Sreewapa P. Effects of domperidone on augmentation of lactation following cesarean delivery at full term. *Int J Gynaecol Obstet*. 2012;116(3):240-243.
51. Wannapat M, Suthutvoravut S and Suwikrom S. Effectiveness of domperidone in augmenting breastmilk production measured by manual expression in postpartum women in Charoenkrung Pracharak hospital. *RMJ*. 2018;41:17-26. https://he02.tci-thaijo.org/index.php/ramajournal/article/view/8523.