

## *Nigella sativa* as a Galactagogue: A Systematic Review (*Nigella sativa* sebagai Penggalak Susu: Suatu Ulasan Sistematik)

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### ABSTRACT

*Nigella sativa* is a herb with various pharmacological properties and has been used widely for medicinal purposes and acts as a milk booster. The aim of this systematic review was to provide information on the galactagogue property of *N. sativa*. Electronic searches were conducted in two databases, namely, Medline via EBSCOhost and Scopus, for relevant studies published between the 1865 and March 2020. Additional records identified through Google Scholar showed one eligible article. Only articles published in English and related to the galactagogue effect of *N. sativa* were included in this review. A total of 110 potential articles were identified, but only four fulfilled the inclusion criteria. Four animal studies were included in this review. All of the selected studies reported positive galactagogue effects of *N. sativa* as determined by serum prolactin level, breast tissue changes, milk production and composition, and weight of litter, thereby suggesting its effect as milk booster. However, the review found no evidence supporting the effect of *N. sativa* as a galactagogue in humans.

**Keywords:** Breastfeeding; galactagogue; milk production; *Nigella sativa*

### ABSTRAK

*Nigella sativa* merupakan sejenis herba yang mempunyai pelbagai ciri farmakologi dan telah digunakan secara meluas bagi tujuan perubatan dan juga sebagai penggalak susu. Ulasan sistematik ini menyediakan maklumat mengenai aktiviti *N. sativa* sebagai penggalak susu dengan mengenal pasti penerbitan yang berkaitan dengannya. Pencarian artikel secara elektronik dilakukan dengan menggunakan dua pangkalan data iaitu Medline melalui EBSCOhost dan Scopus dan artikel yang relevan antara tahun 1865 dan Mac 2020 dikenal pasti. Rekod tambahan telah dikenal pasti melalui Google Scholar iaitu sebanyak satu artikel. Sejumlah 110 artikel yang berpotensi dikenal pasti dan hanya empat artikel menepati kriteria yang ditetapkan. Empat kajian haiwan dimasukkan di dalam ulasan ini. Kesemua kajian menunjukkan kesan positif penggalak susu oleh *N. sativa* melalui penentuan aras prolaktin dalam serum, perubahan tisu payudara, penghasilan dan komposisi susu dan berat anak haiwan yang disusui. Hasil kajian seterusnya mencadangkan *N. sativa* sebagai agen penggalak susu. Namun begitu, ulasan sistematik ini mendapati tiada bukti yang menyokong kesan *N. sativa* sebagai penggalak susu pada manusia.

**Kata kunci:** *Nigella sativa*; penghasilan susu; penggalak susu; penyusuan

### INTRODUCTION

Breastfeeding provides several benefits for both mothers and babies. All essential ingredients for the baby's development are provided in breastmilk. Breastmilk also prevents the development of several chronic diseases. Breastfeeding plays a role in the baby's immune system development, nutrient absorption, and neurodevelopment and in maternal psychological well-being (Othman et al. 2014).

In addition, women who breastfeed have reduced risk of developing breast and ovarian cancers. With each year that women breastfeed, the risk of developing breast cancer is reduced by 7% (Anstey et al. 2017). Furthermore,

a prolonged period of breastfeeding is associated with reduced incidence of ovarian cancer (Jordan et al. 2012). The World Health Organization (WHO) recommends breastmilk as the only source of nutrition for infants until the age of 6 months. In Islam, a mother is encouraged to breastfeed her baby up to 2 years old.

According to the National Health Morbidity Survey 2016 (IPH 2016), the rate of babies that were exclusively breastfed up to 6 months in Malaysia did not achieve the WHO global nutrition targets of 2025 (WHO 2017) even after the National Breastfeeding and Infant Feeding Policy by the Ministry of Health Malaysia has been implemented. In addition, various campaigns on the benefits of breastfeeding have also

been conducted by non-government organizations to create breastfeeding awareness among mothers. Despite the increasing trend of breastfeeding in Malaysia, the duration of breastfeeding remains low due to challenges faced by mothers in breastfeeding their babies. Among breastfeeding mothers, 54.4% discontinued breastfeeding exclusively as early as 1 month postpartum due to the delayed initiation of breastfeeding and difficulties in breastfeeding (Tengku Alina et al. 2013). The key challenges that most mothers encounter is the perception of insufficient milk supply that may lead to the cessation of milk production. The mother's medical problem and poor breastfeeding technique also hinder breastfeeding. To overcome the insufficient milk supply, women have used galactagogues.

Galactagogues are defined as substances or medicine that help to initiate and maintain adequate milk supply (Zuppa et al. 2010). They include conventional medicine or substances of herbal origin. Conventional medicines that are commonly used clinically are domperidone and metoclopramide. Both medicines increase serum prolactin level, thereby increasing milk supply and production. These medicines act by blocking the dopamine receptor in the central nervous system, resulting in an increase of prolactin synthesis by lactotroph cells in the anterior pituitary. However, both medicines have been reported to have adverse effects on mothers. Metoclopramide can cross the blood-brain barrier, resulting in central nervous system side effects, such as involuntary movement, dizziness, and headache (Hale et al. 2018). Furthermore, a high dose of domperidone is associated with gastrointestinal disorders, headache, and increased risk of cardiac problems (Anderson 2013; Doggrel & Hancox 2014).

Alternatively, women throughout the world choose to use herbal sources as galactagogues, because herbal galactagogues are believed to be safe and easily available in the market. Herbal supplements that have been associated with galactagogue effect are shatavari (*Asparagus racemosus*) (Sharma & Bhatnagar 2011), fennel (*Foeniculum vulgare*) (Hale & Hartmann 2007), fenugreek (*Trigonella foenum-gracum*) (Liu et al. 2015), and black seed (*Nigella sativa*) (Hosseinzadeh et al. 2013).

*N. sativa* commonly grows in Eastern Europe, Middle East, and Western Asia and belongs to Ranunculaceae family. The tiny seeds of *N. sativa* are dark black in color, hence its common name 'Habba Al-Barakah' or 'Habba Al-Sauda' in Arabic and black seed in English. Both the seed and oil of *N. sativa* are very popularly used in ancient remedies to treat various ailments and diseases (Unani, Ayurveda, Chinese, and Arabic) in Asian countries and the Middle East (Aljabre et al. 2015). In Islamic literature, *N. sativa* is a great healing medicine, as it was mentioned in a Prophetic hadith. Moreover, the

uses of *N. sativa* seeds have also been documented by Ibne-Sina (980-1037), a renowned Muslim scholar in his famous book, *Al-Qanoon fi el-Tibb* (Aljabre et al. 2015).

The chemical composition and therapeutic potential of *N. sativa* have been extensively studied using *in vitro* and *in vivo* models (Aljabre et al. 2015; Babazadeh et al. 2012; Nasuti et al. 2019). The major active compounds isolated and identified in *N. sativa* seeds are thymoquinone (30-48%), p-cymene (7-15%), carvacrol (6-12%), 4-terpineol (2-7%), t-anethole (1-4%), and sesquiterpene longifolene (1-8%) (Ali & Blunden 2003; Boskabady & Shirmohammadi 2002; Huchchannavar et al. 2019). The seeds reportedly contain fats (28.5%), proteins (26.7%), carbohydrates (24.9%), and total ash (4.8%). They also contain vitamins and minerals, such as Cu, Fe, P, and Zn (Al-Jassir 1992; Nickavar et al. 2003). Interestingly, the composition of *N. sativa* varies depending on its origin (Haron et al. 2014). *N. sativa* has various pharmacological properties, including antioxidant (Erboga et al. 2016), anti-schistosomiasis (El Shenawy et al. 2008), anti-fungal (Kul'ko et al. 2016), anti-diabetic (El Rabey et al. 2017), anti-cancer (Ng et al. 2011) anti-inflammatory (Alemi et al. 2013), anti-hypertensive (Jaarin et al. 2015), anti-malaria (Abdullelah et al. 2007), anti-osteoporotic (Shuid et al. 2012), and hepatoprotective properties (Yesmin et al. 2013). Furthermore, *N. sativa* possesses galactagogue effects and helps stimulate milk production in rats (Hosseinzadeh et al. 2013). However, the galactagogue effects of *N. sativa* in humans is yet to be determined. Regarding acute and chronic toxicity, *N. sativa* fixed oil has low toxicity, as indicated by high LD<sub>50</sub> values and biochemical and histopathological changes in rodents (Zaoui et al. 2002).

Despite several narrative reviews on the pharmacological effects of *N. sativa*, reviews on its galactagogue effect are limited. Therefore, the purpose of this study was to systematically review existing studies on the galactagogue effect of *N. sativa* and to provide information on the topic for further research.

#### MATERIALS AND METHODS

A computerized literature search was conducted to identify the original research articles reporting the potential of *N. sativa* as a natural herb galactagogue. The literature search was conducted using two databases, Medline via EBSCOhost (articles published between 1865 and March 2020) and Scopus (articles published between 1823 and March 2020) with the following keywords: '*Nigella sativa* or black cumin' and 'galactagogue or lactation or prolactin'. In order to find literatures that might be missed during the database search, additional record was identified through Google Scholar using similar set of keywords.

## STUDY INCLUSION AND EXCLUSION CRITERIA

The eligible articles were reviewed independently by two authors (AFZ and AAH) based on the following criteria: Only full-text articles published in English were included; reported the galactagogue effect of *N. sativa* such as changes in milk production and composition, breast tissue and hormones involved in breastfeeding. Review articles, news, case reports, book chapters, conference proceedings, and editorial letters were excluded.

## DATA EXTRACTION AND MANAGEMENT

Selection of the articles was conducted in two stages. In the first stage, the titles and abstracts of the articles were

screened. The studies that did not fulfill the inclusion criteria were excluded. In the second stage, the full-text of selected articles was retrieved and reviewed based on the same inclusion and exclusion criteria. The sample size, type of animal involved, study design, results and conclusion were recorded in Table 1.

## RESULTS AND DISCUSSION

The literature search from two electronic databases identified 110 potentially relevant articles, of which 88 articles were from Medline via EBSCOhost, 21 articles from Scopus and one article from Google Scholar. A total of 105 articles were excluded after reviewing the titles and abstracts. Full-text papers were obtained for

TABLE 1. Summary of selected studies included in the review

Reference	Type of animal	Study design	Result	Conclusion
Abo El-Nor et al. (2007)	Buffalo ( <i>N</i> = 15, <i>n</i> =3)	Lactating buffaloes were randomly divided into 5 experimental treatments; (1) Control, concentrated feed mixture (CFM) and rise straw (RS) (2) <i>T</i> <sub>1</sub> , control + 200 g of fenugreek seeds h <sup>-1</sup> day <sup>-1</sup> (3) <i>T</i> <sub>2</sub> , control + 50 g of caraway seeds h <sup>-1</sup> day <sup>-1</sup> (4) <i>T</i> <sub>3</sub> , control + 50 g of <i>N. sativa</i> seeds h <sup>-1</sup> day <sup>-1</sup> ; and (5) <i>T</i> <sub>4</sub> , control+ 100g <i>Lepidium sativum</i> seeds h <sup>-1</sup> day <sup>-1</sup> )  Duration of experiment: 4 weeks before calving and extended for 12 weeks after parturition. Experimental parameters: Lactating buffaloes were machine milked twice daily, and milk yield was recorded daily for 12 weeks. Milk samples were analyzed for fat, total solids (TS), total protein (TP) ash, lactose, and solid non-fat (SNF)  The blood plasma of lactating buffaloes was collected for the evaluation of plasma total protein, albumin, urea, glucose, plasma glutamic-oxaloacetate-transaminase (GOT), glutamic-pyruvate-transaminase (GPT), globulin and albumin/globulin ratio, creatinine, total lipids, cholesterol, and alkaline phosphatase	↑ Significantly higher milk yield from week 1-6 in all treated groups compared with control  ↓ Significantly lower milk yield from week 7-12 until the 12th week in all groups  ↑ Significantly higher increase in milk solid non-fat content in <i>T</i> <sub>4</sub> , <i>T</i> <sub>1</sub> , and <i>T</i> <sub>2</sub> than in <i>T</i> <sub>3</sub> and the control  ↑ Significantly higher increase in milk lactose content in <i>T</i> <sub>1</sub> , <i>T</i> <sub>4</sub> , <i>T</i> <sub>3</sub> than in <i>T</i> <sub>2</sub> and the control  Milk fat, total solids, total protein, and ash content were not significantly different between treatments  ↑ Significantly higher increase in the daily TS, SNF, TP, and lactose yields in <i>T</i> <sub>1</sub> and <i>T</i> <sub>4</sub> than in <i>T</i> <sub>2</sub> and <i>T</i> <sub>3</sub> compared with control  ↑ Significantly higher milk fat yield in <i>T</i> <sub>1</sub> than in <i>T</i> <sub>3</sub> , <i>T</i> <sub>4</sub> , <i>T</i> <sub>2</sub> and the control	Supplementation of lactating buffalo's diet with medicinal plants, such as fenugreek, <i>N. sativa</i> , and <i>Lepidium sativum</i> may improve the productive performance of lactating buffaloes in terms of milk yield, composition, and feed efficiency

			<p>No significant differences among the different treatments in globulin, albumin/globulin ratio, urea, GOT, alkaline phosphatase, total lipids, and cholesterol</p> <p>Total protein, albumin, creatinine, GPT, and glucose increased significantly (<math>p &lt; 0.05</math>) in different groups</p>	
Nurdin et al. (2011)	Holland Cow (N=20, n=4)	<p>Fries Holland lactating cows (bodyweight of 350 kg and milk production of 10-12 liters/head/day) with suspected subclinical mastitis and presence of bacterial pathogens (<i>Staphylococcus</i>, <i>Streptococcus</i>, <i>Escherichia coli</i>, and <i>Corynebacterium</i>) were divided into five groups of treatments: (1) non-herb, (2) 0.03% body weight of black cumin, (3) 0.02% body weight of <i>Curcuma zedoaria</i>, (4) 0.06% body weight of <i>Curcuma mangga</i>, and (5) 0.02% body weight of <i>Curcuma aeruginosa</i></p> <p>Duration of experiment: 3 months</p> <p>Experimental parameters: Milk yield at 4% fat corrected milk (L), milk fat (%), milk protein (%), milk lactose (%), and mastitis status as measured by IPB-1 reagent (indirect method of mastitis)</p>	<p>↑ Significantly of milk yield (2.83-4.86%) in black cumin and <i>Curcuma aeruginosa</i> than the control group</p> <p>The treatment significantly decreased milk fat (<math>P &gt; 0.05</math>)</p>	<p>Herb supplementation (black cumin, <i>Curcuma zedoaria</i>, <i>Curcuma mangga</i>, and <i>Curcuma aeruginosa</i>) may be useful to treat subclinical mastitis and to increase milk yield and enhance milk quality</p>
Hosseinzadeh et al. (2013)	Rodent (N=30, n=6)	<p>For milk production, 30 lactating dams were divided into five groups and received saline and aqueous and ethanolic extracts of <i>N. sativa</i> at 0.5 and 1 g/kg</p> <p>Duration of study: 23 h</p> <p>Experimental parameters: Milk production and weight of pups were measured. For acute toxicity test, different doses of aqueous and ethanolic extracts of <i>N. sativa</i> were administrated orally and intraperitoneally to groups of six male and female albino mice. The number of deaths at 48 h after treatment was recorded</p>	<p>↑ Significantly of milk production and pup weight 23 h after gavage in aqueous (0.5 g/kg) and ethanolic extracts (1 g/kg) groups</p> <p>No mortality was observed in mice administered with aqueous and ethanolic extracts of <i>N. sativa</i> with LD50 of 4.23 g/kg (aqueous extract) and 4.9 g/kg (ethanolic extracts)</p>	<p>Aqueous and ethanolic extracts of <i>N. sativa</i> stimulates milk production in rats</p>
Al-Snafi et al. (2014)	Mice (N=48, n=24)	<p>Forty-eight lactating albino mice with 3 litters for each female were divided into 2 groups, namely, (1) control diet (2) <i>N. sativa</i> diet</p> <p>Duration of study: 15 days</p> <p>Experimental parameters: Weight of the litter at first and 15th days of age, serum prolactin level, and breast tissue histology of lactating mice</p>	<p>↑ Significantly increased litter weight of lactating mice on <i>N. sativa</i>-containing diet compared with the control</p> <p>↑ Significantly increased serum prolactin level in lactating mice on <i>N. sativa</i>-containing diet compared with the control</p>	<p><i>N. sativa</i> exhibits prolactin stimulatory activity and may stimulate the production of milk in mice</p>

The breast tissue of lactating mice on *N. sativa*-containing diet showed large acini with more secretory activity and increased proliferation and thickness of the epithelium compared with the control group

remaining five papers. Finally, one paper was excluded by reading the full-text thoroughly as the paper reported the effect of *N. sativa* treatment on cows with subclinical mastitis, however no result on the effect of *N. sativa* on its galactagogue effect was reported (Azadi et al. 2010). A flowchart of the selection process is shown in Figure 1.

#### STUDY DESIGN CHARACTERISTICS

A summary of the characteristics of all studies is displayed in Table 1. All studies were published between 2007 and 2014. All studies were conducted using animals, namely, rats (Hosseinzadeh et al. 2013), albino mice (Al-Snafi et al. 2014), buffaloes (Abo El-Nor et al. 2007), and cows (Nurdin et al. 2011). Three studies originated from

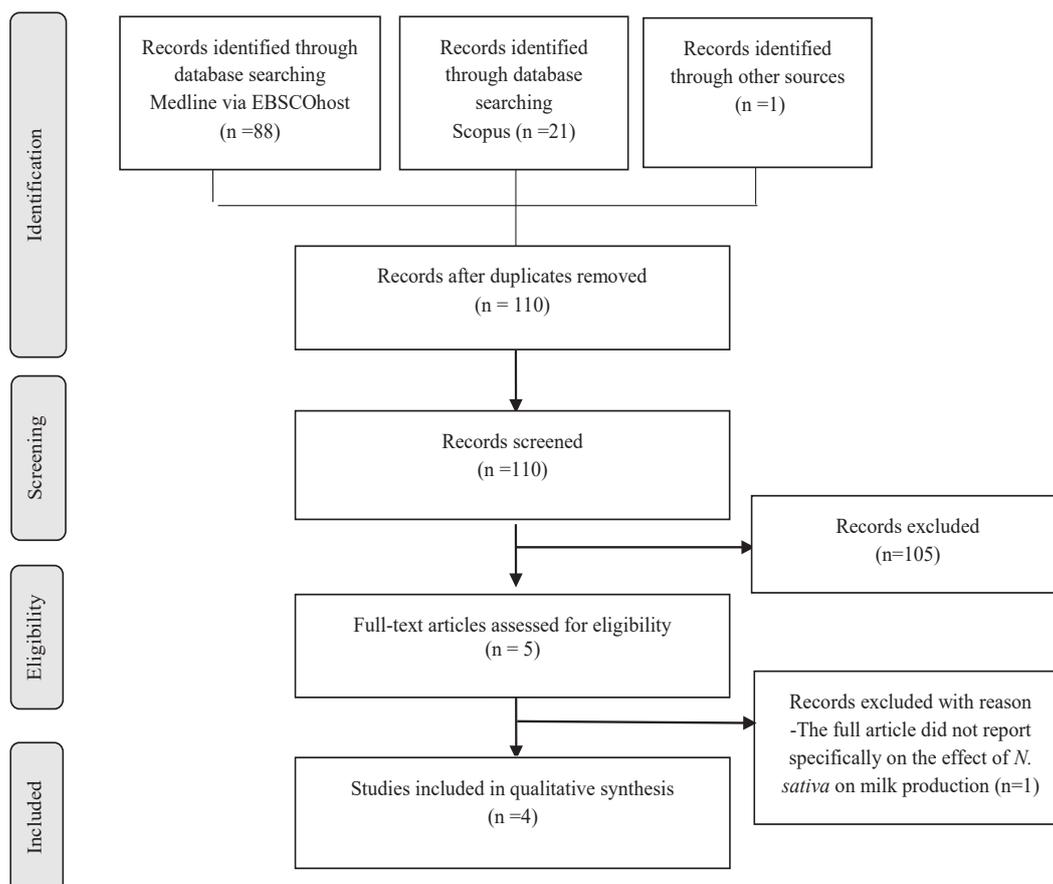


FIGURE 1. Flow chart of the literature search

the Middle East countries, namely, Iran, Iraq, and Egypt. One study originated from Indonesia. In addition to *N. sativa*, other herbs, such as fenugreek seeds, caraway seeds, lepidium seeds (Abo El-Nor et al. 2007), *Curcuma zedoaria*, *C. mangga*, and *C. aeruginosa* (Nurdin et al. 2011), were included in two studies.

In all included studies, the galactagogue effect of *N. sativa* was determined on the basis of these four parameters, as follows: serum prolactin level; milk composition and yield; litter's body weight; and changes of breast tissue as determined through histology. Other than these parameters, one study evaluated hematological and biochemical values of the animals fed with *N. sativa* (Abo El-Nor et al. 2007), and another study determined its toxicity (Hosseinzadeh et al. 2013). Three studies used *N. sativa* seeds in powder form (Abo El-Nor et al. 2007; Al-Snafi et al. 2014; Nurdin et al. 2011), whereas one used the aqueous and ethanolic extracts of the seeds (Hosseinzadeh et al. 2013). *N. sativa* extract was administered to the animals by oral gavage (Al-Snafi et al. 2014; Hosseinzadeh et al. 2013) and as food supplement (Abo El-Nor et al. 2007; Nurdin et al. 2011).

Out of four selected studies, only one (Nurdin et al. 2011) used lactating cows suspected with mastitis. The three other studies used healthy lactating animals (Abo El-Nor et al. 2007; Al-Snafi et al. 2014; Hosseinzadeh et al. 2013). Despite the different methods adopted in each study, the results indicated positive galactagogue effect in animals treated with *N. sativa* compared with the control.

The galactagogue action of *N. sativa* was clearly illustrated in all included studies by measuring serum prolactin level, breast tissue changes, milk production and composition, and the weight of litter. Prolactin is a hormone that is involved directly in breastfeeding. During pregnancy, the level of prolactin in blood increases. However, milk secretion is inhibited by the high serum progesterone and estrogen levels. Immediately following childbirth and placental expulsion, progesterone, and estrogen levels fall dramatically, and milk secretion begins due to the action of prolactin and is stimulated by suckling of the litter. Out of the four studies included in this review, only one tested the galactagogue action of *N. sativa* by measuring the serum prolactin level of female lactating mice fed on diet supplemented with *N. sativa* (Al-Snafi et al. 2014). The serum prolactin level of the lactating female mice fed with the diet was significantly higher compared with the control group.

The initiation phase of lactogenesis also involved changes in breast tissue, which include an increase in size and number of lobules and enlargement of epithelial cells. Among the included studies, one study examined the histology of breast tissue of lactating mice (Al-Snafi et al. 2014). A section of breast tissue in female mice fed with *N. sativa*-containing diet had larger acini, thicker epithelial cells, and more secretory activity compared with the control group. The hyperactivity of breast tissue

of the female mice fed on *N. sativa* well correlated with the increase in serum prolactin. This result may be due to the role of prolactin in stimulating breast tissue growth and development during pregnancy and lactation.

Milk production (L, g or pup or day, or kg h<sup>-1</sup> day<sup>-1</sup>) was estimated in three of the included studies. Three studies measured the milk yield, and these studies showed significantly increased milk yield compared with the control group. Of the three studies that used *N. sativa* seeds, only the study of Hosseinzadeh et al. (2013) used the aqueous and ethanol extracts of seeds, whereas the other three studies used the seeds themselves as part of the daily feed.

The use of small animals, such as mice, allowed administration of the extracts via oral gavage (Hosseinzadeh et al. 2013). However, in large animals, such as cow and buffaloes, *N. sativa* was offered as feed supplements (Abo El-Nor et al. 2007; Nurdin et al. 2011). One study observed increased milk production from day 8 up to day 15 (Hosseinzadeh et al. 2013), whereas study (Abo El-Nor et al. 2007) observed increased milk increases from the second week to the sixth week of treatment. Nurdin et al. (2011) did not state the period of milk collection.

Hosseinzadeh et al. (2013) showed a significant increase in milk production in the groups receiving the aqueous extract at a dose of 0.5 g kg<sup>-1</sup> and ethanolic extract at a dose of 1 g kg<sup>-1</sup> compared with the control. The milk production data were collected 23 h after gavage treatment.

A significant increase in milk yield was observed after *N. sativa* administration ( $p < 0.01$ ). It increased milk yield by 2.83 to 4.86% (799.5 L) compared with the control (777.52 L) (Nurdin et al. 2011). In buffaloes, milk yield significantly increased in the *N. sativa*-treated group compared with the control group and groups treated with other herbs, such as fenugreek seeds, caraway seeds and *Lepidium sativum* seeds (Abo El-Nor et al. 2007).

Two studies estimated milk production using litter weight after feeding as a proxy (Al-Snafi et al. 2014; Hosseinzadeh et al. 2013). Both studies used mice, and the weight of pups was measured daily for 15 days, considering that litters are dependent on mothers' milk within 15 days and cannot nibble any food given. The result from one of the study indicates a significant increase in the weight gain of pups breastfed by mothers receiving aqueous (0.5 g kg<sup>-1</sup>,  $p < 0.01$ ) and ethanolic extracts (1 g kg<sup>-1</sup>,  $p < 0.05$ ) compared with the control group (Hosseinzadeh et al. 2013). Moreover, Al-Snafi et al. (2014) found that the litter weight of their lactating mice fed with *N. sativa* increased compared with the control group.

Out of the four studies, two evaluated milk composition (%) in animals fed with *N. sativa* and used

big animals, namely, cows, and buffaloes. Nurdin et al. (2011) determined milk lactose, fat, and protein. Abo El-Nor et al. (2007) measured similar parameters with the addition of total solid (TS), solid non-fat (SNF), lactose, ash, and acidity. Milk samples were collected twice daily, and all data were recorded daily for each animal for 12 weeks (Abo El-Nor et al. 2007). The milk sampling procedure used by Nurdin et al. (2011) was not clearly stated. Milk fat did not differ significantly in both groups; however, a significant decrease in milk protein (2.56%) was observed in the *N. sativa* group compared with the control (3.56%) in the study conducted by Nurdin et al. (2011). TS, SNF, ash, acidity, and lactose showed no significant differences observed between the treated group and control. Only milk lactose was significantly higher in the treated group than control groups in a study conducted by Abo El-Nor et al. (2007).

Two studies investigated the safety of *N. sativa* consumption in the animals (Al-Snafi et al. 2014; Hosseinzadeh et al. 2013). One study performed an acute toxicity study to determine the safety of *N. sativa* (Hosseinzadeh et al. 2013), whereas another study used blood and specimens obtained from the liver, kidney, intestine, and stomach, which were further processed for histological examinations (Al-Snafi et al. 2014). In acute toxicity test, different doses (0.5, 2, 8, 16, and 32 g kg<sup>-1</sup>) of the aqueous and ethanolic extracts of *N. sativa* were administered orally and intraperitoneally to a group of six mice. After 24 and 48 h of treatment, the number of mortality was recorded. The result from the study indicated no mortality in both aqueous and ethanolic extracts administered orally. However, the intraperitoneal route of administration of aqueous and ethanolic extracts recorded LD<sub>50</sub> values of 4.23 and 4.9 g kg<sup>-1</sup>, respectively, which were considered slightly toxic according to toxicity classification. In the histological, biochemical and hematological study by Al-Snafi et al. (2014), the side effects were not apparent.

In summary, the galactagogue action of *N. sativa* highlighted in the selected studies may be attributed to two main factors. First, *N. sativa* stimulates prolactin, a key hormone in breastfeeding that promotes breast milk production and breast tissue growth. *N. sativa* seeds contain estrogenic constituents, such as t-anethole (1 to 4%) (Huchchannanavar et al. 2019). It may promote menstruation, facilitate birth, and increase milk secretion. Anethole has a similar structure to dopamine and may act as a competitive antagonist at the dopamine receptor site. Given that dopamine is a prolactin inhibitor, the binding of anethole at dopamine receptor sites may eliminate the inhibitory effect of dopamine on prolactin. Consequently, additional prolactin is released. Second, the constituents in the *N. sativa* seed help improve rumen ecology (Nurdin et al. 2011). *N. sativa* seeds contain 28% to 36% of fixed oil, saponin, alkaloid, and proteins and

0.4% to 2.5% of essential oil (Hajhashemi et al. 2004). Saponin helps achieve a balance of microbes in the rumen by depressing the numbers of pathogenic microbes. The numbers of rumen bacteria and the total amount of volatile fatty acid (VFA) increase following the reduction of NH<sub>3</sub> concentration. Numerous rumen bacteria are responsible for increasing VFA production, thereby increasing the production of milk or meat in dairy cows. *N. sativa* oil consists of approximately 35 to 38% fats, 35% carbohydrates and 21% proteins (Al-Jassir 1992.). These contents represent a high energy source that may play a role in the galactagogue effect of *N. sativa* (Al-Snafi et al. 2014).

#### CONCLUSION

This review concluded that *N. sativa* has galactagogue effects in animals as demonstrated by serum prolactin level, breast tissue changes, milk composition, and milk production. Thus, *N. sativa* can be developed as an herbal supplement that can be consumed by breastfeeding mothers. However, further research should be conducted to study the effect of this herb on humans.

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