LACTATION FAILURE AND POTENTIAL OF TRADITIONAL HERBS AS GALACTOGOGUES

Olubunmi Elemo¹, Ibrahim Oreagba², Akinyede Akinwunmi³, Gloria Elemo⁴, Viola Nicholas-Okpara⁵

> ^{1, 2, 3}College of Medicine, University of Lagos, Lagos, Nigeria ^{4,5}Federal Industrial Institute of Research Oshodi, Lagos, Nigeria

Abstract: Lactation is an important process needed in the life of every female mammal to provide adequate nutrition to an offspring as soon as possible after delivery. Thus, lactation failure can adversely affect the nutrition of a child and diminish immunity, predisposing the child to risk of chronic diseases. As a result, lactation failure requires immediate pharmacological intervention. Plants have been used as medicine due to their diverse phytochemical contents responsible for their pharmacological activities. Moreover, they have proven safer, cheaper and have widespread availability compared to conventional drugs. Some of these medicinal plants are commonly used as herbs by lactating mothers in Africa and other parts of the world because they have been able to meet the various nutritional requirements of lactating mothers. However, there is still limited knowledge on their use and efficacy as lactogenic agent. Thus, this review broadens the knowledge on lactation failure and lactogenic potential of some medicinal herbs because of their common traditional use among women in stimulating milk production.

Keywords: Lactation, Herbs, Galactogogue, Plants.

I. INTRODUCTION

Lactation, also referred to as "breast milk production" is a very important process involved in supplying essential nutrients to an infant offspring commencing as soon as possible after delivery. The breast milk is the only infant food that contains the necessary amounts of nutrients, digestive enzymes and antibodies required by an infant [1]. The mother also obtains some benefits through breastfeeding such as; reduction of post-patrum bleeding, reduction of uterus size and reduction of excess weight gain associated with pregnancy. Thus, the benefits obtained from lactation cannot be overemphasized for both the mother and new born. However, the number of women with lactation failure arising from insufficient milk production is increasing worldwide [2]. It has been suggested to be more common in developed countries than in developing countries due to the increased exposure to some factors responsible for lactation failure in developed countries [3]. Lactation failure usually devastates mothers who intend to easily breastfeed their infants. Thus, it requires immediate intervention as it remains one of the common reasons for discontinuation of breastfeeding and early weaning.

Several conventional drugs such as metoclopramide, sulpiride, domperidone, and chlorpromazine have been used for the management of lactation failure. However, they are associated with unwanted side effects such as sedation, depression, weight gain, gastrointestinal disturbances, headache, nausea and dry mouth [4],[5]. Thus, this encourages the need for safer and more natural sources of treatment. Plants are rich natural sources of phytochemicals and essential nutrients that serve as appropriate chemical weapons against several diseases and correct disturbances in normal physiological functions in the body. The phytochemicals present in plant are responsible for their biologic activities. Tannins have been reported Page | 427

Vol. 4, Issue 1, pp: (427-434), Month: April 2016 - September 2016, Available at: www.researchpublish.com

to increase milk production [6]. Moreover, most pregnant women and nursing mothers in Asia and Africa include medicinal plants as part of their diet in order to meet some of their health requirements [7]. During lactation, they use medicinal plants to stimulate the production of milk. However, the lactogenic potential of some of these traditional herbs have been underestimated. This study aims to broaden the understanding of lactation failure and review some of the commonly used medicinal herbs.

II. LITERATURE REVIEW

Breast milk remains the most complete source of nutrition for infants due to the vital nutritional compositions in the milk. In addition to containing the appropriate amounts of carbohydrate, protein, fat, vitamins and minerals, breast milk contains hormones, digestive enzymes and antibodies that would assist the infant in regulating metabolic functions, properly digesting food and strengthening the immune system respectively [8]. Thus, this has proven the superiority of breast milk over most infant formula because of the vast and constantly changing array of essential nutrients. Moreover breast milk flow improves maternal health by reducing postpartum bleeding, excess weight gain, uterine involution, postpartum depression and lactational amenorrhea [9]. Some studies have even shown that it decreases the risk of breast and ovarian cancer in women [10], [11].

Lactation:

Lactation refers to the process of production and secretion of milk from the mammary glands. The process of lactation has to be well understood so as to ensure proper breast feeding of the newly born, as the human species is the only among mammals in which breast feeding is not governed only by instinct but has to be properly learned [12]. Moreover, milk production and secretion is a complex physiologic process involving physical and emotional components, and interaction of multiple hormonal factors, some of which are yet to be acknowledged [13].

For the process of lactation to take place, the breasts must be fully developed and prepared. The process of growth and development of mammary gland is referred to as mammogenesis. Mammogenesis commences from puberty, when the mammary gland is exposed to estrogen and it is completed in the third trimester of pregnancy. During pregnancy, in preparation for lactation, the breast undergoes extensive glandular and ductal development as seen from its developed lobular alveolar complexes. Under the influence of the rising concentration of hormones such as estrogen, prolactin and progesterone, the breast increases in water, fat and electrolyte content [14]. This is responsible for the increase in volume of the breasts. The volume of the breast at this stage is also accompanied by an increase in vascularization as observed in its prominent dilated subcutaneous mammary veins. The process of milk protein synthesis is also important in lactation. This process requires the availability of amino acids and a large supply of energy [15]. This automatically suggests that nutrition can play an essential role in increasing milk protein synthesis through increased availability of energy which can be metabolized.

Pathophysiology of Lactation:

The mechanism by which lactation occurs involves the interplay of several female sex hormones. One of such hormones is prolactin. The function of prolactin on the mammary gland facilitates mammogenesis, lactogenesis and galactopoiesis [16]. After delivery, the rise in the level of prolactin and reduction in progesterone simultaneously stimulates the copious milk production. Progesterone also promotes the development of mammary glands. Though, high levels of progesterone inhibit lactation before birth by preventing lactose and lipid production in mammary glands. This is referred to as lactogenesis I. After birth and placenta detachment, progesterone levels fall and prolactin levels rises to initiate milk production (Lactogenesis II) [17]. Oxytocin plays a major role in the milk ejection reflex by stimulating the contraction of the myoepithelial cells surrounding the alveoli, to squeeze the newly produced milk into the duct system (Renfrew *et al.*, 2000). The increased pressure causes milk to flow through the duct and be released through the nipple. Growth hormone, another important sex hormone supports milk production when prolactin is reduced.

Dopamine antagonism also facilitates lactation. Dopamine is a neurotransmitter that inhibits the process of lactation. Dopamine binds to the D2 receptors present on the cell membrane of the lactotrophs (prolactin secreting cells). This activation result in the reduction of prolactin exocytosis and gene expression by a variety of intracellular signaling mechanisms [18]. Dopamine thus, inhibits prolactin release. This has led to the use of most dopamine antagonists as lactogogues. Noteworthy is the fact that the amount of dopamine in blood is enough to account for about two thirds of the prolactin inhibition normally [19].

Vol. 4, Issue 1, pp: (427-434), Month: April 2016 - September 2016, Available at: www.researchpublish.com

Lactation Failure:

Perceived insufficient milk supply is common among postpartum women and is a major reason for early weaning. It has been claimed, but without sufficient evidence, that at least 5% of women cannot produce enough milk for their infants. Moreover, a study has evaluated breastfeeding success at three weeks postpartum and found that approximately 15% of women experience inadequate supply of their breast milk [20]. Nevertheless, the number of lactating women who have insufficient breast milk produced is on the rise, as lactation consultants around the world are reporting increase in the number of women who cannot produce enough milk [2].

There are a number of well known causes of low milk supply that is primarily related to breast feeding management. These factors are less difficult to control and require only a good knowledge of breastfeeding practices. Some of these factors include; schedule breastfeeding, skipping breastfeeding, supplementing the diet of the baby with infant formulas and poor latching of the baby on the breast. However, there are more complicated causes of low breast milk supply such as; insufficient mammary tissue (hypoplasia), medications (hormonal contraceptive pills), retained placenta, diseases (diabetes, jaundice), metabolic conditions (obesity), previous breast surgeries, caesarean section, thyroid and other hormonal disorders. Another cause is environmental toxins. A study found that daughters of women who grew up in a pesticide contaminated valley of Mexico had much higher incidence of insufficient mammary tissue than those living on the hill top of such area [21].

Conventional drugs used in managing lactation failure:

The drugs used in the management of lactation failure are referred to as galactogogues or lactogogues. They are medications that assist in the initiation, maintenance or augmentation of maternal milk production [22]. However, the use of galactogogues for increasing milk production are only reserved for situations, after which thorough evaluation for treatable causes and increased frequency of breast feeding or pumping has not been successful. Common indications for use of galactologues are in relactation (reestablishment of milk supply after weaning), adoptive nursing (induction of lactation in a woman who did not give birth to the infant) and increasing faltering milk supply due to maternal or infant illness or separation.

There are really no conventional drugs specifically manufactured to increase the supply of breast milk, most are prescription drugs designed for other disease conditions. Nevertheless they are used as galactogogues because they increase the production of prolactin. The mechanisms of action of some of these drugs are unknown; however, most of these drugs exert their mechanism of action through antagonism of dopamine receptors, resulting in increased prolactin secretion [23]. Some of these drugs include metaclopramide, domperidone, sulpride and chlorpromazine. These drugs have been able to successfully increase milk supply but they have been associated with major side effects such as sedation and depression. There have also been reported cases of maternal restlessness, drowsiness, sleeplessness, confusion, fatigue, abdominal cramp and diarrhea associated with the use of these drugs [24].

Traditional medicine:

Traditional medicine consists of using medicinal plants to protect and restore health. These medicinal plants contain inherent active ingredients to cure disease or relieve pain [25]. Women remain the largest users of traditional medicine [26]. It has been discovered that when women express dissatisfaction with conventional treatment due to side effects, they opt for a holistic approach. This partly explains the increase in the use of medicinal herbs among women especially during pregnancy and lactation. Women show preference and are comfortable using medicinal plants because of their perceived safety. Thus, it has been suggested that with the increase in use of various forms of medicinal plants among women during pregnancy and lactation, there is an arising necessity for a rigorous approach in assessing the medicinal plants that are of benefits and understanding the mechanism through which they act [27].

Herbal Galactogogues:

Around the world and throughout history, women have used certain herbs to enhance their milk supply. Most of these herbs have not been scientifically evaluated but their traditional use, suggests safety and some efficacy. Some of these medicinal herbs include; fenugreek, roselle, asparagus, goat's rue and milk thistle. Fenugreek (*Trigonella foenum-graecum*) has a substantial reputation for increasing breast-milk production in nursing mothers [28]. However, the ingestion has been associated with a maple-like odor to sweat, milk, and urine, which usually mislead medical practitioners to diagnose maple syrup–urine disease. Fenugreek is reportedly rich in flavanoid, tannin, alkaloids and saponins [29].

Vol. 4, Issue 1, pp: (427-434), Month: April 2016 - September 2016, Available at: www.researchpublish.com

Seeds of roselle plant (*Hibiscus sabdariffa*) are also being used traditionally as a galactogogue. They have demonstrated good lactogenic activity with favorable enhancement ability in increasing serum prolactin level [30]. Its mechanism of action occurs through the inhibition of dopaminergic receptors. *Hibiscus sabdariffa* is a herb used as source of many food and beverages mostly in local community in Africa and part of the world. However, it is gradually gaining recognition globally and is being used in functional foods or as nutraceuticals. *Hibiscus sabdariffa* has been used in traditional medicine as astringent, demulcent, aphrodisiac, diuretic, purgative, stomachic lactogenic and tonic. They exert antioxidant, antibacterial, anti-inflammatory, anti-diabetic, antipyretic, antihypertensive, hypocholesterolemic, hepatoprotective and antinociceptive effects [31]. The plant is rich in ascorbic acid, anthocyanins, flavanoids and phenols [32].

The roots of wild asparagus (*Asparagus racemosus*) have also been widely recommended in the Ayurvedic tradition to increase milk production in lactating women. However, a randomized controlled study of *A racemosus* in women with lactational inadequacy failed to demonstrate any effect on milk production or prolactin levels [33]. Though, animal study reported an increase in milk yield accompanied with the increase growth of mammary glands, alveolar tissue and acini [34]. The mechanism of action behind its lactogenic effect was suggested to be due to the action of released corticosteroids rather than prolactin increase and oxytocic effect [35]. *Asparagus racemosus* is a herb highly effective in treating problems related to the female reproductive system. The roots have been recommended in cases of threatened abortion. The roots are found rich in steroidal saponins, sterols, flavanoids and alkslods [36].

Goat's Rue (*Galega officinalis*) is another widely recommended traditional galactogogue. Animal studies have reported increased milk production, although no controlled human trials have reported lactogenic efficacy [37]. *Galega officinalis* is commonly used in animal farming to increase milk production of sheep, cows and goats. However the species of Galega have been included in lists of poisonous plants in United States, where *Galega officinalis* is considered an unpalatable and toxic weed majorly attributed to its content of guanidine derivative alkaloids galengine and hydroxyl-galagine. It also contains quinazoline alkaloids vasicine and its oxidation product vascicinone [38].

Milk thistle (*Silybum marianum*) has been known as a galactogogue for centuries. Clinical trials regarding the use of the plant for its lactogenic activity showed efficacy but was limited due to small sample size, indirect measurement of milk production and inadequate detailed information of mother and infant [39]. However, the American Herbal Products Association suggests that the herb may be safely consumed [40]. It is suggested that the lactogenic effect of *Silybum marianum* is due to an increase in prolactin levels, as seen in female rats [41]. The milk thistle extract is rich in silymarin and fatty acids, especially linoleic acid [42].

Gunnera perpensa is also used in Zulu traditional medicine to stimulate milk production. Animal studies have confirmed its lactogenic activity and suggested that it exerts its mechanism of action through stimulation of mammary gland development and contraction of the myoepithelial cells in the alveoli [43]. *Gunnera perpensa* is also used in the treatment of other female reproductive health disorders. The rhizomes are used to relieve menstrual pains, induce labour and expel the placenta after birtntah. Phytochemical screening of the rhizomes revealed the presence of flavanoids, alkaloids, steroids, saponins, tannins and glycosides. The pharmacological studies of the various extract obtained from the plant has shown antioxidant activities, antimicrobial activity, anti-inflammatory activity, anti-nociceptive and uterine contractile activity [44], [43].

Milk weed (*Euphorbia heterophylla*), has also been recommended as a lactogenic agent in traditional medicine [45]. The young leaves, fruits, roots and flower infusion can be independently administered for milk secretion through oral administration or massaging the breast with the poultice of the leaf [46]. The plant has a characteristic milky latex present in most part of it and the leaves serves diverse ethnomedicinal purpose in different cultures as they have been used in treating constipation, respiratory diseases, gonorrhea, diabetes mellitus, malaria. The plant is rich in phytochemicals such as flavanoids, alkaloids, tannins and sterols that may be responsible for its pharmacological activities; antioxidant activity, anti-inflammatory activity, anti-sickling activity, antimicrobial activity, hypoglycemic activity and uterine contractile activity as reported by several studies [47], [48].

Acacia nicolita spp adansonaii (AN) is a plant widely used in Burkina Faso as folk medicine especially for treating lactation problems in women. The plant has been reported to have lactogenic activity in an animal study using rats [49]. Lampo suggested that the aqueous extract of the leaf stimulated milk secretion by increasing the release of prolactin [49] Traditionally, 100g of the dry leaf extract of the plant is usually administered once in a day to nursing mothers. The

Vol. 4, Issue 1, pp: (427-434), Month: April 2016 - September 2016, Available at: www.researchpublish.com

phytochemical analysis of the leaves revealed the presence of alkaloids, tannins and sterols [50]. *Acacia nicolita spp adansonaii* have been reported to have antimicrobial activity, anti-inflammatory activity, anti-platelet aggregating activity and hyperglycaemic activity [51][52].

Afalfa (*Medicago Sativa*) is also used traditionally especially in Asian countries for stimulating milk secretion in women. The leaf of *Medicago Sativa* promotes the development of breast glandular tissue function of the pituitary gland. *Medicago Sativa* leaf has a rich nutritional profile as it contains a host of minerals such as magnesium, phosphorus, potassium, zinc, vitamins (A,C, E and K), essential and non-essential amino acids. As a result it has been promoted as a dietary supplement. The leaves and seed of Medicago Sativa have been found to contain saponins, alkaloid, sterols, flavones, isoflavones and coumarin derivatives [53]. Moreover the plant has been shown rich in phytoestrogens which acts like the female hormone estrogen [54]. The leaf has antifungal activity, anti-oxidant activity, antibacterial activity and anti-inflammatory activity [55].

Other herbs commonly recommended traditionally as herbal galactogogue include anise, borage, caraway, chasteberry, cumin, echinacea coriander, dandelion, dill, garlic, hops, marshmellow root, oats, red clover, stinging nettle, vervain, raspberry, nettle, aniseed, cinnamon, umbel and fennel.

III. CONCLUSION

Lactation failure is a crucial physiological short coming in mammals that should be treated with utmost importance as it can affect the delivery of essential nutrient to an infant after birth. Moreover, the World Health Organization (WHO) has recommended the first six months for exclusive breast feeding in the newly born. Mothers suffering from lactation failure, who are not able to meet up with the WHO standard may become frustrated. Lactation failure also affects mothers by not providing the additional benefits of reduction in postpartum bleeding and assisting decrease in weight gain associated with pregnancies. Nevertheless, plants have provided a promising potential for the treatment of lactation failure and are not associated with the adverse effect common to conventional drugs. Moreover, the diverse nutrients and phytochemical constituents contained in the plants are responsible for most of their lactogenic activity. Though, safety considerations are still important in the utilization of plants as galactogogues.

REFERENCES

- Chantry C, Wiedeman J, Buehring G, Peerson J, Hayfron K, Kaluoch O, Lonnerdal B, Israel-Ballard K., Coutsoudis A and Abrams B. (2011) Effect of flash-heat treatment on antimicrobial activity of breast milk. Breastfeeding Medicine 6 (3): 111-116.
- [2] Sultana A, Rahman K. and Manjula S. (2013) Clinical update and treatment of lactation insufficiency. Medical Journal of Islamic World Academy of Sciences 21 (1): 19-28.
- [3] Centers for disease control and prevention (US); Office of the Surgeon General (US); Office on Women's Health US (2011) Barriers to breastfeeding in the United States. The Surgeon General call to action to support breastfeeding. Rockville (MD).
- [4] Parkman H, Mishra A, Jacobs M, Pathikonda M, Sachdeva P, Gaughan J and Krinetskiy E. (2012) Clinical response and side effects of Metaclopromide: Associations with clinical, demographic and pharmacogenetics parameters. Journal of Clinical Gastroenterology 46 (6):494-503.
- [5] Balikci A and Balibey H. (2012) Postpartum depression due to use of metaclopramide: A case report. Anatolian Journal of Clinical Investigation 6(1): 258-260.
- [6] Bhatta R, Krishnamoorthy U and Mohammed F. (2000) Effect of feeding tamarind (*Tamarindus indica*) seed husk as a source of tannin on dry matter intake, digestibility of nutrients and production performance of crossbred dairy cows in mid lactation. Animal Feed Science Technology 83:67-74.
- [7] Djah F and Danho F. (2011) Traditional practices and medicinal plants used during pregnancy by Anyi-Ndenye Women (Eastern Cote d'Ivore). African Journal of Reproduction Health 15 (1): 85-93.
- [8] Olivia B. (2013) Human Milk Composition: Nutrient and Bioactive factors. Pediatr Clin North Am 60 (1): 49-74.

Vol. 4, Issue 1, pp: (427-434), Month: April 2016 - September 2016, Available at: www.researchpublish.com

- [9] Ip S, Chung M, Raman G, Chew P, Magula N, DeVine D, Trikalinos T and Lau J. (2007) Breast feeding and maternal and infant health outcomes in developing countries. Evid Rep Technol Assess 153: 1-186.
- [10] Woodman I. (2002) Breast feeding reduces risk of breast cancer. BMJ 325 (7357), 184.
- [11] Marilyn L, Philip S, Candyce H, Rachel, E, Laurel A, Erin K., Adrienne C, Erica P, Kaylynn S, Inge, J, Bryan M, Charles P, Lawrnce H, Carol S and Bette J. (2015) Breastfeeding, PAM50 Tumor Subtype and breast cancer prognosis and survival. Journal of the National Cancer Institute, 107: 7.
- [12] Anthony A. (2009) Human Breastfeeding is not automatic: why that's so and what it means for human evolution. Journal of Social, Evolutionary and Cultural Psychology 3 (4): 305-314.
- [13] Neville M, McFadden T and Forsyth I. (2002) Hormonal regulation of mammary differenciation and milk secretion. Journal of Mammary gland biology and Neoplasia 7: 1083-3021.
- [14] Lamote I, Meyer E, Massart A and Burvenich C. (2004) Sex steroids and growth factors in the regulation of mammary gland proliferation, differenciation and involution.. Steroids 69: 145.
- [15] Doepel L, Pachecho D, Mark H and Ignacio F. (2004) Milk protein synthesis as a function of amino acid supply. Journal of Dairy Science 87 (5): 1279-1297.
- [16] Horseman D. (1999) Prolactin and mammary gland development. Journal of Mammary Gland Biology and Neoplasia, 4 (1): 79-88.
- [17] Hanita O and Hanisah A. (2009) The role of progesterone in detecting early pregnancy failure. Pathology 41: 69-70.
- [18] Ben-Jonathan N and Hnasko R. (2001) Dopamine as a prolactin (PRL) inhibitor. Endocrine Reviews 22(6): 724-763.
- [19] De Greef W and Neill J. (1979) Dopamine levels in hypophysial stalk plasma of the rat during surges of prolactin secretion induced by cervical stimulation. Endocrinology 105: 1093–1099.
- [20] Neifert M, Demarzo S, Seacat J, Young D, Leff M and Orleans M. (1990) The incidence of breast surgery, breast appearance and pregnancy induced breast changes on lactation sufficiency as measured by infant weight gain. Birt 17 (1): 31-38.
- [21] Rudel R, Fenton S, Ackerman J, Euling S and Makris, S. (2011) Environmental exposures and mammary gland development: State of the science, public health implications and research recommendations. Environmental Health Perspectives 119: 8.
- [22] Anne M and Nancy W. (2004) Use of galactogogues in initiating or augmenting maternal milk supply. The Academy of breast feeding medicine, Inc.
- [23] Felipe P, Juliana V and Zulma T (2014) Pharmacological overview of galactologues. Vertinary Medicine International 1:20.
- [24] Fife S, Gill P and Hopkins M (2011) Metacolpromide to augment lactation, does it work? A randomized trial. Journal of Maternal Fetal Neonatal Medicine 24: 1317-1320.
- [25] Soetan K and Aiyelagbe O. (2009) The need for bioactivity-safety evaluation and conservation of medicinal plants-A review. Journal of Medicinal Plants Research 3 (5): 324-328.
- [26] Vickers K., Jolly K. and Greenfield S. (2006) Herbal medicine: women's views, knowledge and interaction with doctors: a qualitative study. BMC Complement Altern Med 7 (6): 40.
- [27] Tieraona L. (2009) The use of botanicals during pregnancy and lactation. Altern Ther Health Med 15 (1): 54-58.
- [28] Swafford S and Berens P. (2000) Effect of fenugreek on breast milk volume. ABM News and Views 6 (3): 21.
- [29] Nadagopal S, Dalanakashmi D, Kumar G and Sujitha D. (2012) phytochemical and antibacterial studies of fenugreek. *Trigonella Foenum-graecum* L.-A multipurpose medicinal plant. Journal of Pharmacy Research, 5 (1): 413-415.

Vol. 4, Issue 1, pp: (427-434), Month: April 2016 - September 2016, Available at: www.researchpublish.com

- [30] Bako I, Abubakar M, Mabrouk M and Mohammed M. (2014) Lactogenic Study of the Effect of Ethyl-acetate Fraction of *Hibiscus sabdariffa* Linn (Malvaceae) Seed on Serum Prolactin Level in Lactating Albino Rats. Advance Journal of Food Science and Technology 6 (3): 292-296.
- [31] Ali B, Al Wabel N and Bluden G. (2005) Phytochemical, pharmacological and toxicological aspects of *Hibiscus Sabdariffa L*: A Review. Phytother Res 19 (5): 365-375.
- [32] Rocha I, Bonnlaender B and Heinrich M. (2014) *Hibiscus Sabdariffa* L- A Phytochemical and Pharmacological Review. Food Chemistry 165: 424-443.
- [33] Sharma S, Ramji S, Kumari S and Bapna J. (1996) Randomized control trial of *Asparagus racetnosus* (Shatavari) as a lactogogue in lactational inadequacy. Indian Pediatrics 33: 675-677.
- [34] Behera p, Tripathy D and Parija S. (2013) Shatavari: Potential for galactogogues in dairy cows. Indian Journal of Traditional Knowledge12 (1): 9-17.
- [35] Joglekar G, Ahuwa R and Balwani J. (1967). Galactogogue effect of *Asparagus Racemos*. Indian Medical Journal 61: 165.
- [36] Alok S, Jain S, Verma A, Kumar M, Mahor A and Sabharwai M. (2013) Plant profile, phytochemistry and Pharmacology of *Asparagus Racemos* (Shatavaru): A Review. Asian Pacific Journal Tropical Dis 3(3): 242-251.
- [37] Gonzalez-Andre F, Redondo P, Pescado R and Urbano B. (2004) Management of *Galega officinalis L*. and preliminary results on its potential for milk production improvement in sheep. New Zealand Journal of Agricultural Research 47: 233-245.
- [38] Laakso I, Virkajavi P, Airakisinem I, Varis E. (1990) Determination of vasicine and related alkaloids by gas chromatography- mass spectrometry. Journal of Chromatography 505: 424-428.
- [39] Pierro F, Callegari A, Caretonuto D, Tapia M. (2008) Clinical efficacy, safety and tolerability of BIO-C (micronized silymarin) as a galactogogue. Acta Biomed 70: 205-210.
- [40] McGuffin, M, Hobbs C, Upton R and Goldberg A. (1997) American Herbal Product Association Botanical Safety Handbook. Boca Raton, FL, CRC Press. p 107.
- [41] Capasso R, Aviello G and Capasso F. (2009) Silymarin-Bio C, an extract from *Silibum Marianum* Fruits, induces hyperprolactinaemia in intact female rats.Phytomedicine, 16: 839-844.
- [42] Sherif F, Khattab S, IbrahimA, Ahmed S. (2013) Improved Silymarin content in elicited multiple shoot cultures of Silybum maranium L. Physiology and Molecular Biology of Plants 19 (1): 127-136
- [43] Simelane M. (2012) Lactogenic activity of *Gunnera perpensa* L. (*Gunneraceae*) from South Africa. *African* Journal of Traditional Complementary Alternative Medicine, 9: 4.
- [44] Khan F, Peter X, Mackinzie R, Katsoulis M, Gehring R, Munro O, Herden F, Drewes S. (2004) Venusol from Gunnera perpensa: structural and ctivity study. Phytochemistry 65: 117-1121
- [45] Dokosi, O. (1998). Herbs of Ghana. Ghana University Press. 2ND Edition, Accra. P 746.
- [46] Padal S and Sathyavathi K. (2013) Traditional uses of Euphorbiaceae family of Khammam District, Andra Pradesh, India. International Journal of Pharmacy and Biological Sciences 3 (2): 585-591.
- [47] Mucsi, I., Molnar, J., Hohmann, J. and Redei, D. (2001) Cytotoxicities and anti-herpes simplex virus activities of diterpenes isolated from Euphorbia species. Planta Med 67 (7): 672-674.
- [48] Okeniyi, S., Adedoyin, B. and Garta, S. (2013) Phytochemical screening, cytotoxicity, antioxidant and antimicrobial activities of stem and leaf extract of *Euphorbia Heterophylla*. Journal of Biology and Life Science 4 (1): 24-31.
- [49] Lampo Z, Heide D, Beek E, Swarts H, Mattheij J and Sawadogo L. (2004) Effect of aqeous extract of Acacia nicolita spp adansonii on milk production and prolactin release in rats. Journal of Endocrinology182: 257-266.
- [50] Okoro S, Kawo A and Arzai A. (2014) Phytochemical screening, antibacterial and toxicological activities of *acacia nicolita* extracts. Bayero Journal of Pure and A plied Science 7 (1).

- Vol. 4, Issue 1, pp: (427-434), Month: April 2016 September 2016, Available at: www.researchpublish.com
- [51] Hussein G, Miyashiro H, Nakamura N, Hattori M, Kakiuchi N and Shimotohno K (2000) . Inhibitory effect of Sudanese Plant extracts on HIV-1 replication and HIV-1 protease. Phytotherapy Research, 14: 510-516.
- [52] Gelani A, Shaeen F, Zarman M, Janbaz K, Shah B and Akhtar M (1999). Studies of anthypertensive and antispasmodic activities of *Acacia nicolita* pods Phytotherapy Research, 13: 665-669.
- [53] Newall C, Anderson L and Philipson J (1996) Anise in: Herbal medicines. Great Britain at the University Press, Cambridge
- [54] Malak A and Yawer A (2011). Effect of Herbs contatining Phytoestrogen on rat testis: A histological, histochemical and biochemical study. The IRAQI Post Graduate medical Journal 10 (4): 562-572.
- [55] Sadowsk B, Budzynsa A, Wieckowska M, Paszkiewicz M, Stochmal A and Moniuszko B (2014). New Pharmacological properties of *Medico Sativa* and *Saponaria officinalis*, saponin rich fractions addressed to Candida albicans, Journal of Medical Microbiology 63: 1076-1086.