Original Article

Role Of Prolactin, Natural Galactagogues: An Alternative Strategy For Hyperprolactinemia

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DOI: 10.47750/pnr.2022.13.S10.353

Abstract

Ayurveda is regarded as an antiquated kind of medicine that is nevertheless useful today. One of the three rogas described in Ayurveda is artavakshyaya. The crucial anovulatory gynaecological pathologies during human reproduction is hyperprolactinemia. Anterior pituitary produces prolactin for secretion. It is crucial for the start and continuation of lactation. The most common symptom of hyperprolactinemia, galactorrhea, is seen in the majority of patients. One of the effects in people with hyperprolactinemic amenorrhea brought on by oestrogen deprivation is osteoporosis. It needs effective therapeutic supervision. Numerous instances of hyperprolactinemia, or elevated prolactin levels, are also seen in women who ovulate normally and do not require medical attention. Dopamine agonists are the mainstay of therapy in contemporary science. Ayurveda plays a significant role in the treatment of hyperprolactinemia by using natural galactagogues such as *shatavari* that have been incorporated into a nanoscience formulation to increase the drug's pharmacological activity. In this paper we have reviewed the importance of prolactin, mechanism of action, treatment methods and the herbs used, their role and importance.

Keywords: Galactagogues, prolactin, hyperprolactinemia, nanoscience, *shatavari*

INTRODUCTION

When a hormone is present in the bloodstream in excess or insufficient amounts, hormonal imbalances result. Due to the vital function that hormones play in the body, even minor hormonal abnormalities can have an impact on the entire body. Endocrine system glands create hormones, which are chemicals. Hyperprolactinemia is a condition when there is an elevated amount of prolactin in the blood. Its cause may be idiopathic, pathological, or physiological [1]. A key hormone in the regulation of several reproductive processes is prolactin. The hormone prolactin plays a crucial function in breastfeeding following delivery of the infant, but there is also intense curiosity because it affects reproduction [2]. Different gynaecological conditions may be raised by this high prolactin, yet individuals may not even experience any symptoms. The hypothalamus's control of prolactin hormone release keeps it in check. Prolactin production is not negatively impacted by peripheral hormones either directly or indirectly [3]. It starts to secrete hypothalamic dopamine after being self-inhibited by a counterflow in the hypothalamo-pituitary system. Additionally, it prevents GnRH from

secreting. Inadvertently, this keeps the pituitary hormones, which are in charge of gonadal function, from being secreted [4].

Female hormonal imbalances

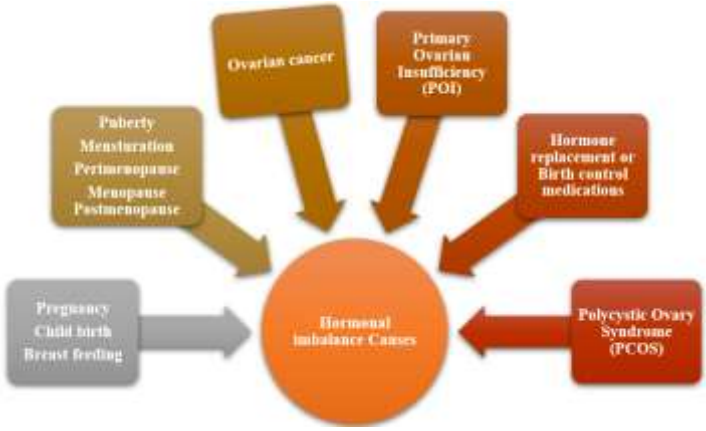

Figure 1: *Hormonal imbalance causes* [5,6]

Symptoms of hormonal imbalances in women include [7]:

- hot flashes and night sweats
- vaginal dryness
- heavy, irregular, or painful periods
- osteoporosis (weak, brittle bones)
- uterine bleeding not associated with menstruation
- increased hair growth on the face, neck, chest, or back
- breast tenderness
- indigestion
- constipation and diarrhea
- acne during or just before menstruation
- infertility
- weight gain
- thinning hair or hair loss
- skin tags or abnormal growths
- deepening of the voice
- clitoral enlargement

PROLACTIN

A polypeptide hormone called prolactin is generated by lactotrophic cells in the anterior pituitary gland as well as, to a lesser extent, by endometrial and lymphoid cells as a luteotropic hormone (LTH) or luteotropin. Throughout pregnancy and after delivery, prolactin induces the breasts to expand and produce milk. For expectant moms and new mothers, prolactin levels are typically high. For both men and non-pregnant women, levels are typically low [8]. Normal levels of prolactin for men 2-8ng/ml, women 2-29 ng/ml and pregnant women 10-209 ng/ml [9].

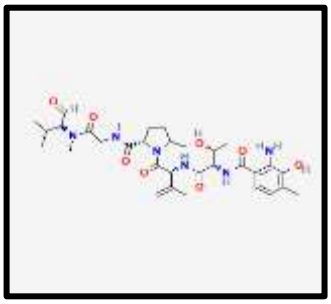

Figure 2: *Structure of Prolactin*

IMPORTANCE OF PROLACTIN

Prolactin's main function in women is to start and maintain breastfeeding. The tactile stimulation of the breast and nipples by the nursing child prevents the release of hypothalamic dopamine, which typically suppresses prolactin, into the pituitary gland's hypophyseal-portal circulation [10]. This causes a sudden increase in serum prolactin levels, which quickly decline when feeding ends. High blood prolactin levels may also prevent gonadotropins from acting on the gonads by preventing the release of gonadotropin-releasing hormone (GnRH) from the brain, which reduces the production of gonadotropins (luteinizing hormone and follicle-stimulating hormone). Therefore, high blood prolactin levels during breastfeeding decrease fertility, preventing nursing women from becoming pregnant too soon [11]. Prolactin contributes to the

maintenance of pregnancy by maintaining the corpus luteum of the ovary, which is the source of the female sex hormone progesterone. Furthermore, prolactin output gradually rises throughout pregnancy [12]. High oestrogen doses can also stimulate prolactin secretion, which is also momentarily stimulated by stress and exercise. It is unknown what prolactin does in guys.

Figure 3: *Importance of Prolactin*

PROLACTIN LEVEL CONDITIONS

HYPERCONDITION; Men and non-pregnant women who have hyperprolactinemia have too much prolactin in their blood. In women, hyperprolactinemia is rather typical [13]. Hyperprolactinemia affects around one-third of pregnant women with irregular periods but healthy ovaries. If this occurs, a woman may find it difficult to become pregnant or her breasts may begin to produce milk outside of pregnancy (galactorrhea). High levels of prolactin prevent other hormones like progesterone and oestrogen from being produced normally. This may alter or prevent ovulation (the release of an egg from the ovary). Additionally, it may cause missing or irregular menstruation. Some women have high levels of prolactin but no symptoms [14]. Infertility, impotence, decreased sex desire, galactorrhea, and impotence are all symptoms of high prolactin levels in men. Untreated hyperprolactinemia can cause a man to produce less or no sperm at all [15].

HYPOCONDITION

After giving birth, inadequate milk production can result from a decrease in prolactin secretion. Although preliminary research suggests they may have diminished immune responses to some infections, the majority of people with low prolactin levels do not have any specific medical issues [16].

Causes

Prolactin levels in men and non-pregnant women are typically very low. When your levels are high, this may be brought on by:

- Prolactinoma (a benign tumor in your pituitary gland that produces too much prolactin)
- Diseases affecting the hypothalamus(the part of the brain that controls the pituitary gland)
- Anorexia(an eating disorder)
- Drugs that are used to treat depression, psychosis, and high blood pressure
- Chest injury or irritation (for example, scars, shingles, or even a bra that's too tight)

The body's capacity to eliminate prolactin can also be impacted by liver disease, polycystic ovarian syndrome (a hormone imbalance that affects the ovaries), and kidney disease.

Regulation of Prolactin Secretion

Prolactin is subject to dual control by hypothalamic hormones transported through the hypothalamic-pituitary portal circulation, like the majority of anterior pituitary hormones. The neurotransmitter dopamine often mediates the primary signal, which is inhibitory and prevents prolactin secretion [17]. Thyrotropin-releasing hormone, a hormone produced in the hypothalamus, mediates the stimulatory signal. The quantity of prolactin produced from the anterior pituitary gland depends on the balance between the two signals. 2 Prolactin levels in the blood are also influenced by how much is excreted by the kidneys [18].

Causes of hyperprolactinemia

Prolactin (PRL) is regulated by both the hypothalamus and dopamine, with dopamine acting as an inhibitory signal to stop PRL secretion and thyrotropin-releasing hormone (TRH) acting as a stimulant in specific circumstances to boost PRL synthesis and release [19]. An adenoma that produces PRL or inflammation can lead to an increase in anterior pituitary hormone production (hypophysitis). However, circumstances that cause either increased TRH signalling or decreased dopamine transport, or both, will also cause increased PRL release. Generally, the anti-dopaminergic effects of medicines lead to an increase in PRL production. Breast stimulation and chest wall damage act as peripheral autonomic control triggers that have an impact on the central neurogenic pathways that govern the release of dopamine into the hypophyseal portal circulation. PRL is cleared from the systemic circulation more slowly in some conditions, such as renal or hepatic insufficiency, leading to higher blood levels of PRL [20].

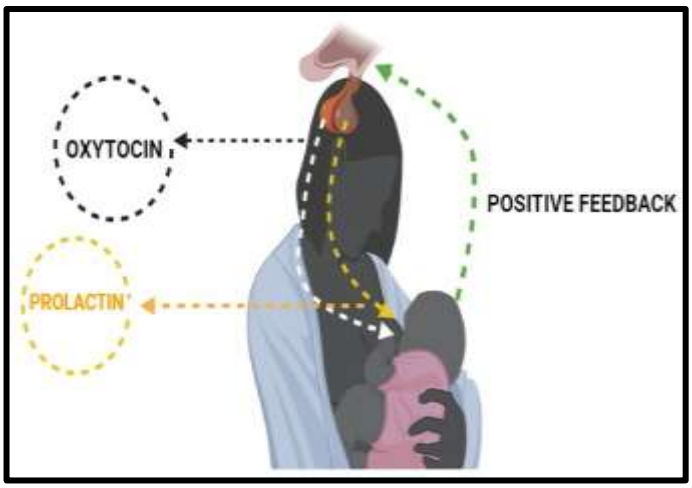

Figure 4: *Prolactin role in Lactation mechanism*

Treatment of Hyperprolactinemia with Hormones

Correcting the biochemical effects of the hormonal excess is the goal of hyperprolactinemia treatment. When a large (macro) tumour is present, its compressive characteristics must also be reduced [21], and the tumor's regrowth must be stopped.

Medical therapy

Agonists of the dopamine, which functions as a physiologic inhibitor of prolactin, have been used in medicine for a long time. Although it was once believed that patients would require dopamine agonist therapy for the rest of their lives, the usage of these drugs today is now a dynamic process that depends on the requirements and circumstances of the patient [22].

Surgical therapy

Surgery for prolactin excess-related tumours requires careful consideration of the intended effects of the procedure. It is recommended for people who have nonfunctional pituitary adenomas or other nonlactotroph adenomas linked to hyperprolactinemia, as well as for people for whom medical therapy has not worked or has been poorly tolerated. Only the most experienced centres can get the best prolactinoma transsphenoidal resection outcomes. Hyperprolactinemia recurrence following surgery, however, is not always a permanent condition and does not always signify a failure of the procedure. An updated assessment of long-term results shows that surgical removal of microprolactinoma has a success rate of roughly 75%. With only a 26% long-term success rate, surgery for macroprolactinoma yields subpar results [23,24].

Herbal Treatment for Hyperprolactinemia

Deepana pachana: Hot water is used to administer Chitrakadi vati three times daily until Nirama Lakshana is observed.

Snehapana: In Arohana Snehapana Karma, *Shatavari Grita* began with a minimum dose of 30ml. A following dosage of gritha was administered based on how long it took to digest the prior day's dose of sneha.

Vamana karma: followed classical method with Madanaphala yoga. Vamana Karma, also known as Medicated Emetic Therapy, cleanses vitiated and accumulated Kapha from the upper channel. Only when there is a significant Kapha imbalance or kapha avarana condition is this intervention performed. Samsarjana karma: Followed as per the shuddi [25].

Agneya dravya prayoga: After samsarjana krama Lashuna, Hingu & Krishnatila vati was given for 3 cycles.

Figure 4: *Deepana pachana* ***Figure 5:*** *Snehapana*

SHATAVARI (Asparagus racemosus)

Figure 6*: Asparagus racemosus*

PLANT PROFILE:

Kingdom: Plantae
Clade: Angiosperms
Clade: Monocots
Order: Asparagales
Family: Asparagaceae
Subfamily: Asparagoideae
Genus: Asparagus
Species: A. racemos

It was first described botanically in 1799. A. racemosus is in high demand due to its variety of applications. The plant is now regarded as endangered in its natural environment because to destructive harvesting, habitat damage, and deforestation. In Ayurvedic scriptures, A. racemosus is advised for the treatment and prevention of dyspepsia, stomach ulcers, and as a galactogogue. Some Ayurvedic doctors have also treated neurological diseases with A. racemosus with success. Varied Indian languages have different names for shatawari, including shatuli, vrishya, and other meanings. It is referred to as Kurilo in Nepal. Shat: "hundred"; variety: "curer" is how the name Shatawari is translated [49].

Characteristics

A.racemosus is a woody climber that may reach heights of 1-2 m. The blooms are white and have short spikes, while the leaves are uniformly tiny and shaped like pine needles. This plant belongs to the genus Asparagus, which recently transferred to the newly established family Asparagaceae from the subfamily Asparagae in the family Liliaceae.

Habitat

Its habitat is widespread throughout Asia, Australia, and Africa at low elevations with shade and in tropical climes. The most popular species of asparagus produced in India is A. racemosus, which is also used often in traditional medicine [50].

Phytochemicals

The following list of photochemical components found in shatvari:

- **Steroidal saponins**, known as shatvarins. Shatvarin I to VI are present. Shatvarin I is the major glycosidewith 3-glucose and rhamnose moieties attached tosarsapogenin;
- **Oligospirostanoside** referred to as Immunoside;
- **Polycyclic alkaloid**-Aspargamine A, a cage type pyrrolizidine alkaloid;
- Isoflavones-8-methoxy-5, 6, 4-trihydroxy isoflavone-7-0-beta-D-glucopyranoside;
- **Cyclic hydrocarbon**-racemosol, dihydrophenantherene;
- **Furan compound**-Racemofuran;
- **Carbohydrates**-Polysacharides, mucilage;
- **Flavanoids**-Glycosides of quercitin, rutin and hyperoside are present in flower and fruits;
- **Sterols**-Roots also contain sitosterol, 4, 6-dihydryxy-2-O (-2-hydroxy isobutyl)
- **Trace minerals** are found in roots-zinc (53.15), manganese (19.98 mg/g), copper (5.29 mg/g), cobalt (22.00 mg/g) along with calcium, magnesium, potassium zinc andselenium;
- **Kaepfrol**- Kaepfrol along with Sarsapogenin from woodyportions of tuberous roots could be isolated;
- **Miscellaneous**-Essential fatty acids-Gamma linoleinicacids, vitamin A, diosgenin, quercetin 3-glucourbnides [51].

PHOTOCHEMICAL CONSTIUENT STRUCTURE

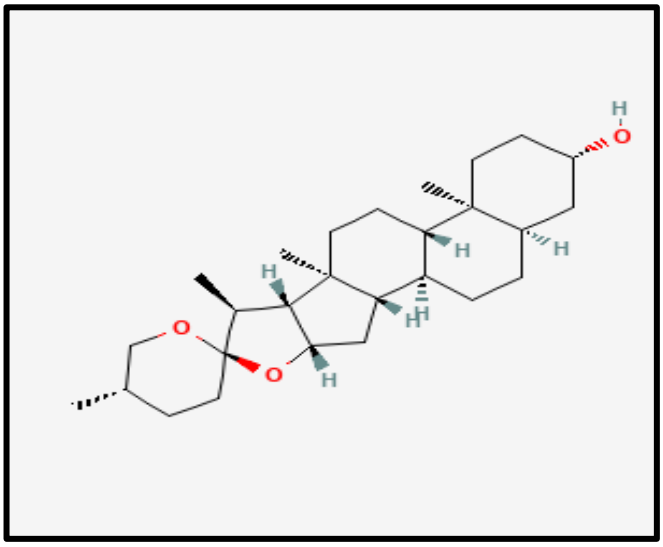

Figure 7: *Sarasasapogenin*

Sarasasapogenin

- *Shatavari* translates as "who has a hundred husbands or is liked by many." It is regarded as a general tonic and a tonic for female reproduction. *Shatavari* can be translated as "100 spouses," suggesting that it has the power to boost vigour and ferocity. This remarkable plant is referred to as the "Queen of herbs" in Ayurveda since it fosters attachment and affection. The primary Ayurvedic rejuvenation remedy for women is *shatavari*, and for men, withania. One of the well-known Ayurvedic medications, Asparagus racemosus (family Asparagaceae), commonly known as *Shatavari*, is useful for treating internal heat, chronic fever, madhur rasam, madhur vipakam, seet-veeryam, and som rogam [47].
- This herb is quite successful in treating issues with the female reproductive system. The two primary scriptures on Ayurvedic medicine, Charak Samhita and Ashtang Hridyam, both cite Asparagus racemosus (A. racemosus) as a component of the formulae to cure women's health disorders. A. racemosus is a well-known Ayurvedic rasayana that helps with nerve diseases, dyspepsia, tumours, inflammation, neuropathy, and hepatopathy. It also prolongs life, boosts immunity, improves mental function, energy, and adds vitality to the body. According to reports, A. racemosus root extract has pharmacological effects that include antiulcer, antioxidant, antidiarrheal, anti-diabetic, and immunomodulatory properties.
- The root of A. racemosus has been specifically advised in situations of imminent abortion and as a galactogogue, according to research of old classical Ayurvedic literature. The root of A. racemosus has been described as bitter-sweet, emollient, cooling, nervinetonic, constipating, galactogogue, and astonic. It is also said to be diuretic, rejuvenating, carminative, stomachic, antibacterial, and aphrodisiac. The root of A. recemosus may be helpful for treating some infectious illnesses, hyperacidity, tumours, inflammations, dyspepsia, diarrhoea, dyssentry, tumours, hyperdipsia, neuropathy, and mental disorders [48].
- The roots of A. racemosus contain steroidal saponins (Shatavarins I-IV), which are the plant's main active ingredients. In cell free assays, shatavarin IV has been shown to exhibit significant activity as a core golgi enzyme transferase inhibitor, and recently, immuno-modulation activity against specific T-dependent antigens in immunocompromised animals has also been reported.
- A. racemosus is widespread in the Himalayas, India, and Sri Lanka. It can reach heights of one to two metres and prefers to establish itself in rocky, gravelly soils at an elevation of 1 300 to 400 metres in the piedmont plains.

Galactagogue

Galactagogues are drugs or herbal supplements that help women who are unable to produce enough breast milk to start and maintain adequate milk production.

Galactagogues may be:

- Pharmaceutical Galactogogue
- Herbal Galactogogue

Table 1: *Pharmaceutical Galactogogue drugs*

Galactagogue drug	Proposed mechanism	Doses&dosage form	Adverse effects	Half-life
Metoclopramide	D2R antagonist, increase PRLsecretion.	Human: 10mg PO TID. Canine/feline: 0.1-0.2mg/kg,	Humans: several gastrointestinal disorders, insomnia severe depression, and seizures and in infants that consume milk from treated mothers causing intestinal discomfort.	Humans: 156.7 minutes. Dogs: 90 minutes

Domperidone [33]	D2R antagonist, increase PRLsecretion.	Human: 10mg PO TID. Canine/feline: 2.2mg/kg SC, every 12 hours for 4–6 days. Equine: 1.1mg/kg PO BID	Humans: xerostomia, gastrointestinal disorders, cardiac arrhythmia, and sudden death.	Humans: 7.5 hours.
Chlorpromazine [34]	D2R antagonist, increase PRLsecretion.	Human: 25mg PO TID. Rat:15mg/kg.	Humans: extrapyramidal symptoms in mothers and lethargy in infants. Feline: in high doses tremors, shivering, rigidity, and loss of the righting, reflexes, lethargy, diarrhea, and loss of anal sphincter tone.	Humans: 16–30 hours.
Sulpiride [35]	D2R antagonist, increase PRL secretion.	Human: 50mg PO TID. Equine: 1.1mg/kg PO BID or 0.5 BID IM.	Humans: headache, fatigue, extrapyramidal symptoms, acute dystonic reactions, and endocrine disruption	Dogs: 1.6–3.4 hours. Humans: 7.15 hours.
Oxytocin [36]	Induce milk ejection and this promotes milk synthesis by FILdecrease.	Canine and feline: 0.5–2.0 IU/kg dose SC EM. Bovine: 20 IUSC EM Sheep and goat: 1–5 IUEM. Swine: 0.025 and 0.05 IU IVEM. Equine: 20 UI IMEM.	When used appropriately at reasonable dosages, oxytocin rarely causes significant adverse reactions Result of using the drug in inappropriate individuals (adequate physical exam and monitoring of patient are essential) or at too high doses. In high doses they may cause discomfort, uterine cramping, hazardous of uterine rupture, and fetuses-placental compromise.	Goat: 22 minutes. Swine: 127 seconds Rat: 1.46 Bovine: 7–9 minutes and 25 minutes. Equine: 6.8 minutes. Humans: 272 seconds.
Recombinant bovine somatotropin (rBST) [37–38]	Increase basal metabolic rate and nutrients bioavailability, in mammary gland Increase MEC proliferation, survival and milk synthesis	Bovine: 500mg SC every 14 days.	Bovine: low pregnancy rates, increased open days, increase incidences of retained placenta, clinical and subclinical, reduced food intake, allergic reactions, laminitis digestive disorders, decreased hemoglobin and hematocrit, and mastitis.	Bovine: 54.8 minutes.

Table 2: *Summary of Selected Studies on Herbal Galactagogues*

Participants	Treatment(s), Dosage, and Duration of Treatment	Outcome of Interest	Results	Reported Side Effects	Reference
Mothers of term infants between 14 and 90 days postpartum who were experiencing lactation inadequacy	Some lactation counseling was given to all mothers. Asparagus racemosus (shatavari) root extract, twice daily, mixed with other herbs at a ratio of 15 9 per 100 g of mixture (n=32) Placebo (n=32) Duration: 4 weeks	Median serum prolactin levels (ng/mL) Mean infant weight gain velocity (g/d) Volume of supplemental milk (mL/d)	No significant difference was found in median serum prolactin levels (25 ng/mL in the treatment group vs 38 ng/mL in the placebo group), mean weight gain velocity (30 g/d vs 26 g/d, respectively), or mean volume of supplementary milk feeds (163.2 214 ml/d vs 262 118 mL/d, respectively) between the 2 groups after treatment.	Not reported	[40]
Lactating mothers of infants ≤6 months old who were experiencing various issues	Asparagus racemosus (shatavari) root extract, 60 mg/kg body weight per day (n-30) Placebo (n=30) Duration: 30 days	Serum prolactin level (ng/mL). Mean percent increase in infant weight	Mean prolactin increase of 32.87% 6.48% in the treatment group vs a mean increase of 9.56% 4.57% in the placebo group from baseline (P<0.05). Mean increase of the babies' weight was 16.13% 3.65% in the	No side effects were observed in human trials. In mice, mortality occurred in long-term trials	[41}

with breast-feeding			treatment group vs 5.68% 2.57% in the placebo group (P<0.05).	at a dose of 5,000 mg/kg.	
Mothers who delivered full-term, healthy infants	Coleus amboinicus Lour (torbangun) leaves, 150 g/d as a soup (n=23) Fenugreek seeds in capsules, 600 mg. 3 times daily (n-22) Placebo, capsule (n-22) Duration: 1 month starting on day 2 after birth	Amount of milk consumed based on infants' weight before and after feeding (collected at 2-week intervals)	No significant difference was observed in the fenugreek group or the placebo group from day 14 to 28 (P>0.05). Mean breast milk consumption was 466.9 253.0 mL at day 14 and 400.3 215.1 at day 28 for the fenugreek group vs 438.8 192.6 mL at day 14 and 385.1 201.9 mL at day 28 for the placebo group. (Note: Results for torbangun leaves are not reported here because the herb was not selected for inclusion in this review.)	Not reported	[42]
Mothers of healthy neonates	A lactation consultant was provided to all mothers. Fenugreek herbal tea, 200 ml., 3 times daily (n-22) Placebo tea (n=22) Control group, routine advice (n-22)	Breast milk produced (mL) on the third day after birth during 15 min of pumping both breasts	Mothers who consumed the galacatagogue tea produced significantly (P-0.004) more milk (mean milk production 73.2 53.5 mL) than mothers in the placebo (38.8 16.3 mL) or control (31.1 12.9 mL) groups.	Not reported	[43]
Mothers experiencing borderline-normal milk production (700 mL/d)	BIO-C (silymarin), 420 mg/d (n-25) Placebo (n=25) Duration: 63 days	Milk production (g) based on baby's weight before and after suckling followed by breast pump until empty	Significantly more milk was produced in the treatment group (989.76 102.33 g. 64.43% increase) vs the placebo group (649.76 + 78.35 g. 22.51% increase) on day 30 compared to baseline (P<0.01). On day 63, mothers in the treatment group produced 85.95% more milk compared to day 0, while mothers in the placebo group produced 32.09% more milk (P<0.01).	Not reported	[45]
Healthy mothers whose infants were exclusively breast-feeding	Participants were instructed to eat a bland diet on days 1-11. Group 1: Placebo on days 8-10 (n=10) Group 2: 1.5 g garlic extract capsule on days 5-7 (n=10). Group 3: 1.5 g garlic extract capsule on days 8-11 (n=10) Duration: 11 days	Milk intake (mL) based on child's weight before and after feeding on days 4 (baseline) and 11 (endpoint)	No significant difference was observed in the amount of milk consumed (mL) between any of the groups at endpoint (P>0.05).	Four mothers in treatment groups 2 and 3 reported children were colicky during treatment period. Four mothers in the placebo group also reported that the children were colicky.	[46]
Mothers 18-38 years who delivered term infants via normal spontaneous delivery	Moringa oleifera (malunggay) leaves in capsules (Prolacta), 350 mg/capsule, 2 capsules daily (n=35) Placebo capsule (n-38) Duration: 8 days starting the third day postpartum	Milk production (mL) collected via manual pump at a minimum of 5 min on each breast every 4 hours	For each day, more milk was produced by participants in the treatment group than in the placebo group; however, the difference was not significant. On day 10, mothers receiving treatment produced an average of 395.9+ 36.3 mL breast milk while those receiving a placebo produced 150.8 ±16.5 mL.	No adverse events were reported.	[44]
Healthy Filipino mothers and term infants weighing	Moringa oleifera (malunggay) leaves (Natalac) 250 mg/capsule. twice daily (n=58) Placebo (n=58) Duration: 4	Serum prolactin levels (mIU/L) collected within 6 hours	Prolactin levels in the treatment group were significantly higher (P<0.01) than in the placebo group for the second (5,235 2,2524 mIU/L vs 3,398 1,939.5 mIU/ respectively) and third	Not reported	[39]

2,500-5,000 g at birth	months starting within 6 hours of delivery	of delivery before apsule administration and infant suckling, at 48 hours after delivery 30 min after infant suckling. and at 4 months after delivery 30 min after infant suckling Infant weight (kg) at birth and at 1 week, 2 weeks, 1 month, and 4 months	measurements (2,389 1,019.7 mIU/L vs 412.64 ± 13.27 mIU/L respectively). Babies weighed significantly more in the treatment group than in the placebo group at 4 months of age (6.646 1.8 kg vs 5.304 +1.2 kg, respectively; P<0.01).		

Table 3. *Summary of Selected Studies on Domperidone*

Participants	Treatment(s), Dosage, and Duration of Treatment	Outcome of Interest	Results	Reported Side Effects	Reference
Mothers of preterm infants experiencing partial or complete lactation failure	All women received lactation support before start of study. Domperidone, 10 mg, 3 times daily (n=19) Placebo (n=19) Duration: 14 days	Mean milk production (mL/d) during 24 hours expressed breast pump	At day 14, mean breast milk volume was 380 mL for the domperidone group and 250 mL for the placebo group. Mean within-subject volume increase from day 0 was 267% in the domperidone group vs 19% in the placebo group (P=0.005).	No adverse events were reported by participants.	[29,30]
Puerperal mothers of premature infants experiencing low milk production	All women received counseling before start of study. Domperidone, 10 mg, 3 times daily mixed with lactose (n=7) Placebo (lactose powder) (n=9) Duration: 7 days	Mean milk production (mL/d) during 24 hours expressed breast pump	The domperidone group experienced a significantly hours expressed via greater (P<0.05) mean increase in participants. milk volume from 130.4 mL on day 2 to 183.5 mL on day 7 (44.5% increase) while the placebo group increased from 54.7 mL to 66.1 mL (16.6% increase).	No adverse events were reported by participants.	[28]
Women who delivered healthy babies at term via cesarean	Participants were encouraged to breast-feed within 24 hours of delivery. Domperidone, 10 mg, 4 times daily (n=22) Placebo (n=23) Duration: 4 days, beginning within 24 hours of delivery	Mean milk production (mL/d) after pumping both hours after breast- feeding, collected twice daily.	Gradual increase in mean milk volume observed in both groups from days 1 to 4 but significantly breasts for 15 min 2 higher in the treatment group treatment group. (P<0.05). The domperidone group increased from 3.9 ± 4.6 mL on day 1 to 191.3±139.1 mL on day 4 vs an increase of 3.49.3 mL on day 1 to 91.4 ± 60.3 mL on day 4 in the placebo group.	Dry mouth was reported by 31.8% of women in the treatment group.	[31]
Multiparous women who had previously experienced (group A) or primiparous Placebo currently experiencing (group B) some degree of lactation failure	Domperidone, 10 mg, 3 times Group A: n=8, Group B: n=9 Group A: n=7 Group B: n=8 Duration: Group A: 4 days starting the second day after birth Group B: 10 days	Volume of milk produced (mL/d) estimated based on infant weight before and after feeding	Group A: Mean daily milk yield was significantly higher in the estimated based on treatment group, increasing from or neonates. 105 35 mL/d on the second before and after day postpartum to 475±51 mL/d on the fifth day postpartum. Group B: Mean daily milk yield was significantly (P<0.01) higher in the treatment vs the control group on treatment days 4-10.	No side effects were reported for mothers or neonates.	[32]

"Intentional design, characterization and manufacture of materials, structures, and systems by regulating their size and form in the nanoscale range of 1 to 100 nm" is how nanotechnology is described. Nanotechnology has the potential to be helpful for medical applications since the nanoparticles are similar in scale to biological molecules and systems but may be created to have different functions. The goal of nanomedicine is to cure illnesses at the molecular level by using the capabilities and physical traits of nanoparticles. One of the newest fields of study in the modern discipline of material science is the topic of nanotechnology. Nanoparticles exhibit entirely new or better characteristics, such as size, particle dispersion, and shape, among others. Nanoparticles and nanomaterials are finding new uses in a variety of scientific fields, including pharmacy, medicine, and other fields [26].

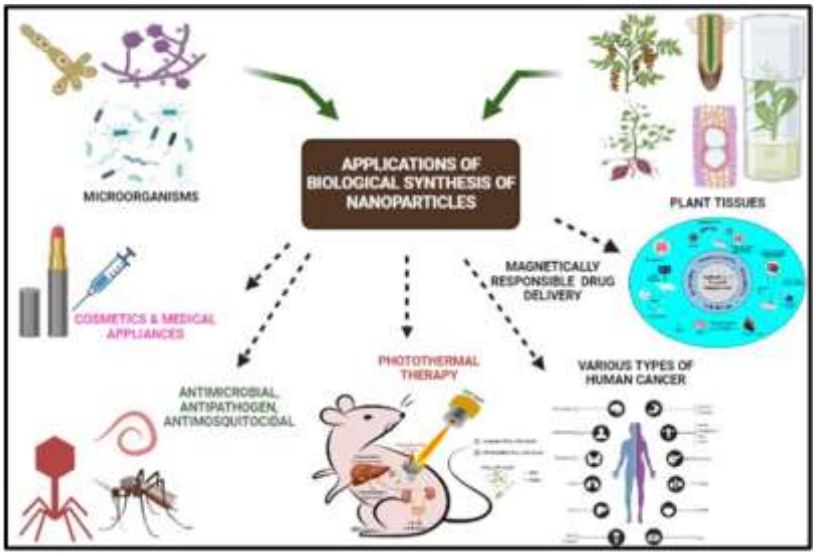

Figure 8: *Applications of nanotechnology*

Selenium nanoparticles (SeNPs)

Origin and the relevance of nanoselenium

The improved safety of nanomedicine is a well acknowledged benefit. The usage of Se in the form of nanoparticles has significantly allayed the toxicity worries related to Se. In the case of Se, the main barrier from bench to bedside translation is the tiny therapeutic window with minimal margin of dosage error. SeNPs may be created using a variety of techniques, such as biological or synthetic ones. The focus of the current study does not include a full discussion of the numerous techniques utilised to synthesise SeNPs, which may be found in previously reported studies. Se is a crucial component of several selenoenzymes, including GPXs, TXNRDS, and deiodinases (DIO), all of which are necessary for a variety of biochemical processes, including the body's natural antioxidant defence mechanism. Depending on the dosage, duration, and oxidation state, it exhibits distinct antioxidantand pro-oxidant actions. In a mouse model, the use of SeNPs significantly lowers the mortality caused by acute toxicity linked with Se by up to four times. Additionally, SeNPs significantly minimise the liver damage caused by large Se dosages, as seen by the indicators of heap totoxicity [27].

Therapeutic applications of selenium nanoparticles (SeNPs)

SeNPs provide a number of medical advantages, such as anticancer, antioxidant, anti-inflammatory, and anti-diabetic effects. The anticancer action is primarily caused by the substance's prooxidant characteristics, which cause these cells to produce reactive oxygen species (ROS), which damage the mitochondria and endoplasmic reticulum and result in DNA damage.

Differential activity of SeNPs on cancer cells and normal cells

Due to the different osmotic and redox states of cancerous cells, SeNPs exhibit prooxidant activity inside malignant cells. Se's regulated release characteristic and increased cellular bioavailability are both provided by the nanoparticulate form. SeNPs are less lethal than their inorganic counterparts due to this distinct distinction between cancer cells and normal cells, even if the essential mechanism of cellular death is the same.

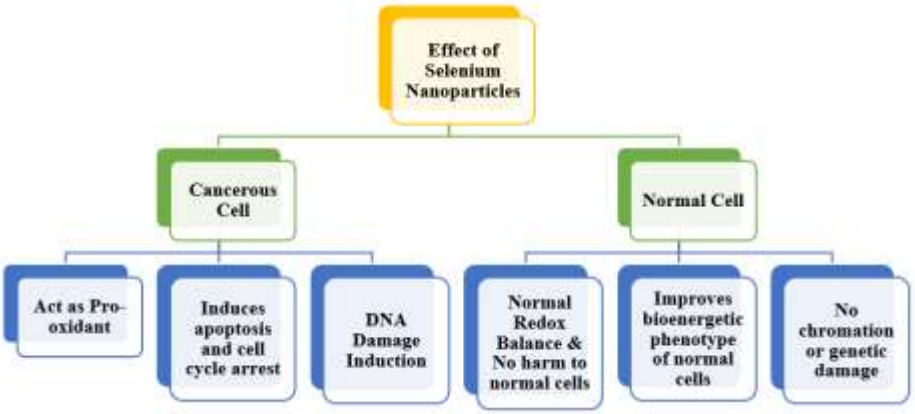

Figure 9: *Differential activity of SeNPs on cancer cells and normal cells*

Putative mechanism of anticancer activity of SeNPs.

Endocytosis mediated by receptors is how SeNPs internalise. The pH condition of the cancerous cells is acidic, and there is a redox imbalance. The prooxidant conversion of SeNPs in this milieu of cancerous cells promotes the additional generation of free radicals, which on the one hand break the mitochondrial membrane and cause the leaking of mitochondrial (Mt) proteins and on the other hand induce endoplasmic reticulum (ER) stress. When the Mt membrane is damaged, different proteins seep out and caspases are activated, which causes apoptosis. Multiple molecular pathways, including the NF-B, PI3K/Akt/mTOR, Wnt/-catenin, MAPK/Erk, and apoptotic pathways, are orchestrated by this cellular stress state. Cellular homeostasis is disturbed by the NF-B pathway, which increases inflammatory and oxidative stress signaling. Oncogenic signalling involves the PI3K/Akt/mTOR, MAPK/Erk, VEGF, and Wnt/-catenin pathway, and SeNPs' modulation of these pathways impairs cellular proliferation and hinders signalling that encourages growth in the tumour microenvironment [28]. Additionally, it has been demonstrated that SeNPs reduce angiogenic signalling in cancer cells, which further inhibits their ability to proliferate and grow. Combining these cellular disruptions results in DNA damage, which causes cell cycle arrest and ultimately leads to cell death.

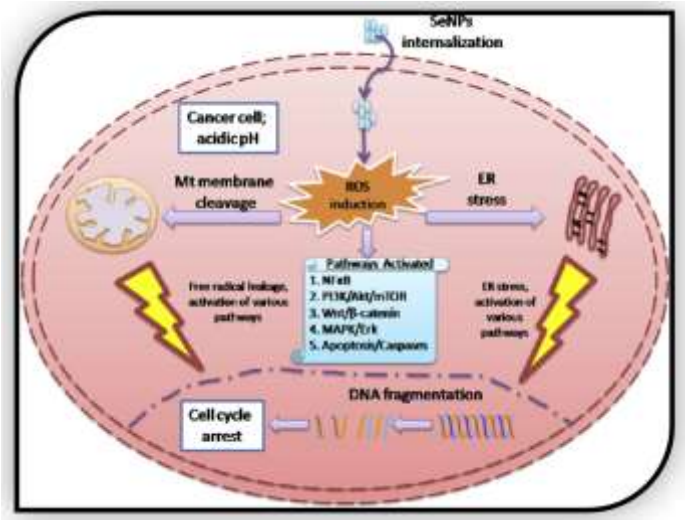

Figure 10: *Mechanism of SeNPs against anti-cancer activity*

CONCLUSION:

Prolactin being a hormone released by pituitary gland at the base of the brain regulates the body's balance and stimulates the breast development and milk production. Because of hyperprolactinemia now a days children are more prone to auto immune disorders. By this review we have analyzed the importance of prolactin in one's life and as a whole if we can enhance the chance for treating hyperprolactinemia with collaboration of herbals and nanotechnology it will a great evolutionary in every individual life and medical field.

CONFLICT OF INTEREST

The authors declare no conflict of interest

ACKNOWLEDGEMENT

One of the authors express sincere gratitude towards Department of Pharmacognosy, JSS College of Pharmacy, Ooty for providing necessary facilities to carry out the research work.

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