HERBAL-BASED MEDICINE APPROACH IN THE TREATMENT OF INFERTILITY: A REVIEW

Pandey Priya Arun[1], Gaurav Kumar*[2] and Raj Kumar Tiwari[2], Bhawna Sharma[2]

1. Medical chemistry department, faculty of ayurveda, institute of medical science, Banarashindu university, Varanasi, Uttar Pradesh, India 221001

2. Department of pharmacy, Dr. K.N. Modi Institute of Pharmaceutical Education and Research, Modinagar, Uttar Pradesh, India, 201204

***Corresponding author's details**

Name – Mr. Gaurav Kumar

E-mail: gktarapur@gmail.com

Mob. no.7409070736

ABSTRACT

The objective of this review is to contribute an exhaustive summary of ayurvedic and herbal plants used extensively for the treatment of infertility throughout the world. We have conducted a detailed literature review through different channels such as review papers, valued textbooks, and with the best scientific databases (Science Direct,Pubmed,ResearchGate,SAGE). Terms such as "fertility potential", "Female fertility", "male fertility", "folliculogenesis "spermatogenesis" ,"ovulatory", "estrogenicity", "galactogogue", "PCOS" were used for screening of the review papers .When the human body's natural, unprotected sexual activity fails to produce an egg after 12 months or more of incubation, this condition is known as infertility. Approximately 18-20% of couples enduring bareness may well be female or male bareness. Female infertilities seem to be more prevalent within the populace compared to guys. Medicinal plants as mentioned in the literature of Ayurveda involving roots, stem, leaves, and extracts prepared from them used traditionally to influence fertility in males and females, are considered exceptionally valuable in conventional pharmaceuticals and treatments. Ahead of controlling the regenerative framework, it is additionally accommodated by reducing the endocrine framework and hormonal issues such as ovarian insufficiency, libido, variocella, vaginal atrophy, bendometriosis, untimely menopause and polycystic ovarian syndrome. These plant-based medications werereliable with exclusive activities such as antioxidants, immunomodulator, antimicrobial, laxative, purgative, and anticancer, which appear to be secure and promising for treatment in conventional remedies from the perspective of women health care.

KEYWORDS

Inferility, ayurveda, herbal, medicine, hormones, female infertility, male infertility, phytochemical antioxidant, rasayana.

INTRODUCTION

Infertility and infecundity are the terminologies used interchangeably. here fertility and infertility are defined as reproductive performance rather than capacity, and are used according to whether there is actual childbearing or not during the period under review, while the capacity of a man, a woman or a couple to produce a live birth is called fecundity[1]. An alternative of the term fecundity implies the ability to conceive, rather than to produce a live child1.Sexual function greatly affects an individuals' quality of life, the normal male sexual response cycle consists of five phases: libido, erection,ejaculation,orgasm and detumescence subsequently[2].Infertility is featured because of the failure of a successful gestation after 12 months or more of vulnerable sexual activity[3]. Probably 1 in 10 ladies struggling within side a variety of 18-38 yrs of age have extreme trouble in gestation. At puberty and before pregnancy, sexual activity appears and large amounts of sex hormones, estrogen and progesterone are produced, which helps to prepare uterus, vagina, and oviducts.Therefore, estrogen, progesterone, and prolactin contribute significantly to pregnancy and fetal growth and should be investigated closely[4]. Diminished or lack of functionality to conceive and endure offspring is a medical condition where extensively women have unsuccessfully pregnancy. Such circumstances occurred in either of males or females, the reasons for male infertility are reported followed up by low sperm concentration and demised movement[5]. Major causes of male infertility are varicocelltumour, infections,problems in ejaculation and erection, hormone imbalance, and obstruction in tubular structures that help in transporting of sperms[6].This etiology ends up in alteration of spermatogenesis and abnormal or improper release during ejaculation of spermatozoa. The pathophysiologies behind the occurrence of female infertility are dysfunction of HPA[7]hypothalamus-pituitary-adrenal axis because they are broadly answerable for the secretion of GRH Gonadotropin Releasing hormone which releases FH and LH in females. Follicle stimulating hormones may help in proper regulation of menstruation and stimulate the event and growth of eggs within the ovaries.

Luteinizing Hormones play a significant role in systemic functioning and development of sexual action and therefore the release of eggs from the ovary gets provoked by it. Those danger factors which influence infertility are lifestyle disorders such as diabetes, obesity, and working in stressful surrounding age of 35 years, frequent drinking and eating activities, high consumption of nicotine and alcohol and continuous exposure to radiation environment. The explanation for herbal-based medicine takes all eyes as they're rich in high phytochemicals, antioxidants, and minerals. Animal studies suggest that the cholesterol level is lowered by increased phytoestrogen intake and there is also some evidence from human studies to suggest that phytoestrogens may reduce cholesterol levels in persons with preexisting hypercholesterolemia[8].Nowadays method used extensively for fertilization are Artificial inseminations (AI),In-vitro fertilization(IVF) , intrauterine inseminations ,natural cycle IVF,egg freezing ,surrogacy and fertility drugs[9]. AI stands for Artificial insemination associated with the placement of healthy sperms directly into the cervix during the time of ovulation in women's. Artificial insemination (AI) also referred as intrauterine insemination (IUI), alternative inseminations or donor insemination is extensively used for women trying harder to conceive but unable to do so after a year. Intrauterine insemination is a kind of artificial insemination procedure that helps with infertility. IVF is a type of assisted reproductive technology (ART), referred as a method of fertilization where the combination of egg and sperm occurs through In-vitro and involves routine regulation, monitoring and stimulation ovulation in women. Mode of action in IVF is medication and surgery simultaneously helping sperm to fertilizeeggs and thereafter they get implants in the uterus for further growth and development. In the natural cycle IVF stimulation of ovulation through drugs is prevented and involves naturally selection of respective follicles. Following the procedure of IVF, sperm got administered directly into the uterus with the help of catheters. The main objective of this technique is ameliorating the chances of fertilization via surrounding eggs with healthy sperms that could reach the fallopian tubes successfully during the time of ovulation. The treatments for infertility require modern advance technology and expensive

medical healthcare, however, the developing countries have a shortage of availability of those technologies,and the plants based medicine will plays a prominent role in pharmaceutical and healthcare society for these severe medical ailments[10].

Ayurvedic perspective on infertility:

The origination of Ayurveda is from India, while going through the etymology of it "Ayurveda" is the consolidation of two words which are "ayus" stands for longevity or viability and "Vedas" stands for the purest form of knowledge, hence Ayurveda is referring as righteous knowledge of longevity. Ayurveda believes the five basic elements Panchamahabhutas (space,air,fire,water, and earth) manifest in the human body as three basic humors known as tridosas(Vata,Pitta and Kapha)[10]. These three govern the creation,maintenance, and destruction of bodily tissues as well as the assimilation and elimination.Ayurveda emphasis more on the science of self-healing, which is the heart and soul of the nonconventional system of medicine. Along with the following concepts of self healing, herbal plants based. Medicine also plays an important role in Indian traditional system of medicine[11].The global recognition of Ayurveda among the population is still lacking behind comparing to the conventional medicine. Allopathic drugs achieve more attention due to their rapid mode of action. Unfortunately, the side effects and the expense of conventional medicine being high could be the reason people shift to Ayurveda and herbal-based medicine as there are affordable and efficient activity against various chronic disease. Ayurveda encourages healthiness via promoting the inner framework self –restoration process and strengthening the quality of life. It more precisely focuses on ameliorating the lifestyle and standard of liveliness of a person individually without consuming any foreign compound in the framework that may affect the structured physiology. In Ayurveda, Vandhyatva (infertility) is a condition where, due to factors like SukraDosha (unhealthy semen), Ativyayama (over exercise), loss of Bala (low strength) and improper Ahara (food) and Vihara (lifestyle) etc., the Beejamsha (spermatozoa and ova) gets defected and finally leads to reduced fertility of

Sukradhatu (sperm)[10]. Some studies concluded infertility cases close to 48 million couples worldwide,50%infertility cases are women related ,30% infertility are caused due to male infertility, and rest are by other factors[10].In ayurvedic literature vandhyatva is the terminology used for infertility . There are 3 basic Srotas(small channel) responsible for infertility[11]:

1. Rajovahasrotas(the uterus, cervix part)

2. Artavahasrotas(ovary and fallopian tubes)

3. stanyavahasrotas(breast tissue with blood supply)

Ayurveda embelish the interior balance and suppresses exterior factors influence to the problems constructing ojas(in Ayurveda,ojas means essence of vitality),enhancing the comprehensive healthcare of individuals, stimulate the hypothalamus and pituitary gland bring about ovaries to ripe and eggs to release[12].As the foremost concentration of Ayurveda rely on balancing out the internal physiology rather than only treating the individuals , Ayurveda is considered as low potential towards side effects. Vajikarana‟ is the ayurvedic medicine that deals with issues of infertility and the word “Vaji” means “horse,” so Vajikarana means “to make one potent like a horse.” Guhyaroga is used for the diseases of the female reproductive system[12].As per Ayurveda; major factors responsible for healthy conception are as mentioned below:

1. Ritu(Fertile period)

2. kshetra(female genital tract)

3. ambu(nutritive fluids)

4. Beeja(ovum and sperm)

In Sanskrit, dosha is referred as defect (which causes issue) and they are 3 types of dosha present in an individual. Vata (space and air),Pitta (fire and water), and Kapha (earth and water) aredosha which controls our mind and body. InAyurveda, Agni is monitored and regulates the proper digestion of food and metabolic products in body.Agni functions as conversion of food in to the form of energy essential for the vital activity of our body. In Ayurveda, imbalance in the Doshas and Agni may cause infertility abnormalites in Ritu, Kshetra, Ambu, and Beeja hinders the process of conception. Obstruction in the normal path of sperm such as obsturacted hymen, obstruction in the cervical canal, absence of infected ovaries, or membranous dysmenorrhoea is some other factors responsible for infertility[12].

Ayurvedic medicinal plants:

(Asparagus racemosus) Shatavari:

Figure 1 Shatavari plant

Shatavari basically referred as "who possesses a hundred mates or readily accessible to many". Sometimes shatavari is also defined as “100mates", so called due to its ability to influence fertility and liveliness. Asparagus racemosus is the botanical name of shatavari, commonly

known as satawar, satavari, and satamuli.They act accordingly as general tonic and female reproductive tonic. Shatavari have different chemical constituents present in different parts of plants such as leaves, stem, flower, roots, shoots (as shown in Figure 1) but root are beingconsidered essential, for important or medicinal purposes acting as diuretic and helps in ulcer preventing effects via cytoprotective action. According to the documented mention in Ayurveda,Shatavari is considered as the "queen of herbs" Because it bringslove, affection, and wisdom. Shatavari is a truelyrejuvenative herbal plant that acts as a strong fertility booster in females in a similar way as withania acts for male fertility. A. racemosusis considered as well-known ayurvedicrasayan that combat against aging, influence lifefullness, benefit brain cells too properly, and increase immunity. For from a long period of time, they have been referred as emollient, carminative, galactogogue, constipating, soothing, and stomachic and tonic. Shatavari have been highly recommended for the prevention of abortion and as a galactogogues[13]. There are therapeuticallyt active due to the present of steroidal saponins commonly known as shatavarin 1,shatavarin 2, shatavarin3, andshatavarin 4 are lying in the roots of shatavari. It is one of the most common herbal plants used worldwide and possesses various chemical constituents such as Racemoside A, B, C, Shatavarins, Asparanin A, Immunoside, 27 α-dimethyl-1β, 2β,3β-trihydroxy-25-spirost-4-en-19β-oic, 27 α-dimethyl-1β, 2β,3β-trihydroxy-25-spirost-4-en-19β-oic and many others14.The geographical region where A. racemosus are broadely available in India, Srilanka and himalaya. The vast pharmacological activities shown by Shatavari are as given below:

1. Shatavari have superefficient activity as a female tonic, rejuvenating lifeliness and influence libido in both males and females.
2. It helps to reduce the tiredness and inflammation of genital organs.
3. Shatavari benefits the dry tissue of female reproductive organs by balancing the optimum hydration and pH level.

4. The post partum action gets influenced by satavar via increasing in lactation and helps the mother in maintaining and balancing uterus and ovarian hormones[14].

Withania somnifera (Ashwangandha):

Figure 2 Ashwagandha plant

Withania is a reverberating herbaceous plant (as shown in fig 2) of Indian ayurvedic system of medicine as a rasayan (tonic) [15]. From almost 6000 years ago ashwagandha were used as rasayan as the roots smell like somewhat horse (ashwa), they have been referred as ashwagandha. Withaniasomnifera is a well-known Indian medicinal plant widely used in the treatment of many clinical conditions in India and an important drug commonly known as Asgand, which has been used either single or in combination with other drugs in Unani as well as Ayurvedic systems of medicine for centuries[16]. Anciently, Indian Ayurveda and Unani system have plentiful knowledge of withania therapeutically active against infection, stress, aging process, and restoring power in male genitals issues such as infertility, lipido, impotence.The botanical name of ashwangandha is withania somnifera are also popular by common name as winter cherry, Kaknaje Hindi, is a well- known medicinal plant in Solanaceae family. The phytochemicals obtained from the extract of leaves and roots of ashwagandha are essential from the medicinal point. It is reported through different investigations that WS possess antiseratogenic, anticancer

and antianabolic activity, antianxiety, aphrodisiac, immune modulation and is beneficial in the treatment of arthritis, geriatric problems, stress and male sexual dysfunctional16. Chemical analysis of Asgand shows that it contains several alkaloids such as withsomine, withaferin A, withanolide A and withanolide D and various other constituents[17].This plant has been known to contain more than 80 types of phytochemicals such as steroidal and nonsteroidal alkaloids, steroidal lactones, and saponins like isopelletierine, anaferin, anahygrine, hygrine, cuscohygrine, tropine, pseudotropine, withananine, ashwagandha, with- aferins, withananinine, pseudowithanine, somnine, som- niferine, somniferinine, 3-tropyltigloate, withanine, withasomine, visamine, mesoanaferine, hentriacontane, amino acids such as aspartic acid, glycine, tryptophan, proline, alanine, tyrosine, hydroxyproline valine, cystine, glutamic acid, and cysteine, calcium, phosphorus, iron, flavonoids, starch, reducing sugars, proteolytic enzyme "chamase," glycosides, dulcitol, and volatile oil6.The leaves are bitter widely used as paste form against fever ,swelling and inflammation. Withaniasomnifera, also known as Indian ginseng, has been described in folk medicine as an aphrodisiac and geriatric tonic4.As ashwagandha hold high adaptogenic value they are being compared with other natural adaptogen of finds in different countries is the only reason behind calling it as "Indian ginseng"[18].The pharmacological activity ashwagandha consists are as given below

- As an antioxidant with free radicle scavenging property
- In denegrative disease (Parkinson,Huntington, and Alzheimer's)
- Used widely as cognition enhancer
- By stimulating and improving the working efficiency of brain cells help individuals in improving memory and learning capabilities
- Act as protective against stress-induced gastric ulcer
- Prominent effects on inflammation and osteoarthritis
- Widely used against rheumatism and cancer

- Improves cell-mediated immunity.

Ashwagandha in Ayurveda is referred as rasayan and categorised into a subgroup of rasayan called as "medhyarasayan" here medhya in Ayurveda stands for mind or mental ability to do work and "rasayan" means promoting intellectual property therefore the meaning of medhyarasayan is having properties to endorse the brain activity. Studies have suggested WS consist of antistress effects hence are highly recommended in stress-induced diseases like atherosclerosis, arrhythmia,cardiac arrest,early aging, hypertension and malignant tumour[19].In a study while administration to the group of Wistar rats with milk injection a significant reduction of lecucocytosis[15].Meanwhile Investigating withania pharmacological activity witnessed to have inhibitory effect on growth of tumourecous cells representing a promising confirmation of noteworthy effects in preventing and treatment of malignant tumour. There are mainly responsible for the improvement of white blood count and function which got disturbed while going through chemotherapy in cancerous individuals. As in the prevention of fibroids, the tumour of the uterus showed a decrease significantly of uterine bleeding tendency and disappearance of fibroids after long treatment.Few studies have demonstrated that the oxidative stress is directly influencing the shortage of antioxidants with a decrease in hormonal levels affecting negatively the sperm quality and quantity. The consequences of oxidative stress resulting from under-developed and abnormal spermatozoa are due to the degradation of lipids and proteins which satisfy the nutrition level of sperms. In the study of have reported, WS significantly reduces the level of lipid per oxidation and protein carbonyl group in infertility. Stress plays an important role in male infertility that produces biogenic amines such as catecholamine's and serotonin, which directly affect the function of the hypothalamus. Adrenal medulla is located in the adrenal cortex of the adrenal glands, which is reason behind the secretion of adrenaline, also called as stress hormone. Stress is a condition which disturbs systematic regulation, production, and secretion of hormone monitoring through brain.W. somnifera has the capability of combating stress

induced infertility, the reason could be WS is enriched with high amount of flavonoids, a neurotransmitter. Several investigator reports have suggested that W. sumnifera is beneficial in the treatment of male infertility. Experimental evidences have shown that treatment with W. Somnifera induced testicular development and spermatogenesis in immature Wistar rats by directly affecting the somniferous tubules, improved prosexual behavior of sexually sluggish mice, and increased testicular daily sperm production and serum testosterone level[19].

Zingiberofficinale (Ginger):

Figure 3: Rhizome of ginger plant

From thousands of years, the medicinal prospects of ginger are well known. Gingers have the perspective of promoting heath quality of individuals are well known. Ginger (zinger officialis) belongs to Zingerberaceae.The foundations of ginger are south-east Asia and have been used up in developed countries such as spices and continents. Accompanied with cooking, ginger rhizome is having high value from a medicinal perspective (rhizomes of ginger plant as shown in Fig 3). Anciently, the natives of India found ginger to be very promising and helpful for having a high antioxidative property. The pharmacological action includes immune modulators, anti-tumourgenesis,anti-inflammatory,anti-apropotic,antihyperglycemia,anti-lipidemia and anti-emetic[20].Large numbers of active chemical constituents are mainly present in ginger. Those active ingredients are categorized as volatile and nonvolatile compounds, volatile hydrocarbon

monoterpenoids, and sesqueterpens, while the aroma and pungent taste of ginger is because of nonvolatile compounds including zingerone,shoqaol,paradol and gingerol[21] .Ginger is that the underground root(rhizome) parts of plants which is thick and knotted has been employed in Indian culture as homemade remedy to assist digestion and treat diarrhoe, nausea ,vomiting and arthritis for quite a centuries.

- Endocrine disorder(menstruation ,infertility,vaginalatrophy,lipido,variocele),
- degenerative disorders (rheumatic and arthritis),
- digestive disease(faltulence, blotting,acidity,ulcers),
- cardiovascular disease (cardiac arrest,arrythmia),
- cancer(leucoderma,colon cancer)
- GIT Tract disorder (flatulence,acidity,constipation)

Studys have explained that ethanol decreases significantly enzymes such as dismutase,superoxidedismutase,glutathione reductase, catalase succeeding in the damage of hepatic tissue while following effects of rats treatment with ginger leads to improvement of tissue. The damage through ethanol treatment improved by treating rats with ginger witnesses, it supports the protective effects against ethanol-induced hepatotoxicity.Various studies have explained the antimutagenic and anticarcinogenic activity attributed to ginger against gastrointestinal cancer[22]. Major biochemicals present in ginger rhizomes areterpenes, carbohydrates, and phenolic compounds. Zingiberene, farnesene, bisabolene, curcumene are the most dominant of the terpenes present in ginger. They are used widely to treat GIT diseases such as heartburn, colic pain, gas ,blotting,flatuelence[21].Ginger is helpful for relieving pain associated with dysmenorrhea, rheumatoid arthritis, osteoarthritis, and gastrointestinal symptoms such as diarrhea, nausea, and vomiting[23].ROS stands for reactive oxygen species which are highly reactive in nature and formed because of oxidative stress. The biological level of ROS is

important for the systematic function of different cellular pathways and maintaining homeostatis[24]Those are the radical like oxide, singlet oxygen, superoxide and nitric oxide to blame for the oxidative damage of cellular pathways. ROS is that one amongst the critical factors that adversely affect the genital system in both males and female[25]. The unequal coordination between ROS synthesis and there elimination results in the main cause behind oxidative stress in semen destroying the per-oxidative sperm membrane, which disturbs the functionality of sperm.

Foeniculum vulgare (Fennel):

Figure 4 fruits of fennel plants

Foeniculum vulgare is the plant name for fennel and belongs to the Umbelliferaefamily(as shown in Figure 4). Due to its important properties, this herbaceous plant occupies a valuable position in Indian spice society and folk remedies. For decades, they have been widely used to increase milk production for lactating mothers. In addition to this fennel, there are treasures of therapeutic activities such as carminative, antiseptic, palliative anti-inflammatory, cold, asthma and menstruation[26]. In some studies, the useful effects of F. vulgare were demonstrated to the increase in milk secretion in breastfeeding[27].Traditionally, fennel seeds have excellent antispasmodic effects, so fennel has been used primarily to treat colic and respiratory illnesses in

children. Diuretics, laxatives, galactatogogues, and mucolytics are among the many widely used activities of fennel, while the extract of fennel powder is used against abdominal and infantile colic[26]. From the literature review it's well documented that fennel has a promising and significant role in medical ailments as like PCOS, vaginal atrophy, menopause, dysmenorrhea, infertility and amenorrhea. Here we are visiting and understand the important role of fennel in the management of women healthcare and medical issues. The main chemical constituents of fenchon, anthon, and essential oils. Among other things, one of the most important activities of fennel is to increase the weight of the female reproductive organs of. Several studies have also reported that they are involved in affecting the total protein content of rat seminal vesicles. Fennel essential oils have beneficial effects on uterine contraction, infertility, and enhanced genital function. In a different studies, they have explained precisely the effects of extractedfennel, fennel which shows a moderate increase in the number of graffiti, follicular and multilayered follicles, and an improvement in the process of folliculogenesis in the ovaries[28] .This study suggests that daily intake of fennel fruit is beneficial in improving fertility in women and helps alleviate the symptoms of menstrual irregularities[23]. The pharmacological activity exhibited by fennel may be due to the estrogenic activity of this herbal plant.

Punicagranatum(Pomegranate):

Figure 5,Fruit of pomegranate plant

Pomegranates are commonly referred as Dadima in Ayurveda or Anar in Hindi are a treasure of numerous nutrients that have been used for health promoting benefits formore than centuries. Pomegranates are commonly known as "blood purifiers" while the daily consumption of pomegranate juice ameliorates blood circulation and purification. The botanical name of pomegranate is Punicagrantus which is a deciduous shrub belonging to pumicaceas family, and it is one of the oldest edible fruits in India (as shown in Figure 5) .They are originated from central Asian countries, Mediterranean area and Middle East. The seed oil of pomegranate is considered as inhibitor of cancerous cell, specially breast cancer and skin cancer. Pomegranate is characterized by several local accessions and cultivars widespread across different countries, each with different bio-agronomic features[29].Having served as a symbolic fruit since ancient times, pomegranate (Punicagranatum) has also gained considerable recognition as a functional food in the modern era and they contain polyphenols, particularly anthocyanins (ATs) and hydrolyzable tannins (HTs), to the health-promoting activities of pomegranate juice and fruit extracts30.Pomegranate contains a large percentage of water and is rich in vitamin C while seeds contain phytoestrogens likes genistein, daidzein, coumestrol.The seeds of pomegranate are enriched with high amountsof anthrcynanin and tannins, including gallagic acid, punicalagicacid, punicalin acid, and punicalagin. Some of the reported studies explained that thered pigmentation of pomegranate is due to anthrocynanins such as delphinidin, pelargonidin, and cyanidin. HT holds the special place for being the mostwidely studied due to the phytoconstituents present in pomegranate, these tannins are grouped into 2 groups such as HT and GT ,based on the different phenolic acids that are esterified to the core cyclic polyol molecule (it is often a glucose molecule)[30].Historically it is mentioned pomegranate is a strong antioxidant property and have different pharmacological action such as antiviral, anti-diabetic, antimicrobial, anti-atherosclerotic, , antiepileptic, antihepatoprotective and other different disease. Sometimes the

consequences of PCOS lead to infertility in females. Here pcos means polycycstic ovarian syndrome, which is defined as a human endocrine disorder feature via the formation of cysts in the ovaries. Women suffering from PCOS have heavy periods, painful period, irregular period, and disturbed menstruation cycle, blotting and acne[31] .There cause could be environmental and genetically, whereas PCOS women have high amount of male hormones known by androgens which obstruct the functionality of ovaries in releasing the eggs process called as ovulation resulting in abnormal menstruation cycles. Studyon phenolic compounds revealed that these compounds have anti-androgenic properties and apply their inhibitory effect on the formation of dihydrotestosterone receptor complexes. The scenario behind the decrease of hormones is due to phytosterols ,a naturally occurring compound in plants similar as cholesterol that basically obstruct the absorption of cholestrerol which corresponds to the elimination of LDL(low density lipid) commonly known as bad cholesterol and trigylcerides and acts a significant role in eliminating of androgen and testosterone hormone. This study was well documented and explained through the obtained results showing the concentration of testosterone, estrogen and andrastenedione in the treated group had a significant increase of steroidal sexual hormone compared to the control group of female wistar rat in animal study[31]. Therefore, it is endorsed to use the pomegranate extract for the treatment and managements of polycystic ovarian syndrome[30].Major biochemical present in pomegranate are fatty acids, tannins, anthocyanins, flavonoids, polyphenols, vitamin a and sugar to larger extent.

- The sweet taste of pomegranate is due to monosaccharides and disaccharides such as glucose, fructose, sucrose, and maltose.
- Along with this, different vitamins are present in the pericarp such as vit B1, B2, B3, C, and beta-carotene.
- Organic acids such as malic acid, oxalic acid, succinic acid, citric acids, and tartaric acid are present.

- Alkaloids such as ellagic acid, Pelletierine, pseudo-pelletierine, and N-methylpelletierine appeared in high amounts.

Phytoestrogen compounds appeared larger in seed oil while ellagic acid and gallic are the chief constituent assembly in pomegranate .The former is a chemical dimeric form of the latterone havingstrong antioxidant activity. Seedsplay significantroleacting as tonicsfor the throatand heart.Pomegranate peelsare highly enriched with glycosides, seem like a lack of estrogenic activity, and are broadly used against dysentery and diarrhoea. Although the pericarp polyphenols and the fermented juice have remarkable estrogenic activity having similarity in estrogenicity compared to estrogen flavanoids. Experiments have mentioned the anticarcinogenesis and antimutagenesis effects of pomegranate could be due to its free radicle scavenging property. Many research proposed pomegranates are strong astringents effects although the presence of high amount of tannin in it. Routine uptake of freshly prepared juice is highly recommended for spontaneous recovery against gall bladder disease. The extracts obtained from leaves are tremendously helpful in maintaining the blood sugar level and reducing the blood pressure to an optimumlevel[31].Luteolin and naringenin are compounds attributing similar activity as hormones secreted during pregnancy .The extracted essential oil of pomegranate seed has inhibitory effects on prostaglandins and leukotrines and seem to have anti-inflammatory activity through suppressing enzymes such as cyclooxygenase, lipoxygenase mediate the occurrence of inflammation.

Cinnamomum zeylanicum (Cinnamon) :

Figure 6 bark of cinnamon plant

The Cinnamon bark has precise species which some of the maximum famous and vital spices used significantly for cooking; however, they are also used conventionally in herbal- based medicine. The bark (Fig 6 is shown above)of various cinnamon species is one of the most important and popular spices used worldwide not only for cooking but also in traditional and modern medicines[32].As the cinnamon consist of pleasant fragrance has a high market value in food industry and pharmaceutical companies for aiding essence and flavor to a variety of food items, bakery item and medicinal formulation. For a long period of time , they have been using it as carminative, analgesic, antifungal, stomachic, antispasmodic, and antiseptic medicinally[33].There are four types of cinnamon bark species available and used widely. Based on the region cinnamons found here is the type given as following:

- True cinnamon or Ceylon cinnamon or Mexican cinnamon (Cinnamomum zeylancium)
- Indonesian cinnamon (cinnamomum Burmanni)
- Vietnamese cinnamon (Cinnamomum Loureiroi)
- Cassia, cinnamon, or Chinese cinnamon (Cinnamomum Aromaticulum)

Cassia bark there are an abundance of chemical constituents as it contains volatile oil, tannins,

sugars, mucilage, and calcium oxalates, whereas cinnamic, aldehydes, hydrocarbons, terpens, eugenol and to a less extent polyphenols and ketones are some of the volatile oil present in it. Additionally, cinnamon contains cinnamyl acetate, eugenol, l-borneol, caryophyllene oxide, b-car- yophyllene, l-bornyl acetate, E-nerolidol, α-cubene, α-terpineol, terpi- nolene, and α-thujene that perform different biological activities[34].Cultivation of cassia are done mainly in geographical areas such as West Indies, Jamaica, Brazil, India and Mauritius. Above all activities cinnamon has one of the most important activity is the enhancement of sexual pleasure due to which it has been under study more than a years[32]. Clearly explained is the major pharmacological activity of cinnamon as an antioxidant, anti- inflammatory, antidiabetic, antimicrobial, anticancer, lipid-lowering, and cardiovascular-disease- lowering compound. In a few recent studies, they have mentioned cinnamon extract may have beneficial activity against hyperlipidemia activity and have proposed that cassia helps against male infertility. Cassia extract restored the damage done in the male reproductive system and infertility. Obesity occurred due to high intake of cholesterol which substantially results into male reproductive dysfunction and infertility. Few of the study on male animals have mentioned and recorded that high fat diet animals have an increase in body weight, high concentration of gonadal fatleading to hypercholestremia, and declined in sperm numbers. C. zeylanicum caused significant increased luteinizing hormone, follicle stimulating hormone, testosterone hormone, and increased activity of Ley dig cells, this effect could be due to the presence of compounds in cinnamon which affect the hypothalamus-pituitary axis and thus increased levels of luteinizing hormone, follicle stimulating hormone, testosterone hormone[34]. In the experiment, the results showed a significant increase of spematogonia, spermatocytes, spermatids, sertoli, and Leydig cells in the treatment groups through which the concentration of testosterone, LH, FSH witnesses that cinnamon increases the sex cells of mice in somniferous tubules[35].

Glycyrrhizaglabra(Liquorice):

Figure 7, Leave of Liquorice plant

Glycyrrhizaglabra Linn (family Fabaceae) is a medicinal plant found in Asia, the Mediterranean, and parts of southern Europe[36].They are common with name such as licorice, liquorice, sweet wood, mulahatti and yastimadhu (Fig as shown in no. 7). The genus Glycyrrhiza (Fabaceae) consists of about 30 species, such as G. glabra, G. uralensis, G. inflata, G. aspera, G. korshinskyi, or G. eurycarpa37.These plants are plentiful phytocompounds, such as glycryrricn, 18-b,flucrrrhetinicacid, glabrin A and B , and isoflavones, that have demonstrated various pharmacological activity[37]. The extract of liquorice contains a compound whose activities are quite similar to ovarian steroid hormones and commonly referred to as a. phytoestrogens36. Ayurveda considered liquorice to be a "rasayana" with implicated use in the treatment of respiratory and digestive disorders[36].Licorice showed estrogenicity by the presence of phytoestrogens such as glabridin found to be the main isoflavan present in gylceraglabra acts as agonist at steroidal estrogenic receptor.Glabridin and 17-beta estradiol have three fused rings of phenanthrene shape and an aromatic ring substituted with a hydroxy group at the para or 3 position[38].The functional group resemblance could be feasible for the binding of glabridin to the same receptor as estradiol and mimeting ovarian hormones. PMS stands for premenstrual syndrome caused due to the increasingratio of estrogento progesterone ratio. Therefore, it acts beneficially via reducing estrogen level and enhancing progesterone levels.Allosteric interaction

occursbetween serotonin and estrogenic or progesterone accomplished byinhibition of serotonin reuptake which leads to the consequenceof depression. Hence,glabridin could be used against menstruation issuessuffering from depression also at the same time.HEK-293 cells have illustrated that isoflavane,glabridin, and 4-O methylglabridin and isoflavaneglabrene inhibited Serotonin reuptake[36]

Conclusions

This study was designed to explore the structure qualitative properties of herbal medicine against severe medical ailments. The traditional medicine system can have more than 1000 of herbal plants reported, but we have examined 7 effective medicinal herbs acting beneficially on against infertility. Furthermore, a systematic and organized study is necessary to investigate additional analysis, identification, characterization, and systemizing more about traditional herbal plants will help in combating in future obstruction and consequences. The Herbal system of medicine in India uses a variety of effective traditional herbs for different severe disorders, among which 7 plant have been studied deeply against infertility. It is suggested that plants-based phytoestrogen acts beneficial in male and female infertility due to different phytocompounds that are biologically active against hormonal distortion .This study showed that these herbs can be used safely for the treatment and cure of diseases such as infertility, menopause, libido, impotence, hormone disturbance, PCOS and PMS.

REFERENCES

1. *Habbema JDF, Collins J, Leridon H, Evers JLH, Lunenfeld B, teVelde ER. Towards less confusing terminology in reproductive medicine: A proposal. Hum Reprod. 2004; 19(7):1497-1501. doi:10.1093/humrep/deh303*
2. *Alahmadi B. Effect of Herbal Medicine on Fertility Potential in Experimental Animals - an Update Review. Mater Socio Medica. 2020;32(2):140. doi:10.5455/msm.2020.32.140- 147*
3. *Fereshteh B, Ali-Reza A, Nastaran M, Mohsen T, Mirhashemi SM. Evaluating the effects of vanadyl sulfate on biomarkers of oxidative stress and inflammation in renal tissue of rats with diabetes type 2. Brazilian J Pharm Sci. 2020;56:1-5. doi:10.1590/s2175-97902019000318586*
4. *Noh S, Go A, Kim D Bin, et al. Withaniasomnifera improves semen quality by regulating reproductive hormone levels and oxidative stress in seminal plasma of infertile males. J Chinese Med Assoc. 2011;9(3):5869-5882. doi:10.1016/j.fertnstert.2009.04.046*
5. *Ahmad MK, Mahdi AA, Shukla KK, et al. Withaniasomnifera improves semen quality by regulating reproductive hormone levels and oxidative stress in seminal plasma of infertile males. FertilSteril. 2010;94(3):989-996. doi:10.1016/j.fertnstert.2009.04.046*
6. *Nasimi R, Azgomi D, Zomorrodi A, et al. Effects of Withaniasomnifera on Reproductive System : A Systematic Review of the Available Evidence. 2018;2018. doi:10.1155/2018/4076430*
7. *Shukla KK, Mahdi AA, Ahmad MK, Shankhwar SN, Rajender S, Jaiswar SP. Mucunapruriens improves male fertility by its action on the hypothalamus-pituitary-gonadal axis. FertilSteril. 2009;92(6):1934-1940. doi:10.1016/j.fertnstert.2008.09.045*
8. *Glazier MG, Bowman MA. A review of the evidence for the use of phytoestrogens as a replacement for traditional estrogen replacement therapy. Arch Intern Med. 2001;161(9):1161-1172. doi:10.1001/archinte.161.9.1161*
9. *Akbaribazm M, Goodarzi N, Rahimi M. Female infertility and herbal medicine: An overview of the new findings. Food SciNutr. 2021;9(10):5869-5882. doi:10.1002/fsn3.2523*
10. *Bhatt KL, Khader A. Role of Ayurveda in the management of Vandhyatvaw .s .r .to Infertility.*
11. *Kumar S, Dobos GJ, Rampp T. The Significance of Ayurvedic Medicinal Plants. J Evidence-Based Complement Altern Med. 2017;22(3):494-501. doi:10.1177/2156587216671392*
12. *Khazaei MRM, Montaseri A, Khazaei MRM, et al. Ayurvedic concepts of female fertility-A Review. IntAyurvedic Herb Med J. 2015;5(1):2313-2320. doi:10.5812/ircmj.17(4)2015.27032*
13. *Shashi a., , S. K. Jain , A. Verma, M. Kumar , A. Mahor MS. P lant profile , phytochemistry (S hatavari): A review and pharmacology of A sparagusracemosus. 2013;3(3):242-251.*
14. *Thakur S, Kaurav H, Chaudhary G. Shatavari (Asparagus Racemosus) - The Best Female Reproductive Tonic. Int J Res Rev. 2021;8(5):73-84. doi:10.52403/ijrr.20210511*
15. *Singh N, Bhalla M, de Jager P, Gilca M. An overview on Ashwagandha: A Rasayana*

(Rejuvenator) of Ayurveda. African J Tradit Complement Altern Med. 2011;8(5 SUPPL.):208-213. doi:10.4314/ajtcam.v8i5S.9

16. *Jahan N, Majeedi S, Road MM. Medicinal properties ,phytochemistry and pharmacology of Withaniasomnifera : an important drug of Unani Medicine Medicinal properties , phytochemistry and pharmacology of Withaniasomnifera : an important drug of Unani Medicine. 2016;(January):7-12.*
17. *Boruah JJ, Kalita D, Das SP, Paul S, Islam NS. Polymer-anchored peroxo compounds of vanadium(V) and molybdenum(VI): Synthesis, stability, and their activities with alkaline phosphatase and catalase. Inorg Chem. 2011;50(17):8046-8062. doi:10.1021/ic200368g*
18. *Of E, Trials C, The IN, et al. Original Research Paper Medical Science DISORDERS AND CANCER TREATMENT USING ALKALOIDS , STEROIDAL Prof . Dr .G .Manoj KEYWORDS : 2017;(10):33-36.*
19. *Kumar V, DeyA, Hadimani MB, Marcovic T, Emerald M. Chemistry and pharmacology of withaniasomnifera: An update. Tang [Humanitas Med. 2015;5(1):1.1-1.13. doi:10.5667/tang.2014.0030*
20. *J.M. Saeid AKS and MMM. Effect of Ginger extract on semen of broilers.pdf. Int J Poult Sci. 2011;10(8):629-633.*
21. *Anh NH, Kim SJ, Long NP, et al. Ginger on Human Health : A Comprehensive Controlled Trials. Nutrients. 2020;12(1):1-28.*
22. *Prasad S, Tyagi AK. Ginger and its constituents: Role in prevention and treatment of gastrointestinal cancer. Gastroenterol Res Pract. 2015;2015. doi:10.1155/2015/142979*
23. *Xu Y, Yang Q, Wang X. Efficacy of herbal medicine (cinnamon/fennel/ginger) for primary dysmenorrhea: a systematic review and meta-analysis of randomized controlled trials. J Int Med Res. 2020;48(6). doi:10.1177/0300060520936179*
24. *Yılmaz N, Seven B, Timur H, et al. Ginger (zingiberofficinale) might improve female fertility: A rat model. J Chinese Med Assoc. 2018;81(10):905-911. doi:10.1016/j.jcma.2017.12.009*
25. *Noh S, Go A, Kim D Bin, Park M, Jeon HW, Kim B. Role of antioxidant natural products in management of infertility: A review of their medicinal potential. Antioxidants. 2020;9(10):1-65. doi:10.3390/antiox9100957*
26. *Mahboubi M. Foeniculum vulgare as Valuable Plant in Management of Women's Health . J Menopausal Med. 2019;25(1):1. doi:10.6118/jmm.2019.25.1.1*
27. *Shabanian S, Bahmani M, Asadi-Samani M. The medicinal plants effective on female hormones: A review of the native medicinal plants of Iran effective on estrogen, progesterone, and prolactin. J Chem Pharm Sci. 2016;9(3):1270-1276.*
28. *Khazaei M, Montaseri A, Khazaei MR, Khanahmadi M. Study of foeniculum vulgare effect on folliculogenesis in female mice. Int J FertilSteril. 2011;5(3):122-127.*
29. *Tahvilzadeh M, Hajimahmoodi M, Rahimi R. The Role of Date Palm (Phoenix dactylifera L) Pollen in Fertility: A Comprehensive Review of Current Evidence. J Evidence-Based Complement Altern Med. 2016; 21(4):320-324. doi:10.1177/2156587215609851*
30. *Wu S, Tian L. Diverse phytochemicals and bioactivities in the ancient fruit and modern functional food pomegranate (punicagranatum). Molecules. 2017;22(10). doi:10.3390/molecules22101606*
31. *Jahromi HK, Tavakol E, Shafiei N, Mohammad P. The Effect of Pomegranate Juice*

Extract on Hormonal Changes of Female Wistar Rats Caused by Polycystic Ovarian Syndrome The Effect of Pomegranate Juice Extract on Hormonal Changes of Female Wistar Rats Caused by Polycystic. 2015 ;(December). doi:10.13005/bpj/849

32. *Rao PV, Gan SH. Cinnamon: A multifaceted medicinal plant. Evidence-based Complement Altern Med. 2014; 2014. doi:10.1155/2014/642942*
33. *Jaafarpour M, Hatefi M, Najafi F, Khajavikhan J, Khani A. The Effect of Cinnamon on Menstrual Bleeding and Systemic Symptoms with Primary Dysmenorrhea. Iran Red Crescent Med J. 2015; 17(4). doi:10.5812/ircmj.17(4)2015.27032*
34. *Arisha SM, Sakr SA, Abd-Elhaseeb FR. Cinnamomumzeylanicum alleviate testicular damage induced by high fat diet in albino rats; histological and ultrastructural studies. Heliyon. 2020;6(11):e05584. doi:10.1016/j.heliyon.2020.e05584*

35. Jahromi VH, Parivar K, Forozanfar M. The Effect of Cinnamon Extract on Spermatogenesis Hormonal Axis of Pituitary Gonad in Mice. Iran J ApplAnim Sci. 2011;1(2):99-103.
36. Saxena S. Glycyrrhizaglabra: Medicine over the millennium. Indian J Nat Prod Resour. 2005;4(5):358-367.
37. Pastorino G, Cornara L, Soares S, Rodrigues F, Oliveira MBPP. Liquorice (Glycyrrhizaglabra): A phytochemical and pharmacological review. Phyther Res. 2018;32(12):2323-2339. doi:10.1002/ptr.6178
38. Poh MSW, Yong PVC, Viseswaran N, Chia YY. Estrogenicity of glabridin in Ishikawa cells. PLoS One. 2015;10(3):1-12. doi:10.1371/journal.pone.0121382