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## **SECONDARY METABOLITE PRODUCTION FROM MEDICINAL PLANTS FOR THE TREATMENT OF FEMALE INFERTILITY: A REVIEW**

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**ABSTRACT:** Folk medicines play an important role to cure human diseases. In India, there are various system of medicinal practices like Ayurveda, Unani, Homoeopathy, Allopathy, and Siddha etc. The common female gynecological disorders are such as amenorrhea, dysmenorrheal, leucorrhea, menometrorrhagia, metrorrhagia, oligomenorrhea, hemorrhage, gonorrhea, syphilis which leads to the female infertility. Plant tissue culture technique occupies the key role in the enhancement of secondary metabolites production by using different elicitors which yield an interesting product of plant constituents leads to second green revolution. In this review, updated information is gathered on scientifically proven medicinal plants used for the treatment of female infertility. The aim of this review is to highlight on various plant drugs which is enhanced by different elicitors that may help investigators to identify suitable medicinal plants to cure female infertility.

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**KEYWORDS:** Secondary metabolites, Infertility, Gynecological disorder, Elicitors.

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### **1.INTRODUCTION**

According to the United Nations Population Division, “Fertility is the natural human capability of producing offspring [1]. According to recent studies by the World Health Organization (WHO), approximately 8-10% of couples are facing some kind of infertility problems [2]. Infertility is an inability to conceive and produce the child. Eight out of every ten women trying for a baby, will fall pregnant within the first six months [3] and the reasons behind it are such as weight, diet, smoking,

other substance abuse, environmental pollutants, infections, medical conditions, medications, the quantity and quality of the sperm and family medical history could affect conception in couples [1]. Assisted Reproductive Technology has been carried out such as IVF, ICSI but common people cannot afford the cost of such procedures [3]. There is various system of medicine like Ayurveda, Unani, Homoeopathy, Allopathy, Siddha and physiotherapy with acupuncture are been effective to enhance the pregnancy [4]. Approximately 90% of the ingredient used in Ayurveda, Unani, Siddha and Homeopathy medicine are plant based over in modern Allopathic medical system has 25% of its formulation from herbal medicine [5]. Hence, the use of herbal medicine is increasing day by day, due to the concept of natural drugs are cheaper with no fear of any side effects [6,7.8.9]. Due to over exploit of traditional medicinal plants, low yielding and loss of growth habitat, the genetic biodiversity of traditional medicinal plants is under a continuous threat of extinction [10]. Because of this there is need to provide alternate methods to propagate, cultivate and conserve the common as well as endangered medicinal plants and also to maintain the balance of eco-system [5].

**Table 1: Significance of medicinal plants used to cure female infertility**

Common name	Botanical name	Family	Parts used	Activities	References
Guyebabla	<i>Acacia farnesiana</i> Willd. (T)	Mimosaceae	Bark	To cure leucorrhea and menorrhagia	[4]
Satamuli	<i>Asparagus racemosus</i> Willd.(H)	Liliaceae	Root	To cure leucorrhea and abnormal discharges of semen.	[4,11]
Neem	<i>Azadirachta indica</i> A.Juss (T)	Meliaceae	Stem, bark and fruit	To control menstrual cycle and also help in follicular	[4,12]
Bhuikumra	<i>Ipomoea paniculata</i> L.R.Br	Convolvulaceae	Root	To cure menorrhagia, gonorrhoea, and syphilis. It also acts as an aphrodisiac.	[4,11]
Kemanch	<i>Mucuna pruriens</i> (Linn.) DC (C)	Fabaceae	Seed	To cure leucorrhoea and menorrhagia. And also effective both for men and women in case of impotency	[4,11]

Bhuiamala	<i>Phyllanthus niruri</i> Hoof.f. non Linn (H)	Euphorbiaceae	Whole plant	To cure menorrhagia and gonorrhoe	[4]
Pila berela	<i>Sida acuta</i> Burm. f.(S)	Malvaceae	Leaf, root ,seed	To cure leucorrhoea and gonorrhoea	[4,11]
Aswagandha	<i>Withania somnifera</i> Dunal. (H)	Solanaceae	Root	To cure leucorrhoea , menstrual troubles and very effective in case of female	[4]

There are two main approaches in the conservation of medicinal plants – in-situ and ex-situ conservation. In *in-situ* conservation of plants in their natural habitats, while in *ex-situ* methods, plant biotechnology offers the most appropriate way of conservation and large-scale production of plants using plant tissue culture techniques. Plant tissue culture is the science & art of growing plant cell, tissues, organs or whole plants on semi-solid or in liquid synthetic nutrient media under aseptic and controlled environmental condition. Higher plants are valuable source for natural drugs, which include flavours, fragrances, essential oils, phytochemical compounds collectively referred as Secondary metabolites [13]. This review, highlights the important medicinal plants and their drugs which help to cure female infertility and conserve by using the advanced biotechnological methods. Plant cell and organ cultures are important techniques to obtain valuable metabolites through callus and cell suspension culture. In vitro propagation via indirect organogenesis or embryogenic calli is an important for isolation of active secondary metabolites which are valuable sources of pharmaceutical industries. Plant cell cultures have great advantages in biosynthesis and metabolite production from a very small amount of plant material leads to develop a higher amount of natural drugs for herbal medicines in short period of time. Cell suspension culture offer an effective mechanism when incorporated with elicitors into the cell which can lead to production of novel natural drugs not previously found in whole plants [13]. Elicitors is a stress agent which enhances the production of secondary metabolites in particular tissue, organ and cells. There are two types of elicitors, biotic (biological origin) and abiotic (non-biological origin) [14,15]. Biotic elicitors are polysaccharide, yeast extract, bacterial and fungal [16] while abiotic elicitors are divided into three group chemicals (heavy metals, mineral salts and gaseous toxins), Physical (light, thermal, osmotic, drought and salt stress), and Hormonal (salicylic acid, jasmonic acid, sucrose etc.). In the recent developments, elicitors have opened a new avenue for the production of secondary metabolite compounds [17].

**Table 2: Different elicitors used in production of crucial secondary metabolites from some important medicinal plants**

Sr No.	Plant Names	Explants	Elicitors	Compounds	References
1	<i>Azadirachta indica</i> A.Juss (T)	Seeds	Glucose, Hydrolyzed casein and Methyl jasmonate	Azadirachtin	[18]
2	<i>Azadirachta indica</i> A.Juss (T)	Seeds	Cyanobacteria: <i>Anabaena sp.</i> , <i>Nostoc carneum</i> ,	Azadirachtin	[19]
3	<i>Azadirachta indica</i> A.Juss (T)	Shoot segments	Salicylic acid, Jasmonic acid, Cadmium chloride and Sodium chloride	Azadirachtin	[20]
4	<i>Azadirachta indica</i> A.Juss (T)	Hairy root	<i>Claviceps purpurea</i>	Azadirachtin	[21]
5	<i>Azadirachta indica</i> A.Juss (T)	Seeds	Salicylic acid, Chitosan, Jasmonic acid, Methyl jasmonate, Yeast extract	Azadirachtin	[22]
6	<i>Asparagus racemosus</i> Willd.(H)	Nodal segments and roots	<i>Fusarium oxysporium</i> and <i>Rhizopus stolonifera</i> UV and Salicylic acid	Shatavarins	[23]
7	<i>Asparagus racemosus</i> Willd.(H)	Nodal segments	UV-B	Shataverins	[24]
8	<i>Mucuna pruriens</i> (Linn.) DC (C)	Seeds	Methyl jasmonate, Chitin, Pectin, Yeast extract	L-Dopa (3, 4-dihydroxy-L-phenylalanine)	[25]
9	<i>Withania somnifera</i> Dunal. (H)	Roots	Cadmium chloride, Aluminum chloride and Chitosan,	Withanolides	[26]
10	<i>Withania somnifera</i>	Cell	pH and Sucrose	Withanolide A	[27]

	Dunal. (H)	suspension			
11	<i>Withania somnifera</i> Dunal. (H)	Hairy root	pH	Withanolide A	[28]
12	<i>Withania somnifera</i> Dunal. (H)	Hairy root	Methyl jasmonate and Salicylic acid	Withanolide A, Withanone, and Withaferin A	[29]
13	<i>Withania somnifera</i> Dunal. (H)	Leaves	Calcium chloride, Copper sulphate and Cinnamic acid, <i>Fusarium solani</i> , <i>Alternaria alternate</i> and <i>Verticillium dahliae</i>	Withaferin A	[30]
14	<i>Withania somnifera</i> Dunal. (H)	leaf, cotyledon and internode explants	Aluminium chloride, Chitosan	withanolides	[31]
15	<i>Withania somnifera</i> Dunal. (H)	leaf	Methyl jasmonate and Salicylic acid	withanolide A, withanolide B, withaferin A, and withanone, 12-deoxy withastramonolide, withanoside V, and withanoside IV	[32]
16	<i>Withania somnifera</i> Dunal. (H)	leaf	Chitosan, Nitric oxide, Jasmonic acid, Acetyl salicylic acid	withaferin A, withanolide A	[33]

## 2. CONCLUSION

Greater efforts are required to document this traditional knowledge of local medicinal plants which are safe, less costly and eco-friendly method for the treatment of gynecological disorders. There is a scope for the large-scale production of secondary metabolites available from these plants by using the elicitors as an agent. Biotic and abiotic elicitors enhanced the secondary metabolites production

for isolation of bioactive compound from important medicinal plants to cure gynecological disorders. One of the main problems for secondary metabolites production is the limited knowledge of biosynthetic pathways and their controlling enzymes and genes regulation. As the little information about pathways of these plants is needed to understand, for isolation of large amount of natural drugs, to treat many gynecological disorders.

### CONFLICT OF INTEREST

The authors report no conflicts of interest.

### REFERENCES

- 1 Karamchedu S. Women's Infertility-An Ayurvedic Perspective,2013. pp.7.
- 2 Roupa Z, Polikandrioti M, Sotiropoulou P, Faros E, Koulouri A, Wozniak G, Gourni M. Causes of infertility in women at reproductive age. Health Science Journal. 2009 ;3(2).
- 3 Gaware, V. M., Parjane, S. K., Merekar, A. N., Pattan, S. R., Dighe, N. S., Kuchekar, B. S., & Godge, R. K. Female infertility and its treatment by alternative medicine: a review. J Chem Pharm Res, 2009 ;1(1), 148-162.
- 4 Tripathi R, Dwivedi SN, Dwivedi S. Ethno-medicinal plants used to treat gynecological disorders by tribal people of Madhya Pradesh, India. International Journal of Pharmacy and Life Sciences (IJPLS). 2010;1(3):160-9.
- 5 Washimkar VB, Shende M. Plant tissue culture in herbal medicinal plants–review. Ejpmr,2016; 3(11),696-699.
- 6 Memon AR, Randhawa MA, Arain AA. Herbal medicine use: knowledge and attitude in patients at tertiary care level in northern border region of Kingdom Saudi Arabia. JSZM2017;8(3):1241-1244
- 7 Tangkiatkumjai M, Boardman H, Praditpornsilpa K, Walker DM. Prevalence of herbal and dietary supplement usage in Thai outpatients with chronic kidney disease: a cross-sectional survey. BMC complementary and alternative medicine. 2013;13(1):153.
- 8 Gawde SR, Shetty YC, Pawar DB. Knowledge, attitude, and practices toward ayurvedic medicine use among allopathic resident doctors: A cross-sectional study at a tertiary care hospital in India. Perspectives in clinical research. 2013;4(3):175.
- 9 Chaudhari VM, Avlaskar AD Role of Shivlingi in Infertility. J Homeop Ayurv Med.2013; 2: 141.
- 10 Chaturvedi M, Chaturvedi AK. Concept of Plant Tissue Culture in Ancient Science WSR Vriksha-Ayurveda. Imperial Journal of Interdisciplinary Research. 2016; 20;3(1)
- 11 Das DC, Sinha NK, Das M. The use of medicinal plants for the treatment of gynaecological disorders in the eastern parts of India. Indian J Obstet Gynecol Res. 2015 ;2(1):16-27.
- 12 Roop JK, Dhaliwal PK, Guraya SS. Extracts of *Azadirachta indica* and *Melia azedarach* seeds Inhibit folliculogenesis in albino rats. Brazilian Journal of Medical and Biological Research. 2005;38(6):943-7.

- 13 Razdan MK. Introduction to plant tissue culture. Science Publishers; 2003.
- 14 Gorelick J, Bernstein N. Elicitation: An underutilized tool in the development of medicinal plants as a source of therapeutic secondary metabolites. In *Advances in agronomy* 2014; 124: 201-230. Academic Press.
- 15 Namdeo AG. Plant cell elicitation for production of secondary metabolites: a review. *Pharmacogn Rev.* 2007; 1;1(1):69-79.
- 16 Ramirez-Estrada K, Vidal-Limon H, Hidalgo D, Moyano E, Golenioswki M, Cusidó RM, Palazon J. Elicitation, an effective strategy for the biotechnological production of bioactive high-added value compounds in plant cell factories. *Molecules.* 2016;21(2):182.
- 17 Naik PM, Al-Khayri JM. Impact of abiotic elicitors on in vitro production of plant secondary metabolites: a review. *J Adv Res Biotech.* 2016;1(2):7.
- 18 Rodrigues M, Festucci-Buselli RA, Silva LC, Otoni WC. Azadirachtin biosynthesis induction in *Azadirachta indica* A. Juss cotyledonary calli with elicitor agents. *Brazilian Archives of Biology and Technology.* 2014; 57(2):155-62.
- 19 Devi BP, Vimala A, Sai I, Chandra S. Effect of cyanobacterial elicitor on neem cell suspension cultures. *Indian Journal of Science and Technology.* 2008;1(7):1-5.
- 20 Garoosi G, Gholami B, Hosseini R. Considerable Azadirachtin Production in Neem Cell Culture under Abiotic Elicitor Induction. *Journal of Medicinal Plants and By-products.* 2016; 2: 195-204
- 21 Satdive RK, Fulzele DP, Eapen S. Enhanced production of azadirachtin by hairy root cultures of *Azadirachta indica* A. Juss by elicitation and media optimization. *Journal of Biotechnology.* 2007;128(2):281-9.
- 22 Prakash G, Srivastava AK. Statistical elicitor optimization studies for the enhancement of Azadirachtin production in bioreactor *Azadirachta indica* cell cultivation. *Biochemical Engineering Journal.* 2008;40(2):218-26.
- 23 Pise M, Rudra J, Begde D, Bundale S, Nashikkar N, Upadhyay A. Elicitor induced production of Shatavarins in the cell cultures of *Asparagus racemosus*. *Indian J Plant Sci.* 2013; 2:100-6.
- 24 Pise M, Upadhyay A. Medium alkalization and induction of phenylalanine ammonia lyase are involved in the early responses of UV-B mediated hyperproduction of shatavarin. *Int.J.Curr.Res.Aca.Rev.*2015;5(3):153-160
- 25 Raghavendra S, Ramesh CK, Kumar V, Moinuddin Khan MH. Elicitors and precursor induced effect on L-Dopa production in suspension cultures of *Mucuna pruriens* L. *Frontiers in Life Science.* 2011;5(3-4):127-33.
- 26 Sivanandhan G, Selvaraj N, Ganapathi A, Manickavasagam M. Enhanced biosynthesis of Withanolides by elicitation and precursor feeding in cell suspension culture of *Withania somnifera* (L.) Dunal in shake-flask culture and bioreactor. *PLoS One.* 2014 ;9(8):e104005.

- 27 Nagella P, Murthy HN. Establishment of cell suspension cultures of *Withania somnifera* for the production of withanolide A. *Bioresource technology*. 2010 ;101(17):6735-9.
- 28 Praveen N, Murthy HN. Synthesis of withanolide A depends on carbon source and medium pH in hairy root cultures of *Withania somnifera*. *Industrial crops and products*. 2012;35(1):2413.
- 29 Sivanandhan G, Dev GK, Jeyaraj M, Rajesh M, Arjunan A, Muthuselvam M, Manickavasagam M, Selvaraj N, Ganapathi A. Increased production of withanolide A, withanone, and withaferin A in hairy root cultures of *Withania somnifera* (L.) Dunal elicited with methyl jasmonate and salicylic acid. *Plant Cell, Tissue and Organ Culture (PCTOC)*. 2013 ;114(1):121-9.
- 30 Chitturi D, Venisetty RK, Molmoori RK, Kokate CK, Apte SS. Enhanced bioproduction of withaferin A from suspension cultures of *Withania somnifera*. *Annals of Biological Research*. 2010;1(2):77-86.
- 31 Sivanandhan G, Arun M, Mayavan S, Rajesh M, Mariashibu TS, Manickavasagam M, Selvaraj N, Ganapathi A. Chitosan enhances withanolides production in adventitious root cultures of *Withania somnifera* (L.) Dunal. *Industrial crops and products*. 2012;37(1):124-9.
- 32 Sivanandhan G, Arun M, Mayavan S, Rajesh M, Jeyaraj M, Dev GK, Manickavasagam M, Selvaraj N, Ganapathi A. Optimization of elicitation conditions with methyl jasmonate and salicylic acid to improve the productivity of withanolides in the adventitious root culture of *Withania somnifera* (L.) Dunal. *Applied biochemistry and biotechnology*. 2012;168(3):681- 96.
- 33 Doma M, Abhayankar G, Reddy VD, Kishor PB. Carbohydrate and elicitor enhanced withanolide (withaferin A and withanolide A) accumulation in hairy root cultures of *Withania somnifera* (L.). *Indian Journal of Experimental Biology*. 2012;50:484-490.