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Herbal Nanoparticles to Control Fertility and Regulation: A Review

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ABSTRACT: Nowadays rapidly and continuously increasing population is creating a significant problem with adverse social, economic, personal, and health outcomes and environmental damage. There are many options available in the market for birth control. Due to the side effects of allopathic or synthetic medicine, herbal medicines are becoming popular day by day since herbal drugs are found safe, economical, and readily available for therapeutic uses. Medicinal plants are regarded as rich resources of traditional medicines; many modern medicines are produced from these plants. The usefulness of herbal medicines can be increased with the help of nanoparticles. A nanoparticle can be defined as a particle of matter that is between 1- 100 nanometers in diameter. Nanoparticles have several properties that distinguish them from bulk materials simply by size, chemical reactivity, absorption, and biological mobility. Herbal nanoparticles are also used in anticancer, anti-diabetic, antimicrobial and antioxidant drugs. Plants have various metabolites that can cause potent antifertility and fertility. This is high time when active components of herbal plants should be further investigated for their antifertility activity. This review aims to provide glimpses and emphasize the importance of herbal nanoparticles in fertility control.

Keywords: Population, nanoparticles, plants, antifertility, anticancer.

I. INTRODUCTION

The world population is growing in an uncontrolled manner. The continued rise in population is a major concern in both developed and developing countries today. It is expected that the world population will reach more than 11 billion by 2050 (Census of India, 2011). The current average population rise is approximately 81 million people per year, and the present world population is 8 billion (World population clock, 2022). Among developing countries, India is highly populated and predicted to reach approx. 9.2 billion by the year 2050. The rapidly increasing human population leads to increased demands for natural resources and creates pressure since resources are limited [7,70].

Particularly in growing countries like India, overpopulation is a critical matter because it has many fatal effects –

- Degradation of environment and natural resources
- Conflicts and wars
- Rise in unemployment
- High cost of living
- Malnutrition and starvation
- Water shortage
- Lower life expectancy
- Extinction of wildlife
- Faster climate change [69]

To control population exploitation and its detrimental impacts, contraception is an essential measure [14]. The available modern methods to control fertility in males and females are as follows (Fig. 1) [68].

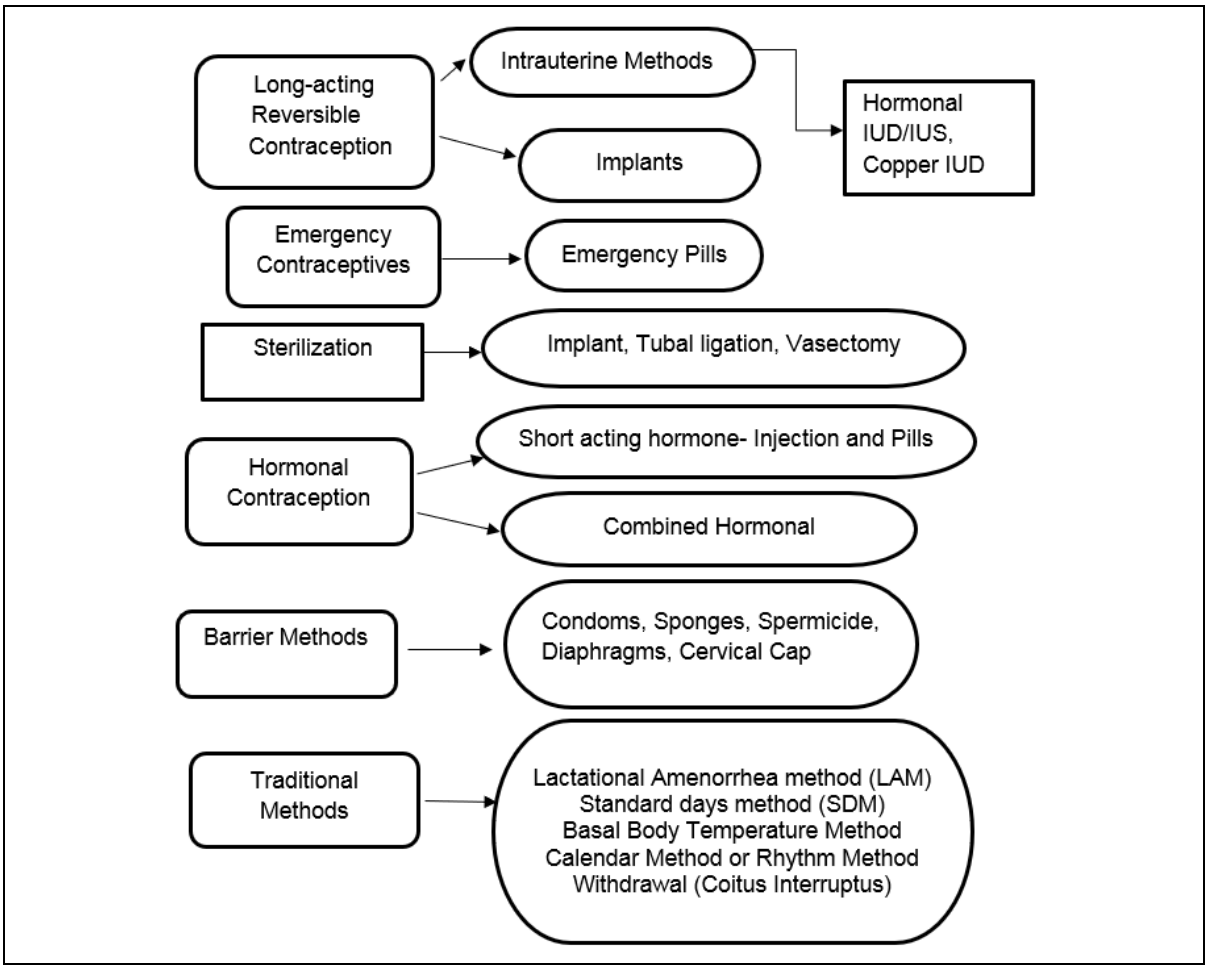

Fig. 1. Modern contraceptive methods used by men and women to control fertility (Curtsy WHO).

A. Need for Herbal contraceptives

Contraceptive devices, hormonal and chemical contraceptives have many adverse effects on human health like irregular menstrual cycle, amenorrhea, hormonal imbalance, obesity, cholelithiasis, gastric dysfunction, carcinoma of breast and cervix, metabolic disorder, asthma, thromboembolism etc. [14, 8]. They are also expensive, with a high failure rate [5, 31]. Because of better acceptability by the human body and lesser side effects, plant-based herbal medicines are a better contraceptive option [18]. Plants have many valuable elements like flavonoids, terpenes, tannins, quinines, diterpenoids and lactones that have an antifertility effect on both male and female reproductive systems. In India, numerous plants have been reported with antifertility activity [70].

B. Plants with antifertility activity

Since ancient times medicinal plants have been used in household remedies to regulate the birth rate and fertility. WHO established seven centres in six countries around the world to explore plants and their products to evaluate antifertility and fertility-regulating effects in animals. Several plants and their products have also been used in modern pharmacopoeia to enhance fertility and check fertility potential in humans [13] (Table 1). Ethanolic extracts of many plants like Citrullus, Euphorbia, Martynia, Solanum and Withania exhibit contraceptive activity in rats [26].

1. Anti-implantation activity

- The plant *Allium cepa* belongs to the family Amaryllidaceae, also known as onion. It contains many chemical compounds like kaempferol, β-sitosterol, ferulic acid, and myristic acid. Its antifertility activity was observed in rats [62].
- The plant *Ricinus communis* belongs to the family Euphorbiaceae and is commonly known as castor oil plant. Its chemical composition is ricinine and isoquinoline. This activity was observed in rats and rabbits [42].
- The plant *Rubia cordifolia* belongs to the family Rubiaceae, also known as Indian

madder. It includes chemical compounds like munjistin, purpurin, and pseudopurpurine [34].

2. **Abortification activity**

- The plant *Trianthema portulacastrum* belongs to the family Aizoaceae, commonly known as Horse purslane. It contains many chemical compounds like alkaloids, flavonoids, saponins, phenolic compounds and terpenoids. This activity of the plant observed in rats [14].
- The plant *Balanites roxburghii* belongs to the family Zygophyllaceae, commonly known as Ingudi, have many chemical components- alkaloids, saponins, tannins, flavonoids, phenolic compounds, gum and mucilage, exhibits abortifacient effects *in vitro* [55].
- The plant *Cannabis sativa* belongs to the family Cannabinaceae, is commonly known as Hemp. Its chemical composition is flavonoids, phenolic compounds, alkaloids, steroids, saponines, terpenoids, tannins, and reducing sugar. Abortification activity of this plant was observed in rats [71].

3. **Antispermatogenic activity**

- The plant *Plumbago zeylanica* belongs to the family Plumbaginaceae, is commonly known as Chitrak. It contains many chemical compounds like Plumbagin, isoshinanolone, trans-cinnamic acid, vanillic acid, beta-sitosterol, 4-hydroxy benzaldehyde and plumbagic acid. This plant's effect on male fertility was observed in rats [41].
- The plant *Piper nigrum* belongs to the family Piperaceae, commonly known as black pepper. It contains many chemical compounds- thujone, piperettine, piperolin A, piperolin B, terpene, volatile oil, starch, piperin, calcium, phosphorus, iron, thiamine, riboflavin, nicotinic acid, vitamin C, carotene, piperidine. Antifertility activity of this plant was observed in mice [37].
- The plant *Azadirachta indica* belongs to the family Meliaceae, commonly known as Neem. It contains many chemical compounds- margosic acid, azadirachtin, polysaccharides, nimbine, nimbidinate, nimbidol, nimbidin. The study of this activity was performed in rats [13].

4. **Anti-ovulation activity**

- The plant *Polygonum hydropiper* Linn belongs to the family Polygonaceae, is also known as Marsh pepper. It contains many chemical compounds- formic acid, acetic acid, beldianic acid, tannin, essential oil, and oxy methyl-anthraquinones. Kapoor *et al.,* observed this activity in rabbits [17].

5. **Anti-androgenic activity**

- The plant *Tropaeolum majus* L. belongs to the family Tropaeolaceae, is commonly known as Indian cress. It contains many chemical compounds- fatty acids, benzyl isothiocynate, flavonoids, glucosinolates, tetra-cyclic triterpenes. Lourenco *et al* observed this activity *in vivo* [24].
- The plant *Caesalpinia bonducella (Roxb.)* belongs to the family Caesalpiniaceae, is also called Sagar Gota. It contains many chemical compounds like β- caesalpin, citrulline, bonducellin, stearic acid, palmitic acid, arginine and aspartic acid. The anti-androgenic activity of this plant was observed in rats [61].
- The plant *Withania somnifera* belongs to the family Solanaceae, is commonly known as Ashwagandha. Its main phytochemical is withanoid. The activity of this plant was observed in male rats [27, 28].

Table 1: List of plants with potential antifertility activity.

Plant name	Common name	Family	Part used	Activity	References
Abrus precatorius	Goonj	Fabaceae	Seed	Contraception	[40]
Achyranthus aspera	Aaghada	Amranthaceae	Root	Antiimplantation	[40]
Artemisia vulgaris	Mugwort	Asteraceae	Leaf	Antiimplantation	[45]
Caesalpinia Bonducella	Fever nut	Caesalpiniacceae	Seed	Antispermatogenic	[63]
Carica papaya	Papaya	Caricaceae	Seed	Abortifacient	[7, 35]
Cassia tora	Chakvat	Fabaceae	Seed & Stem	Antiandrogenic	[19]
Crataeva nurvala	Varuna	Capparidaceae	Stem	Antioestrogenic	[40]

Crocus sativus	Saffron	Iridaceae	Flower	Antiimplantation	[72]
Crotalaria juncea Linn.	Sunn hemp	Asteraceae	Seed	Antispermatogenic	[21]
Ficus religiosa	Peepal	Moraceae	Fruit	Antiimplantation	[48, 16]
Gloriosa superba Linn.	Langli	Colchicaceae	Root	Abortifacient	[30]
Jatropha variegata	Ebki shrub	Euphorbiaceae	Fruit	Abortifacient	[4]
Maytenus emargineta	Kankhera	Celastraceae	Fruit	Contraceptive	[10]
Michelia champaca	Champa	Magnoliaceae	Leaf	Antiimplantation	[54]
Moringa oleifera	Drumstick Tree	Moringaceae	Leaf	Antiimplantation	[1, 29]
Musa paradisiaca L.	Banana	Musaceae	Stem	Antiovulatory	[57]
Ocimum gratissimum	Clove basil	Lamiaceae	Leaf	Antispermatogenic	[25]
Piper betle	Paan	Piperaceae	Petiole	Antiestrogenic	[44]
Piper nigrum	Black pepper	Piperaceae	Fruit	Antispermatogenic	[54]
Plumbago rosea	Rakta Chitrak	Plumbaginaceae	Leaf	Antiovulatory	[49]
Rhodomyrtus tomentosa	Haramonting	Myrtaceae	Leaf	Antispermatogenic	[56]
Tecoma stans	Yellow bells	Bignoniaceae	Leaf	Antispermatogenic	[59]
Tecomella undulata	Rohida	Bignoniaceae	Leaf	Antispermatogenic	[58]
Trigonella foenum-graecum	Fenugreek	Leguminosae	Seed	Antispermatogenic	[51]
Trillium govanianum	Nag Chhatri	Melanthiaceae	Bark	Abortifacient	[47,53]
Vitex negundo	Nirgundi	Lamiaceae	Stem	Spermicidal	[64]

C. Uses of herbal nanoparticles

In the recent past, nanoparticles have been the focal point of research because of their engrossing electronic, optical, and chemical properties and advantageous bio-medical applications [52]. Nanoparticles are molecules with less than 100 nm diameter and can be used for herbal drug delivery in reproductive biology [43]. Hurdles faced by the use of herbal medicine have been overcome using herbal nanoparticles [6]. Herbal nanoparticles are more useful than an herbal extract because of the following reasons (Table 2).

- They decrease the dose amount of the drug [53].
- Because of their small size, nanoparticles show better incorporation in cellular and physiological processes without disturbing the standard biological system [43].
- Nanoparticles have high loading capacity, so they deliver a high amount of drugs to targeted sites [3].
- Nanoparticles increase the stability of drug/proteins against enzymatic degradation.
- Nanoparticles as an effective stabilizing agent [32].
- Nanoparticles need no additional capping agent because green synthesis provides stability [52].
- Green synthesis of nanoparticles is a simple and low-cost procedure [36].
- Nanoparticles with plant extract are nature friendly and free from toxic chemicals [73].
- Nanoparticles can cross barriers like the acidic pH of the stomach, and the metabolism of the liver, so nanoparticles with plant extracts can carry an optimal amount of the drug to their site of action [39].

Table 2: List of herbal nanoparticles with their medicinal activities.

Botanical Name	Family	Part used	Nanoparticle	Size (nm)	Uses	Reference
Ammannia baccifera	Lythraceae	Aerial part	Ag	10-30	Antimalarial	[60]
Azadirachta indica	Meliaceae	Leaf	Ag	90.13	Insecticides	[22]
Bergenia ciliata	Saxifragaceae	Rhizome	ZnO	30	Antibacterial, Anticancer	[15]
Borago officinalis	Boraginaceae	Leaf	Ag	30-80	Anticancer, Antibacterial	[50]
Cannabis sativa	Cannabaceae	Leaf	Au	18.6	Anti-acute leukaemia	[9]
Carica papaya	Caricaceae	Seed	Au	7-16	Antispermatogenic	[38]
Cocos nucifera,	Arecaceae	Inflores -cence	Ag	22	Insecticides	[22]
Curcumae kwangsiensis	Zingiberaceae	Leaf	Au	8-25	Antiovarian cancer	[12]
Eclipta prostrata,	Asteraceae	Leaf	Ag	35-60	Insecticides	[22]
Jurinea dolomiaea	Asteraceae	Leaf& Root	Ag	28& 40	Antioxidant, Anticancer	[2]
Laurus nobilis	Lauraceae	Leaf	ZnO	20-30	Antibacterial	[11]
Mentha piperita	Lamiaceae	Leaf	Ag	35	Antimicrobial	[20]
Moringa oleifera	Moringaceae	Leaf	Ag	19-24	Anti-arthritic	[65]
Ocimum americanum	Lamiaceae	Leaf	ZnO	50	Anticancer, Antimicrobial	[67]
Petiveria alliacea	Phytolaccaceae	Leaf	Ag	16.70-33.74	Antioxidant, Antimicrobial	[23]
Plumeria alba	Apocynaceae	Flower	Ag	36.19	Antioxidant	[33]
Psoralea corylifolia	Fabaceae	Seed	Ag	18	Antidiabetic	[46]
Red ginseng	Araliaceae	Root	Ag& Au	83 & 183	Antimicrobial	[43]
Salvinia molesta	Salviniaceae	Leaf	Ag	10	Antimicrobial	[66]
Vaccinium arctostaphylus	Ericaceae	Fruit	ZnO	8-20	Antidiabetic	[3]

FUTURE SCOPE

The main aim of this review is to focus on developing an herbal drug for fertility regulation with the help of nanotechnology so that it can act on a molecular basis for fertility control.

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Conflict of interest. None.

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