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Natural Product with Potential for Hormonal Female Contraception

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ABSTRACT:

This abstract examines the possibility of natural chemicals as a workable approach for the development of hormonal female contraception. Due to the unfavorable consequences and challenges associated with many modern contraceptive methods, there is growing interest in researching natural compound-based alternatives. Many substances derived from plants have shown promise in regulating hormones, impacting key reproductive system pathways in females. Because of their bioactive components, these natural remedies demonstrate the ability to regulate hormone levels, particularly those associated with ovulation and implantation. By specifically targeting particular receptors or enzymes involved in intricate hormonal cascades, these compounds exhibit potential contraceptive effects without requiring the artificial complexity associated with conventional birth control approaches.

This review aims to present an overview of different contraceptive properties, focusing on the use of these plant phytochemicals in female contraceptives, including current developments, discussing the potential and plant activity, and how well each method performs for delivering the contraceptives and preventing pregnancy.

The present review is an attempt to summarise the ovulation regulatory plants with their parts used, medicinal use, reported phytochemicals, and pharmacological action. The literature covered three plants showing the pharmacological action of the female reproductive system, and this review seeks to collate such information from the past few decades to advance the alkaloidal group as a viable platform for anti-ovulatory and fertility activity.

KEYWORDS- Natural product, Hormonal female contraception, Contraceptive discontinuation, Cnidoscolousaconitifolius, Vaginal administration, Oral administration, Anti-fertility activity, Medicinal plants, Reproductive hormones, Pharmacological effects

Abbreviations

DHS (Surveys on Demographics and Health), **(COC)**combined oral contraceptive, **(LARC)** reversible long-acting contraceptives**, (VTE)**venous thromboembolism**, (STIs)**sexually transmitted infections,

INTRODUCTION-

According to reports, 33 million unintended births occur among women using conventional or contemporary contraceptives worldwide. This compendium provides extensive information on contraception usage from 60 surveys conducted between 1990 and 2009 in 25 countries participating in the Surveys on Demographics and Health (DHS) DHS Programme. It enhances several comparative studies (9–18) based on the chosen groupings of nations. The Compendium provides by far the most knowledge as well as tabulations. It includes 422478 episodes in Eastern, African, Asian, Latin American, and European countries. Important indicators include contraception use's kinetics and cessation likelihood [1].

The World Health Organisation is focusing on research on conventional medical procedures to regulate population growth. Traditional hormonal contraceptives have been insufficient for developing nations due to their high cost, complexity, and adverse effects. Natural remedies are being explored for fertility regulation and treating various illnesses. Research is being conducted to develop herbal anti-fertility drugs that are more appealing, suitable, and effective than synthetic steroidal contraceptives. This is crucial, as no herbal anti-ovulatory medication has been reported to be effective [2].

Our ethnomedical survey indicates that the plant is used to treat a wide range of illnesses, and the leaves are commonly consumed in numerous locations across Nigeria. But this isn't without data regarding how it affects hormones used in reproduction among women. Thus, this investigation was created. to offer details regarding the impact of a watery extract from the leaves of C. aconitifolius on female hormonal reproduction. Numerous studies (9–11) have demonstrated that chemical substances, such as reproductive hormone levels and concentrations, may change as a result of plant extracts. Roles that women play [3]

India was one of the first nations in 1952 to introduce the family planning scheme. The most likely future scenario was that overall development would only be attained if the population stayed in check. But the objective is still far off. India's population is increasing at a startling rate. 1.28% yearly; by 2030, 1 might surpass China.

The Second The significance of having a small family was widely recognized at the onset of civilization. The mantra of Rigveda 3 is that a father with several children who gives up on his misery is most often the earliest disapproval of huge families. It is a cultural notion that having one wise son is preferable to having several illiterate sons. The history of the use of control methods predates civilization. Pregnancy prevention is usually done through contraception. There are several different forms of contraception in use today [4].

Multifunctional prevention Technology delivered vaginally has been seen as a potentially effective approach to addressing issues related to sexual and reproductive health, and as such, it can be especially advantageous for both users and the healthcare system.

The purpose of this review is to go over current methods of contraception as well as the research being done on the creation of innovative vaginal contraceptive systems [5].

In 1960, Enovid-Searle was the first combined oral contraceptive (COC), which has since become the most popular form of birth control in developed and developing countries. The first COC was linked to side effects like irregular bleeding, nausea, headaches, weight gain, and episodes of venous thromboembolism. Over time, new administration regimens have been developed to lower health risks and adverse effects. Most early regimes were monophasic, with biphasic and triphasic formulations developed in the 1980s to replicate physiological fluctuations and lower the overall dose of steroids in each cycle. However, there was insufficient evidence of a significant clinical advantage for multiphasic pills in terms of safety and efficacy. Over the years, changes have been made to reduce the frequency and duration of menstrual cycles and minimize adverse effects, such as dysmenorrhea and migraines [6].

According to estimates, 213 million pregnancies occur each year, and up to 99 million of these are unintended. Numerous studies on contraceptive methods and strategies have been done to address unplanned pregnancies as well as minimize the side effects impacts and address the potential serious health issues. However there are still certain constraints, like high expense and the requirement for expert expertise for the placement of reversible long-acting contraceptives (LARC). When administering medication orally, there is additionally, the danger of adverse effects from high doses of progestogen and estrogen.

Many research investigations have also been conducted to find novel contraceptive delivery methods that can boost efficacy through better user compliance [4]. The percentage of women who become pregnant unintentionally within the first year of using oral contraceptives with perfect use (0.3%) and typical use (8%) is largely due to poor adherence to pill regimens [7].

India, a nation long concerned with population issues, has screened medicinal plants for potential contraceptive properties as well as anti-fertility effect explosion. Research on anti-fertility medications Nowadays, activity is necessary, and plants need it frequently. The anti-fertility properties of extracts have been studied impact on creatures [4]. Given the accessibility of herbal medications Additionally, the current study was side effect-free executed [8].

The population of the world today is estimated to be 6.46 billion, with India accounting for 1.1 billion of that total. The geometric rise in the human population is one of the main issues facing developing nations like India.

Humans have always relied on plants and their products as sources of medications and therapeutic agents, even though synthetic drugs are now widely used in contemporary medical systems. This makes the development of new fertility-regulating drugs from medicinal plants an appealing proposition. Nonetheless, a lot of contemporary medications have been created using the knowledge gleaned from studying phytochemicals. Furthermore, phytochemicals are valuable resources for therapeutic applications. In recent times, plant-based products have gained more popularity than synthetic drugs. It is primarily attributable to the drugs' low toxicity and extensive history of use in traditional medical systems like Ayurveda [9].

Wie Gratz (2011) and Cavazos-Regh (2010) state that most people are unaware of the availability of natural birth control methods. Natural family planning is a technique used to manage a woman's fertility and infertility. It is also referred to as the Creighton Model, Symptothermal Method, and Billings Ovulation Method. By preventing sexual activity during infertility, these techniques help women take charge of their chances of becoming pregnant. However, making an informed decision requires a detailed comparison of these approaches. For many, natural birth control methods might be a better choice [10].

Plant-based products are increasingly popular due to their extended shelf life and minimal toxicity. They are particularly popular among women in rural developing countries like India, China, Bangladesh, and Nigeria who struggle with modern contraceptive options. Herbal contraceptives may gain more credibility if their toxicity and potency are believed to have birth control properties. However, the search for an effective plant preparation remains ongoing due to incomplete fertility inhibition or adverse effects [11].

CONTRACEPTIVE-

Over 140 million women use oral contraceptives worldwide, making it the most widely used method [14, 15]. The progestin and estrogen found in combined oral contraceptives prevent ovulation and alter cervical mucus, which stops sperm from penetrating.

Since all combined oral contraceptives must be taken daily, hormonal fluctuations may result, which could lead to low compliance. Oral contraceptive use has been linked to several side effects, such as depression, headache, nausea, vaginal dryness, breast tenderness, loss of libido, weight gain, and

irritability [17, 18]. Because estrogen-progesterone contraceptives are carcinogenic, so are cervical cancer, venous thromboembolism, HIV, and breast cancer, some studies have linked the use of combined oral contraceptives to an increased risk of breast cancer [19, 20, 21, 23]. Thus, as a result of the negative impact of combined oral contraceptives, there is an immense need to focus on herbal analogs of these contraceptives, which can provide safe and effective contraception. The development of the combined hormonal transdermal contraceptive patch dates back to the early Nineties. The FDA approved Ortho EvraTM, the first contraceptive patch, in 2002. Norelgestromin (6 mg) and ethinyl estradiol (0.75 mg) are released into the weekly systemic circulation [25]. In comparison, contraceptive patches are more effective than non-hormonal barriers; their affordability and simplicity of use are their benefits. But still, a few dangerous side effects, like venous thromboembolism (VTE), brought on by elevated levels of excess of thirty micrograms of estrogen, inadequate defense against sexually transmitted infections (STIs), and in certain situations, skin irritation may prevent the use of contraceptive patches [5].

PLANT PROFILE

1.NEEM-

Neem is inexpensive, readily available, and safe. It also has a promiscuous potential for reversible antifertility activity in both males and females. Commercially available contraceptives have a long list of negative effects and are not safe. The non-toxic, safe, and effective herbal birth control method is neem. To boost the use of neem as a contraceptive globally in the upcoming year and to focus more research on it, this review discusses [13].

NEEM PLANT: LEAF, STEM

BIOLOGICAL SOURCE-

Azadirachta indica is a mahogany tree in the Meliaceae family of plants, also referred to as Indian lilac, nimtree, margosa, or neem. In the genus Azadirachta, there are only two species, including this one [12].

FAMILY-

Neem belongs to the Meliaceae family of mahogany [15].

Synonyms:

Hin. -Nira, nimb; Mal. – Veppa; Mar. – Limba, Oriya- Nimba; Tam- Vembu[14].

GEOGRAPHICAL SOURCE-

- Azadirachta are native to India.
- Additionally, Nepal, Pakistan, Bangladesh, and Sri Lanka grow it.
- Neem trees grow quickly and rarely reach a height of 35 to 40 meters. It doesn't fade [17].

Taxonomical Classification -

Kingdom	Plantae
Subkingdom	Tracheobionta
Division	Magnoliophyta
Class	Eudicot
Subclass	Rosidae
Order	Sapindales
Family	Meliaceae
Genus	Azadirachta
Species	A. indica

[16].

MORPHOLOGY-

Neem trees have thick, furrowed bark and rounded, visually pleasing crowns. They can grow to a height of 5 to 10 meters. The compound leaves are normally evergreen but may drop in times of severe drought. They have toothed leaflets. Bisexual, the tiny, fragrant white flowers are carried in clusters in the leaf axils. The fruit is a smooth, green-yellow drupe with a pulp that tastes sweet [18].

CHEMICAL CONSTITUENT –

Apart from a variety of triterpenoids, the most well-researched and well-known of which is azadirachtin, neem oil also contains steroids (campesterol, beta-sitosterol, and stigmasterol). Terpenoids: azadirachtin, salannin, nimbin, nimbidin, etc. Depending on the extraction method and quality of the crushed neem seeds, neem oil's azadirachtin content can range from 300 ppm to over 2500 ppm [19].

TABLE-[19]

COMMON NAME	ACID NAME	COMPOSITION NAME
Omega-6	Linoleic acid	6-16%
Omega-9	Oleic acid	25-54%
Palmitic acid	Hexadecanoic acid	16-33%
Stearic acid	Octadecanoic acid	9-24%
Omega-3	Alpha-linolenic acid	-
Palmitoleic acid	9-Hexadecenoic acid	-

% active constituents of neem oil

PHARMACOLOGICAL ACTION-

When female albino rats were given intravaginal neem leaf extract at doses of 150 and 200 mg during their menstrual cycle and mated with male rats, the results of the in-vivo study demonstrated the contraceptive efficacy of the extract on implantation sites. It was discovered that each rat in the control group had between four and seven implantation sites. This group of rats had no implantations in the cyclicity study, and the effectiveness of the contraceptive was 100%[31].

2. MORINGA OLEIFERA-

Many therapeutic plants have been tested at various testing facilities across the globe in the plant kingdom. The antifertility properties of Moringa oleifera Lam. (English: drumstick; Hindi: sahajanal), a member of the Moringaceae family, have been noted in the literature. According to Casey (19601) and Soejarto (19781), it is a plant that inhibits fertility. It has been reported that in the later stages of pregnancy, both an ethanolic extract of the root (Prakash and Mathur, 19761) and the entire plant without a root (Dhawan et al., 1977) can induce fetal resorption [20].

M.O. Plant, Leaf, stem

BIOLOGICAL SOURCES-

The sub-Himalayan regions of India, Pakistan, Bangladesh, and Afghanistan are home to the Moringa oleifera, or "munga," plant, which is a member of the Moringaceae family [24].

FAMILY-

Moringa Adans is the only species in the family Moringaceae[21].

SYNONYMS

Guilandia moringa l.
Hyperanthera arborea J.F.Gmel.
Hyperanthera Decandra Willd.
Hyperanthera moringa(L.) Vahl
Moringa polygona DC.

TABLE [23]

GEOGRAPHICAL SOURCE-

Geographical distribution and origin of the Moringa oleifera L. tree. M. oleifera L. is native to Nepal, Pakistan, and the northern foothills of India [29].

TAXONOMICAL CLASSIFICATION

Kingdom	Plantae
Sub kingdom	Sub kingdom
Super Division	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Dilleniidae
Order	Capparales
Family	Moringceae
Genus	Moringa
Species	oleifera

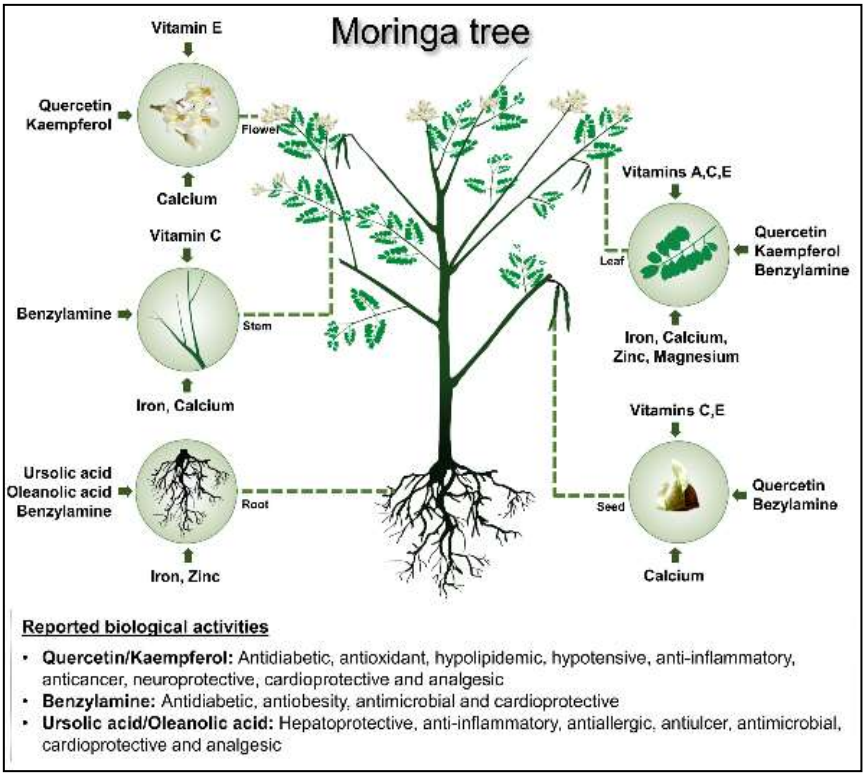
TABLE [22]

MORPHOLOGY-Moringa is a small to a medium-sized deciduous or evergreen tree that can grow up to 12 meters in height. Usually, it has an open crown that spreads widely like an umbrella. The roots are profound [25]. Its tripinnate leaves are feathery, and its thick, corky, whitish bark complements its spreading, open crown of drooping, fragile branches [26].

CHEMICAL CONSTITUENTS-It has been determined that certain MO tree parts are excellent providers of distinct glucosinolates, carotenoids, tocopherols, flavonoids, and phenolic acids, polyunsaturated fatty acids (PUFAs), highly bioavailable minerals, and folate. The most common glucosinolate found in M. oleifera's stem, leaves, flowers, pods, and seeds is 4-O-(a-L-rhamnopyranosyloxy)-benzyl glucosinolate, also known as

glucomoringin. Though the most noticeable is benzyl glucosinolate, also known as glucotropaeolin, the roots, leaves and seeds have the highest concentration of glucosinolate[27].

[44].



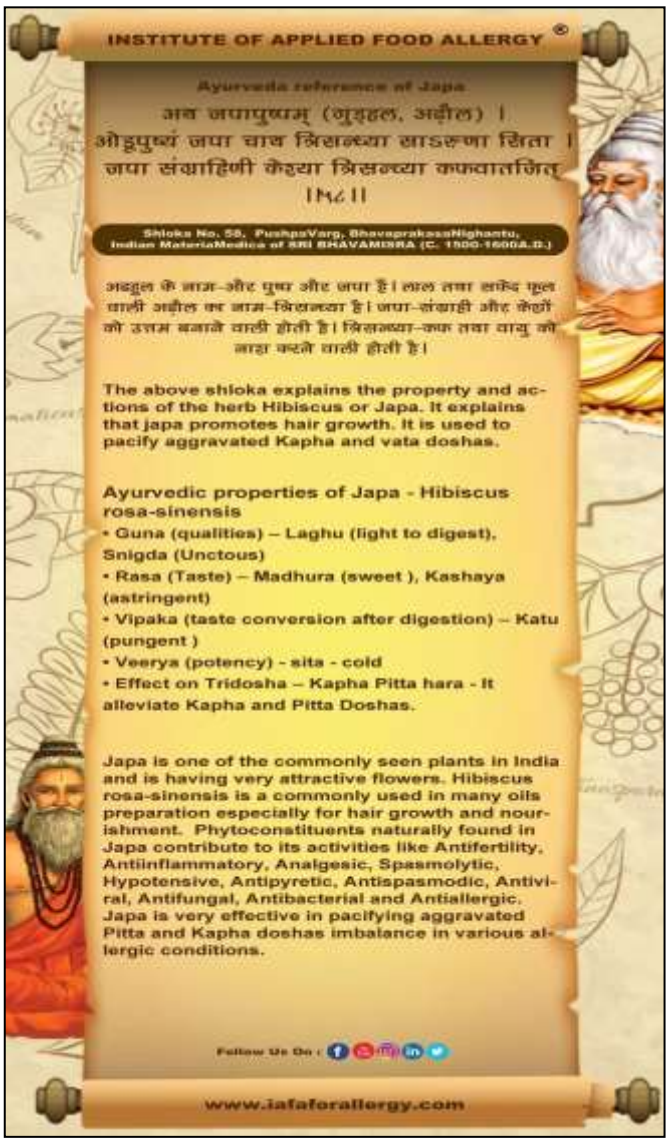
PHARMACOLOGY ACTION-

Oral administration of M. oleifera leaf ethanol extract from post-coital days 1–7 demonstrated antifertility activity at dose levels of 100, and 250 mg/kg, and complete antifertility activity at the dose of 500 mg/kg. It was determined that the M. oleifera extract hampered the implantation process in Wistar rats because antiimplantation loss at each dose was greater than post-implantation loss.

The current study demonstrated that M. oleifera ethanol extract produced antifertility by preventing implantation and also posed the question of whether it was beneficial during pregnancy. This investigation also revealed that, to determine the primary active component causing the antiimplantation activity, a thorough investigation is necessary[30].

3. Hibiscus rosa-sinensis –

The Hibiscus rosa-sinensis flower is widely used in Brazilian traditional medicine for the treatment of diabetes and has shown antifertility activity in female Wistar rats[32]. Hibiscus rosasinensis flowers were used in ancient medical systems to treat reproductive issues. In Bhaavaprakaasha, Japanese literature recommended using them as contraceptives, crushed with sour gruel and jaggery. In "Garbha Anaasthaapaka Yoga," flower buds were used as contraception[33]. Hibiscus rosa sinensis Linn's chemical constituents and all of its parts are used for their antifertility, anovulatory, anti-inflammatory, analgesic, antiestrogenic, antipyretic, antispasmodic, antiviral, antifungal, antibacterial, hypoglycemic, spasmolytic, CNS depressant, hypotensive, and juvenoid properties [34].



AYURVEDA REFRENCE OF ARUNA- Hibiscus rosa-sinensis [38]

BIOLOGICAL SOURCES- In Species Plantarum, Carl Linnaeus published the first description of Hibiscus rosa-sinensis in 1753. Although the plant is not native to China nor closely related to real roses, the specific name rosa-sinensis translates to "rose of China [35].

FAMILY- A green herbaceous plant native to tropical climates, Hibiscus rosa-sinensis is a member of the Malvaceae family [36].

SYNONYMS-

• Hibiscus arnottii Griff. ex Mast.
• Hibiscus boryanus DC.
• Hibiscus cooperi auct.
• Hibiscus festalis Salisb.
• Hibiscus liliiflorus Griff. ex Mast.
• Hibiscus rosiflorus Stokes
• Hibiscus storckii Seem.
• Hibiscus tricolor Dehnh[37].

GEOGRAPHICAL SOURCE- Widely cultivated as an ornamental hedge in tropical and subtropical climates across the world, hibiscus is the most popular species of hibiscus. Although its origins are unknown, some experts believe that Chinese hibiscus originated in Southeast Asia, while others point to Vanuatu in Oceania or other tropical locations. There are currently no known wild populations of the plant [39].

TAXONOMICAL CLASSIFICATION

Kingdom	*Plantae* - Plants
Subkingdom	*Tracheobionta* - Vascular plants
Superdivision	*Spermatophyta* - Seed plants
Division	*Magnoliophyta* - Flowering plants
Class	*Magnoliopsida* - Dicotyledons
Subclass	*Dilleniidae*
Order	*Malvales*
Family	*Malvaceae* Juss. - Mallow family
Genus	*Hibiscus* L. - rosemallow
Species	*Hibiscus rosa-sinensis* L. - shoeblack plant

[40].

MORPHOLOGY- The evergreen shrub species described in this literature has woody stems and can reach heights of 1 to 5 meters. Simple, spiral, alternating leaves with petioles and stipules are present. Ovate or elliptic-ovate in shape, the lamina tapers at the base and becomes acuminate at the apex. With pedicels and lobes on the epicalyx, the flowers are axillary and solitary on the upper branches. Bisexual flowers often occupy a solitary, axillary inflorescence. The fruit capsule is globose and infrequently forms, and the staminal column is 4–8 cm long. With five locular, axile, and stigma discoid, the ovary is superior. The seeds are dark brown to black and reniform[41].

CHEMICAL CONSTITUENT-The phytochemical examination revealed the presence of flavonoids, anthraquinones, quinines, phenols, tannins, alkaloids, terpenoids, saponins, cardiac glycosides, protein, free amino acids, mucilage, essential oils, and steroids in Hibiscusrosa-sinensis[42].

PHARMACOLOGY ACTION- The anti-implantation activity is expressed as a percentage of animals showing absence of implantation in uteri when laparotomized on day 10 of pregnancy. The ethanol extract given orally to the rats at a dose of 400 mg/kg exhibited a very potent anti-implantation activity since no implants, in all the treated animals, were observed, indicating 100% anti-implantation activity [43].

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13. Neem - natural contraceptive for male and female - an overview

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