A REVIEW ON ANTIFERTILITY EFFECTS OF INDIAN PLANTS USED TRADITIONALLY FOR CONTRACEPTION

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ABSTRACT

Rapid rise in human population creates so many problems in developing countries like India. As population increased natural resources declined and increase pollution due to increased demands of urbanization, employment and healthcare. Since ancient time contraceptives have been used to control population including natural methods. In modern time many natural and synthetic agents have been used to check the population at a constant and sustainable level. Attention has now been paid to indigenous medicinal plants since many plants used for contraceptive effects. Thus, there is a need of replace these agents by plants. The investigation of plant constituents with the development of an effective, reversible and safe male contraceptive represents a potential alternative approach to birth control from the existing available methods. These reviews give a detailed introduction on Indian herbal plants explored for fertility regulating effects in male animals. Most of these plants were evaluated in the Department of Zoology, University of Rajasthan, Jaipur since a long back.

KEYWORDS: Medicinal plants, fertility, contraception, animals

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INTRODUCTION

Now a days population explosion is one of the major problems in the world it’s inevitable consequences are unemployment, global warming, housing, health care, economy and pollution. Currently, the world population crosses the 8 billion and increasing continuously day by day, therefore fertility regulation in human becomes an issue of global concern. There is a great need to support at individuals in family-planning since increasing growth rate of world's population caused a negative impact on resources and sustainable development leads to poverty especially in developing countries. Currently India is the second most populous country with a population of 1.22 billion and its population will exceed with that of China before the end of 2030 and it becomes the most populous country. According to World Health Organization despite many achievements in human health care in the twentieth population in developing countries lack regular access to affordable essential drugs. Apart from the advantages of traditional medicine many problems must be tackled to maximize the potential of traditional medicine as a source of health care. Medicinal plants, is a common word which can utter in every one’s mouth that are helpful in treating many diseases which can’t be done by even allopathic medicine. Here we try to updated information gathered on scientifically proved medicinal plants used for fertility regulation. Many scientists around the World supports the antifertility effects of traditional herbal medicines. Main aim of this review on traditional medicinal plants is to highlight the work done on antifertility activities. Several plant(s) or there products have been reported inhibiting male and female fertility, may be used to develop contraceptives. Even though, many indigenous plants have been shown to prevent the birth, only a few plants have so far been investigated for antifertility activity. The World Health Organization (WHO) has set up a task force on plant research for fertility regulation with an objective to find a new orally active non-steroidal contraceptive compounds. Various medicinal plant(s) extracts have altered hormone levels. It is necessary to use biologically active botanical substances or fertility regulating agents of plant origin which are eco-friendly effects.

Plants with antifertility activity

Research on Indian plants with antifertility activity has been exhaustively reviewed recently. Isolated and independent studies by different investigators and institutes on this topic have been continued. Ethanolic extract of *Achyranthes aspera* showed promising antifertility activity. Administration of ethanolic extract of *Achyranthes aspera* (ACE) showed non dose dependant effect on the oestrous cycle doses of 200 and 400 mg/ Kg body weight showed highly significant decrease in the duration of oestrous & metestrous phase. *Achyranthes aspera* (ACE) exhibit antimplantation property due to antiestrogenic effects.

Contraception in the male

Antifertility effect in the male has been demonstrated in a few plants. Notable among these are *Azadirachta indica* leaves, *Aristolochia indica* root, *Ananas comosus* ripe fruit, *Embelia ribes* fruits, *Carica papaya* seeds, flowers of *Hibiscus rosa sinesis* and *Malva vsicus conzatti*. *Aristolochia indica* root (chloroform fraction) revealed on antispermatogenetic effect in mice while as its derivative p–coumaric acid showed an anti-prolactin effect in male mice. *Azadirachta indica* leaves, on the other hand, showed an antifertility activity in the male mice which was not due to inhibition of spermatogenesis. *Embelia ribes* fruits administered to male bonnet monkeys for months reduced the circulating testosterone levels without affecting normal spermatogenesis. The aqueous and alcoholic extracts of *E . ribes* fruits did not reveal any toxic effect on the male reproductive organs in rats. Antispermatic effect of the flower extract of *Hibiscus rosasinensis* was demonstrated in *Rhinopama kineari* – a non-scrotal bat. *Malvaviscus conzattii* flower extract revealed potent antispermatic effect in gerbils and house rats and albino mice. Spermicidal activity of plants have been reported at the CDRI, Lucknow. Spermicidal saponins were identified from *Sapindus mukrossi* fruit, *Schefflera capitata*, *Pittosporum nilgherense* and *Polemonium"
coeruleum\textsuperscript{29}. Alcoholic extract of several traditional medicinal plants like \textit{Echinops echinatus}\textsuperscript{30}. \textit{Citrullus}, \textit{Euphorbia}, \textit{Martynia}, \textit{Solanum} and \textit{Withania} have been reported contraceptive activity in male Wistar rats\textsuperscript{31}.

\textbf{Cassia occidentalis}

The plant \textit{Cassia occidentalis} L. (Family - Caesalpinaeaceae), commonly known as ‘Kasondi’, is a common weed found throughout India and is employed in indigenous and folk medicine for a variety of purposes\textsuperscript{32-34}. In Unani literature, ‘Kasondi’ has been reported to be used as an antidote of poison, blood purifier, expectorant, anti-inflammatory agent and a remedy for the treatment of liver diseases\textsuperscript{35,36}. Several polyherbal preparations are available in the Indian market for liver disorders in which \textit{C. occidentalis} is one of the constituents. The ethanolic extract of leaves of this plant was recently evaluated for its antihepatotoxic activity using carbon tetrachloride and thioacetamide as hepatotoxins, and reported to be active\textsuperscript{37}. The powder of leaves of \textit{C. occidentalis} was screened for anti-inflammatory activity using two models, i.e. carrageenan induced edema in the rat hind paw (acute inflammation) and cotton pellet granuloma (chronic). In order to find the biochemical mode of action of the drug, the level of lipid peroxide, lysosomal enzymes and γ-glutamyltranspeptidase in the exudate of cotton pellet granuloma and the degree of human erythrocyte membrane stabilization were studied after drug treatment, and reported that the beneficial effects of \textit{C. occidentalis} powdered leaves on inflammation may arise from the inhibition of the formation of mediators of inflammation and/or the stabilization of lysosomes\textsuperscript{38}. The anti-inflammatory and antiplatelet activities of constituents isolated from roots and stems of \textit{C. occidentalis} have also been reported\textsuperscript{39}. Mixture ethanolic extrac of \textit{C. occidentalis}, \textit{Derris brevipes} variety coriacea and \textit{Justicia simplex} show antifertility activities in female albino wistar rats\textsuperscript{40} and not show any toxic effects on pregnant albino female wistar rats\textsuperscript{41}. 50% ethanolic extract of \textit{C. occidentalis} plant possess antifertility activities in male albino rats\textsuperscript{42}.

\textbf{Citrullus colocynthis}

The plant \textit{Citrullus colocynthis} (Family - Cucurbitaceae) and also known as Indryan, Tumba, Bitter apple etc. \textit{Colocynthis} have wide range of traditional medicinal uses including in diabetes, leprosy, common cold, cough, asthma, bronchitis, jaundice, joint pain, cancer, toothache, wound, mastitis, and in gastrointestinal disorders such as indigestion, constipation, dysentery, gastroenteritis, colic pain and different microbial infections. The fruit of \textit{C. colocynthis} has been studied extensively for its wide range of biological activities, which include antioxidant, cytotoxic, antidiabetic, antilipidemic, and insecticide, antimicrobial and anti-inflammatory. Antifertility effect with administration of crude 50% ethanol extract of \textit{C. colocynthis} roots produced an antispermatic effect in male albino rats\textsuperscript{43}. And 50% ethanol extract of \textit{C. colocynthis} Schrad fruit showed an antiandrogenic nature reduced reversible infertility in male albino rats\textsuperscript{44}.

\textbf{Maytenus emargineta}

\textit{Maytenus emarginata} (Wild) (family - Celastraceae) is an evergreen tree that generally grows as small trees, bushes or lianas and has resinous stems and leaves. They tolerate various types of stresses of the desert, locally known as vickado, “Kankero” in Hindi, “Thorny staff tree” in English. Synonyms of this plant are \textit{Celastrus emarginatus} Willd. \textit{Gymnosporia emarginata} (Willd) Thw. \textit{Gymnosporia montana} (Roth) Benth. Traditionally, species of \textit{Maytenus} have been used for fever, asthma, rheumatism and gastrointestinal disorders worldwide. Some bioactive of the \textit{Maytenus} species has been reported to be active against HIV-Protease\textsuperscript{45}, Carcinoma and leukemia\textsuperscript{46} and MDR (Multi Drug Resistance)\textsuperscript{47}. Various parts of this plant contain immense medicinal properties such as shoots of the plant help for mouth ulcer\textsuperscript{48}. The bark is ground to a paste and applied with mustard oil to kill lice in the hair. Pulverized leaves are given in milk to children as a vermifuge\textsuperscript{49}. A decoction of the leaf twigs is used as a mouthwash to relieve toothache. Ash of leaves is used to heal up the sores and wound gives a cooling effect. The leaves are burnt and mixed with ghee to form an ointment used to heal sores\textsuperscript{50}. The tender leaves are chewed raw in the treatment
of jaundice. The fruit is used in medicines to purify blood51. In the present work, various solvent extracts of leaf and stem of M. emarginata were evaluated for its phenol and flavonoid content and antibacterial potential. 50% ethanolic fruit extract of M. emarginata show reversible antifertility activities in male albino rats52.

Withania somnifera
The plant Withania somnifera (family – Solanaceae) and also known as Ashwagandha, Winter Cherry etc have been used for different medicinal properties around the world. W. somnifera have antifertility properties which are described in Ayurveda. It has beneficial effect in treatment of a wide range of disorder as digestive ailments, nerve afflictions, heart ailments, inflammation, nervous system, and rashes. The ethanol extract of W. somnifera was believed to suppress “KamVasna” (desire of sex). In this sequence W. somnifera stem extract was daily orally fed to two months to study its effect on reproductive function of male albino rats. It was observed that control albino rat showed 100% fertility rate. In W. somnifera stem extract treated animals; the antifertility effect was 70%. This study was carried out to evaluate in vitro spermicidal & in vivo antifertility activity of this extract against male albino rats. Thus the results suggest a possible antifertility property of the ethanol extract of W. somnifera in male albino rats53-55. The 50% of ethanol extract of W. somnifera have antifertility activity in male albino rats56. Withanolide-A was isolated from W. somnifera and dissolved in DMSO to administer orally in male albino rat at the different dose levels. Withanolide-A reduce in sperm motility and density significantly and inhibit fertility57.

Euphorbia neriifolia
The plant Euphorbia neriifolia Linn (Family - Euphorbiaceae) popularly known as the Indian Spurge Tree, Oleander Spurge, Hedge Euphorbia, Sehundah (Ayurveda) and Ilachevikalli (Siddha) E. neriifolia leaves are used as aphrodisiac, diuretic and also used in the treatment of bronchitis, bleeding piles and in ano-rectal fistula32. The plant is useful in dominal troubles, bronchitis, tumors, leucoderma, piles, inflammation and enlargement of spleen, anemia, ulcers, fever and in chronic respiratory troubles58. E. neriifolia hydro alcoholic extract was found to contain sugar, tannins, flavonoids, alkaloids, triterpenoidal saponin on preliminary phytochemical analysis. Several triterpenoids like glut-5-en 3b-ol, glut-5(10)-en 1-one, taraxerol and b-amyris have been isolated from powdered plant, stem and leaves of E. neriifolia59,60. Neriifolione, atriterpene and a new tetracyclic triterpene named as neriolene along with euphol were isolated from the latex of E. neriifolia61. Antiquorin have been isolated from ethanol extract. Anti-inflammatory and analgesic effect of E. neriifolia is reported by62. There are reports on the mild CNS depressant, wound healing and immune modulatory activities of the hydro alcohol leaf extract63-65. Root extract of E. neriifolia show antifertility effect in male albino rats66.

Martynia annua
Martynia annua (Family - Martyniaccae), commonly known as scorpion (in Hindi, Bichchhu or Baghnukh), has been used from ancient time in traditional medicine in India. From the available literature, it is known that various parts of the plant possess different medicinal properties. For instance, the leaves are used in epilepsy and applied locally to tuberculous glands of camel’s neck, the juice of the leaves as a gargle for sore throat, fruit in inflammation, paste of the nut has a beneficial effect when applied to the bites of venomous insects, and the leaf paste for wounds of domestic animals67. The whole plant is also used by Santaltribals (India) for fever, hair loss, scabies, sores and carbuncles on the back68. The oral administration of 50% ethanol extract of M. annua root to male rats produced dose related effects on reproduction69. The effects may have an inhibitory influence on gonadotropin release which may be responsible for the decline in testosterone production, leading to changes in spermatogenesis. Further long term studies are in progress for the evaluations of complete and reversible efficacy of the extract.

Development of a herbal male contraceptive
Continued efforts over the past three decades to develop additional methods of male contraception have made some significant
contributions in the field. However, there is still no method available in the field of male contraception that satisfies the essential criteria of safety, efficacy economy and complete reversibility\textsuperscript{70-73}. The development of a viable male contraceptive agent of universal appeal has been a difficult task. For a method to succeed, it must be safe and must ensure that:

(i) Production of good quality spermatozoa is totally blocked (azoospermia) or affected to a highly significant extent (oligozoospermia accompanied by impairment in quality, in particular fertilizing ability) hence causing infertility in >90% of the volunteers tested;

(ii) Androgen-dependent accessory sex gland function and libido should not be impaired; and finally

(iii) The process should be reversible after cessation of drug treatment.

**Mode of action**

**Effect on Male Reproductive Hormones**

Fertility regulating hormones like testosterone, luteinising hormone, follicular stimulating hormone plays an important, pivotal role in maturation, spermatogenesis and the maintenance of accessory sex organs\textsuperscript{74}. The structural and functional integrity of reproductive tissues depends on these circulating hormones. Therefore, any small change in this content may cause infertility. It is noted that antifertility agents work by disrupting or desynchronizing pre-ovulatary and pre-implantation events. Antifertility activity is often due to estrogenic activity, but can also be due to anti-estrogenic activity\textsuperscript{75,76}. Abdel-Magied has been that level of *W. somnifera* effect testosterone level of rat’s in treated rats. The aqueous extract of *W. somnifera* is able to decrease the serum level of FSH and to increase the LH level in male rats\textsuperscript{75}. Impaired action of the LH on the gonadal organ is a suggested mechanism for decreasing the reproductive hormone levels mainly progesterone from luteal cells\textsuperscript{77}.

**Effect on Cholesterol**

Cholesterol is a steroid metabolite found in the cell membranes and transported in the blood plasma of animals. It is an essential structural component of mammalian cell membranes, an important component for the manufacture of bile acids, steroid hormones, and fat soluble vitamins\textsuperscript{78}. The effect of *W. somnifera* on cholesterol is a reduction in cholesterol level of blood in diabetic *W. somnifera* treated group relative to the diabetic control group has been observed.

**Spermicidal activity**

The spermicidal method constitutes a key tool for the prevention of undesired pregnancies. Spermicidal activity is dose and time depended study in which measure the minimum concentration spermicidal agent required to kill hundred percent of one million of sperm within 20 seconds. The complete immobilization of sperm conforms by viability test\textsuperscript{79}. The spermicidal effect could be exploited for the development of a product that avoids the undesirable effect of traditional spermicides, making it possible to evaluate the biodiversity in a different biological context such as human reproduction\textsuperscript{68,80}. During the last few years a more scientific and systematic study has conformed recorded usefulness of number of these plant drugs.

### Table 1

**Antifertility activities of six Indian herbal plants in male**

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Botanical name</th>
<th>Common name</th>
<th>Family</th>
<th>Parts used</th>
<th>Action</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td><em>Cassia occidentalis</em></td>
<td>Kasondi</td>
<td>Caesalpinaceae</td>
<td>Fruit</td>
<td>antifertility/antispermatogenic activity</td>
<td>Khan et al, 2011</td>
</tr>
<tr>
<td>2.</td>
<td><em>Citrullus colocynthis</em></td>
<td>Tumba</td>
<td>Cucurbitaceae</td>
<td>Root, Fruit</td>
<td>Antispermatogenic/antiandrogenic activity</td>
<td>43, 44</td>
</tr>
<tr>
<td>3.</td>
<td><em>Euphorbia neriifolia</em></td>
<td>Sehundah</td>
<td>Euphorbiaceae</td>
<td>Root</td>
<td>antifertility activity</td>
<td>66</td>
</tr>
<tr>
<td>4.</td>
<td><em>Martynia annua</em></td>
<td>scorpion</td>
<td>Martyniaceae</td>
<td>Root</td>
<td>antispermatogenic activity</td>
<td>69</td>
</tr>
<tr>
<td>5.</td>
<td><em>Maytenus emarginata</em></td>
<td>Kankero</td>
<td>Celastraceae</td>
<td>Fruit</td>
<td>antispermatogenic activity</td>
<td>52</td>
</tr>
<tr>
<td>6.</td>
<td><em>Withania somnifera</em></td>
<td>Ashwagandha</td>
<td>Solanaceae</td>
<td>Fruit</td>
<td>antispermatogenic activity</td>
<td>56</td>
</tr>
</tbody>
</table>
CONCLUSION

Medicinal plants since ancient time play an important role in treating various diseases. The herbal plants and their extracts exhibit significant antifertility effect in different animal models. Present review showed that medicinal plants possess antifertility activity with different mode of action on dose dependent manner and may be used as an alternative source to develop oral contraceptives. Hence the review study is concluded that the many herbs exhibits antifertility activity in different animal models may further used to develop a safe and cheap contraceptive. Although several contraceptive available to check human fertility at a constant level. However more contraceptive options are needed.

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