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Herbal options for Contraception: A Review

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ABSTRACT - Due to existing and overwhelming growth rate of world population, oral contraceptive have become need of the time. But steroids have various side effects. This forced us to review the existing options of plants having anti-fertility activity. Plant plethora is rich source of plants having anti-fertility activity. In this review we have also covered the plants having anti-fertility activity by different mechanism in both male and female.

KEY WORDS: Anti-fertility, abortifacient, anti-implantation, spermicidal, estrogen.

INTRODUCTION

The extraordinary growth of the world population stands as one of the significant events of the modern era to think over. The current world population is around 6.46 billion and that of India in particular is around 1.1 billion (1). One of the critical problems of the developing countries like India is its geometrical increase in human population. Today we understand that our sheer numbers have increased so much that they are straining Earth’s capacity to supply food, energy and raw materials. Advances in medicine and public health have led to a significant decrease in mortality and an increased life expectancy. This population explosion will have negative impact on our economic policies and would simultaneously misbalance our socio-economic infrastructure. Thus the control of human fertility in the sense of its limitation is the most important and urgent of all-biosocial and medical problem confronting mankind today.

Contraception is literally the prevention of conception, but generally is taken to mean the prevention of pregnancy (2). The development of new fertility regulating drug from medicinal plants is an attractive proposition, because from times immemorial humans have relied on plants and their products as sources of drugs and therapeutic agents, although in recent times, synthetic drugs are used extensively in modern medicine. However many modern medicines are developed through the clues obtained from phytochemicals. More over the phytochemicals even today are important resources for medicine. The plant products are becoming more popular than the synthetic drugs. In recent times it is mainly attributed to their low toxicity and long standing experience of exposure of these drugs in ethnic medicine system like Ayurveda.

Family planning has been promoted through several methods of contraception, but due to serious adverse effects produced by synthetic steroidal contraceptives, attention has now been focused on indigenous plants for possible contraceptive effect. Although contraceptives containing estrogen and progesterone are effective and popular, the risks associated to the drugs have triggered the need to develop newer molecules from medicinal plants. Hence, there is a need for searching suitable product from indigenous medicinal plants that could be effectively used in the place of pills.

All combination oral contraceptives (COCs) contain both an estrogenic compound and a progestin. Over the years, the amounts and types of these components have changed in attempts to lower side effects and improve efficacy.

Mechanism of steroid hormone action

Estradiol, like other steroids, is thought to exert its action directly on the nucleus of the cell. As a consequence, an estrogen-response tissue must have estrogen receptor and nuclear acceptor sites to which activated receptor can bind. Upon entry into the cytosol of the cell (by diffusion), estradiol is bound to a specific receptor (ERc). In the cytoplasm, the estrogen receptor complex is activated (ERn) and translocated to the nucleus. This complex binds to acceptor sites in chromatin and enhances processes associated with differentiated functions of the responsive tissue, which include the production and utilization of messenger and other classes of RNA needed for the synthesis of constituent enzymic and secretory proteins, as well as the receptor itself. In some cells replication of DNA is also stimulated, followed by cell division. The concentration of estrogen receptors in most tissues is constitutive, but in some instances it is increased by estradiol. The
concentration of progesterone receptors in the uterus and other progesterone response tissues is markedly increased by estrogen. In fact, one of the recognized actions of estradiol is to stimulate synthesis of progesterone receptors. The induction of progesterone receptors with estrogen can explain the synergistic action of these two hormones on the uterus.

Methods of contraception

Hormonal control of fertility
The most effective method of contraception, the birth control pill, is based on oral administration of steroids. Estrogens and progestins are used either combined or, as with the "minipill", progestins are used alone. In addition, various combinations of steroids can also be administered as long-acting injectable preparations or via intrauterine systems.

The pills to be effective via the oral route, estradiol and progesterone cannot be used since they are metabolized in the gastrointestinal tract and liver. As a consequence, synthetic estrogens such as mestranol (50-100 µg/day) or ethinyl estradiol (20-50 µg/day) are
used in combination with various synthetic progestins, such as norethindrone, norethindrone acetate, norgestrel, ethinodiol diacetate or norethynodrel (0.3 - 100 mg/day). The hormones are given in a cyclic fashion for 21 days, beginning on day 5 of the menstrual cycle, followed by 7 days of placebo treatment or no pills.

The elevated estrogen and progestin levels inhibit the midcycle LH surge and ovulation by exerting negative feedback effects on the hypothalamus. Irregular LH peaks are sometimes observed, while FSH levels are usually suppressed. Ovarian progesterone production is diminished, but estrogens continue to be secreted. The effects on the endometrium are variable and depend on the type and dosage of the contraceptive. Rapid progression from proliferation to early secretory changes can be observed within a few days from the start of daily intake, followed by regressive changes. Secretory activity is either minimal or absent. The pregnancy rate for combined pills is approximately 2%.

**Risks**

The reason why some women may be reluctant to take combination oral contraceptives (COCs) consistently and correctly is a fear of possible adverse effects.

**Cardiovascular disease**

Historically, combination oral contraceptives have been associated with increased risks for myocardial infarction and stroke. Overall, oral contraceptives were found to multiply the effects of age and other risk factors for MI and stroke, rather than just add to them. Because cigarette smoking is far more prevalent among women of reproductive age than any of these other risk factors, it becomes by far the most important factor.

Whereas early epidemiological studies of high-dose oral contraceptives found significantly increased risks of developing cardiovascular disease among users of combination oral contraceptives.

Use of oral contraceptives by healthy women who do not smoke does not appear to be associated with an increased risk of either myocardial infarction or stroke.

**Hypertension**

As with the increased risks for MI and stroke, older formulations of combination oral contraceptives have been associated with significant elevations of blood pressure as well. The risk of hypertension appears to be much lower when estrogen and progestin doses are lowered.

The mechanism for contraceptive-induced changes in blood pressure is still unclear, with alterations in plasma angiotensinogen and increases in sodium and water retention being noted. Although these are primarily estrogenic effects, progestins may have a synergistic effect, as significant elevations in blood pressure have only been apparent in the combination products and not with either hormone alone.

**Thrombosis**

As doses of estrogenic were lowered to less than 50 µg, a marked drop in the incidence of fatal and nonfatal pulmonary embolism was noted, thus implying an estrogen dose-related effect.

As with the other concerns for myocardial infarction, stroke, and hypertension, patient selection remains the most important method of reducing the incidence of these adverse effects. Women who are already at high risk for cardiovascular problems (hypertension, smoking and older than 35 years, or diabetes with vascular complications) or have already had a cardiovascular or thromboembolic event should not use combination oral contraceptives.

**Hepatomas**

It may occur in women taking oral contraceptive, the most common of which are focal nodular hyperplasias and liver cell adenomas. Hepatocellular cancer was also felt to be associated with combination oral contraceptives use (3).

Here it is clear that estrogen and progesterone play a crucial role in anti-fertility activity but not without the serious side effects. So in this background we have reviewed some of the plants having anti-fertility activity in both male and female.

Following is the list of plants available for anti-fertility activity with their parts used and somewhere mechanism of action to understand this activity.

**Alangium salviifolium**

The family Alangiaceae consists of twenty-two species out of which *A. salviifolium* (Linn.f) Wang is mainly used as medicine in India, China and Philppines (4). Different parts of this plant are reported to possess acrid, astringent, emollient, anthelmintic, diuretic and purgative properties. It is also used externally in acute case of rheumatism, leprosy and inflammation. Applied externally and internally in case of rabid dog bite. Root bark is an antidote for several poisons. Fruits are sweet, cooling and purgative and used as a poultice for treating burning sensation and hemmorhage period (5). Daily administration of petroleum ether, ethyl acetate, chloroform, methanol or aqueous extracts of *A. salviifolium* at a dose of 100mg/kg body weight for eight days starting from the first day of pregnancy showed significant abortifacient activity in comparison to vehicle treated group. Interestingly, except petroleum ether and ethyl acetate extracts, all the extracts showed no anti-implantation activity. Eight
days of drug treatment lead to resorption of fertilized ovum as noticed by red spots in the horns of uterus. Among the extracts, chloroform extract was found to be least effective followed by petroleum ether extract. Methanol extract showed total resorption sites in two animals. Aqueous and ethyl acetate extracts have also shown good activity. These results indicate that A. salvifolium (Linn.f) Wang produced mainly abortificient activity and less antimplantation activity. It indicates that the herbal drugs may have anti-progesterone effect (6).

Aloe vera
Twenty samples of fresh ejaculate donated by healthy volunteers ranging in age from 20-30 years were obtained. Lyophilized A. barbadensis at concentrations of 7.5% and 10% proved to be spermicidal due to the multiple microelements (boron, barium, calcium, chromium, copper, iron, potassium, magnesium, manganese, phosphorus and zinc) which were toxic to the tail causing instant immobilization. These results suggest the possibility of using lyophilized A. barbadensis as a new, effective and safe vaginal contraceptive (7).

Aristolochia tagala
Aristolochia, a large genus of shrubs, rhizomatous perennial herbs often twining, is distributed in tropical and termarate regions of the world. A. tagala is a perennial herb highly prevalent in Himalayas, Bihar, Assam and southwards in forest cleanings. The root of the plant is reported to contain aristalochic acid, which possesses tumor-inhibiting activity and has been used in the treatment of cancer, snakebite and helmenthiasis (8).

Preliminary phytochemical studies revealed that the ethanol extract showed the presence of alkaloids, saponins, flavonoid glycoside, steroids and phenolic compound. The ethanol extract of A. tagala showed significant reduction in the number of corpora lutea and increase in the number of resorptions in comparison to the control. The extract showed 72% antifertility activity on oral administration of 100mg/kg whereas a remarkable 100% antifertility activity resulted on the administration of 200mg/kg as compared to the untreated control group (9).

Azadirachta indica
Male albino rats were administered orally 100 mg/kg A. indica leaf powder with or without testoestosterone. Suitable controls were maintained. Damaged semineferous tubules and abundance of vacuoles of varying size were observed in A. indica treated rats. The germ cells showed overall decrease in cytoplasmic ground substance. Leydig cells exhibited characteristics of degeneration with condensed nuclei. Total count of spermatocytes, spermatids and Leydig cells were reduced. The cell and nuclear diameter of spermatogonia, spermatocytes, spermatids and Leydig cells were also reduced. From the result obtained, it can be observed that effects of Azadirachta indica on the testis are possibly due to gonadotrophic hormone deficiency, caused directly or indirectly (10). Neem oil proved spermicidal against rhesus monkey and human spermatozoa in vitro (11). In vivo studies showed that intravaginal application of neem oil prior to coitus can prevent pregnancy (11). Antifertility effect of neem oil has also been studied and suggested to be a novel method of contraception (12-14). Oral administration of aqueous extract of neem leaf also shows antifertility effect in mice (15). Purified neem seed extract has also been demonstrated to abrogate pregnancy in both baboons and bonnet monkeys, when administered orally (16). From the hexane extract of neem seed, an active fraction containing six components has been found to completely abrogate pregnancy in rodents when given orally up to a concentration of 10%, with no apparent side effect (17).

Biophytum sanctivum
Different extracts of B. sanctivum were tested for their antifertility activity. Ethyl acetate and n-butanol extracts significantly inhibited pregnancy in 4/6 rats with mean number of implants 3.0±1.92 (P≤0.05). It is also understood that the chloroform and the ethanol extracts significantly inhibited pregnancy in 5/6 rats with a mean number of implants of 2.0±1.23(P≤0.05) and 6/6 rats with mean number of implants of 0.00±0.00 (P≤0.05), respectively (18).

Calotropis procera
90% ethanolic and aqueous extracts of roots of C. procera produced on female Wister rats temporary and reversible modification on oestrous cycle characterized by absence of oestrous and metaoestrous phases and dioestrus stage prolonged. Therefore, extracts provoked inhibition of ovulation with consequent reduction of cyclicity (19). Ethanolic extract of roots shows 100% anti-implantation activity at the dose of 250mg/kg (20).

Cardiospermum helicacabum
Ethanolic extract of whole plant at a dose of 250mg and 500mg/kg body weight /day orally for day 1 to 7 of pregnancy showed significant decrease in the implantation sites. Animals treated with 500mg/kg body weight showed 60% inhibiton of implantation sites.