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Neem - natural contraceptive for male and female - an overview

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Abstract

Neem has been used traditionally as a medicine for various ailments. It has been reported to possess wound healing, antiviral, antiarthritic, anti-hyper glycemic and anti-inflammatory properties and also help in curing skin diseases. A novel use of neem (*Azadirachta indica*) oil, Neem leaf extracts a traditional plant product, for long-term and reversible blocking of fertility after a single intrauterine application is described. Deshpande *et al.*(1980) have studied the anti-fertility activity.neem leaves have shown reversible male anti-fertility activity. A viginal contraceptive has also been developed from NIM-76.It is found that 3mg of neem leaf extract immobilize and kill 100% of spermatozoa within 20 seconds. The block in fertility was, however, reversible as half of the animals regained fertility and delivered normal litters by five months after treatment, without any apparent teratogenic effects. Neem oil appears to be a safe and very effective contraceptive, pre and post coital (before and after sex). The way it was applied in the studies it was 100% effective in preventing pregnancies. During in vitro experiments, neem oil also totally immobilized sperm cells within 20 to 30 seconds of being in contact with neem oil. But as we know now, this didn't spread around the world as predicted. Population is the main problem worldwide today it is necessary to control it on time. To increase the use of neem as contraceptive this review entitled the detail study of ant fertility activity of neem which is safe and effective without producing any side effect as compared to the other available contraceptive in the market.

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Introduction

Nowadays worldwide Population is the major problem and it is necessary to control it on the time. As we know the entire available contraceptive in the market are not safe, mostly they are steroid in nature and they have more or little hazardous side effect. To control the population by saving health it is necessary there will be the avaibility of safe contraceptive. Neem has been used traditionally as a medicine for various ailments. It has been reported to possess wound healing, antiviral, antiarthritic, anti-hyper glycemic and anti-inflammatory properties and also help in curing skin diseases. A novel use of neem (*Azadirachta indica*) oil, Neem leaf extracts a traditional plant product, for long-term and reversible blocking of fertility after a single intrauterine application is described. Deshpande *et al*. (1980Year?) have studied the antifertility activity.neem leaves have shown reversible male antifertility acticivity.A viginal contraceptive has also been developed from NIM-76.It is found that 3mg of neem leaf extract immobilise and kill 100% of spermatozoa within 20 second.The block in fertility was, however, reversible as half of the animals regained fertility and delivered normal litters by five months after treatment, without any apparent teratogenic effects. neem oil appears to be a safe and very effective contraceptive, pre and post coital (before and after sex).Neem is a tree common to India with many medicinally valuable parts. The potential use of neem leaf extracts as contraceptives is not a new idea; research on its use as a spermicidal has been underway since the 1960s. The injection of minute quantities of neem oil into the vas deferens (the tubes that carry sperm) has been successfully tested as an alternative to surgical vasectomy (Upadhyay 1993). Various forms of neem have been studied as potential reversible male contraceptives. Male mice fed water crushed with fresh neem leaves impregnated fewer female mice and had smaller average litter sizes (Deshpande 1980). Researchers obtained similar results in rats (Sadre 1983). Within 11 weeks, the animals in this study had 100% effective contraception. The effects were reversed within 6 weeks. An equivalent body weight dosage was tested in guinea pigs and rabbits, but this dosage was toxic. After 6 weeks of treatment, 75 and 90% of the respective animals had died. Studies of various forms of neem for male contraception in different types of mammals have reported no changes in libido or hormonal function (Jensen 2002). Neither neem leaf extract in water nor neem leaf oil alters the rate spermatogenesis. The contraceptive effect of these two forms of neem comes from a reduction in the motility of the sperm. However, neem bark extract and neem seed oil caused arrest of spermatogenesis within 2 months, with a decrease in the number of Leydig cells (responsible for the manufacturing of testosterone) (Randhawa 1996). Although neem treatment does not trigger a systemic autoimmune response to sperm, researchers speculate that a local immune response of some kind is responsible for its contraceptive effects (Lohiya 2001).

Reports of neem oil use by 20 Indian Army soldiers as a low dose, orally administered male contraceptive are erroneous. Neem oil was indeed administered as a successful post-coital contraceptive to the *wives* of 20 soldiers (National Research Council 1992), but it was not a formal study. There have been no studies of neem as a contraceptive in men. Lots of research has been done in India in regards to neem and its contraceptive effects. It seems to have several contraceptive applications, as spermacide and an oral contraceptive for men, and two other options which would only be available through qualified medical research personal at this time. Neem provides men with an alternative oral contraceptive option, Neem Leaf tablets. Research conducted on 20 married soldiers from the Indian Army over the course of one year showed that a daily oral dose of several drops of neem seed oil placed in gelatin capsules prevented pregnancy in each of the wives during the period of the study. The effect took 6 weeks to become 100% effective. The effects were reversed within 6 weeks after subjects discontinued taking the capsules. During the study, none of the men

experienced any negative side effects and retained their normal capabilities and desires. (Vietmeyer, 1992). Neem is currently being used in India for contraceptive purposes for both men (orally) and women (as a spermacide).

Newer studies showed that neem oil contraceptive indeed kills sperm in the vagina within 30 seconds and remains active for five hours. It causes no irritation or discomfort like the chemical based spermicidal foams do. Sodium nimbinate and sodium nimbidinate is the main constituents for the spermicidal and anti-fertility activity of neem oil.

Pressure extracted neem oil was found to have in-vitro spermicidal activity against rat, monkey and human sperms. On intravaginal application before coitus, neem oil was found to prevent pregnancy in rats, rabbits, monkey and human beings. When neem oil was applied intravaginally after coitus, it was found to prevent implantation and cause abortion in rats. All these effects were systemic and dose dependent. The application of neem oil did not alter the hormonal profile.

In short neem oil was found to be a promising (a) pre-coital vaginal contraceptive and (b) a post-coital contraceptive preventing implantation and also (c) an abortifacient agent. All these effects are reversible. Only one ml of oil is to be applied for these effects every time and the cost is negligible as one litre of neem oil can be used for 30 cycles by a woman if it is daily used as a pre-coital vaginal contraceptive. It is purely of herbal origin available in plenty and indigenous. The smell can be marked by adding lemon grass scent can be used with the help of an applicator.

Further, studies were carried out in the direction of isolation of the active component(s) responsible for spermicidal, anti-implantation and abortifacient activities of neem oil so that standard products(s) which can be synthesised could be identified. Neem oil is subjected to steam distillation and the volatile fraction was isolated and coded as NIM-76. This volatile fraction was found to be a mixture of 28 components containing sulphur containing compounds and esters of fatty acids on GC-MS analysis. This fraction was found to retain the spermicidal activity in-vitro and on pre-coital application in the form of a jelly in rabbits and monkeys prevented pregnancy by its in vivo spermicidal activity. This product (NIM-76) impregnated in a suitable cream base is being taken up for multicentric clinical trials. The volatile fraction of NIM-76 was further fractionated and one of the fractions coded as DK-1, which is a single compound, was found to retain the in-vitro spermicidal activity. On in-vivo pre-coital application in rabbits and monkeys, DK-1 has been found to prevent pregnancy. Another fraction from neem oil isolated by solvent extraction and called bitter contains furano-tetranor terpenoids such as azadirachtin, nimbin, nimbidin, salannin, etc. This fraction on post-coital oral administration was found to prevent implantation or cause abortion in rats and rabbits depending upon the time of administration. This biter has further been fractionated in to 10 fractions out of which one fraction coded as DNM-5 has been found to possess anti-implantation activity and another fraction coded as DNM-7 has abortifacient activity in rats.

Studies on rabbits and monkeys with compound DNM-5 and DNM-7 are progressing. Toxicity studies of whole neem oil has already been done on animals and found to be non-toxic in the doses administered.

As a result of the above studies two contraceptives namely (a) pre-coital vaginal contraceptive and (b) a post-coital (postovulatory) oral contraceptive have been developed form neem oil. In addition an abortifacient agent also has been identified.

Characteristics

Neem oil is generally light to dark brown, bitter and has a rather strong odour that is said to combine the odours of peanut and garlic. It comprises mainly triglycerides and large amounts of triterpenoid

compounds, which are responsible for the bitter taste. It is hydrophobic in nature and in order to emulsify it in water for application purposes, it must be formulated with appropriate surfactants.

Chemical Constituents

Neem oil also contains steroids (campesterol, beta-sitosterol, stigmasterol) and a plethora of triterpenoids of which azadirachtin is the most well known and studied. terpenoids such as azadirachtin, nimbin, nimbidin, salannin, etc. The azadirachtin content of neem oil varies from 300ppm to over 2500ppm depending on the extraction technology and quality of the neem seeds crushed.

Table 1. Average composition of neem oil fatty acids.

Common Name	Acid Name	Composition range
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

Methods of extraction of neem oil

The method of processing is likely to affect the composition of the oil, since the methods used, such as pressing (expelling) or solvent extraction are unlikely to remove exactly the same mix of components in the same proportions. The neem oil yield that can be obtained from neem seed kernels also varies widely in literature from 25% to 45%. The oil can be obtained through pressing (crushing) of the seed kernel both through cold pressing and through a process incorporating temperature controls.

Neem seed oil can also be obtained by solvent extraction of the neem seed, fruit, oil, cake or kernel. A large industry in India extracts the oil remaining in the seed cake using hexane. This solvent-extracted oil is of a lower quality as compared to the cold pressed oil and is mostly used for soap manufacturing. Neem cake is a by-product obtained in the solvent extraction process for neem oil.

Mode of action of neem oil

Antfertility effect of neem oil is due to its effect on the immune system. The body's immune system gets stimulated to a degree where it kills the sperm and rejects (or rather resorbs) the embryo.Neem oil also cause the resorption of some embryos between day 8 pc and day 18 pc. In neem oil-treated mice, EGFR immunostaining decreased in the luminal and glandular epithelium and increased in the stroma as determined at 0600 hr on day 5 pc. Uterine secretions on day 4 through day 6 pc from the neem oil-treated mice showed massive leukocyte infiltration. Unimplanted preimplantationembryos, underdeveloped, degenerated, or at blastocyst stage, were recovered from the uteriafter flushing at 2000 hr on day 5 pc from the neem oil-treated animals. A number of retrieved unimplanted embryos showed the direct attachment of the leukocytes to their zona pellucida. It is believed that the secretions of these leukocytes might be responsible for theunderdevelopment of the early embryos and hence inhibition of implantation. The exactinteraction of these leukocytes and their secretions with the early embryos is under investigation. Postcoital intrauterine treatment of neem oil duringpreimplantation period causes fertility block in mouse by lowering the EGFR localization inthe luminal and glandular epithelium, by causing massive leukocytes infiltration into the uteri,by degenerating the early embryos, and by causing the postimplantation embryonic resorptionsin the uteri.

Dr. Beena Khillare find out the contraceptive efficacy of neem leaf extract on female albino rats The experiment was conducted on female albino ratswith proven fertility.Fifteen female albino rats were taken and divided in to three groups of five female rats of each .After confirmation of estrus phase, the extract was applied intravaginally in doses of 150mgand 200

mg in the two groups of female rats of five numbers each in 0.9% saline solution. Five female rats were taken for control group and only 0.9% saline solution was applied intravaginally.Immediatly after application of the extrat,the female rats were kept for mating with male rats in 2:1 ratio.After 24 hrs.,checked for sperms in the vaginal smears.At 200 mg dose all the sperms were non-motile or dead.and at 150 mg dose only 3-4 % sperms were sluggish and the rest were non-motile or dead.After confirmation of mating,this was taken as day one of pregnancy.Laparotomy was done on day 8 of pregnancy and implantation sites were observed.

A separate group of eight female rats was also studied for cyclicity. The rats were treated intravaginally in the estrus phase with 150 mg neem leaf extract everyday at 9-10 a.m. for complete cycle after 5-6 day of cohabitation with male rats, the female rats were separated and mating was confirmed by checking the vaginal smear.Laparotomy is done on day 8 of pregnancy.

Result- In-vivo study of contraceptive efficacy of aqueous neem leaf extract female albino rats shows that female albino rats in estrus cycle when treated intravaginally in the dose of 150 mg and 200 mg and mated with male rats gave 100% ant fertility effect with on implantation sites. Whereas in the control group of rats, 4-7 number of implantation sites were found in each rat. In the cyclicity study, no implantations were found in this group of rats and contraceptive efficacy was 100%.

Conclusion

Neem is a safe,effective and produces promisible potential reversible antfertility activity in male and female, neem is economically cheaf and easily available. Marketed available contraceptives are not safe it produces list of side effects. Neem is the safe,effective nontoxicherbal contraceptive for birth control. To increase contraceptive use of neem worldwide in coming year and to give more research attention towards it this review discus here.

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