CONTRACEPTION & NEEM

Overview

From the perspective of developing countries - or any woman concerned about the long-term impact of using hormones for birth control -- finding a method of contraception that is effective, inexpensive and easily available is truly a step toward solving global problems. Reports from the University of Florida encourage ongoing research into the use of neem as either a pre- or postcoital contraceptive, noting that it prevented in vitro attachment and proliferation of cells in concentrations as low as .05 to 1%. Another report in the American Journal of Reproduction indicates that purified extracts of neem contained immunomodulators that stimulate Th1 cells and macrophages that terminate pregnancies in rats, baboons and monkeys. Fertility was regained after one or two cycles with no apparent impact to future pregnancies.

Recent Research

Braz J Med Biol Res. 2005 Jun;38(6):943-7. Epub 2005 Jun 1.

Extracts of Azadirachta indica and Melia azedarach seeds inhibit folliculogenesis in albino rats.

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http://www.ncbi.nlm.nih.gov/pubmed/15933789?ordinalpos=2&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum

The seed oil of Azadirachta indica A. Juss (neem) is used in traditional medicine for its antidiabetic, spermicidal, antifertility, antibacterial, and wound healing properties. The present study was undertaken to investigate the quantitative aspects of follicular development in cyclic female albino rats (135 +/- 10 g; 8 groups with 6 animals in each group) after oral administration of polar (PF) and non-polar (NPF) fractions of A. indica seed extract at 3 and 6 mg kg body weight-1 day-1 and Melia azedarach Linn. (dharek) seed extract at 24 mg kg body weight-1 day-1 for 18 days. The extracts were prepared using a flash evaporator at 35 degrees C and then dissolved in olive oil to prepare doses on a per kg body weight basis. There was a significant reduction (P = 0.05) in the number of normal single layered follicles (A. indica: 0.67 +/- 0.33 and 4.67 +/- 2.03 after 3 and 6 mg/kg NPF, and 3.33 +/- 1.67 and 1.00 +/- 1.00 after 3 and 6 mg/kg PF vs control: 72.67 +/- 9.14 and M. azedarach: 0.60 +/- 0.40 and 1.80 +/- 1.2 after 24 mg/kg PF and NPF, respectively, vs control: 73.40 +/- 7.02) and follicles in various stages (I-VII) of follicular development in all treatment groups. These extracts also significantly reduced (P = 0.05) the total number of normal follicles in the neem (14.67 +/- 5.93 and 1.00 +/- 1.00 after 3 and 6 mg/kg PF and 3.67 +/- 0.88 and 5.33 +/- 2.03 after 3 and 6 mg/kg NPF) and dharek (13.00 +/- 3.58 and 14.60 +/- 2.25 after 24 mg/kg NPF and PF)

treatments compared to control (216.00 +/- 15.72 and 222.20 +/- 19.52, respectively). Currently, indiscriminate use of persistent and toxic rodenticides to control rodent populations has created serious problems such as resistance and environmental contamination. Therefore, it becomes necessary to use ecologically safe and biologically active botanical substances that are metabolized and are not passed on to the next trophic level, and that interfere with the reproductive potential particularly growth and differentiation of follicles. This may help elevate the socio-economic status of the country. Thus, the present study is an attempt to investigate the effects of A. indica and M. azedarach seed extracts on reproduction of albino rats.
PMID: 15933789 [PubMed - indexed for MEDLINE]

Sheng Wu Yi Xue Gong Cheng Xue Za Zhi. 2004 Dec;21(6):979-82.

[Preparation of contraceptive pill microcapsule and its anti-fertility effect]

[Article in Chinese]

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http://www.ncbi.nlm.nih.gov/pubmed/15646346?ordinalpos=4&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum

The main component of this pill is 2-Octadecanoic acid-4-Palmitic acid-2, 4-Pentanediyl ester separated from chloroform extract of neem oil. The microcapsules coated by the re-curdle method were fabricated with an average particle size of 100-180 microm. The morphological characteristics, incorporation efficiency, carrier reclamation efficiency of the microcapsule were investigated. Kunming mice were used in the experiment, and the anti-fertility effect of the microcapsule on the histology and apoptosis was studied by light and electron microscopy and the flow cytometry. The data obtained clearly indicated that the microcapsule could lead to the payload of medicine, the incorporation efficiency being 90%. After the microcapsules were given to the male mice orally, its anti-fertility effect came into being and could keep the mice in a state of reversible infertility for a long time. The results of histological study and flow cytometry indicate that the mechanism of its anti-fertility effect involves mainly the inhibition of sperm motility and the arrest of spermatogenic process.
PMID: 15646346 [PubMed - indexed for MEDLINE]

Contraception. 2003 Sep;68(3):225-9.

Spermicidal activity of Azadirachta indica (neem) leaf extract.

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The present study was carried out to evaluate the effective concentration of aqueous extract of old and tender Azadirachta indica (neem) leaves to immobilize and kill 100% human spermatozoa within 20 s. Sander-Cramer test was used to study the spermicidal activity of

neem leaf extract. Under the test conditions, minimum effective spermicidal concentrations for tender and old leaf extracts were 2.91 +/- 0.669 mg/million sperm and 2.75 +/- 0.754 mg/million sperm, respectively. The effect of extracts on morphology and viability of sperm was also studied and no change was observed in morphology of head, mid-piece and tail and no viable sperm seen. The leaf extracts were found to be water soluble and carbohydrate in nature. The effect of different concentrations of extracts (old and tender) on percentage motility of the sperm was also studied. With an increase in concentration, there is a linear decrease in percentage motility, becoming zero at a 3-mg dose within 20 s.
PMID: 14561544 [PubMed - indexed for MEDLINE]

J Ethnopharmacol. 1999 Nov 30;67(3):287-96.

Early post implantation contraceptive effects of a purified fraction of neem (Azadirachta indica) seeds, given orally in rats: possible mechanisms involved.

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Neem seed and leaf extracts have immunomodulators that induce cellular immune reactions. These aspects of neem were exploited in earlier studies, where the oral administration of the neem seed extracts in rodents and primates could completely abrogate pregnancy at an early post implantation stage. Complete restoration of fertility was observed in the animals treated in the subsequent cycles. For the purpose of using neem as a long term contraceptive, an activity guided fractionation, followed by identification and characterization of the biologically active fraction from neem seeds was carried out. Sequentially extracted fractions of neem seeds were tested orally at an early post implantation stage in rats. The hexane extract of the neem seeds was found to be biologically active and was the precursor for the final active fraction. The active fraction, identified as a mixture of six components, could completely abrogate pregnancy in rodents up to a concentration of 10%. No apparent toxic effects could be seen following treatment with the fraction. The treatment with the active fraction caused a specific activation of T lymphocyte cells of CD8+ subtype as well as phagocytic cells followed by elevation in cytokines gamma-interferon and TNF. The results of the present study show that a pure active fraction of neem seeds could be obtained for the purpose of early post implantation contraception when given orally, and its mechanism of action seems to be by activating cell mediated immune reactions.
PMID: 10617063 [PubMed - indexed for MEDLINE]

J Ethnopharmacol. 1998 Apr;60(3):235-46.

Immunocontraceptive activity guided fractionation and characterization of active constituents of neem (Azadirachta indica) seed extracts.

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http://www.ncbi.nlm.nih.gov/pubmed/9613837?ordinalpos=4&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

A novel approach for immunocontraception by intervention of local cell mediated immunity in the reproductive system by using single intrauterine application of neem oil has been described earlier. The reversible block in fertility was reported to last for 107-180 days in female Wistar rats (Upadhyay et al., 1990. Antifertility effects of neem oil by single intrauterine administration: A novel method of contraception. Proceedings Of The Royal Society Of London B 242, 175-180) and 7-11 months in monkeys (Upadhyay et al., 1994. Long term contraceptive effects of intrauterine neem treatment (IUNT) in bonnet monkeys: An alternative to intrauterine contraceptive devices. Contraception 49, 161-167). The present study, describes the identification and characterization of the biologically active fraction from neem seeds (Azadirachta indica A. Juss. Family Meliaceae), responsible for the above activity in adult female Wistar rats. Initial studies with the mechanically extracted oil and solvent extracts of neem seeds have revealed that the antifertility activity was present in constituents of low to intermediate polarity. A hexane extract of neem seeds was reported to be biologically active (Garg et al., 1994. Comparison of extraction procedures on the immunocontraceptive activity of neem seed extracts. Journal of Ethnopharmacology 22, 87-92). Subsequently, hexane extract was sequentially fractionated through the last active fraction using various separation techniques and tested for antifertility activity at each step. Preparative HPLC was used for isolating individual components of the active fraction in quantities, sufficient for characterization. An analytical HPLC method was developed for standardization of the fraction. The active fraction was identified to be a mixture of six components, which comprises of saturated, mono and di-unsaturated free fatty acids and their methyl esters. Dose response study was performed with the last active fractions. The antifertility activity with the active fraction was reversible in nature and it was completely active until 5% concentration. There was no systemic toxic effect following the administration of the active fraction. This study, for the first time, proposes an active fraction from neem seeds, responsible for long term and reversible blocking of fertility after a single intrauterine administration with high efficacy.
PMID: 9613837 [PubMed - indexed for MEDLINE]

Contraception. 1997 Nov;56(5):329-35.

Tests of vaginal microbicides in the mouse genital herpes model.

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http://www.ncbi.nlm.nih.gov/pubmed/9437563?ordinalpos=5&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

Microbicide candidates were selected that have demonstrated activity against sperm or sexually transmitted disease pathogens in vitro, and the efficacy of these agents for preventing vaginal transmission of genital herpes infection was evaluated in the progestin-treated mouse. Each agent was delivered to the vaginas of mice approximately 20 sec prior to delivering a highly infectious herpes simplex virus-2 inoculum. The following agents provided significant protection: anti-HSV monoclonal antibodies III-174 and HSV8, modified bovine beta-lactoglobulin (beta-69), carrageenan, concanavalin A, chlorhexidine, dextran sulfate (average molecular weight 8,000 and 500,000), fucoidan, neem, nonoxynol-9, polystyrene sulfonate, and povidone-iodine. Two agents, gramicidin and heparan sulfate, though highly effective in vitro, were not protective in vivo at the doses tested.
PMID: 9437563 [PubMed - indexed for MEDLINE]

Am J Reprod Immunol. 1997 Jun;37(6):485-91.

Induced termination of pregnancy by purified extracts of Azadirachta Indica (Neem): mechanisms involved.

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PROBLEM: To develop a self-administered, orally delivered method for abrogation of early pregnancy. METHOD: Use of purified Neem extracts containing immunomodulators stimulating Th1 cells and macrophages; test animals, rats, baboons, and monkeys, onset of pregnancy confirmed by surgery and counting of implants on day 7 in rats and by chorionic gonadotropin (CG) and progesterone assays in primates; termination defined by complete resorption on day 15 in rats and by bleeding and decline of CG and progesterone in baboons. RESULTS: Pregnancy was terminated successfully in both rodents and primates with no significant side effects. Fertility was regained in both species after one or two irregular cycles. Progeny born had normal developmental landmarks and mothered normal litters in the course of time. The active principle in Neem has been partially fractionated by activity-guided purification. A cascade of events are involved in abrogation of pregnancy. In primates, a decrease in progesterone is an early event. A transient increase in CD4 and CD8 cells is noted in spleen at 96 hr and in mostly CD8 cells in mesenteric lymph nodes. Treatment causes an elevation of both immunoreactive and bioactive TNF-alpha and gamma-interferon in serum, mesenteric lymph nodes, and foetoplacental tissue. CONCLUSION: Immunomodulators of plant origin are potentially usable for termination of unwanted pregnancy

Immunol Cell Biol. 1997 Apr;75(2):190-2.

Plant immunomodulators for termination of unwanted pregnancy and for contraception and reproductive health.

Talwar GP, **Raghuvanshi P**, **Misra R**, **Mukherjee S**, **Shah S**.

Plant immunomodulators for termination of unwanted pregnancy and for contraception and reproductive health.

http://www.ncbi.nlm.nih.gov/pubmed/9107574?ordinalpos=6&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

Neem (Azadirachta indica) seed and leaf extracts have spermicidal, anti-microbial, anti-fungal and anti-viral properties. They are also immunomodulators that induce primarily a TH1 type response. These properties are being exploited to develop two different useful methods of fertility control. Neem extracts given orally at early post-implantation stage terminate pregnancy in rodents and primates. Treatment has no residual permanent effect and fertility is regained in subsequent cycles. The mechanism by which the action occurs is not fully clear. A transient increase in CD4 and more significantly in CD8 cells is noticed in mesenteric lymph nodes and spleen. A rise in immunoreactive and bioactive TNF-alpha and IFN-gamma in draining lymph nodes, serum and foetal-placental tissue is observed. A polyherbal cream and pessary have been developed containing three active ingredients of plant origin. These have synergistic spermicidal properties on human sperm as determined by the Sander Cramer test. Their use before mating has high contraceptive efficacy in rabbits and baboons. Another interesting property is their inhibitory action on a wide spectrum of micro-organisms, including Candida albicans, C. tropicalis, Neisseria gonorrhoeae, the multidrug-resistant Staphylococcus aureus and urinary tract Escherichia coli, Herpes simplex-2 and HIV-1. Phase I clinical trials have been completed in India, Egypt and the Dominican Republic, and indicate the safety of the formulation, its acceptability and beneficial action invaginosis due to infections.
PMID: 9107574 [PubMed - indexed for MEDLINE]

J Ethnopharmacol. 1997 Jan;55(2):133-9.

Immunomodulatory effects of NIM-76, a volatile fraction from Neem oil.

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http://www.ncbi.nlm.nih.gov/pubmed/9032626?ordinalpos=10&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum

The immunomodulatory properties of NIM-76 have been described in this paper. Pre-treatment of rats with a single i.p. injection of NIM-76 resulted in an increase in polymorphonuclear (PMN) leukocytes with a concomitant decrease in lymphocyte counts. The immunomodulatory activity of NIM-76 was found to be concentration-dependent. At 120 mg/kg body weight, there was an enhanced macrophage activity and lymphocyte proliferation response, while the humoral component of immunity was unaffected. At higher concentrations of NIM-76 (300 mg/kg body weight), there was a stimulation of mitogen-induced lymphocyte proliferation, while macrophage activity remained unaffected. However, a fall in primary and secondary

antibody titres was observed. The study indicates that NIM-76 acts through cell-mediated mechanisms by activating macrophages and lymphocytes.
PMID: 9032626 [PubMed - indexed for MEDLINE]

Contraception. 1996 Dec;54(6):373-8.

Mechanism of action of NIM-76: a novel vaginal contraceptive from neem oil.

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http://www.ncbi.nlm.nih.gov/pubmed/8968666?ordinalpos=7&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The present study was undertaken to elucidate the mechanism of spermicidal action of NIM-76, a fraction isolated from neem oil. The spermicidal activity of NIM-76 was confirmed using a fluorescent staining technique. NIM-76 was found to affect the motility of the sperm in a dose-dependent manner. Supplementation of pentoxifylline, which is known to enhance the motility of the sperm, could not prevent the spermicidal action of NIM-76. There was a gradual leakage of cytosolic LDH from the sperm in the presence of NIM-76. Electron microscopic studies revealed the formation of pores and vesicles over the sperm head, indicating the damage to the cell membrane. Membrane fluidization studies did not reveal any significant change in the fluidity of sperm cell membrane structure.

PIP: Neem oil, an extract of a native plant of India, has been demonstrated to have anti-fertility, anti-implantation, and abortifacient properties. An active fraction, termed NIM-76, was extracted that eliminates its abortifacient properties while retaining spermicidal activity. This fraction kills all human sperm in vitro in under 20 seconds at a concentration of 25 mg/ml. With increases in NIM-76 concentrations from 10 to 1000 mcg/ml, there was a linear decrease in percentages of motile as well as progressively motile sperm with time; also recorded were decreases in percentages of rapid, medium, and slow moving sperm, mean track speed, progressive velocity, mean linearity, and lateral head displacement and an increase in the percentage of static sperm. Electron microscopy revealed the formation of pores and vesicles over the sperm head, indicating damage to the cell membrane. Membrane fluidization studies did not reveal any significant change in the fluidity of sperm cell membrane structure. Since calcium supplementation did not relieve the sperm from the spermicidal action, it was determined that NIM-76 does not cause any depletion of intracellular calcium. The capability of NIM-76 to selectively kill sperm without affecting normal cells makes it a highly desirable potential vaginal contraceptive agent.
PMID: 8968666 [PubMed - indexed for MEDLINE]

J Assist Reprod Genet. 1996 Aug;13(7):578-85.

Contraception potential of neem oil: effect on pregnancy success in the mouse.

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http://www.ncbi.nlm.nih.gov/pubmed/8844316?ordinalpos=8&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

PURPOSE: The aim of this study was to find out the role and mechanism of action of neem oil as a postcoital fertility blocker in mouse. METHODS: Female mice were injected with neem oil (20 or 40 microliters) surgically into each uterine horn on day 2 postcoitum (pc). Both the uterine horns of each mouse were injected. Arachis oil served as vehicle control. Pregnancy success was determined by the number of implanted embryos on day 8 pc and the number of live fetuses in the uteri on day 18 pc. Transforming growth factor-alpha (TGF alpha), epidermal growth factor (EGF), and epidermal growth factor receptor (EGFR) were immunolocalized in the paraffin-embedded sections of the uteri at 0600 hr on day 5 pc. The unimplanted embryos were assessed in the uteri at 2000 hr on day 5 pc. Uterine secretions were assessed for the leukocytes infiltration on day 4 through day 8 pc. RESULTS: The number of implantation sites on day 8 pc and the number of live fetuses on day 18 pc were lower in the neem oil-treated animals compared to their respective control animals at both the concentrations of neem oil (20 and 40 microliters/uterine horn). Neem oil also caused 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 preimplantation embryos, underdeveloped, degenerated, or at blastocyst stage, were recovered from the uteri after 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 the underdevelopment of the early embryos and hence inhibition of implantation. The exact interaction of these leukocytes and their secretions with the early embryos is under investigation. CONCLUSIONS: Postcoital intrauterine treatment of neem oil during preimplantation period causes fertility block in mouse by lowering the EGFR localization in the luminal and glandular epithelium, by causing massive leukocytes infiltration into the uteri, by degenerating the early embryos, and by causing the postimplantation embryonic resorptions in the uteri. The possible mechanism of action of neem oil is discussed.
PMID: 8844316 [PubMed - indexed for MEDLINE]

Contraception. 1996 Jun;53(6):375-8.

Purified neem (Azadirachta indica) seed extracts (Praneem) abrogate pregnancy in primates.

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http://www.ncbi.nlm.nih.gov/pubmed/8773426?ordinalpos=9&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The use of neem (Azadirachta indica) seed extracts (Praneem) given orally for abrogation of pregnancy in subhuman primates is described. Oral administration of Praneem was initiated after confirmation of pregnancy using Leydig cell bioassay estimating rising levels of chorionic gonadotropin (CG) in the blood from day 25 onwards of the cycle and continued for six days. Termination of pregnancy was observed with the appearance of blood in the vaginal smears and decline in CG and progesterone. Pregnancy continued in the control animals treated with peanut oil at the same dose. The effect was observed in both baboons and bonnet monkeys. The treatment was well tolerated; blood chemistry and liver function tests had normal values. The animals regained their normal cyclicity in the cycles subsequent to Praneem treatment.
PMID: 8773426 [PubMed - indexed for MEDLINE]

Indian J Med Res. 1995 Aug;102:66-70.

Safety of intrauterine administration of purified neem seed oil (Praneem Vilci) in women & effect of its co-administration with the heterospecies dimer birth control vaccine on antibody response to human chorionic gonadotropin.

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http://www.ncbi.nlm.nih.gov/pubmed/8834816?ordinalpos=13&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum

Praneem Vilci (PV), purified neem oil was reported to exercise a reversible antifertility effect after a single intrauterine instillation in rodents and primates without any adverse effects. After toxicology, drug regulatory and ethical clearances, a phase I clinical trial was conducted on PV. Eighteen healthy tubectomised women were enrolled to evaluate the safety of a single intrauterine instillation of PV and to determine the effect of its co-administration on anti-hCG response to the heterospecies dimer (HSD) hCG vaccine. Eight women received PV alone and ten women were given the HSD-hCG vaccine in addition. Base-line and post-treatment haematological and biochemical profiles were determined as also the mid-luteal serum progesterone. Endometrial biopsies were examined to assess ovulatory status and the effect of intrauterine treatment with PV on the endometrium. Anti-hCG antibody titres were estimated in women who were concurrently immunized with the HSD vaccine. No untoward reaction was observed in any woman. Menstrual pattern and ovulatory status remained unaltered. Endometrial biopsy after PV instillation in one woman showed non-specific endometritis but

she remained asymptomatic. Mild eosinophilia was seen in two women and this reverted to normal on its own. All women receiving PV and the HSD vaccine generated antibodies against hCG. Our data show that intrauterine administration of PV is safe and does not prevent the antibody response to HSD-hCG vaccine.
PMID: 8834816 [PubMed - indexed for MEDLINE]

Contraception. 1995 Mar;51(3):203-7.

Mode of long-term antifertility effect of intrauterine neem treatment (IUNT).

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http://www.ncbi.nlm.nih.gov/pubmed/7621690?ordinalpos=10&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The mode of antifertility action of intrauterine neem treatment (IUNT) was studied. The effect of IUNT on ovarian functions and uterine responsiveness to ovarian hormones was examined in adult Wistar rats. The treated animals had normal reproductive cycles as indicated by the vaginal smears; serum progesterone levels were also in the normal range. Effect of exogenous estradiol following IUNT in ovariectomized rats showed comparable uterine weight gain as in control group; decidual cell reaction of the uterine epithelium following IUNT was also similar to that of control, indicating normal uterine responsiveness to ovarian hormones. Unilateral IUNT followed by mating resulted in degeneration of embryos on the treated side as noted between days 3-5 post coitum; normal embryos were seen on the contralateral side given peanut oil. The study shows that the mode of antifertility action of IUNT is not because of uterine unresponsiveness to the ovarian hormones but is due to impairment of embryo development. The results of this study thus confirm our earlier observations and show further that the antifertility effect of IUNT is at the pre-implantation stage, localized and without any adverse or toxic effect on the fetal development in the contralateral uterine horn of the unilaterally treated rats. The exact mechanism(s) of antifertility action of IUNT is being investigated.

J Ethnopharmacol. 1994 Oct;44(2):87-92.

Comparison of extraction procedures on the immunocontraceptive activity of neem seed extracts.

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http://www.ncbi.nlm.nih.gov/pubmed/7853869?ordinalpos=13&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

Azadirachta indica (Neem) seed extracts are known to activate the local cell-mediated immune reactions after a single intrauterine administration, leading to a long term reversible block of fertility. In order to identify and characterize the active fraction responsible for this activity, neem seeds were extracted by both mechanical expression and solvent extraction using a range of polar to non-polar solvents which yielded 3 broad fractions. The mechanically expressed oil was fractionated using different approaches and studied for antifertility activity. The hexane

extract and a corresponding column fraction showed potent and reproducible antifertility activity. Other fractions were less stable with regard to reproducibility of effects and composition. It is our conclusion that for subsequent fractionation to reach the last active fraction, the hexane extract is the most useful starting material.
PMID: 7853869 [PubMed - indexed for MEDLINE]

J Assist Reprod Genet. 1994 Sep;11(8):419-27.

Neem oil inhibits two-cell embryo development and trophectoderm attachment and proliferation in vitro.

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http://www.ncbi.nlm.nih.gov/pubmed/7606156?ordinalpos=17&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum

PURPOSE: The in vitro effect of neem oil was studied on the development of mouse two-cell embryos and trophectodermal cell attachment and proliferation. METHOD: Female mice were primed with gonadotropins for superovulation and caged with male mice. Early embryos, at the two-cell and the blastocyst stages, were recovered at 40 and 88 hr post-hCG from the oviducts and the uteri, respectively. In the first experiment, two-cell embryos were exposed to culture medium containing different concentrations of neem oil for 1, 12, and 24 hr and then grown in neem oil-free culture medium and assessed for the formation of total and hatching blastocysts at 96 hr. In the second experiment, partially hatching blastocysts were cocultured with human endometrial stromal cell monolayers in culture medium containing different concentrations of neem oil and assessed for the attachment and proliferation of trophectodermal cells at 96 hr. RESULTS: Exposure of two-cell embryos to neem oil concentrations of 0.050-0.500% for 1 hr, 0.010-0.250% for 12 hr, and 0.005-0.100% for 24 hr caused significant inhibition of the formation of total and hatching blastocysts, in a dose-dependent manner. Neem oil at 0.050-0.100% concentrations inhibited, in a dose-dependent manner, the in vitro attachment and proliferation of trophectodermal cells of partially hatching blastocysts cocultured with human endometrial stromal cells monolayers. CONCLUSION: Neem oil inhibits the development of two-cell embryos and attachment and proliferation of the trophectodermal cells of partially hatching blastocysts in vitro. The study encourages the use of this herbal product as a postcoital contraceptive that warrants further research.
PMID: 7606156 [PubMed - indexed for MEDLINE]

Contraception. 1994 Aug;50(2):185-90.

Synergistic spermicidal activity of neem seed extract, reetha saponins and quinine hydrochloride.

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http://www.ncbi.nlm.nih.gov/pubmed/7956217?ordinalpos=15&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

In order to identify potent spermicidal agents which are free from the side effects of currently available agents, spermicidal activity of purified neem seeds extract (Praneem), reetha saponins and quinine hydrochloride was studied individually and in combination. Sander-Cramer test was used to assess the activity on human sperm. Under the test conditions, minimum effective spermicidal concentrations for Praneem, reetha saponins and quinine hydrochloride were 25%, 0.05% and 0.346%, respectively. At these concentrations, 100% of the sperm were immobilised within 20 seconds. A positive synergistic effect in the spermicidal activity of these components, if used in combination, was observed which implies the use of reduced concentrations of each to bring about the desired action. The selected combination formulated into a suitable dosage form is likely to offer dual benefit of a potent contraceptive and an antimicrobial preparation.

PIP: Contraceptive researchers in India and the United States used a modified version of the Sander-Cramer test to measure the minimum concentration of purified neem seeds extract, reetha saponins (pericarp of Sapindus fruits), and quinine hydrochloride to kill all sperm within 20 seconds. They wanted to determine the individual and combined action of these potential spermicidal agents on sperm motility and survival. The concentrations needed to effect the death of 100% of human sperm within 20 seconds were 25% for neem oil, 0.05% for reetha saponins, and 0.346% for quinine hydrochloride. A mixture of 25% neem extract, 1% reetha saponins, and 0.75% quinine hydrochloride was spermicidal up to a dilution of 72 times. This dilution was much higher ($p = .0004$) than the highest spermicidal dilution attained by reetha saponins, the most potent component of the mixture. The positive synergistic effect in the spermicidal activity of these components indicates reduced concentrations of each to achieve effective spermicidal activity (0.39% neem oil, 0.015% reetha saponins, and 0.0012% quinine hydrochloride). Reetha saponins contains considerable oleanolic acid or hederagenin, which have a mild detergent effect, inactivating sperm. Quinine chloride strengthens spermicidal activity and antimicrobial activity. Neem extract induces local cell-mediated immunity. Contraceptive developers can formulate the combination of these 3 components either as a cream or pessary.
PMID: 7956217 [PubMed - indexed for MEDLINE]

Indian Med Trib. 1994 Aug 15;2(13):7.

Immuno-contraception undergoing promising trials.

Koshy LM.

http://www.ncbi.nlm.nih.gov/pubmed/12179186?ordinalpos=14&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

PIP: Immuno-contraception instructs the body to recognize a self-molecule as foreign, so that the body attacks the molecule, thereby effecting contraception. When researchers in India were developing a contraceptive vaccine, they considered 3 things: the targeted molecule should be crucial for reproduction, it should be transient in nature, and the antibodies against this molecule should not cross-react with other molecules in the body. They have developed a vaccine using beta-human chorionic gonadotropin (hCG). The pregnant woman's body produces beta-hCG. It sustains the corpus luteum for production of progesterone which induces changes in the uterus conducive to implantation of the zygote. Researchers have linked beta-hCG with a carrier molecule (tetanus toxoid or diphtheria) to induce an immune attack. They have successfully completed phase 2 efficacy trials. This vaccine also protects against tetanus or diphtheria. Animal studies show that it does not have any harmful side effects and is reversible. The phase 2 trials included women with 2 children cohabiting with fertile partners. Once the antibody titres surpassed the protective threshold, they discontinued contraceptive use and any avoided pregnancies would be attributed to the vaccine alone. The trials exceeded the norm of 750 protected menstrual cycles for the vaccine to be considered efficacious in April 1993. Researchers continued to monitor the women until their anti-beta-hCG titres reached a near-zero level. They are now ready to begin phase 3 trials. Logistical obstacles to overcome are a 2 month-lapse between 1st dose and sufficient titres to protect against pregnancy and multiple injections. Neem oil use may provide protection during the lag phase since it stimulates immune cells in the reproductive tract and has embryocidal and spermicidal effects. A single injection of biodegradable microcarrier systems releasing the vaccine may address the problem with multiple doses.
PMID: 12179186 [PubMed - indexed for MEDLINE]

Contraception. 1994 Feb;49(2):161-9.

Long-term contraceptive effects of intrauterine neem treatment (IUNT) in bonnet monkeys: an alternate to intrauterine contraceptive devices (IUCD).

Upadhyay S, **Dhawan S**, **Sharma MG**, **Talwar GP**.

National Institute of Immunology, New Delhi, India.

http://www.ncbi.nlm.nih.gov/pubmed/8143455?ordinalpos=16&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

Antifertility effects of intrauterine neem treatment (IUNT) was studied in bonnet monkeys. A single administration of 1 ml of neem oil by an intrauterine insemination catheter blocked fertility for 7 to 12 months. The effect was, however, reversible as all the animals became pregnant subsequently and delivered normal babies. The neem oil treatment had no adverse effect on menstrual cyclicity and ovarian functions. The uterus of neem-treated animals showed normal morphology. Immunohistological studies, however, demonstrated a significant

increase in the number of MHC-II antigen-positive cells in the uterine endometrium following neem treatment, indicating enhanced antigen-presenting ability of the uterus; a feature that may be related to the observed antifertility effect of neem oil. The present investigation demonstrates that an IUNT can be used for long-term, reversible contraception, without any apparent side effects, and that the method could provide an alternate to currently used intrauterine contraceptive devices (IUCD).
PMID: 8143455 [PubMed - indexed for MEDLINE]

Contraception. 1993 Dec;48(6):591-6

Studies on the contraceptive efficacy of Praneem polyherbal cream.

Garg S, **Taluja V**, **Upadhyay SN**, **Talwar GP**.
National Institute of Immunology, New Delhi, India.
http://www.ncbi.nlm.nih.gov/pubmed/8131399?ordinalpos=17&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

Praneem polyherbal cream, a spermicidal formulation, has been developed at the National Institute of Immunology, which makes use of Praneem, a purified extract from the dried seeds of an ancient Indian plant Azadirachta indica (Neem), extract from the pericarp of fruits of Sapindus species and quinine hydrochloride. These ingredients have a synergistic spermicidal activity and an optimised formula was derived. The components were made into a water-soluble cream base prepared by using pharmaceutically acceptable base and stabilised by addition of IP grade antioxidant and preservatives. The cream is devoid of irritation and sensitization potential, as seen with standard Draize test on normal and abraded skin of rabbits and by 21-day cumulative skin sensitivity in human volunteers. The formulation was found to be safe under subacute toxicity studies in monkeys. The formulation has shown high contraceptive efficacy in rabbits and in monkeys after intravaginal application. The shelf-life of the cream at room temperature is estimated to be 18 months by accelerated stability studies.

PIP: In India, the National Institute of Immunology has developed Praneem polyherbal cream as a vaginal spermicide. Scientists combined a purified extract from the dried seeds of an ancient Indian plant Azadirachta indica (Neem), extract from the pericarp of fruits of Sapindus species, and quinine hydrochloride with a pharmaceutically acceptable base to make a water-soluble cream base. They added IP grade antioxidant and preservatives to stabilize the cream base. They applied the cream on a shaved or abraded part of the skin of human volunteers and rabbits and inserted it into the vagina of Bonnet monkeys to test for sensitivity and irritation. They studied the dissolution characteristics of the cream after intravaginal application in the rabbits and monkeys. They compared pregnancy rates of monkeys who received intravaginal application of 2 ml cream every day with those of control monkeys. Praneem polyherbal cream did not irritate the skin of the rabbits or the human volunteers. The accelerated stability studies found the shelf-life of the cream at room temperature to be 18 months. The cream dissolves entirely within 30 minutes in the vaginal secretions of the rabbits and 40 minutes in those of the monkeys. Precoital application of the cream provided complete protection against pregnancy in rabbits in the 1st 30 minutes after application. The conception rate was acceptable at 60 minutes (7%), but thereafter it climbed to unacceptable levels (28.6% at 90 minutes and 75% at 12 hours). The conception rate of monkeys who received precoital application of

Praneem polyherbal cream was only 2.27%. These results suggest that Praneem polyherbal cream can protect against pregnancy without causing irritation. Its antimicrobial properties provide another advantage.
PMID: 8131399 [PubMed - indexed for MEDLINE]

Life Sci. 1993;53(18):PL279-84.

Mouse sperm-egg interaction in vitro in the presence of neem oil.

Juneja SC, **Williams RS**.
Department of Obstetrics and Gynecology, College of Medicine, University of Florida, Gainesville 32610.
http://www.ncbi.nlm.nih.gov/pubmed/8231626?ordinalpos=24&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum

In vitro evidence is presented showing toxicity of neem oil on sperm-egg interaction in mouse. Cumulus oophorus-enclosed ova, inseminated with capacitated spermatozoa, were cultured in 1 ml of in vitro fertilization (IVF) medium and overlayered by 1 ml of different concentrations of neem oil (1, 5, 10, 25, 50 and 100%) for IVF duration of 4h. At the end of incubation, ova were allowed to grow in neem oil-free culture medium and assessed for fertilization, first cleavage (2-cell formation) and blastocyst formation in vitro at 4-14h, 24h and 108h post-insemination respectively. The study showed that the presence of neem oil at concentrations of 10, 25 and 50% caused inhibition of IVF in a dose-dependent manner. The toxic effect of exposure of 25 and 50% neem oil was further carried over to the first cleavage of the resulting fertilized ova and the toxic effect of 5, 10, 25 and 50% was carried over to the blastocyst formation from the resulting fertilized ova when grown in neem-oil free culture medium. A total of 94.1% inhibition of 2-cell formation and 100% inhibition of blastocyst formation from the inseminated ova was observed in 50 and 25% neem oil-treated groups respectively. Neem oil at 100% concentration caused 100% degeneration of ova at 1h of sperm-ova coculture. The study showed a direct toxic effect of neem oil on sperm-egg interaction in vitro and encourages research investigations of this herbal product as a pre-coital contraceptive.
PMID: 8231626 [PubMed - indexed for MEDLINE]

J Androl. 1993 Jul-Aug;14(4):275-81.

Antifertility effects of neem (Azadirachta indica) oil in male rats by single intra-vas administration: an alternate approach to vasectomy.

Upadhyay SN, **Dhawan S**, **Talwar GP**.
National Institute of Immunology, New Delhi, India.
http://www.ncbi.nlm.nih.gov/pubmed/8226307?ordinalpos=18&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

An alternate approach to vasectomy for long-term male contraception following a single intra-vas application of a traditional plant (Azadirachta indica) product having immunomodulatory properties is described. Male Wistar rats of proven fertility were given a single dose (50 microliters) of neem oil in the lumen of the vas deferens on each side; control animals received the same volume of peanut oil. Animals were put on continuous mating 4 weeks after the

treatment, with females of proven fertility. While the control animals impregnated the female partners, all males treated with neem oil remained infertile throughout the 8 months of observation period. Epididymal and vas histology were normal without any inflammatory changes or obstruction. The intra-vas administration of neem oil resulted in a block of spermatogenesis without affecting testosterone production; the seminiferous tubules, although reduced in diameter, appeared normal and contained mostly early spermatogenic cells. No anti-sperm antibody could be detected in the serum. Unilateral administration of neem oil in the vas resulted in a significant reduction of testicular size and spermatogenic block only on the side of application; the draining lymph node cells of the treated side also showed enhanced proliferative response to in vitro mitogen challenge. These results indicate that the testicular effects following intra-vas application of neem oil may possibly be mediated by a local immune mechanism.
PMID: 8226307 [PubMed - indexed for MEDLINE]

IDRC Rep. 1993 Jan;20(4):16-8.

A new family planning tool to slow population growth.

Newton P.

http://www.ncbi.nlm.nih.gov/pubmed/12318006?ordinalpos=19&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

PIP: The National Institute of Immunology in New Delhi, India, is conducting clinical trials of a prototype birth control vaccine. 88 20-36 year old women receive a series of 3 injections of 300 mcg human chorionic gonadotropin (hCG) vaccine to theoretically protect them from pregnancy for 1 year. After 1 year, they receive a booster shot to protect them for another year or not receive the booster, thereby resulting in a return to fertility. So far, only 1 pregnancy in 821 menstrual cycles has occurred. In women who do not use contraception, 821 cycles would normally result in 250-300 pregnancies. The developer of the vaccine thinks that these results confirm its effectiveness. The vaccine stimulates antibodies against hCG, thus keeping hCG from preparing the uterus for implantation. Some advantages include the following: it is reversible and effective for 1 year, does not alter women's physiology, and is less intrusive than other contraceptives. The International Development Research Centre of the Government of Canada has supported this vaccine's research since 1974. The Institute is now conducting research on a new contraceptive method using the purified extract of the neem tree called praneem. Researchers have injected it into the uterus of rats and monkeys. They hope it can be a safe and effective method for women to use during the 3 months when they receive their vaccine shots. The Institute is also working on perfecting the delivery system of the vaccine, e.g., a biodegradable implant releasing the required dosage over 1 year. It is also developing a finger-prick test to determine whether women who have accepted the vaccine are producing enough antibodies. Despite the progress, more research is needed.
PMID: 12318006 [PubMed - indexed for MEDLINE]

Int J Immunopharmacol. 1992 Oct;14(7):1187-93.

Immunomodulatory effects of neem (Azadirachta indica) oil.

Upadhyay SN, **Dhawan S**, **Garg S**, **Talwar GP**.

National Institute of Immunology, New Delhi, India.

http://www.ncbi.nlm.nih.gov/pubmed/1452404?ordinalpos=25&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum

Immunomodulatory effects of neem oil were studied in mice. The animals were treated intraperitoneally (i.p.) with neem oil; control animals received the emulsifying agent with or without peanut oil. Peritoneal lavage, collected on subsequent days, showed a maximum number of leukocytic cells on day 3 following treatment with neem oil; peritoneal macrophages exhibited enhanced phagocytic activity and expression of MHC class-II antigens. Neem oil treatment also induced the production of gamma interferon. Spleen cells of neem oil-treated animals showed a significantly higher lymphocyte proliferative response to in vitro challenge with Con A or tetanus toxoid (TT) than that of the controls. Pre-treatment with neem oil, however, did not augment the anti-TT antibody response. The results of this study indicate that neem oil acts as a non-specific immunostimulant and that it selectively activates the cell-mediated immune (CMI) mechanisms to elicit an enhanced response to subsequent mitogenic or antigenic challenge.

PMID: 1452404 [PubMed - indexed for MEDLINE]

Indian J Physiol Pharmacol. 1991 Oct;35(4):278-80.

Neem oil--a fertility controlling agent in rhesus monkey.

Bardhan J, **Riar SS**, **Sawhney RC**, **Kain AK**, **Thomas P**, **Ilavazhagan G**.

Defence Institute of Physiology and Allied Sciences, Delhi Cantt.

http://www.ncbi.nlm.nih.gov/pubmed/1812107?ordinalpos=26&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum

Neem oil, an oil extracted from the seeds of Azadirachta indica has been found to act as a good spermicidal agent. Pre and post coital application of the oil intravaginally prevented pregnancy in rhesus monkey.

PMID: 1812107 [PubMed - indexed for MEDLINE]

Contraception. 1991 Sep;44(3):319-26.

Antifertility activity of volatile fraction of neem oil.

Riar SS, **Devakumar C**, **Sawhney RC**, **Ilavazhagan G**, **Bardhan J**, **Kain AK**, **Thomas P**, **Singh R**, **Singh B**, **Parshad R**.

Defence Institute of Physiology and Allied Sciences, Delhi Cantt, India.

http://www.ncbi.nlm.nih.gov/pubmed/1764946?ordinalpos=20&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

NIM-76, the odorous and volatile fraction of neem oil, was investigated for its antifertility activity in vivo in rats, rabbits and rhesus monkeys. The drug is effective when applied before

coitus but not so when applied during post-coital stages. It, therefore, appears to act mainly by its spermicidal effect. No alteration in the estradiol (E2) and progesterone (P) values was observed after the application of the drug in monkeys.
PMID: 1764946 [PubMed - indexed for MEDLINE]

Curr Opin Obstet Gynecol. 1991 Aug;3(4):477-81.

Barrier contraceptives, spermicides, and periodic abstinence.

Connell EB.
Department of Gynecology/Obstetrics, Emory University School of Medicine, Atlanta, GA 30305.
http://www.ncbi.nlm.nih.gov/pubmed/1878503?ordinalpos=21&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

Although barrier contraceptives were among the first methods of preventing unwanted pregnancy ever described for human use, with the advent of the non-coitally related oral contraceptives and intrauterine devices, they gradually fell into relative disuse. However, for a variety of reasons, this is no longer the case. There is a renewed interest in these techniques both as a major form of birth control and also as our best protection against the transmission of sexually transmitted diseases, many of which are now occurring in epidemic form. This latter reason has stimulated fresh approaches to both physical barriers and spermicidal agents. In addition, attempts have also been made to assess the true effectiveness of periodic abstinence and ways in which to make its use more accurate and acceptable.

PIP: Concerns about preventing the transmission of sexually transmitted diseases as well as pregnancy have led to a renewed interest in barrier contraception and spermicides. Although the condom has received greatest emphasis, data suggest that the use of a female barrier method such as the diaphragm and sponge may be even more effective; for adolescent females, at highest risk, combined use of barrier and oral contraception may be indicated. Given the documented low acceptability of the condom among groups at greatest risk and a lack of knowledge about its proper use, interest has focused on female condoms that cover the entire vagina, cervix, part of the female perineum, and the base of the penis. Spermicides enhance the effectiveness of barrier contraceptives, and new approaches--including use of neem oil and in vitro cobaltous ions--are under development. Finally, research is underway to enhance the effectiveness of various forms of periodic abstinence and ovulation detection techniques. Promising appears to be the supplemental use of a barrier method at the time of presumed ovulation.
PMID: 1878503 [PubMed - indexed for MEDLINE]

Proc Biol Sci. 1990 Dec 22;242(1305):175-9.

Antifertility effects of neem (Azadirachta indica) oil by single intrauterine administration: a novel method for contraception.

Upadhyay SN, **Kaushic C**, **Talwar GP**.
National Institute of Immunology, New Delhi, India.
http://www.ncbi.nlm.nih.gov/pubmed/1983033?ordinalpos=22&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

A novel use of neem (Azadirachta indica) oil, a traditional plant product, for long-term and reversible blocking of fertility after a single intrauterine application is described. Female Wistar rats of proven fertility were given a single dose (100 microliters) of neem oil by intrauterine route; control animals received the same volume of peanut oil. Whereas all control animals became pregnant and delivered normal litters, the rats treated with neem oil remained infertile for variable periods ranging from 107 to 180 days even after repeated matings with males of proven fertility. 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. Unilateral administration of neem oil in the uterus blocked pregnancy only on the side of application whereas the contralateral uterine horn treated with peanut oil had normally developing foetuses; no sign of implantation or foetal resorption was noted in the neem-oil-treated horn. The ovaries on both sides had 4-6 corpora lutea indicating no effect of treatment on ovarian functions. The animals treated with neem oil showed a significant leukocytic infiltration in the uterine epithelium between days 3 and 5 post coitum, i.e. during the pre-implantation period. Intrauterine application of neem oil appears to induce a pre-implantation block in fertility; the possible mechanisms of the antifertility action are discussed.
PMID: 1983033 [PubMed - indexed for MEDLINE]

Contraception. 1990 Oct;42(4):479-87.

Volatile fraction of neem oil as a spermicide.

Riar S, **Devakumar C**, **Ilavazhagan G**, **Bardhan J**, **Kain AK**, **Thomas P**, **Singh R**, **Singh B**.
Defence Institute of Physiology and Allied Sciences, Delhi Cantt, India.
http://www.ncbi.nlm.nih.gov/pubmed/2257744?ordinalpos=23&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The volatile, odorous fraction of neem oil coded as NIM-76 obtained by steam distillation was investigated for in vitro spermicidal activity. The data showed that the minimum concentration which inhibited spermatozoal motility was 0.25 mg/ml for rat and 25 mg/ml for human spermatozoa. The effect of the drug on spermatozoal motility was found to be dose-dependent. The activity of this drug was not altered in the presence of vaginal or cervical mucus. Intra-vaginal application of NIM-76 in rabbits showed no irritation to the vaginal mucosa.
PMID: 2257744 [PubMed - indexed for MEDLINE]

Indian J Med Res. 1988 Oct;88:339-42.

Mechanism of antifertility action of neem oil.

Riar SS, **Bardhan J**, **Thomas P**, **Kain AK**, **Parshad R**.

http://www.ncbi.nlm.nih.gov/pubmed/3225018?ordinalpos=24&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

PIP: The purpose of this study was to determine whether the antifertility effect of the antiestrogenic substance neem oil, extracted from the seeds of Azadirachta indica, acts directly on the uterus or through absorption from the vaginal epithelium into the general circulation. In 4 groups of rats the left uterine horn was ligated 2 days after coitus. Rats in group A were used as controls. In group B 25 mcl neem oil was administered intravaginally on days 2-4 with the animals in head down position for 3 minutes to ensure that the neem oil was uniformly distributed in the vagina. In group C the neem oil was administered on days 4-6, and in group D on days 7-9, i.e., after implantation. The ligatures were removed on day 12, and no viable implantation sites were found in either horn. The study showed that the neem oil exerts its effect on the endometrium through absorption into the general circulation from the vaginal epithelium. The antiestrogenic quality of neem oil explains its anti-implantation effect. But the postimplantation effect, which caused implanted fetuses to be either resorbed or expelled, may be due to direct toxicity, to a fall in progesterone level, or to interference with the uterine utilization of progesterone.

PMID: 3225018 [PubMed - indexed for MEDLINE]

J Ethnopharmacol. 1988 May-Jun;23(1):53-9.

Non-hormonal post-coital contraceptive action of neem oil in rats.

Prakash AO, **Tewari RK**, **Mathur R**.

School of Studies in Zoology, Jiwaji University, Gwalior, India.

http://www.ncbi.nlm.nih.gov/pubmed/3419204?ordinalpos=31&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum

Neem oil, a natural product of Azadirachta indica was investigated for various hormonal properties in relation to its post-coital contraceptive action. At subcutaneous doses up to 0.3 ml/rat, neem oil did not possess any estrogenic, anti-estrogenic or progestational activity and appeared not to interfere with the action of progesterone. These findings were confirmed using the histo-architecture of the uterus of treated rats. Since the post-coital contraceptive effect of neem oil seems to be non-hormonal, neem oil would be expected to elicit less side effects than the steroidal contraceptives.

PMID: 3419204 [PubMed - indexed for MEDLINE]

Indian J Med Res. 1986 Jan;83:89-92.

Antifertility effect of neem oil in female albino rats by the intravaginal & oral routes.

Lal R, **Sankaranarayanan A**, **Mathur VS**, **Sharma PL**.

http://www.ncbi.nlm.nih.gov/pubmed/3699874?ordinalpos=32&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum

PMID: 3699874 [PubMed - indexed for MEDLINE]

No abstract available.

Indian J Med Res. 1984 Dec;80:708-10.

Anti-implantation effect of neem oil.

Sinha KC, **Riar SS**, **Bardhan J**, **Thomas P**, **Kain AK**, **Jain RK**.

http://www.ncbi.nlm.nih.gov/pubmed/6532974?ordinalpos=33&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum

PMID: 6532974 [PubMed - indexed for MEDLINE]
No abstract available.

Indian J Med Res. 1984 Jan;79:131-6.

Neem oil as a vaginal contraceptive.

Sinha KC, **Riar SS**, **Tiwary RS**, **Dhawan AK**, **Bardhan J**, **Thomas P**, **Kain AK**, **Jain RK**.

http://www.ncbi.nlm.nih.gov/pubmed/6724648?ordinalpos=25&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

PMID: 6724648 [PubMed - indexed for MEDLINE]
No abstract available.

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