SUMMARY AND CONCLUSION
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This study has shown that a single, intrauterine application of neem (Azadirachta indica) oil could block fertility in rodents for a minimum period of three months. The effect was specific for neem oil since equal volume of peanut oil given by the same route did not have any effect on fertility. The block was, however reversible since 50% of animals regained fertility during the observation period of six months. Although the anti fertility effect of the neem oil was seen at lower concentrations as well, the duration of the block was relatively short.

The application of the neem oil into the uterus did not interfere with the ovarian functions. The treated animals had normal follicular development, ovulation, reproductive cyclicity and libido. This was evidenced by ovarian histology and vaginal smears of the treated animals. Progesterone profiles of the treated animals confirmed the functional normalcy of the ovaries. No pathological changes were noted in the uterine morphology following the administration of the oil.

The intrauterine instillation of neem oil did not alter the receptivity of the uterus. This was demonstrated by the uterine weight gain in neem oil treated animals given exogenous estradiol, one month after ovariectomy. The histological study confirmed the estrogenic response of the uterus. The induction of decidualization in the uterus of neem oil treated animals following mechanical stimulation on day 5 post coitum, confirmed the progesterone priming and hormonal conditioning of the uterus.

The antifertility effect of neem oil was localized to the site of application. The animals receiving neem oil in one uterine horn had no fetuses in that horn, while the control horn receiving peanut oil had normally growing embryos. The
block in fertility was at the pre-implantation stage, since no implantation or fetal resorption sites were noted. Embryos flushed out on days 3-5 post-coitum from these animals showed degenerating embryos on the treated side whereas normally developing embryos were seen on the control side. The presence of degenerated embryos corresponded with the phenomenon of transient leukocytic infiltration into the uterine epithelium around the time of implantation. Enhanced antigen presenting capacity, as demonstrated by the presence of Ia antigen was observed in the uterine epithelium of the neem oil treated horn, in comparison to the control horn. These results indicated the involvement of local immune cell population in the antifertility effect observed following neem oil administration.

The involvement of the local immune cell population in causing the embryo degeneration was further confirmed by studies on the local draining lymph node cells. Significantly enhanced proliferative activity was observed in the lymph nodes of neem oil treated animals, following treatment. The supernatant collected from the culture of the lymph node cells showed significant embryocidal effect on the mouse embryo development in vitro. This effect was found to be heat labile and trypsin sensitive indicating the presence of a protein factor(s) responsible for the embryocidal activity.

From the present study, it can be concluded that the intrauterine application of neem oil leads to a long term, reversible block in fertility. The block is at the pre-implantation stage and is mediated by induction of non specific local cellular immune response. Neem oil possibly activates the local immune cell population and enhances the antigen presenting capacity of the uterine epithelium. Subsequently during mating, when the sperms are introduced into the uterus, instead of eliciting a facilitatory immune response as under normal circumstances, they evoke a rejection type of immune response. This is reflected by the transient
leukocytic infiltration and lymphocyte proliferation seen in local lymph nodes. The degeneration of the pre-implantation embryos appears to be mediated by the products of the activated leukocytes. The reversibility of the phenomenon probably corresponds to the life span of tissue macrophages, which normally survive 3-6 months. However the exact mechanism is still a matter of speculation.

The present study proposes for the first time, a novel method of long term, reversible contraception following a single intrauterine administration of neem oil, a traditional plant product, with 100% efficacy. It does not interfere with the hormonal cyclicity and is free from any systemic side effects.