

ANTIVIRAL COMPOUNDS IN NEEM

Overview

From the common cold that sweeps through neighborhoods every winter to AIDS, West Nile and avian flu, viral infections are among the most challenging facing researchers around the world. Neem has traditionally been used as an antiviral, and animal and laboratory research shows promising results. While researchers still have not pinpointed how neem works, it appears that compounds in neem may make it difficult for the virus to reproduce, thus minimizing the impact of an infection.

From a purely pragmatic perspective – how soon will I feel better? -- neem also boosts your body's immune system, kicking both the lymphocytic and cell-mediated immune systems into overdrive. Killer-T cells, part of the cell-mediated system, destroy microbes, viruses and cancer cells by injecting toxic chemicals into the invaders. Neem also boosts the body's macrophage response, which stimulates the lymphocytic system and boosts production of white blood cells.

That combination of antiviral activities and immunostimulatory action may be why researchers in Nigeria (partially funded through an agency of the US government) reported that 10 AIDS patients given neem leaf extract for 30 days gained an average of three kilograms – more than 6.5 pounds – plus saw significant increases in key parameters including CD4+, hemoglobin and platelet counts. The researchers also found that neem leaf extract protected 75% of human cells in a test tube from the HIV virus.

One of the first modern reports of neem being used as a medicinal herb focuses on the use of a neem leaf extract as an effective antiviral published in a 1969 article in the Indian Journal of Medical Research. Nearly 20 years later, research at Johns Hopkins University in Baltimore showed that neem "provided significant protection" against the herpes simplex virus-2 in mice infected with the highly infectious virus. ([Contraception. 1997 Nov; 56\(5\):329-35](#)).

More recently, a 2002 study reports that neem leaf extract inhibits the growth of Dengue virus, type 2, a viral hemorrhagic fever related to Ebola. Symptoms of viral fevers include malaise, headache, sore throat, abdominal pain, vomiting, diarrhea, fever and hemorrhaging, typically followed by multiorgan failure and bleeding. The study used water extracts of neem at maximum non-toxic concentrations. In vitro (test tube) tests showed it completely inhibited the virus. In vivo tests conducted on mice showed the neem extract resulted in inhibition of the virus as confirmed by the absence of symptoms. ([Journal of Ethnopharmacology, 2002 Feb;79\(2\):273-8](#)).

Another study of "in vitro" tests indicates that neem leaf extract inactivated and interfered with the reproduction of the coxsackie B virus, one of a group of enteroviruses that are second only to the "common cold" as the most infectious viral agents in humans. The enteroviruses cause an estimated 10 to 15 million or more symptomatic infections a year in the United States. In the study, neem leaf extract inhibited plaque formation in six types of the Cocksackie virus at

concentrations of 1000 micrograms per milliliter. The reports note that the neem leaf extract was most effective as a virucidal agent, and also interfered with the virus's reproductive cycle at an early stage. Additionally, researchers say the evidence suggests that the entire "battery" of compounds in neem have antiviral action for the coxsackie B group of viruses. ([Indian Journal of Experimental Biology, 1998 Nov; 36\(11\):1151-3](#)).

The Indian Journal of Experimental Biology also reported that neem "significantly enhanced" antibodies against the Newcastle Disease virus - a highly contagious and generally fatal disease affecting all species of birds. The chickens in the study had been naturally infected with infectious bursal disease (IBD), a devastating virus that causes an immuno-suppressive disease in chickens. IBD is a major economic problem in most of the world, so increased antibodies against highly infectious viruses like Newcastle Disease are critically important. ([Indian J Exp Biol. 1998 Nov; 36\(11\):1151-3](#))

Along with neem's proven ability as an antiviral agent, it also is a highly effective immune system booster. In fact, it's so effective that many researchers attribute its contraceptive properties - in both men and women - to an enhanced immune system. While scientists have not yet determined specifically how neem works, they do know it carries a one-two-three punch, boosting both the lymphocytic and cell-mediated immune systems, at the same time it kills or slows the growth of many disease-causing organisms such as bacteria, virus and fungus.

Current Research

[Curr Med Chem Anticancer Agents](#). 2005 Mar;5(2):149-6.

Medicinal properties of neem leaves: a review.

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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15777222&query_hl=45&itool=pubmed_docsum

Azadirachta indica, commonly known as neem, has attracted worldwide prominence in recent years, owing to its wide range of medicinal properties. Neem has been extensively used in Ayurveda, Unani and Homoeopathic medicine and has become a cynosure of modern medicine. Neem elaborates a vast array of biologically active compounds that are chemically diverse and structurally complex. More than 140 compounds have been isolated from different parts of neem. All parts of the neem tree- leaves, flowers, seeds, fruits, roots and bark have been used traditionally for the treatment of inflammation, infections, fever, skin diseases and dental disorders. The medicinal utilities have been described especially for neem leaf. Neem leaf and its constituents have been demonstrated to exhibit immunomodulatory, anti-

inflammatory, antihyperglycaemic, antiulcer, antimalarial, antifungal, antibacterial, antiviral, antioxidant, antimutagenic and anticarcinogenic properties. This review summarises the wide range of pharmacological activities of neem leaf.

Publication Types: [Review](#)

PMID: 15777222 [PubMed - indexed for MEDLINE]

[J Ethnopharmacol.](#) 2002 Feb;79(2):273-8.

Inhibitory potential of neem (*Azadirachta indica* Juss) leaves on dengue virus type-2 replication.

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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11801392&query_hl=45&itool=pubmed_docsum

In the present study we report in vitro and in vivo inhibitory potential of crude aqueous extract of neem leaves and pure neem compound (Azadirachtin) on the replication of Dengue virus type-2. In vitro antiviral activity of aqueous neem leaves extract assessed in C(6/36) (cloned cells of larvae of *Aedes albopictus*) cells employing virus inhibition assay showed inhibition in dose dependent manner. The aqueous extract of neem leaves at its maximum non-toxic concentration of 1.897 mg/ml completely inhibited 100-10,000 TCID₅₀ of virus as indicated by the absence of cytopathic effects. The in vivo protection studies with neem leaves extract at its maximum non-toxic concentrations 120-30 mg/ml resulted in inhibition of the virus replication as confirmed by the absence of Dengue related clinical symptoms in suckling mice and absence of virus specific 511 bp amplicon in RT-PCR. The pure neem i.e. Azadirachtin did not reveal any inhibition on Dengue virus type-2 replication in both in vitro and in vivo systems.

PMID: 11801392 [PubMed - indexed for MEDLINE]

[J Ethnopharmacol.](#) 2000 Aug;71(3):377-82.

Anti-microbial activity of a new vaginal contraceptive NIM-76 from neem oil (*Azadirachta indica*).

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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10940573&query_hl=45&itool=pubmed_docsum

Efficacy of NIM-76, a spermicidal fraction from neem oil, was investigated for its antimicrobial action against certain bacteria, fungi and Polio virus as compared to whole neem oil. The NIM-76 preparation showed stronger anti-microbial activity than the whole neem oil. It inhibited growth of various pathogens tested including *Escherichia coli* and *Klebsiella pneumoniae* which were not affected by the whole neem oil. NIM-76 also exhibited antifungal

activity against *Candida albicans* and antiviral activity against Polio virus replication in vero cell lines. It also protected mice from systemic candidiasis as revealed by enhanced % survival and reduced colony forming units of *C. albicans* in various tissues. This shows that NIM-76 has a potent broad spectrum anti-microbial activity.
PMID: 10940573 [PubMed - indexed for MEDLINE]

[J Commun Dis.](#) 1999 Jun;31(2):79-90.

'In vitro' antiviral activity of neem (*Azadirachta indica*. A. Juss) leaf extract against group B coxsackieviruses.

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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10810594&query_hl=45&itool=pubmed_docsum

The antiviral and virucidal effect of methanolic extract fraction of leaves of neem (*Azadirachta indica* A. Juss) (NCL-11) was studied regarding its activity and possible mechanism of action against Coxsackie B group of viruses. NCL-11 inhibited plaque formation in 6 antigenic types of Coxsackie virus B at a concentration of 1000 micrograms/ml at 96 hrs. 'in vitro'. Additionally virus inactivation, yield reduction and effect of time of addition assays suggested that NCL-11 was most effective against coxsackie virus B-4 as a virucidal agent besides interfering at an early event of its replicative cycle. The evidence suggested that presence of a battery of compounds besides flavonoids, triterpenoids and their glycosides in NCL-11 have antiviral action for coxsackie B group of viruses 'in vitro.' The minimal inhibitory concentrations were not toxic to Vero (African green monkey kidney), cells; subtoxic concentration was 8,000 micrograms/ml and cytotoxic concentration 10,000 micrograms/ml, which was confirmed by trypan blue dye exclusion test.
PMID: 10810594 [PubMed - indexed for MEDLINE]

[Analyst.](#) 1999 Jan;124(1):19-21.

Rapid preconcentration method for the determination of azadirachtin-A and -B, nimbin and salannin in neem oil samples by using graphitised carbon solid phase extraction.

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http://www.ncbi.nlm.nih.gov/pubmed/10563041?ordinalpos=5&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

A simple and rapid method involving solid phase extraction and liquid chromatography for the determination of azadirachtin-A and -B, nimbin and salannin at nanogram levels in neem oil samples is presented. The neem oil samples are defatted and the compounds of interest extracted by mixing the sample with hexane and passing the hexane solution through a graphitised carbon black column. After washing the column with 2 ml of hexane, azadirachtin-A and -B, nimbin and salannin are eluted with 5 ml of acetonitrile and quantified using HPLC

with UV detection. The recoveries of azadirachtin-A and -B, nimbin and salannin in fortified oil samples were 97.4-104.7%. The upper limit of quantification is up to 100 micrograms ml⁻¹ without any additional clean-up and with little interference from lipids during the analysis by HPLC. The method was successfully applied to various neem oil samples collected from different locations in India.

PMID: 10563041 [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/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9437563&query_hl=45&itool=pubmed_docsum

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]

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

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

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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]

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