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A REVIEW ON ANTIVIRAL POTIENTIAL OF NEEM AGAINST DIFFERENT TYPE OF VIRUS

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ABSTRACT

Neem (Azadirachta indica), also known as Indian Lilac, has been known in India for centuries for its many healing properties. Neem has been commonly used in Ayurvedic medicine by Indians for over 2000 years. Neem contains a variety of biologically active ingredients that are help in the prevention and treatment of various virus disorder. Various studies, clinical trial and molecular docking reveals that extraction obtained from different part of Neem have been found to exert antiviral effect and may target a wide range of viral protein. Purpose of this review to highlight the in vitro inhibitory potential of crude aqueous, acetone and alcoholic extract of neem leaves, barks and pure neem compound and the neem extract significantly inhibit Chickenpox, HIV/AIDS, HSV, Duck Plague Virus, Polio Virus, Coxsackie B group Virus, Hepatitis B and C Virus, COVID -19 Virus. Also suggesting research on barks extract reveals that neem may help fight future corona variants.

KEYWORDS: Antiviral, Neem, Virus, Methanolic Extract, Acetone Extract.

INTRODUCTION

The purpose of this paper is to review the most recent literature regarding the antiviral evidence of neem. Of the papers studied, Neem have been most consistently associated with treatment of acne, nourishes skin treat fungal infections, useful in detoxification, insect and mosquito repellent, antibacterial, anthelmintic, antiviral, anticancer and Immunomodulatory agent. The 1969 study on the use of neem as a medicinal plant published in the Indian Journal of Medical Research directed on the use of neem leaf extract as an effective antiviral agent. Scientific and researchers' reports have shown that neem reduce progressive growth of many viruses, including polio, HIV, coxsackie B, and dengue in the early stages of their replication.

Reported uses of neem as follows:

1. Acne
2. Nourishes Skin
3. Fungal Infections
4. Detoxification.
5. Insect & Mosquito Repellent
6. Prevents Gastrointestinal Diseases
7. Wounds.
8. Reduces Dandruff
9. Reduces Joint Pain
10. Exfoliates skin[1]

Bioactive compound present in neem

Medicinal property of neem due to Azadirachtin, Nimbin,Selanin, Azadiradione, Gedunin, Phytol, epoxy azadiradione, methylsterate. Biological active compound can be found in neems are alkaloids, flavonoids, triterpenoids, phenolic compound, carotenoids, steroids, ketones. Others are volatiles oil.

Chemical investigation in different part of Neem

Part	Chemical[2-7]	Role[2-7]
Leaves	Quercetin (Flavonoid) and Nimbosterol (Sitosterol)	Antibacterial and antifungal
Flower	Sesquiterpene, Nimbosterol and	Antifungal

	flavonoid, Kaempferol, melcitrin	
Bark	Nimbin,Nimbidin,Nimbinin ,nimbosterol,margosine,	Antitumor, Anti-inflammatory
Gum	L-arabinose,L-galactose,,L-glucoronic acid	Treatment of weakness and skin diseases.
Seed	Azadiachtin, Azadirone, salannin Salannol, vepinin	Antiviral

Chemical	**role**
Nimbin (triterpene)	Antipyretic, Antifungal , antihistamine, antiseptic, Anti-inflammatory and anti-oxidant
Flavonoid	Prostaglandin inhibitor, endoperoxide inhibitor

Taxonomical classification [8]

Reported selective constituents of neem[8]	
Meliacinanhydride	Salannin (Azadirachtin)
IsoNimocinolide	beta-Sitosterol
Nimocinol	Nimbolin
Nimonol,	Quercetin
Isomeldenin	Kaempferol
Nimbin	Hexadecanoic acid
Nimbanal	Hexylicosane
Nimbinene	Gamma-elemene
Azadirachtin	Nimbaflavone

Kingdom	***Plantae***
Subkingdom	*Viridiplantae*
Infrakingdom	*Streptophyta*
Division	*Tracheophyta*
Class	*Magnoliposida*
Order	*Sapindales*
Family	*Maliaceae*
Genus	*Azadirachta*
Species	*Azadirachta India*

METHOD

Science direct, Google scholar, Web of Science and PubMed were accessed to review the ANTIVIRAL POTENTIAL OF NEEM IN DIFFERENT VIRUS.

Antiviral potiential of neem in different virus

Antiviral action of neem in chickenpox virus

Chickenpox is an infection caused by varicella zoster virus. It causes an itchy rash with small, fluid blisters. The itchy blisters rash caused by chickenpox infection appear 10 to 21 days after exposer to the virus and usually last about 5 to 10 days. It can spread through direct contact with the rash. It can spread when a person with the chickenpox coughs or sneezes.[9]

Leaves of neem plant with innumerable medicine benefits also serve as natural treatment for chickenpox. It is the best and most effective remedy that not only cures the chickenpox but also prevent from spreading.Bath with neem leaves water, allow the leaves to soak in the water for at least10-15 minutes before it taking the bath. a paste of neem leaves is prepared and apply it on skin. Leave it on the skin for as long as you can. Another way to use neem for chicken pox treatment is to extract the juice of neem leaves and apply it on skin. The unaffected cell prevents from infection by neem extract which absorb the viruses.[10]

Antiviral action of neem in Hiv/Aids virus

HIV[11] is stand for Human immunodeficiency Virus. It is commonly spread by unprotected sex, body fluids of a person with AIDS, through sharing injection. HIV virus attacks Helper T cells that cannot signal B cells to produce T cell to kill this virus. In 1933, The National Institute of Health circulated that an aqueous bark extract of neem was prepared by soaking the bark in water and then tested in vitro, killing the AIDS virus. Dr. Van Der Nat found that the extract produced a strong immune stimulatory response. Neem-derived polysaccharides are responsible for increasing antibody production and amplifye immune function. The components of neem bark can help reduce the infection spread by the virus AIDS.[12] A clinical trial on neem as an antiviral agent was conducted in Nigeria, funded in part by the U.S. government. In a 60 HIV patient, they determined the effect of neem on viral load and verified its efficacy by preparing acetone-water neem leaf extract (IRAB). The patients with CD4+ count less than 300 cells/mL were

given oral IRAB (1.0 gm daily for 12 weeks). Resulted was found at the end of the trial, extract could increase CD^{+4} cells, body weight by 12%, haemoglobin by 24%, lymphocytes by 20%. and support the safety of acetone water extract and no abnormalities were found in liver and kidney.[13]

Antiviral action of neem in duck plague virus[14]
Anatid alphaherpesvirus 1 belongs to the Herpesviridae family and causes the disease duck plague which leads to acute illness and mainly affects flocks of ducks, geese, and swans. It is mainly caused by migratory waterfowl, which are mainly responsible for the spread of this disease, and symptoms appear within 3 to 7 days.

An experiment was performed to check the antiviral properties of alcoholic seed kernel extract of neem in duck plague virus (DPV) in vitro and extract was prepared from different chromatographic fratcion and then treated with infected Duck embryo fibroblast (DEF). Results shown one fraction obtained from neem seed kernel could reduce the cytopathic effect in virus infected cell at a concentration of 10.9µg/ml.[15-16]

Antiviral action of neem in polio virus
Poliovirus[17] is a member of family Picornaviridae. Its genome is a single stranded RNA consist of 7500 nucleotide long. It is a causative agent of polio. It is of three types 1, 2, 3.

An experiment was conducted with neem polysaccharides to verify the antiviral property against polio virus. The polysaccharides present in neem inhibited the polio virus. The two polysaccharides (P1 and P2) were isolated from neem leaves. MTT analyzed the cytotoxicity of the compound and plaque reduction assay determined the antiviral activity. Result reported that Polysaccharides shown antiviral action at inhibitory concentration (IC_{50}) of 80µg/ml) ,37.5µg /ml,17.5 µg/ml and 12.1 µg/ml.[18]

Antiviral action of neem in coxsackie virus
Coxsackie[19] belong to a family Picoravridae and it is characterised by fever, poor appetite and running virus. of a family of viruses called enteroviruses. Faecal-oral route are responsible for spread of infection.

The Antiviral and Virucidal effect of methanolic extract fraction of leaves of neem (Azadirachta indica a. juss).
A study on the methanolic extract of neem leaves (NCL-11) as antiviral and virucidalactivity and possible mechanism of action against coxsackie B. The plaque formation of NCL-11 was inhibited in 6 antigenic types of coxsackie B at a concentration of 1000 micrograms/ml, and NCL-11 was found to be effective against coxsackie virus B.[20]

Antiviral action of neem in herpes simplex virus[21]
Herpes Simplex Virus 1 and 2 are the two members of the family Herpesviridae family." Herpes is a viral infection caused be Herpes Simplex Virus.

An aqueous extract of neem bark against HSV-1 infection as potent entry inhibitor.It exhibit significant anti-viral potency at concentration ranging from 50 to 100 μg/mL and blocked HSV-1 (Herps Simplex Virus entry into cell) , suggesting a direct anti-HSV-1 property of the neem bark.[22]

Antiviral action of neem in hepatits c virus
Hepatits C is caused by the hepatitis C virus and leads to a chronic stage characterised by liver cirrhosis and hepatocellular carcinoma. [23] In the molecular docking and simulation study, the compound 3-deacetyl-3-cinnamoyl azadirachtin (phytochemical of neem) was used against hepatitis C virus NS3 protease and this phytochemical shows good binding property against hepatitis C virus (HCV).[24]

Antiviral action of neem in hepatits b virus
Hepatitis B[25] is caused by the hepatitis B virus (HBV) and leads to liver cirrhosis and liver cancer. A research paper reports that neem leaf extract[26] may prevent moderate inhibition of viral DNA polymerase of hepatitis B virus.

Antiviral action of neem in covid-19 virus
COVID-19 pandemics been a deadly pandemic that has affected the whole world. Corona Virus is an infectious disease and is commonly called COVID 19.It was first reported in Wuhan, China.

In a study conducted by researchers at IISER (Indian Institute of Science Education and Research), they used computer modelling to test an extract of neem bark in an animal model and found that it had antiviral properties against SARS-CoV-2 spike protein Nagel's lab in University of Colorado test an extract of neem bark in SARS-CoV-2 human lung cells and found that it is effective against viral replication and reduce viral infection.[27-28]

CONCLUSION
Evidence suggests that Neem extracts rich in antiviral action. From these evidences, it appears that neem may play an important role in reducing the risk of a variety of viral infection, also may play a key role in reducing the risk of covid 19 infection. Extract of neem should be taken into consideration in order to reduce viral infection, advance research is required for isolation, purification and identification of principal bioactive compound.

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