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Antifungal activity of Azadirachta Indica(Neem tree): A Review

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Abstract : Recognized worldwide for its wide therapeutic potential, the Neem tree (Azadirachta indica) has moved from traditional healing systems like Ayurveda to a focus in modern medical research. This botanical powerhouse contains a complex mix of over 140 biologically active molecules, including important compounds such as azadirachtin, nimbin, and nimbidin, which support its strong anti-fungal properties. Scientific studies show that extracts from Neem leaves, using solvents like ethanol, methanol, and ethyl acetate, effectively reduce the growth of various pathogens, including Candida albicans, Aspergillus species, and Malassezia furfur. The strength of this growth reduction usually increases with the extract's concentration, with higher levels offering more effective protection against fungal growth and spore development.

The effectiveness of Neem does not come from a single "active ingredient" but from the teamwork of its components. For example, while the isolated compound nimonol has no independent antifungal power, removing it weakens the extract's overall effectiveness. Neem works through several methods, such as damaging the structure of fungal cell walls, stopping the formation of biofilms, and blocking the release of harmful mycotoxins. As global health faces rising microbial resistance to synthetic drugs like Ketoconazole, Neem offers a sustainable, low-cost, and eco-friendly alternative. Its low toxicity and biodegradable nature make it a promising choice for future use in pharmaceuticals and agriculture, as long as further clinical standardization takes place.

To understand how Neem operates, think of it as a complex security system protecting a building. Instead of depending on a single lock that a burglar (the fungus) might eventually figure out, Neem uses multiple layers of defense, including cameras, motion sensors, and reinforced glass that work together. If you remove just one sensor, the entire system becomes weaker. This highlights that the strength lies in the combined network rather than in any individual part.

Keywords – Neem, Azadirachta indica, azadirachtin, nimbin, and nimbidin, antifunal activity.

I. INTRODUCTION

Neem or the "Indian Lilac," Azadirachta indica is a well-known member of the Meliaceae family that is native to the Indian subcontinent. This plant has been a mainstay of traditional Ayurvedic, Unani, and homeopathic medicine for more than two millennia. It was revered in ancient Sanskrit texts as sarva roga nivarini the healer of all illnesses. Although the tree is frequently referred to as a "village pharmacy because of the therapeutic value of its leaves, bark, seeds, and flowers, its antifungal potential has garnered more attention from scientists in recent years. The rise in drug-resistant fungal strains around the world and the shortcomings of traditional treatments like azoles have contributed significantly to this change, making the search for safe, affordable and natural substitutesa medical priority.

The plant's complex chemical composition, which includes over 140 different bioactive compounds like azadirachtin, nimbin, nimbidin, and gedunin, is the basis for its effectiveness against infections. Neem's phytochemicals take a broad-spectrum approach, in contrast to synthetic drugs that frequently target a single biological pathway; they damage mitochondrial health, impair fungal cell membrane integrity, and obstruct vital enzyme activities. According to research, neem extracts are very effective against a range of human threats, such as Aspergillus species, Candida albicans, and dermatophytes that cause skin infections. Neem is a strong candidate for future pharmaceutical development because it attacks several cellular targets at once, which not only inhibits growth and spore development but also greatly lowers the risk of fungi developing resistance. Consider a building's security system to comprehend neem's complex attack. A typical antifungal medication might only attempt to jam the front door lock, but the different compounds in neem act as a full-scale security breach, cutting the power, disabling the cameras, and weakening the structure's foundations all at once, making it almost impossible for the fungal "intruder" to maintain its defenses.

II. Classification of Neem

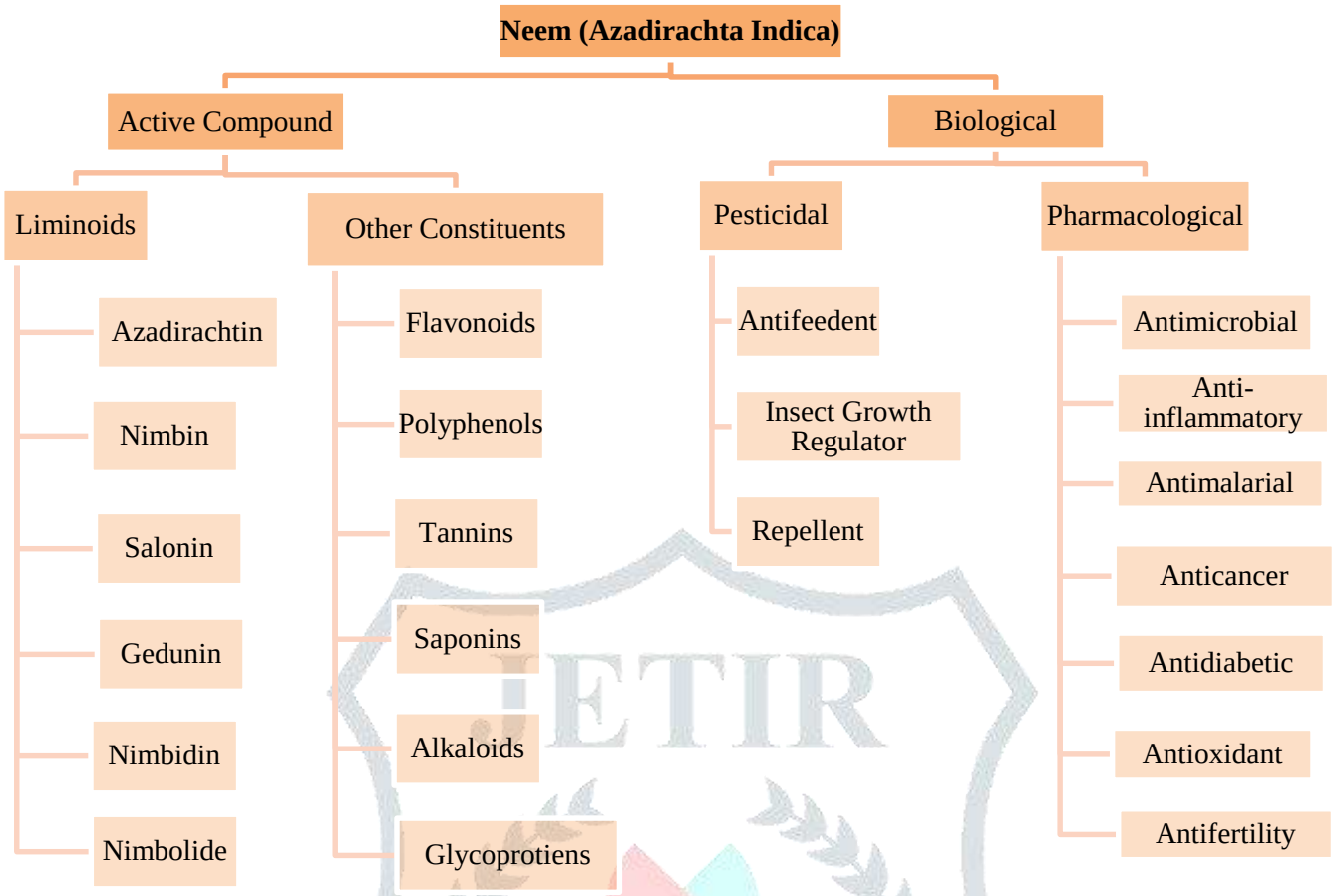

Fig: Leafs and fruits Of Neem(Azadirachta Indica)

III. NEEM COMPOUND SOURCES WITH ITS BIOLOGICAL ACTIVITY

Neem Compound	Source	Biological Activity
Nimbidin	Seed oil	Antiarthritic
Sodium nimbidate		Anti-inflammatory.
Nimbin	Seed oil	Spermicidal.
Nimbolide	Seed oil	Antibacterial, Antimalarial
Gedunin	Seed oil	Antifungal, Antimalarial
Azadirachtin	Seed	Antibacterial
Mahmoodin	Seed oil	Antibacterial
Gallic acid, (−) epicatechin and catechin	Bark	Antiinflammatory, immunomodulatory
Margolone , margolonone and isomargolonone	Bark	Antibacterial
Cyclic trisulphide and cyclic tetrasulphide	Leaf	Antifungal
Polysaccharides		Anti-inflammatory
Polysaccharides GIa , Gib	Bark	Antitumour
Polysaccharides GIIa , GIIIa	Bark	Anti-inflammatory
NB-II peptidoglycan	Bark	Immunomodulatory

IV. ANTIFUNGAL ACTION.

The Neem (Azadirachta indica) antifungal mechanism of action (MOA) is multidrug as there is a complex interaction between bioactive compounds that act on different cellular structures and physiological processes of fungal pathogens.

1 Breach of Fungal Cell Membranes.
Neem interferes with the integrity and functionality of the fungal cell membrane which is very vital in preserving the internal cell environment.

Change of Permeability: Azadirachtin, one of the main bioactive compounds changes the permeability and integrity of the fungal cell membrane. This causes destabilization and ultimate rupture of the membrane compromising structural integrity and cell death.

Cellular Contents Leakage: The substance Nimbidin particularly affects the membrane integrity, and causes the leakage of important internal cellular material.

Inhibition of Ergosterol Synthesis: Nimbin inhibits production of ergosterol a major sterol that the fungal membrane needs to remain stable and functional.

2.Cytotoxicity of Cell Wall Synthesis.
The cell wall of the fungi is rigid and defends the fungus against environmental stress. Neem disrupts its formation and it acts enzymatically and structurally.

Key Enzyme Inhibition: Chitin synthase and glucan synthase are inhibited by the neem extracts. They are crucial enzymes needed in synthesis of chitin and glucans, the major structural elements of cell wall of fungi.

Structural Compromise: Neem compounds inhibit the synthesis of chitin and glucans thereby rendering the wall less rigid. The immune responses and environmental stressors make the fungal cells very susceptible to such interference and thus growth and proliferation are hampered.

3.Fungal Gene Expression.
The Neem has the genetic level control over the pathogen and the survival and virulence.

Targeting Survival Genes: Bioactive components can be used to regulate gene expression by targeting individual genes that deal with fungal metabolism, cell cycle, and stress response pathways.

Alteration of Vital Functions: Neem interferes with these key processes in the body causing impaired growth and ultimate cell death.

4.Enzyme Inhibition of the Fungal Enzymes and Mycotoxins.
Additional effects of Neem on cell wall enzymes include further action on metabolic pathways and the synthesis of toxic secondary metabolites.

Systemic Enzyme Inhibition: Salannin is reported to inhibit different fungal enzyme systems and this is also involved in the inhibition of fungal growth.

Inhibition of Mycotoxins: The neem compounds are able to suppress the production of mycotoxins that in most cases are the pathogenicity and virulence factors of fungi such as Fusarium and Alternaria species.

5.Spora germination and adherence are inhibited.

Neem can be used as prevention of early infections and fungal infection spreading.

Anti-germination: neem cake extracts and such compounds as Azadirachtin have been found to inhibit the germination of spores of a variety of species, such as Aspergillus niger and some sporing fungi.

Anti-Adherence Properties: Neem powder has been demonstrated to undermine adherence of Candida albicans, an important step in the colonization of the surfaces and escalation of a condition like denture stomatitis.

6.Biofilms and Multidrug-Resistant Strains Eradication.

Among the most crucial features in the MOA of Neem is its ability to treat the resistant types of fungi.

Biofilm Disruption: Neem extracts have the potential of attacking both planktonic (free-floating) and biofilm forms of fungi. It can interfere with development of new biofilms as well as eliminating old biofilms that are normally very resistant to traditional antifungal agents.

Resistance Neem-based preparations have been shown to prevent the proliferation of multidrug-resistant (MDR) strains of fungi, which is why it can be used as a substitute in treating recalcitrant infections when the current treatment is not effective.

Therapeutic Applications:

Skin Conditions	Other Diseases
• Acne (Breakouts & Cysts) • Psoriasis (Itching, Pain, Redness, Scaling) • Eczema (Dry, Cracked Skin) • Ringworm • Warts • Radiodermatitis	• Alopecia • Ulcers • Leprosy • Malaria • Cancer

Conclusion:

The Neem (azadirachta indica) with its potent antifungal agent with broad range of applications in human and veterinary healthcare with its unique antifungal mechanism of action peak with efficacy opposed to common fungal pathogens like Aspergillus Niger, Candida albicans and dermatophytes response to scalp and skin infections. Neem extracts are biologically degradable, safe, and rarely produce its adverse effects, Neem is highly suitable for long term use in herbal formulations emerges a valuable natural source with significantly antifungal properties. Neem is advantageous to prevent and treat of numerous diseases. The Antiviral, immunomodulatory, anti-oxidant, anti- ulcer, anti- inflammatory, antifungal, antihyperglycemic, and anti- carcinogenic properties of neem.

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