

Fungi in medicine

Pharmaceutical preparation derived from Fungi (commercial level)

Many microbial strains produce certain secondary metabolites which have applications as Pharmaceuticals eg antibiotics

1. **Antibiotics** : are secondary metabolites produced by microorganisms which adversely affects the growth of other microbes for example penicillin is an antibiotic produced by fungus *Penicillium chrysogenum*
 - this antibiotic is able to kill bacteria eg *Staphylococcus*
 - was discovered in 1945
 - reduces growth of both gram positive and Gram Negative bacteria
 - Strain P reduces growth of Gram Positive Bacteria
 - Strain N reduces growth of Gram Negative bacteria
 - Other antibiotics have been commercially obtained from strains of *Actinomyces* and *Streptomyces* species
- ❖ *Penicillium griseofulvum* produces an antibiotic griseofulvin which inhibits the growth of dermatophytic fungus which infects the skin hair
 - its antifungal activities by inhibiting assembly of fungal microtubules
 - also produces fusidic acid against Gram Positive Bacteria
- ❖ Antibiotic fumagillin is produced from *Aspergillus* species & it acts against protozoa
2. **Immunosuppressive drugs**
 - ❖ cyclosporins from *Tolypocladium inflatum* have been used as an immunosuppressive drug which is required during skin , bone marrow, and organ transplant.
 - Drug attacks on the t-Lymphocytes of our immune system and synthesis of interleukin 2
 - thus prevents rejection of transplanted organ
 - ❖ Gliotoxin produced by *Trichoderma virens* is also immunosuppressant
3. **Cholesterol and blood pressure lowering drugs :**
 - ❖ these are small organic acids which interacts with the main enzyme in the biosynthesis pathway for production of cholesterol in the liver
 - ❖ Mevastatin from *Penicillium citrinum*
 - ❖ Lovastatin from *Monascus ruber*
4. **Ergot alkaloids:** nitrogen containing compounds produced by sclerotia of *Claviceps purpurea* and has been used as a poison to many animals and in medicine
 - ❖ originally this alkaloid was obtained from Rye infected with *Claviceps purpurea*
 - ❖ the disease called as ergotism. Ergot alkaloids act as mycotoxins and caused a condition known as St Anthony's fire as it gives burning sensation to the victim
 - ❖ derivatives of some Ergot alkaloids are used during childbirth for contractions of uterus specifically ergometrine and methyl ergometrine
 - ❖ they are also used for vasoconstriction that is narrowing of blood vessels to control bleeding
 - ❖ ergotamine is used to treat migraine
 - ❖ ergot derived drug called LSD (lysergic acid diethylamide) is used for treatment of Parkinson's disease and Alzheimer's disease

Topic II : Fungi : effect on human health

Mycotoxins

- are low molecular weight secondary metabolites produced by many fungi, called as toxigenic fungi
- most commonly studied mycotoxins are produced from species of *Aspergillus*, *Fusarium*, *Penicillium*, *Myrothecium*
- **What is significance of mycotoxins for the fungus itself?**
- eliminating The Other microorganisms which would be competing for resources in the same environment
- in waiting the host which could be plants humans livestock population insects
- ❖ **How it affects humans?**
- many crops are damaged after harvest and during storage leading to huge economic losses in agriculture
- health problems in human ranging from acute toxicity called mycotoxicoses to milder effects as reduced reproductive efficiency
- ❖ most important Mycotoxins are aflatoxins, fumonisins, ochratoxins, patulin, trichothecenes
- ❖ In 1960s, Turkey-X disease outbreak was there in England where the aflatoxins from *Aspergillus* species lead to Extreme toxicity and carcinogenicity
- ❖ Aflatoxin b is one of the most potent carcinogen known 18 many aflatoxins are associated with human liver cancer
- ❖ Aflatoxin producing toxigenic strains are *Aspergillus flavus* & *A parasiticus*
- ❖ Mycotoxins effect production of many food crops adversely the crops may get contaminated before harvest during harvest or during storage once there is contamination by *A flavus* and *A parasiticus*, aflatoxins would be produced most of this contamination arises due to improper storage of food products
- ❖ greatest which products are corn peanuts rice nuts Brazil nuts pistacio nuts
- ❖ *Aspergillus alternata* is the most important mycotoxin producing species in serials sunflower seeds oilseeds olives fruits

How it affects the animal and human health?

- ❖ aflatoxin : damage liver
- ❖ in livestock decrease the milk and egg production suppress immunity
- ❖ Trichothecene : is a large group of mycotoxin causing necrosis hemorrhage in digestive tract and causing change in spleen and reproductive organs and suppression of immunity
- ❖ Ochratoxins damage kidney of animals which consume contaminated feed it also causes liver damage and intestinal necrosis
- ❖ Aflatoxins, ochratoxin and Sterigmatocystin are known to induce tumors in many species of animals the carcinogenic effect has been seen on liver kidney urinary system lungs digestive tract
- ❖ *Alternaria* mycotoxins are also associated with both animal and human health disorders

Refer Table 28.3 (Walia and Sethi)

Topic III: **Medical Mycology : Disease causing fungi**

- ❖ causes are diseases of humans caused by poisoning in humans is due to injection of infected food contaminated by mycotoxins which are secondary metabolites produced by a certain fungi

Fungal pathogens are different types:

1. Dermatophytic fungi/Dermatophytes:

- ❖ Also called as **ringworm fungi** and the name dermatophyte comes from the term 'dermal' which means skin as these mainly affect the keratinized tissue of skin hair and nails
- ❖ It starts with infection on the superficial layer and it gradually penetrates and causes symptoms like irritations shedding of skin which may lead to even secondary invasion by bacteria as seen in case of dandruff
- ❖ many fungal species are associated as *Trichophyton*, *Epidermophyton*, *Microsporum*
- ❖ Although dermatomycosis is most commonly causing skin infection. there are other parts of body also which can get attacked by like
 - respiratory tract : bronchomycosis,
 - nails : onychomycosis
 - ears : otomycosis
 - lungs: pneumomycosis
- ❖ Another common name of mycoses is ringworm or tinea
 - Eg Tinea capitis : infection of scalp
 - Tinea unguium : infection of nails
- ❖ Fungal species which survive on humans are called as anthrophillic example
 - *Epidermophyton floccosum* & *Trichophyton interdigitale* : both cause infection in between toe fingers ; athlete's foot
 - *Microsporum audouinii* causes head ringworm

2. Harmless commensals

- some fungi don't cause major harm to the individuals but reside within the body and the symptoms take over whenever there is the natural defence of the body is low one such fungus is ***Candida albicans*** which is found in the mucosal membranes of humans and mammals . the disease condition caused by this fungus is called **candidiasis** or mouth thrush
- it shows symptoms requiring clinical attention in some cases especially those suffering from diabetes, HIV, leukaemia and other immune disorders,
- in such individual the fungus gets systemically spread via blood and lymph tissue
- In newborn babies it causes thrush a condition of mouth and throat where small white pustules are produced
- *Candida* is also commonly found in women and causes vulvovaginitis, inflammation of reproductive canal
- causes inflammation of mouth in persons using dentures the condition is called stomatitis

3. Opportunistic pathogens

- ❖ These are These are commonly found on different organic materials example *Aspergillus* species are normally saprotrophic but in case of in immunocompromised individuals, it can be pathogenic and cause infection
- ❖ species as *Aspergillus flavus* and *Aspergillus niger* reproduce through conidia which are airborne and can reach the lungs once it infects, it can cause localised damage and subcutaneous mycosis

- ❖ condition having these localised colonies is called aspergillomas
- ❖ is common in case of poultry which are fat on grains infected by this fungus it also occurs in humans where it causes impaired respiratory function
- ❖ Another condition Aspergillosis: *Aspergillus* in which the person's lungs are affected and they are respiratory problems mostly normally people are able to overcome but immune-compromised individuals have low defence system and they get infected and the fungus grows is systemically in the body

4. Endemic dimorphic fungi

- ❖ fungi which are endemic that means geographically localised and those which also have different growth forms come under this category
 - for example *Candida albicans* in environment grows as mycelium while once it enters human body it transforms into yeast like form. It is spread through air and infect the lungs
 - *Coccidioides immitis* is soil borne fungus and survives in arid dry condition through spores, It gets dispersed through wind and which infects lungs of humans and cause disease called coccidioidomycosis.
 - In a valley of Southern California it is very common infection there thus it is also known as valley fever.
 - the symptoms are presence of blistering Rash and pneumonia like symptoms, later it spread systemically to other tissues as lungs skin brain and other vital organs
 - *Histoplasma capsulatum*: is soil borne dimorphic fungus that causes histoplasmosis a disease common to humans dogs and cats
 - infection is caused by inhaling contaminated air
 - there are two kinds of spores which are produced :large thick walled macroconidia and smaller microconidia
 - it mainly causes respiratory troubles along with fever, chest pain and dry cough and can be fatal if left untreated
 - Cryptococcosis : caused by *Cryptococcus neoformans* This disease is airborne and the fungus produces basidiospores and once it reach lungs it starts growing and causes pneumonia like symptoms which can lead to lung dysfunctionit can systemically spread to nervous system affecting cerebral cortex brain cerebellum, meninges.