CHAPTER - II

Review of Literature
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Vision, the priceless gift from God, a blessing to enjoy the beauty of the world. Millions of people are deprived of God given gift of vision. Twenty five percentage of the world’s visually challenged People are Indians. The relevance of this study topic and its location becomes apparent, when considering that India holds one of the largest blind and at - risk - for - blindness populations in the world (Malik. 1990). Of the total estimated 39 million blind persons in the world, 15 million people live in India (WHO, 2013).

OCULAR PATHOGENS

The ocular pathogenicity of a micro - organism can be calculated by the number of ocular infections divided by the number of eyes harbouring the same micro - organism (Wilhelmus, 2008). A primary pathogen will regularly cause infection, an opportunistic pathogen causes infection in immunocompromized individuals, while normally occurring micro-organisms may act as incidental pathogens, replicating and causing disease when host defence mechanisms have been impaired (Wilhelmus, 2008).

A great number of bacterial species is generally recovered from adults than from children. Facultative anaerobic species, particularly Corynebacteria, are found significantly more frequently in adults, while Streptococci are obtained more frequently form children (Singer et al., 1988). Worldwide, S. aureus is the most frequently occurring cause of bacterial conjunctivities (Mannis and Plotnik, 2005). (Weiss et al., 1993) suggested that eyelids commonly harbor Staphylococci, Corynebacteria and alpha - haemolytic Streptococci.
Reports of Coagulase-negative *Staphylococci* and *Corynebacteria* are frequently found to be present on the healthy conjunctiva, but more traditionally pathogenic organisms, such as *Coagulase-positive Staphylococci, Streptococci, Haemophilus specius, Maraxellae* and Gram-negative *Coliform* rods, are also occasionally isolated from normal, non-inflamed eyes (Olafsen et al., 1986 and Mannis et al., 2005). *Bacillus cereus* has emerged as the most important ocular pathogen and one of the most destructive organism to affect the eye (Daven Port et al., 1952 and O’Day et al., 1981).

Fungi have replaced bacteria as the predominant cause of infectious Keratitis in some of the countries (Hagan et al., 1995; Poole et al., 2002). The incidence of fungal keratitis is increasing nowadays. Factors correlated with this increasing incidence include the growing number of trauma cases, wide-spread abuse of broad-spectrum antibiotics and steroids, and increasing use of corneal contact lenses (Xie et al., 2001 and Gopinathan et al., 2002). A number of recent studies have reported emerging fluoroquinolone resistance among ocular isolates, particularly among gram-positive organisms (Alexandrakis et al., 2000). Emerging Ciprofloxacin resistance among ocular gram-negative isolates such as *P. aeruginosa* also has been reported by Chaudhry et al., (1999) and Rhee et al., (2004).

The frequency of life-threatening infections caused by pathogenic microorganisms has increased worldwide and is becoming an important cause of morbidity and mortality in immune compromised patients in developing countries (Al-Bari et al., 2006). The increasing prevalence of multi-drug resistant strains of bacteria and the recent appearance of strains with reduced susceptibility to antibiotics raised the specter of “untreatable” bacterial infections and adds urgency to the search
for new infection - fighting strategies (Zy et al., 2005, Rojas et al., 2006). Around the world *Moringa* is the subject of legends and praise, awe and respect - so much that it is also called “Miracle Tree”, “Mothers best friend”. Literature review of the antifungal activity of *M. oleifera* seeds, leaves and flowers revealed the best extract as seed alchohal against tested sixteen fungal species. *Candida* were found to be totally resistant (Sahar et al., 2015).

**PLANT REMEDY FOR EYE INFECTION**

According to World Health Organization (WHO), any plant which contains substance that can be used for therapeutic purposes or which are precursors of chemopharmaceutical semi synthetic new drug is reoffered as medicinal plant (Hassanali, 2003). Medicinal plant would be the important source of obtaining a variety of drugs as phytochemicals are more specific, bio degradable and are supposed to have fewer side - effects. Phytochemicals offer unique platform for structural diversity and biological functionality, which is indispensable for drug discovery (Verpourte, 2002).

The list of benefits of plants bioactive compounds to human health such as anti - cancer, anti - hypertension, anti - hypoglycemia, anti - oxidants and antimicrobial activities have been reported by Chandra et al., (2012) and Arora et al., (2012).

Kala, (2005) reported that Allopathic medicine may cure a wide range of diseases; however it’s high prices and side - effects are causing many people to herbal medicines which have fewer side - effects. Literature reports of Satyavati et al., (1987) reveal that in India, almost 95% of the prescriptions were plant based in the traditional systems of Unani, Ayurveda, Homeotherapy and Siddha. Nearly 80% of the world’s population relies on traditional medicines for primary health care, most of which involve the use of plant extracts (Sandhya et al., 2006). Out of the 250,000 to 500,000
species of plants in earth, *Moringa* is one of the 10% which has a profound potential in pharmaceutical industry as a source of bioactive constituents for drug development (Cowan, 1999).

**MORINGA**

In a study reported by Chatterjee and Pakrashi (1992), *M. oleifera* flowers are found to possess antibacterial, antiulcer, antitubercular, antiviral, fertility, depressant, antiinflammatory and anticancer property. *M. oleifera* is rich in various phytochemicals like carotenoids, vitamins, minerals, aminoacids, sterols, glycosides, alkaloids, flavonoids, moringine, phytoestrogens, caffeoytquinic acids and phenolics in flowers, leaves, roots, fruits and seeds (Guevara et al., 1999; Fugile, 1999 and Anwar et al., 2007).

The function of flavonoids in flowers is to provide colors attractive to plant pollinators (Skibola et al., 2000). The antibacterial activity of flavonoids is being interestingly documented. Crude extract from plants with history of use in folk medicine have been screened invitro for antibacterial activity by many research groups (Dall’ Agnol et al., 2003). Spiolotis et al., (1997) reported antimicrobial activity from varieties of *Moringa oleifera* seeds. All the varieties are investigated against *Bacillus cereus, Candida albicans, Streptococcus faecalis, Staphylococcus aureus, Staphylococcus epidermidis, Bacillus subtilis, Pseudomonas aeruginosa, E. coli* and *Aspergillus niger*. Prashith et al., (2010) investigated antibacterial and antifungal efficacy of steam distillate of *M. oleifera*. Among bacteria tested, more inhibition was observed in case of *E. coli* followed by *S. aureus, K. pneumoniae, P. aeruginosa* and *B. subtilis*. Chuang et al., (2006) stated that ethanol extracts of seed and leaf of *Moleifera* showed antifungal activites invitro against *Trichophyton rubrum*,
*Epidermophyton, Microsporum canis.* Reports of antibacterial properties of flowers of *M. oleifera* is subtle. The highlight of usage of flowers of *M. oleifera* in siddha medicine gave us an idea to study its antimicrobial activity against isolated ocular pathogens. Moreover *M. oleifera* is also rich in antioxidants as stated by various researchers Ruckmani et al., (1998) in their study revealed the presence of the active phenolic compound quercetin, a powerful antioxidant, in the flowers of *M. oleifera.* Various findings have also shown that the phenolic - rich hydroethanolic fractions of plants contain catechin, rutin, quercetin, Kaempherol and isorhemnetin (Zu et al., 2006).

**NADIYAVATTAM**

Nadiyavattam (*Tabernaemontana divaricata*) - “The best herb for all eye diseases as well as a rejuvenator for eyes” if considered a herbal medicine and Natural Remedy for eye diseases. In the siddha medicine the flower juice is mixed with oil and used as eye drops. The flower juice is also used in the treatment of eye infection (Kanthal, 2011).

*T. divaricata* is also mentioned in Ayurvedic system of medicine to cure diseases like diarrhoea and neuronal acetylcholinesterase problems (Chattipalcorn et al., 2007). The genus *Tabernaemontana* has evoked interest due to the important biological activity of its extracts, particularly, antimicrobial (Federici, 2000), antitumoral (Mansour, 2012), antioxidant (Pereira et al., 2005), anticholinesterasic (Pereira et al., 2008), and antiinflammatory (Taesotikul et al., 2003) activities. Most of which have been associated with indole alkaloids. Previous studies on the phytochemistry and chemical constituents of leaves, stems and roots of *T.divaricata* reported the presence of alkaloids (Arambewela et al., 1991) and non alkaloids such as terpenoids (Sharma et al., 1998), steroids, flavonoids (Dagino et al., 1991), phenyl
propanoids (Dagino et al., 1991), phenolic acids and enzymes (Stevens et al., 1992). The literature survey revealed the presence of alkaloids, tannins, xanthoproteins, carboxylic acid, coumarins and carbohydrates in flowers (Sharma et al., 2010). Sumitha et al., (2014) in their earlier studies reported the antibacterial effect of Jasminium officionale flower extract (Water and Methanol) on eye pathogen S.aureus.

Among all elements found in the plants, alkaloids are the most powerful components. Hence, it is little surprising that the alkaloids have been researched and examined the most by the modern day scientists. Voacongine and Coronaridine are the major indole alkaloids that have been extensively studied. Monoterpenic indole alkaloids have been extensively investigated for exhibiting numerous biological activities such as antitumor, antimicrobial and antihypertensive functions (Andrate et al., 2005).

Literature review shows that the leaves of T. divaricata possess good antioxidant potential (Rebecca et al., 2013). Many Polyphenolics in flowers exert more powerful antioxidant effect than vitamin E and inhibit lipid peroxidation by chain-breaking peroxyl - radical scavenging. They can also directly scavenge reactive oxygen species (ROS), such as hydroxyl, superoxide and peroxynitrite radicals (Tsao and Akhtar, 2005).

Valli et al., (2014) reported that beneficial properties of T. divaricata are antioxidant, antiinfective, antitumour action and enhancement of cholinergic activity. Thambi et al., (2006) reported that the ethanolic and the aqueous extracts of T. corinata flowers possessed significant invitro superoxide - hydroxyl radicals, nitric oxide scavenging and lipid peroxidation inhibiting activities.
Phytochemical studies on *Moringa oleifera* by Ndong et al., (2007) revealed the presence of major polyphenols such as quercetin glycosides, rutin, Kaempferol glycosides and chlorogenic acids. Bennett et al., (2003) isolated various glucosinolates and phenolic compounds from various parts of *M. oleifera*. The seeds only contained 4 - (alpha - 1-rhamnopyranosyloxy) - benzylglucosinolate at high concentrations. Roots of *M. oleifera* contains high concentrations of both 4 - (alpha-1-rhamnopyranosyloxy) - benzylglucosinolate and three monoacetyl isomers of this glucosinolate. The leaves also contain quercetin - 3 - 0 - glucoside and quercetin - 0 - (6”- malunyl - glucoside) and lower amounts of Kaempferol - 3 - 0 - glucoside and Kaempferol -3-0 (6-malunyl - glucoside), 3 - clfeoylquinic acid and 5 - calfeoylquinic acid.

Phytochemical studies on *M. oleifera* flowers are limited. Hence the present study has been planed to fill up the lacunae. Chaung et al., (2006) stated that ethanol extracts of seed and leaf of *M. oleifera* showed antifungal activities against *Trichophyton rubum, Epidermophyton* and *Microsporum canis*. Reportsof antibacterial properties of flowers of *M. oleifera* is subtle. The highlight of usage of flowers of *M. oleifera* in siddha medicine gave us an idea to study its antimicrobial activity against isolated ocular pathogens.

The literature reports of Denise et al., (1991) revealed the presence of major compounds such as O - acetylvallesamine, voaphyilline and apparicine in the alkaloid extracts of *T. divaricata* cell suspension. A study by Pranav et al., (2011) revealed the presence of amino acids such as Proline and 2 - aminobutyric acid in *T. divaricata* leaves. Hemalatha et al., (2012) in their studies on phytochemical isolation and characterization of different extracts of *T. divaricata* flowers, revealed the presence of Campesterol - D glucoside, stigmosterol, α - amyrin acetate, Asiatic acid (n - hexane extract) Kamferol (Ethyl acetate extract), 11 - hydroxyl voabacristine heyneanine
They are found to have antioxidant activity. Renitta et al., (2009) investigated various phytochemicals present in the leaves, seeds and flowers of ethanolic extract of *M. oleifera* by GC-MS.

Molecular methods involving the use of polymerase chain reaction (PCR) here recently been applied in genetic studies of various organisms. Sequencing of the 16s rRNA gene (16s) is a reference method for bacterial identification. It’s expanded use has led to increased recognition of novel bacterial species, (Tringe et al., 2008). A 16s ribosomal DNA clone library analysis for microbiological diagnosis in a clinical case of buckle infection revealed the presence of *Achromobacter* (Hotta et al., 2014). PCR has often been used to provide evidence of bacterial involvement in the eyes with suspected intraocular infections (Okhravi et al., 2006). Abyar et al., (2012) in their studies isolated and identified *Achromobacter* from the polluted sediment of Persian Gulf using PCR amplification technique and Gene sequencing on BLAST search software. The internal transcribed spacer (ITS) region of the nuclear ribosomal repeat unit is the most popular locus for species identification in sequence-based mycological research (Nilsson et al., 2008). Phytogenetic systematic reconstructs evolutionary history and studies the pattern of relationship among organisms (Linder et al., 2005). The endophytic fungi *Cochliobolus* belonging to Ascomycota has been identified by Phylogenetic analysis from *Lycium chinense* (Paul et al., 2014).

Current techniques are applied in the present study to identify the unknown bacterial and fungal species from eye infected patients. The present review summarizes some important studies on ocular pathogens, pharmacological studies on *M. oleifera* and *T. divaricata*. Phytochemical investigations and isolated principles from them can be investigated further to get any lead molecules in the search of novel drugs.