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Review Article

Natural Compounds as Anti Microbial Agents with In Silico Technique: A Review

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ABSTRACT

The present review gives the use of natural product/isolated compound as antibacterial agents as microbes are the main cause for number of life threatening complication/diseases. Modern techniques like in silico method can identify the target compounds which has selective affinity for particular microorganism and can be effective in treatment of even resistant strains. Not much work is done in this direction, this review can be used as lead for finding the selective target for finding a better antimicrobial for society at an affordable price.

Key words: Antifungal; Antimicrobial; Gram positive and gram negative microorganism; Isolated phytoconstituents; Medicinal plants.

1. INTRODUCTION

The term antimicrobial, derived from three Greek words anti (against), mikros (little) and bios (life) and refers to the agents that act against micro-organisms. It is a similar term derived from the Greek word anti (against) and biotikos (concerning life). "Antibiotic" means substances produced or synthesized by microorganisms which acts against another microorganism. Thus, antibiotics do not include antimicrobial substances that are purely synthetic (quinolones and sulfonamides), or semisynthetic (amoxicillin and methicillin), or those which derived from plants (alkaloids and quercetin) or animals (lysozyme). In contrast, "antimicrobials" include all substances that act against all kinds of microorganisms –as antibacterial (acts

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against bacteria), antiviral (acts against viruses) antifungal (against fungi) and antiprotozoal (against protozoa).

An antibiotic is a low molecular weight substance which produced by microorganism that inhibits or kills other microorganisms at a low concentration. Antimicrobial is any substance from natural, semisynthetic or synthetic origin that inhibits the growth or kills microorganisms but causes little or no damage to the host cell. Not all antimicrobial agents are antibiotics but all antibiotics are antimicrobial agents.

Bacterial infections caused can be prevented and treated through anti-bacterial agents including antibiotics. When bacteria are exposed to an antibiotic, they cause either inhibition of the growth or remain resistant or unaffected.

Infections caused by bacteria, viruses, fungi and parasites are major causes of mortality, morbidity, disability, and socio-economic disruption of millions of people. The symptoms of bacterial infection are fever, chills, headache, nausea and vomiting, if untreated it can lead to life threatening complications such as sepsis, kidney and liver failure, toxic shock and even death.

However in the developing countries, infectious diseases still remain a major cause of global disease burden with high mortality and morbidity. On other side, there have been threats of new diseases during the past three decades due to the evolution and adaptation of micro-organisms and the re-occurrence of old diseases due to the development of resistance towards antimicrobials. The present trend for treating bacterial infections is antibiotic therapy. But use of antibiotics is associated with mild to severe toxicities and failure of treatment due to the development of resistance to antibiotics.

Before the introduction of modern medicines, disease treatment was entirely managed by herbal remedies. As per WHO, it is estimated that about 80% of the world population in developing and under developed countries still rely mainly on medicinal plants. Medicinal plants are the only affordable and accessible source of primary health care for them, especially in the absence of access to modern medical facilities. There is a need discovery of herbal medicines for their antibacterial properties in this millennium. Use of herbal medicines to treat bacterial infections is consider to be safe due to less toxicity, effective since development of resistance is rare and convenient due to their easy availability. Newer techniques can be used like in silico model/docking studies can be done to check whether the isolated natural products can be the lead molecule against the drug resistance microbes.

It is estimated that, 50% of Western drugs shows either the plant phytoconstituents or synthetic derivatives of phytoconstituents. Commercially proven drugs used in modern practices were initially used in various traditional or folk healing practices in the crude form that suggested potentially useful pharmacological activity. The main benefits of plant derived medicines are that they are relatively safer than synthetic agents, offering profound therapeutic benefits and more affordable treatment.

Plants consisting of active compounds are important as beneficial medicinal effects, typically result from the combinations of secondary metabolite such as tannins, alkaloids, phenolic compounds and steroids, which are synthesized and deposited in specific parts of the plant. These constituents are more complex and specific and are found in certain taxa such as family, genus and species. The medicinal properties of plants are unique to a particular plant species or group, consistent with the concept that the combination of secondary metabolites in a particular plant is taxonomically distinct.

Plants have become a source of potential antimicrobial substances. Laboratories of the world have found literally thousands of phyto-constituents which have inhibitory effects on all types of microbes *in vitro*. Most of these compounds should be subjected to preclinical and clinical studies to determine their effectiveness in whole-organism systems, including in particular toxicity studies as well as an examination of their effects on beneficial normal micro-organisms. It would be advantageous to standardize methods of extraction and *in vitro* evaluation so that the search could be more systematic and interpretation of results would be facilitated. Also, alternative mechanisms of infection prevention and treatment should be included in initial activity screenings.

Disruption of adhesion and in silico docking techniques are examples and currently, the anti-microbial activity not commonly screened using these mechanisms. Attention in this direction is needed in era of chemotherapeutic treatment of infection by using plant-based principles.

In silico docking techniques, the compounds which are complementarily at the molecular level of a ligand and a protein target is studied. Docking studies can identify the structural features that are important for binding and for in silico screening efforts in which suitable binding partners can be identified[1].In silico method can become an important tool in drug discovery taking the lead from the herbal medicinal plants which have already shown as a potential source of drugs as an alternate source. Phytoconstituents which have shown/ isolated / the extract which have shown good activity against microbes can be good source as antiinfectives. Structural activity relation[SAR] for the isolated compounds can be studied by in silico molecular docking studies and best molecule with potential can be made available to the society at a affordable price with effective treatment free from side effects.

The present work aim is to give a review of isolated compound from the plants which has shown activity against microbes viz., bacteria and fungi in alphabetic order. Not much work is done in this direction of studying in silico docking of microbes, this review can be used as lead for finding the selective target for finding a better antimicrobial after SAR and docking studies.

1.1 Ageratum conyzoides

Antibacterial activity of an isolated compound (AC-1) from the leaves of Ageratum conyzoides Linn was evaluated against four Gram-negative bacteria like *Escherichia coli*, *Shigella dysenteriae*, *Pseudomonas aeruginosa* and *Salmonella typhi* as well as four Gram +ve bacteria viz. *Staphylococcus aureus, Streptococcus pyogenes, Bacillus subtilis* and *Bacillus megaterium* using Disc diffusion method. Result showed that compound AC-1had large zone of inhibition in disc diffusion against the said bacteria. Antibacterial activity was more in Gram - positive bacteria than Gram - negative bacteria. Highest activity was noted against *Staphylococcus aureus* and lowest was found for *Salmonella typhi*. The MIC (minimum inhibitory concentration) values of AC-1 against the bacteria ranged from 8 – 32 µg/ml. Results, thus, suggests that the compound (AC-1) isolated from the leaves of *Ageratum conyzoides* Linn. had good anti bacterial activity against the tested bacteria[2].

1.2 *Ambrosia maritime*

Five pseudoguaianolide sesquiterpenes (neoambrosin, damsinic acid, damsin, ambrosin, and hymenin) isolated from the aerial parts of *Ambrosia maritima* were investigated for their antimicrobial activity against two plant pathogenic bacteria, *Agrobacterium tumefaciens* and *Erwinia carotovora*. The tested compounds exhibited variable degree of antibacterial activity against both tested bacteria as minimum inhibitory concentrations (MIC) ranged 90–520 mg/l. Neoambrosin showed the highest antibacterial activity among the tested sesquiterpenes with MIC values of 150 and 90 mg/l against *A. tumefaciens* and *E. carotovora*, respectively.

On the contrary, hymenin was the least effective compound with MIC values of 520 and 310 mg/l against *A. tumefaciens* and *E. carotovora*, respectively. Neoambrosin, damsinic acid, and damsin caused significant reduction in sulfhydryl group content with the former being the most effective. The tested sesquiterpenes significantly inhibited polygalacturonase and pectin-lyase activities of A. tumefaciens and E. carotovora except for hymenin which caused a significant activation of E. carotovora enzymes[3].

1.3 *Berberis heterophylla*

The *in-vitro* antifungal activity of aqueous extracts of *Berberis heterophylla* were evaluated as well as the antifungal activity of berberine isolated from *Berberis heterophylla*. In Addition acute toxicity on fish and toxicity of berberine to embryo-larval stages of *Bufo arenarum* were tested. Berberine has shown a moderate but significant antifungal activity against dermatophytes fungi. Thus, the *in vivo* or *in vitro* antifungal activity of this compound, combined with their lower toxic effect in comparison with the reference compounds, indicate that the potential of this alkaloid as a novel class of antifungal agent[4].

1.4 *Baccharis dracunculifolia*

The antimicrobial activities of *B. dracunculifolia* and some of its isolated compounds were evaluated. The results have shown that the leaves extract of *B. dracunculifolia* (BdE) presents antifungal and antibacterial activities, especially against *Candida krusei* and *Cryptococcus neoformans*, for which the BdE showed IC_{50} values of 65 µg/ml and 40 µg/ml respectively.

Also, a phytochemical evaluation of the BdE was performed with the isolation of ursolic acid (1), 2a-hydroxy-ursolic acid (2), isosakuranetin (3), aromadendrin-4'-methylether (4), baccharin (5), viscidone (6), hautriwaic acid lactone (7), and the clerodane diterpene (8). Among these isolated compounds, 1 and 2 showed significant antibacterial property against Methicillin-Resistant *Staphylococcus aureus* (MRSA) with IC_{50} values of 5 µg/ml and 3 µg/ml respectively. Compound 3 was active against *C. neoformans* with an IC_{50} value of 15 µg/ml and a MIC value of 40 µg/ml, while compounds 4 to 8 were inactive against all tested microorganisms[5].

1.5 *Boscia albitrunca*

The extracts of *Boscia albitrunca* and martynoside were evaluated for antimicrobial activities using the micro dilution technique. All the extracts and compound were active against the tested Gram +ve, Gram –ve bacteria and fungi. Minimum inhibitory concentration (MIC) values for extracts ranged from 390.0 to 6250 µg/ml and martynoside isolated from the butanol fraction was the most active with the lowest MIC values of 7.81 and 31.2 µg/ml against *B. subtilis* and *K. pneumoniae* respectively. The activity demonstrated by the extracts and martynoside obtained from *B. albitrunca* against tested bacteria and fungi suggests that they could be helpful in the management of eye infections[6].

1.6 *Bougainvillea glabra*

Antibacterial property of Oleananoic acid acetate isolated from *Bougainvillea glabra* leaves were evaluated against *Streptococcus mitis* and *Lactobacillus spp*. by examining the zone of inhibition by well diffusion method at a concentration of 25µg/25µl. The terpenoid has shown significant antibacterial activity. The isolation method adopted is simple, cost effective and efficient[7].

1.7 *Butea monosperma*

Crude extract of flowers [CVP-1] and roots [CVP-2]of *Butea monosperma* were subjected for antibacterial activity against gram-negative and gram-positive bacteria like *Bacillus megatarium*, *Bacillus subtilis*, *Escherichia coli and Pseudomonas aeruginosa* using standard protocols with MIC in range of 7.5 to 25 µg/ml. The antifungal activity was also carried out against strains of *Alternaria*, *Fusarium* and *Aspergillus flavus* in the range of10 µg/ml to 300 µg/ml . The fraction CVP-1 was found to be active against the bacterial strain *Escherichia coli* MTCC–442 with 3.5 µg/mL concentration. Similarly, fraction CVP-2 was found excellent active against the bacterial strain *Bacillus subtilis* MTCC–441 with 6.4 µg/ml concentration. The fraction

CVP-1 was found excellent active against *Alternaria* MTCC—149 with 10 µg/ml concentration and fraction CVP-2 was found excellent active against *Alternaria* MTCC—149 with 50 µg/ml concentration. Four compounds were isolated viz., 3,4,5 trihydroxy Benzoic acid,2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy- 4H -chromen-4-one(quercetin), (E)-3- (4 hydroxy-3-(3,4,5-rihydroxy methyl) tetrahydro-2H pyran-2-yloxy)phenyl)-1-(2-hydroxy-4-(3,4,5-trihydroxy-6(hydroxyl methyl) tetrahydro- 2H -pyran-2- yloxyl) phenyl)prop -2-en-1 -oneand2-(4-hydroxy-2-(3,4,5trihydroxy) tetrahydo -2H-pyran-2-yloxy)phenyl)-7-(4,5, 6 -trihydroxy- 3 (hydroxymethyl)tetrahydro-2H-pyran-2- yloxyl) chroman -4-one from the plant and antimicrobial activity could be attributed this compounds[8].

1.8 *Calophyllum brasiliense*

Crude methanol extracts (CME) of *Calophyllum brasiliense* and two fractions, denoted non-polar (soluble in chloroform) and polar (insoluble in chloroform), were prepared from different parts of the plant (roots, stems, leaves, flowers and fruits) and evaluated. Isolated compounds from methanol extract of *Calophyllum brasiliense* viz., brasiliensic acid (1), gallic acid (2), epicatechin (3), protocatechuic acid (4), friedelin (5) and 1,5-dihydroxyxanthone (6) were evaluated for antimicrobial activity against *Bacillus cereus*(ATCC 14579), *Enterobacter cloacae* (ATCC35030), *Escherichia coli* (ATCC 11775), *Proteus mirabilis* (ATCC 14273), *Pseudomonas aeruginosa* (ATCC 35032), *Salmonella typhimurium* (ATCC14028), *Staphylococcus aureus* (ATCC 6538P), *Staphylococcus saprophyticus* (ATCC 35552) and *Streptococcus agalactiae* (ATCC 13813), *Candida albicans* (ATCC 10231) and *Candida tropicalis* (ATCC 7349). The results of the present indicated that all the parts of the plant exhibited antimicrobial activity against Gram-positive bacteria, which are selectively inhibited by components of *C. brasiliense*. No activity was found against Gram-negative bacteria and yeasts tested. Among the isolated compounds, substance 4 showed antimicrobial property against all the tested microorganisms, where as compound 6 has shown antimicrobial activity only against Gram-positive bacteria [9].

1.9 *Chamaecyparis formosensis*

The chemical composition of the volatile oil of *Chamaecyparis formosensis* wood has been tested. GCMS data and retention indices for reference samples were used to identify 32 constituents. α Eudesmol (18.06%), β-guaiene (8.0%), (–)-β-cadinene (7.89%), γ-costal (7.03%), α-muurolol (6.49%), 4α-hydroxy-4bmethyldihydrocostol (5.52%), s -selinene (4.78%), santolina triene (4.60%), eremophilene (4.32%), humulene (4.11%), myrtenol (4.11%), and t-cadinene (3.25%) were the most abundant components. The wood oil was evaluated against typical wood decay fungi, *Laetiporus sulphureus* and *Trametes versicolor*, proved the antifungal activity of the essential oil, as the growth of *L. sulphureus* and *T. versicolor* was inhibited at concentrations of 50 and 100 µg /ml respectively. The volatile compounds were isolated and purified from ethyl acetate fractions of *C. formosensis* were epicubenol, chamaecynone, myrtenol, cis-myrtanol, 12-hydroxyisointermedenol and 4α-hydroxy-4β methyldihydrocostol. Out of the isolated compound, Chamaecynone possessed the strongest antifungal activity, with an antifungal index of 88.2% and 67.3% for *L. sulphureus* and *T. versicolor* at a dose of 50 mg/ ml respectively[10].

1.2.0 *Cichorium intybus*

The ethyl acetate extract of chicory root were tested for anti-bacterial and anti-fungal properties using Gram Positive (*Bacillus subtilis, Staphylococcus aureus, Rhizobium leguminosarum*) and three Gram negative (*Vibrio cholerae,Escherichia coli, Pseudomonas fluorescens*) bacterial species & two fungal (*Aspergilus niger* and *Saccharomyces cerevisiae*) species. Fractionation by column chromatography of ethyl acetate extracted root powder contains the compound, inhibiting both Gram positive and Gram negative bacteria and was found to be bacteriostatic rather than bacteriocidal. The effect of chicory root extract has more bacteriostatic effect on Gram Positive bacteria than Gram negative bacteria as MIC value is more in case of Gram negative bacteria than Gram positive bacteria[11].

1.2.1 *Chromolaena Spp.*

The crude extracts (dichloromethanic and ethanolic) and compoundsisolated (8 flavonoids and 5 steroids stigmasterol 9, β-sitosterol 10, campesterol 11, espinasterol 12, Δ7 -stigmastenol 13.) isolated from *Chromolaena squalida* (leaves and stems) and *Chromolaena hirsuta* (leaves and flowers) have been investigated against 22 strains of microorganisms including bacteria (Gram- positive and Gram-negative) and yeasts[*Escherichia coli* - ATCC 10538; *E. coli* 6.1 (fieldstrain); *Pseudomonas aeruginosa* - ATCC 27853; *P.aeruginosa - Pn* (field strain); *Micrococcus luteus* - ATCC9341; *Staphylococcus aureus* - ATCC 25923, 6538 and 29213; *S. aureus - 7+ penicillinase producer*; *S. aureus -8-penicillinase non-producer*; *Staphylococcus epidermidis* - 6ep (field strains); *Candida albicans* - ATCC 1023;*Candida albicans-cas* and *Candida tropicalis - ct* (field strains), cultivated for 24 hours at 37 °C in Mueller Hinton broth (Difco)-MHb; *Enterococcus faecalis* – ATCC 10541; *Streptococcus mutans* - ATCC 25175; *S. mutans* (strains Fab3; 87.1; 203.1; 211.1; 213.1) and *Streptococcus sobrinus* - 87.3 (field strains).

All crude extracts, flavonoids and steroids evaluated have been shown actives, mainly against Gram-positive bacteria. The flavonoids 6, 7 and 8 were the most bioactives. The mixture of steroids (500 µg/ml) showed to be active mainly against *Streptococcus mutans* and *S. sobrinus* strains, however with very limited activity. The flavonoids 1 and 2 were active against *S. aureus* (ATCC 6538 and ATCC 29213), *S. sobrinus* (87.3) and *Enterococcus faecalis* (ATCC-10541) strains. From all test-drug only the flavonoid 7 showed activity against the Gram-negative (*Escherichia coli, Pseudomonas aeruginosa*) bacteria and yeast (*Candida*

albicans and C. tropicalis). *C. hirsuta* showed antimicrobial activity, mainly against Gram-positive (*Staphylococcus* and *Streptococcus)* bacteria[12].

1.2.2 *Clerodendrum phlomidis*

The *in vitro* antimicrobial activity of the extracts and isolated compounds [Phenyl acetic acid, Ethyl- 2- hydroxy - 4- methyl benzoate, 3,6,7-trihydroxy-2-(3-methoxyphenyl)-4H-chromen-4- one] from roots of *Clerodendrum phlomidis* against *Staphylococcus aureus*, *Streptococus pyogenes*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Candida albicans*, and *Aspergillus niger* were evaluated. Experiment showed that ethanol extract of *Clerodendrum phlomidis* at 106.66µg/ml showed a significant result against *Escherichia coli*.Chloroform extract also shows good antimicrobial activity against *Staphylococcus aureus* with a zone of inhibition of (14.67mm). Among the isolated compounds, Ethyl- 2- hydroxy -4- methyl benzoate shows good antimicrobial activity against *Staphylococcus pyogenes*, and *Candida albica*[13]. In the isolated compounds, ethyl- 2- hydroxy -4- methyl benzoate shows good antimicrobial activity than other two compounds, this may be due to the presence of ester group and phenolic hydroxyl group. All the isolated compounds showed no inhibition against *Pseudomonas aeruginosa*. Ethyl- 2- hydroxy -4- methyl benzoate, possess the chemical structure similar to parabens, may exert the similar antimicrobial activity like that of parabens.

1.2.3 *Combretum woodii*

Acetone extracts of *C. woodii* leaf powder was separated by solvent-solvent partition into six fractions. The highest total activity was in the chloroform fraction. The compound was isolated by bioassay-guided fractionation using silica gel open column chromatography as the stilbene 2',3',4-trihydroxyl-3,5,4' trimethoxybibenzyl (combretastatin B5). Causative agents of nosocomial infections were used which were *Staphylococcus aureus* (ATCC 29213), *Pseudomonas aeruginosa* (ATCC 25922), *Escherichia coli* (ATCC 27853) and *Enterococcus faecalis* (ATCC21212).

It has shown significant anti-bacterial activity against *S. aureus* with an MIC of 16 mg/ l but with lower activity towards *P. aeruginosa* (125 mg/ l), *E. faecalis* (125 mg/ l) and slight activity against *E. coli*. Its concentration in the leaves was in the order of 5-10 mg/g which makes the use of extracts for clinical purposes a viable possibility particularly in poor communities[14].

1.2.4 *Curcuma longa*

The three isolated compounds from *Curcuma longa* viz, curcuminoids [curcumin, bisdemethoxycurcumin and demethoxycurcumin] were screened for antibacterial activity against medically important bacteria viz. *B. subtilis, K. pneumonia, E. coli, Enterobacter aerogenes, Pseudomonas aeruginosa, S. auresus* and *P. Mirabilis* by Agar diffusion method. Two fungi were selected viz. *Aspergillus niger* and *Candida albicans* for antifungal activity of three isolated curcuminoids by Agar well diffusion method. Out of three curcuminoids, curcumin has shown better antibacterial as well as antifungal properties as compared to bisdemethoxycurcumin and demethoxy curcumin. Curcumin has shown very good significant activity against *B.subtilis, E. coli, S. auresus* and *P. mirabilis*, whereas it exhibited moderate activity against *K. pneumonia, Enterobacter aerogenes* and *Pseudomonas aeruginosa.* Bisdemethoxycurcumin exhibited good activity against *B. subtilis* and *S. auresus* whereas it showed moderate activity against *E. coli, P. mirabilis, K. pneumonia, Enterobacter aerogenes and Pseudomonas aeruginosa*. Demethoxycurcumin has shown some degree of activity against *B. subtilis, S. auresus, E. coli, P. mirabilis, K. pneumonia* and *Enterobacter aerogenes*. It was inactive against *Pseudomonas aeruginosa*. Curcumin showed very good activity against both fungi, viz., *A.niger* and *C.albican*. Bisdemethoxycurcumin has shown moderate activity against *A.niger* and *C.albican*. Demethoxycurcumin exhibited some degree of activity againgt *C.albican* and no activity against *A. niger*[15].

1.2.5 *Ficus lyrata*

The aqueous and ethanol extracts of *F. lyrata* and two pure compounds i.e. Ursolic acid (FL-1) and Acacetin-7-O-neohesperidoside (FL-2) isolated from *F. lyrata* were tested against several standard bacterial strains by the Kirby Bauer method for determining the MIC. *F. lyrata* showed potent antibacterial activity against *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Shigella dysenteriae*, *Shigella boydii*, *Citrobacter freundii*, *Proteus vulgaris*, *Proteus mirabilis* and *Klebsiella*. The aqueous extract was more potent than alcoholic extract. The isolated compounds were more potent and showed better activity when compared to the crude extract. The minimum inhibitory concentration (MIC) of aqueous extract of *F.lyrata* and the isolated compounds were found to be significantly low for all the tested bacterial strains. The study suggests that the extracts obtained from the leaves of *F. lyrata* possess excellent antibacterial activity which could possibly be attributed to the two compounds i.e. FL-1 and FL-2[17].

1.2.6 Flavonoids

Flavonoids are ubiquitous in photo-synthesising cells and are commonly found in vegetables, nuts, fruit, seeds, stems, flowers, tea, wine, honey and propolis. For centuries, preparations consisting of flavonoid compounds have been used to treat various human diseases. Now a days this class of natural products is becoming the subject of research as anti-infectives, and several groups have isolated and identified the structures of flavonoids possessing antimicrobial (antifungal, antiviral and antibacterial) activity. Several groups of flavonoids have demonstrated synergistic properties between active flavonoids as well as between flavonoids and existing chemotherapeutic agents. In addition, several research groups have sought to elucidate the mechanisms of action for antibacterial activity of selected flavonoids. For example, the activity of quercetin

has been at least partially attributed to DNA gyrase inhibition. Also it has been proposed that sophoraflavone G and (−)-epigallocatechin gallate diminishes cytoplasmic membrane function, and that licochalcones A and C inhibit energy metabolism. Other flavonoids for which mechanisms of action for antimicrobial properties have been investigated include apigenin, rutin, robinetin, myricetin, galangin, 2,4,2-trihydroxy-5-methylchalcone and lonchocarpol A. These compounds represent novel leads future studies may allow the development of a pharmacologically acceptable antimicrobial agent or class of agents[18].

1 .2.7 *Kigelia africana*

Crude extracts of stembark and fruits of *Kigelia africana* were prepared with distilled water, ethanol or ethyl acetate. In the microtitre plate bioassay, fruits and stembark extracts have shown similar antibacterial activity against Gram-negative and Gram-positive bacteria. A mixture of three fatty acids [palmitic acid was the major compound and non anoic acid and 8-heptadecenoic acid, the minor compounds] showing antibacterial effects were isolated from the ethyl acetate extract of the fruits using bioassay- guided fractionation. The results confirm antibacterial activity of *K. africana* fruits and stembark, and support the traditional use of the plant in therapy of bacterial infections[19].

1.2.8 *Mangifera indica*

Five flavonoids, viz. (–)-epicatechin-3-O-β-glucopyranoside (1), 5-hydroxy- 3-(4- hydroxylphenyl)pyrano[3,2-g]chromene-4(8H)-one (2), 6-(p-hydroxybenzyl) taxifolin-7-O-β-D- glucoside (tricuspid) (3), quercetin-3-O-α glucopyranosyl-(1→2)-β-glucopyranoside (4) and (–)-epicatechin(2-(3,4-dihydroxyphenyl)- 3,4-dihydro-2H-chromene-3,5,7-triol) (5) were isolated from the leaves of mango (*Mangifera indica* L.). The antibacterial properties of different concentrations of the flavonoids (100, 300, 500, 700, 900 and 1000 ppm) were tested against four bacterial species, namely *Azospirillium lipoferum, Bacillus spp., Escherichia coli* and *Lactobacillus spp.* The five flavonoids significantly inhibited the growth of all the five tested species of bacterial. However, differences in the antibacterial properties of the flavonoids were evident. Compound 1 has shown the lowest antibacterial property, resulting in a 7–75 % reduction in the growth of the different bacterial species. Compound 5 has shown the maximum antibacterial activity and the different concentrations inhibited the bacterial growth by 45–99.9 %. *A. lipoferum* and *Bacillus sp*p. has shown the highest susceptibility to this compound. Compounds 2–4 also exhibited pronounced antibacterial activity. Different concentrations of the flavonoid compounds reduced bacterial growth by 52–96 %. The results of the present study concluded that compound 5 is the most effective of the tested flavonoids against *A. lipoferum* and *Bacillus* spp[20].

Potential antimicrobial compounds from *Mangifera indica* L. seed kernel were isolated by the bioassay guided fractionation process and characterized by NMR and LC-MS as gallic acid, gallic acid ethyl ester,hydroxyl xanthone –C-glucoside and Quercetin 3 sulphate. The extracts and isolated fractions were evaluated for their antimicrobial property against *Bacillus subtilis, Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa*, and the fungal strains *Aspergillus niger* and *Candida albicans*. The minimum inhibitory concentration (MIC) of ethyl acetate extract ranged between 4.0 and 5.0 µg/ml, *Bacillus subtilis* (MIC 4.5µg/ml), *S. aureus* (MIC 4.0 µg /ml), *Escherichia coli* (MIC 4.5 µg /ml) and *Pseudomonas aeruginosa* (MIC 5 .0 µg/ml) and *Candida albicans* (MIC 4. 5 µg /ml)[21].

1.2.9 *Monanthotaxis littoralis*

The study evaluated the antifungal activity of a mixture of two closely related flavonoids namely 3, 7, 5'- trihydroxy anthocynidines and 3, 5-dihydroxy-7-methoxyanthocynidines isolated from *Monanthotaxis littoralis* (Annonaceae) against mycotoxigenic fungi from three genera (*Aspergillus, Fusarium and Penicillium*) isolated from maize samples. The highest activity of the flavonoids was against *Aspergillus ochraceus* with inhibition zone of 20.17mm and MIC of 1 µg/ml. The activity of the flavonoids against the mycotoxigenic fungi had Minimum Inhibitory Concentration (MIC) values ranging from 1 µg/ml to 4 µg /ml. These results show that the two flavonoids from *M. littoralis* have antifungal activities against fungi that are the producers of poisonous mycotoxins found in foods. These compounds are potential antimicrobials that can be used in food preservation systems to inhibit the growth of moulds and retard subsequent mycotoxin production[22].

1.3.0 *Nyctanthes arbortristis*

The antimicrobial activity of stem bark extracts of *Nyctanthes arbortristis* were evaluated by cup plate method against *Staphylococcus aureus, Micrococcus luteus, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa, Candida albicans* and *Aspergillus niger*. The chloroform extract was found to have both antifungal and antibacterial properties whereas the petroleum ether and ethanol extracts has shown only antibacterial property.

The antibacterial potential of β sitosterol isolated from the ethanolic extract of leaves of *Nyctanthes arbortristis* were evaluated on gram +ve (*Staphylococcus aureus*) and gram –ve (*Escherichia Coli and Pseudomonas aeruginosa*) bacteria. Isolated compound, β sitosterol shown higher zone of inhibition against *Pseudomonas aeruginosa* as compared with the other tested bacteria[23].

1.3.1 *Psidium guajava*

Ten new aliphatic compounds pentapentacont-17, 31-diol (1), 11-hydroxy-tricont-35- pentatriacontanoate (2), 34 octahexacontanol (3), heptatriacont-8-ol (4), 14,15-dimethyl (cyclopropayl)-9-oloctadecayl- 3-(4-hydroxyphenyl) propanoate (5), hexaeicosan-16-ol (6), pentatetracosan-10, 25-diol (7), untricontan-11, 19-diol (8), tricosan -17-ene-5-ol (9), and nonacosan-23-ene-3-ol (10) were isolated from the ethanol extract of the leaves of *P. guajava* .The

antimicrobial activity of 10 compounds were evaluated against *E. coli, P. aeruginosa, Staphylococus aureus, Klebsiella pneumoniae, Shigella boydi, S. typhimurium* and *Bacillus subtilis.* All compounds exhibited moderate activity against *Staphylococcus aureus* and poor activity against *Shigella* spp and *Klebsiella pneumoniae*.

All compounds isolated from benzene: acetone fraction of *P. guajava* gave moderate activity against *Staphylococus aureus*. All of compounds showed noticeable activity against *Salmonella typhimurium, Pseudomonas aceruginosa* and *Bacillus subtilis*. All compounds showed very poor activity and no activity against *Shigella spp, E. coli* and *Salmonella typhimurium*. The plant can be used for the formulation of oral antibacterial drugs to manage surgical, skin and soft tissue infections[24].

Four antibacterial compounds were isolated from leaves of guava (*Psidium guajava* L.), which were morin-3-O-α-L-lyxopyranoside,morin-3-O- α -L-arabopyranoside, guaijavarin and quercetin. The minimum inhibition concentration of morin-3-O-α- Llyxopyranoside and morin-3-O-α-L- arabopyranoside was 200 µg/ml for each against *Salmonella enteritidis* and 250 µg/ml and 300 µg/ml against *Bacillus cereus*, respectively[25].

1.3.2 *Pseudognaphalium luteoalbum*

Invasive and weedy species such as *Pseudognaphalium luteoalbum* may serve as a source of biologically active extracts or compounds with application in crop and ornamental plant protection, among other uses. The acetone crude extract of *P. luteoalbum* leaves had strong antifungal activity when tested against a selection of plant pathogenic fungi *in vitro*. The compounds were identified as: 5,4′-dihydroxy-6-methoxy-7-O-β-glucopyranosideflavone (hispidulin-7-O-glucopyranoside) (1) and stigmasterol-3 O-β-glucopyranoside (2). The crude extract and isolated compounds were moderately to highly active against a selection of phytopathogenic fungal organisms with MIC values ranging from 0. 02 to 1.25 mg/mL. No cytotoxicity of the isolated compounds was found against Vero kidney cells at 200 µg/ml[26].

1.3.3 *Reboulia hemispherica*

Comparative evaluation of antimicrobial activity of methanolic extract and phenolic fraction of a liverwort, *Reboulia hemispherica* were carried out by Agar well diffusion technique. Four Gram positive (*S. aureus*, clinical isolate; *E. faecalis*, clinical isolate; *B. subtilis*, MTCC 121*; B. cereus*, MTCC 430) and three Gram negative (*E. coli*, MTCC 1673; *P. aeruginosa*, MTCC 1934; K. sp., clinical isolate). Fungal species included *A. niger*, MTCC 1344 and *P. notatum*, MTCC 1898.The Gram +ve bacteria were more sensitive than the Gram -ve ones, while the fungal species were least sensitive. *R. hemispherica* extract exhibited best results against *Staphylococcus aureus*, although it was active against all tested microbes. The antimicrobial activity increased with the increase in the concentration of the extract except in *Klebsiella sp. S. aureus, E. faecalis* and *Bacillus* cereus were inhibited more by the crude methanol extract of *R. hemispherica* than the phenolic compounds isolated from the extract. A. niger was inhibited equally by the crude methanol extract as well as the phenolic compounds. *B. subtilis, E. coli, P. aeruginosa, K. sp.* and *P. notatum* were inhibited more by phenolic compounds than the crude methanol extract of *R. hemispherica*[27].

1.3.4 *Solanum spirale*

The hexane and chloroform extracts of *Solanum spirale* inhibited antibacterial activity against *E. coli* and *S. aureus* with the MIC values were in the range between 375-1500 µg/ml. All isolated compounds [trans-cinnamic acid, lupeol and protocatechuic acid] showed equal antibacterial activity against *E. coli* with the MIC of 250 µg/ml, and trans-cinnamic acid showed better antibacterial activity against *S. aureus* with the MIC of 250 µg/ml than lupeol and protocatechuic acid[28].

1.3.5 *Tectona grandi*

The isolated compound from *Tectona grandis* were evaluated for anti-mycobacterial activity against *S. aureus, K. pneumoniae, S. paratyphi* and *P. mirabilis* and also against *Mycobacterium tuberculosis*. Cytotoxicity of isolated compounds was evaluated. Two compounds isolated from chloroform extract of leaf has shown significant activity against *S. aureus* (Compound 1: MIC – 2.5µg/ml, IC_{50} - 72µg/ml ; Compound 2: MIC - 5 µg/ml, IC_{50} - 98 µg/ml) and *K. pneumoniae* (Compound 2: MIC – 6.2 µg/ml, IC_{50} – 113.5 µg/ml). These compounds failed to show anti-mycobacterial activity on testing against *M. tuberculosis*. On cytotoxicity analysis of both compounds against chick embryo fibroblast (CEF), HEK293, HCT119 and L929 cells, compound 2 showed activity against HEK293 (IC_{50} - 2 µg/ml)[29].

1.3.6 *Tragia involucrata*

The fresh roots of young matured plants of *Tragia involucrata* Linn. were selected for phytochemical and antimicrobial examination to justify the folklore and traditional uses of the plant parts in various microbial infections. The antimicrobial activities were noted in the selected isolated compounds from the plants [10, 13-dimethoxy-17-(6-methylheptan-2-yl)-2, 3, 4, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16,17 tetradecahydro-1Hcyclopenta [α]phenanthrene[TIR-01], Stigmasterol [TIR-02], Quercetin [TIR-03], Rutin [TIR-04] and 3-(2,4-dimethoxyphenyl)-6,7-dimethoxy-2,3-dihydrochro-men-4- one; TIR-05] in a concentration of 200µg/ml were well comparable with that of the standard drugs in the concentrations of 25µg/ml against some selective strains of bacteria and fungi[*S. aureus* (MTCC 7443), *B. subtilis* (MTCC 619), *B. brevis* (MTCC 4832) and *S. epidermidis* (MTCC 2639); gram –ve bacteria such as *E. coli* (MTCC 1687), *Shigella dysenteriae* (Lab. isolate from stool), *Pseudomonas aeruginosa* (MTCC 1688) and *Vibrio cholera* (MTCC 3904) and fungi such as *Trichophyton rubrum*(MTCC 296) and *Malassezia furfur*

(MTCC 1765). Maximum ZOI of 20.1 mm was found in case of TIR-01 against the gm. +ve bacteria, *Staphylococcus aureus*; 16.2 mm in case of TIR-05 against the gm. –ve bacteria, *Escherichia coli* and 12.6 mm in case of TIR-01 against the fungi, *Malassezia furfur*. While comparing the MIC values of the two selected isolated compounds (TIR-01 and TIR-05), the lower MIC was observed in TIR-01 against almost all selected bacteria (Gm. + ve and – ve) and fungi with a few exceptions against *P. aeruginosa* (Gm. – ve bacteria) and *M. furfur* (fungi) and these were found to have low MIC in TIR-05[30].

2. IN SILICO ANTIMICROBIAL ACTIVITY

2.1 *Annona reticulate*

The antimicrobial activities of methanolic root extract of *Annona reticulata* Linn were evaluated using the agar cup method whereas Poison plate method was used to assess sensitivity of fungal strains. The biological potential of major phytoconstituents as antimicrobial agent was screened by new software based tool, PASS. The probable activity (Pa) of neoannonin using PASS was found to be 0.541. The extract was significantly active against all strains of bacteria but the largest zone of inhibition was found against *B. cereus*. Predominant growth reduction was observed in fungi *Tricoderma viride* and *Candida albicans*. The results indicate that the extract show potential as a source of new antimicrobial drug and may impart health benefits by its antioxidant property[31].

2.2 *Sesamum indicum*

Pathogenic bacteria constitute an important cause of hospital-acquired infections. However, the misuse of available bactericidal agents has led to the appearance of antibiotic-resistant strains. Thus, efforts to seek new antimicrobials with different action mechanisms would have an enormous impact. Here, a novel antimicrobial protein (SiAMP2) belonging to the 2S albumin family were isolated from *Sesamum indicum* kernels and evaluated against several bacteria and fungi. Furthermore, in silico analysis was conducted in order to identify conserved residues through other 2S albumin antimicrobial proteins (2S-AMPs). SiAMP2 specifically inhibited Klebsiella sp. Specific regions in the molecule surface where cationic (RR/RRRK) and hydrophobic (MEYWPR) residues are exposed and conserved were proposed as being involved in antimicrobial activity. This study reinforces the hypothesis that plant storage proteins might also play as pathogen protection providing an insight into the mechanism of action for this novel 2S-AMP and evolutionary relations between antimicrobial activity and 2S albumins[32].

3.CONCLUSION

We have given a review of 38 plants with their isolated compounds against number of bacteria and fungi. Each isolated compound have shown to possess antimicrobial activity with different MIC values. Future plan will be that SAR of the isolated compounds can be done and check which has a better antimicrobial activity. Industry can take the lead and isolated the compound in bulk quantities and prepare formulation. This review gives an idea about their antimicrobial potential of isolated compounds which can be utilized by Industry and coming out with a formulation at a cheaper rate which could be helpful to treating the disease related to microbes at an affordable price.

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