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Antimicrobial properties of natural products: A review

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Abstract

Natural products are known for their antimicrobial factors since time immemorial. By virtue of their antimicrobial factors, natural products play an important role in modern drug development programmes. Numerous naturally occurring antimicrobial agents can be of plant origin, animal origin, mineral origin, microbial origin etc. Many plant and animal products have antimicrobial activities due to the presence of a variety of active principles or secondary metabolites or phytochemicals (in case of plants) like alkaloids, tannins, terpenoids, essential oils, flavonoids, lectins, proteins & polypeptides, quinones, coumarins, polyphenols & phenolic compounds, enzymes, lysozymes, phagocytic cells and many other organic constituents. Neem leaves show anti-dermatophytic activity. The 5% Neem oil placed over breeding places inhibited breeding of *Anopheles stephansi* and *Aedes aegypti* mosquitoes in 45 days. Essential oils from Thyme, cinnamon & Eucalyptus showed antibacterial activity. Glycyrrhizin, a triterpenoid from *Glycyrrhiza glabra* (licquorice) was tested effective against RNA viruses like measles virus, polio virus etc. Quinine the antimalarial drug is obtained from the bark of cinchona tree. Leaves of *Cassia alata* show *in vitro* antibacterial activity against *Staphylococcus aureus*, *E. coli*, *Bacillus subtilis*, *Salmonella typhi* etc. Antimicrobial properties of milk are due to presence of many proteins and peptides like immunoglobulins, lactoperoxidase system, lactoferrin, some lysozymes etc. The black meat and blood of Kadaknath breed of poultry is famous for its medicinal value. The cow urine concentrate and cow dung showed antibacterial activity against many bacteria like *B. subtilis*, *P. asoginosa* etc. Co-ordinated approach is required among the planners, researchers, scientists, industrialists, Ayurveda exports, developmental agencies, administrators, extension workers, growers and funding agencies & users to utilize the immense potential of natural products to serve as an alternate source of combating infections.

Keywords: Antimicrobial, natural products, antibacterial and infections

Introduction

We all might have heard, watched or read somewhere that “certain seeds treated with some oracles (mantras) were thrown on somebody to entice him, certain roots were chewed to increase the longevity of life and few drops of juice of the Amar-Sanjevani plant put in the mouth of the dead brought him back to life. The sacred water of Ganges, cow dung and cow urine were used to purify a place or an object. And we all are familiar with the old American proverb “An apple a day, keeps the doctor away”. All these lead to the thought of some miraculous and supernatural cures. But these might be true to some extent because there are references of some natural products with magical properties to cure some deadly diseases in many of our ancient literatures and even in few modern researches also.

Nature is the wonderful gift of God. Nature has been the source of numerous antimicrobial agents since thousands of years. An impressive number of modern drugs have been isolated from natural sources. Natural products play an important role in modern drug development programmes. Majority of modern clinical drugs are of natural origin and mostly herbal origin. A big part of world population relies mainly on traditional medicines of natural origin for primary healthcare solutions.

History

Perhaps Neanderthal man was the first to use some natural antimicrobials for pain relief. But it was by chance. While moving on the hill tops, he felt hungry and ate some plants which relieved his pain. Since then, *Homo sapiens*, being the most intelligent among the species evolved, based on the principles of necessity and trial could observe the effectiveness of many natural products to relief of his pain and sufferings. The 1st written record of use of natural antimicrobials is by Sumerian and Babylonian physicians around 3000 B.C. Hippocrates mentioned about 300-400 medicinal plants with antimicrobial properties.

He burned some aromatic plants to combat the deadly epidemic plague of Athens in the Medieval Europe. Discorides wrote the 1st *materia medica*, which was a medicinal catalogue describing about many naturally occurring antimicrobials. Galen's poly pharmacy, The Chinese *Pen Tsao*, The *Rigveda*, the *Ayurveda* (a sub-section of *Atha0r vaveda*), Charaka Samhita, Sushruta Samhita, Ramayana and even the holy Bible also describe about antimicrobial properties of many natural products.

What are the naturally occurring antimicrobials?

Numerous naturally occurring antimicrobial agents can be of plant origin, animal origin, mineral origin, microbial origin etc. They are derived from plant parts like seed, bark, stem, leaves, flowers, fruits, root, rhizome, tuber, bulb, wood and even from the whole plant, and form various animal products like milk, curd, eggs, meat, cow dung, cow urine, marine fishes, sponges and other marine animals, honey etc. they can also be derived from minerals, microbes and many more. The scientific discipline dealing with the study of these natural antimicrobial agents is called as "Ethno-pharmacology" whose goal is to utilize the impressive array of knowledge assembled by indigenous people of a particular culture and region about the various plant and animal products they have used to maintain their health. The antimicrobial activity refers to the ability to fight against the microbes and the infections caused by them. Many plant and animal products have antimicrobial activities due to the presence of a variety of active principles or secondary metabolites or phytochemicals (in case of plants) like alkaloids, tannins, terpenoids essential oils, flavenoids, lectins, proteins & polypeptides, quinones, coumarins, polyphenols & phenolic compounds, enzymes, lysozymes, phagocytic cells and many other organic constituents.

Advantages

1. No problem of antibiotic resistance or multi drug resistance (MDR) and cross-resistance to other drugs.
2. Broader spectrum of action.
3. Lesser side effects, if used properly.
4. Abundantly available in nature.
5. Less expensive or cheap and effective.
6. Self-medication with these agents is a common practice.
7. Several natural antimicrobials have already been tested on human beings showing positive results.

There has been a revival / renewal of interest in natural antimicrobials due to

1. Increased awareness among people about the limited ability of synthetic pharmaceutical products to control many infectious diseases due to drug resistance developed by misuse and over prescription of modern drugs.
2. Many synthetic chemical are toxic and have many side effects or unwanted effects.
3. Now, people are more interested in having autonomy over their medical care and to avoid unnecessary chemicals and toxins, when an alternative is available.

Before use, screening is done to identify, isolate and extract the pure compounds from natural sources. The antimicrobial activities should be tested against appropriate microbial models in labs to confirm their activity.

Classification of natural antimicrobials

Natural antimicrobial agents are classified as antibacterial, antifungal, antiviral, antiprotozoal and insecticidal agents.

1. Anti-bacterial agents

- Leaves of *Cassia alata* show *in vitro* antibacterial activity against *Staphylococcus aureus*, *E. coli*, *Bacillus subtilis*, *Salmonella typhi* etc. [1]
- Extracts of dry nuts of *Samecarpus anacardium* showed bactericidal activity against 3 Gram -ve strains - *E. coli*, *S. typhi* & *Proteus vulgaris* and 2 Gram +ve strains like *Staphylococcus aureus* & *Corynebacterium diphtheriae*. [2]
- Essential oils from Thyme, cinnamon & Eucalyptus showed antibacterial activity. [3]

2. Anti-fungal agents:

- Neem leaves show anti-dermatophytic activity. [4]
- The percentage of antifungal activities of different plants- Eucalyptus (88%), Tulsi (85.5%), Neem (84.66%), Castor (75%) and Jatropa (10%). [5]
- Essential oils from *Aegel mermelos* (Bael) leaves exhibited antifungal activity and 100% sporicidal activity. [6]
- Leaves of *Cassia alata* showed antifungal activity against *Aspergillus niger* and *Candida albicans*. [7]
- Roots of *Withania somnifera* (Aswagandha) are found to be effective against *Aspergillus fumigatus*. [8]

3. Anti-viral agents

- Glycyrrhizin - a triterpenoid from *Glycyrrhiza glabra* (licquorice) was tested effective against RNA viruses like measles virus, polio virus -type 1, 2 & 3, HIV virus at higher concentration and inhibits DNA viruses at lower concentration. [9]
- Certain mangrove plant extracts showed antiviral activity against HIV virus by inhibiting the viral adsorption to host cells. [10]
- *Hemdesmus indica* leaves and *Cassia fistule* stem extracts inhibit viral replication & cytopathic effect (CPE) of Ranikhet Disease (RD) virus. And vaccinia virus due to presence of some interferon like factors in them. [11]

4. Anti-protozoal agents

- Quinine the antimalarial drug is obtained from the bark of cinchona tree. [3]
- Extracts of *Artemisia japonica* inhibited schizont stage of chloroquine sensitive strains of *Plasmodium falciparum*. [12]
- Extracts of *Swertica charata* inhibited catalytic activity of topoisomerase-I enzyme of *Leishmania donovoni* and showed anti-leishmanial activity. [13]
- Extracts of *Parthenium hysteroporos* (congress grass) exhibited trypanocidal activity against *Trypanosoma evansi*. [14]

5. Insecticidal agents

- 5% Neem oil placed over breeding places inhibited breeding of *Anopheles stephani* and *Aedes aegypti* mosquitoes in 45 days. [15]
- Application of oil of camphor and cream of neem on exposed body parts @ 2g / person significantly protected against *Aedes*, *Culex* and *Anopheles* mosquito bites. [16]
- Roots of *Derris elliptica* yields, 'rotenone' against head lice, scabies & other ectoparasites. [11]
- Pyrethrum from pyrethrum flowers is none of the oldest insecticides known.

By killing all these insect vectors, indirectly the natural antimicrobial agents kill the pathogenic microbes is them and hence show their antimicrobial properties.

Table 1. Antimicrobial properties of some traditionally used plants

S. No.	Common Name	Scientific Name	Active principle and plant parts	Antimicrobial activity
1.	Aloe	<i>Aloe vera</i>	Latex from succulent stems	<i>Salmonella</i> & <i>Streptococcus</i> spp.
2.	Apple	<i>Malus sylvestris</i>	'Phloretin' - a flavonoid from fruit	General antimicrobial
3.	Ashwagandha	<i>Withania somniferum</i>	'Withafarin A' - a lactone from roots & leaves	Antibacterial & antifungal
4.	Asafoetida/ Hing	<i>Ferul narthax</i>	Roots & rhizomes	Cholera whooping cough
5.	Bael / wood-apple	<i>Aegel marmelos</i>	Essential oils/terpenoids from leaf, fruit & root extracts	Antifungal
6.	Barberry	<i>Barberis vulgaris</i>	'Barberine' an alkaloid from root & stem bark	<i>M. tuberculosis</i> , <i>Vibrio cholera</i> , <i>Plasmodium</i> & <i>Trypanosomes</i>
7.	Basil / Sacred basil/ Holy basil	<i>Ocimum sanctum</i>	a. Essential oils from leaves and seed b. Root extracts	a. <i>Salmonella</i> , Ringworm, common cold virus b. In malarial fever to bring sweating
8.	Bay	<i>Laurus nobilis</i>	Essential oils from leaves	Antibacterial and antifungal
9.	Black pepper	<i>Piper nigrum</i>	'Piperine' - an alkaloid from dried seeds	Fungi, <i>Micrococci</i> , <i>E. coli</i>
10.	Brahmi	<i>Bacopa monnieri</i>	'Brahmine' - an alkaloid from whole plant	Anthelmintic property
11.	Calamus / sweet flag	<i>Acorus calamus</i>	Volatile oils from rhizomes roots & leaves	Enteric bacteria, insecticidal
12.	Cashew	<i>Anacardium pulsatilla</i>	Salicylic acids & polyphenols from fruit, seed	<i>P. acenes</i>
13.	Castor	<i>Ricinus communis</i>	Castor oil from seed	Antifungal (in dermatitis)
14.	Cinnamon	<i>Cinnamomum verum</i>	Essential oils from barks and leaves	General antimicrobial
15.	Cinchona	<i>Cinchona officinalis</i>	'Quinine' - an alkaloid from bark	Antimalarial
16.	Chilli	<i>Capsicum annum</i>	'Capsaicin' - a terpenoid from fruits	Antibacterial
17.	Chalmogra	<i>Hydnocarpus kurzii</i>	Essential oil	<i>Mycobacterium leprae</i> (in leprosy)
18.	Clove	<i>Syzygium aromaticum</i>	'Eugenol' - a terpenoid in clove oil from dried flowers	Antiseptic, general antimicrobial
19.	Coca	<i>Erythroxylum coca</i>	'Cocaine' - an alkaloid	Gram +ve & Gram -ve cocci
20.	Coriander	<i>Coriandrum sativum</i>	Whole plant, leaves & seeds	Antibacterial & antifungal
21.	Eucalyptus	<i>Eucalyptus globulus</i>	Tannins and terpenoids / essential oils from leaves	Antibacterial, antiviral antifungal
22.	Euphorbia	<i>Euphorbia nerifolia</i>	Entire plant stem	Anthelmintic & antitubercular
23.	Fava beans	<i>Vicia faba</i>	'Fabatin' from seeds	<i>E. coli</i> , <i>Pseudomonas aeruginosa</i>
24.	Garlic	<i>Allium sativum</i>	Sulfated terpenoids from bulbs	General antimicrobial
25.	Green tea	<i>Camellia sinensis</i>	'Catechin' - a flavonoid from leaves	<i>Shigella</i> , <i>Vibrio</i> , <i>S. mutans</i> , viruses.
26.	Henna	<i>Lawsonia inermis</i>	Gallic acid from leaves	1. Paste applied on skin diseases like boil. ^[24] 2. As gargle in sorethroat caused by <i>S. aureus</i> 3. TB, Typhoid
		Additional use- Orange dye for colouring hairs, palms & nails		
27.	Ipecac / Ipecacuanha	<i>Cephaelis ipecacuanha</i>	Root extracts	Amoebic dysentery
28.	Kamela	<i>Mallotus Phillippensis</i>	Tannins from red glandular fruits	Tapeworm, Ring worm, Scabies
		Additional use – dried powder of fruits used as vermilion / sindur		
29.	Long pepper	<i>Piper longum</i>	Dried fruits & leaves	Antibacterial
30.	Licquorice	<i>Glycyrrhiza glabra</i>	1. 'Glycyrrhizin' - a terpenoid 2. 'Glabrol' - an alcohol	1. HIV virus & other viruses 2. <i>M. tuberculosis</i> <i>S. aureus</i>
31.	Marigold	<i>Calendula officinalis</i>	Essential oils/ Terpenoids from leaves flowers	General antimicrobial
32.	Mint	<i>Mentha arvensis</i>	'Menthol' - an alcohol from leaves	Antiseptic, Mouth wash
33.	Neem / Margosa tree ^{[40][41]}	<i>Azadirachtus indica</i>	1. 'Azadirachtin' 2. 'Nimbin' 3. 'Nimbidin' 4. 'Gedunin' 5. 'Salannin' 6. 'Quercetin' (these are obtained from root, leaves bark, fruit, flower)	1. Repellant & antifeedant 2. Antifungal 3. Antibacterial, antifungal 4. Anti malarial & antifungal 5. Repellant 6. Antibacterial, antiprotozoal
34.	Oak	<i>Quercus rubra</i>	1. Tannins & polyphenols 2. 'Quercetin' from leaves	1. General antimicrobial 2. Antibacterial antiprotozoal
35.	Olive oil	<i>Oleo europoea</i>	'Hexanal' - an aldehyde	General antimicrobial
36.	Onion	<i>Allium cepa</i>	'Allicin' - a sulfoxide & other sulfated terpenoids from bulb	Bacteria, <i>Candida</i> (fungi)
37.	Orange	<i>Citrus sinensis</i>	Terpenoids from fruit peels, leaves	Antifungal
38.	Papaya	<i>Carica papaya</i>	Terpenoids, organic acids and alkaloids from latex of plant & fruit	General antimicrobial
39.	Palas/Flame of forest	<i>Butea monosperma</i>	Tannins from seed & leaves	Round worm, Ring worm, Dhobi-itch

40.	Peppermint	<i>Mentha piperita</i>	1. 'Menthol'- an alcohol 2. Peppermint oil- terpenoid from whole plant	1. General antimicrobial, 2. Mouth freshener ^[25]
41.	Poppy	<i>Papaver somniferum</i>	'Opium'- an alkaloid	General antimicrobial
42.	Potato	<i>Solanum tuberosum</i>	Potato starch from tuber	In skin ointment ^[24] , antibacterial & antifungal
43.	Rauwolfia	<i>Rauwolfia serpentina</i>	'Reserpine'- an alkaloid from root	General antimicrobial
44.	Red sandal wood	<i>Pterocarpus santalinus</i>	Terpenoids from wood	Antiseptic, used in skin infections & inflammations, Antibacterial
45.	Sadabahar	<i>Catharanthus roseus</i>	'Ajmalicine', 'serpentine', 'reserpine' (alkaloids)	General antimicrobial, anti-cancer drug
46.	Sandal ^[44]	<i>Santalum album</i>	Terpenoids, saponins, phenolic compounds from wood	Antibacterial, skin infections, TB of gallbladder
47.	Somraj / Kalazira	<i>Centratherum anthelminthium</i>	Dried seeds	Thread worm
48.	Sida	<i>Sida cardifolia</i>	Entire plant and root with ginger	General antimicrobial, fever
49.	Thyme	<i>Thymus vulgaris</i>	'Caffeic acid', 'thymol' & tannins	Antibacterial, antiviral, antifungal
50.	Tamarind	<i>Tamarindus indica</i>	Pulp of fruit	GIT infections and toxicity
51.	Turmeric	<i>Curcuma longa</i>	'Curcumin', turmeric oil, terpenoids from root / rhizome & leaves	Antibacterial, antiprotozoal, intestinal worms
52.	Willow	<i>Salix alba</i>	'Salicin', tannins, & essential oils	General antimicrobial
53.	Wintergreen	<i>Gaultheria fragrantissima</i>	Tannins & polyphenols	Hook worms, mosquito & fly repellent, anti-cancer drug
54.	Wormseed/ Ajvain	<i>Atremisia maritime</i>	Immature flowers & leaves	Anthelmintic (expels thread worms & round worms), GIT infections
55.	Triphala (3 fruits)	1. <i>Terminalia chebula</i> 2. <i>Terminalia bellerica</i> 3. <i>Embilica officinalis</i>	Seed extracts and powder of dried fruits	<i>S. aureus</i> , <i>E. coli</i> , <i>P. aeruginosa</i> , <i>M. tuberculosis</i> , common cold virus etc.

Anti-microbial properties of some animal products

Milk: Antimicrobial properties of milk are due to presence of many proteins and peptides like immunoglobulins, lactoperoxidase system, lactoferrin, some lysozymes etc. which are effective against many bacteria & viruses like *Listeria monocytogenes*, *E. coli*, *Enterobacter*, *Salmolnella* etc. having a broad spectrum of action. This antibacterial property of milk is used in prevention of mastitis in cattle & improving the health of man. ^[26]

Meat: Beef extracts show antifungal activity against *Candida albicans* due to presence of some lysozyme and phagocytic cells. ^[27]

The black meat and blood of Kadaknath breed of poultry is famous for its medicinal value. Along with treating male sterility problems aphrodesiac cases, it is used for treating TB, asthma, headaches, heart and nervous disorders etc. ^[28, 35]

Egg: Egg white lysozyme is effective against *Listeria monocytogenes* and other bacteria showing antibacterial activity. ^[29, 30]

Honey: Honey shows extreme antimicrobial activity. About 70 species of bacteria are susceptible to honey including methicillin resistant *Staphylococcus aureus* (MRSA) and vancomycin resistant *Enterococci* (VRE). ^[37]

Cow urine: The cow urine concentrate showed antibacterial activity against many bacteria like *B. subtilis*, *P. asoginosa*, *S.typhi*, *K. pneumoniae* and antifungal activity against *Aspergillus flavus* and *Aspergillus Niger*.

- Its anthelmintic property is found to be superior to the standard drug piperazine citrate.
- It is known for its anti-cancerous property and anti-HIV property.
- Cow urine with Neem extracts act as a potent insect repellent.

Cow dung: It is used as an antiseptic. Hence washing the floor of houses and sprinkling of cow dung solution is an Indian custom. Medicinal plants like ginger, garlic grown on

cow dung slurry showed increased antibacterial activity against *S. aureus*, *E. coli*, *P. aeruginosa* and higher antifungal activity against *Aspergillus Niger*. ^[32]

Marine animals: Marine actinomycetes, fungi, algae, sponges, fishes, crabs, molluscs, sea weeds show many antimicrobial activity against *S. typhi*, *L. monocytogenes* & *E. coli*.

Panchagavya: Milk, curd, ghee, dung and urine when mixed is called panchagavya. The concoction is seen to increase resistance of body, cure cancer and reduce dependence on antibiotics. ^[33, 34]

Antimicrobial properties of some other natural products

Microbes: Certain bacterial like lactic acid bacteria in curd, rice field *Cyanobacteria* and fungi like mushroom show various antimicrobial properties.

Minerals: Certain minerals, like Silver, Iodine, Iron, slat or NaCl show antimicrobial properties and used as antiseptic. Drinking water placed in copper pots shows proven antimicrobial properties.

Soil: Some actinomycetes present in laterite soil and loamy sand soil showed antimicrobial activities. Multani soil is known for its antimicrobial activities and is used in face pack, face cream etc. ^[31, 36]

Ganga water: The water of the Ganges is still believed to have some antimicrobial activity in spite of heavy pollution. It is believed to be self-purifying and active against various pathogens due to its constituents which are the reasons of its uniqueness among all perennial rivers, anywhere in the world. ^[17]

The bacteriophages and predatory bacteria like *Bdellovibrio bacteriovorus* (a G-ve curved rod with predatory action on other bacteria) present in the Ganges water against *Vibrio cholera* and other bacteria show the antibacterial property and can be used in preparation of antibiotics.

It has been observed that an 8 yr old Ganga water sample produced 14 mm zone of inhibition against *Streptococcus* spp.

And a 10 year old Ganga water sample produced 16 mm zone of inhibition. [17]

Sea water: The sea water shows anti-coliform activity against *E. coli* and antibacterial activity against other bacteria. It is effective in skin disease treatments. [20, 42, 43]

Limitations

1. Poor knowledge on scientific cultivation of many medicinal plants.
2. Lack of application of modern innovative for enhancing productivity of natural antimicrobials.
3. Lack of researches / funding.
4. Real concern about product safety.
5. Concern about liability.
6. Difficulty in extraction of pure and unchanged active principles.
7. Unrecognized trade and limited marketing support for naturally occurring antimicrobials.
8. Lack of awareness among people about properties of different natural antimicrobials.
9. In some cases, possible efficacy of a compound or few compounds depends on the presence of all other compounds of the intact whole plant or animal. Solution sometimes some compounds extracted from some well-known natural products show distinctively negative results.
10. Problem of sever toxicity in case of over doses and in association with some toxic factors.
11. Time of collection state of growth, locality of natural occurrence, place of cultivation etc all influence the antimicrobial properties of natural products.
12. The greatest difficulty for research worker is that the information on use of natural antimicrobials are scattered and most of it are found in some books or periodicals, which are either out of print and are not available even in large libraries.

What should be done for improvement of natural antimicrobials?

1. Awareness campaigns, training programmes, distribution of literatures/ medicinal catalogues in local languages should be done to popularize the use of natural antimicrobials.
2. Use of latest, economically viable, modern scientific technologies in cultivation, harvesting, processing, storage, extraction, study of pharmacodynamic properties and marketing of various natural products.
3. Special emphasis on conservation of valuable, rare, wild species of medicinal plants.
4. Backyard cultivation of important natural antimicrobials should be encouraged by every family, schools and educational institutes.
5. Financial support and supply of quality planting materials by government and transfer of scientific production technologies to the farming community.
6. Local, traditional and indigenous valuable medicinal products need to be patented in favour of a country's economy and geographical/topographical identification.
7. Co-ordinated approach is required among the planners, researches, scientists, industrialists, Ayurveda exports, developmental agencies, administrators, extension workers, growers and funding agencies & users to utilize the immense potential of natural products to serve as an alternate source of combating infections.

Conclusion

Modern man is so much indebted to microbial drugs that he can't think of the condition of life without those useful agents. Antimicrobials have become the very sinews of modern civilization, the arterial system of modern life. Wonders of these drugs for excel the wonders of god. But the inappropriate use and over prescription multi drug resistance (MDR) and cross-resistance to other drugs and has become a worldwide concern today. This emerging problem has ushered the 'Era of Responsibility'. Warning bells can be heard from every quarter. The urgent need of this age is to discover some novel alternatives to help combat this great problem. Many works are going on the antimicrobial properties of natural products. The plethora of literatures in the area indicates an urgent need for a coordinated effort for meaningful research and discovery of the novel alternatives by exploring the natural products.

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