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A REVIEW ON ANTIMICROBIAL COMPOUNDS ISOLATED FROM ENDOPHYTES, ALGAE AND PLANTS

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Abstract – Antimicrobial compounds are the vital tools to fight against pathogenic microorganisms. Discovery of antibiotics saved many lives during World War II. Extensive use of antibiotics in 20th century has led in the evolution of antibiotic resistant microbes. The problem of antibiotic resistance is a global problem and it is rising exponentially. Infections caused by such resistant microbes are difficult to treat. Under such a scenario, there is an urgent need for searching, identifying and compiling the antimicrobial compounds from diverse and natural sources. The secondary metabolites from plant, algae and endophytes seem to be prominent alternatives to fight against antibiotic resistance microorganisms. This review has compiled 40 such potential antimicrobial compounds from fungal endophytes, algae and plants.

INTRODUCTION

Antimicrobial compounds inhibit or kill microbes. Discovery of antimicrobial compounds has revolutionized medicine and protected humans from death causing infectious diseases. The mechanism of killing microbes is by attacking and terminating their biochemical and molecular pathways. Antibiotic Penicillin was the first antimicrobial compound that was isolated from fungi *Penicillium notatum*. This accidental discovery opened the door for many other antibiotics discovery and their production. This period is called the modern antibiotic era, which has substantially reduced the mortality rate. The ability to produce antibiotics is the natural strategy of bacteria and fungi to protect themselves from competitive microbes.

The doctors unknowingly indulge in prescribing antibiotics.The antibiotics are also extensively used in Animal Husbandry for improving animal growth and for protecting them from pathogenic microorganisms. Repeated and frequent use of antibiotics has caused the evolution of antibiotic resistant microbial populations.

To raise awareness, WHO is constantly conducting various programmes? Antibiotic resistance is escalating dangerously in all parts of the world. New resistance mechanisms are developing and spreading worldwide, threatening in the treatment of infectious diseases (Ortiz-Martínez *et al.*, 2018). The Center for Disease Control, USA, estimated in 2020 that antibiotic-resistant microbes cause 2.8 million infections and at least 35,000 deaths per year (CDC.gov). The three fundamental mechanisms of antimicrobial resistance are (1) enzymatic degradation of antibacterial drugs, (2) alteration of bacterial proteins that are antimicrobial targets, and (3) changes in membrane permeability to antibiotics (Dever and Dermody, 1991). The evolution of resistance is caused by mutation of genes and spreading it by horizontal gene transfer.

Under such a scenario, there is an urgent need for searching, identifying and compiling the antimicrobial compounds from diverse and natural sources. The secondary metabolites from plant, algae and endophytes seem to be prominent alternatives to fight against antibiotic resistance microorganisms. The secondary metabolites are the part of their defence system that works against all types of abiotic stress. Medicinal plants, microalgae and fungi that are rich in compounds, such as alkaloids, terpenoids, tannins, steroids, coumarins and flavonoids are antimicrobial in nature, and do not normally cause resistance (Lewis and Ausubel,

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Table 1. Antimicrobial compounds and mechanism of action from natural sources

Sr. No.	Name of antimicrobial compound	Source of isolation	Mode of action	Reference
		Anti-microbial compounds produced by Fungal Endophytes		
1.	Diketopiperazine (DKPs)	*Gliocladium* sp.	Diketopiperazine that kills Pythium by coagulation of proteins in the cytoplasm.	(Musetti *et al.,* 2007)
2.	Trichodermin	*Trichoderma harzianum*	Trichodermin has been shown to be a very potent inhibitor of eukaryotic protein synthesis, specifically by inhibiting peptide-bond formation at the initiation stage of translation and by inhibiting peptidyl transferase activity required for translational elongation and/or termination.	(Carter *et al.,* 1976; Wei *et al.,* 1974)
3.	Phomenone	*Xylaria sp*., associated with Piper aduncum,	Phomenone induces electrolyte loss and dysfunction of cell membrane permeability.	(Capasso *et al*., 1984)
4.	Phomenone	*Penicillium roqueforti*,	Inhibits RNA polymerase and protein synthesis at the initiation step as well as elongation	(Moule *et al*., 1976)
5.	Paclitaxel	*Taxomycesandreanae*	Paclitaxel acts by stabilizing microtubules and inhibiting spindle function leading to disruptions in normal cell division.	(Horwitz, 1994; Stierle *et al.,* 1995)
6.	Sordaricin	*Xylaria* sp. isolated from the leaves of *Garciniadulcis*, a tropical fruit tree	Sordarin was shown to inhibit fungal protein synthesis by selectively binding and inhibiting elongation factor 2 (EF-2) catalyzes ribosomal translocation during translation.	(Justice *et al.,* 1998; Pongcharoen *et al.,* 2008)
7.	Guanacastepene	Fungus CR115 isolated from the branch of a *Daphnopsis* americana tree	Damage and breakdown bacterial cell wall.	(M. P. Singh *et al*., 2000)
8.	Podophyllotoxin	*Podophyllum* plant species	The anti-viral activity of Podophyllotoxin appears to be due to its ability to disrupt viral replication and inhibit reverse transcriptase	(Canel *et al*., 2000; Stähelin and von Wartburg, 1991)
9.	Cytonic acids A and B (Tridepsides)	obtained from *Cytonaema* sp., an endophytic fungus of *Quercus* sp.	Inhibitory activity against the opportunistic human pathogen cytomegalovirus by inhibiting a protease required for normal assembly of the viral nucleocapsid	(Guo *et al*., 2000)
10.	Helvolic acid	*Pichiaguilliermondii* (Candida guilliermondii)	In A. fumigatus, a major human pathogen, evidence was presented that the helvolic acid gene cluster may be transcriptionally regulated by the major virulence-controlling transcription factor LaeA.	(Bok *et al.,* 2005; Zhou *et al.,* 2010)

Table 1. *Continued ...*

Sr. No.	Name of antimicrobial compound	Source of isolation	Mode of action	Reference
11.	Brefeldin A	*Eupenicellium brefeldianum*	BrefeldinA blocks the transport of proteins from the endoplasmic reticulum to the Golgi apparatus resulting in inhibition of secretion.	(Härri *et al*., 1963; Misumi *et al*., 1986)
		Antiviral compounds from algae (microalgae and cyanobacteria)		
12.	Naviculan	Microalgae *Naviculadirecta*	Inhibition of hyaluronidase	(Lee *et al*., 2006)
13.	Sulfated polysaccharides	Microalgae *Chlorella autotrophica*	Replication inhibition 47.4-67.4 %	(Fabregas *et al*., 1999)
14.	Spirulan	(Cyanobacteria) *Spirulinasp.*	Inhibits reverse transcriptase	(R. K. Singh *et al.,* 2011)
15.	Cyanovirin-N	(Cyanobacteria) *Nostoc ellipsosporum*	Interacts with high mannose groups of envelope glycoproteins, gp120 and blocks its interaction with target cell receptors	
16.	Scytovirin N	(Cyanobacteria) *Scytonemavarium*	Interacts with oligosaccharides conaining α1–2, α1–2, α1–6, tetramannose units of envelope glycoproteins, gp120, gp160, gp41	(Bokesch *et al.,* 2003; Xiong *et al*., 2006
17.	Sulfoglycolipid	(Cyanobacteria) *Scytone*ma sp.	Inhibit reverse transcriptase and DNA polymerases	(Loya *et al*., 1998)
18.	.α-dimorphecolic acid	*Oscillatoria redekei*	Inhibited the growth of Gram-positive bacteria	(Mundt *et al.,* 2003)
19.	Coriolic acid	*Oscillatoria redekei*	Inhibited the growth of Gram-positive bacteria	
20.	Abietane -diterpenoids	Plant and Cyanobacteria *Microcoleouslacustris*	They have ability to cross or damage microbial cell membranes due to themamphiphilic nature. Disruption of the membrane topology leads to increased membrane fluidity and permeability, disturbance of membrane embedded proteins, inhibition of respiration, and alteration of ion transport processes in both Gram-positive and Gram-negative bacteria.	(Neto *et al*., 2015)
21.	Ambigol A	*Fischerellaambigua*	Exhibited a strong inhibition of cyclooxygenase (in the range of indometacin) and of the HIV-1 reverse transcriptase as well as a potent antibacterial activity against *Bacillus subtilis*.	(Falch *et al*., 1993)
22.	Sulfated polysaccharides	*Chlorellaautotrophica*, *Ellipsoidon* sp.	Replication inhibition in vitro of *C. autotrophica*: range 47.4–67.4%; *Ellipsoidon* sp.: up to 44%	(Guedes *et al*., 2011)

Table 1. *Continued ...*

Sr. No.	Name of antimicrobial compound	Source of isolation	Mode of action	Reference
		Antibacterial compounds from plant		
23.	Piperine	*Piper nigrum L.* (Black paper)	This substance shows antibacterial activities by inhibition of bacterial efflux pumps.	(Khameneh *et al.,* 2015)
24.	Berberine	*Berberis spp.* and *Hydrastisspp.*	Inhibition of the bacterial cell division protein FtsZ.	(Boberek *et al*., 2010)
25.	solasodine-3-*O*-β-D-glucopyranoside	*Solanum nigrum* L.	Destruction of bacterial membrane.	(Chang *et al*., 2017)
26.	Tomatidine	*Solanaceae* (Tomato)	Bacterial ATP Synthase as the cellular target. (ATP synthase inhibitor).	(Ruiz-Rubio *et al*., 2001)
27.	Allicin (diallylthiosulfinate)	*Allium sativum* (Garlic)	Sulfhydryl-dependent enzyme inhibitor, DNA and protein synthesis inhibitor	(Reiter *et al*., 2017)
28	Resveratrol	waste skins and seeds of Pinot noir grapes	Efflux pump inhibitor.	(Klanènik *et al*., 2017)
29.	3-*p-trans*-coumaroyl-2-hydroxyquinic acid(CHQA),	*Cedrus deodara*	CHQA damaged the cytoplasmic membrane of *S. aureus*, causing a significant membrane hyperpolarization with a loss of membrane integrity.	(Wu *et al*., 2016)
30.	Sophoraflavanone B	*Desmodiumcaudatum*	ATPase inhibitors, Direct interaction with peptidoglycan.	(Mun *et al*., 2014; Sasaki *et al*., 2012)
31.	Artocarpin	leaves of *Artocarpus anisophyllus*	Inhibition of bacterial enzymes (such as tyrosyltRNA synthetase).	(Jamil *et al.,* 2014)
32.	Artonin I	*MorusmesozygiaStapf*	Inhibition of the bacterial efflux pump and increase in the susceptibility of existing antibiotics (by inducing depolarization of the cell membrane).	(Farooq *et al*., 2014)
33.	Diosmetin and Alpinumisoflavone	*Sophora moorcroftiana*	Inhibition of the NorA efflux protein.	(Wang *et al*., 2014)
34.	Kaempferol 3-rutinoside	*Sophora japonica* (flowers)	Inhibition of the action of sortase A that plays a key role in the adhesion to and invasion of hosts by Grampositive bacteria	(Yang *et al*., 2015)
35.	6, 8 -diprenyleriodictyol	*Dorstenia*	Deactivated *S. aureus* via depolarization of membrane and inhibition of DNA, RNA, and protein synthesis. This compound rapidly reduced the bacterial cell density and caused lysis of *S. aureus.*	(Dzoyem *et al*., 2013)
36.	licochalcone A	*Licorice*	Inhibitory activity of bacterial infection by decreasing expression of bacterial genes, inhibiting bacterial growth, and reducing the production of bacterial toxin	(Wang *et al*., 2015)
37.	licochalcone E	*Licorice*		
38.	2′,4′,4-trihydroxy-3,6′--dimethoxychalchone	Piper delineatum	Inhibitory effect on biofilm formation, without inhibition of bacterial growth	(Martín-Rodríguez *et al*., 2015)

Table 1. *Continued ...*

Sr. No.	Name of antimicrobial compound	Source of isolation	Mode of action	Reference
39.	Hyperenone A	*Hypericum acmosepalum*	Inhibited the ATP-dependent MurE ligase of *M. tuberculosis*, a crucial enzyme in the cytoplasmic steps of peptidoglycan biosynthesis.	(Osman *et al*., 2012)
40	Catechins	Tea plant *Cameliasinensis*	Inactivation of specific bacterial enzymes	(Betts *et al*., 2011)

2006; Singh, 2019; Yother, 2011).

Understanding the need and scope of identifying potential antimicrobial compounds this paper has reviewed and compiled different antimicrobial compounds isolated from endophytes, algae and plants in Table 1. The table includes information about Antimicrobial compound name, its source, mode of action and its reference.

CONCLUSION

Over usage of antibiotics has caused the evolution of antibiotic resistant microbes. An antibiotic resistance among the pathogenic microbes is because of transfer of genes. Due to which, the available antibiotics have rendered futile and hence it is becoming difficult for us to treat them. Moreover, the treatment of such resistant pathogens is very costly. In this situation, the best possible solution seems to be the secondary metabolite from plants, algae and endophyte. This review brings light on many hidden such potential antimicrobial compounds, which could be further used to make antimicrobial drugs. This could help us to fight with Antibiotic resistant microbes.

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Conflict of interest

The authors have no conflicts of interest to declare.

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