

Azaphilones: Their Role in Various Biological Activities

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Abstract

Azaphilones which can be isolated from various natural resources like fungi and plant have range of potent biological activities that can be exploited against various diseases. Structure of numerous azaphilones has already been described. The present review talks about activities of azaphilones like anti-cancerous, anti-HIV, anti-nematicidal, anti-bacterial, anti-fungal which have been extensively explored and efforts are going on to use azaphilones in drug formulation. This review is an effort to shift focus from complex synthetic products to natural products which are known to have less toxicity and have less side effect for the treatment of various diseases.

Keywords: Fungi; *Penicillium*; Immunosuppression; Antifungal; Natural Products.

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Introduction

Natural products, produced by sources present in nature like plants, fungi, algae etc., have been used to cure diseases from the ancient time. In ancient literature like that of Charka and various other literature available one can easily find how extracts from leaves, seeds and various other parts of the plant were utilized to treat various diseases and for healing of the wounds. Early ayurvedic practices and even today these natural products either in extracted or as in some cases whole plant or leaves are applied to the wounds. These natural products, even in today's world are contributing a lot for fight against diseases. Traditionally natural products have been employed for discovery of drugs and laid the foundation of early medicines but unfortunately with advent of new technologies and procedure for drug discovery like rational drug designing, crystallography, NMR's results into the shifting of focus from natural products. Despite of all of these discoveries there is still a shortage of medicines in the field like oncology, immunosuppression and various metabolic diseases where natural products can play a vital role.

Fungi which have been considered as a potent source of various biologically active compounds and have been used to produce some valuable compounds that are still the active component of lots of medicines. Various different chemical compounds have been identified in fungi these include organic acids, polyynes, polyketides, polysaccharides etc.

The role of fungi in producing biological active compounds have been widely spread and is known to be used in medicinal purposes in Africa and Asia [1,2]. Our knowledge for fungi is very limited as of about 1.5 million species of fungi we know only about 7% of the total population and out of 7% of the population very few of these species have been cultivated and screened for drug production. The contribution of fungi is extraordinarily in managing human and animal diseases. Fungi are being explored for secondary metabolites for clinical applications and compounds extracted through them are active

ingredients of modern drugs including antifungal agents and stains. Due to their wide spread uses many publications have focused on novel active compounds [3-6].

One such interesting set of secondary metabolites is azaphilones. Azaphilones are natural products belong to structurally diverse family having an oxygenated bicyclic core and quaternary center. They possess large groups of pyrano-quinone and have chromophoric properties. Their colour depends upon their chemical structure and they got their name from the reaction with ammonia which led to the formation of gamma pyradone derivatives. To classify as azaphilone both pyrone-quinone structure and quaternary center is necessary. For most of azaphilones their absorption spectrum lies within the visible range. They have been identified in various filamentous fungi well known producers of these compounds include the genera *Monascus*, *Penicillium* and *Chaetomium*. They are also identified in *Aspergillus*, *Cochliobolus lunata* and *Emericella falconensis*.

Many secondary metabolites are being produced by fungi and which sorts out the fungi into different groups on the basis of the secondary metabolites and different chemicals produced. Some of the secondary metabolites follow certain combinatorial chemistry and are synthesized by combination of biosynthetic pathways. Genes involved in the production of enzymes of secondary metabolites are nucleic acids to form red or purple vinyllogous c-pyridones due to the exchange of pyrane oxygen for nitrogen [7-9]. This appears to be a characteristic reaction. It can take place both with ammonia alone as found in the case of monascorubramine and rubropunctamine [10,11] and the side chain of a macrocyclic polypeptide as discovered for chlorofusin [12,13]. They possess large groups of pyrano-quinone and have chromophoric properties. Their colour depends upon the chemical pyradone derivatives. To classify azaphilones both pyrone-quinone structure and quaternary center is necessary. For most of azaphilones their absorption spectrum lies within the visible range. They have been identified in various filamentous fungi

(*Manascus*, *Penicillium* and *Chaetomium*). They are also identified in *Aspergillus*, *Colchlioboluslumata* and *Emericellaalcalconensis*.

It is necessary, however, to note that azaphilones are not the only structural class reacting with primary amines. Thus, fluorones isolated from *Echinodontumtinctorium* and *Pyroformesalbomarginatus* also change their colour on exposure to ammonia [14]. However, they are not azaphilones and should not be mistakenly included in the azaphilone class. Azaphilones exhibit a wide range of interesting biological activities, such as anticancerous, antimicrobial, inhibitory effects on HIV-1 replication and gp120-CD4 activity, antifungal, nematicidal and anti-inflammatory activities. Several secondary metabolites from microbial origin inhibit 15-lipoxygenase (15-LOX) [15,16]. More recently the fungal pigment, (+)-sclerotiorin [1], was found to inhibit lipoxygenase-1, also known as 15-LOX [17]. Geumsanols were isolated from *Penicillium* sp. KCB11A109, a fungus derived from ginseng field. The isolates were evaluated for their anti-cancer, anti-bacterial, anti-malarial activities in zebrafish development [18]. Endophytic fungus *Colletotrichum* sp. secondary metabolites showed anti-bacterial activities against two commonly dispersed environmental strains of *Escherichia coli* and *Bacillus subtilis*, as well as against two human pathogenic clinical strains of *Staphylococcus aureus* and *Pseudomonas aeruginosa* [19]. The potent nonselective biological activities of azaphilones may be related to their production of vinylogousc-pyridones [20]. Azaphilones were also found to be a new class of heat shock protein Hsp90 inhibitors [21]. Recently, It has been reported that azaphilones inhibit tau aggregation and dissolve tau aggregates [22]. *A. nidulans* secondary metabolites were tested for their ability to inhibit tau aggregation in vitro and it was found that several were active inhibitors at micromolar concentrations, although they did not have tau disaggregation properties [23].

Materials and Methods

PUBMED database, MEDLINE database, Google Scholar and other online journals such as Journal of Natural Products, Mycological Research and others were searched with no date restrictions for published articles using keywords azaphilones, secondary metabolite, and natural products. Some additional articles of interest were selected from reference lists of included articles. Only those articles were eligible to be included which showed azaphilones having numerous biological activities and can be isolated from natural resources like plant and fungi. Screening of the literature was also done on the same basis. Literature search began in January 2013 and ended in January 2016. The prime focus of the literature search was to screen the literature on the basis of eligibility criteria. Publications only in English were used and there was not any limitation on date of publication. Data extraction was based on which secondary metabolite can be isolated from natural resources and further incorporated into drug formulation. If many separate studies were present with similar conclusions, then only those were selected to be included which were most

relevant to the objectives of the study and research question. No unpublished study was used or included (Tables 1 and 2).

Table 1. Azaphilones showing anti- cancerous activity.

Azaphilones	Species	Activity	Reference
Chaetomugilin	<i>C. globosum</i>	Growth inhibition of P388, HL-60, L1210, and KB lines; selective cytotoxic activity against 39 human cancer cell lines.	[24]
Harziphilon	<i>Trichodermaharzianum</i>	Cytotoxicity against the murine tumour cell line M-109; inhibitor of Rev-protein to RRE RNA binding.	[25]
Sclerotiorin	<i>P. multicolor F1753</i> <i>P. sclerotiorum X11853</i> <i>P. frequentans</i> <i>P. hiramayae</i> <i>Udagawa</i>	Inhibits binding between Grb2-SH2 domain and phosphopeptide derived from the Shc protein; aldose reductase inhibitor; antibacterial activity against <i>Bacillus</i> spp.; chlamyospore-like cell-inducing agent; Endothelin receptors binding agent	[26-29]
Chaetogloblins A and B	<i>C. globosum</i>	Antitumor activity in cell line MCF-7 and colon cancer cell line SW1116	[30]
Chaetomugilins A and B	<i>C. globosum</i>	Antifungal agent; cytotoxic activity against cultured P388 leukemia cells and HL-60 cells; selective cytotoxicity activity against 39 human cancer cell line	[31-33]
Chaetomugilin C	<i>C. globosum</i>	Cytotoxic activity against cultured P388 cells and HL-60 cells	[24,31,34]
Chaetomugilin F	<i>C. globosum</i>	Selective cytotoxicity activity against 39 human cancer cell lines	[31,32,34]

Seco-chaetomugilins A and D	<i>C. globosum</i>	Seco-chaetomugilin [34] A is not active; Seco-chaetomugilin D: growth inhibitory activity against cultured murine P388 leukemia cell lines P388 and L1210; the human leukemia cell line HL-60 and KB epidermoid carcinoma
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Role of Azaphilones in anticancer activity

Sclerotiorin and azaphilone was found to be potent anti-proliferative against different cancer cells and found to be involved in different pathways. It activates BAX which induces apoptosis in colon cancer (HCT-116) and it involved in the down regulation of BCL-2, and which leads to the activated cleaved caspase-3 causing apoptosis of cancer cells. Enzyme K-Ras is activated in many colon cancers. The enzyme Ras protein farnesyltransferase (PFTase), which catalyze the initial step of RAS signalling, has been reviewed as a potential target for cancer therapy [35]. Sclerotiorin have been identified to exhibit PFTase inhibitory activity. Its role in RAS inhibitor in time and dose dependent caspase mediated apoptosis in cells has been reported earlier [36]. Screening for anticancer activity was done with cell proliferation assay and LDH release assay. Sclerotiorin showed IC₅₀ in the range of 0.63 to 2.1 μ M in different cancer cell lines viz. ACHN, Panc-1, Calu-1, HCT-116 having IC₅₀ of 0.63 \pm 0.08, and H460 along with the normal breast epithelial cell (MCF10A) having IC₅₀ of >10 μ M [26]. Seco-chaetomugilin D exhibited significant cytotoxic activity against the murine P388 leukemia cell line, the human HL-60 leukemia cell line, the murine L1210 leukemia cell line, and the human KB epidermoid carcinoma cell line [37]. Harzophilone demonstrated cytotoxicity at 38 μ M against the murine tumor cell. Chaetomugilins are similar to some of azaphilones, the compound which shows significant cytotoxic activity against P388 and HL-60 cell lines have the double bond between C-2 and C-3 intetracyclic ring systems [38].

Table 2. Azaphilones showing inhibitory effects on HIV-1 replication and gp120-CD4 activity.

Azaphilones	Species	Activity	Reference
Helotialins A and B	Unidentified species Of Helotiales.	inhibitory effects on HIV-1 replication in C8166 cells	[39]
Isochromophilone II	<i>P. multicolor</i> FO-2338	gp120-CD4 binding inhibitor	[30,40]
Isochromophilone III	<i>P. multicolor</i> FO-2338	gp120-CD4 binding inhibitor	[28,30,41]
Isochromophilone IV	<i>P. multicolor</i> FO-2338	gp120-CD4 binding inhibitor; Acyl-CoA	[28,30,41]

	<i>P. multicolor</i> F1753	inhibitor	
Isochromophilone V	<i>P. multicolor</i> FO-2338	gp120-CD4 binding inhibitor	[30,41]
Isochromophilone VI	<i>P. multicolor</i> FO-2338 <i>P. multicolor</i> F1753	gp120-CD4 binding inhibitor; Acyl-CoA inhibitor	[30,41]
Luteusin A	<i>P. multicolor</i> FO-2338 <i>P. sclerotiorum</i> X11853 <i>P. vonarxii</i> <i>T. luteus</i>	gp120-CD4 binding inhibitor; MAO inhibitor <i>in vitro</i> ; Endothelin receptors binding agent	[8,24,27,30,42,43]
Phomoeuphorbins A and B	<i>Phomopsis</i> <i>Euphorbiae</i>	Phomoeuphorbin A: Inhibitor of HIV replication in C8166 cells <i>in vitro</i> ; Phomoeuphorbin B is not active	[44]
Phomoeuphorbins C and D	<i>Phomopsis</i> <i>Euphorbiae</i>	Phomoeuphorbin C: Inhibitor of HIV replication in C8166 cells <i>in vitro</i> ; Phomoeuphorbin D is not active	[44]
Bromochrephilone	<i>P. multicolor</i> FO-2338	gp120-CD4 binding inhibitor	[30]
Fleephilone	<i>T. harzianum</i>	HIV REV/RRE binding inhibitor	[26]
Isochromophilone I	<i>P. multicolor</i> FO-2338	gp120-CD4 binding inhibitor	[28,30,40]
(+)-Isorotiorin (5-chloroisorotiorin)	<i>P. multicolor</i> <i>P. sclerotiorum</i> X11853	gp120-CD4 binding inhibitor; Endothelin receptors binding agent	[27,30]
Ochrephilone	<i>P. multicolor</i> FO-2338 <i>P. sclerotiorum</i> X11853	gp120-CD4 binding inhibitor; Endothelin receptors binding agent	[28, 27,30,45]
(-)-Rotiorin	<i>C. cupreum</i> CC3003	Antifungal activity against <i>C. albicans</i> ; CETP inhibitor <i>in vitro</i> ; gp120-CD4 binding inhibitor; (+)-Rotiorin is not active	[30,46]
Rubrorotiorin	<i>C. cupreum</i> CC3003 <i>P. hirayamae</i> <i>Udagawa</i> <i>P. multicolor</i> FO-2338	Antifungal activity against <i>C. albicans</i> ; CETP inhibitor <i>in vitro</i> ; gp120-CD4 binding inhibitor	[28,30,46-48]

Tetrahydroisochromophilone	<i>P. multicolor</i> FO-2338	gp120-CD4 binding inhibitor	[30]
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It has been reported that Isochromophilone I and Isochromophilone II isolated from *Penicillium multicolor* FO-2338 showed inhibitory activity against gp120-CD4 binding. Though the strain FO-3216 also produced Isochromophilone I and II with Isochromophilone III & VI, the inhibitory activity of Isochromophilone III & VI against gp120-CD4 binding was weaker than that of Isochromophilone I and II [20]. The novel 5-bromo-derivative 9, showed the most potent inhibition with an IC₅₀ value of 2.5 μ M [30] (Tables 3 and 4).

Table 3. Inhibitory activities of azaphilones against gp120-CD4 binding [30].

Inhibitor	IC ₅₀ μ M
Isochromophilone I	6.6
Isochromophilone II	3.9
Ochriphilone	114
Sclerotiorin	>250
Rubrorotiorin	>240
Dechloroisochromophilone	>300
Isotiorin	>260
5- Bromoochriphilone 9	2.5
Rotiorin	>240

Table 5. Azaphilones showing Anti-inflammatory.

Azaphilones	Species	Activity	Reference
Falconensins A, B, C and D	<i>Emericella falconensis</i>	Anti-inflammatory activity induced by TPA (12 Otetradecanoylphorbol-13-acetate)	[49,50]
Falconensin E	<i>E. falconensis</i>	Anti-inflammatory activity induced by TPA	[49,50]
Falconensins F and G	<i>E. falconensis</i>	Anti-inflammatory activity induced by TPA	[49,50]
Falconensin H	<i>E. falconensis</i>	Anti-inflammatory activity induced by TPA	[49,50]
Falconensins I and J	<i>E. falconensis</i> <i>E. fruticulosa</i>	Anti-inflammatory activity induced by TPA	[50,51]

Luteusin	9.4
Isochromophilone III	14.6
Isochromophilone IV	48
Isochromophilone V	96
Chaetoviridin A	>230
Chaetoviridin B	140
Lunatoic acid	>260

Azaphilones showing Anti-HIV activity

Phomoeuphorbin A and Phomoeuphorbin C isolated from cultures of *Phomopsis euphorbiae*, an endophytic fungus isolated from *Trewia nudiflora* were tested for in vitro inhibitory effects against HIV replication in C8166 cells. Phomoeuphorbin A and Phomoeuphorbin C both exerted minimal cytotoxicity against C8166 cells (CC₅₀>200 μ g/mL) and each showed anti-HIV activity with EC₅₀=79 μ g/mL and 71 μ g/mL [44] (Tables 4 and 5).

Table 4. Anti-HIV activities of Phomoeuphorbins A and Phomoeuphorbins C

	EC ₅₀ (μ g/ml)	CC ₅₀ (μ g/ml)	TI
Phomoeuphorbins A	79	>200	>2.5
Phomoeuphorbins C	71	>200	>2.8

Chaetoviridin A	<i>C. globosum</i> var. <i>flavo-viridae</i> <i>P. multicolor</i> FO-2338	Antifungal agent; inhibitor of cholesteryl ester transfer protein (CETP) in vitro; antiinflammatory Activity	[28,27,48,52]
Monascin	<i>M. pilosus</i>	Food dye; anti-inflammatory activity (TPA-induced); inhibitory effects on NOR 1 activation; Epstein-Barr virus early antigen activator	[10,11]
Monascorubramine	<i>M. pilosus</i>	Anti-inflammatory activity (TPAinduced); inhibitory effects on NOR 1 activation; Epstein- Barr virus early antigen activator	[10,11]
Monascorubrin	<i>Monascus</i> sp.	Food dye; antiinflammatory Activity (TPA-induced); inhibitory effects on NOR 1 activation; Epstein-Barr virus early antigen activator	[10,11,34,53]
Rubropunctamine and Rubropunctatin	<i>M. pilosus</i>	Anti-inflammatory activity (TPAinduced); inhibitory effects on NOR 1 activation; Epstein- Barr virus early antigen activator	[11]

Role of Azaphilones (Harziphilone and Fleephilone) as two new HIV REV/ RRE binding inhibitors produced by Trichodermaharzianum

Table 6. 12-O-tetradecanoylphorbol-13-acetate (TPA) induced inflammatory ear edema in mice with ID50 values and confidence intervals [50].

Compounds	ID50		
	µG/ear	µM/ear	95% confidence interval
FalconensinA	526	1.09	0.679-1.75
FalconensinB	721	1.49	1.12-1.98
FalconensinC	641	1.22	0.923-1.75
FalconensinD	506	0.962	0.789-1.17
FalconensinE	167	0.373	0.248-0.560
FalconensinF	509	1.23	1.11-1.37
FalconensinG	927	2.03	1.41-2.94
FalconensinH	677	1.46	1.00-2.13
FalconensinI	315	0.787	0.577-1.07
FalconensinJ	202	0.502	0.326-0.778

FalconensinK	240	0.553	0.447-0.682
FalconensinL	543	1.25	0.860-1.80
FalconensinM	195	0.417	0.318-0.549
FalconensinN	488	1.04	0.817-1.32
Monomethylmitorubirin	>1.000	>2.53	-
Monascorubrin	411	1.07	0.868-1.33
Indomethacin	325	0.908	0.755-1.09
Hydrocortisone	25.1	0.0692	0.0640-0.0753

Azaphilones (Falconensins) showing inhibitory effects on 12-O-tetradecanoylphorbol-13-acetate-induced inflammatory ear edema in mice

Falconensin have found to be having anti-inflammatory activity induced by TPA. Falconensins anti-inflammatory activity was tested using 12-O-tetradecanoylphorbol-13-acetate (TPA) induced inflammatory ear edema in mice. Their ID50 value of 526 µg/ear and 1.09 µmol/ear is a clear indication of

its effectiveness as an anti-inflammatory agent [50] (Tables 6 and 7).

Table 7. Azaphilones showing Nematicidal activity.

Azaphilones	Species	Activity	Reference
Pseudohalonestrin A	<i>Pseudohalonestria Adversaria</i>	Nematicidal activity against the pine wood nematode <i>Bursaphelenchus xylophilus</i>	[54]
Pseudohalonestrin B	<i>P. adversaria</i> <i>YMF1.01019</i>	Nematicidal activity against the pine wood nematode <i>B.xylophilus</i>	[54]
(-)-Mitorubrin	<i>E. cinnabarina</i> <i>H. aucklandiae</i> <i>H. croceoplum</i> <i>H. dingleyae</i>	Nematicidal activity against <i>Caenorhabditis elegans</i> ; antimicrobial	[55-57]
(-)-Mitorubrinol	<i>T. austrocalifornicus</i> <i>T. convolutes</i>	Nematicidal activity against <i>C. elegans</i> ; antimicrobial activity against <i>B. subtilis</i> , <i>Y. lipolytica</i> ; antifungal agent	[57]
Mitorubrinic acid	<i>H. fragiforme</i> <i>P. rubrum</i> <i>P. funiculosum</i> <i>P. porrecta</i> <i>Pyrenomyxa invocans</i> <i>T. austrocalifornicus</i> <i>T. convolutes</i> <i>T. flavus</i> <i>T. macrosporus</i> <i>T. mimosinus</i> <i>T. udagawae</i> <i>T. wortmannii</i>	Trypsin inhibitor; nematocidal activity against <i>C. elegans</i> ; antimicrobial activity against <i>B. subtilis</i> , <i>Y. lipolytica</i> ; antifungal agent; inhibits NO production in RAW 264.7 cells; chlamydospore-like cell-inducing agent	[27,57,58-62]
Mitorubrinol	<i>E. cinnabarina</i> <i>H. aucklandiae</i> <i>H. croceoplum</i> <i>H. dingleyae</i> <i>H. fedleri</i> <i>H. fragiforme</i> <i>H. haematostroma</i> <i>H. howeianum</i> <i>H. julianii</i> <i>H. laschii</i> <i>H. rutilum</i> <i>H. subcroceoplum</i> <i>H. subgilvum</i> <i>H. subticinese</i>	Nematicidal activity against <i>C. elegans</i> ; antimicrobial activity against <i>B. subtilis</i> , <i>Y. lipolytica</i> ; antifungal agent; inhibits NO production in RAW 264.7 cells	[8,55-58,62-64]

H. ticiense
P. funiculosum
P. rubrum
P. vermiculatum
P. wortmannii
P. invocans
T. wortmannii

Bulgaria lactones A and B	<i>Bulgaria inquinans</i>	Antimicrobial activity against <i>B. brevis</i> , <i>B. subtilis</i> and <i>Micrococcus luteus</i> ; cytotoxic agent; nematicidal agent; inhibitor of 3H-SCH 23390 binding to the dopamine D1 receptor	[7]
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Two new azaphilones metabolites, named Pseudohalonestrin A (1) and B (2), were isolated from the culture of the aquatic fungus *Pseudohalonestria adversaria* YMF1.01019, originally separated from submerged wood in Yunnan Province, China. The nematicidal activity of pseudohalonestrin A and B was measured and the results revealed that of pseudohalonestrin A and B displayed moderate nematicidal activity against *B. xylophilus* [55] (Table 8).

Table 8. Azaphilones showing antibacterial activity.

Azaphilones	Species	Activity	Reference
RP 1551-2	<i>Penicillium SPC-21609</i> sp.	Inhibitor of platelet derived growth factor (PDGF) binding to its receptor; antibacterial activity against <i>Bacillus subtilis</i> , <i>Enterococcus faecium</i> , <i>Staphylococcus aureus</i>	[65]
RP 1551-M2	<i>Penicillium SPC-21609</i> sp.	Inhibitor of (PDGF) binding to its receptor; antibacterial against <i>B. subtilis</i> , <i>E. faecium</i> , <i>S. aureus</i>	[65]
Sassafrin D	<i>Creosphaeria sassafras</i>		[65]
Deflectins 1a, 1c and A (1b)	<i>A. deflectus</i>	Deflectins 1a and 1c are not active; Deflectin A 1(b): Antibacterial and weak antifungal agent; cytotoxic	[66]

			activity against Ehrlich carcinoma cells of mice; lytic activity towards bacteria and erythrocytes	
Deflectins B (2a) and 2b	<i>A. deflectus</i>		Antibacterial and weak antifungal agent; cytotoxic activity against Ehrlich carcinoma cells of mice; lytic activity towards bacteria and erythrocytes; Deflectin 2b is not active	[66]
RP 1551-1, RP 1551-6 and RP 1551-M1	<i>Penicillium SPC-21609</i>	sp.	Antibacterial activity against <i>B. subtilis</i> , <i>E. faecium</i> , <i>S. aureus</i>	[66]
RP 1551-3 and RP 1551-4	<i>Penicillium SPC-21609</i>	sp.	Antibacterial activity against <i>B. subtilis</i> , <i>E. faecium</i> , <i>S. aureus</i>	[66]
RP 1551-5	<i>Penicillium SPC-21609</i>	sp.	Antibacterial activity against <i>B. subtilis</i> , <i>E. faecium</i> , <i>S. aureus</i>	[66]

Azaphilones anti-microbial activity

The antimicrobial activity of RP-1551-1, RP-1551-6, RP-1551-M1, RP-1551-3, RP-1551-4, RP-1551-5 was measured and the results revealed that they showed weak anti-microbial activity against activity *Bacillus subtilis*, *Enterococcus faecium*, and *Staphylococcus aureus* [66]. The two major components were used Deflectins A (1b) and B (2a), for the evaluation of the biological activities of the Deflectins. Both compounds showed antibacterial and weak antifungal activity with minimum inhibitory concentrations (MIC) ranging from less than 1 µg/ml to 150 µg/ml, depending on the medium. In synthetic media the MIC's were 20~100 fold lower than in complex media. *Bacillus brevis* and *B. subtilis* were the most sensitive organisms. Deflectin B was slightly more active than Deflectin A. Besides the inhibitory effects on the growth of bacteria and fungi, these compounds showed lytic activity towards bacteria and erythrocytes and cytotoxic activity towards cells of the ascitic form of Ehrlich carcinoma of mice.

Conclusion

Fungi have been used for medical purposes for a long time. Fungal kingdom appears to be very rich and diverse in area of secondary metabolites. Fungi have evolved its secondary metabolic pathways in such a way producing various compounds having diverse array of biological activities. The chemical composition and biochemical activity of many fungi

has not been yet studied in detail. Identification of novel herbal compounds and further to explore its wide range potential secondary metabolite has become a trend in the last decade. Speaking of that, more and more novel azaphilones are being identified and is being used in drug formulation. Azaphilones has shown a wide spectrum of biological activities against various target organisms, including bacteria, fungi, and nematodes including the anti-cancerous and anti-HIV activity, lipogenase activity and recently it has been reported that reported that azaphilones inhibit tau aggregation and dissolve tau aggregates. Concerning the pharmaceutical science, finding new secondary metabolites enriches the possibilities of new drug discovery.

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