A Review on Bioactive/Phytoconstituent Molecules Reported in Oman

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Abstract: **Bioactive molecules have been documented since ages in providing medicinal benefits towards various ailments. Recent advances in biotechnological methods have expanded the use of naturally derived bioactive molecules in diverse applications apart from pharma. The demand of better and more potent molecules require continuous exploration of biota from different parts of the world. The environmental conditions do have an impact on not only the quantity but also the potency of bioactive molecules. Arid regions have a peculiar environment where plants need a more robust self-defense system for survival. Such regions hold a promising array of bioactive molecules. There have been reports of some very interesting bioactive molecules from the Middle East. Oman is one such country that harbors huge unexplored species of flora and fauna. The country is abundantly rich in the marine, plant, microbial and animal ecosystems, with over 250 species of medicinal plants. This review provides collective information of the bioactive/phytoconstituent molecules reported so far in Oman from the plants, marine and other plant associated sources.**

I. INTRODUCTION

Bioactive compounds are generally regarded as plant derived secondary metabolites having pharmacological effect on human system [1]. Owing to the ever growing demand of replacing chemicals,bioactive compounds are finding extensive applications in wide areas such as food industry, dietary supplements, cosmetics, pharmaceuticals, agrochemicals and so on. It is a well-established fact that typically medicinal plants or toxic plants produce bioactive molecules that are more potent and have the potential to replace a chemical in any process as mentioned above. To add on to this, plants when subjected to harsh environmental conditions produce more bioactive quantitatively as a tool for survival [2]. Thus, perhaps, plants growing in arid regions have plethora of bioactive molecules that need to be explored more extensively. This thought leads to a need of summarizing the bioactive molecules discovered or reported in plants growing in arid environments. In this review, a collective and comprehensive report of bioactive molecules reported in Oman is presented. The bioactive/phytoconstituents molecules from plant, marine and endophytic sources are listed.

II. BIOACTIVE COMPOUNDS FOUND IN OMAN

The bioactive molecules reported so far in Oman have been categorized in three groups-terrestrial, marine and plant associated microbes [endophytes].

A. Bioactive compounds reported from terrestrial sources

There have been several plants in Oman reported to have secondary metabolites such as phenolics, flavanoids, alkaloids, essential oils etc. These compounds have been extracted using solventextraction methods where a high polarity solvent such as methanol is used [3], [4] and [5]. The extracts mostly constitute of water soluble flavonoids and alkaloids. When the polarity of solvent was reduced using chloroform, hexane, ethyl acetate, butanol etc. it was found that more alkaloids and terpenoids could also be separated. The phytochemical extraction offlavonoids/alkaloids from the leaves of two plants *Rhamnuscathartica*and *Lawsoniainermis* was done using two solvents in two different methods. Soxhalation using petroleum ether and maceration using hexane showed an entirely different profile of the molecules obtained [6]. The extraction method definitely results in difference of secondary metabolites found in a particular source. Hence, important plants which are a source of real potential candidate that can be effectively used in an application should be screened for bioactive components using more than one solvent profile or extraction methods.

Many of the bioactive/phytoconstituent components reported in Oman have been studied for their anti-inflammatory, antioxidant and/or analgesic effects. *Ochradenusarabicus* is of particular interest since it has been shown to possess varied activities. The plant belonging to the species *arabicus* is endemic to Oman and is widely used in traditional medicine [7]. The extract of whole plant was found to exhibit anticancer properties against four cancer cell lines colorectal adenocarcinoma [HT29], colorectal adenocarcinoma [HCT116]; breast cancer cell line [MCF-7] and Human hepatoma derived cell line [HepG2]. Apart from exhibiting antioxidant activity, the extract also showed antifungal activities against several pathogenic fungi. Most interestingly, the aqueous extract showed allelopathic effects, which could potentially lead to a molecule that can be used as an agrichemical [7]. Recent HPLC purifications done on the aerial parts of plant resulted in separation a new cyclopropyltriterpenoid. The structure of compound 1 was assigned as (3b,13a)13,27-cyclours-21-ene-3,20-diol as determined by NMR [8].

Acridocarpusorientalis, a flowering plant found in Oman is traditionally used in inflammatory diseases. Two bioactive

compounds morin[I] and morin-3-O-β-D-glucopyranoside[II] were isolated from the plant. Compound II possessed significant anti-cancer activity towards human hepatoma[HepG2] and colorectal adenocarcinoma [HCT116] derived cell lines. Both the compounds also exhibited antifungal activities against plant pathogenic fungi [9].

Anogeissusdhofarica,is a species endemic to the dhofar region of Oman. Conventionally it is used for wound healing and for antiseptic purposes. The extracts of the plant reported to have tannins and elagic acid were found to have anti-microbial activity for *Pseudomonas aeruginosa*, *Staphylococcus aureus*and *Candida albicans.* Interestingly, the extracts were also found to possess a strong anti-oxidant activity [10].

Another species belonging to the dhofar region of Oman *Boswelliasarca*was studied. The methanol extract of frankincense when subjected to fractionation using polar, medium polar and non-polar solvents resulted in two fractions. The first fraction was found to have anti-inflammatory activity while the second fraction had analgesic and anti-inflammatory properties [11]. Traditionally the aqueous extracts of frankincense from *B. sarca*has been used to treat inflammatory disorders and for pain relieving. Further investigation of the fractions obtained can reveal the composition of extracts and structures of the compounds.

These few examples listed above demonstrate the potential hidden in this region of Middle East and the need to explore more from various resources in Oman.

TABLE I

BIOACTIVE/PHYTOCONSTITUENT MOLECULES REPORTED in PLANTS

Plant	Part of the plant	Bioactive/Phyto constituent compound	Extraction method	Potential use	Reference
Zizyphusspina-christi	Seeds and Fruits	Tannins, alkaloids, flavonoids, cardiac glycosides	Alcoholic extract	Anti- inflammatory	3
*Trigonellafoenumgraecum*L	Seeds	Tannins, flavonoids, oxalates, saponins	Alcoholic extract	Antioxidant	4
Punicagranatum L.	Peels	Phenolics, flavonoids, 61 different polyphenols	Alcoholic extract	Antioxidant particularly neuroprotective	5
Rhamnuscathartica	leaves	Alkaloid, flavonoid, resin	Maceration using hexane	Antioxidant	6
Lawsoniainermis	leaves	Steroids	Soxhalation using petroleum ether	Wound healing, cosmetics	
Ochradenusarabicus	Whole plant	Cyclopropyltriterpenoid[3b,13a] 13,27-cyclours-21-ene-3,20-diol	Ethyl acetate, methanol, chloroform, butanol, hexane, water	Allelopathic, antioxidant, antimicrobial, anticancer	8
Acridocarpusorientalis	Leaves and stem	morin[I] and morin-3-O-β-D-glucopyranoside[II]	Methanol followed by hexane, chloroform, ethyl acetate, butanol	Antifungal, phytotoxic, anticancer, anti- lipid peroxidation	9
Anogeissusdhofarica	Leaves and stem bark	Tannins, ellagic acid	Alcoholic extract	Antimicrobial, antioxidant, cytotoxic	10
Boswellia sacra	Resin	Terpenoids	Methanol followed by hexane	Analgesic	11
Neem	Leaves	Terpenoids, alkaloids, phenolics	Chloroform, butanol, ethyl acetate, hexane, methanol	Antioxidant	12
*Menthapiperita*L	Whole plant	Phytoanticipins	Hexane, chloroform, ethyl acetate, butanol	Medicinal drugs	13
*Phoenix dactylifera*L.	Fruit	Phenolics and flavonoids	Methanol water	Antioxidant	14
Lactuca sativa L.	Leaves	Monoterpenes, sesquiterpenes	Dichloromethane	Antioxidant, antifungal	15
Juniperus excels	Whole plant	Terpenes	Solvent free microwave	Medicinal drugs	16
Helianthemumlippii	Whole plant	Terpenes	Solvent free microwave		
Lawsoniainermis	leaves	Phenols, carboxylic acid	Maceration using hexane		
Medicago sativa linn	leaves	Phenolics, flavonoids	Alcohol extract	Antioxidant	17

It is evident from the table that most of the bioactive/phytoconstituent molecules have been extracted using similar methods. The flavonoids and phenolic are shown to exhibit anti-inflammatory properties, while the essential oils exhibit analgesic properties.

The data presented leads to a detailed physiologic role of the said molecule and a structural study of the same in future studies. The data also shows a lack of applications of the bioactive molecules in fields other than medicine, for example, agrochemicals etc.

B. Bioactive compounds reported from marine sources

Fisheries are the second main revenue source for Oman after oil and gas. However, the other marine resources are not yet tapped to a large extent. A survey between Oman and Norway shows how the latter has expanded its marine potential through areas like aquaculture, animal feed, human health care, polymers, enzymes and drug development [18]. Compared to the neighboring countries in the Arabian Peninsula, Oman has the longest coastal habitats along the Arabian Sea, the Gulf of Oman, and the Arabian Gulf. Oman contributes a rich environment to marine biodiversity; one example is Ras Al-Hadd, one of the largest nesting beaches for marine turtles around the world. Oman provides a perfect zone for an extensive investigation of the marine flora and fauna.

There is a huge potential in marine biotechnology given the plethora of its flora and fauna. However, the difficulties in the collection of marine samples and the difficulties in culturing marine microorganisms may underlie the main reasons for the slow progress in this field. However, recent advances in technologiesto i] isolate and maintain less-culturable marine microbes, ii] to bypass culture-dependent issues through development in the field of metagenomics, and iii] to isolate and characterize secondary metabolites using new robust technologies may promote faster progress [19].
The bioactive/phytoconstituent molecules reported so far in Oman from the marine sources are listed in table 2.

TABLE II

BIOACTIVE/PHYTOCONSTITUENT MOLECULES REPORTED in SEA

Source	Bioactive/phytoconstituentcoumpound	Extraction method	Potential use	Reference
Codiumdwarkense[green alga]	Triterpenoic acid [dwarkenoic acid]	Methanol extract	Anti-diabetic, α-glucosidase inhibitor	[20]
Nizamuddiniazanardinni[brown alga]	Hydroperoxy sterols [24 [R]-hydroperoxy-24-vinyl cholesterol]		Anti-cancer particularly human adenocarcinoma	[21]
Actinomycetes	Extra cellular medium		Anti-bacterial [human pathogens]	[22]
Gracilariafoliifera and *Cladophoropsis* sp. [Algae]	Total extract	Ethanol extract	Anti-cancer	[23]
Holothuriaatra and *Holothuriaedulis*[sea cucumbers]	Total extract	Methanol+Chloroform	Anti-larval	[24]

As shown in table 2, there is limited information about bioactive molecules reported from marine sources in Oman. The two reports of particular interest are from the green and brown algae *Codiumdwarkense* and *Nizamuddiniazanardinni* respectively. The bioactive molecule dwarkenoic acid isolated from *Codiumdwarkense*showed a potential as anti-diabetic candidate molecule. The molecule showed significant inhibition of α-glucosidase activity independent of concentration [20]. The hydroperoxy sterol [HVC] from *Nizamuddiniazanardinni*could be a potential anti-cancer drug molecule. HVC exhibited cytotoxic activity for MCF-7 and HT-29 cell lines. The cytotoxicity of HVC is attributed to its sterol structure and also the peroxygroup [21].

The other source that holds a very promising area is actinomycete. The one reported here in table 2 was isolated from the Lipar area of Oman Sea. Out of the 35 isolated actinomycete strains, 94% showed antibacterial activity. The anti-bacterial activity was attributed to several exogenous enzymes secreted by the actinomycete [22].

C.Bioactive compounds reported from plant associated microbial sources

The innate capability of plants to survive in extreme climates is a coherent action by the plants and the associated microbial population. It has been postulated and investigated that microbial colonies in the rhizosphere and endophytes are primarily responsible for secreting metabolites that are used for self- defense by the plants. Various bioactive compounds having immense utility as bio control agents have been isolated from the rhizosphere [25]. The interesting fact is that the microbial flora associated with plants grown in desert climate is completely different from plants grown in humid climate. Martina *et al* reported gram positive bacteria (*Bacillus* sp.) abundantly existed in plants growing in arid climate whereas, gram negative bacteria (*Pseudomonas* sp.) predominates in plants growing in humid soil [26]. It is an important area that should be explored more in depth. The bioactive molecules/secondary metabolites isolated from microbial sources associated with plants in Oman is discussed below-

There is a very limited study done so far in Oman in the area of phyto-metabolites secreted from plant associated microbes. Abdul *et al* isolated an endophytic fungus Bipolarissorokiniana LK12 from the leaves of ethno-medicinal and alkaloidal rich *Rhazyastrictaa*. A new radicinol derivative, biopolarisenol isolated from the fungus LK12 was found to have moderate antioxidant ability. The bioactive molecule also exhibited inhibitory activity for urease and acetyl choline esterase enzymes thereby having a potential in pharma[27]. A group from the University of Nizwa, isolated an endophytic fungus associated with *Boswellia sacra, Ziziphusspina-christi* and *Z. hajanensis*. Of the 43 isolates, in *Boswellia sacra*, 35 species are new reports to the mycoflora of Oman, whereas 12 species were added to the list of fungal flora of the Arabian Peninsula [28]. In the endophytes isolated in Ziziphus plants 45 species were found to be new to the micoflora of Oman, whereas 27 species are new to Arabian Peninsula [29].

Endophytic fungi are an unexplored trove of treasure, and their association with plants can alleviate many long standing problems of abiotic stress, low biomass, pathogens etc.

III. CONCLUSION

In the reviewed literatures here in present study, bioactive/phytoconstituents compounds from three different sources has been presented. From the terrestrial sources, plants like *Ocradenusarabicus* have been studied in details with respect to characterization of the bioactive molecule. In marine flora algae have been studied extensively, however, other sources such as actinomycetes need more exploration. The arid region does provide a unique environment for plants to struggle and survive. The phytochemicals/bioactive molecules reported from Oman are very limited though the diversity is huge. There is a tremendous potential in the area of plant associated microbes such as endophytes and rhizosphere. A metagenomic approach should be looked into more deeply with respect to isolation of genes from un-cultivable plant associated microbes.

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