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WILD *ASPARAGUS* SPECIES OF ISRAEL AND PALESTINE – A MINIREVIEW

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ABSTRACT

Compared with Europe, the communities of Israel and Palestine (the reviewed region, RR) did not consume WILD species of *Asparagus* and hardly grew domesticated species. This fact reflects also on lack of clear reported ethnomedicinal and ethnobotanical uses. Contrary to this, modern research found notable interest in these plants, with clear differences between published literature about each one. In this minireview article, the published ethnomedicine, ethnobotany, along with findings of modern studies about these plants will be presented. Among the medicinal activities-properties, some were largely published (anticancer) while others were hardly reported or not at all. The chemical compositions of these plants were also partially reported, and among the isolated natural products, saponins were some of the earliest.

KEYWORDS: wild *Asparagus*, *Asparagus acutifolius*, *Asparagus aphyllus*, *Asparagus setaceus*, anticancer, antimicrobial, antioxidant, chemical composition, saponins, ethnomedicine.

Abbreviations ABTS 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid), ahc and her/his colleagues, AChE acetylcholine esterase, βCBM β-Carotene bleaching method, CAT catalase, CUPRAC cupric reducing antioxidant capacity, DCM dichloromethane, DEE diethyl ether, DPPH 2,2-Diphenyl-1-picrylhydrazyl, EO essential oil, EtOAc ethyl acetate, FRAP ferric reducing activity power, GABA γ-amino butyric acid, GCC general chemical composition, GC-MS gas chromatography mass spectrometry, GSH glutathione, LC-MS liquid chromatography mass spectrometry, LPS lipopolysaccharide, MDA malondialdehyde, ORAC oxygen radical absorbance capacity, OSI oxidative stress index, PBD phosphomolybdenum (assay), PE petroleum ether, RR reviewed region, SOD superoxide dismutase, STZ streptozotocin, Syn synonym, TFC total flavonoid content, TPC total phenolic content, TTC total tannins content.

1. INTRODUCTION: Taxonomy and Ethnomedicine

The genus *Asparagus* (هليون in Arabic, אספרגוס in Hebrew) is part of the Asparagaceae family, and the number of species that this genus includes is very highly debated.[1,2,3] It ranges between 200 and 300 species. However, according to the reliable website of "Plants of Israel and Adjacent Areas"[4], in the RR, there are six WILD *Asparagus* species, and these are: *A. acutifolius*, *A. africanus*, *A. aphyllus*, *A. horridus* (Syn. *stipularis*), *A. palaestinus* and *A. setaceus* (Syn. *plumosus*).

Traditional societies around the world have used plants of the genus *Asparagus* for various ethnomedicinal and ethnobotanical goals. In addition, modern societies cultivate *Asparagus officinalis* for food, where in 2025 the data of the production was: it is cultivated in more than 60 countries, on over 1.6 million hectares, producing an annual yield exceeding 8 million metric tons.[5]

But in the present minireview article the focus will be only on ethnomedicinal and ethnobotanical uses of WILD *Asparagus* species of the RR. These uses are summarized in **Table 1**. Strangely enough, no reports of such uses from the RR.

Table 1: Ethnomedicinal/Ethnobotanical Uses of WILD *Asparagus* Species of the RR.

Species	Region	Use(s), Reference
A. acutifolius	Sardinia	Food: cooked vegetables, omelettes[6]
	Spain	Food: cooked in several ways, rarely eaten raw[7]
	Lebanon	Antihypertensive: decoction of stem tops, 1 cup/day[8]
	Morocco	Digestive problems[9]
A. africanus	Saudi Arabia	Leaf paste, topically, leishmaniosis treatment[10]
	Tanzania	Diabetes, decoction, half tea cup, twice a day[11]
A. horridus	Tunisia	Gout, headache[12]
	Morocco	Young stems as food[13]
	Morocco	Food, to treat cold[14]
A. palaestinus	Pakistan	Antidysenteric[15]
	Turkey	Ornamental[16]
A. setaceus	Pakistan	Gastrointestinal disorders, cardiovascular pains[17]
	Pakistan	Roots, decoction, oral, diarrhea, dysentery, stomach[18]
	DR Congo	Root powder, decoction, oral, impotence, headache[19]
	Bangladesh	Ornamental, shoots extracts for heart diseases[20]

2. Selected Publications about WILD *Asparagus* Species of Israel and Palestine

As listed in **Table 1** and published literature, many cultures and nations around the world consumed both cultivated and wild species of *Asparagus*. In some parts of the Middle East (north), this use for nutritional purposes was much wider than in the RR. This also reflected on ethnomedicine and ethnobotany.

Modern research found relatively limited interest in the six WILD species of *Asparagus* of the RR, and the published findings will be listed below. Unless stated otherwise, percentages of solvent mixtures are given as volume/volume (v/v).

Asparagus acutifolius

Fresh young shoots acetone-ethanol (1:1) extract was tested for adaptogenic (milk induced leucocytosis assay in rats), anti-inflammatory (carrageenan-induced rat paw edema) and antioxidant (DPPH, hydroxyl radical scavenging and NO radical scavenging methods) activities. The extract was analyzed for partial GCC and TPC.[21]

Dried shoots aqueous extract was tested for anticancer activity against T24 and A549 cell lines. It was chromatographed resulting the identification of six known phenolics. *Tamus communis* and *Ruscus aculeatus* were also studied in this research.[22]

Aerial parts were separately extracted with DCM and methanol. The extracts were tested for anticancer (against A549 cell line), antimicrobial (against six bacterial and three fungal species) and antioxidant (OSI and total antioxidant status methods) activities. *Asparagus officinalis* was also studied in this research.[23]

Leaves, precaps, rhizomes and stems were separately extracted with 80% aqueous ethanol. The extracts were tested for anticancer (against HCT-116 and HepG2 cell lines), enzyme inhibition (pancreatic lipase), antioxidant (using ABTS, DPPH and FRAP methods) and antimicrobial (against 16 bacterial and 6 fungal species) activities. The extracts were chromatographed yielding known phenolics. Interestingly, Narcissin (**Figure 1**) was found only in the stems extract. In addition, seven saponins were isolated and identified by molecular formulas.[24]

Fruits and leaves were separately extracted with 96% aqueous ethanol and water (4 extracts). The extracts were analyzed for TFC, TPC and TTC, and tested for antioxidant activity using βCBM, PBD, ABTS and DPPH methods. The cytotoxic activity of the extracts was determined using the Brine shrimp lethality bioassay.[25]

Freeze dried spears were defatted with chloroform and extracted with methanol, and the extract was analyzed for partial GCC, TFC, TPC, amino acids, sugars and microelements. The extract was tested for antioxidant (ABTS, DPPH, FRAP, ORAC and NO scavenging methods) and anticancer (against HepG2, A549, HeLa and SK-N-BE cell lines) activities. The extract was chromatographed for phenolics affording 8 known acids (including Chlorogenic acid, **Figure 1**) and three other compounds.[26]

Freeze dried flowering aerial parts were successively extracted with DEE, acetone, ethanol and water. The extract were tested against 11 bacterial and 4 fungal species (with notable mistake in table 2 of this article, that is supposed to present the results). Three other plant species were studied in this research.[27]

Aqueous, ethanolic and methanolic extracts (plant parts/s not indicated) were tested for antibacterial (against 4 bacterial strains), antioxidant (using ABTS and DPPH methods) and AChE inhibition activities.[28]

Roots 70% aqueous methanolic extract was partitioned with several solvents including *n*-butanol, and this

fraction was chromatographed affording seven saponins (**Figure 1**). These compounds were active against three *Candida* species.[29]

Shoots ethanolic extract was analyzed for TPC and tested for antioxidant activity with ABTS, DPPH and ferrous (Fe^{+2}) chelating methods. Seven other plants species were studied in this research.[30]

Spears were analyzed for extended GCC and nutritional values, amino acids, monosaccharides composition, total sugar content, total lipid content, total amino acids content, fatty acids composition, Ascorbic acid content and Folic acid (**Figure 1**) content. The methanolic extract was prepared and analyzed for TPC and tested for antioxidant activity using DPPH, hydrogen peroxide scavenging and nitric oxide scavenging methods. Some results were compared to *Asparagus officinalis*.[31]

Roots 70% aqueous ethanolic extract was active against CaCO2 cancer cells. Three more *Asparagus* species were studied in this research.[32]

Aerial parts and roots were separately extracted with 70% aqueous ethanol, and the extracts had protective activity in Carbon tetrachloride-induced hepatotoxicity in rats. The positive effect was measured with several parameters including antioxidant biomarkers. The extracts were chromatographed yielding known phenolics like Caffeic acid and Rutin. Three more *Asparagus* taxa were studied in this research.[33]

Asparagus africanus

Roots were defatted with PE and extracted with methanol. The extract was tested for analgesic (using tail-flick and hot-plate tests) and anti-inflammatory (egg albumin-induced paw edema) activities in rats. In the analgesic activity tests Morphine was standard drug and in the anti-inflammatory activity tests, Indomethacin.[34]

Roots aqueous extract had anticonvulsant activity against Pilocarpine-induced convulsions (tonic and clonic) in mice. Sodium valproate was reference drug. The positive effect was measured with several biomarkers including GABA levels in the brain, antitumor necrosis factor-alpha (TNF-α) and oxidant-antioxidant (CAT, GSH, MDA and SOD).[35]

Aerial parts aqueous extract had antidiabetic, anti-inflammatory and antihyperlipidemic activities in diabetic rats, where diabetes was induced by high fat diet and STZ. In addition to whole body and isolated organs weight, the positive effect was measured using 13 biomarkers. The extract was analyzed for extended GCC.[36]

Roots aqueous extract had antidiabetic (mainly lowering blood glucose levels) and antioxidant (mainly increasing CAT and SOD levels) in STZ-induced diabetic rats.[37]

Leaves and roots were separately extracted with water and 90% aqueous ethanol. The four extracts were tested for antifertility activity in rats (both sexes). *In vivo* by administration to living animals and *in vitro* by testing on isolated uterine strip.[38]

Roots aqueous extract was analyzed for GCC, and tested for antifertility activity in female rats, with/without roots extract of *Annona senegalensis*. The combination was more effective than the each one of the extracts.[39]

Roots aqueous extract had antifertility activity in female rats. The extract had no effect on body weight and was not toxic. The extract was analyzed by LC-MS yielding eleven known compounds including Acetylcaranine and Prosopinine (**Figure 2**).[40]

Whole plant 80% aqueous methanolic extract had antimalarial activity in *Plasmodium berghei* infected mice.[41]

Roots 80% aqueous methanolic extract was partitioned with several solvents and analyzed affording thirty-three compounds of which ten were new (**Figure 2**). The antioxidant activity of the isolated phenolics was tested using CUPRAC, DPPH and hydroxyl radical scavenging methods.[42]

Aqueous extract (plant part/s not indicated) had positive effect in high fat fed and STZ-induced diabetic rats. The effect was mainly protection of kidneys (measured by urine biomarkers) and alleviation of oxidative stress (eight biomarkers).[43]

Roots were defatted with PE and successively extracted with DCM, EtOAc and methanol. The EtOAc fraction was chromatographed yielding Muzanzagenin and (+)-Nyasol (**Figure 2**). The crude extracts and the two isolated compounds were tested for antiprotozoal activity against *Leishmania major* promastigotes.[44]

Three new steroidal saponins (**Figure 2**) were isolated from roots methanolic extract that was fractionized ad chromatographed.[45]

GCCs of roots aqueous and methanolic extracts are reported.[46]

Rhizomes were defatted with PE and extracted with methanol and the extract was partially analyzed for GCC, It had diuretic activity in mice.[47]

Stems ash was analyzed for elements resulting the presence of Cr, Fe, K, Mg and Zn, while iodine, which is believed to promote hair growth was absent.[48]

Roots aqueous extract was administered to mice resulting decrease of sleep latency period, increase of sleep duration, increase of GABA and decrease of GABA-T in

the animals brain. Authors concluded that this extract has sedative and hypnotic effects.[49]

Roots ethanolic extract was analyzed for TFC, TPC and extended GCC. It was administered to mice with Gentamicin-induced nephrotoxicity, resulting protective effect was measured by levels of Creatinine, Uric acid, and blood urea nitrogen.[50]

Roots aqueous extract had oestrogenic effect in female rats, with Ethinyl-Estradiol as reference drug. GC-MS analysis resulted the identification of nine compounds with Sarsasapogenin (**Figure 2**) as major component, 40.78%.[51]

Asparagus aphyllus

Roots 70% aqueous ethanolic extract was active against CaCO2 cancer cells.[32]

Aerial parts and roots were separately extracted with 70% aqueous ethanol, and the extracts had protective activity in Carbon tetrachloride-induced hepatotoxicity in rats. The positive effect was measured with several parameters including antioxidant biomarkers. The extracts were chromatographed yielding known phenolics like Caffeic acid and Rutin.[33]

Aerial parts (shown in graphical abstract) 50% aqueous ethanolic extract was active against monocultures and co-cultures of Hepg2 and THP-1-derived macrophages. *Crataegus aronia* and *Ephedra alata* were also studied in this research.[52]

Follow up of the previous research that tested the effect of the extracts on Glucose-tranferase-4 membrane translocation on L6 muscle cells and blood glucose levels in mice.[53]

Aerial parts were separately extracted with PE, chloroform and 70% aqueous ethanol. These extracts were tested against MCF7 and HCT cancer cell lines. The aqueous ethanolic extract was analyzed for TFC, TPC, and single phenolics resulting the identification of 27 compounds. Among these were 15 phenolic acids, where Vanillic acid (**Figure 3**) was major with a concentration of 1037 ppm.[54]

Another publication by the group cited as references 52 and 53. The tested anticancer activity as in reference 52, anti-inflammatory activity in LPS-treated THP1 and HepG2 cells (effect was measured using three biomarkers) and antioxidant activity (using ABTS, DPPH, FRAP and PBD methods). The extracts were analyzed for TFC and TPC.[55]

Leaves were successively extracted with methanol, ethanol, chloroform, EtOAc and water. The extracts were tested against five bacterial strains showing notable activities.[56]

Asparagus horridus (Syn. ***stipularis***)

Methanolic extract (plant part/s not indicated) was tested for anticancer (against HepG2 cancer cells) and anti-inflammatory (protein denaturation assay) activities. It was analyzed for TFC and TPC and tested for antioxidant activity using DPPH and FRAP methods.[57]

Aerial parts 70% aqueous ethanolic extract was tested for anticancer (against HepG2 and HCT116 cancer cell lines) and antidiabetic (inhibition of α-Amylase and α-Glucosidase) activities. The extract was chromatographed resulting known phenolics including Caffeic and Ferulic acids, Tiliroside, Nicotiflorin, Quercetin and Brassicin. Molecular docking for hypoglycemic activity was conducted for the last four compounds. The structures of Tiliroside, Nicotiflorin and Brassicin are shown in **Figure 4.**[58]

Young shoots were analyzed for nutritional values: total carbohydrates composition (8), total fibres, energy and mineral. In addition, it was analyzed for fatty acids composition (17), aliphatic acids (3), volatile compounds (30) and tocopherols (2). Dried young shoots were separately extracted with water and 80% aqueous methanol. The hydro-methanolic extract was chromatographed for phenolics (13, known), tested for anticancer activity (against MCF-7, NCI-H460 and HepG2 cell lines) and antioxidant activity (using ABTS, DPPH, FRAP and TBRAS methods).[59]

Roots methanolic extract was partitioned with several solvents including EtOAc, and this fraction was chromatographed affording two new alkaloids: Aspastipuline and 5-Hydroxyaspastipuline (**Figure 4**). Aspastipuline had moderate activity against MCF-7 cancer cells.[60]

Roots and rhizomes were separately extracted with high pressure super critical CO_2 ad the extracts were analyzed for TPC. They were tested for antioxidant activity using ABTS, DPPH, FRAP and quenching assay.[61]

Follow up of previous research but in this case roots and rhizomes were studied. The extracts were encapsulated and resulting material was tested for availability of its components for biological activity.[62]

Leaves, pericarps, rhizomes and roots were separately extracted with 80% aqueous ethanol. The extracts were analyzed for TFC, TPC and total saponin content. The extracts were tested for antioxidant (using ABTS, DPPH and FRAP methods), anticancer (against (HCT-116 and HepG2 cell lines) and pancreatic lipase inhibition activities. The extracts were chromatographed affording 9 known phenolics and 6 known saponins including Diosgenin (**Figure 4**).[63]

Roots 70% aqueous ethanolic extract was fractionized with several solvents including *n*-butanol and this fraction was chromatographed affording Asparagalin A

(**Figure 4**). This compound had anti-schistosomiasis activity (*Schistosoma mansoni*).[64]

Follow up of the research cited as reference 62: in this research, shoots decoction was used to treat metabolic syndrome in high-fructose diet-fed rats. The decoction was used to prepare nanoparticles, and these were also used for the same treatment. Effect was measured mainly by levels of oxidant-antioxidant biomarkers.[65]

Asparagus palaestinus
Aerial parts were analyzed for GCC, fatty acids composition (3), total carbohydrates and composition.[66]

Asparagus setaceus (Syn. ***plumosus***)
Leaves ethanolic extract had allelopathic activity against *Lactuca sativa* (Lettuce) seeds. The extract was analyzed for extended GCC (15 compound families).[67]

Whole plant EO (hydrodistillation) and the remaining aqueous phase were tested for antibacterial (against four bacterial strains) and antioxidant (using DPPH method) activities. Another 21 plant species were studied in this research.[68]

Leaves methanolic extract was analyzed for TFC, TPC and was tested for antioxidant activity using DPPH method, and for antimicrobial activity against *Escherichia coli*. It was analyzed for chemical composition (GC-MS) yielding 19 compounds after silylation.[69]

Follow up study by the group that published reference 67: in this study they tested antibacterial (against eight bacterial species) and toxicity (against *Artemia salina*). Extensive GCC is reported.[70]

Leaves 90% aqueous methanolic extract was chromatographed affording three new saponins (**Figure 5**).[71]

Another publication by the same group cited by reference 71, using the same methods, afforded two new saponins (**Figure 5**).[72]

Roots 95% aqueous ethanolic extract was chromatographed affording two saponin derivatives of 2-Yamogenin and 2-Furostanol (1 and 2 in **Figure 5**). These compounds caused immobilization of human spermatozoa.[73]

Roots methanolic extract was chromatographed yielding Shatavarin IV (**Figure 5**). Another four *Asparagus* species were studied in this research.[74]

Cladodes were separately extracted with chloroform, EtOAc and methanol, and the extracts were chromatographed for chemical compositions. A very detailed report is presented but no new compounds. Another two *Asparagus* species were studied in this research.[75]

Juices were prepared from fresh fruits, leaves, stems and roots, and these plant parts were dried and extracted with ethanol (total of 8 materials). These materials had larvicidal properties against Aedes aegypti. GCCs is provided.[76]

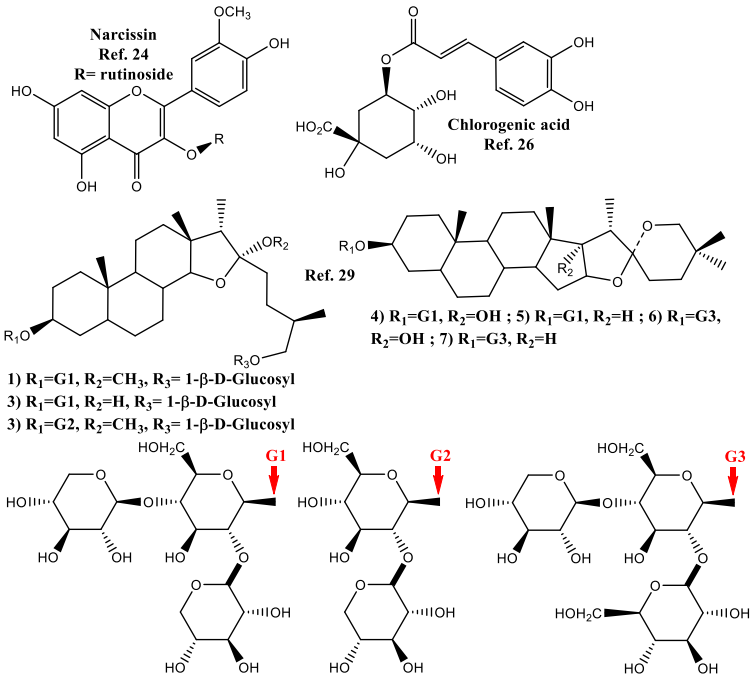

Figure 1: Natural products isolated from *Asparagus acutifolius*.

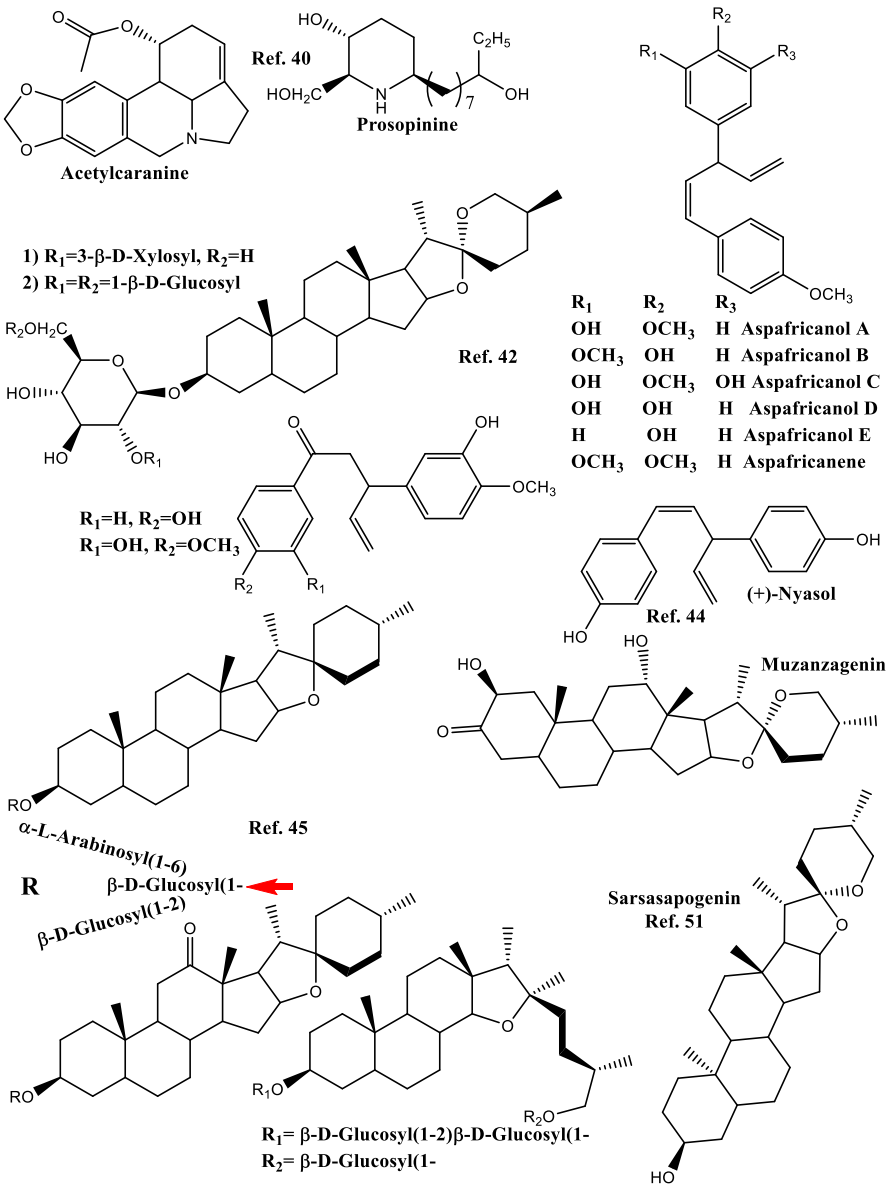

Figure 2: Natural products isolated from *Asparagus africanus.*

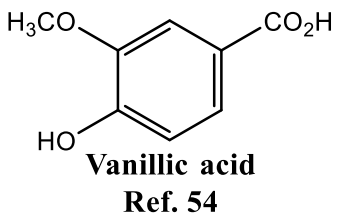

Figure 3: Natural products isolated from *Asparagus aphyllus.*

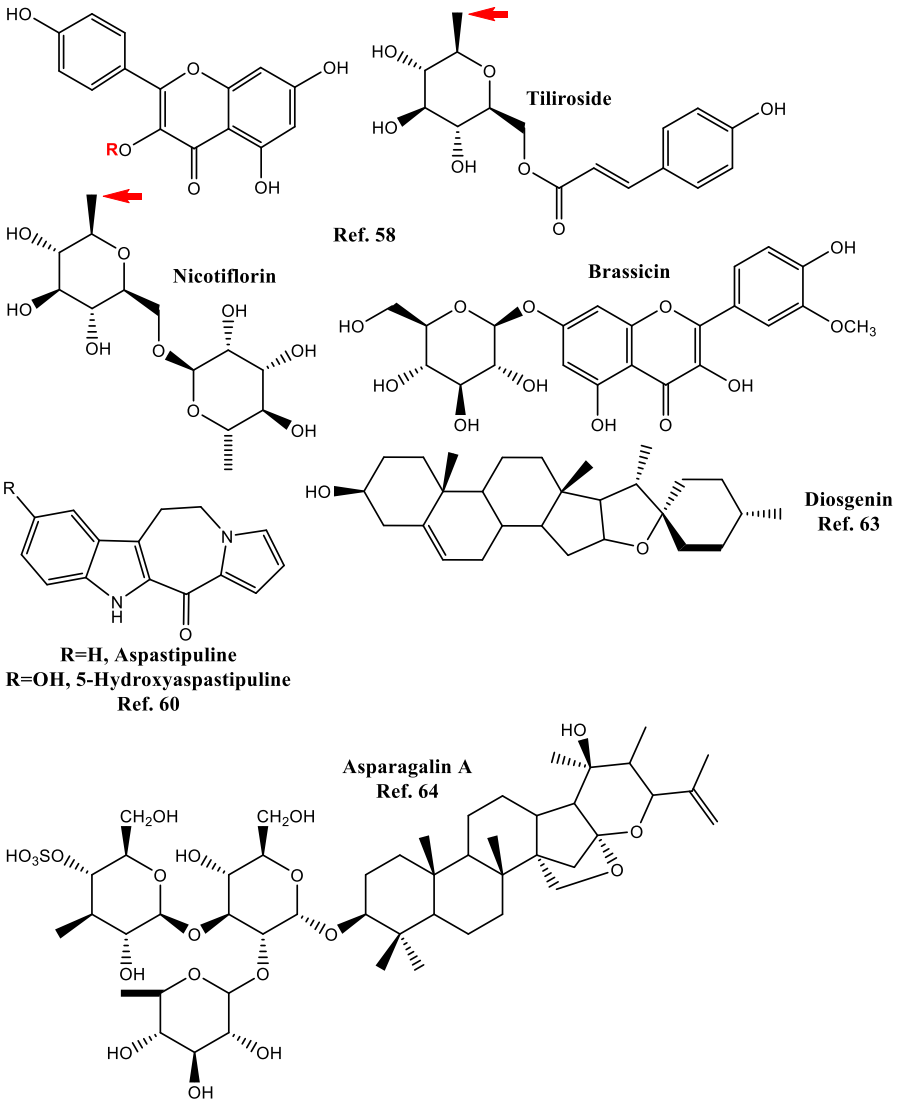

Figure 4: Natural products isolated from *Asparagus horridus*.

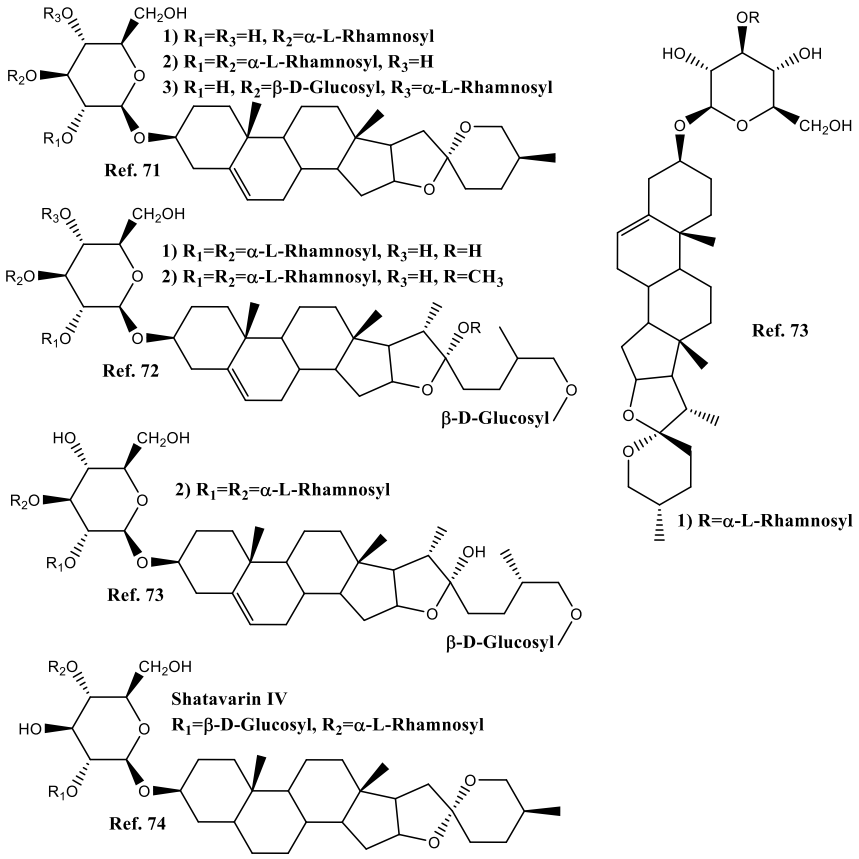

Figure 5: Natural products isolated from *Asparagus setaceus.*

3. DISCUSSION

Among the six WILD *Asparagus* species, the cultivation of *Asparagus acutifolius* drew most attention. O. Alan ahc reported the seasonal variations of quality parameters, phenolic content and antioxidant activity of cultivated and wild plants of this species.[77] In short, they found clear seasonal changes in antioxidants pigments such as phenolics and chlorophylls but not in carbohydrates and compositions. D Mantovani ahc studied the effects of drought and temperature on photosynthesis of this species.[78] They report that optimal growth temperature was about 30°C, while the is a significant decrease over 45°C. As for water shortage, this species demonstrated high tolerance to drought. A. Martínez-Coronado ahc reported that *A. acutifolius* growth was unaffected by high to extremely high concentrations of mercury pollution, even though the metal accumulated in the plant roots.[79]

The enzyme family of Peroxidases is part of a larger family named Oxidoreductases. The major activity of Peroxidases is to catalyse oxidation processes. In recent years, there is growing interest in Peroxidases and the number of their applications and uses is constantly increasing: see the review article of I. Nnamchi ahc.[80] V. Guida ahc isolated a group of Peroxidases from *A. acutifolius* and used them to oxidize phenolic compounds in olive oil production wastewater, a very high environmental and economic application.[81] In a follow up research, the immobilized the enzymes and used them more efficiently for the same purpose.[82]

The concern of possible adverse effects of plants, especially edible and medicinal plants is always present. For this reason, Abubakar El-Ishaq conducted a toxicological study of *Asparagus africanus* in rats.[83] Relying testing several effects of the methanolic extract, this widely used as medicinal plant is safe. Riaz ahc published a computational study of S. Riaz ahc about possible use of this plant species to treat polycystic ovarian syndrome (PCOS).[84] And even though a follow up *in vitro* or *in vivo* studies were not published yet, this work has special significance since PCOS is "one of the most prevalent endocrine system conditions affecting women of reproductive age".[85]

The search of improved conditions for cultivation of *Asparagus* species is continuous due to the high nutritional value and fine taste of these plants. S.S. Mustafa reported a study where she managed to increase the growth and production of beneficial secondary metabolites of *Asparagus aphyllus.*[86] K. Ulukapi ahc analyzed nutrients content in cultivated and naturally growing (Turkey) in *A. horridus.*[87]

Finally, natural and synthetic saponins have special importance as drugs and drugs carriers.[88,89] C. Paczkowski ahc managed to glycolyze some steroidal

compounds using Glucosyltransferases that they isolated from *Asparagus setaceus* (Syn. *plumosus*).[90]

4. CONCLUSIONS

1) *Asparagus* species of Israel and Palestine have special nutritional value.
2) These species contain important medicinally active natural products, especially saponins.
3) Some of these species were significantly studied and published while others were not.
4) Based on item 3, there is a notable need for extensive additional investigations.
5) The chemical compositions on these plants are partially known and must be completed.

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