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REVIEW

The chemistry and biological activities of natural products from Northern African plant families: From Aloaceae to Cupressaceae

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Traditional medicinal practices play a key role in health care systems in countries with developing economies. The aim of this survey was to validate the use of traditional medicine within Northern African communities. In this review, we summarize the ethnobotanical uses of selected plant species from the Northern African flora and attempt to correlate the activities of the isolated bioactive principles with known local uses of the plant species in traditional medicine. The literature is covered for the period 1971 to 2014. Part I of this series focuses on plant families with names beginning with letters A to C, with the ethnobotanical uses of 32 plant species correlated with the bioactivities of 176 compounds identified.

1 Introduction

Before the advent modern or Western medicine, people from several civilizations have depended on medicinal plants/herbs for the treatment of various diseases and ailments. This is particularly the case in the Northern African civilization of Egypt.[1] Ancient Egyptians are known to have been familiar with a catalogue of plant-derived traditional remedies, having used a range of plant organs; roots, rhizomes, flowers, leaves, fruits, seeds, and oils in the form of powders, pills, suppositories, creams, pastes, and ointments.[2,3] In modern Egyptian society, plant-derived remedies are popularly sold in herbal shops and used by the local populations, often without the need for scientific evidence for their use.[1] Some of the knowledge derived from the Ancient civilization of Egypt has been transmitted throughout North Africa and the Middle East.

According to the United Nations Organization (UNO), the geographical region of Northern Africa comprises the countries; Algeria, Egypt, Lybia, Morroco, North Sudan, South Sudan, Tunisia and Western Sahara (Fig. 1), covering a land surface area of about 8,935,659 km^2 and a total population of 198,996,526 inhabitants.[4] The inhabitants of North Africa are generally divided in a manner roughly corresponding to the principal geographic regions of North Africa: the Maghreb, the Nile Valley, and the Sahara. This region is mostly desert (the Sahara), while the rest is made of oases and grasslands, with a few species of trees.[5] According to the analyses of Vilà *et al*., a total of 343 vascular plant species from 69 families non-native to this region were found in the literature.[5] The authors mentioned that alien species richness ranged from 143 (Algeria) to 60 (Tunisia). Most of these were of Mediterranean and North American origin.[5] For the purposes of this study, the terminology "North Africa" is slightly different from that defined by the World Geographical Scheme for Recording Plant Distributions,[6] since the latter excludes the countries of Northern and Southern Sudan.

Recently, our research team has started to explore the components of African traditional medicines, by documenting the current available knowledge on the biological activities of natural products (NPs) isolated from the African flora (from dispersed data/literature sources), to aid in drug discovery programs on the continent. This includes the development of NP databases for use in virtual screening campaigns,[7-10] the pharmacokinetic profiling of NP databases from African flora,[10-13] developing focused reviews on NPs isolated from floral matter from particular countries/regions,[14-19] as well as NPs with interesting biological activities against specific diseases/ailments.[20-23] Our focus has been on the NPs whose measured biological activities correlate with the use of the plant in African traditional medicine (ATM), with the aim of validating the

use of these plant species in traditional medicine. In this survey, the ethnobotanical uses of the plant species from Northern Africa *versus* the bioactivities of the derived NPs are presented by plant family and in alphabetical order. Wherever the bioactivities of the isolated metabolites correlate with the ethnobotanical uses of the plant species, these are highlighted in bold in the Tables. In the first part of this review series, only plant families with names beginning with letters A to C have been considered.

2 Aloaceae (now Xanthorrhoeaceae-Asphodeloideae), Anacardiaceae and Apiaceae

The traditional uses of the studied species from the above families, as well as the isolated compounds and their respective bioactivities are shown in Table 1, while the chemical structures are shown in Figs. 2 and 3. The species from the Aloaceae; *Aloe vera*[24] and *Aloe sinkatana*[25] from North Africa have been investigated. *A. vera* is a well known medicinal plant with diverse applications, in horticulture, medicine and commerce.[24-27] Milardi *et al*. investigated the antioxidant properties of the ethanolic extract of *A. vera* leaf skin harvested in Kairouan, Tunisia.[24] This was fractionated by liquid-liquid partition using hexane, ethyl acetate, chloroform-ethanol and butanol. The chloroform-ethanol fraction showed the highest proportion of total phenolics (40.500 ± 0.041 µg gallic acid equivalents/g of extract), the highest scavenging activity and the greatest reducing power, followed by ethyl acetate, butanol and hexane extracts. ELhassan *et al*. also investigated the leaves of *Aloe sinkatana*, collected from Arkawit, Sudan. In Sudanese traditional medicine, the leaves and leaf exudates of this plant are valued to treat a variety of ailments, including skin disease, constipation, fever and inflamed colon,[28] as well as in the treatment of diabetes.[29] The phytochemical investigation of this plant led to the identification of a new anthraquinone, 2,8-dihydroxy-6-(hydroxymethyl)-1-methoxyanthracene-9,10-dione (**1**), along with 10 known compounds.[25] The known compounds include; aloe-emodin (**2**), feralolide (**3**), 1-hydroxy-5-methoxy-3-methyl-9,10 dihydroanthracene 9,10-dione (**4**), β-sitosterol (**5**), β-sitosterol with glycosidic bond (**6**), microdontin (**7**), homoaloins A (**8**) and B (**9**) and aloins A (**10**) and B (**11**). Scientific evidence for the use of this plant in the treatment of diabetes lies in the fact that compound **1** also showed significant inhibitory effects against glucose-induced advanced glycation end-products.[25]

From the Anacardiaceae (cashew or sumac family), foliage from the pepper tree, *Schinus molle*, is traditionally used as a repellent against house flies, *Musca domestica*, in Ethiopia.[30] It is also valuable as a purgative, diuretic, parasiticide and vulnerary.[31] The repellent ability of the ethanol and petroleum ether extracts from the leaves and fruits of *S. molle* against adult *Blattella germanica* have been investigated,[32] while hexane extracts from the leaves and the fruits have been tested for repellent and insecticidal activities against nymphs and eggs of the Chagas' disease vector, *Triatoma infestans*.[33] Abdel-Sattar *et al*. have investigated the insecticidal and insect repellent activities of essential oils from the leaves and fruits of the plant species *S. molle*, harvested in Saudi Arabia and attempted to establish a correlation with the chemical compositions of these oils documented.[30] GC-MS analysis led to the identification of sixty five (65) components, showing that hydrocarbons dominated the oil composition, with monoterpenes occurring in the largest amounts in the fruits and leaves, 80.43% and 74.84%, respectively. Additionally, *p*-Cymene (**12**) was identified as a major component in both oils. It could be concluded that the high yield and efficacy of *S. molle* essential oil against *T. granarium* and *T. castaneum* suggest that the oil may provide leads for active insecticidal agents.[30]

Daucus carota carota (Apiaceae: celery, carrot or parsley family) is native to the continents of Europe, Asia and Africa. Extracts of the plant are used traditionally for the treatment of hepatic and renal insufficiency as well as for skin disorders.[34] Extracts of the wild plants are also known to exhibit antioxidative and iron-chelative properties. Ahmed *et al*. have isolated three new sesquiterpene daucane derivatives (**13** to **15**) and four known compounds (**16** to **19**) from the roots of wild *D. carota carota*, that showed antifungal activity.[35] The methanol extract of the seeds of this plant also showed antibacterial activity.[36] Marzouli *et al*. investigated essential oils and supercritical CO_2 extracts of umbels from wild *Daucus carota carota* from two different sites in Tunisia.[37] It was shown that eudesm-7(11)-en-4-ol (**20**) (8.2 - 8.5%), carotol (**21**) (3.5 - 5.2%), sabinene (**22**) (12.0 - 14.5%), α-selinene (**23**) (7.4 - 8.6%) and 11-α-(*H*)-himachal-4-en-1-β-ol (**24**) (12.7 - 17.4%) were dominant in the oil from the species harvested in Sejnane, whereas the oils from Tunis were predominantly composed of elemicin (**25**) (31.5 - 35.3%) and carotol (**21**) (48.0 - 55.7%). The antimicrobial activity of the essential oils were assayed by using the broth dilution method on *Escherichia coli* ATCC 35218 and *Staphylococcus aureus* ATCC 43300, and clinical strains of *Candida albicans* and *C. tropicalis* 1011 RM. The MIC values obtained were all > 2.5% (v/v).

Traditional plant remedies have been extensively evaluated for their antihepatotoxic activity through *in vivo* and *in vitro* test models (since effective treatments against liver disease are rare). Ozbek *et al*. have presented an extensive report on the hepatoprotective efficacy of certain plants from the Apiaceae.[38] This has warranted some investigation of apiaceous species from Egypt.[39] The hepatoprotection of the ethanolic extract and fractions of the aerial parts of *Torilis radiata* (Apiaceae), from Egypt, were assessed in terms of the reduction in histological damage, accompanied by restoration of the liver enzymes; alanine amino transferase, aspartate amino transferase, lactate dehydrogenase, and a reduction in the inflammatory markers (tumour necrosis-α, nitric oxide, *N*-acetyl-β-*D*-glucosaminidase and myloperoxidase) in serum.[39] An investigation of the aqueous ethanolic extract of the aerial parts of the plant yielded two triterpenes; lupeol acetate (**26**) and α-amyrin (**27**), along with spinasterol (**28**) from the *n*-hexane fraction; while acacetin (**29**), scopoletin (**30**) and ferulic acid (**31**) were derived from the chloroform fraction and luteolin-7-*O*-glucoside (**32**) from the *n*-butanol fraction.[39] The isolated compounds have exhibited a number of bioactivities. Lupeol acetate, for example, is known to exhibit anti-inflammatory[40] and antiarthritic[41] activities, while α-amyrin has shown anti-inflammatory,[42-43] antihyperglycemic[44] and antimicrobial[45] activities, along with antinociceptive properties in mixture with β-amyrin.[46] *In vivo* studies clearly demonstrated that spinasterol exhibits antitumorigenic activity against skin tumors with neither co-tumour nor co-carcinogen promoter activities.[47] The compound exhibits its cytoprotective and anti-inflammatory effects *via* the induction of heme oxygenase-1 in murine hippocampal and microglial cell lines.[48] Acacetin is known to inhibit cell growth and cell cycle progression, and induces apoptosis in human prostate cancer cells,[49] along with other cancer types.[50-53] Scopoletin exhibits a host of biological activities, including acetylcholinesterase inhibitory activity,[54] hepatoprotective activity,[55] xanthine oxidase inhibition and uricosuric activities[56] and antimicrobial activities.[57-58] Ferulic acid and some of its derivatives are known to exhibit antioxidant[59-60] and hypoglycaemic[60-61] activities, among other activities,[62] while luteolin-7-*O*-glucoside displayed antiasthmatic,[63] antioxidant,[64] antiviral,[65-66] and antibacterial properties.[67] Thus, the hepatoprotective activity of scopoletin could justify the use of this

apiaceous plant in the treatment of liver disorders among other ailments.

Dahia *et al*. also investigated the methanolic and aqueous extracts of *Pituranthos scoparius*, another apiaceous medicinal plant harvested from Southern Algeria.[68] Fifteen metabolites were identified, including two cinnamic acids; 5-*O*-caffeoyl quinic acid (**33**) and 5-feruloyl quinic acid (**34**), along with thirteen known flavonoids, including vicenin-2 (**35**), six quercetin and six isorhamnetin *O*-glycosylated derivatives. Among the isolated metabolites, 5-*O*-caffeoyl quinic acid was the main component, while, of the flavonoids, the isorhamnetin derivatives were present to a greater extent. The major component of this plant (compound **33**) is known to exhibit several bioactivities, including antioxidant, antibacterial, anticancer, antihistamic, and other biological effects.[69]

3 Arecaceae, Asclepiadaceae (now Apocynaceae-Asclepiadoideae) and Asteraceae

The medicinal uses of plants in these plant families are shown in Table 2. Also indicated in the Table are the NPs from different plant species with some biological activity which can be correlated with ethnobotanical studies. The chemical structures of the isolated metabolites have been shown in Figs. 4 to 6.

From the Arecaceae (palm tree family), a number of compounds of medicinal value were isolated and screened for biological activities against various diseases. A new flavone glycoside, tricin 7-O-β-glucopyranoside-2''-sulphate sodium salt (**36**) and fourteen known flavonoids (**37- 50**) were isolated from the leaves of *Livistona australis* and screened for antioxidant and cytotoxicity properties.[70] Compound **36** and the methanol extract of the leaves of *L. australis* significantly restored the reduced levels of GSH in diabetic rats. Compound **36** also indicated potent cytotoxic activity against liver carcinoma Hepg2, breast carcinoma MCF7 and colon carcinoma HCT116 cell lines, with IC_{50} values of 13.5, 15.2 and 16.5 μg/mL, respectively. The ethanol extract showed less activity against HEPG2 and MCF7 cell lines with IC_{50} values of 21.9 and 22 μg/mL respectively, and the weakest activity against colon carcinoma HCT116 cell line, with IC_{50} values of 45.8 μg/mL.[71] The known compounds isolated, alongside compound **36** are genkwanin-6-*C*-β-glucopyranoside (**37**), genkwanin 8-*C*-β-glucopyranoside (**38**), isovitexin (**39**), isoorientin (**40**), orientin (**41)** tricin 7-*O*-β-glucopyranoside (**42**), tricin 4'-*O*-β-glucopyranoside (**43**), luteolin 7-*O*-β-glucopyranoside (**44**), quercetin 3-*O*-β-glucopyranoside (**45**),qurecetin 3-*O*-β-galactopyanoside (**46**), tricin (**47**), quercetin (**48**), apigenin (**49**) and luteolin (**50**).

Calotropis procera (Aiton) (Asclepiadaceae) is a traditional medicinal plant that has been used for the treatment of various ailments in Africa and Asia. The root bark is used in treating skin diseases, enlargement of the abdominal viscera, intestinal worms and ascites. The root has also been used as a carminative in the treatment of indigestion. The latex of the plant is used in India as a purgative and the flowers as a digestive and has also shown anti-asthmatic properties.[72] An aqueous extract of the latex inhibits cellular infiltration as well as protecting against the development of neoplastic changes in the transgenic mouse model of hepatocellular carcinoma.[73] The chloroform extract of the root has been shown to have protective activity against carbon tetrachloride-induced liver damage.[74] The ethanol extract of fresh vegetative parts of *Calotropis procera* from Egypt afforded three new metabolites: 5-hydroxy-3,7-dimethoxyflavone-4'-*O*-β-glucopyranoside (**51**), 2β,19-epoxy-3β,14β-dihydroxy-19-methoxy-5α-card-20(22)-enolide (**54**) and β-anhydroepidigitoxigenin-3β-*O*-glucopyranoside (**55**), along with two known compounds, uzarigenine (**52**) and β-anhydroepidigitoxigenin (**53**).[71] Compound **56** was used as a reference for structural analysis. Ibrahim *et al.* also isolated four new ursane-type triterpenes, namely, calotroprocerol A (**57**), calotroproceryl acetate A (**58**), calotroprocerone A (**59**) and calotroproceryl acetate B (**60**) from the root bark of *C. procera* along with five known compounds: pseudotaraxasterol acetate (**61**), taraxasterol (**62**), calotropursenyl acetate B (**63**), stigmasterol (**64**) and (*E*)-octadec-7-enoic acid (**65**).[75] The bioactivities of the newly identified metabolites are still to be determined.

Compounds **51-55** were tested *in vitro* for cytotoxicity against the human cells HT29 and Hepg2 and the mouse fibroblast cell line NIH-3T3. Uzarigenine (**52**) decreased the metabolic activity of HT29 and HEPG2 cells at 50 μM concentration by 59% and 35%, respectively, and no decrease of the metabolic activity of the NIH-3T3 cells was noted. Compound **51** (50 μM) decreased the metabolic activity of NIH-3T3 and HEPG2 cells by 18% and 10%, respectively, but compounds **52**, **53** and **55** indicated no activity. The metabolites displayed no significant antimicrobial activity against a panel of bacterial strains.[71] Compounds **57 – 65** were all evaluated against three human cancer cell lines including the A549 non-small cell lung cancer (NSCLC), the U373 glioblastoma (GBM) and the PC3 prostate cancer lines. Only compound **57** showed *in vitro* growth inhibitory activity in all three cancer cell lines. Compounds **59** and **64** indicated weak *in vitro* inhibition in A549 NSCLC cancer cell only. The presence of the OH group in compound **57** may be responsible for the *in vitro* growth inhibition of cancer cells as this property is lost when the OH is protected or oxidized (as opposed to compounds **58, 60, 61** and **63**).

Two new taraxastane-type triterpenes (**66** and **67**), along with eight known compounds (**68 -75**) were isolated from *Pergularia tomentosa* (Asclepiadaceae) from Algeria.[76] The new compounds were named pergularine A (**66**) and pergularine B (**67**). The known compounds were oleic acid (**68**), (9*Z*,12*Z*)-octadecadienoic acid (**69**), α-amyrin (**70**), 3-acetyltaraxasterol (**71**), 3-taraxasterol (**72**), 16α-hydroxytaraxasterol-3-acetate (**73**), 3-epimicromeric acid (**74**) and (9*Z*,12*Z*)-octadecadienoic acid glucoside (**75**). Although this plant is poisonous, it is used in folk medicine as a tanning agent and for the treatment of skin diseases in Nigeria. It is used as a depilatory, a poultice, a laxative, an anthelmintic and an abortifacient in Egypt. A decoction of the leaves and stem is used as a remedy for bronchitis and tuberculosis as well as a molluscide. Unfortunately, the new compounds were not tested for any biological activities.

A number of medicinal plants in the Asteraceae (aster, daisy, composite, or sunflower family) have been investigated in North Africa, mostly for their antimicrobial and anticancer activities.[77-80] From *Artemisia herba-alba*, harvested from Eastern Algeria, Laid isolated six compounds, comprising two new sesquiterpene lactones from the methylene chloride/methanol extract of the aerial parts; 1b,9b-diacetoxyeudesm- 3-en-5a,6b,11bH-12,6-olide (**76**) and 1b,9b-diacetoxyeudesm-4-en- 6b,11bH-12,6-olide (**77**), together with 4 known compounds (**78** to **81**).[77] The species *A. herba-alba* is famous plant used tremendously in our folk medicine. Tea preparations with components of this species have exhibited a number of therapeutic properties, including analgesic, antibacterial, anthelminthic and diuretic.[77] Among the popular compounds from this plant are the terpenoid thujone (**82**)[81] and the flavonoid hispidulin (**83**).[82] However, no correlation between the bioactivities of the isolated metabolites and the ethnobotanical of this plant has been recorded.

Hegazy *et al*. isolated and characterized eight new (**84 – 91**) and eight known metabolites (**92 - 99**) from the CH_2Cl_2/MeOH (1:1) extract of the aerial parts of *Chiliadenus montanus*.[78] In Egypt, this plant is known locally as "haneida" and it used as a herbal tea for the treatment of renal problems and some of its constituents have shown anti-diabetic, antimicrobial, anti-obesity, antiatherogenic and antioxidant properties.[79-80] The new compounds include 3-oxo-γ-costic acid β-D-glucopyranoside (**84)**, 3β-methoxy isocostic acid (**85)**, 3α-methoxy isocostic acid (**86),** eudesm-11,13-ene-1β,4β,7α-triol (**87)**, chiliadenol A (3,6,7-trihydroxy-11-methoxy-3,7,11-trimethyldodeca-1,9-diene) (**88**), chiliadenol B (3-hydroxy-3,7,11-trimethyl-1,6-dodecadien-9-one) (**89)**, chiliadenol C (3-hydroxy-3,11-dimethyl-6β,9α-epidioxy-dodeca-1,7(14),10-triene) (**90**), chiliadenol D (3-hydroxy-3,11-dimethyl-6β,9α-epidioxy-dodeca-1,10,7(14)-ene (**91**) and the known ones include; 3-oxo-γ-costic acid (**92**), 3-oxo-γ-costic acid methyl ester (**93**), 3α-acetyl-γ-costic acid (**94**), 5α-hydroxy-4α,15-dihydrocostic acid (**95**), 5α-hydroxycostic acid (**96**), eudesmane-1β,4β,7α-triol (**97**), kaempferol-3-*O*-(6''-O-acetyl)-β-D-glucopyranoside (**98**), and thymol-β-D-glucopyranoside (**99**). All these isolates were tested for antimicrobial activity against gram-positive bacterial strains, for *Staphylococcus aureus* and *Bacillus subtilis* and the gram-negative bacterial strains, *Klebsiella pneumoniae, Alcaligenes faecalis* and *Escherichia coli*. The fungal yeasts used were *Saccharomyces cerevisiae* and *Candida albicans.* Compound **98** indicated antimicrobial activity preventing the growth of *Staphylococcus aureus*, *Bacillus subtilis*, *Klebsiella pneumoniae*, *Alcaligenes faecalis* and *Candida albicans* with MIC values 25, 25, 25, 12.5 and 3.125 μg/mL, respectively, using chloramphenicol (< 6 μg/mL) as positive control.

Chrysanthemum macrocarpum (Asteraceae) is an endemic species, which is used in traditional medicine as a scabicide and for the treatment of intestinal infections in Algeria. It is also used in food flavoring and as a herbal tea by the Touaregs.[83-86] From the aerial parts of this plant were isolated and characterized three new metabolites: a triterpenic diester (**100**) and two natural cyclitols, conduritol C (**101**) and viburnitol (**102**), in addition to four known triterpenes (**103 -106**) and seven known flavonoids (**107 – 113**). Compound **100** was identified as 3,21-dipalmitoyloxy-16β,21α-dihydroxy-β-amyrine and compounds **101** and **102** were determined to be cyclohex-5-ene 1β,2β,3β,4α-tetraol (conduritol C) and cyclohexa-1β,2α,3β,4α,5α-pentaol (viburnitol), respectively. The chloroform, EtOAc and *n*-BuOH extracts and compounds **103** and **106** were screened for antibacterial activity using two gram-positive bacterial strains (*S. aureus and Enterococcus faecalis)* and gram negative bacterial strains *(Pseudomonas aeruginosa*, *E. coli* and *K. pneumoniae*) using ampicillin as the standard. Compound **103** (taraxasterol) showed weak antibacterial activity, while compound **106** showed no activity on either bacterial strain. However, the chloroform fraction showed good activity against gram negative bacteria (*P. aeruginosa, K. pneumoniae, E. coli.*), with MICs of 0.5, 4 and 8 μg/mL, respectively. Both compound **103** and the chloroform extract were evaluated for their cytotoxic activity against human colon cancer HT-29 cells and human prostate cancer carcinoma PC3 cells. The chloroform fraction and taraxasterol prevented cell proliferation of both HT-29 and PC3 cancer cells in a dose-dependent manner. It was concluded that taraxasterol may be responsible for the activity of the extract since it is known to possess antiproliferative properties against various cancer cells.[86] The search for cytotoxic compounds has also led to the bioactivity-guided isolation of ten known compounds from the leaves of *Gaillardia aristata* (Asteraceae). The compounds are, neopulchellin (**114**), 6α-hydroxyneopulchellin (**115)**, β-sitosterol-3-O-β-D-glucoside (**116**), apigenin (**117**), quercitin (**118**), eupafolin (**119**), kaempferol-3-methoxy-7-O-α-L-rhamnoside (**120**), apigenin-7-O-β-D-glucopyranoside (**121**), α-amyrin (**122**) and β-sitosterol (**123**).[83] The antiproliferative activity of these compounds was evaluated against two human cell lines (breast (MCF7) and colon (HCT116)). Compounds **114** and **115** isolated from the chloroform extract indicated the highest cytotoxicity with IC_{50} values of 0.43, 0.32 μg/mL against MCF7 and 0.46, 0.34 μg/mL against HCT116, respectively. Compounds **122** and **123** isolated from the hexane extract showed lower IC_{50} values of 3.05, 2.35 μg/mL against MCF7 and 2.9, 2.85 μg/mL against HCT116, respectively. The compounds obtained from the EtOAc extract indicated the lowest cytotoxicity.

The ornamental medicinal plant, *Wedelia prostrata* (Asteraceae) has yielded known compounds from its callus cultures.[87-88] The compounds consist of two methyl esters of fatty acids, namely, methyl stearate (**124),** methyl palmitate (**125**); four cinnamyl alcohol derivatives, namely sinapyl alcohol (**126)**, coniferyl alcohol (**127**), *p*-coumaryl alcohol (**128**) and coniferyl alcohol 4-*O*-glucoside (**129**). These compounds were not tested for any biological activity. Meanwhile, essential oils have been extracted from *Conyza bonariensis* (Asteraceae), an annual perennial weed endemic in Tunisia.[89] The ethanol extract of the aerial parts of *Centaurea nicaeensis* All. var. *walliana* M. (Asteraceae), yielded a new flavone glucoside, apigenin 4'-(6''-methylglucoside (**130**)), together with six known compounds, namely, cirsilineol, jaceosidin, melitensin, apigenin, apigenin 7-(6''-methylglucuronide) and prunasin.[90] Mamdouh *et al*. also isolated and characterized fifteen known flavonoids from the leaves of *Psiadia punctulata* (Asteraceae), but the isolated compounds were not tested for any biological activity.[91] The compounds include apigenin, acacetin, luteolin, chrysoeriol, luteolin 7-glucoside, orientin 7-glucoside, isoorientin, isoorientin 7-glucoside, cirsilineol 5,4'-dihydroxy-6,7,3'-trimethoxyflavone, gardenin B (5-hydroxy-6,7,8,4'-tetramethoxyflavone), 5-hydroxy-3,6,7,8,4'-tetramethoxyflavone, 5,3'-dihydroxy-6,7,4',5'-tetramethoxyflavone, 5-hydroxy-6,7,3',4',5'-pentamethoxyflavone, and gardenin C (5,3'-dihydroxy-6,7,8,4',5'-pentamethoxyflavone).

4 Balanitaceae, Bignoniaceae, Bombacaceae (now Malvaceae-Bombacoideae) and Burseraceae

A summary of the medicinal uses and biological activities of the compounds of the plant families are indicated in Table 3. The chemical structures of the isolated compounds are shown in Fig. 7

Balanites aegyptiaca (Balanitaceae) is used in Sudanese folk medicine for the treatment of jaundice and the fruits are used in Egypt for the treatment of diabetes.[84] Apart coumarins, flavonoids, saponins and steroids which, have been isolated from *B. aegyptiaca*, new constituents such as *N-trans*-feruloyltyramine (**131**) and *N-cis*-feruloyltyramine (**132**) were isolated from the plant along with vanillic acid, syringic acid, and 3-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone.[92] These compounds were not tested for any biological activities. The work of de Abreu *et al*. led to the isolation and characterization of a new glycosylated lignan, 5-hydroxysesamin 5-*O*-β-D-glucopyranosyl-(1→2)-[β-D-glucopyranosyl-(1→6)]-β-D-glucopyranoside (**133**), from the leaves of *Tabebuia argentea* (Bignoniaceae) and a new phenolic glycoside, 1-benzyl-[6-*p*-hydroxybenzoyl]-β-D-glucopyranosyl-(1→3)-β-D-glucopyranoside, (**134**) from the petioles of *Catalpa bignonioides* (Bignoniaceae), along with five known phenolic glycosides; 1,6-di-*O*-*p*-hydroxybenzoyl-β-D-glucopyranoside, benzyl β-D-glucopyrano-side, 1-*O*-ethyl-6-(p-hydroxybenzoyl)-β-D-glucopyranoside, 1-O-*p*-hydroxybenzoyl-β-D-glucopyranoside, 6-*p*-

hydroxybenzoyl-D-glucose (α,β), along six flavonol glycosides; kaempferol 3-*O*-β-D-glucopyranoside, quercetin 3-*O*-β-D-glucopyranoside, kaempferol 3-*O*-rutinoside, quercetin 3-*O*-sambubioside, quercetin 3-*O*-robinobioside, and rutin.[93] *T. tabebuia* is used in Egyptian folk medicine as an anti-inflammatory and against influenza and *C. bignonioides* is known to have a sedative and a narcotic effect and it has also been used in the treatment of whooping cough and asthma. Many iridoids from these plants have been evaluated for their Hsp90 inhibitory activity.[94] *Jacaranda mimosaefolia* (Bignoniaceae) is a useful medicinal plant whose bark decoction has been used to treat veneral diseases and to purify blood in Ecuador.[95-96] The plant has also been reported to be used as an antisyphilitc, astringent and in applications against buboes.[97] The phytochemistry of the stem bark of *J. mimosaefolia* afforded two new glycosides, 2-(3',4'-dihydroxyphenyl) ethyl-3-O-α-L-rhamnopyranosyl-4-*O*-*p*-hydroxyphenylacetyl-6-*O*-caffeoyl-β-D-glucopyranoside (**136)** and 2-(3',4'-dihydroxyphenyl) ethyl-3-*O*-α-L-rhamnopyranosyl-4-*O*-piperidine-3-carboxylic acid-6-*O*-caffeoyl-β-D-glucopyranoside (**137**). In addition, the known compounds lupeol (**138**), betulinaldehyde (**139**), terminic acid (**140**), betulinic acid (**141**), maslinic acid (**142**), β-sitosterol glucoside (**143**) and isoacteoside (**135**) were isolated and identified. Although different biological activities have been reported for this plant, such as antimicrobial activity[98] and antioxidant activity,[99] these new metabolites were not tested for any biological activities.

Bombax malabaricum DC (Bombacaceae: bignonias family) has been used in traditional medicine for the treatment of enteritis, dysentery, lymphadenoma, menorrhagia, and hepatitis.[100-101] It has also been employed as a diuretic, demulcent, aphrodisiac, and an emetic and for curing impotence, in addition to showing significant anti-*Heliobacter pylori* activity.[102] Seven flavones were isolated from the methanol extract of the flowers of *B. malabaricum* DC (Bombacaceae) and fourteen compounds from the *n*-hexane extract including cholesterol, stigmasterol, campestrol, α-amyrin and ten hydrocarbons. The seven flavonols include, vicenin 2 (**144**), linarin (**145**), saponarin (**146**), cosmetin (**147**), isovitexin (**148**), xanthomicrol (**149**) and apigenin (**47**)[100] (Fig. 8). These pure compounds were not screened for biological activity but the *n*-hexane and methanol extracts showed significant antioxidant and antimicrobial activity.[100] The *n*-Hexane extract scavenged the free radical 1,1-diphenyl-2-picrylhydrazoyl (DPPH) over concentrations ranging between 0.55 – 0.0343 mg/mL and the methanol extract scavenged DPPH over the range 0.5 – 0.0312 mg/mL. The maximum scavenging being observed was 0.55 – 0.5 mg/mL for both extracts. Both extracts were screened for antimicrobial activities against different bacterial, fungal and yeast strains using tetracycline (antibacterial) and fluconazole (antifungal) as standard drugs. The methanol extract showed significant activity against *Stapylococcus aureus, Bacillus subtilis, Strptococcus faecalis* (gram-positive strains), *Escherichia coli, Neisserria gonorrhea, Pseudomonas aeruginosa* (gram negative strains) and *Candida albicans* (yeast), but the hexane extract displayed between weak and moderate activity against the tested microorganisms. The *n*-hexane extract indicated no antifungal activity against *Aspergillus niger and Aspergillus flavus* (filamentous fungi) but the methanol extract revealed moderate activities.

Commiphora molmol, from the Burseraceae (torchwood family) is indigenous to desert areas of Somalia, Ethiopia and part of Kenya and exudes a gum (oleo-resin), which has been used as an insect repellent, antiseptic and an anti-inflammatory for the remedy of mouth and throat infections. In search of anti-staphylococcal agents from plants, Rahman *et al*. isolated two octanordammaranes; mansumbinone (**150**) and 3,4-*seco*-mansumbinoic acid (**151**) and two sesquiterpenes; β-elemene (**152**) and T-cadinol (**153**) (Fig. 8).[103] These compounds were assessed for anti-staphylococcal activity against multi-drug and methicillin-resistant strains of *Staphylococcus aureus*. The most significant anti-staphylococcal activity was displayed by compound **151**. It revealed the highest potency against the multi-drug effluxing strain SA1199B (MIC = 4 μg/mL) two times more potent than the control antibiotic norfloxacin. The crude chloroform extract of the oleo-resin of *C. molmol* indicated potentiation of ciprofloxacin and tetracycline in several strains of the bacteria.[103]

5 Celastraceae, Chenopodiaceae, Cleomaceae, Cucurbitaceae and Cupressaceae

A summary of the medicinal uses and biological activities of the compounds of the plant families are indicated in Table 4, while chemical structures of identified metabolites are shown in Figs. 8 and 9.

Cleome paradoxa (Cleomaceae) has shown noticeable antidiabetic activity.[104-105] A new cembranoid diterpene, paradoxenoic acid (**154)** and a new alkaloid, paradoxonine (**155a**) and its tautomer (**155b**) were isolated and characterized from *C. paradoxa.* No biological activity has been reported of these metabolites. A decoction of the root bark of *Maytenus senegalensis* (Celastraceae: staff vine or bittersweet family) is widely used folk medicine in Sudan to treat malaria. Bioactivity-guided fraction of the root bark of this plant led to the isolation of a new quinonemethide triterpene, (20α)-3-hydroxy-2-oxo-24-nor-friedela-1(10),3,5,7-tetraen-carboxylic acid-(29)-methylester commonly known as pristimerin (**156**). Pristimerin revealed *in vitro* antiplasmodial activity against the chlorquine-resistant strain (Dd2) of *Plasmodium falciparum* (IC_{50} = 0.50 μg/mL),[106] thus supporting the local use of this plant as medication for malaria. Pristimerin also showed antileishmanial activity (IC_{50} = 6.8 ± 0.8 μg/mL against promostigotes of the WHO reference vaccine strain of *Leishmania major*. The cytotoxic activity of this compound was measured by the lymphocyte proliferation model and was detected at IC_{50} = 6.8 ± 0.8 μg/mL

Our survey of the Cucurbitaceae (gourd family) indicated three species (Table 4). These are *Citrullus colocynthis*, used in treating several diseases such rheumatism and hypertension, and many contagious diseases such as dermatological, gynecological, and pulmonary infections;[107] *Citrullus lanatus* var. *citroides* used to treat rheumatism, swellings, gout and as a laxative[108] and *Cucurbita pepo* L., used in the remedy of several ailments (antidiabetic, antihypertensive, antitumor, immunomodulation, antibacterial, antihypercholsterollemia, intestinal antiparasitia, antalgic).[109] The antibacterial and anticandidal activities of the aqueous and diluted acetone extracts of various parts (roots, stems, leaves, fruits and seeds) of *C. colocynthis* were measured against gram-positive and gram-negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Enterococcus faecalis*) and various *Candida* spp. (*Candida glabrata*, *Candida albicans*, *Candida parapsilosis* and *Candida kreusei*).[107] All the extracts showed activity against all the strains with the highest activity from the fruit aqueous extracts (MIC 0.10 mg/mL against *Candida albicans* and *Candida glabrata*, 0.20 mg/mL against *Escherichia coli* and *Pseudomonas aeruginosa*) and the lowest activity from the roots. These studies validate the use of this plant as a broad-spectrum antimicrobial agent. Cucurbitacin E (**157**), extracted from the powdered fruit pulp of *Citrullus lanatus* exhibited *in vitro* and *in vivo* anti-inflammatory activity through the inhibition of COX and

RNS enzymes but not reactive oxygen species (ROS), corroborating the use of this plant as anti-inflammatory. In addition, compound **157** does not affect normal human liver cells. Badr *et al*. separated six compounds from the rind, flesh and seeds of the pumpkin, *Cucurbita pepo*.[109] These compounds include, a triglyceride fatty acid mixture (**158**), tetrahydrothiophene (**159**), linoleic acid (**160**), calotropoleanly ester (**161**), cholesterol (**162**), and 13(18)-oleanen-3-ol (**163**). Extracts of the various parts of this plant were screened for antimicrobial, antiviral, antitumor and cytotoxicity activities in comparison with the isolated components.[109] The rind and flesh extracts revealed moderate antimicrobial activity against gram-positive bacteria, *Bacillus subtilis* and *Bacillus cereus*, while the oil from the seeds displayed strong antifungal activity against *Saccharomyces cerevesiae*. On the contrary, the defatted seed showed no antimicrobial activity. Extracts of the rind, flesh and the defatted seed showed significant antiviral activity against Live Newcastle Disease Virus (NDV) vaccine strains and Live Infectious Bursitis Viruses (IBDV) vaccine strain, D_{78} in the range 4 – 6 µL/mL at therapeutic indices of >100, >80 and 50 respectively. Extracts of different parts of the pumpkin (rind, flesh, seed oil and defatted seeds) showed potent *in vitro* antitumor activities against liver carcinoma (Hepg2) (IC_{50} range from 0.6 – 5.03 µg). Apart from the seed oil, the extracts exhibited cytotoxicity activity against breast carcinoma (MCF7), with an IC_{50} in the range 0.40 – 1.01 µg. Comparing the extracts with the pure compounds, only linoleic acid (**160**) showed potent antimicrobial activity against gram-positive bacteria (*Streptomyces viridochromogenes)* and moderate activity against yeast (*Candida albicans*) and the fungi, *Mucor miehi.* The other compounds were inactive. Linoleic acid exhibited potent cytotoxic activity against brine shrimp compared to the rind and flesh extracts, while the other isolated compounds were inactive against brine shrimp. The use of the plant as a remedy for several diseases is justified.

The genus *Salsola* (Chenopodiaceae: goosefoot family) consists of several species found mostly in dry parts of Africa, Asia and Europe, very few of them having been utilized in folk medicine. Oueslati *et al*. have isolated the new norisoprenoid 3*β*-hydroxy-5α,6α-epoxy-*β*-ionone-2α-*O*-*β*-D-glucopyranoside (**164**) and the long-chain hydroxyl fatty acids 9,12,13-trihydroxyoctadeca-10(*E*),15(*Z*)-dienoic acid (**165**) and 9,12,13-trihydroxyoctadeca-10(*E*)-dienoic acid (**166**) from *Salsola tetrandra* aerial parts, together with 3,4,5-trimethoxyphenyl-*β*-D-glucopyranoside (**167**), 9-hydroxylinaloyl glucoside (**168**), taxiphyllin (**169**), *trans*-*N*-feruloyltyramine (**170**), and *S*-(-)-*trans*-*N*-feruloyloctopamine (**171**).[110] All the eight compounds were screened for antimicrobial activity against gram-positive evaluated against Gram-positive *Staphylococcus aureus* ATCC 29213, *Staphylococcus epidermidis* NCIMB 8853, and *Micrococcus luteus* NCIMB 8166 and gram-negative *Escherichia coli* ATCC 35218 and *Pseudomonas aeruginosa* ATCC 27853 using microdilution methods on liquid medium. Compounds **169** and **171** revealed moderate antimicrobial activity by preventing the growth of *S. aureus* (MIC 200 µg/mL). Two new compounds, tetranins A and B, 1-(3,5-dihydroxy-4'-methoxyphenyl)-2 phenylethanol (**172**) and 5,2'-dihydroxy-5'-methoxy-6,7-methylenedioxy-isoflavone (**173**), were isolated from the EtOAc extract of *Salsola tetrandra* roots.[111] The two compounds displayed significant antioxidant effect in the DPPH and 2,2'-azinobis(3-ethylbenzothiazoline)-6-sulphonic acid (ABTS) assays. Another *Salsola* species, widely growing in Egypt, which has been studied, is *S. imbricata* from which two new triterpene glycosides have been isolated and characterized but not biologically screened: 3-*O*-β-D-xylopyranosyl-(1→2)-*O*-β-D-glucuronopyranosyl-akebonic acid 28-*O*-β-D-glucopyranoside (**174**) and 3-*O*-β-D-xylopyranosyl-(1→2)-*O*-β-D-glucuronopyranosyl-29-hydroxyoleanolic acid 28-*O*-β-D-glucopyranoside (**175**).[112] The extracts of the berries of *Juniperus phoenicea* (Cupressaceae: cypress family) indicated significant antioxidant activity in the DPPH and ABTS assay.[113] The berries of the plant are rich in minerals, unsaturated lipids and polyphenols which may account for their antioxidant properties.

6 Conclusions

The results presented in this review represent an overview of the biological activities of selected NPs isolated from plants used in traditional medicine in North Africa, which could be useful in drug discovery programs. Our intention has been to focus on those plants whose ethnobotanical uses correlate with the biological activities of the derived NPs. Even though this report does not claim to be exhaustive, the goal of documenting the baseline knowledge, from which further investigations could be carried out, has been achieved. The plant sources, geographical collection sites, chemical structures of pure compounds as well as their spectroscopic data, were retrieved from literature sources comprising data collected from major international journals on natural products and some available PhD theses, spanning the period 1971 to 2014. Our survey consisted in collecting data from the literature sources, mainly using author queries in major natural product and medicinal chemistry journals. The collected data includes plant sources, uses of plant material in traditional medicine, plant families, region of collection of plant material, isolated metabolites and type (e.g. flavonoid, terpenoid, etc.), measured biological activities, etc. The data was collected on a Excel sheet and analyzed. In the second part of this review series, emphasis will be on the remaining plant families.

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8 Notes and references

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Figure captions

Fig. 1: Map showing geographical region of North Africa.

Fig. 2: Chemical structures of compounds **1** to **28** and **138**.

Fig. 3: Chemical structures of compounds **29** to **35**.

Fig. 4: Chemical structures of compounds **36** to **69** and **75**.

Fig. 5: Chemical structures of compounds **70** to **74** and **76** to **113**.

Fig. 6: Chemical structures of compounds **114** to **130** and **143**.

Fig. 7: Chemical structures of compounds **131** to **137** and **139** to **142**.

Fig. 8: Chemical structures of compounds **144** to **155**.

Fig. 9: Chemical structures of compounds **156** to **175**.

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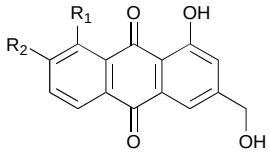
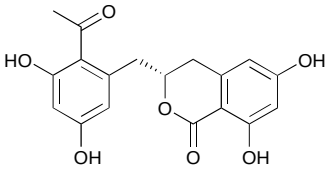


1: R_1 = OCH_3 and R_2 = OH
2: R_1 = OH and R_2 = H



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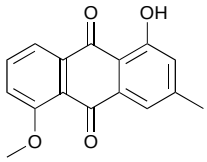

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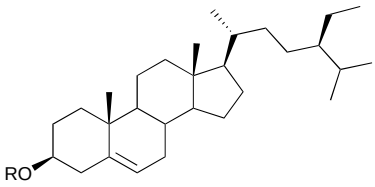
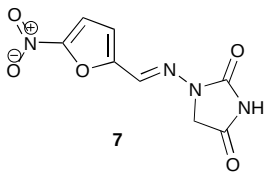


5: R = H, **6**: R = Glc



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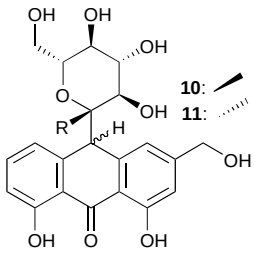
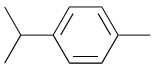


10:
11:
10: R = H, **11**: R = OH



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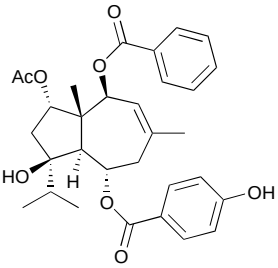

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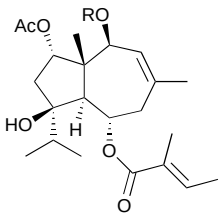
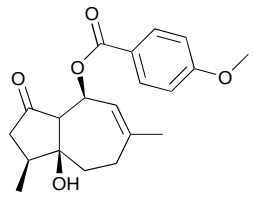


14: R = benzoate
15: R = cinnamate



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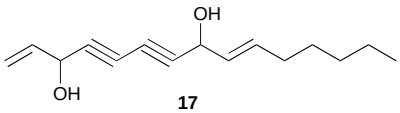

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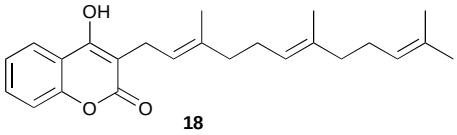

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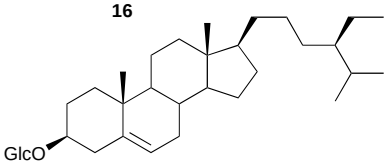

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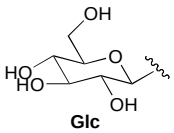
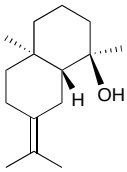


Glc



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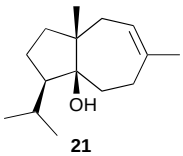

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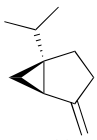

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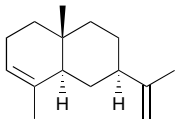

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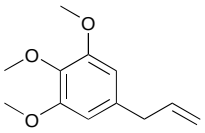

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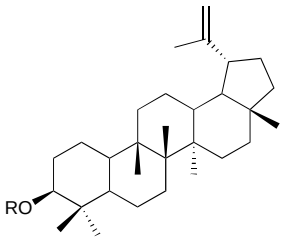
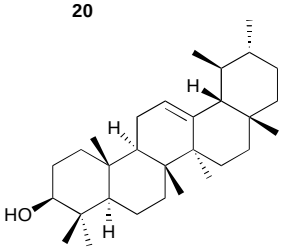


26: R = Ac, **138**: R = H



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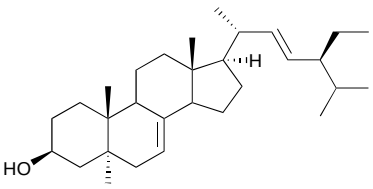

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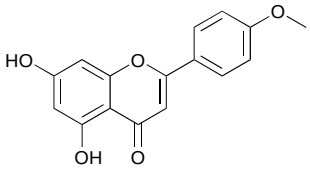

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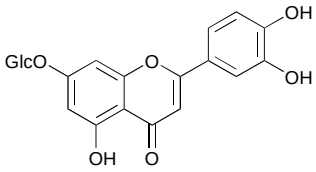

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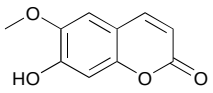

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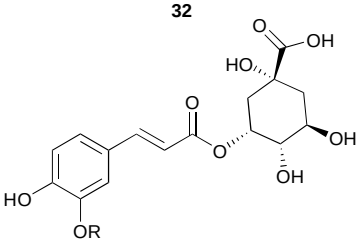
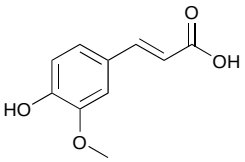


33 R = H

34: R =CH_3



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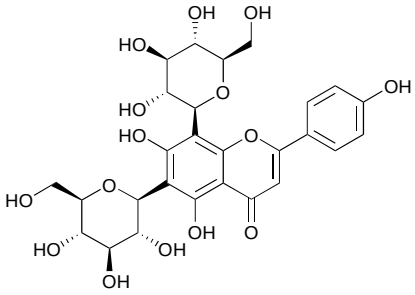

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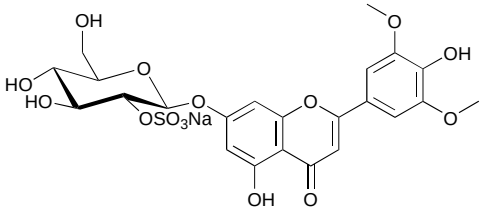

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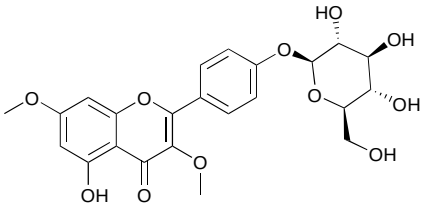

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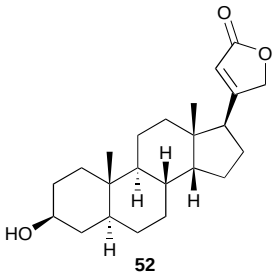

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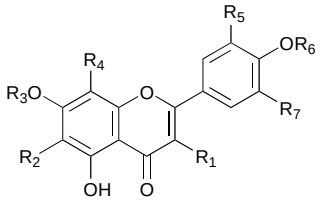
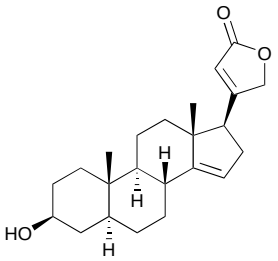


37: $R_1 = R_4 = R_5 = R_6 = R_7 = H$, $R_3 = CH_3$, $R_2 = Glc$
38: $R_1 = R_2 = R_5 = R_6 = R_7 = H$, $R_3 = CH_3$, $R_4 = Glc$
39: $R_1 = R_2 = R_3 = R_5 = R_6 = R_7 = H$, $R_4 = Glc$
40: $R_1 = R_4 = R_6 = R_7 = H$, $R_3 = R_5 = OH$, $R_2 = Glc$
41: $R_1 = R_2 = R_3 = R_4 = H$, $R_5 = R_7 = OH$, $R_6 = Glc$
42: $R_1 = R_2 = R_4 = R_6 = H$, $R_5 = R_7 = OCH_3$, $R_3 = Glc$
43: $R_1 = R_2 = R_3 = R_4 = H$, $R_5 = R_7 = OCH_3$, $R_6 = Glc$
44: $R_1 = R_2 = R_4 = R_6 = R_7 = H$, $R_5 = OH$, $R_3 = Glc$
45: $R_2 = R_3 = R_4 = R_6 = R_7 = H$, $R_5 = OH$, $R_1 = O\text{-}Glc$
46: $R_2 = R_3 = R_4 = R_6 = R_7 = H$, $R_5 = OH$, $R_1 = O\text{-}Gal$
47: $R_1 = R_2 = R_3 = R_4 = R_6 = H$, $R_5 = R_7 = OCH_3$
48: $R_2 = R_3 = R_4 = R_6 = R_7 = H$, $R_1 = R_5 = OH$
49: $R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = R_7 = H$
50: $R_1 = R_2 = R_3 = R_4 = R_6 = R_7 = H$, $R_5 = OH$



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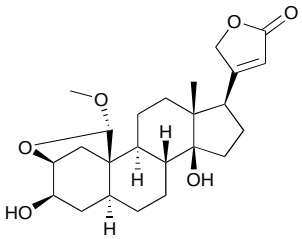

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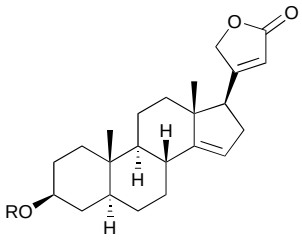
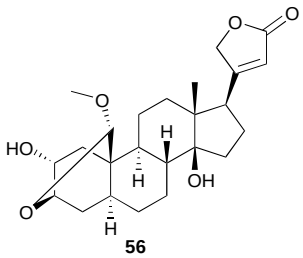


55: R = β–Glc



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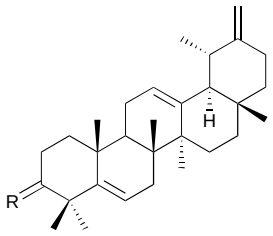
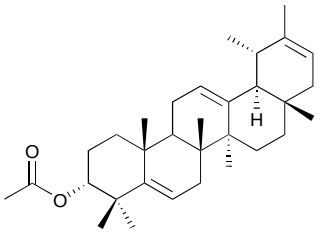


57: R = β-H, α-OH
58: R = β-H, α-OAc
59: R = O



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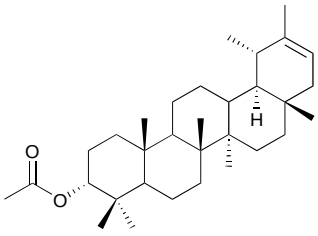

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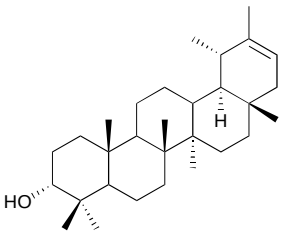
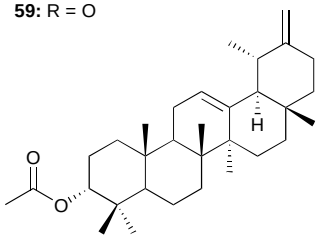


62



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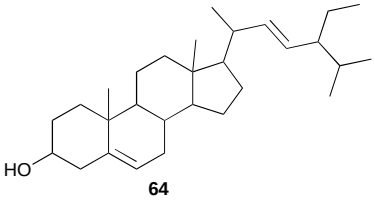

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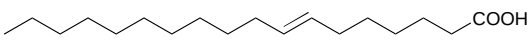

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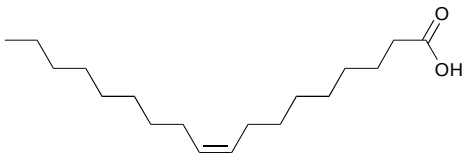

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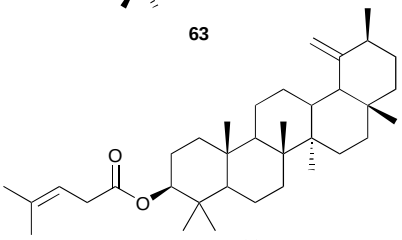
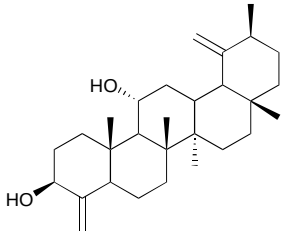


66



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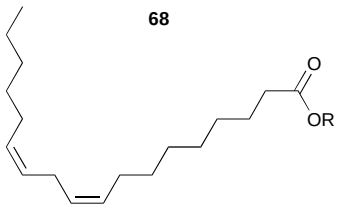
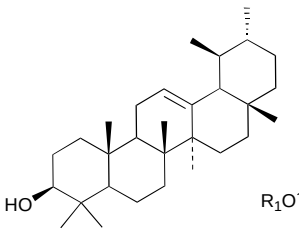


69: R = H, **75:** R = Glc



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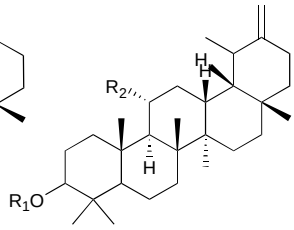
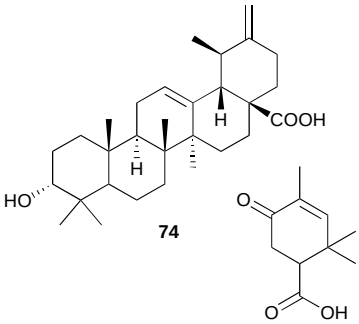


71: R_1 = Ac, R_2 = H
72: R_1 = H, R_2 = H
73: R_1 = Ac, R_2 = OH



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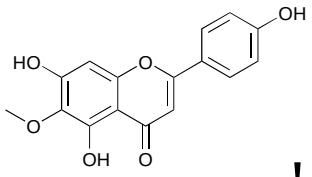
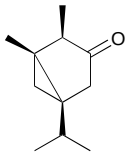


83



82

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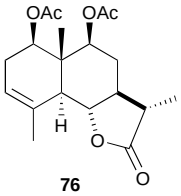

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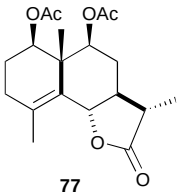

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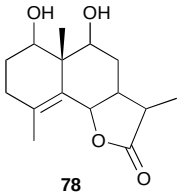

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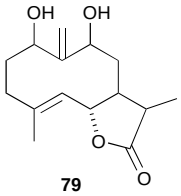

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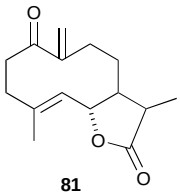
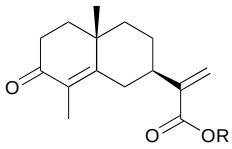
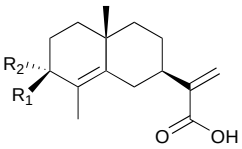


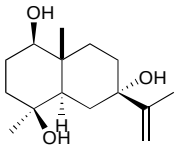
81



84: R = Glc
92: R = H
93: R = CH_3



85: R_1 = OCH_3 , R_2 = H
86: R_1 = H, R_2 = OCH_3
94: R_1 = H, R_2 = OAc



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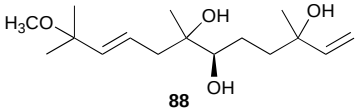

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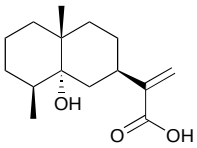

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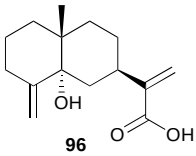

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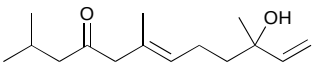

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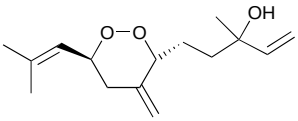

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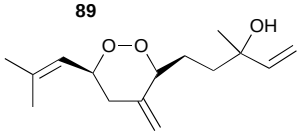

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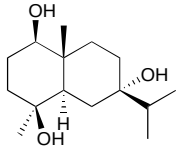

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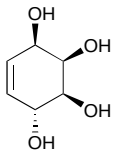
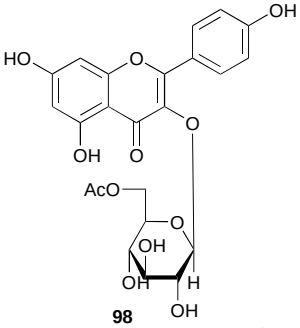


101



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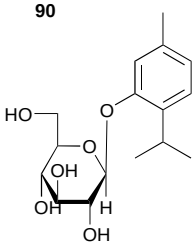

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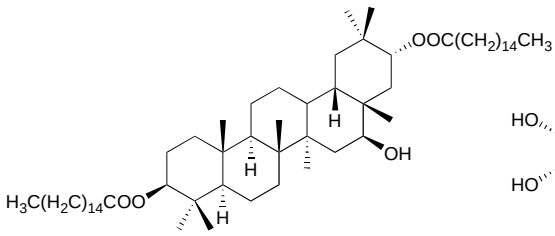

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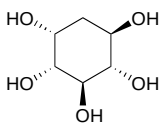
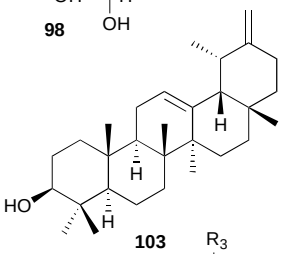
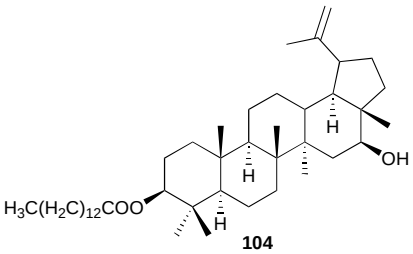


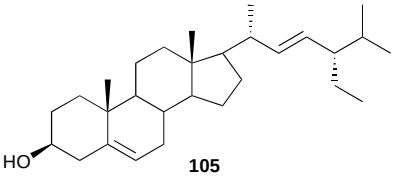
102



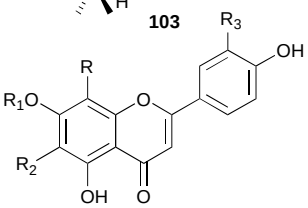
103



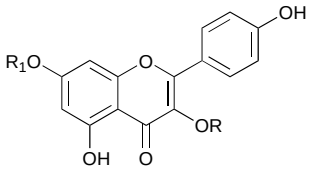
104



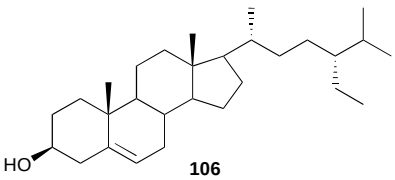
105



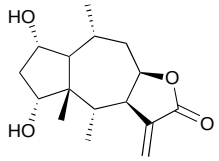
107: R = R_1 = R_2 = R_3 = H, **108**: R = R_2 = R_3 = H, R_1 = CH_3
109: R = R_2 = R_3 = H, R_1 = Glc, **112**: R = R_1 = R_2 = H, R_3 = OGlc
113: R = Ara, R_1 = R_3 = H, R_2 = Glc



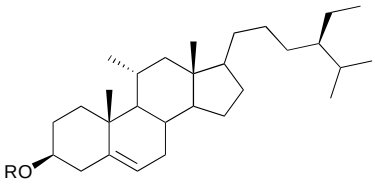
110: R = Glc, R_1 = H
111: R = H, R_1 = Glc



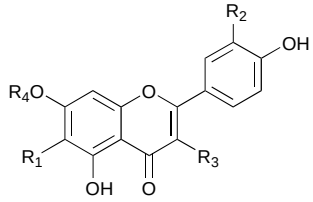
106



114: R = H, **115**: R = OH



116: R = β-Glu, **123**: R = H, **143**: R = β-D-Glu



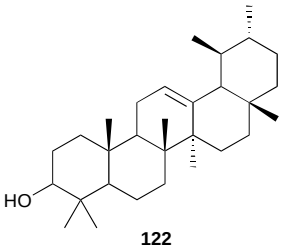
117: $R_1 = R_2 = R_3 = R_4 = H$

118: $R_1 = R_4 = H$, $R_2 = R_3 = OH$

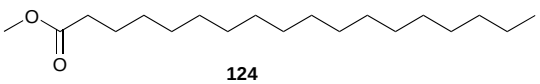
119: $R_1 = OCH_3$, $R_2 = OH$, $R_3 = R_4 = H$

120: $R_1 = R_2 = H$, $R_3 = OCH_3$, R_4 = Rhamnose

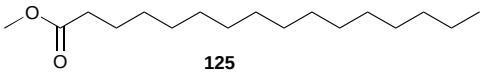
121: $R_1 = R_2 = R_3 = H$, R_4 = Glucose



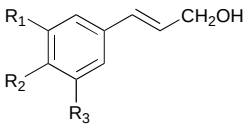
122



124



125

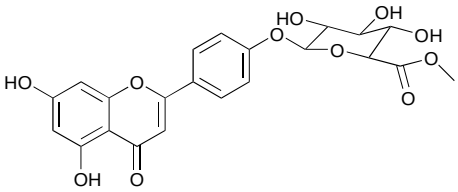


126: $R_1 = R_3 = OCH_3$, $R_2 = OH$

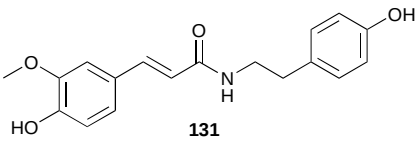
127: $R_1 = OCH_3$, $R_2 = OH$, $R_3 = H$

128: $R_1 = R_3 = H$, $R_2 = OH$

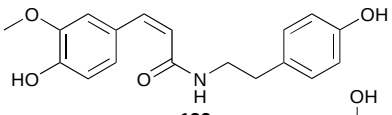
129: $R_1 = OCH_3$, R_2 = O-Glu, $R_3 = H$



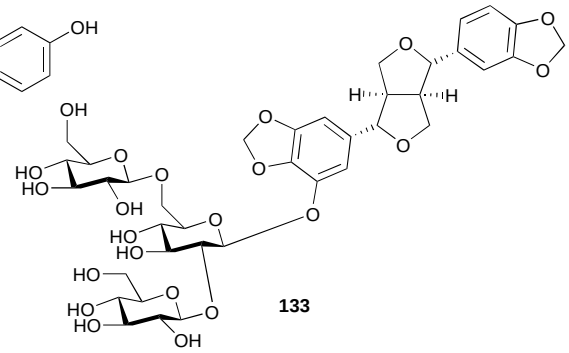
130



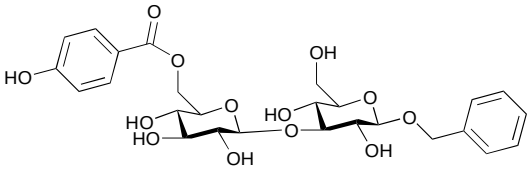
131



132



133



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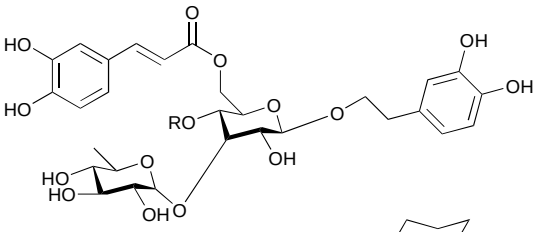
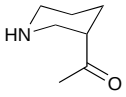
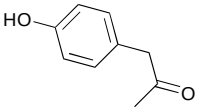


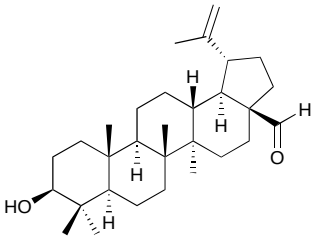
135: R = H

137: R =



136: R =





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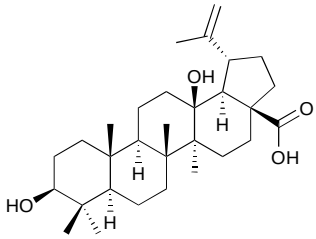

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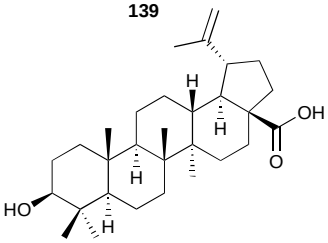

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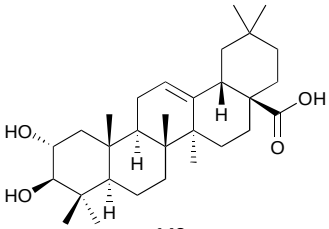

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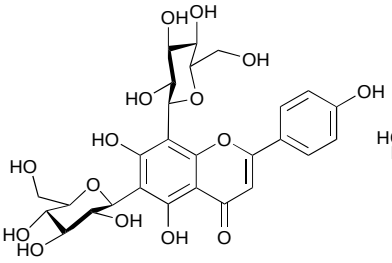

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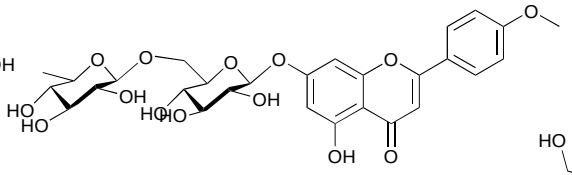

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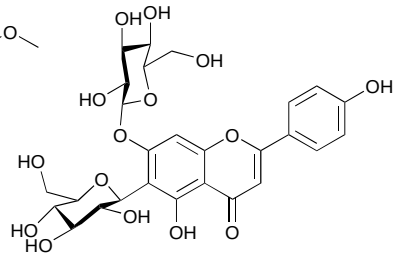

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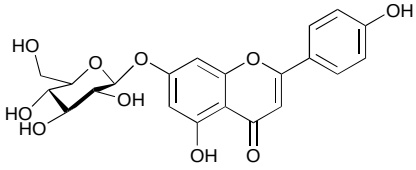

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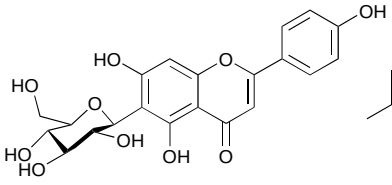

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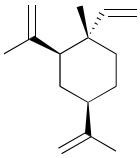

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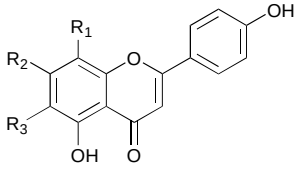

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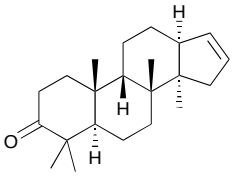

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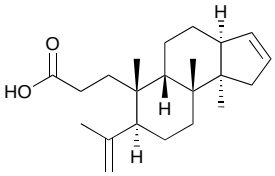

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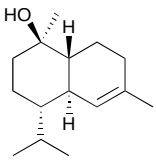

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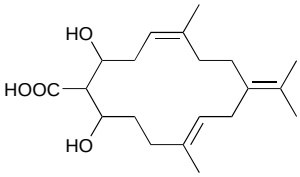

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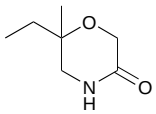

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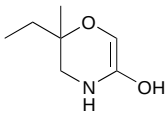

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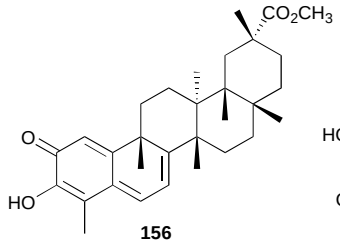

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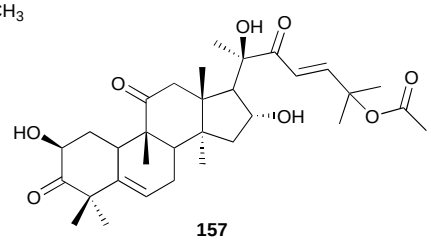

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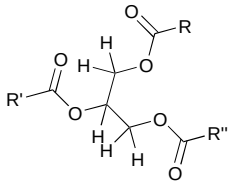

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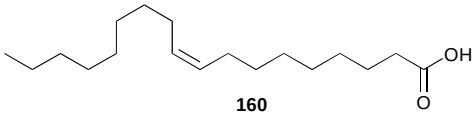

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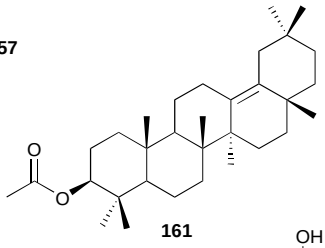

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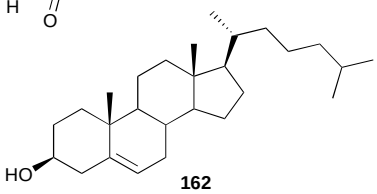

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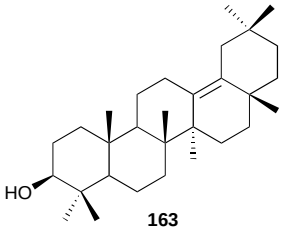

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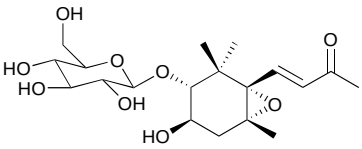

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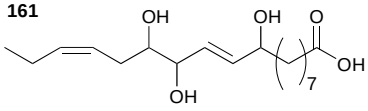

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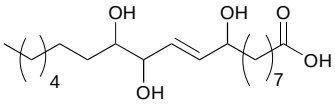

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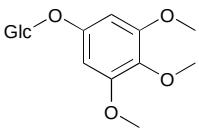

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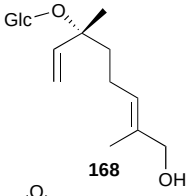

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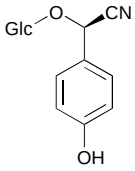

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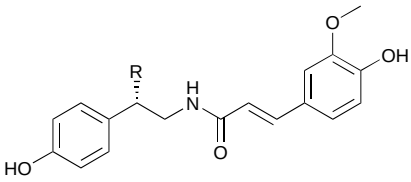
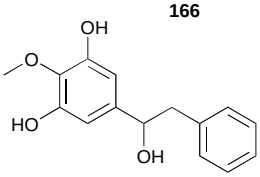


170: R = H, **171**: R = OH



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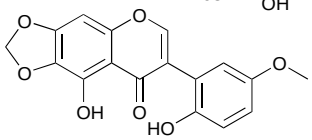

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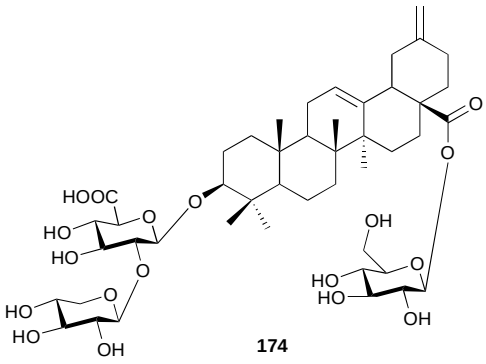

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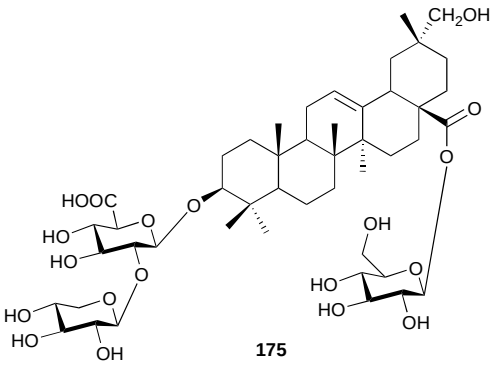

175

Table 1: Summary of ethnobotanical uses *versus* measured biological activities of isolated secondary metabolites from Aloaceae, Anacardiaceae and Apiaceae plant families

Plant family	Plant name (country)	Use in traditional medicine	Part of plant studied	Active principle	Measured activity	Author and Reference
Aloaceae (now Xanthorrhoeaceae-Asphodeloideae)	*Aloe vera* and *Aloe sinkatana* (Tunisia, Sudan)	Well known medicinal plants with diverse applications, in horticulture, medicine and commerce	Whole plant	**1** to **11**	inhibitory effects against glucose-induced advanced glycation end-products	Miladi *et al.*,[24] ELhassan *et al.*[25]
Anacardiaceae	*Schinus molle* (Saudi Arabia)	Traditionally used as a **repellent against house flies**, *Musca domestica*	fruits and leaves	**12**	**Insect repellent activity**	Abdel-Sattar *et al.*[30]
Apiaceae	*Daucus carota carota* (Tunisia)	Used traditionally for the treatment of hepatic and renal insufficiency as well as for skin disorders	roots	**13 -19**	antifungal activity	Ahmed *et al.*[35]
	Torilis radiata (Egypt)	Hepatoprotective	aerial parts	**26-32**	Diverse biological activities	Ezzat *et al.*[39]
	Pituranthos scoparius (Algeria)	Used in traditional medicine in the treatment of asthma and rheumatism and in **food as flavouring**.	aerial parts	**33-34**	**Antioxidant**, antibacterial, anticancer, antihistamic, and other biological effects	Dahia *et al.*[68]

Table 2: Summary of ethnobotanical uses versus measured biological activities of isolated secondary metabolites from Arecaceae, Asclepiadaceae and Asteraceae plant families.

Plant family	Plant name (Country)	Use in traditional medicine	Part of plant studied	Active principle	Measured activity	Author and Reference
Arecaceae	*Livistona australis* (Egypt)	To treat **tumors**	Leaves	**36**	Antioxidant, **cytotoxic**	Kassem *et al.*[70]
Asclepiadaceae	*Caloptropis procera* (Egypt)	Indigestion, stomach pains, **tumors**, snake bites, malaria, skin diseases, abdominal viscera, intestinal worms, dyspepsia	Vegetative stems	**51 -56, 57 - 60**	**Cytotoxicity**, **anticancer**	Shaker *et al.*,[71] Ibrahim *et al.*[75]
	Pergularia tomentosa (Algeria)	Skin diseases, bronchitis, tuberculosis, abortifacient, worms, scorpion bites, stomach pains, used as arrow poisons, used for tanning	Whole plant	**66 -67**	none	Babaamer *et al.*[76]
Asteraceae	*Artemisia herba-alba* (Algeria)	Tea preparations with components of this species have exhibited a number of therapeutic properties, including	Whole plant	**68-83**	Not determined	Laid[77]

		analgesic, antibacterial, anthelminthic and diuretic				
	Chiliadenus montanus (Egypt)	Renal problems, used as herbal tea	Aerial parts	**84 -91**	Antimicrobial	Hegazy *et al.*[78]
	Chrysanthemum macrocarpum (Algeria)	Inflammation, headache, ulcerative colitis, vertigo, **eye irritation**, hypertension, intestinal infections, scabies	Aerial parts	**103, 106**	**Antimicrobial**, anticancer	Boutaghane *et al.*[83]
	Gaillardia aristata (Egypt)	Used as a diuretic, to relieve painful urination	Leaves	**76, 77**	Cytotoxicity	Salama *et al.*[87]
	Wedelia prostrata (Egypt)	Kaurene diterpenes have shown antibiotic activity	Fresh young shoots		Not tested	Ahmed *et al.*[88]
	Conyza bonariensis (Tunisia)	Inflammation, vermifuge, diarrhoea, haemorrhoids, used as a diuretic	Leaves, stem, roots		Not tested	Mabrouk *et al.*[89]
	Centaurea nicaeensis (Algeria)		Aerial parts	**120**	Not tested	Hammoud *et al.*[90]
	Psiadia punctulata (Saudi Arabia)	Used in casts for broken bones	Leaves and stems			Abou-Zaid *et al.*[91]

Table 3: Summary of ethnobotanical uses *versus* measured biological activities of isolated secondary metabolites from Balantiaceae, Bignoniaceae, Bombacaceae and Burseraceae plant families

Plant family	Plant name	Use in traditional medicine	Part of plant studied	Active principle	Measured activity	Author and Reference
Balanitaceae	*Balanites aegyptiaca* (Mali)	Treatment of jaundice and diabetes	Stem bark	**131, 132**	Not tested	Sarker *et al.* [92]
Bignoniaceae	*Tabebuia argentea* (Mali)	Inflammation, influenza	leaves	**131**	Not tested	de Abreu *et al.*[93]
	Catalpa bignonioides (Egypt)	Whooping cough, asthma, asthmatic cough	petioles	**132**	Not tested	de Abreu *et al.* [93]
	Jacaranda mimosaefolia (Egypt)	Anti-malarial, antioxidant, anti-inflammatory, antisyphilitic astringent; veneral diseases	Stem bark	**135 - 137**	Not tested	Zaghloul *et al.* [95]
Bombacaceae (now Malvaceae-Bombacoideae)	*Bombax malabaricum* (Egypt)	Diuretic, demulcent, aphrodisiac, emetic; importance, enteritis, **dysentery**, lymphadenoma, menorrhagia,	Flowers	*n*-hexane, methanol extracts	Antioxidant, **antimicrobial**	El-Hagrassi *et al.*[100]

		hepatitis				
Burseraceae	*Commiphora molmol* (North Africa)	Insect repellent, **antiseptic**, anti-inflammatory; mouth and throat infections including gingivitis, tonsillitis and **mouth ulcers**.	Bark	**151 -154**, extract	**Antibacterial**	Rahman *et al*. [88]

Table 4: Summary of ethnobotanical uses versus measured biological activities of isolated secondary metabolites from Celasterceae, Chenopodiaceae, Cleomaceae, Cucurbitaceae and Cupresaceae plant families

Plant family	Plant name (Country)	Use in traditional medicine	Part of plant studied	Active principle	Measured activity	Author and Reference
Cleomaceae	*Cleome paradoxa* (Saudi Arabia)	Treatment of diabetes	Whole plant	**155, 156a, 156b**	Not tested	Azza R. Abdel-Monem[104]
Celastraceae	*Maytenus senegalensis* (Sudan)	Treatment of **malaria**	Root bark	**157**	**Antiplasmodial**, antileishmanial, cytotoxicity	Khalid *et al.*[106]
Cucurbitaceae	*Citrullus lanatus* var. *citroides* (Sudan)	Treatment of **rheumatism**, swelling, gout; used a laxative	Fruit pulp	**158**	**Anti-inflammatory**	Abdelwahab *et al.*[107]
	Citrullus colcoynthis (Tunisia)	Treatment of rheumatism, hypertension and **contagious infections.**	Roots, stems and leaves	Extracts	**Antibacterial**, anticandidal	Marzouk *et al.*[108]
	Cucurbita pepo (Egypt)	Treatment of diabetes, hypertension, tumor, immunomodulation; used as an **antibacterial**, antihypercholesterolemia, intestinal	Ripe fruit	Extracts	**Antimicrobia**, cytotoxicity	Badr *et al.*[109]

		antiparasitia, anti-inflammatory				
Chenopodiaceae	*Salsola tetranda* (Tunisia)	Members of this genus are used in folk medicine as antihypertensive and for the treatment of tapeworm infestations.	Aerial parts	**165 - 172**	Antibacterial	Oueslati *et al*. [110]
	Salsola tetranda (Tunisia)	Treatment of hypertension, tapeworm infestations	Roots	**173, 174**	Antioxidant	Beyaoui *et al*.[111]
	Salsola imbricate (Egypt)	Treatment of inflammations; used as a diuretic, an antioxidant and CNS depressant	Roots	**175, 176**	Not tested	Hamed *et al*.[112]
Cupressaceae	*Juniperus phoenicea* (Tunisia)	Treatment of cough; also used as a hypoglycaemic, an antiseptic and a diuretic	Berries (seeds)	**Extracts**	Antioxidant	Nasri *et al*.[113]