



# ARUM: A PLANT GENUS WITH GREAT MEDICINAL POTENTIAL

Abdullatif Azab<sup>[a,b]\*</sup>

**Keywords:** Arum, alkaloids, toxicity, anticancer, antibacterial, volatile amines

Plants belonging to the genus *Arum* are being used for nutritional and medicinal purposes for many centuries, despite their toxicity. Few subspecies of this genus were widely investigated by modern research, mainly for potential therapeutic goals and drug discovery. Other subspecies were never studied by current research despite the fact that some of them have known and well documented traditional medicinal and other uses. In this review article, we will present the traditional uses of this plant genus and summarize the published results of modern medicinal and other studies of these plants. Special attention will be drawn to effective, natural products that were isolated from these plants. The toxicity of the plants will be discussed extensively.

\* Corresponding Authors

E-Mail: [eastern.plants@gmail.com](mailto:eastern.plants@gmail.com); Tel: +972-(0)4-6357011

[a] Triangle Research & Development Center, Box 2167, Kfar-Qari, Israel 30075, Fax: +972-(0)4-6356168

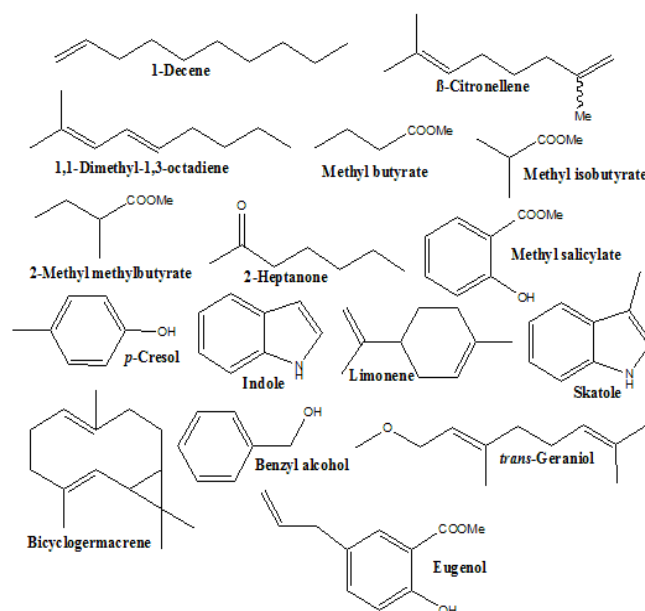
[b] Eastern Plants Company, Box 868, Arara, Israel 30026, Fax: +972-(0)4-6205906

## Introduction

The genus *Arum* (Araceae) is native to Asia, Europe, and northern Africa. The number subspecies of this genus is not definite: while some researchers consider 29 subspecies,<sup>1</sup> the "U.S. National Plant Germplasm System" counts 44.<sup>2</sup> However, the number of subspecies that have known (reported) traditional uses and were reported in current studies for biological/medicinal activities hardly exceeds two dozens. Archeological evidence indicate uses of *Arum* by humans since ancient times.<sup>3</sup>

*Arum* subspecies are well known for their *thermogenesis*.<sup>4</sup> This is to say that alteration of light and dark in the environment of the plant stimulates the primordia of the male plant to produce salicylic acid that triggers thermogenic reactions. For some subspecies like *A. italicum* and *A. maculatum*, the temperature of the flower can be higher by 15-25 °C than the surrounding air. This phenomenon is one of two major pollination strategies that aim to attract potential pollinators like insects. The other strategy is releasing a very strong odor that attracts insects. In most subspecies of *Arum*, this odor is foul (dung, *A. palaestinum*, *A. dioscoridis*, *A. elongated* and others) but in some subspecies, it can be from not perceptible (*A. jacquemontii*) to even pleasant (*A. gratum*).<sup>4</sup> In addition to many volatile amines that will be presented in next sections, many compound families are represented in these pollination odors.<sup>4,5</sup> Some important compounds are shown in Figure 1.

Detailed study of the floral odor of *A. italicum* was published earlier in 2004, where several methods of isolation and trapping volatile compounds were used.<sup>6</sup> In this study, very similar results were obtained comparing with the previously cited publications (4,5), and only stereochemical and structural isomerization can be noticed, comparing with the compounds shown in Figure 1.



**Figure 1.** Major compounds that compose the pollination odors of *Arum* subspecies

## Traditional uses of *Arum* subspecies

Most listed subspecies of *Arum* have no documented traditional uses. Most of this group was not reported by modern research studies as well. But scanning the literature of *Arum* traditional uses reveals two significant findings:

a) The vast majority of documented traditional users are aware of the *toxicity* of these plants and in

Most texts this property is mentioned and potential users are explicitly warned. Modern research approved this as shown in below (discussion).

b) It is notable that the most important traditional uses of *Arum* are for nutritional purposes then by medicinal use as an anticancer agent. This using field is also in agreement with current research results.

**Table 1.** Traditional uses of *Arum* subspecies

<i>Arum</i> subspecies	Country/Region	Used parts	Uses; Administration (References)
<i>A. balansanum</i>	Bulgaria	Tubers	Against haemorrhoids, direct contact <sup>7</sup>
<i>A. conophalloides</i>	Iran	Leaves	Food, flavor, elimination of seasonal allergies <sup>8</sup>
	Turkey	Leaves	Food ( <i>Srama</i> ) <sup>9</sup>
<i>A. cyrenaicum</i>	Libya	Corms	Food, ornaments <sup>10</sup>
<i>A. detruncatum</i>	Bulgaria	Tubers	Against hemorrhoids, direct contact <sup>7</sup>
	Turkey	Leaf/Root	Anti-diarrhea, kidney stones, stomachic; infusion (internal)/ Antidiabetic; decoction (internal) <sup>11</sup>
<i>A. dioscorides</i>	India	Stems	Boils rure; aqueous extract, direct contact <sup>12</sup>
	Jordan	Leaves	Anticancer; decoction <sup>13</sup>
	Palestine	NS*	Cancer, prostate disorders <sup>14</sup>
	Palestine	Leaves	Anticancer: liver, stomach; decoction (detailed) <sup>15</sup>
	Turkey	Leaves	Food ( <i>Srama</i> ) <sup>9</sup>
	Turkey	Roots, flowers	Treatment of inflamed wounds; poultice, to cure hemorrhoids; direct contact <sup>16</sup>
<i>A. elongatum</i>	Bulgaria	Tubers	Against hemorrhoids, direct contact <sup>7</sup>
	Turkey	Leaves	Abdominal pain, antihypertensive, antidiabetic, rheumatism; infusion, compress or drink <sup>17</sup>
<i>A. italicum</i>	Turkey	Tuber	Haemorrhoids; tubers is crushed to powder and consumed <sup>18</sup>
	Iraq	Leaves	Food <sup>19</sup>
	Italy	Leaves	Anti-warts; topical application <sup>20,25</sup>
	Italy	Tubers, leaves	Food for pigs <sup>21,22</sup>
	Italy	Rhizomes	To heal contusions; pieces are locally applied <sup>23</sup>
	Italy	NS	Vesicatory, treatment of CNS disorders; NS <sup>24</sup>
	Italy	Leaves, rhizomes	Rheumatic pains; leaves and rhizomes macerated in oil <sup>26</sup>
	Italy	Tubers, leaves	Against warts, rheumatic pains <sup>7</sup>
	Slavic culture (Italy)	Leaves, tubers	Food, unclear; NS <sup>27</sup>
	Spain	Leaves, tubers	Skin, muscles, skeleton; very detailed <sup>28</sup>
	Spain	Spathe	Ludic; NS <sup>29</sup>
	Tunisia	NS	Vesicatory, treatment of CNS disorders; NS <sup>24</sup>
	Turkey	Flowers/Tubers/ Tubers & fruits	Hemorrhoids; decoction/Women diseases, cancer, eczema; decoction, decoction, consumed/ hemorrhoids; consumed <sup>30</sup>
	Turkey	Tubers	Treatment of hemorrhoid, expectorant; infusion <sup>31</sup>
	Turkey	Leaves	Food (soup); boiled <sup>32</sup>
	Turkey	Tubers/aerial parts	Treat hemorrhoid; crushed, direct contact/ hepatitis, muscle pain; crushed, decoction <sup>33</sup>
	<i>A. hygrophilum</i>	Turkey	Tubers
Jordan		Leaves	Anticancer; decoction <sup>13</sup>
<i>A. maculatum</i>	Bulgaria	Tubers	Against haemorrhoids, direct contact <sup>7</sup>
	Czech Republic	Rhizomes	Food; boiled <sup>35</sup>
	Europe	NS	Antimalarial; NS <sup>36</sup>
	Iraq	Leaves	Treat intestinal worms, rheumatism; decoction <sup>37</sup>
	Italy	NS	NS; NS <sup>38</sup>
	Turkey	NS	Anti colitic, abortive; NS <sup>39</sup>
	Turkey	Corms	Treat hemorrhoids; crushed and swallowed <sup>40</sup>
	Turkey	Leaves	Food; eaten fresh in salads <sup>41</sup>
	Turkey	Leaves	Food ( <i>Srama</i> ); cooking stuffed leaves <sup>9</sup>
<i>A. palaestinum</i>	Greco-Arab region	Leaves	Anticancer, urinary disorders; NS <sup>42</sup>
	Greco-Arab region	Leaves	Anticancer (especially colon), internal bacterial infections, poisoning, disturbances of the circulatory system.; cooking <sup>43</sup>
	Islamic-Arab region	NS	Anticancer; NS, but modern results presented <sup>44</sup>
	Jordan	Leaves	Anticancer; decoction <sup>13</sup>
	Jordan	Leaves	Anticancer; cooked with onion and salt <sup>45</sup>
	Lebanon	Leaves	Rheumatism; decoction, maceration <sup>46</sup>

.Table 1 cont			
	Middle-East	NS	Anticancer; NS, links modern research <sup>47</sup>
	Middle-East	NS	Anticancer; NS, links to modern homeopathy <sup>48</sup>
	Palestine	Leaves, flowers	Internal bacterial infection, cancer, poisoning, circulatory system; decoction (detailed) <sup>49</sup>
	Palestine	NS	Anticancer; NS <sup>50</sup>
	Palestine	Leaves	Food; detailed procedure <sup>51</sup>
	Palestine	Leaves	Anticancer: liver, colon, kidney, breast; decoction (detailed) <sup>15</sup>
NS	Turkey	Roots/flowers	Rheumatism; pounded/ treat oxyuris; NS <sup>52</sup>

\*NS, Not specified

In Table 1, we summarize the traditional uses of *Arum*, arranged by regions/countries. Roots and fruits of the plants are very toxic, so it's highly recommended to pay attention to the plant parts used.

### Modern research reports of *Arum* subspecies

Many *Arum* subspecies were studied so far, where the most investigated are *A. dioscorides*, *A. maculatum*, and *A. palaestinum*. It is interesting to see that unlike other plant families that are used by humans for millenia, modern research of *Arum* started just little more than three decades ago, while other plant families are being studied for much longer periods of time. Many medicinal and other biological activities of *Arum* plants were reported. In Table 2 a summary of these reports is presented.

## Discussion

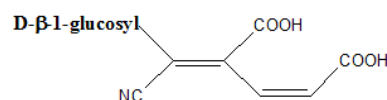
*Arum* subspecies are known and used by humans since ancient times. But new subspecies are still identified once in a while. *Arum megobrebi* was identified and classified as wild subspecies of *Arum* that grows in Turkey and Georgia.<sup>107</sup>

Reading data in Tables 1 and 2 reveals a wide variety of activities of the genus *Arum*. But it is crucial to notice that many *Arum* subspecies were never mentioned for traditional uses or reported by recent research publications. These include *A. alpinariae*, *A. besserianum*, *A. byzantinum*, *A. concinatum*, *A. cylindraceum*, *A. gratum*, *A. hainesii*, *A. jacquemontii*, *A. lucanum*, *A. megobrebi*, *A. pictum*, *A. purpureospathum*, *A. rupicola*, *A. sintenisii*. It is evident as well that modern research has studied (so far) more *Arum* subspecies than those that were documented as having traditional uses. Most investigated subspecies is *A. palaestinum*.

It is interesting to pay attention to *A. cyrenaicum*, an endemic subspecies that grows wild only in Libya. In reference 8, authors report two traditional uses of this plant (food and ornaments), and it is interesting to notice that the used parts are corms, not leaves, contrary to most *Arum* subspecies, where corms are highly toxic. But these authors have mistakenly classified this plant into the Poaceae family, while the correct classification is in the Araceae family.<sup>55</sup>

One of the most important properties of *Arum* that was consistently mentioned by traditional users and approved by modern research is the toxicity of these plants. Despite being recommended for use as food and medicine, the toxicity of *Arum* is indicated in most texts.<sup>108</sup> Modern reports rank *Arum* subspecies as one of the most important causes of children poisoning in Brazil.<sup>109</sup> Among these, *A. italicum* is responsible for the largest number of poisoning cases, and all parts of the plant are toxic.

Toxicity of *Arum* subspecies results from several single compounds or compound families. Calcium oxalate is one of the primary toxic compounds in *Arum* plants,<sup>55</sup> but it decomposes with cooking. The same occurs to cyano glycosides such as triglochinin,<sup>76</sup> a toxic compound present in *Arum*, that its structure is shown in **Figure 2**



**Figure 2.** Structure of triglochinin

Among reported *Arum* subspecies in the toxic context, *A. maculatum* is the most published by current research publications so far. One of the earliest reports was published in 1861, and it presents some poisoning cases.<sup>110</sup> Part of this toxicity is due to the presence of toxic odorants, especially volatile amines.<sup>111</sup> In addition to oxalates and cyano compounds, the toxicity of *A. maculatum* is intensified by alkaloids and saponins.<sup>112</sup> The orange-colored fruits of *A. maculatum* are very attractive yet very poisonous, and they are responsible for most poisoning events caused by this plant.<sup>113</sup> The toxicity of *A. palaestinum* is also known and published: ethanolic extract of the plant was found toxic to the liver of female rats.<sup>114</sup> Despite that, unlike other natural, plant-derived anticancer therapies, *A. palaestinum* has no herb-drug contradictions with synthetic drugs.<sup>115</sup>

An interesting modern research report presented in **Table 2** is about *A. Conophalloides*.<sup>54</sup> All 18 compounds identified in the essential oil of this plant do not contain nitrogen. No amines or alkaloids. This situation can be understood from two reasons: nitrogen containing compounds, especially amines are volatile and alkaloids are not volatile and mostly water soluble, so they are not present in the essential oil that contains mainly hydrophobic compounds.

**Table 2.** Overview of modern research finding of *Arum* studies

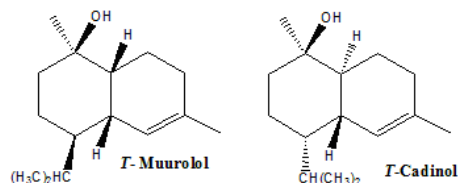
<i>Arum</i> subspecies	Activity/property	Major findings (References)
<i>A. apulum</i>	Odor components	Traces of indole, terpinolene <sup>53</sup>
<i>A. creticum</i>	Odor components	Presence of benzaldehyde, benzyl alcohol, indole <sup>53</sup>
<i>A. Conophalloides</i>	Essential oil	18 Compounds were found including (>5%): nonanal, $\beta$ -ionone, <i>T</i> -cadinol, <i>T</i> -muurolol, fitone, methyl palmitate <sup>54</sup>
<i>A. cyrenaicum</i>	Odor components Antioxidant, toxicity	Traces of indole <sup>53</sup> Moderate antioxidant activity (DPPH), toxicity is a result of the presence of calcium oxalate and cyanogenic glycosides <sup>55</sup>
<i>A. dioscorides</i>	Flowering amines Antilipoperoxidation Fatty acids in seeds Antioxidant, composition Antimicrobial Antibacterial Minerals content Antioxidant Enzyme inhibition Antioxidant activity	Methylamine, skatole <sup>56</sup> Both aqueous and methanolic extracts showed moderate antioxidant capacity <sup>57</sup> Methanolic and acetone extracts were prepared and their antioxidant capacities were tested by three methods. Methanolic extract showed higher capacity and its full fatty acid composition is presented <sup>58</sup> Three extracts were prepared and their antioxidant capacities (DPPH) were tested. Methanolic was highest and contained highest number (5) of tested antioxidants <sup>59</sup> Four extracts were prepared: water, ethanol, methanol and acetone. Testing against 6 microbes showed that aqueous extract was most active <sup>60</sup> Ethanol extract was tested against 6 bacteria types: weak <sup>61</sup> Magnesium, 24.6 g/Kg, sulfur 39.4 (cites other studies) <sup>62</sup> Four extracts (water, ethanol, methanol, acetone) were prepared and tested for reducing power (ferric, ethanol highest) and scavenging of DPPH (methanolic highest) <sup>63</sup> Ethanol and aqueous extracts were tested for <i>in vivo</i> and <i>in vitro</i> enzyme inhibition. Both were active as inhibitors of gastrointestinal enzymes involved in carbohydrate and lipid digestion and absorption <sup>64</sup> Methanolic and aqueous extracts were prepared, analyzed for phenolic content and tested for antioxidant activity. Methanolic extract was more active <sup>65</sup>
<i>A. elongatum</i>	Chemical composition Antioxidant activity	Minerals were quantified. Iron highest (134 mg/Kg) <sup>66</sup> Methanolic and aqueous extracts were prepared, analyzed for phenolic content and tested for antioxidant activity. Methanolic extract was more active <sup>65</sup>
<i>A. euxinum</i>	Macroelement content Antibacterial	Macroelement (N, P, K) content was quantified during different growth phases. Various localities were also tested <sup>67</sup> Aqueous, ethanol and methanolic extracts were tested for antibacterial activity: ethanol>methanolic. Aqueous inactive <sup>68</sup>
<i>A. hygrophilum</i>	Antimicrobial Antimicrobial Antioxidant activity	95% Ethanol-water extract was tested for antimicrobial activity: active against some species and inactive against others <sup>69</sup> Four extracts were prepared: water, ethanol, methanol and acetone. Testing against 6 microbes showed only methanolic and ethanol extracts were active just against <i>C. albicans</i> <sup>60</sup> Methanolic and aqueous extracts were prepared, analyzed for phenolic content and tested for antioxidant activity. Methanolic extract was more active <sup>65</sup>
<i>A. idaeum</i>	Odor components	Presence of benzaldehyde, benzyl alcohol, nonanal <sup>53</sup>

<i>.Table 2 cont</i>		
<i>A. italicum</i>	Flowering amines	Isobutylamine, diethylamine, ethylamine, dimethylamine, methylamine, 2-aminoethanol, 1,2-propanediamine, 1,6-hexanediamine, agmatine, cadaverine, histamine, putrescine <sup>56</sup>
	Hydroperoxysterols	In addition to known sterols and hydroperoxysterols, 6 new of the second class were isolated and characterized <sup>70</sup>
	Carotenoids	Ethanol extract of the fruits was prepared during maturation and ripening stages. 18 different carotenoids were isolated and identified, along with chlorophyll precursor ( <i>cis</i> -OH-phytoene), chlorophylls A and B, and chlorophyll-like, pheophytin <sup>71</sup>
	Accumulation of metals	Among 13 plant species, <i>A. italicum</i> was best accumulator of Zn <sup>+2</sup> , Cd <sup>+2</sup> and Cu <sup>+2</sup> . It was not successful with Pb <sup>+2</sup> . This suggests a bioremediation method of contaminated soils <sup>72</sup>
	Fatty acids in seeds	Essential oil of the plant was isolated and fatty acids were methylated (esters, BF <sub>3</sub> /MeOH), isolated and analyzed. 21 acids were found from caprylic (C8:0) to legnocerac (C24:0) <sup>73</sup>
<i>A. korolkowii</i>	Lipids in tubers	Hydrophobic compounds were isolated by column chromatography. Composition is reported by groups <sup>74</sup>
<i>A. maculatum</i>	Odor components	Presence of indole, nonanal, $\alpha$ -pinene, $\beta$ -pinene, tepinolene, $\alpha$ -Copaene <sup>53</sup>
	Unsaponifiable lipids	Spadices were treated with concentrated base and the hydrosylate was extracted with ether, resulting long chain hydrocarbons, long chain alcohols and carotenoids <sup>75</sup>
	Triglochinin in spathes	The toxic cyanoglycoside was isolated and identified <sup>76</sup>
	Fatty acids contents	Fatty acids of seed oil were isolated by picolinyl esterification and purification. In addition to medium chain acids (C14:0), acids with aromatic residues (including pyridyl) were detected <sup>77</sup>
	Pro-inflammatory	A monocot lectin (ptotein) was isolated from the tubers of the plant. It acts as agglutinin and has pro-inflammatory activity <sup>78</sup>
	Insecticidal	Mannose binding lectin was isolated from the tubers. It binds to the glycosylated insect gut receptors <sup>79</sup>
	Cytogenetic	Aqueous extract inhibited cell mitosis of bone marrow of mice <sup>80</sup>
	Antioxidant capacity of food	Antioxidant capacity of leaves were tested in three forms: fresh, powder and stored. All forms showed similar capacities <sup>81</sup>
	Analgesic	Aqueous extract analgesic activity was compared with that of declofenac-Na and morphine. It was more active than the first and had similar activity of the second <sup>82</sup>
	Antibacterial	Ethanol extract tested against 7 types of bacteria: weak <sup>83</sup>
Antibacterial	Four extracts (petroleum ether, chloroform, ethyl acetate and 70% methanol) of aerial parts were tested against two bacteria. Hydromethanolic extract showed high activity <sup>84</sup>	
Antioxidant	Methanolic extract of whole plant was by DPPH assay and found very active, even more than ascorbic acid <sup>85</sup>	
Essential oil, antibacterial, antioxidant	Essential oil was tested for antibacterial (3 bacteria) and antioxidant (DPPH) activities. Composition found: palmitic acid 23.31 %, phytol 13.02 %, methyl 9,12,15-octadecatrienoate 10.34 %, methyl linolenate 8.64 % <sup>86</sup>	
<i>A. nigrum</i>	Odor components	Presence of indole <sup>53</sup>
<i>A. orientale</i>	Glucomannan	Major glucomannan (with other minor polysaccharides) was isolated from the tubers. It is composed of D-glucose and o-mannose (2: 3.1), and traces of uronic acid <sup>87</sup>
<i>A. palaestinum</i>	Isoorientin	Isoorientin (luteolin 6-C-glucoside) that was isolated by soaking aerial parts in ethanol, then partitioned and chromatographed. The compound myolytic activity on smooth muscle-containing preparations from the rat and the guinea-pig <sup>88</sup>
	Piperazirum	Piperazirum was isolated and characterized as a novel alkaloid (1 in Figure 6 in the discussion section) <sup>89</sup>

.. Table 2 cont

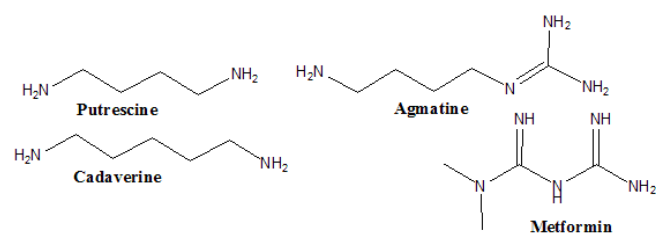
<i>A. palaestinum</i>	New Alkaloid	(S)-3,4,5-trihydroxy-1H-pyrrol-2(5H)-one (2 in Figure 6) was isolated from the aqueous extract and characterized. The ethyl acetate extract showed strong antioxidant and sufficient anticancer activities <sup>90</sup>
	Antioxidant, antidiabetic	Aqueous and methanolic extracts were prepared and tested for antioxidant activity (DPPH): moderate. This result is in agreement with total phenolics content and antidiabetic traditional use <sup>91</sup>
	Anticancer modern herbal medicine	Aerial parts, especially leaves are used as anticancer agents in modern herbal Palestinian medicine. It is used raw, cooked (food) or as a decoction <sup>92</sup>
	Anticancer, antioxidant	Aqueous and ethanolic extracts were tested for anticancer and antioxidant activities. Anticancer was very strong (aqueous >> ethanolic), antioxidant was weak (aqueous > ethanolic) <sup>93</sup>
	Diketopiperazines	Two new alkaloids were isolated from the aqueous extract and characterized. Only 3 in Figure 6 showed cytotoxic activity <sup>94</sup>
	Antimicrobial	70% Aqueous ethanol extract was tested for antibacterial activity against six types of bacteria (weak), and for antidermatophyte activity (2 fungi): moderate <sup>95</sup>
	Phenolics, protein	70% Aqueous methanol extract was analyzed for proteins and phenolics <sup>96</sup>
	Phthalates	Three phthalates isolated from ethanolic extract: Diisobutyl phthalate, di-n-propyl phthalate, di-n-octyl phthalate <sup>97</sup>
	Antioxidant, antitumor	Ethanolic extract was tested for antioxidant activity: moderate. The title of this publication include <i>in vitro</i> antitumor testing but this does not exist in the article <sup>98</sup>
	Phenolics	Phenolic extract was analyzed for phenolic compounds <sup>99</sup>
	Metabolites of leaves	Comprehensive metabolite profiling of Arum liquid chromatography–tandem mass spectrometry (UHPLC–DAD–ESI–MS/MS) revealed 191 compounds, with detailed analysis of selected entries <sup>100</sup>
	Partial composition and antioxidant	Concentrations of minerals, phenolic and anthocyanins were determined, and antioxidant (DPPH) capacity of methanolic extract of leaves was tested (high) <sup>101</sup>
	Cytotoxic	Ethereal and ethyl acetate extracts as well as four flavonoids isolated from the plant, showed significant antiproliferative activity <sup>102</sup>
	Antioxidant, Anti-inflammatory, Anti-diarrheal	Ethanolic extract was prepared from the plant along with other plants. Total phenolic was determined (low), antioxidant capacity (DPPH, moderate), anti-inflammatory (moderate) and anti-diarrheal (inactive) <sup>103</sup>
	Locality influence on content	Leaves of the plant from different localities in Palestine were extracted by various methods. The results show clear variations <sup>104</sup>
	Anticancer (prostate), fortified extract	Aqueous extract with/without isovanillin, linolenic acid and $\beta$ -sitosterol was tested for anticancer activity. These compounds have significantly fortified the activity <sup>105</sup>
	Endangered plant	This mini-review presents the latest publications of the medicinal activities of the plant and classify it as endangered. This might be true in some regions, however, this is not the case in Israel <sup>106</sup>
	Enzyme inhibition	Ethanolic and aqueous extracts were tested for <i>in vivo</i> and <i>in vitro</i> enzyme inhibition. Both were active as inhibitors of gastrointestinal enzymes involved in carbohydrate and lipid digestion and absorption <sup>64</sup>
	Antioxidant activity	Methanolic and aqueous extracts were prepared, analyzed for phenolic content and tested for antioxidant activity. Methanolic extract was more active <sup>65</sup>

Two of the major (>5%) compounds are both chemically and biologically interesting. These are the structurally isomeric alcohols *T*-cadinol (8.9% in the essential oil of *A. Conophalloides*) and *T*-muurolol (24.4%). Their structures are shown in **Figure 3**.



**Figure 3.** Structures of *T*-cadinol and *T*-muurolol

These compounds have many biological activities such as antibacterial of *T*-cadinol.<sup>116</sup> They are present in relatively high concentrations, and it might be useful to try to isolate them from other subspecies of *Arum*.



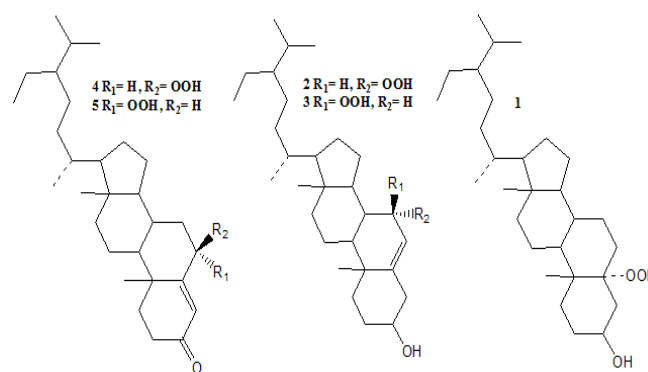
**Figure 4.** Selected flowering amines of *A. italicum* and metformin

*A. italicum* produces a wide variety of amines during the flowering season.<sup>56</sup> Some of these amines are very interesting regarding the number of nitrogen atoms that they contain. In **Figure 4**, the structures of three of these amines are shown (with metformin).

The structures of agmatine and metformin are relatively close. Metformin is very well known synthetic antidiabetic drug, and the great medicinal potential and activities of agmatine are being studied, including antidiabetic activity,<sup>117</sup> but this research must be expanded.

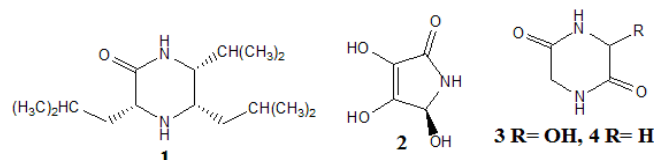
Antibacterial and antimicrobial activities are tested for almost every studied medicinal plant. In the case of *Arum* subspecies, some were reported, and these reports are not consistent. Even after taking into account the different subspecies, various parts of the plants that were extracted and the various solvents that were used, the overall reporting is confusing and even contradicting.<sup>60,61,68,69,83,84,95</sup> For example, M. Obeidat *et al.*<sup>60</sup> reported that they tested four extracts (water, ethanol, methanol and acetone) and found the aqueous extract most active. On the contrary, A. Ucar Turker and her colleagues,<sup>68</sup> used aqueous, ethanolic and methanolic extracts, and the aqueous extract was inactive.

In 1994, M. Della Greca *et al.* isolated and characterized phytosterols and hydroperoxy sterols from *A. italicum*, where some were new.<sup>70</sup> Despite the fact that similar compounds were isolated from other plants and marine animals,<sup>118</sup> and proved to have significant biological activities, a follow-up study was never reported. It is worth trying to find this compound family in other *Arum* subspecies, characterize them and test them for biological activities, especially antimicrobial and antifungal activities. The presence of the peroxy group ensures oxidant activity, while the entire compound is hydrophobic and can penetrate the lipophilic membranes of microbes and fungi. The structures of the new hydroperoxy sterols that were reported by M. Della Greca *et al.* are presented in **Figure 5**.



**Figure 5.** Structures of new hydroperoxy sterols reported in reference 70

Alkaloids are the major compound family in *Arum* subspecies. Their toxic and psychoactive influence affected users of this genus since very ancient times. But the isolation and characterization of these compounds from *Arum* started relatively late.<sup>89</sup> The polyhydroxy alkaloid that was isolated in the same year,<sup>90</sup> provides an interesting starting material for synthetic purposes. Two other new alkaloids were reported later, and they have even simpler structures. *Arum* subspecies can be the natural source for such heterocyclic alkaloids. See **Figure 6**.



**Figure 6.** Selected alkaloids isolated from *Arum* subspecies

Reading the papers of M. M. Farid *et al.*<sup>96</sup> of K. I. Ereifej *et al.*<sup>99</sup> reveals some confusion regarding the presence of caffeic acid in *A. palaestinum*. The first reports that it is present, while the second clearly indicated (ND) that it is not. But studying other reports show that this compound is present in *A. palaestinum*, and many of its derivatives.<sup>90,100</sup>

In the same sense, it is not clear why M. M. Farid *et al.*<sup>102</sup> claim that isovitexin was "isolated (by them) for the first time from the studied taxa," while they reported the isolation of the same compound in one of their earlier works.<sup>96</sup>

## Conclusions

1) Many subspecies of the genus *Arum* were never studied, which is a very vast field of future potential research.

2) It is important to invest more research in nitrogen containing compounds of *Arum* subspecies. The structures of the known compounds so far (very few ssp.) indicate a high potential for antidiabetic activity, which might result from a single compound or synergy of several compounds.

3) Antibacterial activities of *Arum* subspecies need further studies and organization.

4) Some activities like the antidiabetic potential of *Arum* were hardly investigated. There is an urgent need to expand the research of these activities.

5) Very few attempts were made so far to prepare synthetic modifications of active natural products isolated from *Arum* which could be intensified.

## References

- <sup>1</sup>Linz, J., Stokl, J., Urru, I., Krugel, T., Marcus C. Stensmyr, M. C., Hansson, B. S., *Taxon*, **2010**, *59*, 405.
- <sup>2</sup> U.S. National Plant Germplasm System: <https://npgsweb.ars-grin.gov/gringlobal/taxon/taxonomysimple.aspx>
- <sup>3</sup>Espindola, A., Buerki, S., Bedalov, M., Kupfer, P., Alvarez, N., *Bot. J. Linn. Soc.*, **2010**, *163*, 14. <https://doi.org/10.1111/j.1095-8339.2010.01049.x>
- <sup>4</sup>Gibernau, M., Macquart, D., Przetak, G., *Aroideana*, **2004**, *27*, 148.
- <sup>5</sup>Urru, I., Stokl, J., Linz, J., Krugel, T., Stensmyr, M. C., Hansson, B. S., *Biol. J. Linn. Soc.*, **2010**, *101*, 991. <https://doi.org/10.1111/j.1095-8312.2010.01537.x>
- <sup>6</sup>Gibernau, M., Favre, C., Talou, T., Raynaud, C., *Aroideana*, **2004**, *27*, 142.
- <sup>7</sup>Kochmarov, V., Kozuharova, E., Naychov, Z., Momekov, G., Mincheva, I., *Int. J. Pharm. Chem. Biol. Sci.*, **2015**, *5*, 394.
- <sup>8</sup>Mohammadi, H., Sajjadi, S-E., Noroozi, M., Mirhosseini, M., *J. Herb. Med. Pharm.*, **2016**, *5*, 54.
- <sup>9</sup>Dogan, Y., Nedelcheva, A., Luczaj, L., Drăgulescu, C., Gjoshe Stefkov, G., Maglajlic, A., Ferrier, J., Papp, N., Hajdari, A., Behxhet Mustafa, B., Zora Dajic-Stevanovic, Z., Pieroni, A., *J. Ethnobiol. Ethnomed.*, **2015**, *11*, 26. <https://doi.org/10.1186/s13002-015-0002-x>
- <sup>10</sup>El-Darier, S. M., El-Mogaspi, F. M., *World J. Agric. Sci.*, **2009**, *5*, 353.
- <sup>11</sup>Altundag, E., Ozturk, M., *Proc. Social Behav. Sci.*, **2011**, *19*, 756. <https://doi.org/10.1016/j.sbspro.2011.05.195>
- <sup>12</sup>Sajem, A. L., Gosai, K., *J. Ethnobiol. Ethnomed.*, **2006**, *2*, 33. <https://doi.org/10.1186/1746-4269-2-33>
- <sup>13</sup>Afifi-Yazar, F. U., Kasabri, V., Abu-Dahab, R., *Planta Med.*, **2011**, *77*, 1203. <https://doi.org/10.1055/s-0030-1270832>
- <sup>14</sup>Ali-Shtayeh, M. S., Yaniv, Z., Mahajna, J., *J. Ethnopharmacol.*, **2000**, *73*, 221. [https://doi.org/10.1016/s0378-8741\(00\)00316-0](https://doi.org/10.1016/s0378-8741(00)00316-0)
- <sup>15</sup>Jaradat, N. A., Al-Ramahi, R., Zaid, A., Ayeshe, O. I., Eid, A. M., *BMC Complement. Altern. Med.*, **2016**, *16*, 12. DOI [10.1186/s12906-016-1070-8](https://doi.org/10.1186/s12906-016-1070-8)
- <sup>16</sup>Ozhatay, N., Kocak, S., *J. Fac. Pharm. Istanbul Univ.*, **2011**, *41*, 75.
- <sup>17</sup>Polat, R., Cakilcioglu, U., Satıl, F., *J. Ethnopharmacol.*, **2013**, *148*, 951. <https://doi.org/10.1016/j.jep.2013.05.050>
- <sup>18</sup>Ari, S., Temel, M., Kargioglu, M., Konuk, M., *J. Ethnobiol. Ethnomed.*, **2015**, *11*, 84. <https://doi.org/10.1186/s13002-015-0067-6>
- <sup>19</sup>Ahmad, S. A., Askari, A. A., *Harvard Papers in Botany*, **2015**, *20*, 85. <https://doi.org/10.3100/hpib.v20iss1.2015.n8>
- <sup>20</sup>Pieroni, A., Quave, C. L., Santoro, R. F., *J. Ethnopharmacol.*, **2004**, *95*, 373. <https://doi.org/10.1016/j.jep.2004.08.012>
- <sup>21</sup>Guarrera, P. M., Forti, G., Marignoli, S., *J. Ethnopharmacol.*, **2005**, *96*, 429. <https://doi.org/10.1016/j.jep.2004.09.014>
- <sup>22</sup>Guarrera, P. M., Giovanni Salerno, G., Caneva, G., *J. Ethnobiol. Ethnomed.*, **2006**, *2*, 37. <https://doi.org/10.1186/1746-4269-2-37>
- <sup>23</sup>De Natale, A., Pollio, A., *J. Ethnopharmacol.*, **2007**, *109*, 295. <https://doi.org/10.1016/j.jep.2006.07.038>
- <sup>24</sup>Leporatti, M. L., Ghedira, K., *J. Ethnobiol. Ethnomed.*, **2009**, *5*, 31. <https://doi.org/10.1186/1746-4269-5-31>
- <sup>25</sup>Montesano, V., Negro, D., Sarli, G., De Lisi, A., Gaetano Laghetti, G., Hammer, K., *J. Ethnobiol. Ethnomed.*, **2012**, *8*, 15. <https://doi.org/10.1186/1746-4269-8-15>
- <sup>26</sup>Leto, C., Tuttolomondo, T., Le Bella, S., Licata, M., *J. Ethnopharmacol.*, **2013**, *146*, 90. <https://doi.org/10.1016/j.jep.2012.11.042>
- <sup>27</sup>di Tizio, A., Luczaj, L. J., Quave, C. L., Redzic, S., Pieroni, A., *J. Ethnobiol. Ethnomed.*, **2012**, *8*, 21. <https://doi.org/10.1186/1746-4269-8-21>
- <sup>28</sup>Menendez-Baceta, G., Aceituno-Mata, L., Molina, M., Reyes-García, V., Tardío, J., Pardo-de-Santayana, M., *J. Ethnopharmacol.*, **2014**, *152*, 113. <https://doi.org/10.1016/j.jep.2013.12.038>
- <sup>29</sup>Gras, A., Garnatje, T., Bonet, M. A., Carrio, E., Mayans, M., Parada, M., Rigat, M., Valles, J., *J. Ethnobiol. Ethnomed.*, **2016**, *12*, 23. <https://doi.org/10.1186/s13002-016-0097-8>
- <sup>30</sup>Genc, G. E., Ozhatay, N., *Turk. J. Pharm. Sci.*, **2006**, *3*, 73.
- <sup>31</sup>Fakir, H., Korkmaz, M., Guller, B., *J. Appl. Biol. Sci.*, **2009**, *3*, 33.
- <sup>32</sup>Kizilarlan, C., Ozhatay, N., *Marmara Pharm. J.*, **2012**, *16*, 194. <https://doi.org/10.12991/201216398>
- <sup>33</sup>Sagiroglu, M., Topuz, T., Ceylan, K., Turna, M., *SAÜ Fen Edebiyat Dergisi*, **2013**, *11*, 13.
- <sup>34</sup>Akbulut, S., Ozkan, Z. C., *J. Forestry Fac., Kastamonu Univ.*, **2014**, *14*, 135. <https://doi.org/10.17475/kuofd.48636>
- <sup>35</sup>Simkova, K., Polensy, Z., *J. Appl. Botany Food Qual.*, **2015**, *88*, 49.
- <sup>36</sup>Adams, M., Alther, W., Kessler, M., Kluge, M., Hamburger, M., *J. Ethnopharmacol.*, **2011**, *133*, 278. <https://doi.org/10.1016/j.jep.2010.10.060>
- <sup>37</sup>Ahmed, H. M., *J. Ethnobiol. Ethnomed.*, **2016**, *12*, 8.
- <sup>38</sup>Leporatti, M. L., Impierim M., *J. Ethnobiol. Ethnomed.*, **2007**, *3*, 34
- <sup>39</sup>Everest, A., Ozturk, E., *J. Ethnobiol. Ethnomed.*, **2005**, *1(6)*, 6.
- <sup>40</sup>Demirci, G., Ozhatay, N., *Turk. J. Pharm. Sci.*, **2012**, *9*, 75.
- <sup>41</sup>Polat, R., Cakilcioglu, U., Uluhan, M. D., Paksoy, M. Y., *Indian J. Tradit. Knowledge*, **2015**, *1*, 69.

- <sup>42</sup>Zaid, H., Rayan, A., Said, O., Saad, B., *The Open Nutraceut. J.*, **2010**, *3*, 203. <https://doi.org/10.2174/18763960010030100203>
- <sup>43</sup>Zaid, H., Silbermann, M., Ben-Arye, E., Saad, B., *Evid. Based Complement. Alternat. Med.*, **2012**, Article ID 349040, 13 pages. doi:10.1155/2012/349040
- <sup>44</sup>Ahmad, R., Ahmad, N., Naqvi, A. A., Shehzad, A., Al-Ghamdi, M. S., *J. Trad. Compl. Med.*, **2016**, in press, 10 pages. <http://dx.doi.org/10.1016/j.jtcm.2016.05.002>
- <sup>45</sup>Oran, S. A., Al-Eisawi, D. M., *J. Biodivers. Environ. Sci.*, **2015**, *6*, 381.
- <sup>46</sup>Baydoun, S., Chalak, L., Dalleh, H., Arnold, N., *J. Ethnopharmacol.*, **2015**, *173*, 139. <https://doi.org/10.1016/j.jep.2015.06.052>
- <sup>47</sup>Ben-Arye, E., Schiff, E., Hassan, E., Mutafoglu, K., Lev-Ari, S., Steiner, Lavie, O., Polliack, A., Silbermann, M., Lev, E., *Annals Oncol.*, **2012**, *23*, 211. <https://doi.org/10.1093/annonc/mdr054>
- <sup>48</sup>Ben-Arye, E., Samuels, N., *J. Med. Person*, **2015**, *13*, 65. <https://doi.org/10.1007/s12682-014-0196-z>
- <sup>49</sup>Said, O., Khalil, K., Fulder, S., Azaizeh, H., *J. Ethnopharmacol.*, **2002**, *83*, 251. [https://doi.org/10.1016/s0378-8741\(02\)00253-2](https://doi.org/10.1016/s0378-8741(02)00253-2)
- <sup>50</sup>Saad, B., Azaizeh, H., Said, O., *eCAM*, **2005**, *2*, 475. <https://doi.org/10.1093/ecam/neh133>
- <sup>51</sup>Ali-Shtayeh, M. S., Jamous, R. M., Al-Shafie', J. H., Elgharabah, W. A., Kherfan, F. A., Qariah, K. H., Khair, I. S., Soos, I. M., Musleh, A. A., Isa, B. I., Herzallah, H. M., Khlaif, R. B., Aiash, S. M., Swaiti, G. M., Abuzahra, M. A., Haj-Ali, M. M., Saifi, N. A., Azem, H. K., Nasrallah, H. A., *J. Ethnobiol. Ethnomed.*, **2008**, *4*, 13. <https://doi.org/10.1186/1746-4269-4-13>
- <sup>52</sup>Akaydin, G., Simsek, I., Arituluk, Z. C., Yesilada, E., *Turkish J. Biol.*, **2013**, *37*, 230.
- <sup>53</sup>Formisano, C., Senatore, F., Della Porta, G., Scognamiglio, M., Bruno, M., Maggio, A., Rosselli, S., Zito, P., Sajeve, M., *Molecules*, **2009**, *14*, 17.
- <sup>54</sup>Haghighi, H., *Iranian J. Pharm. Sci.*, **2016**, *12*, 11.
- <sup>55</sup>Ben Ramadan, L., Zwawi, A., Almaghour, H., Saad, M., Alfalah, A., Ben Amer, L., Auzi, A.; *Egypt J. Forensic Sci. Appl. Toxicol.*, **2012**, *12*, 31. <https://doi.org/10.12816/0005072>
- <sup>56</sup>Smith, B. N., Meeuse, B. J., *Plant Physiology*, **1966**, *41*, 343. <https://doi.org/10.1104/pp.41.2.343>
- <sup>57</sup>Janakat, S., Al-Thnaibat, O., *J. Food Qual.*; **2008**, *31*, 1. <https://doi.org/10.1111/j.1745-4557.2007.00180.x>
- <sup>58</sup>Uguzlar, H., Malras, E., Yildiz, S., *Biosci. Biotechnol. Res. Asia*, **2011**, *8*, No paging. <http://dx.doi.org/10.13005/bbra/825>
- <sup>59</sup>Uguzlar, H., Malras, E., Yildiz, S., *J. Food Biochem.*, **2012**, *36*, 285. <https://doi.org/10.1111/j.1745-4514.2010.00537.x>
- <sup>60</sup>Obeidat, M., Shatnawi, M., Al-alawi, M., Al-Zu'bi, E., Al-Dmoor, H., Al-Qudah, M., El-Qudah, J., Otri, I., *Res. J. Microbiol.*, **2012**, *7*, 59. <https://doi.org/10.3923/jm.2012.59.67>
- <sup>61</sup>Ali-Shtayeh, M. S., Al-Assali, A. A., Jamous, R. M., *Afr. J. Microbiol. Res.*, **2013**, *7*, 2560. <https://doi.org/10.5897/ajmr12.1875>
- <sup>62</sup>Tunçturk, M., Özgökçe, F., *Turkish J. Agric. Forestry*, **2015**, *39*, 55. <https://doi.org/10.3906/tar-1406-153>
- <sup>63</sup>Karahan, F., Kulak, M., Uurlu, E., Gul Gozuacik, H., Boyumez, T., Sekeroglu, N., Doganturk, I. H., *Natural Prod. Res.*, **2015**, *29*, 1678. <https://doi.org/10.1080/14786419.2014.991320>
- <sup>64</sup>Afifi, F. U., Kasabri, V., Litescu, S. C., Abaza, I. M., *Natural Prod. Res.*, **2016**, *30*, 1777. <https://doi.org/10.1080/14786419.2015.1072713>
- <sup>65</sup>Jaradat, N. A., Abualhasan, M., *Pharm. Sci.*, **2016**, *22*, 120. <https://doi.org/10.15171/ps.2016.19>
- <sup>66</sup>Tunçturk, M., Eryigit, T., Sekeroglu, N., Özgökçe, F., *Am. J. Essential Oils Natural Prod.*, **2015**, *2*, 31.
- <sup>67</sup>Kilinc, M., Bilgin, A., Yalcin, E., Kutbay, H. G., *Pak. J. Biol. Sci.*, **2005**, *8*, 267. <https://doi.org/10.3923/pjbs.2005.267.272>
- <sup>68</sup>Ucar Turker, A., Birinci Yildirim, A., *Trop. J. Pharm. Res.*, **2013**, *12*, 1003. <https://doi.org/10.4314/tjpr.v12i6.20>
- <sup>69</sup>Khalil, A., Dababneh, B. F., Al-Gabbiesh, A. H., *J. Food, Agric. Environ.*, **2009**, *7*, 103.
- <sup>70</sup>Della Greca, M., Fiorentino, A., Molinaro, A., Monaco, P., Previtera, L., *Natural Prod. Lett.*, **1994**, *5*, 7. <https://doi.org/10.1080/10575639408043928>
- <sup>71</sup>Bonora, A., Pancaldi, S., Gualandri, R., Fasulo, M. P., *J. Exp. Botany*, **2000**, *51*, 873. <https://doi.org/10.1093/jxb/51.346.873>
- <sup>72</sup>Ducceschi, L., Marras, A. M., Cellini Legittimo, P., *Chem. Ecol.*, **2001**, *17*, 255. <https://doi.org/10.1080/02757540108035558>
- <sup>73</sup>Sacliik, S., Alpinar, K., Imre, S., *J. Food Lipids*, **2002**, *9*, 95. <https://doi.org/10.1111/j.1745-4522.2002.tb00212.x>
- <sup>74</sup>Chernenko, T. V., Glushenkova, A. I., Kotenko, L. D., *Chem. Natural Compd.*, **2000**, *36*, 565. <https://doi.org/10.1023/a:1017503522970>
- <sup>75</sup>Hemming, F. W., Morton, R. A., Pennock, J. F., *Proc. Royal Soc. B*, **1963**, *158*, 291. <https://doi.org/10.1098/rspb.1963.0049>
- <sup>76</sup>Nahrstedt, A., *Phytochemistry*, **1975**, *14*, 1870. [https://doi.org/10.1016/0031-9422\(75\)85315-5](https://doi.org/10.1016/0031-9422(75)85315-5)
- <sup>77</sup>Christie, W. W., *Eur. J. Lipid Sci. Technol.*, **2003**, *105*, 779. <https://doi.org/10.1002/ejlt.200300865>
- <sup>78</sup>Alencar, V., Alencar, N., Assreuy, A., Mota, M., Brito, G., Aragao, K., Bittencourt, F., Pinto, V., Debray, H., Ribeiro, R., Cavada, B., *Int. J. Biochem. Cell Biol.*, **2005**, *37*, 1805. <https://doi.org/10.1016/j.biocel.2005.02.027>
- <sup>79</sup>Majumder, P., Mondal, H. A., Das, S., *J. Agric. Food Chem.*, **2005**, *53*, 6725. <https://doi.org/10.1021/jf051155z>
- <sup>80</sup>Modallal, N., Abderrahman, S., Papini, A., *Caryologia*, **2008**, *61*, 383. <https://doi.org/10.1080/00087114.2008.10589650>
- <sup>81</sup>Dayisoylu, K. S., *Asian J. Chem.*, **2010**, *22*, 6595.
- <sup>82</sup>Abbasi, N., Karkondi, V. R., Asadollahi, K., Tahmasebi, M., Ghobad, A., Taherikalani, M., Parisa, A., *J. Med Plant Res.*, **2014**, *8*, 1025. <https://doi.org/10.5897/jmpr2013.5239>
- <sup>83</sup>Safari, E., Amiri, M., Bahador, A., Amiri, M., Esmaeili, D., *Int. J. Current Microbiol. Appl. Sci.*, **2014**, *3*, 301.
- <sup>84</sup>Mansour, O., Salamma, R., Abbas, L., *Int. J. Pharm. Sci. Rev., Res.*, **2015**, *31*, 231.
- <sup>85</sup>Mohammed, Z. H., Ibraheem, R. M., *Ibn Al-Haitham Journal for Pure & Applied Sciences*, **2015**, *28*, 7. <http://www.iasj.net/iasj?func=fulltext&aId=105107>
- <sup>86</sup>Kianinia, S., Farjam, M. H., *Iranian J. Sci. Technol., Trans. A: Sci.*, **2016**, *40*, 1. <https://doi.org/10.1007/s40995-016-0051-6>
- <sup>87</sup>Achtardjiev, C. Z., Koleva, M., *Phytochemistry*, **1973**, *12*, 2897. [https://doi.org/10.1016/0031-9422\(73\)80503-5](https://doi.org/10.1016/0031-9422(73)80503-5)
- <sup>88</sup>Afifi, F. U., Khalil, E., Abdalla, S., *J. Ethnopharmacol.*, **1999**, *65*, 173. [https://doi.org/10.1016/s0378-8741\(98\)00147-0](https://doi.org/10.1016/s0378-8741(98)00147-0)
- <sup>89</sup>El-Desouky, S. K., Ryu, S. Y., Kim, Y.-K., *Tetrahedron Lett.*, **2007**, *48*, 4015. <https://doi.org/10.1016/j.tetlet.2007.04.032>
- <sup>90</sup>El-Desouky, S. K., Kim, K. H., Ryu, S. Y., Eweas, A. F., Gamal-Eldeen, A. M., Kim, Y.-K., *Arch. Pharm. Res.*, **2007**, *30*, 927. <https://doi.org/10.1007/bf02993958>
- <sup>91</sup>Al-Mustafa, A. H., Al-Thunibat, O. Y., *Pak. J. Biol. Sci.*, **2008**, *11*, 351. <https://doi.org/10.3923/pjbs.2008.351.358>
- <sup>92</sup>Ali-Shtayeh, M. S., Jamous, R. M., Jamous, R. M., *Complement. Therap. Clin. Pract.*, **2011**, *17*, 235. <https://doi.org/10.1016/j.ctcp.2011.06.002>

- <sup>93</sup>Aboul-Enein, A. M., Abu El-Ela, F., Shalaby, E. A., El-Shemy, H. A., *J. Med. Plants Res.*, **2012**, *6*, 689.
- <sup>94</sup>El-Desouky, S. K., Usama W. Hawas, U. W., Kim, Y-K., *Chem. Natural Compd.*, **2014**, *50*, 1075. <https://doi.org/10.1007/s10600-014-1162-y>
- <sup>95</sup>Husein, A. I., Ali-Shtayeh, M. S., Jamous, R. M., Abu Zaitoun, S. Y., Jondi, W. J., Zatar, N. A., *Afr. J. Microbiol. Res.*, **2014**, *8*, 3501. <https://doi.org/10.5897/ajmr2014.6921>
- <sup>96</sup>Farid, M. M., Hussein, S. R., Ibrahim, L. F., El-Desouky, M. A., Elsayed, A. M., Saker, M. M., *Afr. J. Biotechnol.*, **2014**, *13*, 3522. <https://doi.org/10.5897/ajb2014.13935>
- <sup>97</sup>Husein, A. I., Ali-Shtayeh, M. S., Jamous, R. M., Jondi, W. J., Zatar, N. A., *Int. J. Current Res. Acad. Rev.*, **2014**, *2*, 195.
- <sup>98</sup>Husein, A. I., Ali-Shtayeh, M. S., Jondi, W. J., Zatar, N. A., Abu-Reidah, I. M., Jamous, R. M., *Pharm. Biol.*, **2014**, *52*, 1249. <https://doi.org/10.3109/13880209.2014.886274>
- <sup>99</sup>Ereifej, K., I., Feng, H., Rababah, T., Alu'datt, M., Gammoh, S., Oweis, L. I., Alkasrawi, M., *J. Plant Sci. Res.*, **2015**, *2*, 5. <http://www.opensciencepublications.com/wp-content/uploads/JPSR-2349-2805-2-139.pdf>
- <sup>100</sup>Abu-Reidah, I. M., Ali-Shtayeh, M. S., Jamous, R. M., Arraez-Roman, D., Segura-Carretero, A., *Food Res. Int.*, **2015**, *70*, 74. <https://doi.org/10.1016/j.foodres.2015.01.023>
- <sup>101</sup>Ereifej, K., I., Feng, H., Rababah, T., Almajwal, A., Alu'datt, M., Gammoh, S. I., Oweis, L. I., *Food Nutr. Sci.*, **2015**, *6*, 581. <https://doi.org/10.4236/fns.2015.67061>
- <sup>102</sup>Farid, M. M., Hussein, S. R., Ibrahim, L. F., El-Desouky, M. A., Elsayed, A. M., El-Oqlah, A. A., Saker, M. M., *Asian Pac. J. Trop. Biomed.*, **2015**, *5*, 944. <https://doi.org/10.1016/j.apjtb.2015.07.019>
- <sup>103</sup>Khalaf, N. A., Naik, R. R., Shakya, A. K., Shalan, N., Al-Othman, A., *Orient. J. Chem.*, **2015**, *31*, 1923. <https://doi.org/10.13005/ojc/310408>
- <sup>104</sup>Jaradat, N., Eid, A.M., Assali, M., Zaid, A., *Int. J. Pharmacogn. Phytochem. Res.*, **2015**, *7*, 356.
- <sup>105</sup>Cole. C., Burgovne. T., Lee. A., Stehno-Bittel. L., Zaid. G., *BMC Complement. Altern. Med.*, **2015**, *15*,264, DOI 10.1186/s12906-015-0774-5
- <sup>106</sup>Farid, M. M., Hussein, S. R., Saker, M. M., *Asian Pac. J. Trop. Disease*, **2016**, *6*, 832. [https://doi.org/10.1016/s2222-1808\(16\)61141-6](https://doi.org/10.1016/s2222-1808(16)61141-6)
- <sup>107</sup>Lobin, W., Neumann, M., Bogner, J., Boyce, P. C., *Willdenowia*, **2007**, *37*, 445-449. <https://doi.org/10.3372/wi.37.37206>
- <sup>108</sup>Armoosh, H., Al-Omari, M., *Herbs in a Book*, Damascus: Al-Nafaes Publishers; **2004**; 811-2.
- <sup>109</sup>Cuadra, V., Cambi, V., Rueda, M., Calfuan, M., *Ethnobotany Res. Appl.*, **2012**, *10*, 77. <https://doi.org/10.17348/era.10.0.077-094>
- <sup>110</sup>Frazer, W., *British Med. J.*, **1861**, *1*, 654. <https://doi.org/10.1136/bmj.1.25.654>
- <sup>111</sup>Kite, G. C., *Biochem. Systemat. Ecol.*, **1995**, *23*, 343. [https://doi.org/10.1016/0305-1978\(95\)00026-q](https://doi.org/10.1016/0305-1978(95)00026-q)
- <sup>112</sup>Wink, M., *Wirbeltierforsch. Kulturlandschaft*, **2009**, *421*, 93.
- <sup>113</sup>Tamilselvan, N., Thirumalai, T., Shyamala, P., David, E., *J. Acute Disease*, **2014**, *3*, 85. [https://doi.org/10.1016/s2221-6189\(14\)60022-6](https://doi.org/10.1016/s2221-6189(14)60022-6)
- <sup>114</sup>Al-Qudah, M. M., *J. Appl. Environ. Biol. Sci.*, **2016**, *6*, 7.
- <sup>115</sup>Ben-Arye, E., Samuels, N., Hilary Goldstein, H., Mutafoglu, K., Omran, S., Schiff, E., Charalambous, H., Dweikat, T., Ghrayeb, I., Bar-Sela, G., Turker, I., Hassan, A., Hassan, E., Saad, B., Nimri, O., Kebudi, R., Silbermann, M., *Cancer*, **2016**, *122*, 598. <https://doi.org/10.1002/cncr.29796>
- <sup>116</sup>Claeson, P., Radstrom, P., Skold, O., Nilsson A., Hoglund, S., *Phytotherapy Res.*, **1992**, *6*, 94. <https://doi.org/10.1002/ptr.2650060209>
- <sup>117</sup>Somang Kang, S., Kim, C-H., Jung, H., Kim, E., Song, H-T., Lee, J. E., *Neuropharmacology*, **2017**, *113*, 467. <https://doi.org/10.1016/j.neuropharm.2016.10.029>
- <sup>118</sup>Sung, P.-J., Lin, M-R., Chen, J-J., Lin, S-F., Wu, Y-C., Hwang, T-L., Fang, L-S., *Chem. Pharm. Bull.*, **2007**, *55*, 666. <https://doi.org/10.1248/cpb.55.666>

Received: 25.02.2017.

Accepted: 20.03.2017.