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Comparative Study on Phytochemical Profile and Cytotoxic Effect for Phenolic Content of Arum maculatum Family (Araceae)

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Abstract

Arum maculatum L. of the Araceae family is a yearly perennial that is renowned for its medicinal applications and diverse phytochemical properties. It has been traditionally used to treat maladies such as kidney stones, colitis, hemorrhoids, and hyperacidity, despite its toxicity, and is indigenous to Europe, Turkey, and the Caucasus. Alkaloids, saponins, flavonoids, and organic volatile compounds are among the many physiologically active molecules found in the plant. These substances exhibit antioxidants, antibacterial, and anti-inflammatory characteristics. A. maculatum showed the cytogenetic and cytotoxic effects on cancer cell and wound healing studies that made it a bright candidate for further studies. Its pharmacological effects are significantly influenced by substantial amount of unsaturated fatty substances, phenolic acids, and essential oils, as indicated by phytochemical analyses. Studies have demonstrated its efficacy in mitigating oxidative stress, enhancing wound healing, and offering potential therapeutic benefits for obesity and ulcerative colitis. This research consolidates ethnobotanical knowledge with contemporary pharmacological insights, highlighting the plant's therapeutic promise and the need for careful handling due to its toxic components.

Introduction

The species *Arum maculatum L.,* which is found throughout Europe, Turkey, and the Caucasus, belongs to the Araceae family (Lack, 2001), The Temperate and Mediterranean regions of the Old World are home to 29 species of tuberous plants in the genus Arum L. (Erbil et al., 2018b, Kozuharova et al., 2020), Common names for the perennial, deciduous woodland plant *Arum maculatum L.* include cuckoo pint, lords and ladies, devils and angels, cows and bulls, Adam and Eve, adder's root, and sneaks head. It is widespread in Europe, East Ukraine, and Anatolia (Kozuharova et al., 2018, Kianinia and Farjam, 2018b).

Bulgarians recognize *Arum maculatum L.* as a medicinal herb, albeit it may not be the most well-known (Gibernau and Momekov), likely due to its toxicity. For hyperacidity, kidney stones, colitis, and liver disease, *Arum maculatum* has been used in traditional and folk medicine of Bulgaria (Ergene and Karaaslan, 2023). Moreover, the plant has been documented as an exceptionally potent treatment for hemorrhoids, a medical problem with few other effective remedies aside from surgery.

In Jordan, it is referred to as Arun and is identified as a source of allergic reactions to the skin (Al-Qura'n, 2005). Rheumatic pain, abscesses, convulsions, plague sores, gout, and fever are among the ailments for which the herb has been used in traditional Turkish medicine (Uzun et al., 2004) for an extended duration and possesses numerous therapeutic benefits for human health. Furthermore, it exhibits pro-inflammatory effects, as well as antibacterial and antifungal activity (Alencar et al., 2005a).

Plant Description

The plant's tubers are unevenly cylindrical along a horizontal axis, from which the shoots emerge at the end. Juvenile leaves are more obovate in shape, and adult leaves are more oblong-hastate to oblong-lanceolate. The hue of the foliage is green. In contrast to *Arum maculatum* var. immaculatum, which does not have any spots on its leaves, *Arum maculatum* var. maculatum has deep violet markings on its leaves. The leaves are lanceolate and petiolate. In most cases, the spathe is small, lanceolate, acuminate, and pale green in color, while the stem is shorter than the petioles. The basal sections of the spathe converge to create a tubular structure. The tube features a lavender band traversing its center, as depicted in (figure 1) (Düz, 2024). It has protogynous blooms. The pollen has a consistent shape and size, with a spiced surface texture. The oxalate crystals found in the plant's orange-red berry cause epidermal and mucous membrane irritation and discomfort when they ripen in the fall (Erbil et al., 2018b).

There are two recognized subdivisions of the genus Arum L. based on present taxonomical knowledge. One section is the subgenus Arum, which includes plants that blossom in march or the beginning of summer (Croat and Ortiz, 2020). A. maculatum and A. italicum are two examples of the taxa in section Arum that have horizontal rhizomatous tubers with side branches that emerge from the soil that create offsets that eventually become independent. The Dioscorides section comprises taxa characterized by a discoid tuber that exhibits exterior spontaneous branches (e.g., A. elongatum, A. orientale, A. palestinum) (Kozuharova et al., 2023). It is a toxic plant (Kozuharova et al., 2014).

Figure 1: *Arum maculatum L.*

Taxonomical Classification

The Araceae is a widespread family with 144 genera and 3645 known species (Boyce and Croat, 2011). It is one of the oldest angiosperms and the third biggest family of monocots. It is further subdivided into eight subfamilies, all of which arose prior to the Cretaceous/Tertiary K/T boundary (Croat, 2019, Hesse and Zetter, 2007, Nauheimer et al., 2012, Stevens, 2020) contains ancient pollen indicating that the clade Pothoideae–Monsteroideae originated between 120 and 110 million years ago during the Late Barremian–Aptian (Early Cretaceous) epoch (Friis et al., 2004), and macrofossils seemingly associated with Aroideae, discovered in other layers of comparable age (Friis et al., 2010), taxonomical classifications shown in table 1 (USDA, 2024).

Table. 1. Taxonomical classification of *Arum maculatum*.

Rank	Scientific Name and Common Name
Kingdom	*Plantae* - Plants
Subkingdom	*Tracheobionta* - Vascular plants
Super division	*Spermatophyta* - Seed plants

Division	*Magnoliophyta* - Flowering plants
Class	*Liliopsida* - Monocotyledons
Subclass	*Arecidae*
Order	*Arales*
Family	*Araceae* Juss. - Arum family
Genus	*Arum* L. - arum
Species	*Arum maculatum* L. - cuckoo pint (USDA, 2024)

A

Traditional Use of *Arum maculatum*

Arum species, such as A. Dioscorides and *A. palaestinum*, are utilized in folk medicine (Afifi-Yazar et al., 2011, Zaid et al., 2012, Naseef et al., 2017) been employed in the management of malignancy. Cuckoo pint (A. maculatum) is a forest plant indigenous to northern Iraq, where it is referred to as 'kardi.' The indigenous populace consumes the palatable leaves of cuckoo pint after the hazardous components have been eliminated through preparation. Amines, calcium oxalates, cyano compounds, alkaloids, saponins, and poisonous volatiles are what make A. maculatum toxic (Azab, 2017).

Historically, A. maculatum has been used for millennia. The plant's usage to treat snake bites was noted in Dioscorides' "De Materia Medica." (Kochmarov et al., 2015). According to reports, the plant has been traditionally used to treat several conditions, including burns and wounds, hemorrhoids, discomfort, inflammation, sore throat, mumps, antihypertensive, antirheumatic, and antidiabetic. Fasciola hepatica (Kozuharova et al., 2018, Karaköse, 2022, Kochmarov et al., 2015, Kozuharova et al., 2020). Jordanian people consume plant parts belonging to the *Arum maculatum* species, and the folk medicine of the country uses them as a method of birth control (YAYLA, 2021).

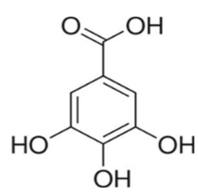
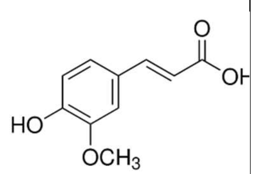
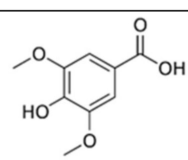
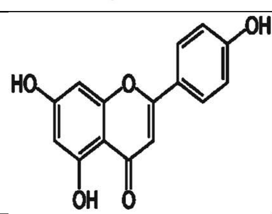
On the Syrian front, the mixture that is made from the stems, roots, and foliage is taken by the locals as a treatment for cancer and constipation (Alachkar et al., 2011). The powdered roots are used as traditional medicine in Northern Morocco to treat a variety of stomach issues (El-Hilaly et al., 2003). In Serbia, the cleaned tubers are used as folk medicine after being chopped into little pieces and let to dry for at least five days. For 30 days, one piece should be used three times a day to prevent hemorrhoids (Jarić et al., 2015). In Lebanon, the ethanol-based leaf macerate is utilized as an antirheumatic and antineuralgic (Nelly et al., 2008). After being gathered by the Roma people in the area of Sliven (Central Balkan Mountains), the leaves of Arum maculutum L. were dried and then boiled with multiple water changes before cooking to make them more palatable. Nevertheless, the Roma people lack awareness regarding the plant's toxicity and do not associate the preparation method with its mitigation (Ivanova et al., 2023).

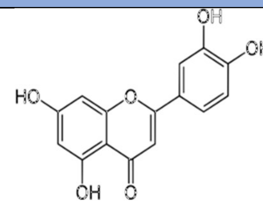
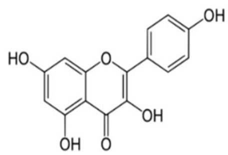
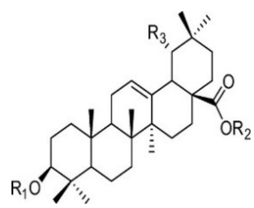
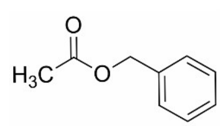
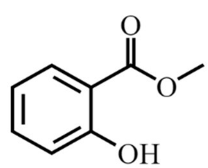
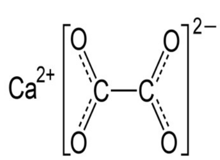
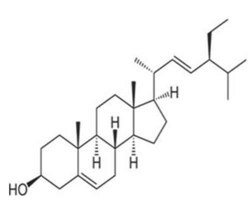
Phytochemistry

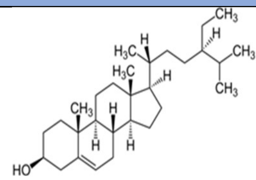
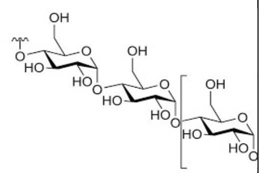
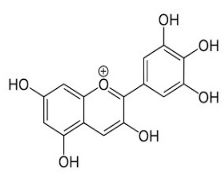
The leaves and tubers of arum plants are rich in a variety of vital chemical components. Table 2 contains a list of compounds, including alkaloids, polyphenols, glycosides (including saponins and flavonoids), proanthocyanidins, 2-heptanone, p-cresol, (E)-caryophyllene, monoterpenes, sesquiterpenes, and lectins. The tubers also include bioactive substances such starch, mucilage, gum, carotenoids, and volatile amines (Safari et al., 2014, Ceylan and Sahingoz, 2022, Comlekcioglu et al., 2021, Allen, 1995, Kochmarov et al., 2015, Van Damme et al., 1995, Azab, 2017, Demir et al., 2020, Farhan et al., 2019). The cyanogenic glycoside triglochinin was discovered to be present in the plant's leaves and spathes (Dring et al., 1995). The leaves also contain other compounds such as nicotine, ethylamine, isoamylamine, isobutylamine, caffeic acid, p-coumaric acid, and chlorogenic acid (Kozuharova et al., 2020, Baytop, 1984). Carotenoids and unsaponifiable lipids, such as long-chain alcohols and hydrocarbons, are present in the spadices (Azab, 2017). In addition to minerals including iron, calcium, sodium, phosphorus, magnesium, potassium, copper, manganese, and zinc, the raw material is known to contain protein, fat, carbs, fibers, and vitamin C (Ceylan and Sahingoz, 2022, ÇOLAK et al., 2009, Ceylan, 2019, Akpınar, 2021). The amount of starch in the tubers is especially high (Atalay and Yıldız, 2020).

The investigation conducted by Kochmarov et al. (2020) unveiled the existence of hydrocarbons, alcohols, thiols, carbonyl derivatives, terpenoids, and fatty acid esters, alongside the nitrogen-containing compound N-(2-ethyl phenyl) benzamide. The extracts with 70% ethanol exhibited a greater percentage area of the identified species, with the sole exception of the latter chemical (Kochmarov et al., 2020).

Table 2. Major Chemical Constituents Reported in *Arum maculatum* and Their Chemical Structure, Molecular Weight & Activity

No	Category	Compound	Structures	Molecular Formula	Molecular Weight (g/mol)	Biological Activity
1	Phenolic Compounds & Flavonoids	Gallic Acid		$C_7H_6O_5$	170.12	Antioxidant, anti-inflammatory.
		Ferulic Acid		$C_{10}H_{10}O_4$	194.19	Antioxidant, UV protection.
		Syringic Acid		$C_9H_{10}O_5$	198.17	Antimicrobial, antioxidant.
		Apigenin		$C_{15}H_{10}O_5$	270.25	Antioxidant, anticancer.

		Luteolin		C15H10O6	286.25	Anti-inflammatory, antimicrobial.
		Kaempferol		C15H10O6	286.25	Antioxidant, anticancer.
2	Saponins	Triterpenoid Saponins		Complex structure	1000 – 1500	Antimicrobial, anti-inflammatory, irritant.
3	Volatile Organic Compounds (VOCs)	Benzyl Acetate		C9H10O2	150.17	Aromatic, mild antimicrobial.
		Methyl Salicylate		C8H8O3	152.15	Anti-inflammatory, aromatic.
4	Oxalates	Calcium Oxalate		Ca(C2O4)	128.1	Defense mechanism, irritant.
5	Sterols	Stigmasterol		C29H48O	412.71	Anti-inflammatory, cholesterol-lowering.
		β-Sitosterol		C29H50O	414.72	Anti-inflammatory,

						antioxidant.
6	Carbohydrates	Polysaccharides		Glucose polymers	Varies (> 10 kDa)	Energy storage, prebiotic effects.
7	Fatty Acids	Linoleic Acid		$C_{18}H_{32}O_2$	280.45	Anti-inflammatory, structural.
		Palmitic Acid		$C_{16}H_{32}O_2$	256.42	Energy sources, structural.
8	Anthocyanins	Delphinidin Derivatives		$C_{15}H_{11}O_7^+$	~303.26	Antioxidant, pigmentation.

Chemical compound in Seed Oil and Essential oil in *Arum maculatum*

The analysis conducted through gas chromatography mass spectrometry on the picolinyl ester and its derivatives has identified the presence of 13-phenyltridec-9-enoic acid at a concentration of 0.4% and 15-phenyl-pentadec-9-enoic acid at 1% within the seed oil of *Arum maculatum* (Haghighi, 2016). fortified aqueous extract of *Arum palaestinum* contained high levels of isovanillin, linolenic acid and β-sitosterol (Al-Shmgani et al., 2019). Eight saturated and ten unsaturated fatty acids were identified among the 18 fatty acids in the plant extract, even though the oil content was just 2.08%. The fatty acid content of *A. maculatum* extracts is shown in Table 3. Palmitic acid (19.57%), oleic acid (15.25%), linoleic acid (21.84%), and alpha-linolenic acid (15.95%) were the principal constituents of the fixed oil of plant extracts. The findings showed that the following acids were present more than 5%: cis-4,7,10,13,16,19-Docosahexaenoic (5.07%), gamma-Linolenic (7.64%), and stearic (5.20%). The remaining fatty acids were below 5%. Based on the study, the highest fatty acid content was polyunsaturated (PUFA), followed by saturated (SFA) at nearly 1/2 of the fatty acids are polyunsaturated, and the smallest percentage are monounsaturated (MUFA). Higher quantities of unsaturated fatty acids are a result of the primary fatty acids in the sample, oleic (C18:1), linoleic (C18:2), and alpha linolenic (C18:3) acids, which make up 53% of the oil (Comlekcioglu et al., 2021).

Species of *Arum* are recognized for their lectin content (Allen, 1995, Majumder et al., 2005, Mladenov et al., 2002, Alencar et al., 2005b). Non-immune (glyco)proteins known as lectins interact with carbohydrates in a reversible and specific manner. The A. maculatum agglutinin (AMA) lectins (Alencar et al., 2005b) The "tuber" or rhizome of A. maculatum yields a mannose-binding homotetrameric lectin that is approximately 50 kDa in size *(Majumder et al., 2005)*. The Arum lectin contains two separate lectin polypeptides of the same size, as both the 12-kD lectin polypeptides from A. maculatum and the 12-kD storage protein from taro (Colocasia esculenta) show a strong similarity. Additionally, the N-terminal sequencing of each of these polypeptides reveals a dual amino acid sequence (Van Damme et al., 1995). Reason being that Arum lectins are known to have pharmaceutical consequences, one of which being an increase in inflammation, their significance goes well beyond their nutritional value (Alencar et al., 2005b). *Arum maculatum* has been determined to include a variety of bioactive chemicals, as shown in (Table 5) (Kozuharova et al., 2023).

Table 3. Fatty acid compositions of *Arum maculatum (%)*

Fatty Acids	Carbon Numbers	Amount (%)
Butyric acid	C4:0	1.05 ± 0.01
Myristic Acid	C14:0	1.37 ± 0.00
Palmitic Acid	C16:0	19.57 ± 0.02
Stearic Acid	C18:0	5.20 ± 0.01
Arachidic Acid	C20:0	0.23 ± 0.00
Heneicosanoic Acid	C21:0	0.37 ± 0.00
Behenic Acid	C22:0	0.72 ± 0.00
Lignoceric Acid	C24:0	0.41 ± 0.00
Myristoleic Acid	C14:1	0.28 ± 0.00
Palmiteloic Acid	C16:1	0.82 ± 0.00
Cis-10-Heptadecanoic Acid	C17:1	0.90 ± 0.00
Oleic Acid	C18:1	15.25 ± 0.02
Linoleic Acid	C18:2	21.84 ± 0.02
gama-Linolenic Acid	C18:3	7.64 ± 0.01
alfa-Linolenic Acid	C18:3	15.95 ± 0.02
Cis-8,11,14-Eicosatrienoic Acid	C20:3	0.73 ± 0.01
cis-5.8.11.14.17-Eicosapentaenoic Acid	C20:5	2.61 ± 0.01
cis-4,7,10,13,16,19-Docosahexaenoic	C22:6	5.07 ± 0.01
Ratio of saturated fatty acid	28.93	
Ratio of monounsaturated fatty acid	17.24	
Ratio of polyunsaturated fatty acid	53.83	

The volatile oil that is derived from the dehydrated leaves of *A. maculatum* using the steam distillation method at room temperature had a distinctive, pleasant scent. A total of forty-three compounds were found, accounting for 92.69% of the components of the oil (Table 4) (Kianinia and Farjam, 2018a). The principal components discovered were Palmitic acid (23.31%), Phytol (13.02%), Methyl 9,12,15-octadecatrienoate (10.34%), and Methyl linolenate (8.64%) (Kianinia and Farjam, 2018a).

Table 4: Essential oil of A. maculatum GC/MS analytical data

No	Compound	KI	Area %	KI/MS
1	cis-4-Decene	930	1.92	KI/MS
2	4-Propylheptane	944	0.46	KI/MS
3	Cyclopentane, 1,2-dimethyl	947	0.45	KI/MS
4	4-Nonene, 5-methyl-	966	1.43	KI
5	1-Decene	989	0.52	KI
6	trans-4-Decene	992	0.45	KI/MS
7	Cineole	1032	0.36	KI/MS
8	Nonanal	1104	1.21	KI/MS
9	Safranal	1202	0.25	KI/MS
10	a-Cyclocitral	1223	0.26	KI/MS
11	Cuminal	1242	0.30	KI/MS
12	Carvol	1246	0.44	KI/MS
13	Nonoic acid	1265	0.28	KI/MS
14	Thymol	1285	0.29	KI/MS
15	Anethol	1287	0.26	KI/MS
16	Carvacrol (antioxine)	1301	1.29	KI/MS
17	4-Hydroxy-4-methyl-4H-naphthalen-1-one	1390	1.84	/MS
18	p-Cymol	1417	0.51	KI/MS
19	Caryophyllene	1425	0.84	KI/MS
20	Geranyl acetone	1454	0.52	KI/MS

21	Myrcene	1458	0.26	KI/MS
22	a-Ionone	1489	1.45	KI/MS
23	a-Bisabolene	1511	0.40	KI/MS
24	Myristicin	1525	0.24	KI/MS
25	Olivetol	1528	0.80	MS
26	Lauric acid	1560	0.51	KI/MS
27	Spathulenol	1583	0.55	KI/MS
28	Caryophylene oxide	1589	0.99	KI/MS
29	Apiol	1628	0.32	KI/MS
30	Benzene, 1-(3-cyclopentylpropyl)-2,4-dimethyl	1668	1.10	KI/MS
31	Stearaldehyde	1714	0.29	KI/MS
32	Myristic acid (crodacid)	1759	1.40	KI/MS
33	Hexahydrofarnesyl acetone	1846	5.60	KI/MS
34	Phthalic acids	1870	0.39	KI/MS
35	Methyl palmitate	1926	4.33	KI/MS
36	Lignocerol	1940	0.24	KI/MS
37	Phytol	1942	13.02	KI/MS
38	Palmitic acids	1960	23.31	KI/MS
39	Methyl linolenate	2085	8.64	KI/MS
40	8,11-Octadecadienoic acid, methyl ester	2095	2.52	KI/MS
41	Linoleic acids	2131	1.09	KI/MS

42	Methyl 9,12,15-octadecatrienoate	2133	10.34	KI/MS

Table 5. Discoveries made in the genus *Arum maculatum* regarding bioactive chemicals

Compound name	Plant parts
Lectin (Ahmed et al., 2023a)	Rhizome
p-Cresol (Dring et al., 1995)	Leaves
Germacrene B (Dring et al., 1995)	Leaves
Ethylamine (Stahl and Kaltenbach, 1970)	Leaves
Isobutylamine (Stahl and Kaltenbach, 1970)	Leaves
Isoamylamine (Stahl and Kaltenbach, 1970)	Leaves
Indole (Dring et al., 1995)	Leaves
Nicotine (Stahl and Kaltenbach, 1970)	Leaves
Triglochinin (Dring et al., 1995)	Leaves
Saponins (Bonora et al., 2000)	Leaves
p-Hydroxybenzoic acid (Djurdjević et al., 2008)	Leaves
Vanillic acid (Djurdjević et al., 2008)	Leaves
Syringic acid (Djurdjević et al., 2008)	Leaves
p-Coumaric acid (Dring et al., 1995, Djurdjević et al., 2008)	Leaves
Ferulic acid (Djurdjević et al., 2008)	Leaves
Caffeic acid (Dring et al., 1995)	Leaves
Chlorogenic acid (Dring et al., 1995)	Leaves
Carotenoids (Dring et al., 1995)	Spadix
13-Phenyltridec-9-enoic and 15-phenylpentadec-9-enoic acids (Christie, 2003)	Seeds

Pharmacological effects of *Arum maculatum l.*

1. Antioxidant activity

The overall quantity and arrangement of hydroxyl groups, which affect the ability of flavonoids to chelate metal ions, determine their antioxidant activity (El-Lateef et al., 2023), The capacity to scavenge radicals and interact with enzyme functions (Chen et al., 2023, Khamees et al., 2018). Ultrasonic extraction using a 50:50 mixture of ethanol and water yielded 4.42 mg CE/g of total flavonoids from *Arum maculatum* leaves, whereas maceration with the same mixture yielded 4.17 mg CE/g. After that, separate steps of ethanol ultrasonic extraction (2.65 mg CE/g), water maceration (1.67 mg CE/g), and ethanol maceration (3.45 mg CE/g) were performed (Farahmandfar et al., 2019). The consumption of flavonoid-rich foods is recommended because of their capacity to donate hydrogen atoms (Hassanpour and Doroudi, 2023). Therefore, food products can be protected against lipid peroxidation by adding *Arum maculatum* leaf extract, which has the potential to be an antioxidant (Farahmandfar et al., 2019).

Cells are shielded from reactive oxygen species (ROS) damage by antioxidants like catalase (CAT) and superoxide dismutase (SOD). Antioxidants help reduce ROS damage, according to in vitro and in vivo studies, which are linked to heart disease and cancer. In addition to the majority of fruits and vegetables, culinary and medicinal herbs can also be rich sources of antioxidants (Jomova et al., 2023, Khamees et al., 2017). *Arum maculatum's* meal and leaves contain antioxidant properties, according to a study, however they undergo modifications while being stored. Group 1's CAT activity was found to be considerably lower than that of the leaf extracts ($p < 0.05$). However, group 2 had significantly higher SOD activity than the others ($p < 0.05$) (Dayisoylu, 2010).

Another study done by Mohammed and Ibraheem (2017) in the study they assessed the antioxidant properties extracted using methanol from Arum maculatum L. and Physalis *peruviana L. A. maculatum* had higher total flavonoids (535.3±109.9 µg/ml) than *P. peruviana* (352.0±12.7 µg/ml). Both extracts showed effective, concentration-dependent reductive ability, with *A. maculatum* achieving higher absorbance at 0.64 mg/ml (0.929±0.006) compared to *P. peruviana* (0.850±0.050) and trolox (0.278±0.010). In DPPH radical scavenging activity, both extracts were most effective at 0.500 mg/ml, with *A. maculatum* and *P. peruviana* achieving 93.33±0.58% and 95.33±2.52%, respectively, outperforming vitamin C (64.67±5.03%). Both extracts are potent antioxidants and free-radical scavengers (Mohammed and Ibraheem, 2017).

The plant's extracts exhibited strong antioxidant activity by neutralizing free radicals. Furthermore, cytotoxicity tests showed a dose-dependent inhibition of cell viability, indicating potential for therapeutic applications in oxidative stress and cancer treatments. The GC-MS analysis of the plant's bioactive compounds highlighted the presence of significant antioxidant agents, such as methyl esters of fatty acids

2. Antimicrobial activity

Arum maculatum extracts were evaluated for their MIC and MBC against several food-borne illnesses. The susceptibility of different bacterial strains to these extracts varied (Farahmandfar et al., 2019). Based on the results, it seems that the extracts were more effective against Gram-positive bacteria (12.5 mg/ml) than Gram-negative bacteria (25 mg/ml), with S. aureus and L. monocytogenes being the most sensitive pathogens in this test. However, prior research has shown that different plant extracts have varying antibacterial activity against these bacteria. The *Arum maculatum* berries and leaves had the strongest antibacterial action against Pseudomonas aeroginosa, according to the data (Erbil et al., 2018a).

According to Çolak et al., (2009) A. maculatum extracts were effective against a variety of bacteria, including Bacillus cereus, Yersinia enterocolitica, Micrococcus luteus, and Pseudomonas phaseolicola (ÇOLAK et al., 2009). Kianinia and Farjam (2018) examined the antibacterial properties of A. maculatum using extracts derived from petroleum ether, methanol, and ethyl acetate. Ten bacteria, six molds, and one yeast were among the seventeen microorganisms whose Minimum Inhibiting Concentration (MIC) was examined. There was a substantial inhibitory effect of the plant on Staphylococcus aureus (MIC = 32 mg mL-1), Staphylococcus epidermidis (MIC = 4 mg mL-1), and Escherichia coli (MIC = 4 mg mL-1) (Kianinia and Farjam, 2018b). The suppression of Escherichia coli ATCC 35213 bacteria by measuring the amount of leaf extract at 14±1.63 mm, demonstrating greater efficacy compared to root extract. Root extract (9±3.26 mm) exhibited a larger zone of inhibition against Staphylococcus aureus ATCC 12600 than Chloramphenicol (8±1.67 mm), which served as a positive control, indicating superior antibacterial activity. A standard chloramphenicol antibiotic disc (30 µg/disc) was employed as a positive control in antimicrobial activity assays. Leaf and root extracts showed considerable inhibition of Staphylococcus mutans and had the lowest MIC values, according to the microdilution experiment. ASTC 10449 (Ahmed et al., 2023a). A. maculatum is the most interesting species among the Arum for further bioactive study (Comlekcioglu et al., 2021).

The disc diffusion and microbroth dilution methods were used to assess the antibacterial properties of A. maculatum by first extracting the roots with petroleum ether and then with ethanol. The tests incorporated a variety of microbial strains, including Staphylococcus aureus (ATCC 6558), Staphylococcus epidermidis (ATCC 12228), Shigella flexneri, Proteus mirabilis, Escherichia coli (ATCC 8739), Klebsiella pneumoniae (ATCC 4352), Pseudomonas aeruginosa (ATCC 1539), and Candida albicans (ATCC 10231). At 39.1 µg/mL, the petroleum extract's minimum inhibitory concentration (MIC) demonstrated potent action against S. epidermidis. This extract's MIC values against S. typhi and Staphylococcus aureus were determined to be 625 µg/mL and 312.5 µg/mL, respectively (Uzun et al., 2004).

3. Antifungal effect

To ascertain the significant effect of *Arum maculatum* extract on rat fungal infections, Abbood and Salman (2024) isolated fungi from infected broad bean roots and leaves in Kirkuk City's Hawija district. The isolates were then cultivated on PDA medium for morphological and phenotypic analysis. 16 male rabbits from Kirkuk's local markets were used in the study. They were split into four groups, each consisting of four rabbits: a control group, a group that was infected, a group that was infected and got 50 mg of plant leaf extract, and a group that was infected and received 100 mg of leaf extract. Variables related to oxidative stress were then measured. The findings showed that infected rabbits had significantly higher levels of MDA and lower levels of GSH and catalase ($P < 0.05$) compared to normal rabbits. The levels of MDA, GSH, and catalase in the groups treated with leaf extract differed little from those in the control group ($P < 0.05$) (Abbood and Salman, 2024).

Mansour et al. (2015) demonstrated that methanol extracts exhibited the most potent antibacterial action. Additionally, the essential oil of the plant effectively suppressed the growth of fungal species Aspergillus niger and Penicillium digitatum (fungi) with MIC = 8 mg/ml (Kianinia and Farjam, 2018b).

4. Cytogenetic Effect of *Arum maculatum*

One ailment that significantly affects individuals worldwide is cancer. To address and avert this lethal illness, there is an ongoing necessity for innovative medicines. Because they are believed to have less harmful side effects than current treatments like chemotherapy, natural compounds are receiving more scientific and research attention (Ahmed et al., 2023b). *Arum maculatum* extract inhibits the production of DNA, RNA, and proteins in cultured mammalian cells (Li et al., 2024). Across all exposure times, the mitotic index dropped dramatically in bone marrow cells treated with high doses (75 and 100%) (Nazam et al., 2020). This reduction results from the diminished quantity of cells transitioning from G2 to prophase (Baszczynski et al. 1980). Evidently, *Arum maculatum* may alter the frequency of mitotic phases and produce a number of mitotic abnormalities, such as restitution, micro and multinuclei, aberrant prophase, C-metaphase, sticky chromosomes, fragments, bridges, non-congression, and laggards (Nabeel et al., 2008). However, the extract's primary effects were observed during interphase, as well as during metaphase and anaphase.

The plant's hydro-alcoholic extracts were tested for their antiproliferative effects in immortalised human umbilical vein endothelial cell line EA.hy926 after 72 hours of continuous exposure. A modified MTT-dye reduction assay protocol was used to separate the effects of cell growth inhibitory from lethal cytotoxicity. A. maculatum extracts showed a concentration-dependent inhibition of EA. hy926 cell growth (Kochmarov et al., 2020).

The plant's extracts showed strong antioxidant action by neutralising free radicals. In addition, cytotoxicity experiments showed that cell viability decreased with increasing dosage, which might have therapeutic applications in cancer and oxidative stress therapy. The GC-MS study revealed the presence of methyl esters of fatty acids, which are key antioxidant agents contained in the plant's bioactive components.

5. Antimutagenic Effects

For the antimutagenic activity assays, the Salmonella typhimurium TA 98 and TA 100 strains were used. The results revealed that the leaf extract displayed antimutagenic activity against induced mutagenesis in S. typhimurium TA 98 at both the lowest (10 µL/Plaque) and maximum (80 µL/Plaque) dosages, however the berry extract did not exhibit any antimutagenic effects at any of the tested doses (10, 20, 40, and 80 µL/Plaque). It is desirable and advantageous for health to have these antimutagenic results. The berry and leaf extracts (10, 20, 40, and 80 µL/Plaque) did not show any antimutagenic properties against induced mutagenesis in S. typhimurium TA 100, nevertheless (Erbil et al., 2018a). Another study found that Arum euxinum extracts in ethanol (36.1%) and methanol (41.7%) demonstrated anticancer efficacy (Turker and Yıldırım, 2013). Additionally, Larasati et al. reported that the extract of Arum palaestinum exhibited cytotoxic action (Larasati et al., 2014).

6. Wound healing activity

Wounds progressively heal through systematic mechanisms necessitating intercellular communication. This process involves cytokines, growth factors, and components of the extracellular matrix (ECM) (Pang et al., 2020, Abdulrasool et al., 2013). The complex of the skin should be maintained by ECM proteins, which are mostly present in connective tissue and help with wound and skin aging treatment strategies. Additionally, they stimulated clinical trials and new research (Mazini et al., 2019). The Araceae family includes *Arum maculatum L*. (Arum), which is referred to in Turkey as "yılan pancarı, yılan yastığı." Traditionally, the herb has been used to treat rheumatism, cancer, constipation, fungal illnesses, and hemorrhoids. Diaphoresis, sudorific, and expectorant effects are its main uses. Paralysis may be effectively treated with A. maculatum (Alachkar et al., 2011). The ability of the methanol extract from A. maculatum fruits to heal wounds was investigated for the first time in a scientific investigation. Animal models for excisional wound healing and in vitro wound healing were used to study the antioxidant and antibacterial activity of A. maculatum. One hundred and thirty-two Balb-c mice were randomly assigned to one of four groups: control, saline control, A. maculatum, or Centella asiatica extract. Each patient received a topical therapy once daily. We looked at how much of the wound area shrank, how long it took for the epithelium to form, and what percentage of the wound healed. Both in vitro and in vivo wound studies showed that A. maculatum treatment enhanced healing. A. maculatum facilitated healing by promoting angiogenesis, epidermal regeneration, and granulation tissue development (Sakul et al., 2023).

7. Anti- obesity effect

The fundamental strategies for overcoming or controlling obesity include diet, exercise, and medication; herbal remedies are particularly popular due to their natural origin, affordability, and negligible adverse effects (Rahman et al., 2017, AHMED et al., 2020). Many people have unwanted side effects while using traditional pharmacological treatments for obesity, and after they stop taking the prescription, they commonly regain the weight they lost. Consequently, the discovery of a safe and effective medicine for obesity treatment is still underway by researchers (Mopuri et al., 2015). Ibrahim (2021separated thirty male albino rats into five groups: exercise, Nasturtium officinale extract (NOE), *Arum maculatum* extract (AME), high-fat diet control (HFD-C), and normal control (NC). While the others were fed a high-fat diet (HFD) for eight weeks, the NC group was fed a regular diet. Treatments were administered to the designated groups. Each week, participants documented their food intake and weight, and at the conclusion, a number of blood parameters were examined. Results showed HFD-C rats had significant increases in body weight, glucose, lipid profiles, liver function tests, and MDA compared to NC rats, with decreased HDL-C levels. Treatments with AME, NOE, and exercise significantly reduced these changes. To combat obesity and its associated physiological effects, AME, NOE, and exercise may be utilized as dietary supplements or as a potential therapeutic agent (Ibrahim, 2021).

8. Protective effects against colitis

Symptoms of ulcerative colitis (UC), an inflammatory disorder affecting the large intestine, include sores on the mucosa, loose stools, blood in the stool, and discomfort in the abdomen (Kucharzik et al., 2020). Immunosuppressants, corticosteroids, and nonsteroidal anti-inflammatory medications are used to treat UC; however, prolonged use of these medications may result in side effects (Fries et al., 2022). Despite *Arum maculatum*'s long history of use as a digestive system medicine, its efficacy in treating ulcerative colitis remains unproven. Doğan et al. (2023) examined if a methanol extract of A. maculatum could shield rats from experimental UC caused by dextran sulfate sodium (DSS). 32.919 ± 1.125 mg gallic acid equivalent (GAE)/g and 52.045 ± 7.902 µg rutin equivalent (RE)/mg were the extract's total phenolic and flavonoid contents, respectively. The extract has an IC50 value of 105.76 µg/ml when tested for its ability to scavenge radicals using the 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay. A. maculatum extract was tested for its effects on DSS-induced UC using both microscopic and histological methods. There was also an investigation into how A. maculatum extract influenced oxidative stress index (OSI) and malondialdehyde (MDA) levels in rats with normal and UC. It was shown that there was a dose-dependent protection against DSS-induced UC in the colon when A. maculatum extract was administered to it (Doğan et al., 2023).

Kochmarov et al. (2015) conducted a study that focused on the therapeutic effects of *Arum maculatum* L. (Araceae) in the treatment of haemorrhoids. The study collected anecdotal reports from individuals who had used the herb to treat haemorrhoids and gathered current traditional knowledge about its therapeutic effects. The information gathered was analysed to identify the mechanism of action and to determine the efficacy of the herb against haemorrhoids and other medical conditions. Finally, the study examined the prevalence of snakehead as a medicinal plant in Bulgaria today. Between March and November 2013 and June and August 2014, semi-structured interviews were conducted with Bulgarians to investigate their traditional ethnobotanical knowledge of the medicinal properties of *Arum maculatum*. It is reasonable to assume that the plant material 1) reduces inflammation, 2) alleviates pain, and 3) narrows blood vessels in the treatment of various haemorrhoids, chronic traumatic pain, and purulent infections, based on the examination of A. maculatum tuber's therapeutic effects, both directly and indirectly (Kochmarov et al., 2015).

Conclusion

The plant known as *Arum maculatum L.* has both promising and perilous qualities. As an antioxidant, antimicrobial, and wound-healing agent, it has long been utilised in traditional medicine and is now showing promise in contemporary medicine. The plant's variable chemical composition makes it useful for a wide range of therapeutic purposes. According to studies, it has a long history of usage in the treatment of a variety of medical conditions, including cancer, haemorrhoids, and colitis. Scientific evidence supports this traditional usage by showing that the active components may aid with various ailments. Nevertheless, due to its toxicity, the plant must be handled and prepared with extreme care. Serious health problems might arise from mistakes. Future studies should concentrate on isolating and developing safer versions of its beneficial components so that we can maximise its advantages while minimising its hazards. Novel, safe, and effective medications might be created by integrating traditional wisdom with cutting-edge scientific methods.

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