

Checklist of Medicinal Plants of Ait Ayash Valley and their Pharmacological Properties

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Received: 17.08.2023; Accepted: 7.01.2024; Published: 28.08.2024

Abstract: Herbs, for a long time now, have been employed to treat different ailments, such as diabetes, kidney and liver disorders, cancer, and obesity. Considering these facts, we endeavored to realize this review by enlightening the biological properties of different herbs found in the Ait Ayash region. The information is derived from different sources of scientific information like Science Direct, Springer Link, Scopus, and PubMed. Plant bioactive substances have a good effect on both human and animal health. This review intends to investigate the published studies regarding the biological properties of different plants found in the abovementioned region.

Keywords: medicinal plants; Ait Ayash valley; bioactive compounds; pharmacological properties.

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1. Introduction

Rural communities use different wild herbs as a common practice to treat several diseases, especially in the rural culture society of High Moulouya [1]. The population of this region has developed a vast knowledge of the use of wild plants, and modern medicine has never completely supplanted herbal medication. Ait Ayash region is a very fertile valley with a vocation for apple crops in Morocco. The region is framed by the Middle-Atlas and High-Atlas reliefs to the East [2] and characterized by an in-tramontane Mediterranean climate of high plain [3]. The pedoclimatic conditions of this region subserve the development of different medicinal plants, including *Origanum compactum benth*, *Rosamarinus officinalis*, *Chenopodium ambrosioides*, *Mentha pulegium*, *Artemisia herba-alba* Asso, *Lavandula dentate*, *Lawsonia inermis*, *Juniperus phoenicea*, *Rosa canina*, *Salvia aucheri mesatlantica*, *Satureia alpine*, *Juglans regia*, *Salix alba*, *Retama shaerocarpa*, *Peganum harmala*, these plants are frequently used in local phytotherapy[1].

Determining the exact time of acting phytotherapy practice in the Ait Ayash Valley is tough. Additionally, mounting evidence proves that the cultivation of medicinal plants dates approximately 60000 years ago [4]. The inhabitants of this region have long enjoyed knowledge about traditional treatment with medicinal plants and their beneficial properties, but unfortunately, this knowledge is not yet documented. Traditional herbal medicine is practiced for many reasons, including fewer complications, efficacy, low costs, and availability in the

region [5]. Until now, many families in this valley still consider herbal medication an essential element of primary health care.

This review is considered a continuation of our previous studies conducted about local products relevant to human and animal health in our search structure (SNAMOPEQ). This review's findings will be crucial in enriching the Moroccan databases about natural products and their phytochemicals and pharmacological properties.

2. Methodology

The current review is prepared by selecting different articles falling within the scope of the determined objective of this review. The search for data was performed using different keywords, such as medicinal plants, high Moulouya, Ait ayash, and pharmacological properties. A total of 120 articles selected were exploited to prepare the current work.

3. Plants with Pharmacological Effects

3.1. *Rosa canina* (RC).

Research involving RC as a natural product with a wide range of biological properties, including antioxidant, antidiabetic, anti-inflammatory, and anticancer effects. Rural populations use medicinal plants as the first treatment line, which comes to the forefront for many reasons, such as unsatisfactory results of modern medication; they prefer natural remedies with lower costs or inexpensive and have fewer side effects [6].

Rosa canina belongs to a long list of medicinal plants grown naturally in the Ait Ayash valley. Different parts of this plant are widely used in local folk medicine. According to Benlamdini *et al.*, the RC leaves were used as a natural agent of erectile dysfunction and stomachic treatment in the aforementioned studied region [1]. The RC fruits collected in the same region possessed high antioxidant activity and counteract the harmful effects of peroxide hydrogen-induced oxidative stress in an animal model with a high histopreventive effect [7,8]. The hips possess antioxidant and antiproliferative activities due to their bioactive molecules, which protect against oxidative stress [9].

Additionally, the oligosaccharide fraction of hips manages blood glucose levels in diabetic rats and stimulates the expression of insulin Ngn3 and NKx6.1 genes [10]. The administration of oligosaccharide fraction isolated from hips on Streptozotocin-induced diabetic rats for three weeks proved its ability to decrease blood sugar levels better than a standard drug (metformin) [10]. The hepatoprotective effect of *Rosa canina* was examined by Sadeghi *et al.* [11] using the hydroethanolic extract. The obtained results showed that the administration of both doses of 500 and 750 mg for six weeks decreased CCl₄-increased serum levels of alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), and malonylaldehyde (MDA). These findings were supported by ameliorating the histopathological damages induced by CCl₄. In addition, *Rosa canina* fruits provide an interesting antioxidant property evaluated *in vitro* and *in vivo* [11–14]. The formation of advanced glycation end products (AGEs) is linked with the persistence of hyperglycemia as a complication. These compounds are derived from non-enzymatic glycation and oxidation between different biomacromolecules [15]. Within this frame, a study was conducted to examine the ability of the aqueous extract of RC to inhibit the formation of AGEs derived from reactive carbonyl species. The obtained results revealed that the RC exhibited an important inhibitory effect [13]. Based on the high antioxidant potential of RC, it has been tested to treat

numerous types of cancer and furnished a promising outcome in most cases. Several studies were conducted on different tumor cell lines and found a significant decrease in cancer cell viability of lines treated with rose hip extract [16–19]. The different features of RC are not derived from actual knowledge, as there have been numerous centuries since medicinal plants have been used as medication. The analysis of the phytochemical content of RC revealed the presence of numerous bioactive compounds in different amounts, such as vitamin C, ellagic acid, quercetin, kaempferol, and so on (Table 1) [20–22]. The synergistic effect of RC's different bioactive compounds makes it a natural agent with multifaceted potentials.

Table 1. Phytochemistry and pharmacological properties of medicinal plants used in Ayt Ayash Valley.

Plant species	Family name	Used part	Type of extract	Secondary metabolites	Pharmacological effects	Reference
<i>Rosa canina</i> (RC)	Rosacea	Leaves	Aqueous extract	-	Erectile dysfunction	[1]
		Fruits	Hydroethanolic extract	-	Hepatoprotecteur effect	[11]
		Fruits	Hydroethanolic extract	hexadecanoic acid (12.72%), 9,12-Octadecadienoyl chloride, (Z, Z)- (10.45%), glycerol 1,2-diacetate (9.00%), maltose (7.58%), 2-methylcyclopentanone (6.36%), cyclohexanamine, N-3-butenyl-N-methyl- (5.06%), hexadecenoic Acid,1-(hydroxymethyl)-1,2-ethanediyl ester (4.55%), oleic acid (3.41%), hexadecanoic acid, 2,3-dihydroxypropyl ester (3.36%), 7,8 epoxylanostan-11-ol, and 3-acetoxy- (3.29%)	Antioxidant effect	[23]
		Flowers , fruits, and seeds	Methanol extract	Citric acid, Rhamnosylnaringenin, Quercetine-3-O –glucoside, Hydroxycinnamic acid derivative, Pyrogallol-2-O-Glucuronide, Galloylglucose, Kaempferol-3- Glucoside- <i>p</i> -coumaroyl, Quercetin-7-O-hexoside- 3-O-(malonyl)hexoside, Arzanol, Procyanidin trimer monogallate, <i>p</i> -Coumaroyl derivative	Antioxidant and antidiabetic effects	[24]
<i>Juglans regia</i> (JR)	Juglandaceae	Fruits	Fractionation	-	Antioxidant, antibacterial, and antidiabetic effects	[25]
		Fruits	Fruit powder	-	Antidabetic effect	[26]
		Roots	Aqueous extract	Gallic acid, juglone, catechin, vanillic acid, epicatechin, and coumain	Antimicrobial, insecticidal, and anti-leishmanial effects	[27]
		Leaves	Aqueous extract	3- <i>O</i> -caffeoylquinic acid, Procyanidin dimer, 3- <i>p</i> -Coumaroylquinic acid, 4- <i>O</i> -caffeoylquinic acid, Procyanidin trimer, <i>cis</i> 4- <i>p</i> -Coumaroylquinic acid, <i>trans</i> 4- <i>p</i> -Coumaroylquinic acid, Procyanidin dimer, Taxifolin <i>O</i> -pentoside isomer, Taxifolin <i>O</i> -pentoside	Antioxidant and antitumor effects	[28]

Plant species	Family name	Used part	Type of extract	Secondary metabolites	Pharmacological effects	Reference
				isomer, Myricetin 3- <i>O</i> -glucoside, Laricitrin <i>O</i> -hexoside, Taxifolin <i>O</i> -pentoside isomer, Taxifolin <i>O</i> -pentoside isomer, Myricetin <i>O</i> -pentoside, Myricetin <i>O</i> -rhamnoside, Taxifolin <i>O</i> -pentoside isomer, Quercetin 3- <i>O</i> -glucoside, Quercetin <i>O</i> -hexoside, Quercetin <i>O</i> -pentoside, Quercetin <i>O</i> -pentoside, Quercetin <i>O</i> -rhamnoside, Kaempferol <i>O</i> -pentoside, Kaempferol <i>O</i> -pentoside, and Kaempferol <i>O</i> -rhamnoside		
<i>Retama shaerocarpa</i> (RP)	Fabaceae	Leaves	Aqueous extract	-	Rheumatism	[1]
		Grains and stems	Hydromethanolic extract	Gallic acid, p-coumaric acid, taxifolin, naringenin, luteolin, and isorhamnetin	Antioxidant and antibacterial activities	[29]
		Areal parts	Aqueous extract	Daidzin, rutin, genistin, daidzein, luteolin, apugenin, and genistein	Anti-inflammatory effect	[30]
<i>Peganum harmala</i> (PH)	Zygophyllaceae	Seeds	Methanol extract	-	Analgesic effect	[31]
		Seeds	Methanol extract	Harmalacidine, harmine, peganine, and vasicinone	Cytotoxic effect	[32]
<i>Malus domestica</i>	Rosaceae	Peel powder	Aqueous extract	-	Antioxidant and anti-inflammatory effects	[33]
		Apple pomace	Aqueous extract	Phloretin, epicatechin, coumaric acid, phloridzin, and chlorogenic acid	Antioxidant and hepatoprotective effects	[34]
<i>Salix alba</i>	Salicaceae	Leaves	Aqueous extract	Apigenin, quercetin, and salicylic acid	Anti-inflammatory effect	[35]
<i>Herniaria hirsuta</i> (HH)	Caryophyllaceae	Whole plant	Aqueous extract	-	Nephrolithiasis preventive effect	[36]
		Whole plant	Hydromethanolic extract	<i>p</i> -coumaroyl-4- <i>O</i> -hexoside, <i>cis</i> -3-feruloyl quinic acid, licoagroside B, <i>trans</i> -4-FerQA, rutin, quercetin-3- <i>O</i> -hexoside, nicotiflorin, narcissin, and isorhamnetin-3- <i>O</i> -hexoside	Antioxidant and anti-inflammatory effects	[37]
<i>Foeniculum vulgare</i> Mill.	Apiaceae	Seeds	Hydroalcoholic extract	-	Hepatoprotective effect	[38]
		Whole plant	Hydromethanolic extract	-	Antioxidant and hepatoprotective effects	[39]

3.2. *Juglans regia* (JR).

Juglans regia (JR), or walnut tree, is a medicinal plant well known for its defense system against pathogenic agents. It belongs to the family Juglandaceae, widely distributed in the Balkans, Himalayas, and southwest China [40]. JR is used in local folk medicine for multiple purposes, such as producing dyes for hands, hair, and feet; this traditional practice is still ongoing and widely spread in Amazigh culture for honoring female guests or relieving articulation pain.

The JR leaves, or root barks, are commonly incorporated into mouth hygiene. Mounting evidence showed that JR exhibited an antiplaque activity and acted with a high antimicrobial

effect against different pathogenic bacteria, including *Streptococcus mutans*, *Streptococcus sanguis*, *Actinomyces viscosus*, *Streptococcus mutans*, *Streptococcus salivarius*, and *Staphylococcus aureus* [41–46]. Ghorabni *et al.* investigated the ability of walnut consumption on sex hormones perturbed by chronic hyperglycemia in Wistar rats [26]. The obtained findings proved that the diet reinforced with walnuts at doses of 9 and 12% improves blood glucose levels in diabetic rats and positively impacts the release of sex hormones perturbed by chronic hyperglycemia. The biological properties of walnuts have been attributed to their dense phytochemical composition, attracting the attention of several researchers [47–49]. The scrutiny of the phytochemical content of walnuts revealed the presence of numerous bioactive compounds in which hydrolyzable tannins are the major compounds of walnuts, including ellagitannins, ellagic acid derivatives, anthocyanins, and dicarboxylic acid derivatives (Table 1) [50].

Various phytochemicals in walnuts have antioxidant ability and can act as an antiproliferative agent against numerous cancer cell lines, including MCF-7 (breast adenocarcinoma), NCI-H460 (non-small cell lung cancer), HCT-15 (colon carcinoma), HeLa (cervical carcinoma) and HepG2 (hepatocellular carcinoma) [28]. Oxidative stress affects different systems, promoting the pathogenesis of a large number of disorders, such as diabetes, obesity, neurodegenerative diseases, aging, and cancer [51]. Investigations of the antioxidative effect of JR against different toxic agents were conducted on animal models [19,52–54]. The administration of hull extract at a dose of 300 mg/kg for 7 days restored the perturbation induced by isoprenaline (ISO), reducing oxidative stress markers and also reducing histomorphological modifications in rat brains [55]. Furthermore, JR leaf extract was used to evaluate its anti-inflammatory and immunomodulatory effects in preclinical rodent models of arthritis induced by Freund's complete adjuvant. The authors proved that the treatment of mice with leaf extract at a dose of 500 mg/kg sustained 20 days attenuated arthritic development, paw edema, and histopathological markers [56]. They found also that the JR leaves extract-treated mice reduced prostaglandins E₂, TNF- α , NF- κ B, IL-6, IL-1 β , and cyclooxygenase-2 levels. These molecules are an important target in treating inflammation and oxidative stress, which are considered the common point of several diseases.

3.3. *Retama shaerocarpa* (RP).

Retama sphaerocarpa is a perennial shrub widely distributed in North Africa, especially in the Ait Ayash valley [57]. This plant supports critical conditions and has developed a root system that allows deep water access [58]. It is characterized by the open canopy, which facilitates the growth of other plants and enhances the production of nutrient and bioactive compounds [59,60]. The richness of RP in bioactive compounds (Table 1) makes it an excellent herb used widely in folk medicine to treat numerous ailments such as diabetes, inflammation, rheumatism, skin diseases, fever, and so on [61]. An ethnopharmacological study conducted in the abovementioned region (Ait Ayash Valley) reported that the rural population of this area used RS to treat rheumatism [1]. In fact, experimental studies confirm the utility of this plant as a natural remedy for a vast range of disorders [30,62]. It has been proved that chloroform, ethyl acetate, and butanol extracts obtained from aerial parts of RS exhibited a cytotoxic effect with dose-dependent against three human cancer cell lines such as TK-10 (renal adenocarcinoma), MCF-7 (breast adenocarcinoma) and UACC-62 (melanoma) [63]. Advanced glycation end products (AGE) are implicated in the induction of oxidative stress, inflammation, and insulin resistance. At the same time, the reduction of these

compound's production is considered a useful tool in the medicine and food industry [64]. In this regard, Boussahel *et al.* found that both the methanolic and aqueous extracts of RS exhibited a dose-dependent inhibited AGE production [62], which was ascribed to their flavonoid content, as previously confirmed by Grasci *et al.* [65]. RS is a medicinal plant poorly investigated for its pharmacological properties despite its importance in land restoration and bioenergy production [62].

3.4. *Peganum harmala* (PH).

Peganum harmala (PH) or Harmal, as named in the Ait Ayash valley, belongs to the Zygophyllaceae family, which contains about 250 species. It grows in semi-arid rangeland and pre-desertic areas in the south-east of Morocco [66]. Traditionally, PH ethnobotanical preparations are still used for various reasons, such as decoction, infusion, and powder to treat numerous ailments, including subcutaneous tumors and dolorous events [66,67]; it is also used as an emmenagogue and abortifacient [68]. In fact, PH extract proved its ability to possess a central and peripheral antinociceptive effect on animal models through the opioid system [31]. Different parts of PH are thought to induce toxicity due to its content of alkaloids, including harmine and harmaline, known for their ability to accelerate breathing and muscular spasms [68]. Harmine and harmaline are two active alkaloids that interact with alpha 1-adrenergic receptors and enhance the release of nitric oxide, affecting vasorelaxation [69]

Lamchouri *et al.* reported that the PH seeds extract exhibited a cytotoxic effect against several tumor cell lines, including Med-mek carcinoma, UCP-med carcinoma, UCP-med sarcoma, SP2/O-Ag14, and b) and antiproliferative effect on cells of Jurkat, E6-1 clone (inhibition of incorporation of {³H-thymidine} in cellular DNA) [32]. In the same context, it has been proved that the PH possesses an antiproliferative and growth inhibitory effect against two breast cancer cell lines (MCF-7 and MDA-MB-231), melanoma cell line (Hs-294T), and leukemia cell lines such as MV-4-11 [70,71]. Both harmine and harmaline, as two active alkaloids of pH, are shown to reduce and stop cancer cells, activating both intrinsic and extrinsic pathways of the apoptosis process and destructing DNA, which disrupts the cell division process [72,73].

3.5. *Malus domestica*.

Malus domestica, or apple tree, comprises twenty-nine species widely grown worldwide in the temperate areas of the northern and southern hemispheres [74]. It belongs to the family Rosaceae; the genus of *Malus* is characterized by its incredible diversity, high hybridization potential, and apomixes and polyploidy, which complicate species classification [75]. Different epidemiological studies have established possible links between apple consumption and the prevention of various chronic pathologies, including diabetes, obesity, cerebrovascular diseases, and metabolic disorders [76,77]. The beneficial properties of apples have been attributed to their phenolic content, dietary fibers, minerals, and organic acids [78–80]. In fact, research has shown that pharmacologically active compounds have an essential ability to improve health and reduce risk [81]. These beneficial properties have caught the attention of researchers. A study was conducted on healthy people who suffered from moderate loss of joint range of motion and related to persistent pain. Twelve weeks of treatment with dried apple peel powder improved range of motion by ameliorating serum antioxidant status and inhibiting cyclooxygenase-2 and lipoxygenase enzymes [33].

Furthermore, dried apple peel powder proved its ability to reduce reactive oxygen species production. In fact, reactive oxygen species affect different organs, resulting in histopathological damage [82]. Evidence from an experimental study showed that the pretreatment of mice model with pomace apple extract at doses of 200 and 400 mg/kg for 2 weeks prior to the administration of carbon tetrachloride (CCl₄) reduced the necrotic perturbations in the liver. Furthermore, the authors revealed that the levels of antioxidant parameters were improved and showed higher expression of the nuclear erythroid-2 factor as a critical factor of oxidative response [34]. The analysis of the phytochemical content of apples revealed a complex composition containing different bioactive compounds such as phloridzin, (+)-catechin, and (-)-epicatechin [83]. These molecules affect the proper functioning of SGLT1, thereby reducing serum glucose levels [84,85]. Different beneficial properties of apples have been spotlighted as a dense source of bioactive compounds with fewer side effects. Apple contains cysteine, malic acid, and arginine, which are well known for removing the stocked toxic molecules [86]. Apple by-products such as apple vinegar have been spotlighted as a regulator against several pathologies, including diabetes, obesity, oxidative stress, pathogenic bacteria, anemia, Alzheimer and so on [7,87–95].

3.6. *Salix alba*.

Salix alba, or white willow, known in the Ait Ayash area under the vulgar name ‘‘AArish’’, belongs to the family of Salicaceae [96]. The rural population of the Ait Ayash area used it to treat diabetes, as documented previously in the ethnopharmacological survey conducted by Benlamdini *et al.* [1]. Traditionally, it has been documented that the Assyrians and Egyptians used *Salix alba* to treat musculoskeletal pain [97]. In fact, the observations of modern evidence-based medicine proved that the willow tree contains salicin, which means willow in Latin, detected for the first time by Henri Leroux in 1826 [98]. This plant has achieved a kind of representative importance linked with the discovery of analgesic medications such as aspirin [97]. Furthermore, different studies have highlighted salix extract's utility in improving low back pain and proved that the adverse effects appear minimal or absent compared to conventional medication [99,100]. Phytochemical analysis revealed the presence of at least twelve salicylate compounds such as iso salicin, salidroside, salicylic acid, salicyl salicin, salipurposide, saligenin, and salicin [101]. A study examining the willow bark's phytochemical content showed that salicin presents 4 to 8 % of total antioxidant compounds, and other phenolic compounds were detected in different amounts [102].

Salicin is a phenolic compound of willow, a precursor of salicylic acid; this molecule has anti-inflammatory effects explained by inhibiting cyclooxygenase and interrupting the formation of prostaglandins, thereby controlling the inflammation process [35,103]. Inflammation amerces the pathogenesis of different acute and chronic diseases. It is implicated in maintaining the body's integrity against damaging agents [104]. The production of reactive oxygen species (ROS) accompanies the inflammation process and is implicated in the cell's defense mechanism against pathogenic bacteria [105]. While the overproduction of ROS alters different physiological functions, favoring the installation of numerous pathologies [82]. Thus, the control of ROS production constitutes a key factor in controlling inflammation in a study conducted by Khayyal *et al.* on two inflammation models, the 6-day air pouch model in rats and adjuvant-reduced arthritis [106]. The authors found that administering standardized willow extract at doses of 50 and 150 mg/kg completely suppressed the inflammatory exudates raised by the injection of carrageenan and reduced the leukocytic infiltration by about 52-63%. In

addition, they found that the standardized willow bark extract affects other inflammatory markers such as interleukin-1 β , tumor necrosis factor- α , interleukin-6, prostaglandin E₂, leukotriene B₄, cyclooxygenase 1 and 2 [106]. The willow bark extract has interesting effects against toxic agents, inducing inflammation more than standard anti-inflammatory drugs [106]. Willow is a dense source of bioactive compounds acting synergistically to prevent and treat different perturbations, such as rheumatological diseases [107].

3.7. *Herniaria hirsuta* (HH).

Herniaria hirsuta, from the family of Caryophyllaceae, is a medicinal plant well known for its application in treating kidney diseases such as urolithiasis and stones. Accumulated information from ethnobotanical and experimental studies conducted in vivo and in vitro favors nephrolithiasis's protective and curative effects [36,37,108–110]. The findings of a study published in 2004 on the impact of an aqueous extract of HH on experimentally nephrolithiasis rats showed that this extract at a dose of 50mg/ml decreased the deposition of crystals into the kidney when compared with rats intoxicated with ethylene glycol alone [36]. The same author proved that the saponin-rich fraction isolated from HH significantly reduced crystal deposition in lithiasic rats [110]. Crystal deposits disturb kidney homeostasis and promote the formation of reactive oxygen species accompanied by the stimulation of proinflammatory markers release.

Interestingly, HH enjoys wide acceptance by scientists due to its ability to possess both antioxidant and anti-inflammatory activities [37]. In fact, the anti-inflammatory and antioxidant effects of HH were examined using human blood plasma stressed by peroxyinitrite. Authors found that the HH extract affects the cyclooxygenase 1 and 2 activities [37]. The impact of gastrointestinal and hepatic biotransformation of phytochemicals of HH was evaluated using unbiased dynamic metabolomics and data analysis; authors of this publication showed that the HH extract comprises a dense mixture of phytochemicals including saponin aside from bioactive ingredients or prodrugs which are biotransformed leading to loss sugar moieties forming glucuronidated hepatic metabolites. These later are probably implicated in the urolithiatic effects of HH, as previously documented by Peeters *et al.* and Ritter, 2000 [111,112]. Furthermore, glucuronidated metabolites enjoy emulsifying abilities, which could explain the dissolution of kidney stones [113].

3.8. *Foeniculum vulgare* Mill.

Foeniculum vulgare Mill. FV or fennel is known by the vulgar name *Bisbas* in Arabic and *Amsa* in Amazigh. It belongs to the Apiaceae family and occupies an important place in traditional and popular medicine for its long history as a natural medication [114]. Checking a series of published studies on traditional knowledge of FV, we noticed that FV effectively positively affects different functions, including antioxidant status, glycemia, liver function, kidney function, diuresis, galactagogue, and estrogenic activities [115–120]. Within this frame, several experimental studies have been conducted to confirm the beneficial properties of FV both in vitro and in vivo using animal models. Interestingly, it has been proved that the chronic consumption of FV did not induce any harmful effects [114]. The hepatoprotective effect of FV is evaluated against different toxic agents such as carbon tetrachloride and paracetamol [38,121,122]. The authors found that the hepatotoxic effect of FV extract was 80 folds (1g/ml) of the hepatoprotective dose (12.5 μ g/ml). In addition, the observed hepatoprotective effect of

FV is ascribed to the two compounds 3,4-dihydroxyphenethylalcohol-6-O-caffeoyl- β -D-glucopyranoside and 3',8'-binaringenin, detected for the first time by Ghanem *et al.* [39]. The administration of essential oil of FV at a dose of 0.3ml/kg was sustained for seven weeks with a posology of three times a week. The obtained results showed that the FV essential oil significantly decreased the hepatic enzyme (ALT, AST, and ALP) leakage in tetra chloride-intoxicated rats and showed a significant recovery in the histopathological damage of rats treated simultaneously with CCl₄ and FV essential oil [121]. A study published in 2021 was conducted on fish exposed to glyphosate and treated simultaneously with FV extract at a dose of 1 and 2 ml of fennel ethanolic extract for 30 days. The authors revealed that the exposed fish fed with a fennel-supplemented diet attenuated the hepatic oxidative stress translated by increased malondialdehyde fragmentation and reduced the antioxidant defense systems. Additionally, the fennel proved its ability to down-regulate the gene expression of inflammatory cytokines such as tumor necrosis factor-alpha and interleukin 1 beta [123].

4. Conclusions

Ait Ayash Valley is a very fertile region, and different medicinal plants are grown naturally. Rural populations have used these plants for many purposes as a natural medication for ailments due to their pharmacological properties, including antidiabetic effect, anti-inflammatory effect, antimicrobial effect, antioxidant effect, and so on. The beneficial properties of medicinal and aromatic plants and their by-products are attributed to their dense chemical composition that guided the search for clinical trials and safe and effective new drugs.

Funding

This research received no external funding.

Conflicts of Interest

The authors declare no conflict of interest.

References

1. Benlamdini, N.; Elhafian, M.; Rochdi, A.; Zidane, L. Étude floristique et ethnobotanique de la flore médicinale du Haut Atlas oriental (Haute Moulouya). *J. Appl. Biosci.* **2014**, *78*, 6771–6788, <https://doi.org/10.4314/jab.v78i1.17>.
2. Saadi, Z.; Fedan, B.; Laadila, M.; Kaoukaya, A. Les tidalites liasiques de la Haute Moulouya et du Moyen Atlas méridional (Maroc) : dynamique sédimentaire et contexte paléogéographique. *Bull. Inst. Sci.* **2003**, *25*, 55–71.
3. Ghanem, H. Agriculture and Rural Development for Inclusive Growth and Food Security in Morocco. Brookings Global Working Paper Series, **2015**.
4. Jamshidi-Kia, F.; Lorigooini, Z.; Amini-Khoei, H. Medicinal plants: Past history and future perspective. *J. Herbmed. Pharmacol.* **2017**, *7*, 1–7, <https://doi.org/10.15171/jhp.2018.01>.
5. Bellakhdar, J. A new look at traditional medicine in Morocco. *World Health Forum.* **1989**, *10*, 193-199.
6. Kachmar, M.R.; Naceiri Mrabti, H.; Bellahmar, M.; Ouahbi, A.; Haloui, Z.; El Badaoui, K.; Bouyahya, A.; Chakir, S. Traditional Knowledge of Medicinal Plants Used in the Northeastern Part of Morocco. *Evid.-Based Complementary Altern. Med.* **2021**, *2021*, e6002949, <https://doi.org/10.1155/2021/6002949>.
7. Ousaaïd, D.; Laaroussi, H.; Bakour, M.; El Ghouizi, A.; El Menyiy, N.; Lyoussi, B.; El Arabi, I. Effect of a Combination of *Rosa canina* Fruits and Apple Cider Vinegar against Hydrogen Peroxide-Induced Toxicity in Experimental Animal Models. *J. Food Qual.* **2022**, *2022*, 7381378, <https://doi.org/10.1155/2022/7381378>.

8. Ousaaïd, D.; Mansouri, I.; Laaroussi, H.; ElGhouzi, A.; Lyoussi, B.; ElArabi, I. Phytochemical Content and Antioxidant Activity of Flesh Fruits *Rosa canina* Extracts Collected from Ait Ayach Midelt. *Indian J. Agric. Res.* **2020**, *54*, 373-377, <https://doi.org/10.18805/IJARE.A-494>.
9. Fetni, S.; Bertella, N.; Ouahab, A.; Zapater, J.M.M.; Fernandez, S.D.P.-T. Composition and biological activity of the Algerian plant *Rosa canina* L. by HPLC-UV-MS. *Arab. J. Chem.* **2020**, *13*, 1105–1119, <https://doi.org/10.1016/j.arabjc.2017.09.013>.
10. Rahimi, M.; Sajadimajd, S.; Mahdian, Z.; Hemmati, M.; Malekkhatabi, P.; Bahrami, G.; Mohammadi, B.; Miraghaee, S.; Hatami, R.; Mansouri, K.; Moahammadi Motlagh, H.R.; Keshavarzi, S.; Derakhshankhah, H. Characterization and antidiabetic effects of the oligosaccharide fraction isolated from *Rosa canina* in STZ-Induced diabetic rats. *Carbohydr. Res.* **2020**, *489*, 107927, <https://doi.org/10.1016/j.carres.2020.107927>.
11. Sadeghi, H.; Hosseinzadeh, S.; Touri, M.A.; Ghavamzadeh, M.; Barmak, M.J.; Sayahi, M.; Sadeghi, H. Hepatoprotective effect of *Rosa canina* fruit extract against carbon tetrachloride induced hepatotoxicity in rat. *Avicenna J. Phytomed.* **2016**, *6*, 181-188.
12. Aladedunye, F.; Kersting, H.J.; Matthäus, B. Phenolic extract from wild rose hip with seed: Composition, antioxidant activity, and performance in canola oil. *Eur. J. Lipid Sci. Technol.* **2014**, *116*, 1025–1034, <https://doi.org/10.1002/ejlt.201300255>.
13. Kawaguchi, T.; Takano, A.; Tsukatani, T.; Kuroda, R.; Ueda, K.; Tsubata, M. Inhibitory effect of rosehip (*Rosa canina* L.) on the formation of advanced glycation endproducts by scavenging reactive carbonyls. *Glycative Stress Res.* **2016**, *3*, 91–98, https://doi.org/10.24659/gsr.3.2_091.
14. Mármol, I.; Sánchez-de-Diego, C.; Jiménez-Moreno, N.; Ancín-Azpilicueta, C.; Rodríguez-Yoldi, M.J. Therapeutic Applications of Rose Hips from Different *Rosa* Species. *Int. J. Mol. Sci.* **2017**, *18*, 1137, <https://doi.org/10.3390/ijms18061137>.
15. Singh, R.; Barden, A.; Mori, T.; Beilin, L. Advanced glycation end-products: a review. *Diabetologia* **2001**, *44*, 129–146, <https://doi.org/10.1007/s001250051591>.
16. Ayati, Z.; Amiri, M.S.; Ramezani, M.; Delshad, E.; Sahebkar, A.; Emami, S.A. Phytochemistry, Traditional Uses and Pharmacological Profile of Rose Hip: A Review. *Current pharmaceutical design* **2018**, *24*, 4101–4124.
17. Jiménez, S.; Gascón, S.; Luquin, A.; Laguna, M.; Ancin-Azpilicueta, C.; Rodríguez-Yoldi, M.J. *Rosa canina* Extracts Have Antiproliferative and Antioxidant Effects on Caco-2 Human Colon Cancer. *PLoS ONE* **2016**, *11*, e0159136, <https://doi.org/10.1371/journal.pone.0159136>.
18. Tumbas, V.T.; Čanadanović-Brunet, J.M.; Četojević-Simin, D.D.; Četković, G.S.; Ethilas, S.M.; Gille, L. Effect of rosehip (*Rosa canina* L.) phytochemicals on stable free radicals and human cancer cells. *J. Sci. Food Agric.* **2012**, *92*, 1273–1281, <https://doi.org/10.1002/jsfa.4695>.
19. Zhong, L. Anti-cancer effects of bioactive compounds from rose hip fruit in human breast cancer cell lines : carotenoids, triterpenes, and ascorbate evaluated singly or in combination. Doctoral thesis, Swedish University of Agricultural Sciences, Alnarp, Sweden, **2017**.
20. Adamczak, A.; Buchwald, W.; Zieliński, J.; Mielcarek, S. FLAVONOID AND ORGANIC ACID CONTENT IN ROSE HIPS (*ROSA* L., SECT. CANINAE DC. EM. CHRIST.). *Acta Biol. Crac. Ser. Bot.* **2012**, *54*, 105-112, <https://doi.org/10.2478/v10182-012-0012-0>.
21. Hosni, K.; Chrif, R.; Zahed, N.; Abid, I.; Medfei, W.; Sebei, H.; Brahim, N.B. Fatty acid and phenolic constituents of leaves, flowers and fruits of tunisian dog rose (*Rosa canina* L.). *Riv. Ital. Sostanze Grasse.* **2010**, *87*, 117–123.
22. Roman, I.; Stănilă, A.; Stănilă, S. Bioactive compounds and antioxidant activity of *Rosa canina* L. biotypes from spontaneous flora of Transylvania. *Chem. Cent. J.* **2013**, *7*, 73, <https://doi.org/10.1186/1752-153X-7-73>.
23. Soltan, O.I.A.; Gazwi, H.S.S.; Ragab, A.E.; Aljohani, A.S.M.; El-Ashmawy, I.M.; Batiha, G.E.-S.; Hafiz, A.A.; Abdel-Hameed, S.M. Assessment of Bioactive Phytochemicals and Utilization of *Rosa canina* Fruit Extract as a Novel Natural Antioxidant for Mayonnaise. *Molecules* **2023**, *28*, 3350, <https://doi.org/10.3390/molecules28083350>.
24. Mourabit, Y.; El Hajjaji, S.; Taha, D.; Badaoui, B.; El Yadini, M.; Rusu, M.E.; Lee, L.-H.; Bouyahya, A.; Bourais, I. HPLC-DAD-ESI/MS phytochemical investigation, antioxidant, and antidiabetic activities of Moroccan *Rosa canina* L. extracts. *Biocatal. Agric. Biotechnol.* **2023**, *52*, 102817, <https://doi.org/10.1016/j.bcab.2023.102817>.

25. Elouafy, Y.; Mortada, S.; Yadini, A.E.; Hnini, M.; Aalilou, Y.; Harhar, H.; Khalid, A.; Abdalla, A.N.; Bouyahya, A.; Faouzi, M.E.A.; Tabyaoui, M. Bioactivity of Walnut: Investigating the Triterpenoid Saponin Extracts of *Juglans Regia* Kernels for Antioxidant, Antidiabetic, and Antimicrobial Properties. *Prog. Microbes Mol. Biol.* **2023**, *6*, <https://doi.org/10.36877/pmmb.a0000325>.
26. Ghorbani, R.; Mokhtari, T.; Khazaei, M.; Salahshoor, M.R.; Jalili, C.; Bakhtiari, M. The Effect of Walnut on the Weight, Blood Glucose and Sex Hormones of Diabetic Male Rats. *Int. J. Morphol.* **2014**, *32*, 833–838, <http://doi.org/10.4067/S0717-95022014000300015>.
27. Ellafi, A.; Farhat, R.; Snoussi, M.; Noumi, E.; Anouar, E.H.; Ben Ali, R.; El May, M.V.; Sayadi, S.; Aouadi, K.; Kadri, A.; Ben Younes, S. Phytochemical profiling, antimicrobial, antibiofilm, insecticidal, and anti-leishmanial properties of aqueous extract from *Juglans regia* L. root bark: *In vitro* and *in silico* approaches. *Int. J. Food Prop.* **2023**, *26*, 1079–1097, <https://doi.org/10.1080/10942912.2023.2200561>.
28. Santos, A.; Barros, L.; Calhelha, R.C.; Dueñas, M.; Carvalho, A.M.; Santos-Buelga, C.; Ferreira, I.C.F.R. Leaves and decoction of *Juglans regia* L.: Different performances regarding bioactive compounds and *in vitro* antioxidant and antitumor effects. *Ind. Crops Prod.* **2013**, *51*, 430–436, <https://doi.org/10.1016/j.indcrop.2013.10.003>.
29. Touati, R.; Santos, S.A.O.; Rocha, S.M.; Belhamel, K.; Silvestre, A.J.D. Phenolic composition and biological prospecting of grains and stems of *Retama sphaerocarpa*. *Ind. Crops Prod.* **2017**, *95*, 244–255, <https://doi.org/10.1016/j.indcrop.2016.10.027>.
30. González-Mauraza, H.; Martín-Cordero, C.; Alarcón-de-la-Lastra, C.; Rosillo, M.A.; León-González, A.J.; Sánchez-Hidalgo, M. Anti-inflammatory effects of *Retama monosperma* in acute ulcerative colitis in rats. *J. Physiol. Biochem.* **2014**, *70*, 163–172, <https://doi.org/10.1007/s13105-013-0290-3>.
31. Farouk, L.; Laroubi, A.; Aboufatima, R.; Benharref, A.; Chait, A. Evaluation of the analgesic effect of alkaloid extract of *Peganum harmala* L.: Possible mechanisms involved. *J. Ethnopharmacol.* **2008**, *115*, 449–454, <https://doi.org/10.1016/j.jep.2007.10.014>.
32. Lamchouri, F.; Zemzami, M.; Jossang, A.; Abdellatif, A.; Israili, Z.H.; Lyoussi, B. Cytotoxicity of alkaloids isolated from *Peganum harmala* seeds. *Pak. J. Pharm. Sci.* **2013**, *26*, 699–706.
33. Jensen, G.S.; Attridge, V.L.; Benson, K.F.; Beaman, J.L.; Carter, S.G.; Ager, D. Consumption of Dried Apple Peel Powder Increases Joint Function and Range of Motion. *J. Med. Food* **2014**, *17*, 1204–1213, <https://doi.org/10.1089/jmf.2014.0037>.
34. Sharma, S.; Rana, S.; Patial, V.; Gupta, M.; Bhushan, S.; Padwad, Y.S. Antioxidant and hepatoprotective effect of polyphenols from apple pomace extract via apoptosis inhibition and Nrf2 activation in mice. *Hum. Exp. Toxicol.* **2016**, *35*, 1264–1275, <https://doi.org/10.1177/0960327115627689>.
35. Drummond, E.M.; Harbourne, N.; Marete, E.; Martyn, D.; Jacquier, J.C.; O’Riordan, D.; Gibney, E.R. Inhibition of Proinflammatory Biomarkers in THP1 Macrophages by Polyphenols Derived from Chamomile, Meadowsweet and Willow Bark. *Phytother. Res.* **2013**, *27*, 588–594, <https://doi.org/10.1002/ptr.4753>.
36. Atmani, F.; Slimani, Y.; Mimouni, M.; Aziz, M.; Hacht, B.; Ziyat, A. Effect of aqueous extract from *Herniaria hirsuta* L. on experimentally nephrolithiasic rats. *J. Ethnopharmacol.* **2004**, *95*, 87–93, <https://doi.org/10.1016/j.jep.2004.06.028>.
37. Kozachok, S.; Kolodziejczyk-Czepas, J.; Marchyshyn, S.; Wojtanowski, K.K.; Zgórk, G.; Oleszek, W. Comparison of Phenolic Metabolites in Purified Extracts of Three Wild-Growing *Herniaria* L. Species and Their Antioxidant and Anti-Inflammatory Activities *In Vitro*. *Molecules* **2022**, *27*, 530, <https://doi.org/10.3390/molecules27020530>.
38. Nazir, T.; Shakir, L.; Zaka-ur-Rahman; Najam, K.; Choudhary, A.; Saeed, N.; Haroon-urRasheed; Nazir, A.; Aslam, S.; Khanum, A.B. Hepatoprotective Activity of *Foeniculum vulgare* Against Paracetamol Induced Hepatotoxicity in Rabbit. *J. Appl. Pharm.* **2020**, *12*, 270, <https://doi.org/10.35248/2376-0354.20.12.270>.
39. Ghanem, M.T.M.; Radwan, H.M.A.; Mahdy, E.-S.M.; Elkholy, Y.M.; Hassanein, H.D.; Shahat, A.A. Phenolic Compounds from *Foeniculum Vulgare* (Subsp. *Piperitum*) (Apiaceae) Herb and Evaluation of Hepatoprotective Antioxidant Activity. *Pharmacogn. Res.* **2012**, *4*, 104–108, <https://doi.org/10.4103/0974-8490.94735>.
40. Hosseini, S.; Jamshidi, L.; Mehrzadi, S.; Mohammad, K.; Najmizadeh, A.R.; Alimoradi, H.; Huseini, H.F. Effects of *Juglans Regia* L. Effects of *Juglans regia* L. leaf extract on hyperglycemia and lipid profiles in type two diabetic patients: A randomized double-blind, placebo-controlled clinical trial. *J. Ethnopharmacol.* **2014**, *152*, 451–456, <https://doi.org/10.1016/j.jep.2014.01.012>.

41. Al-Rawi, R.; Bashir, Y.; Mustafa, A.; Omar, M.; Al-Rawi, N.; Saeed, M.; Uthman, A.; Al-Rawi, N.H. Teeth Whitening and Antibacterial Effects of *Juglans regia* Bark: A Preliminary Study. *Int. J. Dent.* **2021**, *2021*, 6685437, <https://doi.org/10.1155/2021/6685437>.
42. Deshpande, R.R.; Kale, A.A.; Ruikar, A.D.; Panvalkar, P.S.; Kulkarni, A.A.; Deshpande, N.R.; Salvekar, J.P. ANTIMICROBIAL ACTIVITY OF DIFFERENT EXTRACTS OF *JUGLANS REGIA* L. AGAINST ORAL MICROFLORA. *Int. J. Pharm. Pharm. Sci.* **2011**, *3*, 200–201.
43. Dolatabadi, S.; Moghadam, H.N.; Mahdavi-Ourtakand, M. Evaluating the *anti*-biofilm and antibacterial effects of *Juglans regia* L. extracts against clinical isolates of *Pseudomonas aeruginosa*. *Microb. Pathog.* **2018**, *118*, 285–289, <https://doi.org/10.1016/j.micpath.2018.03.055>.
44. Kavuncuoglu, H.; Kavuncuoglu, E.; Karatas, S.M.; Benli, B.; Sagdic, O.; Yalcin, H. Prediction of the antimicrobial activity of walnut (*Juglans regia* L.) kernel aqueous extracts using artificial neural network and multiple linear regression. *J. Microbiol. Methods* **2018**, *148*, 78–86, <https://doi.org/10.1016/j.mimet.2018.04.003>.
45. Noumi, E.; Snoussi, M.; Trabelsi, N.; Hajlaoui, H.; Ksouri, R.; Valentin, E.; Bakhrouf, A. Antibacterial, anticandidal and antioxidant activities of *Salvadora persica* and *Juglans regia* L. extracts. *J. Med. Plant Res.* **2011**, *5*, 4138–4146.
46. Zakavi, F.; Golpasand Hagh, L.; Daraeighadikolaei, A.; Farajzadeh Sheikh, A.; Daraeighadikolaei, A.; Leilavi Shoostari, Z. Antibacterial Effect of *Juglans Regia* Bark against Oral Pathologic Bacteria. *Int. J. Dent.* **2013**, *2013*, 854765, <https://doi.org/10.1155/2013/854765>.
47. Sheng, F.; Hu, B.; Jin, Q.; Wang, J.; Wu, C.; Luo, Z. The Analysis of Phenolic Compounds in Walnut Husk and Pellicle by UPLC-Q-Orbitrap HRMS and HPLC. *Molecules* **2021**, *26*, 3013, <https://doi.org/10.3390/molecules26103013>.
48. Wu, S.; Shen, D.; Wang, R.; Li, Q.; Mo, R.; Zheng, Y.; Zhou, Y.; Liu, Y. Phenolic profiles and antioxidant activities of free, esterified and bound phenolic compounds in walnut kernel. *Food Chem.* **2021**, *350*, 129217, <https://doi.org/10.1016/j.foodchem.2021.129217>.
49. Zhang, Z.; Liao, L.; Moore, J.; Wu, T.; Wang, Z. Antioxidant phenolic compounds from walnut kernels (*Juglans regia* L.). *Food Chem.* **2009**, *113*, 160–165, <https://doi.org/10.1016/j.foodchem.2008.07.061>.
50. Medic, A.; Jakopic, J.; Hudina, M.; Solar, A.; Veberic, R. Identification and quantification of the major phenolic constituents in *Juglans regia* L. peeled kernels and pellicles, using HPLC–MS/MS. *Food Chem.* **2021**, *352*, 129404, <https://doi.org/10.1016/j.foodchem.2021.129404>.
51. Spector, A. Review: Oxidative Stress and Disease. *J. Ocul. Pharmacol. Ther.* **2000**, *16*, 193–201, <https://doi.org/10.1089/jop.2000.16.193>.
52. D'Angeli, F.; Malfa, G.A.; Garozzo, A.; Li Volti, G.; Genovese, C.; Stivala, A.; Nicolosi, D.; Attanasio, F.; Bellia, F.; Ronsisvalle, S.; Acquaviva, R. Antimicrobial, Antioxidant, and Cytotoxic Activities of *Juglans regia* L. Pellicle Extract. *Antibiotics* **2021**, *10*, 159, <https://doi.org/10.3390/antibiotics10020159>.
53. Fizeşan, I.; Rusu, M.E.; Georgiu, C.; Pop, A.; Ştefan, M.-G.; Muntean, D.-M.; Mirel, S.; Vostinaru, O.; Kiss, B.; Popa, D.-S. Antitussive, Antioxidant, and Anti-Inflammatory Effects of a Walnut (*Juglans regia* L.) Septum Extract Rich in Bioactive Compounds. *Antioxidants* **2021**, *10*, 119, <https://doi.org/10.3390/antiox10010119>.
54. Nasiry, D.; Khalatbary, A.R.; Ahmadvand, H.; Talebpour Amiri, F.B. Effects of *Juglans regia* L. leaf extract supplementation on testicular functions in diabetic rats. *Biotech. Histochem.* **2021**, *96*, 41–47, <https://doi.org/10.1080/10520295.2020.1755893>.
55. Sharma, P.; Verma, P.K.; Sood, S.; Pankaj, N.K.; Agarwal, S.; Raina, R. Neuroprotective potential of hydroethanolic hull extract of *Juglans regia* L. on isoprenaline induced oxidative damage in brain of Wistar rats. *Toxicol. Rep.* **2021**, *8*, 223–229, <https://doi.org/10.1016/j.toxrep.2021.01.006>.
56. Mobashar, A.; Shabbir, A.; Shahzad, M.; Gobe, G. Preclinical Rodent Models of Arthritis and Acute Inflammation Indicate Immunomodulatory and Anti-Inflammatory Properties of *Juglans regia* Extracts. *Evid.-Based Complementary Altern. Med.* **2022**, *2022*, 1695701, <https://doi.org/10.1155/2022/1695701>.
57. Alami, S.; Lamin, H.; Bennis, M.; Bouhnik, O.; Lamrabet, M.; El Hachimi, M.L.; Abdelmoumen, H.; Bedmar, E.J.; El Idrissi, M.M. Characterization of *Retama sphaerocarpa* microsymbionts in Zaida lead mine tailings in the Moroccan middle Atlas. *Syst. Appl. Microbiol.* **2021**, *44*, 126207, <https://doi.org/10.1016/j.syapm.2021.126207>.

58. Prieto, I.; Armas, C.; Pugnaire, F.I. Water release through plant roots: new insights into its consequences at the plant and ecosystem level. *New Phytol.* **2012**, *193*, 830–841, <https://doi.org/10.1111/j.1469-8137.2011.04039.x>.
59. Rodríguez-Echeverría, S.; Pérez-Fernández, M.A.; Vlaar, S.; Finnan, T.M. Analysis of the legume–rhizobia symbiosis in shrubs from central western Spain. *J. Appl. Microbiol.* **2003**, *95*, 1367–1374, <https://doi.org/10.1046/j.1365-2672.2003.02118.x>.
60. Valladares, F.; Villar-Salvador, P.; Domínguez, S.; Fernández-Pascual, M.; Peñuelas, J.L.; Pugnaire, F.I. Enhancing the early performance of the leguminous shrub *Retama sphaerocarpa* (L.) Boiss.: fertilisation versus *Rhizobium* inoculation. *Plant Soil* **2002**, *240*, 253–262.
61. León-González, A.J.; Navarro, I.; Acero, N.; Muñoz Mingarro, D.; Martín-Cordero, C. Genus *Retama*: a review on traditional uses, phytochemistry, and pharmacological activities. *Phytochem. Rev.* **2018**, *17*, 701–731, <https://doi.org/10.1007/s11101-018-9555-3>.
62. Boussahel, S.; Cacciola, F.; Dahamna, S.; Mondello, L.; Saija, A.; Cimino, F.; Speciale, A.; Cristani, M. Flavonoid profile, antioxidant and antiglycation properties of *Retama sphaerocarpa* fruits extracts. *Nat. Prod. Res.* **2018**, *32*, 1911–1919, <https://doi.org/10.1080/14786419.2017.1356835>.
63. López-Lázaro, M.; Martín-Cordero, C.; Cortés, F.; Piñero, J.; Ayuso, M.J. Cytotoxic activity of flavonoids and extracts from *Retama sphaerocarpa* Boissier. *Z. Naturforsch. C* **2000**, *55*, 40–43, <https://doi.org/10.1515/znc-2000-1-209>.
64. Nagai, R.; Shirakawa, J.-I.; Ohno, R.-I.; Moroishi, N.; Nagai, M. Inhibition of AGEs formation by natural products. *Amino Acids* **2014**, *46*, 261–266, <https://doi.org/10.1007/s00726-013-1487-z>.
65. Crasci, L.; Lauro, M.R.; Puglisi, G.; Panico, A. Natural antioxidant polyphenols on inflammation management: Anti-glycation activity vs metalloproteinases inhibition. *Crit. Rev. Food Sci. Nutr.* **2018**, *58*, 893–904, <https://doi.org/10.1080/10408398.2016.1229657>.
66. El Bahri, L.; Chemli, R. *Peganum harmala* L: a poisonous plant of North Africa. *Vet. Hum. Toxicol.* **1991**, *33*, 276–277.
67. Bellakhdar, J. La Pharmacopée marocaine traditionnelle: médecine arabe ancienne et savoirs populaires. Le Fennec, **1997**.
68. Mahmoudian, M.; Jalilpour, H.; Salehian, P. Toxicity of *Peganum Harmala*: Review and a Case Report. *Iran. J. Pharmacol. Ther.* **2002**, *1*, 1–4.
69. Moloudizargari, M.; Mikaili, P.; Aghajanshakeri, S.; Asghari, M.H.; Shayegh, J. Pharmacological and Therapeutic Effects of *Peganum harmala* and its Main Alkaloids. *Pharmacogn. Rev.* **2013**, *7*, 199–212, <https://doi.org/10.4103%2F0973-7847.120524>.
70. Atrooz, O.M.; Wietrzyk, J.; Filip-Psurska, B.; Al-Rawashdeh, I.; Soub, M.; Abukhalil, M.H. ANTIPROLIFERATIVE, ANTIOXIDANT, AND ANTIBACTERIAL ACTIVITIES OF CRUDE PLANT EXTRACTS OF *ASPHODELINE LUTEA* L. AND *PEGANUM HARMALA* L. *World J. Pharm. Res.* **2018**, *7*, 148–167.
71. Seyed Hassan Tehrani, S.; Hashemi Sheikh Shabani, S.; Tahmasebi Enferadi, S.; Rabiei, Z. Growth Inhibitory Impact of *Peganum Harmala* L. on Two Breast Cancer Cell Lines. *Iran. J. Biotechnol.* **2014**, *12*, 8–14, <https://doi.org/10.5812/IJB.18562>.
72. Hamsa, T.P.; Kuttan, G. Harmine activates intrinsic and extrinsic pathways of apoptosis in B16F-10 melanoma. *Chin. Med.* **2011**, *6*, 11, <https://doi.org/10.1186%2F1749-8546-6-11>.
73. Roostae, Z. Effect of Alkaloids Belong to β -Carbolines Family in *Peganum Harmala* on Cancer Cells. *Sarem J. Med. Res.* **2018**, *3*, 73–78, <https://doi.org/10.29252/sjrm.2.2.73>.
74. Robinson, J.P.; Harris, S.A.; Juniper, B.E. Taxonomy of the genus *Malus* Mill. (Rosaceae) with emphasis on the cultivated apple, *Malus domestica* Borkh. *Plant Syst. Evol.* **2001**, *226*, 35–58, <https://doi.org/10.1007/s006060170072>.
75. Dickinson, T.A.; Lo, E.; Talent, N. Polyploidy, reproductive biology, and Rosaceae: understanding evolution and making classifications. *Plant Syst. Evol.* **2007**, *266*, 59–78, <https://doi.org/10.1007/s00606-007-0541-2>.
76. Boyer, J.; Liu, R.H. Apple phytochemicals and their health benefits. *Nutr. J.* **2004**, *3*, 5, <https://doi.org/10.1186%2F1475-2891-3-5>.
77. Zhao, C.-N.; Meng, X.; Li, Y.; Li, S.; Liu, Q.; Tang, G.-Y.; Li, H.-B. Fruits for Prevention and Treatment of Cardiovascular Diseases. *Nutrients* **2017**, *9*, 598, <https://doi.org/10.3390/nu9060598>.
78. Biedrzycka, E.; Amarowicz, R. Diet and Health: Apple Polyphenols as Antioxidants. *Food Rev. Int.* **2008**, *24*, 235–251, <https://doi.org/10.1080/87559120801926302>.

79. Blanco, D.; Quintanilla, M.E.; Mangas, J.J.; Gutierrez, M.D. Determination of Organic Acids in Apple Juice by Capillary Liquid Chromatography. *J. Liq. Chromatogr. Relat. Technol.* **1996**, *19*, 2615–2621, <https://doi.org/10.1080/10826079608014042>.
80. Zhang, Y.; Li, P.; Cheng, L. Developmental changes of carbohydrates, organic acids, amino acids, and phenolic compounds in ‘Honeycrisp’ apple flesh. *Food Chem.* **2010**, *123*, 1013–1018, <https://doi.org/10.1016/j.foodchem.2010.05.053>.
81. Hyson, D.A. A Comprehensive Review of Apples and Apple Components and Their Relationship to Human Health. *Adv. Nutr.* **2011**, *2*, 408–420, <https://doi.org/10.3945/an.111.000513>.
82. Scherz-Shouval, R.; Elazar, Z. Regulation of autophagy by ROS: physiology and pathology. *Trends Biochem. Sci.* **2011**, *36*, 30–38, <https://doi.org/10.1016/j.tibs.2010.07.007>.
83. Ferretti, G.; Turco, I.; Bacchetti, T. Apple as a Source of Dietary Phytonutrients: Bioavailability and Evidence of Protective Effects against Human Cardiovascular Disease. *Food Nutr. Sci.* **2014**, *5*, 1234–1246, <https://doi.org/10.4236/fns.2014.513134>.
84. Honda, M.; Hara, Y. Inhibition of Rat Small Intestinal Sucrase and α -Glucosidase Activities by Tea Polyphenols. *Biosci. Biotechnol. Biochem.* **1993**, *57*, 123–124, <https://doi.org/10.1271/bbb.57.123>.
85. Welsch, C.A.; Lachance, P.A.; Wasserman, B.P. Dietary Phenolic Compounds: Inhibition of Na⁺-Dependent D-Glucose Uptake in Rat Intestinal Brush Border Membrane Vesicles. *J. Nutr.* **1989**, *119*, 1698–1704, <https://doi.org/10.1093/jn/119.11.1698>.
86. Patocka, J.; Bhardwaj, K.; Klimova, B.; Nepovimova, E.; Wu, Q.; Landi, M.; Kuca, K.; Valis, M.; Wu, W. *Malus domestica*: A Review on Nutritional Features, Chemical Composition, Traditional and Medicinal Value. *Plants* **2020**, *9*, 1408, <https://doi.org/10.3390/plants9111408>.
87. Ousaaïd, D.; Ghouizi, A.E.; Laaroussi, H.; Bakour, M.; Mechchate, H.; Es-safi, I.; Kamaly, O.A.; Saleh, A.; Conte, R.; Lyoussi, B.; El Arabi, I. Anti-Anemic Effect of Antioxidant-Rich Apple Vinegar against Phenylhydrazine-Induced Hemolytic Anemia in Rats. *Life* **2022**, *12*, 239, <https://doi.org/10.3390/life12020239>.
88. Ousaaïd, D.; Laaroussi, H.; Bakour, M.; Ennaji, H.; Lyoussi, B.; El Arabi, I. Antifungal and Antibacterial Activities of Apple Vinegar of Different Cultivars. *Int. J. Microbiol.* **2021**, *2021*, 6087671, <https://doi.org/10.1155/2021/6087671>.
89. Ousaaïd, D.; Laaroussi, H.; Bakour, M.; ElGhouizi, A.; Aboulghazi, A.; Lyoussi, B.; ElArabi, I. Beneficial Effects of Apple Vinegar on Hyperglycemia and Hyperlipidemia in Hypercaloric-Fed Rats. *J. Diabetes Res.* **2020**, *2020*, 9284987, <https://doi.org/10.1155/2020/9284987>.
90. Ozturk, I.; Caliskan, O.; Tornuk, F.; Ozcan, N.; Yalcin, H.; Baslar, M.; Sagdic, O. Antioxidant, antimicrobial, mineral, volatile, physicochemical and microbiological characteristics of traditional home-made Turkish vinegars. *LWT - Food Sci. Technol.* **2015**, *63*, 144–151, <https://doi.org/10.1016/j.lwt.2015.03.003>.
91. Shah, Q.A.; Bibi, F.; Shah, A.H. Antimicrobial Effects of Olive Oil and Vinegar against *Salmonella* and *Escherichia coli*. *Pac. J. Sci. Technol.* **2013**, *14*, 479–486.
92. Thinathayalan, D.; Yuan, B.T.; Kaur, J.; Albert, Y.; Yan, N.J. The Effects of Apple Cider Vinegar on Weight, Blood Pressure, Blood Glucose Level and Heart Rate of 60 MMC Medical Students Randomized Controlled Trial. *Med. J.I* **2019**, *6*, 88–100.
93. Tripathi, S.; Mazumder, P.M. Apple Cider Vinegar (ACV) and their Pharmacological Approach towards Alzheimer’s Disease (AD): A Review. *Indian J. Pharm. Educ. Res* **2020**, *54*, s67–s74, <https://doi.org/10.5530/ijper.54.2s.62>.
94. Wakuda, T.; Azuma, K.; Saimoto, H.; Ifuku, S.; Morimoto, M.; Arifuku, I.; Asaka, M.; Tsuka, T.; Imagawa, T.; Okamoto, Y.; Osaki, T.; Minami, S. Protective effects of galacturonic acid-rich vinegar brewed from Japanese pear in a dextran sodium sulfate-induced acute colitis model. *J. Funct. Foods* **2013**, *5*, 516–523, <https://doi.org/10.1016/j.jff.2012.10.010>.
95. Xia, T.; Zhang, B.; Duan, W.; Li, Y.; Zhang, J.; Song, J.; Zheng, Y.; Wang, M. Hepatoprotective efficacy of Shanxi aged vinegar extract against oxidative damage *in vitro* and *in vivo*. *J. Funct. Foods* **2019**, *60*, 103448, <https://doi.org/10.1016/j.jff.2019.103448>.
96. Klasnja, B.; Kopitovic, S.; Orlovic, S. Wood and bark of some poplar and willow clones as fuelwood. *Biomass Bioenergy* **2002**, *23*, 427–432, [https://doi.org/10.1016/S0961-9534\(02\)00069-7](https://doi.org/10.1016/S0961-9534(02)00069-7).
97. Mahdi, J.G.; Mahdi, A.J.; Mahdi, A.J.; Bowen, I.D. The historical analysis of aspirin discovery, its relation to the willow tree and antiproliferative and anticancer potential. *Cell Prolif.* **2006**, *39*, 147–155, <https://doi.org/10.1111/j.1365-2184.2006.00377.x>.

98. Leroux, H. Discovery of Salicine. *J. Chim. Med* **1830**, 6, 340–432.
99. Oketch-Rabah, H.A.; Marles, R.J.; Jordan, S.A.; Dog, T.L. United States Pharmacopeia Safety Review of Willow Bark. *Planta Med.* **2019**, *85*, 1192–1202, <https://doi.org/10.1055/a-1007-5206>.
100. Shara, M.; Stohs, S.J. Efficacy and Safety of White Willow Bark (*Salix alba*) Extracts. *Phytother. Res.* **2015**, *29*, 1112–1116, <https://doi.org/10.1002/ptr.5377>.
101. Kammerer, B.; Kahlich, R.; Biegert, C.; Gleiter, C.H.; Heide, L. HPLC-MS/MS analysis of willow bark extracts contained in pharmaceutical preparations. *Phytochem. Anal.* **2005**, *16*, 470–478, <https://doi.org/10.1002/pca.873>.
102. Förster, N.; Ulrichs, C.; Zander, M.; Kätzel, R.; Mewis, I. Influence of the season on the salicylate and phenolic glycoside contents in the bark of *Salix daphnoides*, *Salix pentandra*, and *Salix purpurea*. *J. Appl. Bot. Food Qual.* **2012**, *82*, 99–102.
103. Phillips, H.N.; Sharpe, K.T.; Endres, M.I.; Heins, B.J. Effects of oral white willow bark (*Salix alba*) and intravenous flunixin meglumine on prostaglandin E₂ in healthy dairy calves. *JDS Commun.* **2022**, *3*, 49–54, <https://doi.org/10.3168/jdsc.2021-0138>.
104. Wu, J.T.; Wu, L.L. Local Inflammatory Diseases Are at Risk of Developing Myocardial Infarction, Stroke, Renal Failure and Cancer via Chronic Systemic Inflammation. *J. Biomed. Lab. Sci.* **2007**, *19*, 35–39.
105. Grigore, A.; Vulturescu, V.; Neagu, G.; Ungureanu, P.; Panteli, M.; Rasit, I. Antioxidant–Anti-Inflammatory Evaluation of a Polyherbal Formula. *Pharmaceuticals* **2022**, *15*, 114, <https://doi.org/10.3390/ph15020114>.
106. Khayyal, M.T.; El-Ghazaly, M.A.; Abdallah, D.M.; Okpanyi, S.N.; Kelber, O.; Weiser, D. Mechanisms Involved in the Anti-Inflammatory Effect of a Standardized Willow Bark Extract. *Arzneimittelforschung* **2005**, *55*, 677–687, <https://doi.org/10.1055/s-0031-1296917>.
107. Bonaterra, G.A.; Heinrich, E.U.; Kelber, O.; Weiser, D.; Metz, J.; Kinscherf, R. Anti-inflammatory effects of the willow bark extract STW 33-I (Proaktiv®) in LPS-activated human monocytes and differentiated macrophages. *Phytomedicine* **2010**, *17*, 1106–1113, <https://doi.org/10.1016/j.phymed.2010.03.022>.
108. Atmani, F.; Slimani, Y.; Mimouni, M.; Hacht, B. Prophylaxis of calcium oxalate stones by *Herniaria hirsuta* on experimentally induced nephrolithiasis in rats. *BJU Int.* **2003**, *92*, 137–140, <https://doi.org/10.1046/j.1464-410x.2003.04289.x>.
109. Bencheikh, N.; Elbouzidi, A.; Kharchoufa, L.; Ouassou, H.; Alami Merrouni, I.; Mechchate, H.; Es-safi, I.; Hano, C.; Addi, M.; Bouhrim, M.; Eto, B.; Elachouri, M. Inventory of Medicinal Plants Used Traditionally to Manage Kidney Diseases in North-Eastern Morocco: Ethnobotanical Fieldwork and Pharmacological Evidence. *Plants* **2021**, *10*, 1966, <https://doi.org/10.3390/plants10091966>.
110. Fouada, A.; Yamina, S.; Nait, M.A.; Mohammed, B.; Abdlekrim, R. In Vitro and in Vivo Antilithiasic Effect of Saponin Rich Fraction Isolated from *Herniaria hirsuta*. *J Bras. Nefrol.* **2006**, *28*, 199–203.
111. Peeters, L.; Beirnaert, C.; Auwera, A.V.d.; Bruyne, T.D.; Laukens, K.; Pieters, L.; Hermans, N.; Foubert, K. Metabolic profile elucidation after *in vitro* biotransformation of *Herniaria hirsuta* by an innovative data analysis strategy for dynamic multiclass experiments. *Planta Med.* **2019**, *85*, 106, <https://doi.org/10.1055/s-0039-3399837>.
112. Ritter, J.K. Roles of glucuronidation and UDP-glucuronosyltransferases in xenobiotic bioactivation reactions. *Chem. Biol. Interact.* **2000**, *129*, 171–193, [https://doi.org/10.1016/s0009-2797\(00\)00198-8](https://doi.org/10.1016/s0009-2797(00)00198-8).
113. Peeters, L.; Van der Auwera, A.; Beirnaert, C.; Bijttebier, S.; Laukens, K.; Pieters, L.; Hermans, N.; Foubert, K. Compound Characterization and Metabolic Profile Elucidation after *in Vitro* Gastrointestinal and Hepatic Biotransformation of an *Herniaria hirsuta* Extract Using Unbiased Dynamic Metabolomic Data Analysis. *Metabolites* **2020**, *10*, 111, <https://doi.org/10.3390/metabo10030111>.
114. Badgular, S.B.; Patel, V.V.; Bandivdekar, A.H. *Foeniculum vulgare* Mill: A Review of Its Botany, Phytochemistry, Pharmacology, Contemporary Application, and Toxicology. *BioMed Res. Int.* **2014**, *2014*, 842674, <https://doi.org/10.1155/2014/842674>.
115. Andrade-Cetto, A. Ethnobotanical study of the medicinal plants from Tlanchinol, Hidalgo, México. *J. Ethnopharmacol.* **2009**, *122*, 163–171, <https://doi.org/10.1016/j.jep.2008.12.008>.
116. Es-Safi, I.; Mechchate, H.; Amaghnoije, A.; Jawhari, F.Z.; Bari, A.; Cerruti, P.; Avella, M.; Grafov, A.; Bousta, D. Medicinal plants used to treat acute digestive system problems in the region of Fez-Meknes in Morocco: An ethnopharmacological survey. *Ethnobot. Res. Appl.* **2020**, *20*, 1–14.
117. Jaradat, N.A.; Zaid, A.N.; Al-Ramahi, R.; Alqub, M.A.; Hussein, F.; Hamdan, Z.; Mustafa, M.; Qneibi, M.; Ali, I. Ethnopharmacological survey of medicinal plants practiced by traditional healers and herbalists

- for treatment of some urological diseases in the West Bank/Palestine. *BMC Complement. Altern. Med.* **2017**, *17*, 255, <https://doi.org/10.1186/s12906-017-1758-4>.
118. Rahimi, R.; Ardekani, M.R.S. Medicinal properties of *Foeniculum vulgare* Mill. in traditional Iranian medicine and modern phytotherapy. *Chin. J. Integr. Med.* **2013**, *19*, 73–79, <https://doi.org/10.1007/s11655-013-1327-0>.
119. Rather, M.A.; Dar, B.A.; Sofi, S.N.; Bhat, B.A.; Qurishi, M.A. *Foeniculum vulgare*: A comprehensive review of its traditional use, phytochemistry, pharmacology, and safety. *Arab. J. Chem.* **2016**, *9*, S1574–S1583, <https://doi.org/10.1016/j.arabjc.2012.04.011>.
120. Singh, A.; Singh, P.K. An ethnobotanical study of medicinal plants in Chandauli District of Uttar Pradesh, India. *J. Ethnopharmacol.* **2009**, *121*, 324–329, <https://doi.org/10.1016/j.jep.2008.10.018>.
121. Özbek, H.; Uğraş, S.; Dülger, H.; Bayram, İ.; Tuncer, İ.; Öztürk, G.; Öztürk, A. Hepatoprotective effect of *Foeniculum vulgare* essential oil. *Fitoterapia* **2003**, *74*, 317–319, [https://doi.org/10.1016/S0367-326X\(03\)00028-5](https://doi.org/10.1016/S0367-326X(03)00028-5).
122. Rabeh, N.M.; Aboraya, A.O. Hepatoprotective Effect of Dill (*Anethum graveolens* L.) and Fennel (*Foeniculum vulgare*) Oil on Hepatotoxic Rats. *Pak. J. Nutr.* **2014**, *13*, 303–309, <https://doi.org/10.3923/pjn.2014.303.309>.
123. Abdelmagid, A.D.; El Asely, A.M.; Said, A.M. Evaluation of *Foeniculum vulgare* impact on glyphosate hepato-toxicity in Nile tilapia: Biochemical, molecular and histopathological study. *Aquac. Res.* **2021**, *52*, 5397–5406, <https://doi.org/10.1111/are.15409>.