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Resistance, Pharmacology Properties and Nutritional Value of a Shrub from Arid Environments *Atriplex halimus*

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ABSTRACT

Several of experimental studies and molecular investigations highlight the power of herbs to evidence-based medicine. In Algeria, a number of medicinal plants have been studied for the treatment of diabetes such as *Atriplex halimus* L., xerohalophyte species, growing in arid and sub-arid areas, known for its hypoglycemic activity and widely used by the local population as remedy to treat diabetes mellitus. The objective of this review is to give value to this important traditional medicinal plant as antidiabetic, to set other biological and nutritional properties and its importance as resistant shrubs and good forage in severe environmental conditions.

Key words: Medicinal plants, bioactive compounds, diabetes, *Atriplex halimus*

INTRODUCTION

The *Atriplex* genus (Amaranthaceae; formerly Chenopodiaceae), of 100-200 species, denominated saltbush is quite variable and widely distributed (Poblete *et al.*, 1991; Djerroudi *et al.*, 2011). These shrubs xerohalophyte are dominant in many arid and semi-arid regions of the world, particularly in saline, arid soils (Manousaki and Kalogerakis, 2009). *Atriplex* are extremely tolerant of salt content in the ground. Their name derives from the fact that they retain salt in their leaves (Djerroudi *et al.*, 2011). Also, *Atriplex* maintains photosynthetic activity with water potentials lower than -1.15 MPa and keeps the photosynthesis/transpiration ration adequate in a range of temperatures between -30 and 40°C (Chatterton *et al.*, 1970).

Saltbush species (*Atriplex* spp.) are use in areas affected by soil salination (Djerroudi *et al.*, 2011), for rehabilitation of degraded lands (Abbad *et al.*, 2004), for animal feed (Otal *et al.*, 2010) and for the production of green forage during the dry season and to control erosion (Le Houerou, 2000).

Atriplex halimus, native of Mediterranean (Lefevre *et al.*, 2009) is a perennial C4 shrub, highly resistant to drought (Le Houerou, 1992, 2000) and salinity (Bajji *et al.*, 1998).

In Algeria, a great number of plants may be shown to have therapeutic value. The ethnopharmacological information from the medicinal plants used in the treatment of diabetes mellitus were reported a diversity of species such as *Zygophyllum album* L., *Atriplex halimus*, *Nigella sativa* L., *Ziziphus lotus* (L.) Lam., *Ficus carica* L., *Aloe vera* (L.) Burm. f., *Olea europaea* L., *Anabasis articulate* (Forssk) Moq., *Punica granatum* L., *Lawsonia inermis* L., *Marrubium vulgare* L., *Mentha pulegium* L., *Salvia officinalis* L., *Artemisia herba-alba* Asso, *Ajuga iva* (L.) Schreb, etc. (Kambouche *et al.*, 2009; Rachid *et al.*, 2012; Boudjelal *et al.*, 2012; Houacine *et al.*, 2012; Benammar *et al.*, 2014; Chikhi *et al.*, 2014). The Algerian species *Atriplex halimus*, know under the name of Guettaf or El-Gtaf, is autochthonous, grown over a wide range of soil, from

coastal areas to mountainous areas at more than 1100 m altitude (Aouissat *et al.*, 2011). The traditional use in phytotherapy by local populations is mainly as a means of lowering hyperglycaemia and to treat anemia.

The aims of this review are to give bioactive phytochemical compounds and to highlight this plant as a species with multiple medicinal efficacies, particularly hypoglycemic effect.

BOTANICAL CHARACTERISTICS OF *Atriplex halimus*

Atriplex halimus is an evergreen shrub growing to 3 m, forming tufts up to 1-3 m in diameter. In absence of grazing, this species can grow up to 4 m in height. It is dense with alternate, ovate or diamond-shaped leaves, to 2-5 cm long, flowers in terminal panicles and reddish seeds (Franclet and Le Houerou, 1971; Quezel and Santa, 1962; Negre, 1961).

Atriplex halimus is perennial monoecious, producing unisexual staminate flowers with five tepals and unisexual pistillate flowers enclosed within two bracts (Kuhn *et al.*, 1993). Five different floral phenotypes were observed and identified in single *Atriplex halimus* plant, which were distributed into two major architectural patterns. The first consisted of pentamerous flowers, with one whorl of yellowish tepals and lacking bracts, which were usually staminate. The second consisted of flowers subtended by a pair of bracts, almost invariably limited to a single pistil (Talamali *et al.*, 2001). This plant does not have salt glands but are characterized by the presence of several layers of balloon-like, vesiculated hairs (trichomes) on the leaf surface (Black, 1954).

BIOACTIVE COMPOUNDS

Atriplex halimus contain a wide range of bioactive metabolites. Qualitative analysis performed by Chikhi *et al.* (2014) in the aqueous extract demonstrated the presence of phytochemicals like tannins, flavonoids, saponins and alkaloids. These substances were potentially useful for the prevention against many human diseases and food preservation. The content of total phenolic determined in the leaves was higher than in the stems, the amount of phenolic compounds in the leaves of *Atriplex halimus*, extracted by water and methanol was 12.47 and 10.12 mg GAE/g respectively, while the amount of phenolic compounds in the stems, extracted by methanol was 3.77 mg GAE/g (Benhammou *et al.*, 2009).

The plant contains free amino acids at different concentrations depending of ecological habitat. The percentage of proline was higher in *Atriplex halimus*. The species contain also unsaponifiable matter and two sterols (n-eicosane, n-docosane, n-tricosane, n-pentacosane, n-hexacosane, n-octacosane, squalene, n-triacontane, cholesterol and stigmasterol), unsaturated fatty acids (palmitoleic, oleic, linoleic and linolenic acids) and free sugars (rhamnose, arabinose, ribose, fructose, glucose, galactose, sucrose and raffinose). Chromatographic investigation of ethyl acetate extract indicated that the plant contained vicenine II and flavonol, flavones, flavanone and isoflavone glycosides (isorhamnetin-3-glucopyranose, rutin-4',7-dimethyl ether, kaempferol-3,7-dirhamnoside-4'-methoxide, isoorientin, 4'-methoxy-7-glucoside-5-hydroxyisoflavone, naringenin-4'-orhamnopyranoside and hesperidin), phenolic acids (p-hydroxy benzoic, gallic, chlorogenic, cinnamic, p-coumaric, ferulic and salicylic acids) and alkaloids (piperine, berberine, ephedrine and palmatine) (Emam, 2011). Furthermore, the investigation on chemical bioactive compounds carried by Kabbash and Shoeib (2012) has yielded two new flavonol glycosides, designated as atriplexoside A (1) [3'-O-methylquercetin-4'-O-beta-apiofuranoside-3-O-(6"-O-alpha-rhamnopyranosyl-beta-glucopyranoside)] and atriplexoside B (2) [3'-O-methylquercetin-4'-O-(5"-O-beta-xylopyranosyl-beta-apiofuranoside)-3-O-(6"-O-alpha-rhamnopyranosyl-beta-glucopyranoside)],

isolated from aerial parts, while Clauser *et al.* (2013) have isolated four new glycosylated flavonoids: (1) 3',5'-dimethoxymyricetin-3-O- β -D-xylopyranosyl-7-O-fucopyranosyl-(1-3)- β -D-glucopyranoside, (2) 3'-methoxyquercetin-7-O- β -D-fucopyranosyl-(1-3)- β -D-glucopyranosyl-3-O- β -xylopyranosyl-(1-4)- β -xylopyranoside, (3) 3'-methoxyquercetin-7-O- α -L-rhamnopyranosyl-3-O- α -arabinofuranosyl-(1-6)- β -D-glucopyranoside, (4) 3',5'-dimethoxymyricetin-7-O-fucopyranosyl-(1-3)- β -D-glucopyranoside and other known phenolic compounds such as myricetin and quercetin.

RESISTANCE OF *Atriplex halimus*

Atriplex halimus L. originated from North Africa is well adapted to saline clay soils under less than 150 mm year⁻¹ of rainfall (Le Houerou, 1980). Ability of this species to tolerate salinity stress was investigated by Sadler *et al.* (2013). Adaptation to salt stress is complex and governed by molecular changes, expressed as physiological processes during plant development. Stressed plants showed increased expression of salt response genes (intermediate-associated protein, acetohydroxy acid reducto-isomerase, early-responsive to dehydration stress-related protein, ER-luminal protein and membrane protein). Their expression was much higher at 150 Mm than 500 Mm stress level, indicating their specificity for low level salt stress. Photosynthetic activity was slightly decreased with both extended stress exposure and increased salt concentration, while total chlorophyll and proline increased under saline stress. The same authors demonstrated that *Atriplex halimus* plants possess in-built potential to regulate osmotic strength in their cells and hence have superior tolerant capacity under stress condition up to 600 Mm NaCl. Also, tolerance might be regulated by reducing growth, to save energy and gas exchange parameters, to improve water use efficiency, as well as increasing Na⁺ uptake and PEPC protein to efficiently re-fix CO₂ that passively leaked from the bundle sheath under stress conditions (Alla *et al.*, 2011).

Mozafar and Goodin (1970) indicates that, in *Atriplex halimus*, the vesiculated hairs play a significant role to removing salt from the remainder of the leaf and preventing the accumulation of toxic salts in the parenchyma and vascular tissues. Tolerance of halophytes to the ionic and the osmotic components of salt stress is linked to their ability to synthesize osmoprotectants in order to maintain a favorable water potential gradient and to protect cellular structure (Sharma and Dietz, 2006). In the chenopodiaceae species, such as those belonging to the genus *Atriplex*, osmotic adjustment is thought to be mainly performed through the accumulation of the glycine betaine, which may protect membranes and other cellular structures against destabilization induced by salinity (Shen *et al.*, 2002). Soluble sugars and proline accumulation play an important role to response to salinity and environmental constraints (Martinez *et al.*, 2004; Morant-Manceau *et al.*, 2004; Ottow *et al.*, 2005). Djerroudi *et al.* (2011) demonstrated the protein synthesis and accumulation capacities in *Atriplex halimus*, stressed with sea water or combined salts (NaCl + CaCl₂). Accumulation of proline occurs first in the roots and moves towards the stems, and finally to leaves. In addition, abscisic acid is involved in both salt and osmotic stress resistance in *Atriplex halimus* through an improvement in stomatal regulation and hence, to an increased WUE (water-use efficiency) (Ben Hassine *et al.*, 2009).

In general, the tolerance of plants of the genus *Atriplex* to the ionic components has been related to various mechanisms, such as the synthesis of osmoprotectants (glycylbetaine) and polyamines (amino acids) and the excretion of trichome, which can accumulate high levels of ions (Na⁺, Cl⁻, Cd²⁺) (Lutts *et al.*, 2004; Walker *et al.*, 2008; Lefevre *et al.*, 2009; Vromman *et al.*, 2011).

In addition, Essafi *et al.* (2006) have studied the impact of water stress on morphological parameters, chemical composition and *in vitro* organic matter digestibility of three Tunisian clones of *Atriplex halimus* (G1, G2, and G3) and two Moroccan ecotypes of the same species (G4 and G5). The results showed that Biomass Dry Matter (BDM) production was significantly reduced in G4, G1 and G5 when water was limited in the T50 treatment. Nitrogen content was higher (8%) in G4 and G2. The BDM reduction induced by water stress was 26% compared to the control. Ash and crude fiber contents increased significantly on a dry matter basis under water stress (T50). Hemicellulose, a significant parameter that expresses well the genotype under water stress conditions, increased by 62% and dry matter digestibility was reduced by water stress except for the G2 genotype. Vazirian *et al.* (2013) have evaluated *Atriplex halimus* effects on some soil properties and carbon sequestration. It showed that *Atriplex* significantly increased the amount of soil organic carbon (0.56%), organic matter (1.96%) and Electrical Conductivity (EC) (7.64 dS m^{-1}) while it caused lower soil pH (7.85), soil bulk density (1.78 g cm^3) and lime percentage (15.14%) as compared to control. The amount of soil carbon sequestration in the *Atriplex* area (30.11 t ha^{-1}) as compared to the control (4.35 t ha^{-1}) has a significant increasing. The authors suggest this species to be introduced as an effective species in order to the soil chemical and physical properties improvement and soil erosion reduction. Also, Henni and Mehdadi (2012) have performed a preliminary assessment of soil and floristic properties of degraded steppes of white wormwood in the region of Saïda (Western Algeria), rehabilitated by the planting of *Atriplex halimus* subsp. *schweinfurthii* and *Atriplex canescens*. The results show the adaptation of these two species to edaphic and climatic conditions of the study area with a success rate above 80%. Compared to the non rehabilitated perimeter (control), in the perimeters where the two species of *Atriplex* were introduced, these authors have note improved recovery rate of vegetation, phytomass, thickness and humidity of soil.

PHARMACOLOGY PROPERTIES

Various species of *Atriplex* have been used for their important medicinal values and several species have been evaluated for their antidiabetic effect, such as *Atriplex halimus* (Rodriguez and Murray, 2010).

Antidiabetic properties: *Atriplex halimus* is widely used in traditional medicine for its antidiabetic properties. Diabetes mellitus is a chronic metabolic disorder characterized by high levels of glucose in the blood, due to the impaired secretion of insulin or insulin insensitivity (American Diabetes Association, 2010). Experimental data on animal model for diabetogenesis proved that this plant is an extremely effective antidiabetic herb and shows an insulin potentiating effect. Saltbush lowered the blood glucose levels and enhanced insulin secretion (Adler *et al.*, 1986).

Chikhi *et al.* (2014) revealed the beneficial effects of the aqueous leaf extract in reducing the elevated blood glucose level and hepatic levels in streptozotocin-induced diabetic rats. Aqueous extract produced significant antihyperglycemic activity at a concentration of $200 \text{ mg kg}^{-1} \text{ b.wt.}$, in diabetic treated rats. Also, authors have not observed any toxic or lethality and confirm the non toxic nature of the *Atriplex halimus* aqueous extract at the previous dose (200 mg kg^{-1}). The phytochemicals present in this aqueous extract are flavonoids, saponins, tannins and alkaloids. Kadan *et al.* (2013) indicate that antidiabetic properties of this medicinal plant are mediated, at least partially, through mediating Glut4 translocation to the plasma membrane.

Antimicrobial and insecticidal properties: *Atriplex halimus* possess antimicrobial properties. Hexane and methanol extracts of fresh aerial parts of *Atriplex halimus* were screened *in vitro* for antibacterial activity against Gram positive and negative pathogenic bacteria (*Escherichia coli*, *Yersinia enterocolitica*, *Enterocolitica*, *Salmonella enterica*, *Klebsiella pneumonia*, *Klebsiella oxytoca*, *Bacillus cereus*, *Clostridium perfringens*, *Listeria innocua*, *Listeria monocytogenes*, *Listeria ivanovii*, *Staphylococcus aureus* and *Staphylococcus epidermis*). Methanol extracts showed strong antibacterial activity than hexane extracts and it is rich on secondary metabolic such as flavonoids, glycosides and alkaloids (Rahman *et al.*, 2011). Furthermore, Abd-Ellatif *et al.* (2011) showed strong antifungal activity of methanolic extracts against some pathogenic fungi at 23 mg mL⁻¹ concentration. These authors revealed a percentage inhibition of 91.4% (*Fusarium solani*), 46.7% (*Bipolaris oryzae*), 38.9% (*Chetomium*), 33.4% (*Alternaria alternaria*), 28.6% (*Fusarium oxysporum*), 26.7% (*Pythium ultimum*), then the same authors revealed anticandidiasis activity against *Candida albicans*. This data provide a scientific support for the ethnomedicinal uses of *Atriplex halimus* in the treatment of fungal diseases and suggest its potential as antimycotic agent.

In addition, *Atriplex halimus* provide insecticidal properties, example against *Tribolium castaneum* and *Culex quinquefasciatus*. Different organic extracts (acetone, ethanol, petroleum-ether, ether and chloroform) have proved a considerable toxicity to *Culex* larvae with LC₅₀ values of 115, 36, 54 and 48 ppm, respectively, a strong aphicidal activity against *Aphis gossypii* with LC₅₀ values of 0.059 and 0.085% with ether and petroleum-ether extracts respectively and also a toxicity has shown with ethanol extract against the cotton leaf-worm (El-Gougary, 1998).

Other medicinal properties: *Atriplex halimus* possessed antioxidant activity (Kadan *et al.*, 2013). The butanolic and ethyl acetate extracts from the leaves have more hydrogen donating ability to reducing iron and have higher DPPH radical scavenging capacities (Benhammou *et al.*, 2009). These antioxidants properties were also observed by Kabbash and Shoeib (2012) in n-BuOH-soluble fraction from aerial parts of *Atriplex halimus* and therefore, secondary metabolites of this plant present a good source for antioxidants that may be involved in the prevention of human cellular damage, caused by free radicals. Also, the same authors have highlighted antileishmanial and anti-multidrug resistance activity.

Atriplex halimus provide inhibitory activity against acetylcholinesterase (AChE). The chloroform fraction obtained from root crude extract presents the highest inhibition (74.60%) at the dose of 125 µg mL⁻¹, followed by ethyl acetate fraction (65.08%). The active compounds were flavonoids and saponins (Benamar *et al.*, 2010). The development of natural Ache inhibitor drugs may be used to treat some symptoms of Alzheimer's Disease (AD).

NUTRITIONAL VALUE OF *Atriplex halimus*

Atriplex species are acceptable to many ruminants (El-Shaer and Kandil, 1990) and very appreciated by camelids (Benchaabane, 1997). *Atriplex halimus* contain 32.10% dry matter, 74.30% organic matter, 25.70% mineral, high value in crude protein (20.40%), higher levels of ash (28.03%), less crude fiber (14.8%) and 4.1% lipids (Abu-Zanat *et al.*, 2003; Selmi *et al.*, 2013). *Atriplex halimus* can yield up to 3 t DM ha⁻¹ on degraded and high salt soils (Nedjimi *et al.*, 2013). The comparative study of dry matter yield and total nitrogen mater of tree species of the genus *Atriplex*, which one is a local Algerian species *Atriplex halimus* and two others introduced plants: *Atriplex canescens* and *Atriplex nummularia*, originating from Australia and America, respectively was monitored by Rahmoune *et al.* (2004). Each species is grown in a separate plot, in an experimental

nursery, in arid steppe region, in the South-West of Algeria. Authors showed that the local species *Atriplex halimus* gave an intermediate yield in dry matter and in total nitrogen matter, unlike the other two species, but this species have stable forage production throughout the two seasons (spring, summer). Authors concluded that in the case of steppe areas, which are often exposed to periods of drought, the species *Atriplex halimus* seems to be the better adapted, as it produces as much forage with a clearly better regularity.

The effects of feeding *Atriplex halimus* silage treated with two developed enzyme cocktails to sheep on feed intake, nutrient digestibility and ruminal fermentation were studied by Alsersy *et al.* (2015). The *Atriplex halimus* silage was treated without or with 2 L of ZAD1[®] (xylanase: 2.32 U mL⁻¹, α -amylase: 61.50 U mL⁻¹, cellulase: 7.05 U mL⁻¹ and protease: 29.20 U mL⁻¹) or ZAD2[®] (xylanase: 6.93 U mL⁻¹, α -amylase: 69.40 U mL⁻¹, cellulase: 8.16 U mL⁻¹ and protease: 12..30 U mL⁻¹)/1000 kg with 5% molasses and ensiled for 30 days. Authors concluded that *Atriplex halimus* silage treated with ZAD1[®] or ZAD2[®] improved digestibility and rumen fermentation in sheep. Also, Stringi *et al.* (2009) showed that lambs grazing *Atriplex halimus* supplemented with both wheat straw and barley grains had a significantly higher live weight than those grazing on *Atriplex halimus* alone. The results suggest that a diet of *Atriplex halimus*, supplemented with an energy source is necessary for lambs to gain weight.

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