Natural Products

Research Reviews

— *Volume 2* —

Editor
V.K. Gupta
Chief Scientist
CSIR-Indian Institute of Integrative Medicine
Canal Road, Jammu – 180 001,
India

ASTRAL

DAYA

Natural Products: Research Reviews Vol. 2 (2014) *Pages* **145–176**
Editor: **V.K. Gupta**
Published by: **DAYA PUBLISHING HOUSE, NEW DELHI**

7

An Overview of *Salicornia* Genus: The Phytochemical and Pharmacological Profile

Vera M.S. Isca[1], Ana M.L. Seca[1,2], Diana C.G.A. Pinto[1] and Artur M.S. Silva[1]*

ABSTRACT

Salicornia L. (Chenopodiaceae) is a genus of annual, apparently leafless halophytic herb that have articulated and succulent stems. The Salicornia species comprise the most salt-tolerant land plant and frequently occur in saline areas. The use of glasswort as food is referred by the forensic palynology as a reality at least from 550 years ago. Nowadays it is much appreciated as a gourmet product in Europe but particularly in Asian countries, where is used in fresh salads and pickles. Some of the Salicornia species display applications on folk medicine (for treatment of bronchitis, hepatitis and diarrhea) and showed important biological properties such as antioxidant, anti-inflammatory, hypoglycemic and cytotoxic activities. The phythochemical studies on this genus reported the presence of fatty acids, sterols, saponins, chlorogenic acid derivatives, alkaloids, flavonoids and other kind of phenolic compounds. The purpose of this review is to highlight the advances in Salicornia genus knowledge by presenting its biological and medicinal applications, phytochemical studies and the relationship between the isolated compounds with the described biological and/or medicinal properties.

Keywords: Biological activities, Medicinal applications, Natural compounds, Phythochemistry, *Salicornia*, Saltmarsh species.

1 Chemistry Department and QOPNA, University of Aveiro, Campus de Santiago, 3810-193 Aveiro, Portugal

2 DCTD, University of Azores, Rua Mãe de Deus, 9501-801 Ponta Delgada, Azores, Portugal

* *Corresponding author*: E-mail: artur.silva@ua.pt

Introduction

The healing power of plants is as old as mankind, even today plants are used not only as household remedies but also as source of new drugs. Important molecules used in medicine were obtained from natural sources, mostly plants, and others were inspired in the natural active compounds (Nicolaou and Montagnon, 2008). On the other hand environmental problems arising from the chemical wastes in the synthesis of new compounds and the fact that synthetic drugs tend to present more side effects are incentives to increase the research in the natural products field. Consequently, more and more plants are the subject of phytochemical studies, not only to know their chemical constituents but most of all to find new biologically active molecules that can be used as drugs and/or as models for the preparation of new ones. In this context *Salicornia* species are of huge importance due their applications on folk medicine. However, *Salicornia* species have a great diversity of applications ranging from the use as a medicinal herb to human consumption to their use as an additive in the production of glass and soap (the latter due to its high ash content) (Davy *et al.*, 2001; Liebezeit, 2008).

Furthermore *Salicornia* species are among the most salt-tolerant land plant and frequently occur in saline areas associated with coastlines, tidal floodways, and salt lakes (Rhee *et al.*, 2009). This explains their use in human nutrition mainly in salads. Still many studies showed that these plants could be advantageously used as alternative feeds to replace common feedstuffs (Yaprak and Yurdakulol, 2008). The typically high content of minerals (mostly NaCl) compromises their usefulness as halophyte forages (Swingle *et al.*, 1996), while their chemical profile in natural products can be unique due to the environmental stress of their habitat. The high salinity in their environment habitat may induce species to develop resistance mechanisms during their evolution.

The referred interesting characteristics and/or properties of the *Salicornia* species highlight the importance to review and update them, which is the purpose of this work. It should be noteworthy that *Salicornia* genus taxonomy is a night-mare and it is difficult to differentiate some species of *Salicornia* (Davy *et al.*, 2001). So in this chapter, we will maintain, for convenience, the names of the species used in the cited articles.

Salicornia Genus

Salicornia L. is a wide-spread annual hygrohalophytic (the natural flora of highly saline soils) and apparently leafless herb that have articulated and succulent stems (Davy *et al.*, 2001). It belongs to the Chenopodiaceae family, one of the more advanced eleven families within the order Caryophyllales (Al-Jaber *et al.*, 1992). *Salicornia* species (Figure 7.1) are small, usually less than 30 cm tall, the main stem and its opposite branches are composed of short, cylindrical or clavate internodes, each with a succulent, photosynthetic covering, conferring the articulated appearance (Davy *et al.*, 2001). Many species are green, but their foliage turns red in autumn. The hermaphrodite flowers are wind pollinated, and the fruit is small and succulent and contains a single seed (Ball, 2004).

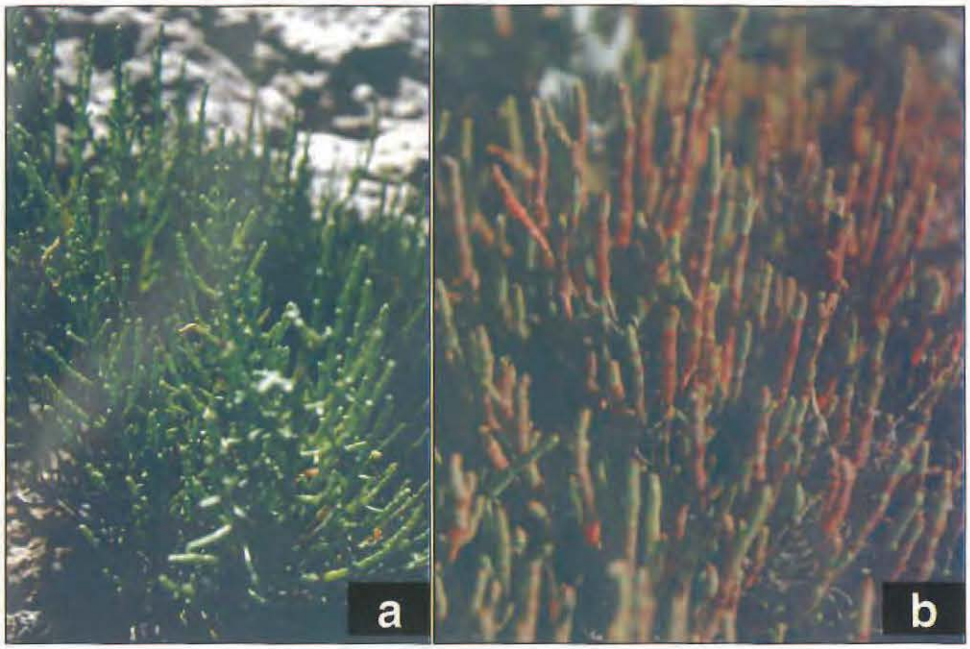


Figure 7.1: *Salicornia* species on (a) spring and (b) autumn seasons.

Salicornia species are environmentally recognized as one of the most important ecosystems in a tidal zone since they play vital roles in the tidal ecology, such as serving as buffers, protecting the shorelines from erosion by the force of waves, and filtering contaminants from the land (Silva *et al.*, 2007; Kong *et al.*, 2008a, Han *et al.*, 2010). For example, *Salicornia bigelovii* is effective to remove selenium from contaminated water and soil (Lin *et al.*, 2000) and can inhibit the growth of *Skeletonema costatum*, a marine bloom forming diatom, playing thus an active role in the prevention of eutrophication and the subsequent harmful algal bloom (HAB) (Jiang *et al.*, 2010).

Salicornia probably originated during the Miocene somewhere between the Mediterranean and Central Asia from the perennial *Sarcocornia* and started to diversify during Late Pliocene/Early Pleistocene (Kadereit *et al.*, 2007). Actually, the genus *Salicornia* include about 117 species, being *Salicornia herbacea, Salicornia bigelovii, Salicornia europea, Salicornia prostata, Salicornia ramosissima* and *Salicornia verginica* those with larger occurrence (GBIF, 2012).

Salicornia is the most complicated group of vascular plants and consequently its taxonomy and species circumscription is considered as a night-mare (Kadereit *et al.*, 2007). In fact, a combination of inbreeding, allowing the development of locally differentiated populations, and a considerable phenotypic plasticity has created great taxonomic complexity. The taxonomic difficulties due to their highly reduced leaves implies that the morphological distinction is only possible between flowering and fruiting and is compounded by very striking morphological parallelism, weak morphological differentiation and the inadequacy of dried material in representing a

succulent growth form (Davy *et al.*, 2001; Kadereit *et al.*, 2007; Silva *et al.*, 2007). There still is no satisfactory taxonomic treatment and it is frequently impossible to assign published information specifically to taxa within *Salicornia* (Davy *et al.*, 2001, Kadereit *et al.*, 2007). For example, the most common *Salicornia* upper intertidal species, *i.e. Salicornia ramosissima*, *Salicornia pusilla* and *Salicornia marshalli*, are only distinguished by their number of flowers (Hupel *et al.*, 2011). Another example are *Salicornia ramosissima* and *Salicornia europaea*, sometimes classified as microspecies (Jefferies and Gottlieb, 1982), and included in the species *S. europaea* agg. because it is extremely difficult to differentiate them. Their morphological similarity, phenotypic plasticity, and frequent local differentiation of populations at different sites are the reasons for this difficulty. The morphological criteria previously found to be most useful for its differentiating was the width of a scarious margin at the upper edge of the segment, which only measure a few tenths of a millimeter. Natural hybrids between them have

Figure 7.2: Morphological aspects of the aerial parts of *Salicornia* species.

not yet been reported, confirming that they maintain reproductive isolation (Jefferies and Gottlieb, 1982) (Figure 7.2).

The *Salicornia* genus is worldwide distributed in saline environments, occupying the most highly saline sites (Silva *et al.*, 2007). It has very wide climatic tolerances: subarctic to subtropical and oceanic to continental (Bashan *et al.*, 2000). Its tolerance of water stress and its annual life history presumably contribute to its ability to survive in extreme conditions at adverse seasons (Davy *et al.*, 2001) (Figure 7.3).

Salicornia is found in the European coastline from the Arctic to the Mediterranean, as well as on the shores of both the Black Sea and Caspian Sea; it is also sporadically present inland where saline occur (Davy *et al.*, 2001). Much of this distribution can be cautiously attributed to the *S. europaea* agg. (*S. ramosissima* J. Woods, *S. europaea* L. and *S. obscura* P.W. Ball and Tutin). From Europe and North African coast, the distribution of *Salicornia* extends through the near East and Caucasus and central Asia, including much of the Russian Federation, where it forms enormous thickets on solonchaks in steppes and deserts (Davy *et al.*, 2001). At the end of eighties *Salicornia* has been discovered in Saudi Arabia (*Salicornia europaea* L.), in salt marshes on the Arabian Gulf coast and in the sabkha of Al-Aushaziya, around 400 km from the coast (Al-Turki, 1997). A few species of *Salicornia* also occur on the southern African coast (Tanzania, Madagascar, Mozambique and South Africa) (O'Callaghan, 1992).

Nutritional Properties of *Salicornia* Species

Salicornia has a long history of applications in human and domestic animals diet. The Gosiute people on the interior plains and plateaus of western North America

Figure 7.3: *Salicornia* species on their natural habitat.

grind the seeds of *Salicornia rubra* (*Salicornia europaea* L. sub sp. *rubra)* to make "sweet bread". Cree women and men from Shoal Creek, Saskatchewan, also used *Salicornia rubra*. The plants are washed and boiled and then the decoction media can be evaporated in a frying pan to produce salt for food use (Mudie *et al.*, 2005). But several other species are used in the human diet (Chevalier, 1922; Geslin and Verbist, 1985).

The young stalks of *Salicornia herbacea*, called hamcho and tungtungmadi in Korea, are consumed in a variety of ways such as a seasoned vegetable, salad, and fermented food in coastal areas of Korea (Kong *et al.*, 2008a; Kong *et al.*, 2008b; Kim *et al.*, 2011) and are favored as a main ingredient of salad in Europe (Jang *et al.*, 2007). Seeds of *Salicornia herbacea* are also used as a tea material (Kang *et al.*, 2011).

In Nova Scotia, Canada, the annual glasswort or saltwort (*Salicornia europaea* L., *Salicornia bigelovii* Torr.) have been used freshly in salad or boiled for jarring as pickles with vinegar, sugar, onion, bayberry leaves, and mixed pickling spice (Mudie *et al.*, 2005). In addition, the aerial parts have been used as an ingredient of vinegar in Italy and France (Kim *et al.*, 2011).

Today, the annual tidal salt marsh herb *Salicornia europaea* L. subsp. *europaea* with long succulent spikes is seasonally common in markets of East Anglia, England, where it is known as samphire, pickleweed or glasswort (Mabey, 1996).

Salicornia species are also consumed by other animals. In Korea, the whole *Salicornia herbacea* is greedily devoured by cattle for its saltish taste (Im *et al.*, 2003). Testas of *Salicornia* seeds have been reported in the fecal pellets of rabbits (*Oryctolagus cuniculus*) on a salt marsh; yellow-necked fieldmice (*Apodemus flavicollis*) sought out and consumed stored seed in preference to potatoes, carrots and apples (Davy *et al.*, 2001). However it may not be a desirable food for some birds. *Salicornia europaea* on New England salt marshes is relatively unpalatable to Canada geese (*Branta canadensis*), whilst *S. bigelovi* has a positive chemical defense mechanism, including a pungent odor, against being eaten by this species (Buchsbaum *et al.*, 1984); in *S. europaea* there is an increase in the percentage of phenolic substances, thought to render the plants unpalatable to Canada geese, from May to September (Buchsbaum and Valiela, 1987).

Nowadays soil salinity has become an important issue in agriculture, which is also one of the most urgent global problems to provide enough water and land to meet the world's food needs (El Shaer, 2010). *Salicornia* has been recognized as one of the most promising crops that could be potentially brought into human or animal food productions (Lu *et al.*, 2010). As previously mentioned many studies showed that *Salicornia* plants could be used as alternative feeds (Yaprak and Yurdakulol, 2008), however the higher content in NaCl compromises its usefulness (Swingle *et al.*, 1996). Several authors envisage that the incorporation of halophyte feedstuffs into mixed diets would minimize potential adverse effects and would probably yield higher economic returns, possible from direct grazing of halophyte resources (Swingle *et al.*, 1996).

Salicornia bigelovii has been grown as an oil-seed and forage crop in arid environments since it may be irrigated with seawater or other saline waters (Swingle *et al.*, 1996; Glenn *et al.*, 1991; Glenn *et al.*, 1998). It can yield 10–20 $t.ha^{-1}$ of seed,

containing 28 per cent oil and 31 per cent protein with only 5-7 per cent fibre and ash (Glenn *et al.*, 1991, Glenn *et al.*, 1999). Despite its high salt content, animals fed moderate levels of *Salicornia* gained as much weight as those whose diet included hay or other terrestrial weeds (Swingle *et al.*, 1996, Bashan *et al.*, 2000). Thus, it is acceptable as the forage component of diets fed to goats (Glenn *et al.*, 1992) and as an ingredient in broiler chicken diets (Attia *et al.*, 1997).

Plants of *Salicornia virginica* are very sensitive to the presence of pollutant like cadmium and the lightweight petroleum, even though metals such as Cd(II) ions, tend to accumulate and be retained in its roots (Rosso *et al.*, 2005). A study about the accumulation of Cd^{2+}, Ni^{2+} and As^{3+} on *Salicornia brachiata* showed its potential for phytoremediation of heavy metal in polluted saline coastal areas (Sharma *et al.*, 2010). A recent study showed that roots of *Salicornia europaea* accumulate much more heavy metals than the above-ground organs (Milic *et al.*, 2012). The accumulation of metals in *Salicornia* species must be taken into account when attempting to use them as food ingredients. Nevertheless several species have been subjected to evaluations of their nutritional potential. For instance, nutritional analyses showed that *Salicornia bigelovii* contained high amounts of vitamins and minerals, which made it an ideal nutritional and diet supplement. The protein level in *Salicornia bigelovii* is lower than in celery leaf (2.6 per cent) and spinach (2.6 per cent) but similar to lettuce (1.3 per cent) and Chinese cabbage (1.4 per cent) level.

In view of the cardinal role of dietary fats in human health and disease, the chemical analysis and, particularly, the fatty acid composition of oil used for domestic consumption have become a research priority of lipid chemistry and nutritional characterization. So *Salicornia bigelovii* was also evaluated in its lipid content. Although the lipid content of *Salicornia bigelovii* was relatively low, it was characterized by a high degree of unsaturated acids, mainly α-linolenic and linoleic acids and its tissue showed high values of β-carotene, ascorbic acid and total chlorophyll which made the plant a good source of vitamin A and C (Lu *et al.*, 2010). The seeds of this plant have a high polyunsaturated fat content, nutlike taste and texture like olive oil, although the raw seeds contain saponins that make them inedible (Mudie *et al.*, 2005). On the other hand, seeds of a hybrid variety *Salicornia bigelovii* (SOS-10) have an oil content of 27.2-32.0 per cent, and the seed oil was found to contain high levels of linoleic acid (74.7-79.5 per cent) and less oleic acid (12.3-16.8 per cent). Saturated fatty acids, palmitic and stearic acids, ranged from 7 to 8.5 per cent and from 1.2 to 1.7 per cent, respectively. Linolenic acid (C18: 3 ω-3) was found within the range of 1.5-2.3 per cent. Many parameters of *Salicornia bigelovii* seed oil were quite compatible with those of safflower oil (Anwar *et al.*, 2002).

The analysis of *Salicornia europaea* seeds oil indicate that its total lipid content is from 26 to 30 per cent, being the linoleic acid the main component, nearly 70 per cent of the fatty acid content (Austenfeld, 1986, Austenfeld, 1988). Seed oil of *Salicornia* (SOS-7), a hybrid variety selected for cultivation as an oil-seed crop, has been analyzed in great detail (El-Shami and El-Negoumy, 1993; El-Mallah *et al.*, 1994). Its fatty acid composition is likewise dominated by linoleic acid (66.9 per cent), with 17.5 per cent oleic acid, only 1.4 per cent linolenic acid and traces of stearic and palmitic acid. The

total lipid content and the fatty acids distribution in *Salicornia europaea* demonstrate the good nutritional quality of this plant (Guil *et al.*, 1996).

Apparently it is also attributed some nutritional benefits to *Salicornia herbacea*. It contains large amounts of salt and other minerals, especially ions of manganese, calcium, iron, potassium and iodine, as well as dietary fibers (Ha *et al.*, 2006; Im *et al.*, 2006; Jang *et al.*, 2007). In addition contains essential aminoacids and a large amount of betaine and choline. The beneficial effects of consuming *S. herbacea* may in part be due to betaine or choline absorption. Betaine has been shown to reduce potentially toxic level of homocysteine, an aminoacid normally found in the body, and a high level of homocysteine has been implicated to increase the chance of developing heart disease, stroke, liver disease, and peripheral vascular disease (Im *et al.*, 2006).

Traditional and Pharmacological Applications of *Salicornia* Species

Salicornia species have been used not only in the human diet but also in traditional medicine. In North America, in 1793–1794, samphire, the common name of *Salicornia europaea* (often incorrectly including young plants of *Salicornia perennis*), which is endemic of the saline wetlands of southeastern Alaska, was known for its antiscorbutic properties (Mudie *et al.*, 2005). Recently, it was reported the oral administration of fresh *Salicornia europaea*, in Edremit Gulf folk medicine, to treat goiter (Polat and Satil, 2012). The same species is used in traditional Chinese Medicine to treat hypertension, cephalalgia and scurvy (Wang *et al.*, 2012).

The rising number of immunosuppressed and immunocompromised patients succumbing to fungal infections and other parasitic diseases, together with the gradual rise in resistance against common antibiotics, increased dramatically the demand for new compounds with potent activity against these eukaryotic microorganisms. And in this contest the ethanol extracts of *Salicornia europaea* L. exhibited the highest inhibition of algal growth and moderated antiyeasts activity, but did not show activity against gram-positive and gram-negative bacteria (Lellau and Liebezeit, 2003a). The same author (Lellau and Liebezeit, 2003b) observed that identical extracts (ethanol extracts of *Salicornia europaea* L.) showed significant cytotoxic activity against *Artemia salina* L. and *Daphnia magna* S. and moderate anti-neoplastic activity. Bhosale *et al.* (1999) found significant antifungal activity of 90 per cent aqueous methanol extract of *Salicornia brachiata* against food poisoning strains of *Aspergillus niger* and reasonably active against *Aspergillus fresenii* and *Aspergillus japonicas*. Recently, Chandrasekaran *et al.* (2008) reported that the methyl ester fatty acid fraction (fatty acid methyl ester extract) from the same species exhibit the highest antibacterial and antifungal activities when compared with other Chenopodiaceae extracts tested. *Salicornia brachiata* preparations are also used, in India, to treat mange and pruritus (Khare, 2007).

"Heiltzuk" (probably the Heiltsuk, a North Wakashan people from the central British Columbia coast) used *Salicornia virginica* (maybe *Salicornia perennis*) as an analgesic and external antirheumatic plant (Mudie *et al.*, 2005). Radwan *et al.* (2007) showed that *n*-butanol and ethyl acetate extracts of *Salicornia fruticosa* display high DPPH radical scavenging effect, which is an evidence for its antioxidant activity.

As far as we could find out the *Salicornia herbacea* is the species of which biological and pharmacological activities are better documented, most likely due to its widespread use in Korea folk medicine. Actually, *Salicornia herbacea*, known in Korea by its common name hamcho, has been used for several disorders such as constipation, obesity, diabetes, cancer (Bang *et al.*, 2002; Kong *et al.*, 2008b), indigestion, gastroenteric disorders, hepatitis, nephropathy (Jang *et al.*, 2007), asthma and arthritis (Im *et al.*, 2003). It was also reported its use for the treatment of intestinal ailment, nephropathy, cancer, asthma, arthritis, hepatitis (Ha *et al.*, 2006; Rhee *et al.*, 2009), hypertension and hemorrhoids (Han *et al.*, 2003; Kang *et al.*, 2011), in other Oriental countries.

Rhee *et al.* (2009) published a review reporting several works where numerous pharmacological studies were conducted with extracts or solvent-extracted fractions of *Salicornia herbacea*. These experiments revealed that solvent-extracted fractions with hexane, chloroform, ethyl acetate, *n*-butanol, methanol and aqueous fractions exhibited antioxidant, anti-microbial, anti-proliferative, and anti-inflammatory activities, and these results are undoubtedly a rationalization for the use of *Salicornia herbacea* in traditional medicine. In fact it is overwhelming the number of reports on biological and physiological effects of *Salicornia herbacea* extracts. Examples such as antihyperlipidemic (Bang *et al.*, 2002), antidiabetic (Bang *et al.*, 2002; Lee *et al.*, 2005; Jang *et al.*, 2007), and more recent anti-cancer (Kong *et al.*, 2008a,), anti-inflammatory (Kong *et al.*, 2008b) and antioxidant (Kong *et al.*, 2008b; Kang *et al.*, 2011; Kim *et al.*, 2011) activities can be found in the literature. Indeed it can be found a patent claiming that *Salicornia herbacea* is effective to improve inflammatory responses and prevent atherosclerosis, hypertension and tumours (Lu *et al.*, 2010).

Im *et al.* (2006) states that plant extracts of *Salicornia herbacea* modulate the production of cytokines and the release of nitric oxide in macrophages. The study on the mechanism of immunomodulatory effect showed that *Salicornia herbacea* extract (SHE) activate RAW cells to produce cytokines such as tumour necrosis factor (TNF)-α and interleukin (IL)-1β, and nitric oxide (NO) dose dependently. SHE also induces the expression of co-stimulatory molecules such as B7-1 and CD40, and increased phagocytic activity on opsonized sheep red blood cells. While increasing these parameters of macrophage activation, SHE inhibited the growth of RAW cells dose dependently, inducing morphological changes from slightly adherent monocytic cells to strongly adherent macrophages.

Several authors suggest that *Salicornia herbacea* extracts can prevent arteriosclerosis, hyperlipidemia, fatty liver, but also inhibit the weight gain (Jo *et al.*, 2002). Some of these studies were *in vivo* assessments (Lee *et al.*, 2005). There are also evidences on *Salicornia herbacea* extracts efficiency in diabetes prevention (Lee *et al.*, 2005; Kim, 2007). Recently, Yu *et al.* (2012) showed the antioxidant and bacteriostatic action of *Salicornia herbacea* extract and therefore suggest the application of this plant as food additives and pharmaceutical ingredients.

Some of the above mentioned studies do not specify the solvent used to obtain the extracts and consequently it is difficult to know if the active compounds are polar or apolar. However, some authors indicate the solvent employed and it is evident that polar extracts of *Salicornia herbacea*, such as ethanol extracts showed two noble

activities, weight gain and hyperglycemia inhibition (Park *et al.*, 2006). Consequently this plant can be suitable to be used as prototype material to develop novel drugs to treat symptoms such as hyperglycemia, hyperlipidemia without concomitant weight gain. A drug with such a combination of properties should be a much better option for up to 90 per cent of type 2 diabetic patients who have diabetes-associated weight problems. Hwang *et al.* (2007) reported the inhibitory activity of ethanol extracts of *Salicornia herbacea* against porcine pancreatic lipase, which may explains the plant effectiveness in controlling hyperlipidemia. In this study, due to the inhibition of pancreatic lipase animal models they claim to enlighten the potential of this plant for type 2 diabetic treatments (Hwang *et al.*, 2007).

Finally, aqueous extract of *Salicornia herbacea* can act as antioxidant modulator. This extract modulates antioxidants such as SOD (superoxide dismutase), CAT (catalase), GPx (glutathione peroxidase) and estradiol, and in doing so may play a significant role in restoration of cellular redox status and minimization of cell damage cause by ROS (reactive oxygen species) (Ha *et al.*, 2006). Another important study showed the potent tyrosinase inhibitory activity of the *Salicornia herbacea* aqueous extracts (Sung *et al.*, 2009). These authors also reported skin whitening effects exhibit by the same extract and propose that it can be a good candidate for skin rejuvenating agent, especially in treatments of B16 melanoma cells where the synthesis of melanin decreases (Sung *et al.*, 2009). One more example is the potent antioxidant activity and the selective cytotoxic effects against HCT 116 and HT-29 colon cancer cells showed by *Salicornia herbacea* seeds extract (Kang *et al.*, 2011) indicating that the consumption of this plant could also be considered as an indirect intake of healthy metabolites.

Phytochemical Studies on *Salicornia* Species: Isolated Compounds and their Structural Pattern

The above mentioned activities prompted several researchers to carry out phytochemistry studies on *Salicornia* species. The main purpose was the isolation and structural characterization of secondary metabolites. Some researchers were also interested in the biological assessments of pure isolated compounds in order to establish relationships between plant activity and their chemical constituents. This relationship can be useful in the development of new natural alike active drugs.

The aim of this part is to present in a straightforward way the structures of the isolated secondary metabolites from *Salicornia* species and when possible to describe their biological properties.

Phytochemical studies on *Salicornia* species as far as we are aware were being reported since 1965 when Borkowski and Drost (1965) reported the isolation of alkaloid derivatives from *Salicornia europaea*, among them saliherbin [$(C_5H_{12}N_2O)^+C1^-$] and salicomine, sometimes identified as salicornin, [$(C_9H_{22}N_5O_4)^+C1^-$]. Apparently there were no attempts to establish the structure of these compounds. More than 10 years later two chromones, 6,7-methylenedioxychromone (**1**) and 6,7-dimethoxychromone (**2**) (Figure 7.4), were isolated from the reddish stems of the same plant (Chiji *et al.*, 1978). In the eighties Arakawa *et al.* (1983) reported the isolation of a glucopyranosylchromone, 7-*O*-β-D-glucopyranosyl-6-methoxychromone (**3**), and the

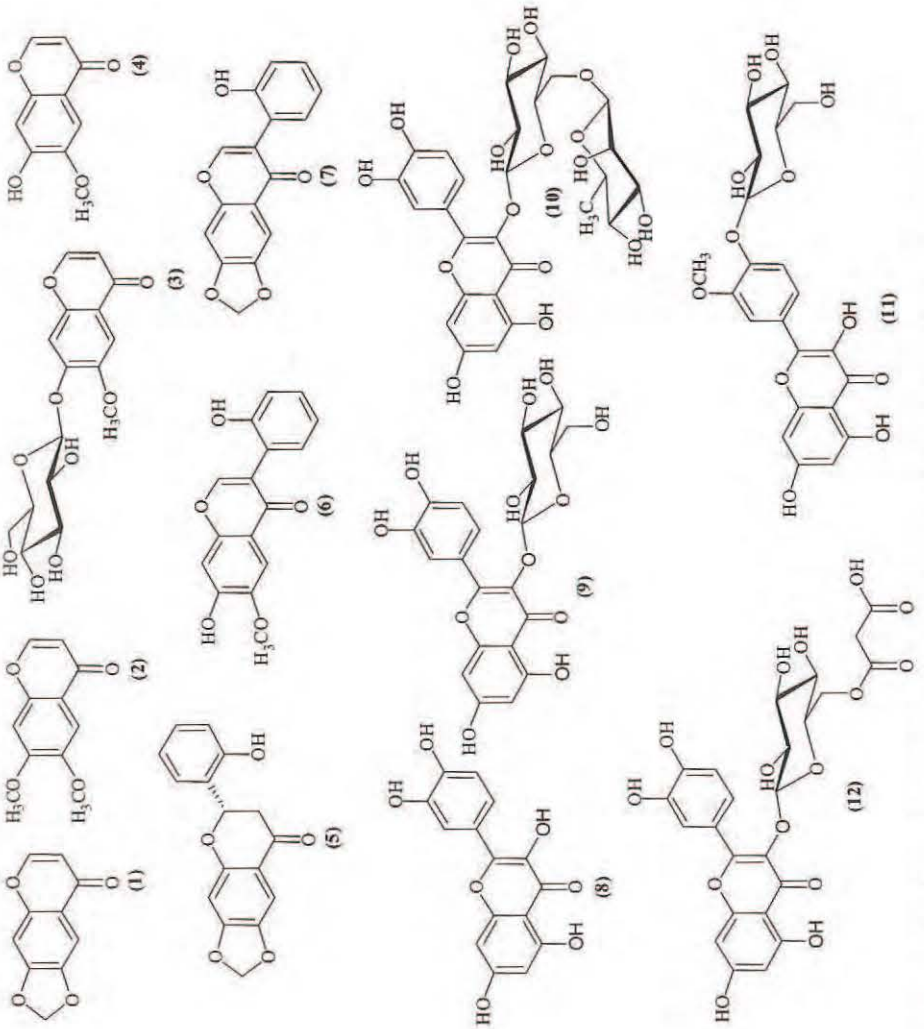


Figure 7.4: Simple chromones and flavonoid derivatives isolated from *S. europaea*.

respective aglycone, 7-hydroxy-6-methoxychromone (**4**) (Figure 7.4), from the methanol extract of *Salicornia europaea* (Arakawa *et al.*, 1983). Arakawa *et al.* (1982) also isolated several flavonoid derivatives, such as (-)-(2*S*)-2'-hydroxy-6,7-methylenedioxy-flavanone (**5**), 2',7-dihydroxy-6-methoxyisoflavone (**6**) and 2'-hydroxy-6,7-methylenedioxyisoflavone (**7**) (Figure 7.4). In the case of flavanone (**5**) the authors established the absolute stereochemistry of the stereocenter and obtained the specific rotation. It appears that *Salicornia europaea* is very rich in flavonoid derivatives; accordingly to Geslin and Verbist (1985) 1.2 per cent of its dried mass is flavonoids. In this phytochemical study they have isolated and characterized quercetin (**8**), isoquercitrin (**9**), rutin (**10**), isorhamnetin 4'-glucoside (**11**) and quercetin 3-(6''-malonylglucoside (**12**) (Figure 7.4) [Geslin and Verbist, 1985; here, the name of the isolated compounds were written according to Harborne and Baxter (1999)]. The latest one seems to be the most abundant which is in agreement with the fact that this quercetin derivative is believed to be an important compound produced by plants in order to protect them against the UV light induced damages (Liebezeit, 2008).

Recently, it was isolated from the ethanol extract of *Salicornia europaea* L. a new triterpenoid saponin, 3β,29-dihydroxy-olean-12-en-28-oic acid 28-*O*-β-D-

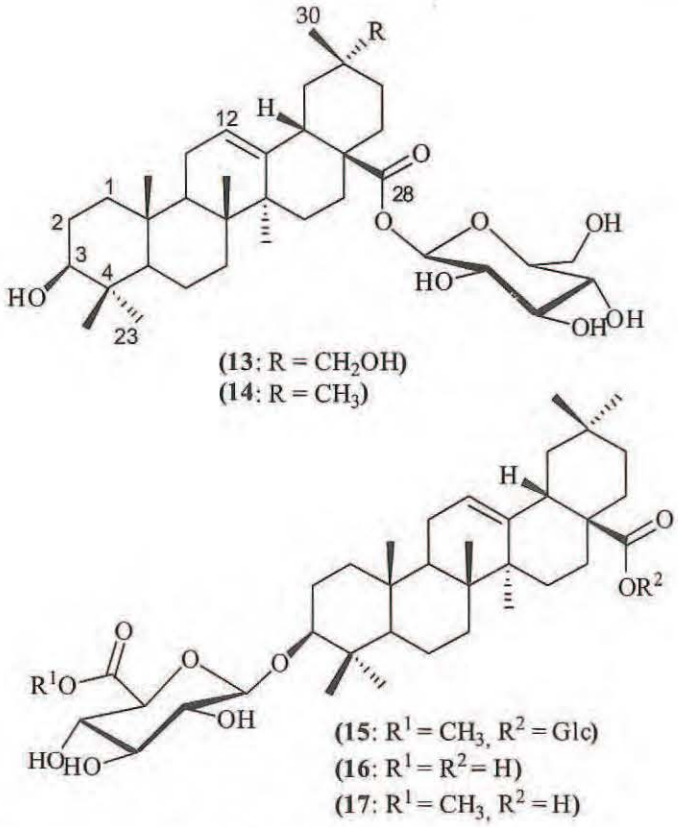


Figure 7.5: Triterpenoid saponins isolated from *S. europaea*.

glucopyranosyl ester (**13**) (Figure 7.5), along with the four known ones, oleanolic acid 28-*O*- β-D-glucoside (**14**), chikusetsusaponin IVa methyl ester (**15**), calenduloside E (**16**), and calenduloside E 6′-methyl ester (**17**) (Figure 7.5) (Yin *et al.*, 2012).

Salicornia europaea extracts also revealed the presence of steroid derivatives (Figure 7.6). Salt and Adler (1985) claimed the isolation and identification of eight different 24-α-ethylsterols being spinasterol (**18**) and stigmasterol (**19**) the major ones (Figure 7.6). These authors have also studied the steroids content of *Salicornia bigelovii* extracts and found out that both species are very similar in the steroid constituents except the lacking of isofucosterol (**20**) (Figure 7.6) from *Salicornia europaea* extracts (Salt and Adler, 1985).

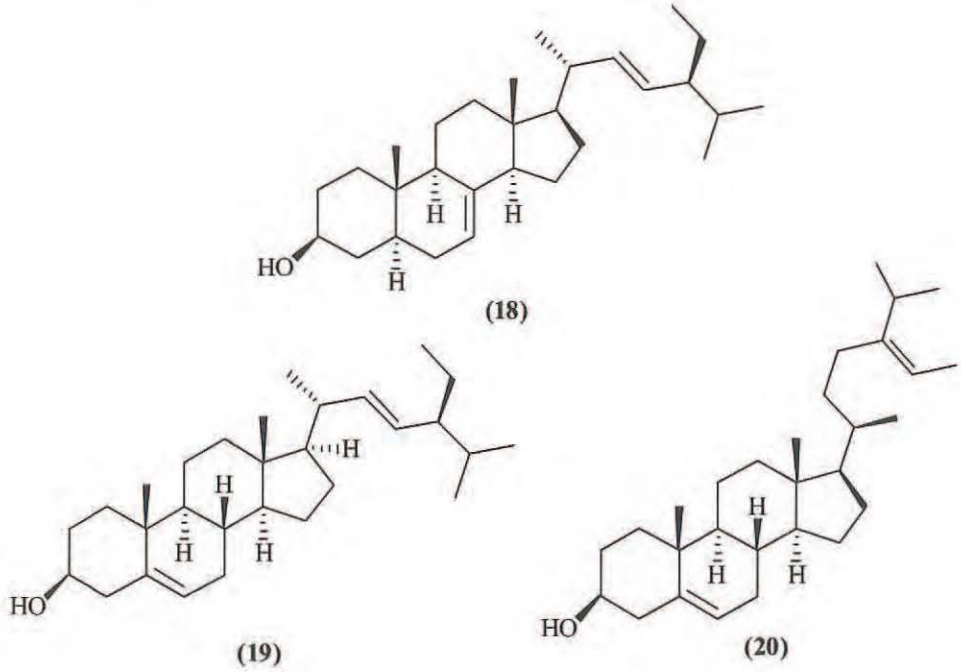


Figure 7.6: Examples of steroids isolated from *S. europaea* and/or *S. bigelovii*.

A study on the *n*-butanol fraction of the ethanol extracts of *Salicornia bigelovii* Torr. allowed the isolation of two new rare oleanane type 30-nortriterpenoid saponins, bigelovii A (**21**) and bigelovii B (**22**) (Figure 7.7) (Wang *et al.*, 2012). The authors have also isolated two known 30-nortriterpenoid glycosides, 3-*O*-β-D-glucuropyranosyl-30-norolean-12,20(29)-dien-28-oic acid-28-*O*-β-D-glucopyranoside (also known as pfaffine B) (**23**) and 3-β-hydroxy-30-norolean-12,20(29)-dien-28-*O*-β-D-glucopyranoside (also known as boussingoside A_2) (**24**), and three oleanane-type triterpenoid glycosides, oleanolic acid 28-*O*-β-D-glucopyranoside (**14**) (Figure 7.5), 3-*O*-β-D-glucuropyranosyl oleanolic acid (**25**), 3-O-β-D-glucuropyranosyl oleanolic acid 28-*O*-β-D-glucopyranoside (**26**) (Figure 7.7).

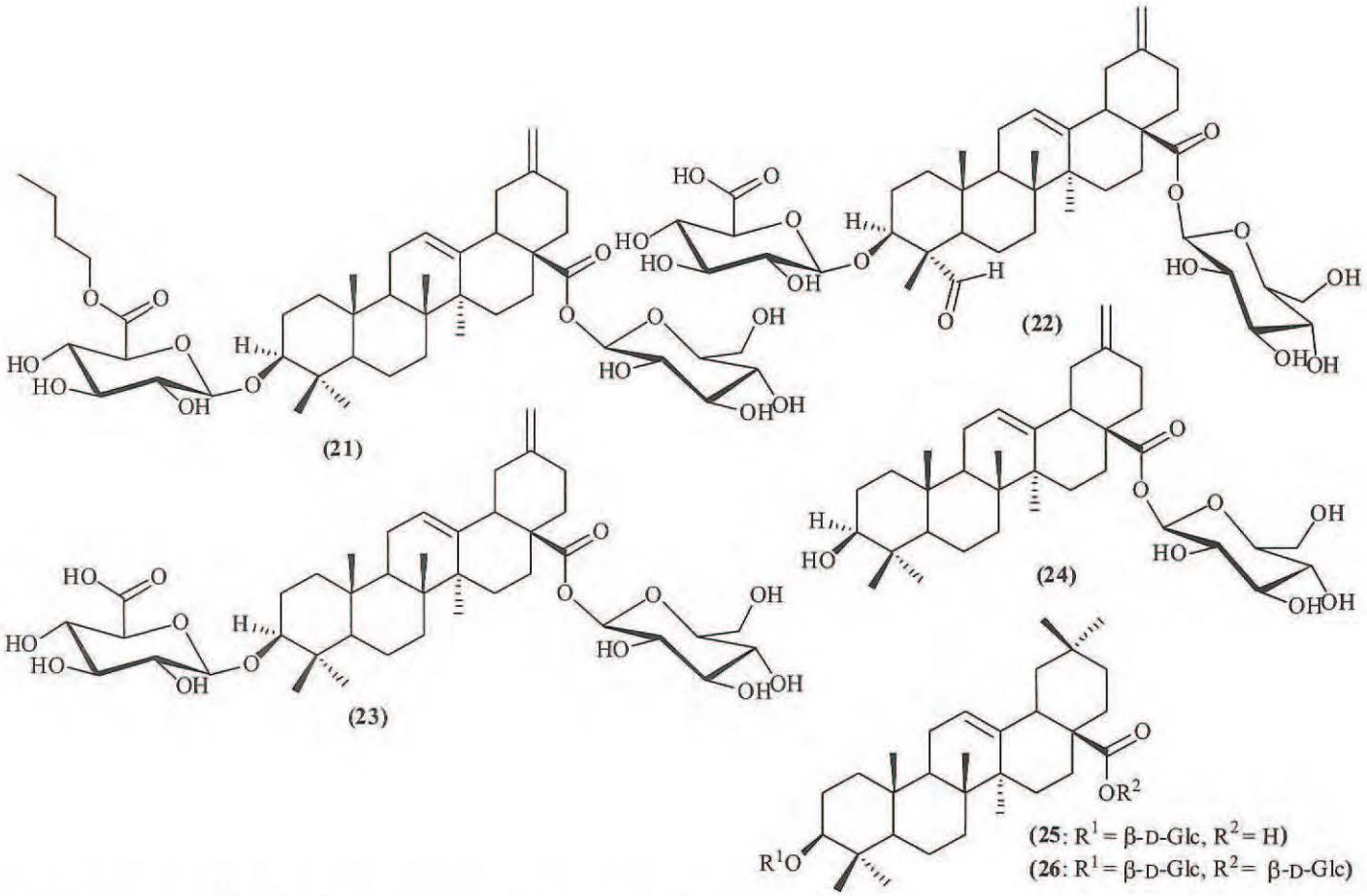


Figure 7.7: Nortriterpenoid and triterpenoid saponins isolated from *S. bigelovii*.

Phytochemical studies on *Salicornia* species increased in the 21st century, especially due to the diversification of the species studied. One of these cases is of *Salicornia fruticosa* L. which attracted Radwan *et al.* (2007). They have identified the lipid content of this species and reported a series of hydrocarbons ranging from C_{13} to C_{31}, the triterpenoid α-amyrin (**27**), cholesterol (**28**) (Figure 7.8) and stigmasterol (**19**) (Figure 7.6). They have also stated that palmitic acid represents the main component of the fatty acid fraction, nearly 32.4 per cent, and fatty alcohol fractions contained mainly hentriacontanol ($C_{31}H_{64}O$, 22.15 per cent), but also octatriacontanol ($C_{38}H_{78}O$, 21.529 per cent). They have also found that the mucilage hydrolysate of the aerial parts of *Salicornia fruticosa* contain xylose, manose, galactose and glucose. These authors (Radwan *et al.*, 2007) have also studied the plant aqueous alcoholic extract; from which after fractionation with chloroform, ethyl acetate and butanol were isolated several flavones derivatives, apigenin (**29**), apigenin-7-*O*-galactoside (**30**) isorhamnetin (**31**), isorhamnetin-3-*O*-galactoside (**32**) and acacetin (**33**) (Figure 7.8).

Other *Salicornia* species attracting the scientific community in this century is *Salicornia herbacea*, from its extracts several natural compounds were isolated. As far as we could find the first reported study involved the analysis of the methanol extract obtained by a hot extraction (Lee *et al.*, 2004). Compounds such as stigmasterol (**19**) (Figure 7.6), β-sitosterol (**34**), uracil (**35**) and isorhamnetin-3-*O*-β-D-glucopyranoside (**36**) (Figure 7.9) were isolated. This diversity of families of compounds is very interesting, especially because this species is one of most used in traditional medicine. Several other authors reports the isolation of isorhamnetin 3-*O*-β-D-glucopyranoside (**36**) and quercetin 3-*O*-β-D-glucopyranoside (**37**) (Figure 7.9) from the *n*-butanol extract of *Salicornia herbacea* (Park and Kim, 2004; Kong *et al.*, 2008b; Kong *et al.*, 2012). Lee *et al.* (2005) have also isolated isorhamnetin 3-*O*-β-D-glucopyranoside (**36**) (Figure 7.9) from this plant employing an aldose reductase inhibitory-guide methodology.

Apparently a careful analysis of methanol extract of *Salicornia herbacea* revealed the presence of several chlorogenic acid derivatives, such as 3-caffeoyl-4-dihydrocaffeoyl quinic acid (**38**) also named tungtungmadic acid (Chung *et al.*, 2005; Kim *et al.*, 2011), methyl 4-caffeoyl-3-dihydrocaffeoyl quinate (salicornate) (**39**), methyl 3,5-dicaffeoyl quinate (**40**) 3,5-dicaffeoylquinic acid (**41**), 3,4-dicaffeoylquinic acid (**42**), and the flavonoid derivatives quercetin 3-*O*-β-D-glucopyranoside (**37**) and isorhamnetin 3-*O*-β-D-glucopyranoside (**36**) and the new isoquercitrin 6″-O-methyloxalate (**43**) (Kim *et al.*, 2011) (Figure 7.10).

In 2007 Oh *et al.*, obtained the *Salicornia herbacea* viscozyme-treated extract and extracted it with ethanol. This methodology allowed the isolation of simple phenolic acids such as protocatechuic (**44**), caffeic (**45**) and ferulic (**46**) (Figure 7.11) and also the flavonol derivatives quercetin (**8**) (Figure 7.4) and isorhamnetin (**31**) (Figure 7.8).

The most recent studies applied new extraction methodologies in order to extract the compounds with less harsh conditions and consequently reducing the possible transformations during the extraction process. One example consider the use of ionic liquids, methodology successfully employed by Zhu and Row (2010) in the extraction and quantification of β-sitosterol (**34**) (Figure 7.9) from *Salicornia herbacea* L. The same methodology was successfully applied in the isolation of protocatechuic (**44**), caffeic

Phytochemical studies on *Salicornia* species increased in the 21st century, especially due to the diversification of the species studied. One of these cases is of *Salicornia fruticosa* L. which attracted Radwan *et al.* (2007). They have identified the lipid content of this species and reported a series of hydrocarbons ranging from C_{13} to C_{31}, the triterpenoid α-amyrin (**27**), cholesterol (**28**) (Figure 7.8) and stigmasterol (**19**) (Figure 7.6). They have also stated that palmitic acid represents the main component of the fatty acid fraction, nearly 32.4 per cent, and fatty alcohol fractions contained mainly hentriacontanol ($C_{31}H_{64}O$, 22.15 per cent), but also octatriacontanol ($C_{38}H_{78}O$, 21.529 per cent). They have also found that the mucilage hydrolysate of the aerial parts of *Salicornia fruticosa* contain xylose, manose, galactose and glucose. These authors (Radwan *et al.*, 2007) have also studied the plant aqueous alcoholic extract; from which after fractionation with chloroform, ethyl acetate and butanol were isolated several flavones derivatives, apigenin (**29**), apigenin-7-*O*-galactoside (**30**) isorhamnetin (**31**), isorhamnetin-3-*O*-galactoside (**32**) and acacetin (**33**) (Figure 7.8).

Other *Salicornia* species attracting the scientific community in this century is *Salicornia herbacea*, from its extracts several natural compounds were isolated. As far as we could find the first reported study involved the analysis of the methanol extract obtained by a hot extraction (Lee *et al.*, 2004). Compounds such as stigmasterol (**19**) (Figure 7.6), β-sitosterol (**34**), uracil (**35**) and isorhamnetin-3-*O*-β-D-glucopyranoside (**36**) (Figure 7.9) were isolated. This diversity of families of compounds is very interesting, especially because this species is one of most used in traditional medicine. Several other authors reports the isolation of isorhamnetin 3-*O*-β-D-glucopyranoside (**36**) and quercetin 3-*O*-β-D-glucopyranoside (**37**) (Figure 7.9) from the *n*-butanol extract of *Salicornia herbacea* (Park and Kim, 2004; Kong *et al.*, 2008b; Kong *et al.*, 2012). Lee *et al.* (2005) have also isolated isorhamnetin 3-*O*-β-D-glucopyranoside (**36**) (Figure 7.9) from this plant employing an aldose reductase inhibitory-guide methodology.

Apparently a careful analysis of methanol extract of *Salicornia herbacea* revealed the presence of several chlorogenic acid derivatives, such as 3-caffeoyl-4-dihydrocaffeoyl quinic acid (**38**) also named tungtungmadic acid (Chung *et al.*, 2005; Kim *et al.*, 2011), methyl 4-caffeoyl-3-dihydrocaffeoyl quinate (salicornate) (**39**), methyl 3,5-dicaffeoyl quinate (**40**) 3,5-dicaffeoylquinic acid (**41**), 3,4-dicaffeoylquinic acid (**42**), and the flavonoid derivatives quercetin 3-*O*-β-D-glucopyranoside (**37**) and isorhamnetin 3-*O*-β-D-glucopyranoside (**36**) and the new isoquercitrin 6″-O-methyloxalate (**43**) (Kim *et al.*, 2011) (Figure 7.10).

In 2007 Oh *et al.*, obtained the *Salicornia herbacea* viscozyme-treated extract and extracted it with ethanol. This methodology allowed the isolation of simple phenolic acids such as protocatechuic (**44**), caffeic (**45**) and ferulic (**46**) (Figure 7.11) and also the flavonol derivatives quercetin (**8**) (Figure 7.4) and isorhamnetin (**31**) (Figure 7.8).

The most recent studies applied new extraction methodologies in order to extract the compounds with less harsh conditions and consequently reducing the possible transformations during the extraction process. One example consider the use of ionic liquids, methodology successfully employed by Zhu and Row (2010) in the extraction and quantification of β-sitosterol (**34**) (Figure 7.9) from *Salicornia herbacea* L. The same methodology was successfully applied in the isolation of protocatechuic (**44**), caffeic

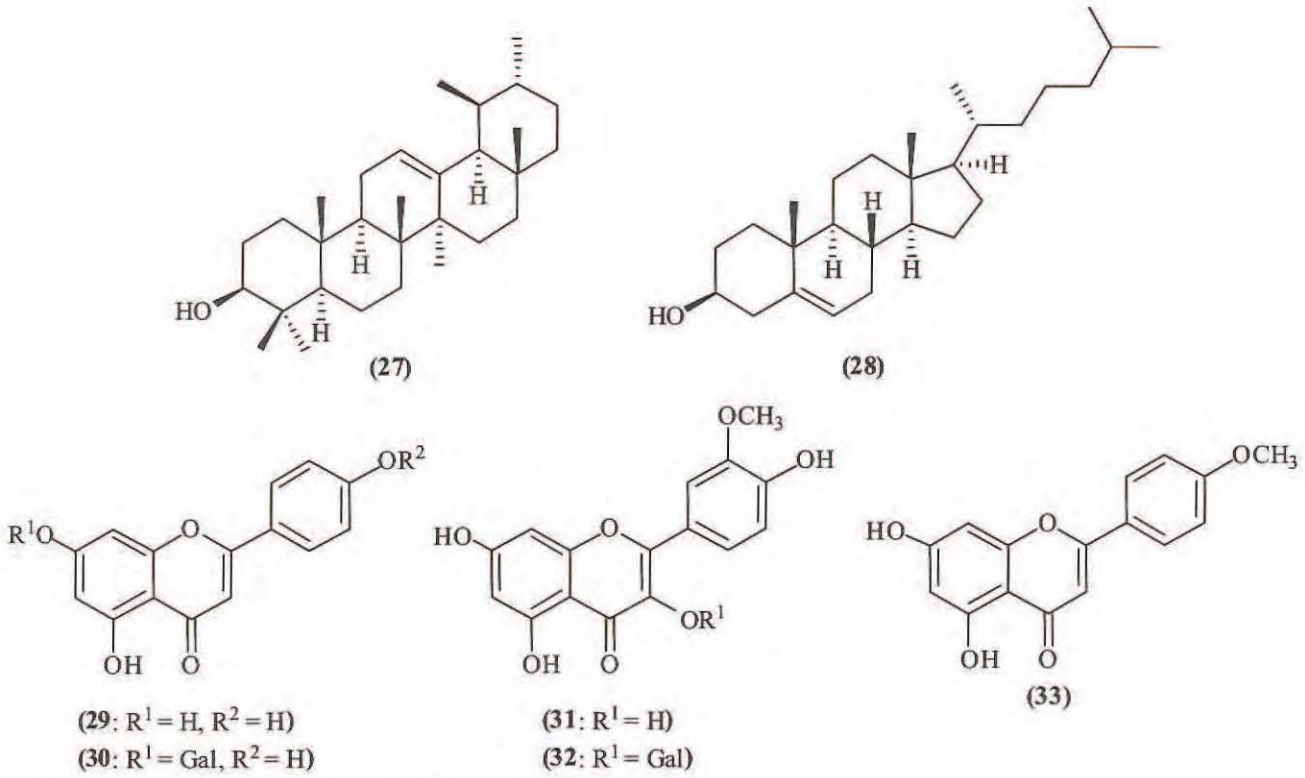


Figure 7.8: Triterpenoids and flavone derivatives isolated from *S. fruticosa*.

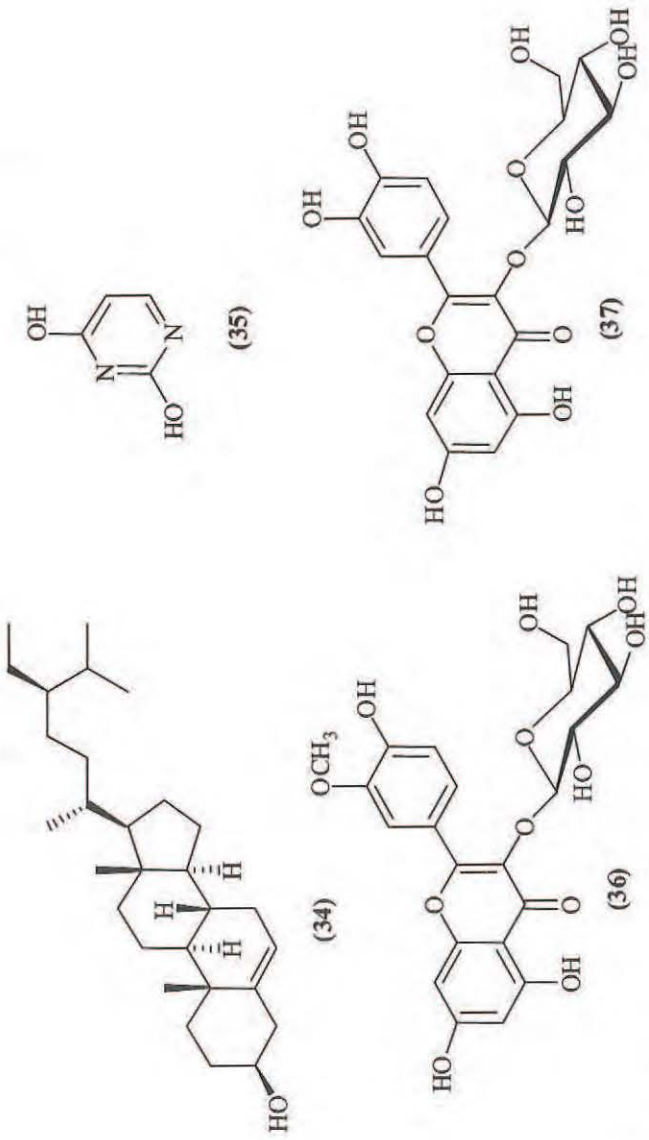


Figure 7.9: Compounds isolated from the methanol extract of *S. herbacea*.

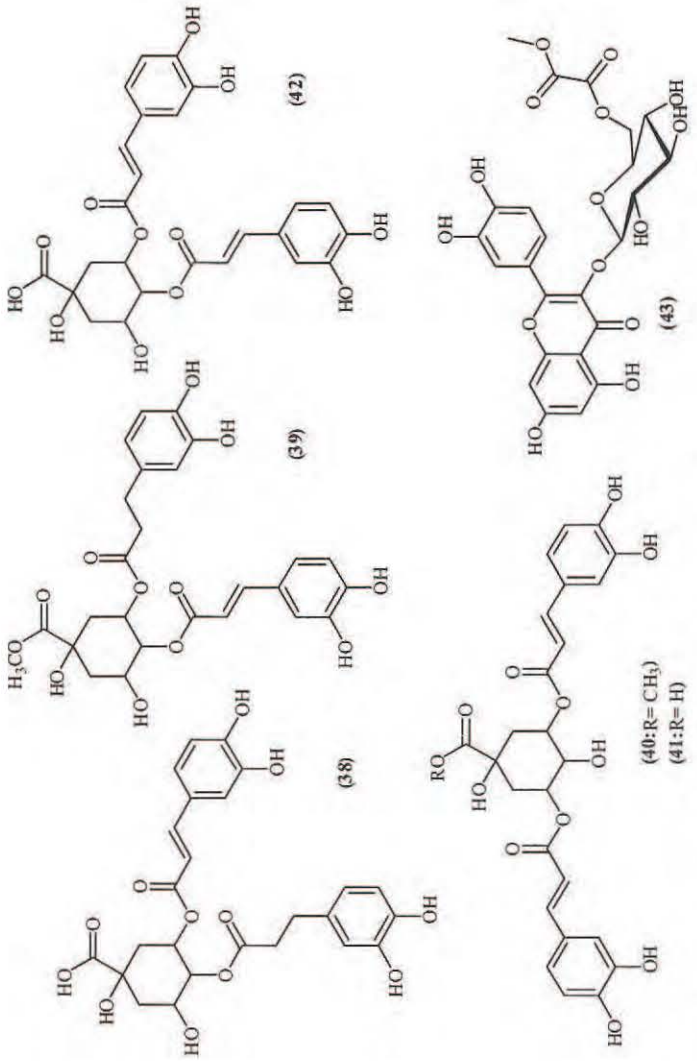
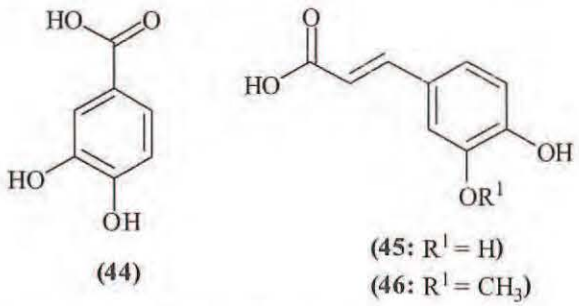


Figure 7.10: Compounds isolated from the methanol extract of *S. herbacea*



(44)

(45: $R^1 = H$**)**
(46: $R^1 = CH_3$**)**

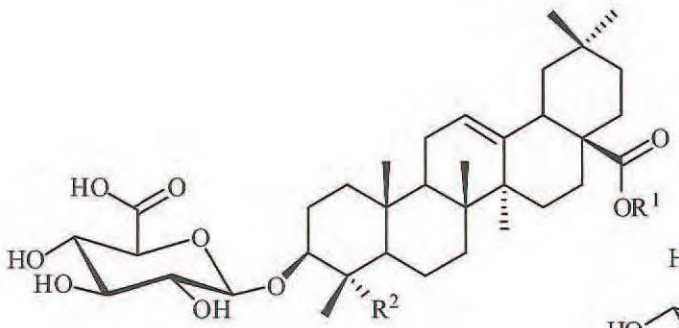
Figure 7.11: Compounds isolated from the viscozyme-treated extract of *S. herbacea*.

(**45**), and ferulic (**46**) acids (Figure 7.11) from *Salicornia herbacea* L. (Zhu *et al.*, 2011). These acids were also isolated from the aqueous extract of *Salicornia herbacea* by Bi *et al.* (2012). In these cases the innovation was not in the extraction methodology but in the purification, since the authors used molecularly imprinted anion-exchange polymer confined ionic liquids to perform the chromatographic separation.

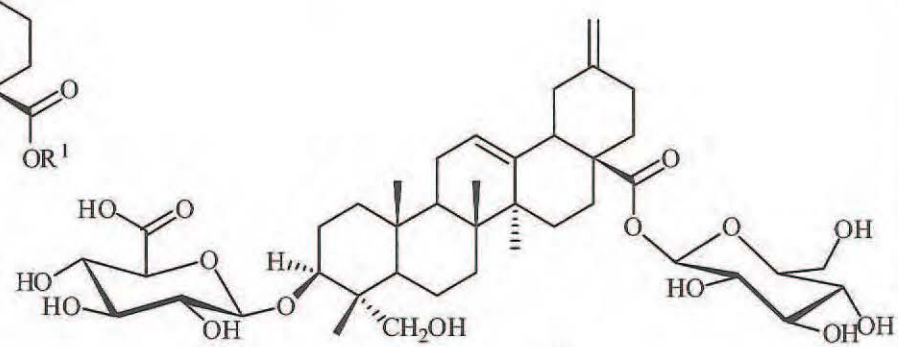
The last reported study on *Salicornia herbacea* describe the isolation of a new natural compound, 3β-hydroxy-23-oxo-30-noroleana-12,20(29)-diene-28-oic acid 3-*O*-β-D-glucuronopyranosyl-28-*O*-β-D-glucopyranoside (**22**) (Figure 7.7), employing a common extraction strategy with n-butanol (Kim *et al.*, 2012). Along with this compound the known saponins gypsogenin 3-*O*-β-D-glucuronopyranoside (**47**), gypsogenin 3-*O*-β-D-glucuronopyranosyl-28-*O*-β-D-glucopyranoside (**48**), and 30-norhederagenin 3-*O*-β-D-glucuronopyranosyl-28-*O*-β-D-glucopyranoside (**49**) (Figure 7.12) were also isolated. It is worth to note that compound (**22**) was isolated for the first time on *Salicornia* genus by Wang *et al.* (2012). These authors named it as bigelovii B (**22**) probably due to the species name, *Salicornia bigelovii*, and their report is available online since March 5, 2012. Kim *et al.*, isolate (**22**) from *Salicornia herbacea* and submitted their results in January 10, 2012. Taking into account the proximity dates of the reported works it is plausible that both authors claimed the isolation of the same new compound.

Salicornia ramosissima is one of the least studied species and in our literature survey we just found one work of Renard *et al.* (1993), where they examined the cell walls and reported the identification of ferulic (**46**) (Figure 7.11) and acetic acids, monosaccharides such as arabinose, glucose and galacturonic acid, and proteins.

Finally we would like to emphasize that the examples given are those that undoubted have been indicated in the plant studied. Sometimes it is difficult to identify which plant was used, for instance El-Mallah *et al.* (1994) reported the isolation of tocopherols (mainly alpha and gamma), sterols (mainly 7-stigmastenol and sitosterol) and sterylglycosides (mainly β-sitosterol and campestigmasterol) from the seeds of a hybrid variety of *Salicornia*, the SOS-7. Another interesting example is the isolation and characterization of betanidin-5-*O*-[2-*O*-(β-D-glucopyranosyl uronic acid)]-β-D-glucopyranoside (**50**) (Figure 7.13), a betacyanin pigment referred by Davy *et al.* (2001) and by Liebezeit (2008). Both authors state that this pigment is responsible for the distinctive typical violet-red colouration of the *Salicornia* species in autumn.

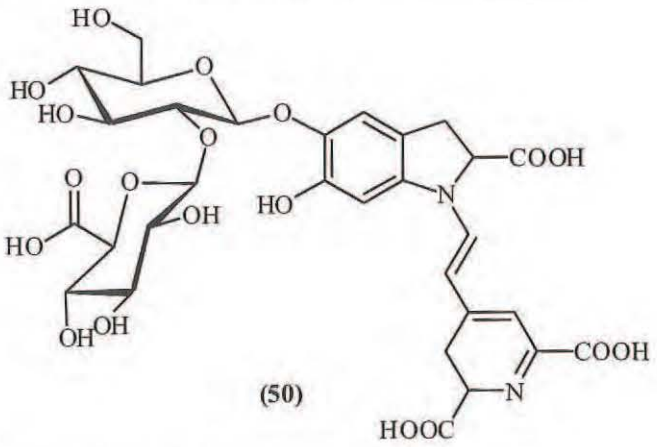


(47: R^1 = H, R^2 = CHO)
(48: R^1 = β-D-Glu, R^2 = CHO)



(49)

Figure 7.12: Compounds isolated from the *n*-butanol extract of *S. herbacea*.



(50)

Figure 7.13: Betacyanin pigment present on *Salicornia* species.

Biological Properties of the Isolated Compounds

In the former items we detailed the reported medicinal applications of *Salicornia* species and the structure of compounds isolated from them. Some researchers dedicate their work to investigate which compounds are responsible for a specific recognized activity. It should be emphasized that the properties attributed to plants usually are the results of synergetic effects between their constituents. Consequently the relationship between the reported activity for a pure compound and the traditional use of a plant cannot be done. We will also describe the biological activities of the compounds isolated from *Salicornia* species.

The polysaccharides found in *Salicornia herbacea* showed potent immunomodulatory activity on monocyte/macrophage lineage cells (Im *et al.*, 2006). Lee *et al.* (2006) reported in the same year a study on macrophage activation mechanism by polysaccharides from *Salicornia herbacea*. They demonstrate that the isolated polysaccharides stimulate macrophages to express iNOS gene through the activation of NF-κB/Rel, and that is the reason why these compounds may represent useful immunopotentiating agents. The immunomodulatory activity of polysaccharides may explain some of the therapeutic efficacies of *Salicornia herbacea*, which has long been used in folk medicine to treat various diseases including cancer.

The tungtungmadic acid (CDCQ) (**38**) (Figure 7.10), also found in *Salicornia herbacea*, was biologically evaluated and the reported properties seems indicate this acid is an important molecule that could be used as lead compound. For instance, Chung *et al.* (2005) evaluated its high ability to scavenge DPPH radical (IC_{50} 5.1 μM) which is an indication of its potential as antioxidant. In addition, they also found that CDCQ prevent the iron-induced liver microsomal lipid peroxidation (IC_{50} 9.3 μM) and is effective in protection of the plasmid DNA against strand break-age induced by hydroxyl radicals (Chung *et al.*, 2005). Later on, the author use serum enzymatic activities of alanine and aspartate aminotransferase and serum TNF-α levels to evidence the suppressive effects of CDCQ on the progress of acute carbon

tetrachloride (CCl_4)-induced hepatic fibrosis and on CCl_4-induced hepatic necrosis and inflammation (Chung *et al.*, 2006).

The CDCQ ability to scavenge radicals was also studied by Hwang *et al.* (2009), especially in the protective effect against *tert*-butyl hydroperoxide (t-BHP)-induced hepatotoxicity in Hepa1c1c7 cells. They suggested that this effect is due to the CDCQ ability to scavenge ROS and to regulate the antioxidant enzyme HO-1 via the PI3K/Akt-Nrf2 signalling pathways (Hwang *et al.*, 2009). More recently these authors reported that CDCQ inhibits tumour cell invasion and migration in human fibrosarcoma HT-1080 cells, by regulating protein kinase Cδ-dependent matrix metalloproteinase-9 expression. They propose that the anti-invasive effects occur through the inhibition of AP-1 and signalling pathways involving PKCδ and three MAPKs (ERK, p38 MAPK, and JNK) leading to the down regulation of MMP-9 expression (Hwang *et al.*, 2010). Additionally this chlorogenic acid derivative inhibit, in a dose-dependent manner, PMA-induced COX-2 protein, gene expression and PGE2 production in murine macrophage RAW 264.7 cells, reduced PMA-induced C/EBPβ and *c*-jun protein expression and significantly inhibited PMA-induced activation of the mitogen-activated protein kinases (MAP kinases), JNK and p38. These findings sustain its anti-inflammatory properties (Han *et al.*, 2010).

Other chlorogenic acid derivatives (**38-42**) (Figure 7.10) isolated from *Salicornia herbacea* showed significantly higher DPPH radical-scavenging and metal-chelating activities than chlorogenic acid, which served as a control (Kim *et al.*, 2011).

The DPPH radical-scavenging and metal-chelating activities of quercetin glucosides (**37**) (Figure 7.9) and (**43**) (Figure 7.10), isolated from the same *Salicornia* species, and having a catechol structure, were similar to those of the dicaffeoylquinic acid derivatives, while (**36**) (Figure 7.9), which has a 3′-methoxyl group on the B ring, showed the lowest radical-scavenging activity (Kim *et al.*, 2011).

Triterpenoid saponins (**22**) (Figure 7.7) and (**47-49**) (Figure 7.12), isolated from *Salicornia herbacea* and *Salicornia bigelovii*, do not have significant scavenge effect on DPPH radical but showed relatively good activity on authentic $ONOO^-$ and induced $ONOO^-$ from morpholinosydnonimine (SIN-1), comparable with those of L-ascorbic acid and penicillamine (Kim *et al.*, 2012). 30-Nortriterpenoid saponins bigelovii A (**21**), bigelovii B (**22**), pfaffine B (**23**) and boussingoside A_2 (**24**) (Figure 7.7) were evaluated for their cytotoxicity against cell lines, HL-60 (promyelocytic leukemia), MCF-7 (breast carcinoma), HepG2 (liver carcinoma) and A549 (lung carcinoma) (Wang *et al.*, 2012). The results reported indicate that just bigelovii A (**21**) and pfaffine B (**23**) were moderately active against HL-60, MCF-7 and HepG2 (6.18, 78.08 and 13.64 μM for (**21**); 31.87, >100, ~100 μM for (**23**), respectively) (Wang *et al.*, 2012).

The use of *Salicornia herbacea* in traditional medicine to prevent and/or treat diabetic complications attracted Lee *et al.* (2005) to investigate the compound and/or compounds responsible for this activity. They found out that isorhamnetin 3-*O*-β-D-glucoside (**36**) (Figure 7.9) not only inhibited AR *(Aldose reductase) in vitro* but also suppressed the serum glucose concentration and sorbitol accumulation in tissues of STZ-induced diabetic rats, therefore can be regard as the antidiabetic principle.

Radwan *et al.* (2007) decided to evaluate the antioxidant activity and antitumour activity against Ehrlich ascites carcinoma of the flavonoids apigenin (**29**), isorhamnetin (**31**), acacetin (**33**), and apigenin- 7-*O*-galactoside (**30**) and isorhamnetin-3-*O*-galactoside (**32**), (Figure 7.8), isolated from *Salicornia fruticosa*. The results revealed that the tested compound present low antitumour activity but higher antioxidant activity than trolox, a standard antioxidant compound (Radwan *et al.*, 2007). The *Salicornia herbacea* flavonoids, isorhamnetin 3-*O*-β-D-glucopyranoside (**36**) and quercetin 3-*O*-β-D-glucopyranoside (**37**) (Figure 7.9), were also evaluate as DPPH scavenging (Park and Kim, 2004) and matrix metalloproteinase-9 (MMP-9) inhibitory agents (Kong *et al.*, 2008b). These compounds, successfully suppressed radical-mediated DNA damage by scavenged the intracellular radicals and had inhibitory effect on MMP-9 expression. These results suggest that these compounds may be used to prevent metastasis involving MMP-9, closely related to ROS (Kong *et al.*, 2008b). They have also studied the inhibitory effects, of these flavonoid derivatives, on two gelatinases, MMP-9 and MMP-2 and the influence on tissue inhibitor of metalloproteinase-1(TIMP-1) in human fibrosarcoma cells (HT1080). Their results showed that isorhamnetin 3-*O*-β-D-glucopyranoside (**36**) and quercetin 3-*O*-β-D-glucopyranoside (**37**) (Figure 7.9) can become natural chemopreventive agents for cancer, since both, MMP-9 and MMP-2, were inhibited and TIMP-1 (tissue inhibitor of metalloproteinase-1) protein level was enhanced (Kong *et al.*, 2008a). Their study on the action mechanisms showed that isorhamnetin 3-*O*-β-D-glucopyranoside (**36**) significantly increased GSH (glutathione) level as well as expression levels of antioxidant enzymes, such as superoxide dismutase (SOD), catalase (CAT), glutathione reductase (GSH-reductase) and heme oxygenase-1 (HO-1), which were closely related with the amount of cellular ROS. In addition, it significantly inhibited oxidative damage of purified genomic DNA and suppressed activity of myeloperoxidase (MPO) in tumour necrosis factor-α (TNF-α) stimulated human myeloid cells (Kong *et al.*, 2009).

The inhibitory effect on lipid accumulation and adipogenic differentiation of the same two flavonoid glucopyranosides, isorhamnetin 3-*O*-β-D-glucopyranoside (**36**) and quercetin 3-*O*-β-D-glucopyranoside (**37**) (Figure 7.9), were also evaluated (Kong *et al.*, 2012). The results showed that glucopyranoside (**36**) applied to adipocytes significantly reduced triglyceride content in adipocytes with decrease of leptin, the adipogenic marker protein which is secreted in proportion to triglyceride stores. Moreover, the specific mechanism mediating the effects of glucopyranoside (**37**) was confirmed by activation of AMP-activated protein kinase (AMPK). Although the structural similarity between glucopyranosides (**36**) and (**37**), the later is more active and the authors propose that the extra hydroxyl group in aromatic ring may be responsible for high antiadipogenic activity of quercetin 3-*O*-β-D-glucopyranoside (**37**). They also suggest that the nutraceutical value of *Salicornia herbacea* as potent anti-obesity agent via alleviation of lipid accumulation is due to its content in quercetin 3-*O*-β-D-glucopyranoside (**37**) (Kong *et al.*, 2012).

The glucopyranoside isorhamnetin 3-*O*-β-D-glucopyranoside (**36**) exhibited dose-dependent scavenging activities of the authentic $ONOO^-$ and $ONOO^-$ from SIN-1. In fact, isorhamnetin 3-*O*-β-D-glucopyranoside (**36**) acts as anti-inflammatory

agent by suppressing the lipopolysaccharide-induced nitric oxide production and the expression of cytokines such as inducible nitric oxide synthase, tumour necrosis factor-α, and interleukin-1β in RAW 264.7 cells (Kim *et al.*, 2009). Furthermore, ROS, including the hydroxyl, superoxide, carbon-centered, and DPPH radicals, were actively quenched in the presence of isorhamnetin 3-*O*-β-D-glucopyranoside (**36**) (Kim *et al.*, 2009).

Conclusion

The phytochemical and pharmaceutical knowledge on *Salicornia* species have been described, which genus include more or less 117 species. It is clear that the phytochemical profile of this genus is very far of being completed, since only a few species were examined. The results found and here presented point out for the importance of this genus as nutritional sources and/or as new sources for new drugs, directly used in traditional medicine or as inspiration for new synthetic ones. Nevertheless it is evident that other species should be phytochemically studied because other interesting and active compounds can be found. Moreover the biological evaluations clearly point that the secondary metabolites isolated from *Salicornia* species can become important as new anti-inflammatory and/or anti-cancer agents, which once more indicate that further studies should be undertaken. We expect, with this review, have not only detailed the information on *Salicornia* genus secondary metabolites constituents and biological properties but, above all, stimulate further studies on the less investigate species.

Abbreviations

A549: Lung carcinoma cells line

AMP: Activated protein kinase (also 5'-adenosine monophosphate-activated protein kinase plays a role in cellular energy homeostasis).

AP-1: Activator protein 1 (a transcription factor that controls a number of cellular processes including differentiation, proliferation, and apoptosis).

AR: Aldose reductase

B7-1: Co-stimulatory molecules involved on T cell co-stimulation process (require to the development of an effective immune response).

***t*-BHP:** *tert*-Butyl hydroperoxide

C/EBPβ: A member of the CCAAT-enhancer-binding proteins (C/EBP proteins interact with the CCAAT (cytidine-cytidine-adenosine-adenosine-thymidine) box motif, which is present in several gene promoters).

CAT: Catalase enzyme (convert molecules of hydrogen peroxide to water and oxygen).

CD40: Co-stimulatory molecules involved on B cell co-stimulation process (require to the development of an effective immune response).

CDCQ: 3-Caffeoyl-4-dihydrocaffeoyl quinic acid (the same as tungtungmadic acid)

c-jun: Name of a gene and protein that, in combination with the cellular proto-oncogene c-Fos, forms the activator protein 1.

COX-2: Cyclo-oxigenase-2.

DNA: Deoxyribonucleic acid

DPPH: 2,2-diphenyl-1-picrylhydrazyl radical

ERK: Extracellular signal-regulated kinases.

GPx: Glutathione peroxidase (main biological role is to protect the organism from oxidative damage).

GSH: Glutathione

HAB: Harmful Algal Bloom

Hepa1c1c7: Murine hepatoma cell line

HepG2: Liver carcinoma cells line

HL-60: Promyelocytic leukemia cells line

HO-1: Heme Oxygenase-1

HT-1080: Human fibrosarcoma cell line

IL-1β: Interleukin-1b, also known as catabolin (is a cytokine protein, important mediator of the inflammatory response).

iNOS: Isoform nitric oxide synthases (involved in immune response)

JNK: c-Jun N-terminal kinases (belong to the mitogen-activated protein kinase family).

MAPKs: Mitogen-activated protein kinases

MCF-7: Breast carcinoma cells line

MMP-2: Matrix metalloproteinase-2

MMP-9: Matrix metallopeptidase 9 (are key effectors of extracellular matrix remodeling and play a role in inflammation)

MPO: Myeloperoxidase (MPO produces several substances used by the neutrophil to kill bacteria and other pathogens)

NF-κB/Rel: A member of the family of nuclear factor kappa-light-chain-enhancer of activated B cells (transcription factors involved in the control of immune and inflammatory responses, developmental processes, cellular growth, and apoptosis. In addition, these transcription factors are persistently active in a number of disease states, including cancer, arthritis, chronic inflammation, asthma, neurodegenerative diseases, and heart disease)

NO: Nitric oxide

$ONOO^-$: Anion peroxynitrite (sometimes called peroxonitrite)

p38 MAPK: A subfamily of mitogen-activated protein kinases that are responsive to stress stimuli

PGE2: Prostaglandin E2

PI3K/Akt-Nrf2: Intracellular signaling pathway involving phosphatidylinositol 3-kinases (PI3K), protein kinase B (Akt) and nuclear factor (erythroid-derived 2)-like 2 (Nrf2)

PKCδ: Protein kinase C delta

PMA: Phorbol 12-myristate 13-acetate (a tumour promoter)

RAW 264.7: Mouse leukemic monocyte macrophage cell line

ROS: Reactive oxygen species

SHE: *Salicornia herbacea* extract

SIN-1: 3-Morpholinosydnonimine (releases NO and superoxide anion under physiological conditions)

SOD: Superoxide dismutases (important antioxidant defense enzymes that catalyze the dismutation of superoxide into oxygen and hydrogen peroxide).

SOS-10: *Salicornia bigelovii* seeds hybrid variety

SOS-7: *Salicornia* oilseed selection n° 7 hybrid variety

STZ: Streptozotocin

TIMP-1: Tissue inhibitor of metalloproteinase-1

TNF-α: Tumour necrosis factor alpha (a cytokine involved in systemic inflammation)

Acknowledgements

Thanks are due to the Universities of Aveiro and Azores and also to Fundação para a Cıκncia e a Tecnologia (FCT) and FEDER for funding the Organic Chemistry Research Unit (project PEst-C/QUI/UI0062/2011). The authors also wish to acknowledge generous contribution of José M G Pereira for the original photographs of *Salicornia* in Aveiro region (Ecomuseu da Troncalhada, 40° 38' 32.32" N, 8° 39' 47.52" W).

References

Al-Jaber, N.A., Mujahid, T.G., and Al-Hazimi, H.M.G. (1992). Secondary metabolites of Chenopodiaceace species. *Journal of the Chemical Society of Pakistan*, **14**: 76-83.

Al-Turki, T.A. (1997). A preliminary checklist of the flora of Qassim, Saudi Arabia. *Fedde Repertorium*, **108**: 259-280.

Anwar, F., Bhanger, M.I., Nasir, M.K.A., and Ismail, S. (2002). Analytical characterization of *Salicornia bigelovii* seed oil cultivated in Pakistan. *Journal of Agricultural and Food Chemistry*, **50**: 4210-4214.

Arakawa, Y., Asada, Y., Ishida, H., Chiji, H., and Izawa, M. (1982). Structures of new two isoflavones and one flavone from glasswort (*Salicornia europaea* L.). *Journal of the Faculty of Agriculture, Hokkaido University*, **6**: 11-12.

Arakawa, Y., Chiji, H., and Izawa, M. (1983). Structural elucidation of two new chromones isolated from Glasswort (*Salicornia europaea* L.). *Agricultural Biology and Chemistry*, **47**: 2029-2033.

Attia, F.M., Al-Sobayel, A.A., Kriadees, M.S., Al-Saiady, M.Y., and Bayoumi, M.S. (1997). Nutrient composition and feedingvalue of *Salicornia bigelovii* Torr. meal in broiler diets. *Animal Feed Science and Technology*, **65**: 257-263.

Austenfeld, F.A. (1986). Nutrient reserves of *Salicornia europaea* seeds. *Physiologia Plantarum*, **68**: 446-450.

Austenfeld, F.A. (1988). Seed dimorphism in Salicornia: nutrient reserves. *Physiologia Plantarum*, **73**: 502-504.

Ball, P.W. (2004). *Salicornia* L. *In*: Flora of North America: North of Mexico. Magnoliophyta: Caryophyllidae, Vol. 4, part 1, Editorial Committee of the Flora of North America (Oxford University Press, ISBN 978-0-19-517389-5, pp.335.

Bang, M.A., Kim, H.A., and Cho, Y.J. (2002). Hypoglycemic and antioxidant effect of dietary hamcho powder in streptozotocin-induced diabetic rats. *Journal of Korean Society of Food Science Nutrition*, **31**: 840-846.

Bashan, Y., Moreno, M., and Troyo, E. (2000). Growth promotion of the seawater-irrigated oilseed halophyte *Salicornia bigelovii* inoculated with mangrove rhizosphere bacteria and halotolerant *Azospirillum* spp. *Biology and Fertility of Soils*, **32**: 265-272.

Bhosale, S.H., Jagtap, T.G., and Naik, C.G. (1999). Antifungal activity of some marine organisms from India, against food spoilage *Aspergillus* strains. *Mycopathologia1*, **147**: 133-138.

Bi, W., Tian, M., and Row, K.H. (2012). Separation of phenolic acids from natural plant extracts using molecularly imprinted anion-exchange polymer confined ionic liquids. *Journal of Chromatography* A, **1232**: 37-42.

Borkowski, B., and Drost, K. (1965). Alkaloide aus *Salicornia herbacea* L. *Pharmazie*, **20**: 390-393.

Buchsbaum, R., and Valiela, I. (1987). Variability in the chemistry of estuarine plants and its effect on feeding by Canada geese. *Oecologia*, **73**, 146-153.

Buchsbaum, R., Valiela, I., and Swain, T. (1984). The role of phenolic compounds and other plant constituents in feeding by Canada geese in a coastal marsh. *Oecologia*, **63**: 343-349.

Chandrasekaran, M., Kannathasan; K., and Venkatesalu, V. (2008). Antimicrobial activity of fatty acid methyl esters of some members of Chenopodiaceae. *Zeitschrift für Naturforschung* C., **63**: 331-336.

Chevalier, A. (1922). Les *Salicornes* et leur emploi dans l'alimentation: Etude historique, botanique, économique. *Revue de Botanique appliqué et d'Agriculture coloniale*, **2**: 697-785.

Chiji, H., Aiba, T., and Izawa, M. (1978): Isolation and identification of two 2,3-unsubstituted chromones from glasswort (*Salicornia europaea* L.). *Agricultural Biology and Chemistry*, **42**: 159-1654.

Chung, Y.C., Choi, J.H., Oh, K.N., Chun, H.K., and Jeong, H.G. (2006). Tungtungmadic acid isolated from *Salicornia herbacea* suppresses the progress of carbon

tetrachloride-induced hepatic fibrosis in mice. *Journal of Toxicology and Public Health*, **22**: 267-273.

Chung, Y.C., Chun, H.K., Yang, J.Y., Kim, J.Y., Han, E.H., Kho, Y.H., and Jeong, H.G. (2005). Tungtungmadic acid, a novel antioxidant, from *Salicornia herbacea*. *Archives Pharmacal Research*, **28**: 1122-1126.

Davy, A.J., Bishop, G.F., and Costa, C.S.B. (2001). *Salicornia* L. (*Salicornia pusilla* J. Woods, *S. ramosissima* J. Woods, *S. europaea* L., *S. obscura* P.W. Ball and Tutin, *S. nitens* P.W. Ball and Tutin, *S. fragilis* P.W. Ball and Tutin and *S. dolichostachya* Moss). *Journal of Ecology*, **89**: 681-707.

El Shaer, H.M. (2010). Halophytes and salt-tolerant plants as potential forage for ruminants in the Near East region. *Small Ruminant Research*, **91**: 3-12.

El-Mallah, M.H., Murui, T., and El-Shami, S. (1994). Detailed studies on seed oil of *Salicornia* SOS-7 cultivated at the Egyptian border of Red-Sea. *Grasas y Aceites*, **45**: 385-389.

El-Shami, S.M., and El-Negoumy, S.I. (1993). Tocopherols and flavonoids of SOS-7 halophyte. *Grasas y Aceites*, **44**: 249-252.

GBIF (2012). Data Portal of the Global Biodiversity Information Facility (GBIF). *"Salicornia"* webpage retrieved June 16, 2012

Geslin, M., and Verbist, J.-F. (1985). Flavonoides de *Salicornia europaea*. *Journal of Natural Products*, **48**: 111-113.

Glenn, E., O'Leary, J.W., Watson, C.M., Thompson, T.L., and Kuehl, R.O. (1991). *Salicornia bigelovii* Torr. an oil seed halophyte for seawater irrigation. *Science*, **251**: 1065-1067.

Glenn, E.P., Brown, J.J., and O'Leary, J.W. (1998). Irrigating crops with seawater. *Scientific American Magazine*, **279**: 76-81.

Glenn, E.P., Brown, J.J., and Blumwald, E. (1999). Salt tolerance and crop potential of halophytes. *Critical Reviews in Plant Science*, **18**: 227-255.

Glenn, E.P., Coates, W.E., Riley, J.J., Kuehl, R.O., and Swingle, R.S. (1992). *Salicornia bigelovii* Torr. – a seawater-irrigated forage for goats. *Animal Feed Science and Technology*, **40**: 21–30.

Guil, J.L., Torija, M.E., Giménez, J.J., and Rodríguez, I. (1996). Identification of fatty acids in edible wild plants by gas chromatography. *Journal of Chromatography A*, **719**: 229-235.

Ha, J.A., Lee, S.H., Kim, H.J., and Lee, J.Y. (2006). The role of *Salicornia herbacea* in ovariectomy-induced oxidative stress. *Biological and Pharmaceutical Bulletin*, **29**: 1305-1309.

Han, E.H., Kim, J.Y., Kim, H.G., Chun, H.K., Chung, Y.C., and Jeong, H.G. (2010). Inhibitory effect of 3-caffeoyl-4-dicaffeoylquinic acid from *Salicornia herbacea* against phorbol ester-induced cyclooxygenase-2 expression in macrophages. *Chemico-Biological Interactions*, **183**: 397-404.

Han, S.K., Kim, S.M., and Pyo, B.S. (2003) Antioxidative effect of glasswort (*Salicornia herbacea* L.) on the lipid oxidation of pork. *Korean Journal for Food Science of Animal Resources*, **23**: 46-49.

Harborne, J.B., and Baxter, H. (1999). The handbook of natural flavonoids. Vol. 1. John Wiley and Sons, New York.

Hupel, M., Lecointre, C.A., M.; Poupart, N., and Gall, E.A. (2011). Comparison of photoprotective responses to UV radiation in the brown seaweed *Pelvetia canaliculata* and the marine angiosperm *Salicornia ramosissima*. *Journal of Experimental Marine Biology and Ecology*, **401**: 36-47.

Hwang, J.-Y., Lee, S.-K., Jo, J.-R., Kim, M.-E., So, H.-A., Cho, C.-W., Seo, Y.-W., and Kim, J.-I. (2007). Hypolipidemic effect of *Salicornia herbacea* in animal model type 2 diabetes mellitus. *Nutrition Research and Practice*, **1**: 371-375.

Hwang, Y.P., Yun, H.J., Choi, J.H., Chun, H.K., Chung, Y.C., Kim, S.K., Kim, B.-H., Kwon, K.-I., Jeong, T.C., Lee, K.Y., and Jeong, H.G. (2010). 3-Caffeoyl, 4-dihydrocaffeoylquinic acid from *Salicornia herbacea* inhibits tumour cell invasion by regulating protein kinase C-δ-dependent matrix metalloproteinase-9 expression. *Toxicology Letters*, **198**: 200-209.

Hwang, Y.P., Yun, H.J., Chun, H.K., Chung, Y.C., Kim, H.K., Jeong, M.H., Yoon, T.R., and Jeong, H.G. (2009). Protective mechanisms of 3-caffeoyl, 4-dihydrocaffeoyl quinic acid from *Salicornia herbacea* against *tert*-butyl hydroperoxide-induced oxidative damage. *Chemico-Biological Interactions*, **181**: 366-376.

Im, S.-A., Kim, G.W., and Lee, C.K. (2003). Immunomodulatory activity of *Salicornia herbacea* L. components. *Natural Product Science*, **9**: 273-277.

Im, S.-A., Kim, K., and Lee, C.-K. (2006). Immunomodulatory activity of polysaccharides isolated from *Salicornia herbacea*. *International Immunopharmacology*, **6**: 1451-1458.

Jang, H.S., Kim, K.R., Choi, S.W., Woo, M.H., and Choi, J.H. (2007). Antioxidant and antithrombus activities of enzyme-treated *Salicornia herbacea* extracts. *Annals of Nutrition and Metabolism*, **51**: 119-125.

Jefferies, R.L., and Gottlieb, L.D. (1982). Genetic differentiation of the microspecies *Salicornia europaea* L. (*SensuStricto*) e *S. ramosissima* J. Woods. *New Phytologist*, **92**: 123-129.

Jiang, D., Huang, L., Lin, S., and Li, Y. (2010). Allelopathic effects of euhalophyte *Salicornia bigelovii* on marine alga *Skeletonema costatum*. *Allelopathy Journal*, **25**: 163-172.

Jo, Y.C., Ahn, J.H., Chon, S.M., Lee, K.S., Bae, T.J., and Kang, D.S. (2002). Studies on pharmacological effects of glasswort (*Salicornia herbacea* L.). *Korean Journal of Medicinal Crop Science*, **10**: 93-99.

Kadereit, G., Ball, P., Beer, S., Mucina, L., Sokoloff, D., Teege, P., Yaprak, A.E., and Freitag, H. (2007). A taxonomic nightmare comes true: phylogeny and biogeography of glassworts (*Salicornia* L., Chenopodiaceae). *Taxon*, **56**: 1143-1170.

Kang, S., Kim, D., Lee, B.H., Kim, M.-R., Chiang, M., and Hong, J. (2011). Antioxidant proprieties and cytotoxic effects of fractions from glasswort (*Salicornia herbacea*) seeds extracts on human intestinal cells. *Food Science and Biotechnology*, **20**: 115-122.

Khare, C.P. (2007). Indian medicinal plants, Springer Science and Business Media, LLC, 1st ed., New York.

Kim, J.Y., Cho, J.Y., Ma, Y.K., Park, K.Y., Lee, S.H., Ham, K.S., Lee, H.J., Park, K.H., and Moon, J.H. (2011). Dicaffeoyl quinic acid derivatives and flavonoid glucosides from glasswort (*Salicornia herbacea* L.) and their antioxidative activity. *Food Chemistry*, **125**: 55-62.

Kim, M.W. (2007). Effect of *Salicornia herbacea* L. suplementation on blood glucose and lipid metabolites in streptozotocin-induced diabetic rats. *Korean Journal of Nutrition*, **40**: 5-13.

Kim, Y.A., Kong, C.-S., Lee, J. I., Kim, H., Park, H.Y., Lee, H.-S., Lee, C., and Seo, Y. (2012). Evaluation of novel antioxidant triterpenoid saponins from the halophyte *Salicornia herbacea*. *Bioorganic and Medicinal Chemistry Letters*, **22**: 4318-4322.

Kim, Y.-A., Kong, C.-S., Um, Y.R., Lim, S.-Y., Yea, S.S., and Seo, Y. (2009). Evaluation of *Salicornia herbacea* as a potential antioxidant and anti-inflammatory agent. *Journal of Medicinal Food*, **12**: 661-668.

Kong, C.-S., Kim, J.-A., Qian, Z.-J., Kim, Y.A., Lee, J.I., Kim, S.-K., Nam, T.J., and Seo, Y. (2009). Protective effect of isorhamnetin 3-O-β-D-glucopyranoside from *Salicornia herbacea* against oxidation-induced cell damage. *Food and Chemical Toxicology*, **47**: 1914-1920.

Kong, C.-S., Kim, Y.A., Kim, M.M., Park, J.S., Kim, J.A., Kim, S.K., Lee, B.J., Nam, T.J., and Seo, Y. (2008a). Flavonoid glycosides isolated from *Salicornia herbacea* inhibit matrix metalloproteinase in HT1080 cells. *Toxicology in Vitro*, **22**: 1742-1748.

Kong, C.S., Kim, Y.A., Kim, M.M., Park, J.S., Kim, S.K., Lee, B.J. Nam, T.J., and Seo, Y. (2008b). Antioxidant activity and inhibition of MMP-9 by isorhamnetin and quercetin 3-O-β-D-glucopyranosides isolated from *Salicornia herbacea* in HT1080 cells. *Food Science and Biotechnology*, **17**: 983-989.

Kong, C.-S., Lee, J.I., Kim, Y.A., Kim, J.-A., Bak, S.S., Hong, J.W., Park, H. Y., Yea, S.S., and Seo, Y. (2012). Evaluation on anti-adipogenic activity of flavonoid glucopyranosides from *Salicornia herbacea*. *Process Biochemistry*, **47**: 1073-1078.

Lee, K.Y., Lee, M.H., Chang, I.Y., Yoon, S.P., Lim, D.Y., and Jeon, Y.J. (2006). Macrophage activation by polysaccharide fraction isolated from *Salicornia herbacea*. *Journal of Ethnopharmacology*, **103**: 372-378.

Lee, Y.S., Hye, S.L., Kuk, H.S., Kim, B.K., and Lee, S. (2004). Constituents of the halophyte *Salicornia herbacea*. *Archives Pharmacal Research*, **27**: 1034-1036.

Lee, Y.S., Lee, S.H., Kim, B.K., Oguchi, K., and Shin, K.H. (2005). Inhibitory effects of isorhamnetin-3-O-β-D-glucoside from *Salicornia herbacea* on rat lens aldose reductase and sorbitol accumulation in streptozotocin-induced diabetic rat tissues. *Biological and Pharmaceutical Bulletin*, **28**: 916-918.

Lellau, T.F., and Liebezeit, G. (2003a). Activity of ethanolic extracts of salt marsh plants from Lower Saxonian Wadden sea coast against microorganisms. *Senckenbergiana Maritima*, **32**: 177-181.

Lellau, T.F., and Liebezeit, G. (2003b).Cytotoxic and antitumour activities of ethanolic extracts of salt marsh plants from Lower Saxonian Wadden Sea, Southern North Sea. *Pharmaceutical Biology*, **41**: 293-300.

Liebezeit, G. (2008). Ethnobotany and phytochemistry of plants dominant in salt marshes of the Lower Saxonian Wadden Sea, southern North Sea. *Senckenbergianan Maritima*, **38**: 1-30.

Lin. Z.Q., Schemenauer, R.S., Cervinka. V., Zayed. A., Lee. A., and Teny, N. (2000). Selenium volatilization from a soil-plant system for the remediation of contaminated water and soil in the San Joaquin Valley. *Journal of Environmental Quality*, **29**: 1048-1056.

Lu, D.H., Zhang, M., Wang, S.J., Cai, J.L., Zhou, X., and Zhu, C.P. (2010). Nutritional characterization and changes in quality of *Salicornia bigelovii* Torr. during storage. *LWT Food Science and Technology*, **43**: 519-524.

Mabey, R. (1996). Flora Britannica. Sinclair-Stevenson, Reed International Books Ltd., London.

Milic, D., Lukovic, J., Ninkov, J., Zeremski-Škoriæ, T., Zoriæ, L., Vasin, J., and Milic, S. (2012). Heavy metal content in halophytic plants from inland and maritime saline areas. *Central European Journal of Biology*, **7**: 307-317.

Mudie, P.J., Greer, S., Brakel, J., Dickson, J.H., Schinkel, C., Peterson-Welsh, R., Stevens, M., Turner, N.J., Shadow, M., and Washington, R. (2005). Forensic palynology and ethnobotany of *Salicornia* species (Chenopodiaceae) in northwest Canada and Alaska. *Canadian Journal of Botany*, **83**: 111-123.

Nicolaou, K.C., and Montagnon, T. (2008). Molecules that changed the World. Wiley-Vch Verlag GmbH and Co. KGaA, Weinheim, ISBN 978-3-527-30983-2

O'Callaghan, M. (1992) The ecology and identification of the southern African Salicornieae (Chenopodiaceae). *South African Journal of Botany*, **58**: 430-439.

Oh, J.-H., Kim, E.-O., Lee, S.-K., Woo, M.-H., and Choi, S.-W. (2007). Antioxidant activities of the ethanol extract of Hamcho (*Salicornia herbacea* L.) cake prepared by enzymatic treatment. *Food Science and Biotechnology*, **1**: 90-98.

Park S.H., and Kim K.S. (2004). Isolation and identification of antioxidant flavonoids from *Salicornia herbacea* L. *Journal of the Korean Society for Applied Biological Chemistry*, **47**: 120-123.

Park, S.H., Ko, S.K., Choi, J.G., and Chung, S.H. (2006). *Salicornia herbacea* prevents high fat diet-induced hyperglycemia and hyperlipidemia in ICR mice. *Archives of Pharmacal Research*, **29**: 256-264.

Polat, R., and Satýl, F. (2012). An ethnobotanical survey of medicinal plants in Edremit Gulf (Balýkesir–Turkey). *Journal of Ethnopharmacology*, **139**: 626-641.

Radwan, H.M., Nazif, N.M., and Abou-Setta, L.M. (2007). Phytochemical investigation of *Salicornia fruticosa* (L.) and their biological activity. *Research Journal of Medicine and Medical Sciences*, **2**: 72-78.

Renard, C.M.G.C., Champenois, Y., and Thibault, J.F. (1993). Characterizaton of the extractable pectins and hemicelluloses of the cell-wall of glasswort, *Salicornia ramosissima*. *Carbohydrate Polymers*, **22**: 239-245.

Rhee, M.H., Park, H.J., and Cho, J.Y. (2009). *Salicornia herbacea*: Botanical, chemical and pharmacological review of halophyte marsh plant. *Journal of Medicinal Plants Research*, **3**: 548-555.

Rosso, P.H., Pushnik, J.C., Lay, M., and Ustin, S.L. (2005). Reflectance properties and physiological responses of *Salicornia virginica* to heavy metal and petroleum contamination. *Environmental Pollution*, **137**: 241-252.

Salt, T.A., and Adler, J.H. (1985). Diversity of sterol composition in the family Chenopodiaceae. *Lipids*, **9**: 594-601.

Sharma, A., Gontia, I., Agarwal, P.K., and Jha, B. (2010). Accumulation of heavy metals and its biochemical responses in *Salicornia brachiata*, an extreme halophyte. *Marine Biology Research*, **6**: 511-518

Silva, H., Caldeira, G., and Freitas, H. (2007). *Salicornia ramosissima* population dynamic sand tolerance of salinity. *Ecological Research*, **22**: 125-134.

Sung, J.H., Park, S.H., Seo, D.H., Lee, J.H., Hong, S.W., and Hong, S.S. (2009). Antioxidative and skin-whitening effect of an aqueous extract of *Salicornia herbacea*. *Bioscience, Biotechnology, and Biochemistry*, **73**: 552-556.

Swingle, R.S., Glenn, E.P., and Squires, V. (1996). Growth performance of lambs fed mixed diets containing halophyte ingredients. *Animal Feed Science and Technology*, **63**: 137-148.

Wang, Q.-Z., Liu, X.-F., Shan, Y., Guan, F.-Q., Chen, Y., Wang, X-Y., Wang, M., and Feng, X. (2012). Two new nortriterpenoid saponins from *Salicornia bigelovii* Torr. and their cytotoxic activity. *Fitoterapia*, **83**: 742-749.

Yaprak, A.E., and Yurdakulol, E. (2008). *Salicornia freitagii* (Chenopodiaceae), a new species from Turkey. *Annales Botanici Fennici*, **45**: 207-211.

Yin, M., Wang, X., Wang, M., Chen, Y., Dong, Y., Zhao, Y., and Feng, X. (2012). A new triterpenoid saponin and other saponins from *Salicornia europaea*. *Chemistry of Natural Compounds*, **48**: 258-261.

Yu, X., Zhang, Y., Shao, R., and Xu, W. (2012). Study on antibacterial and antioxidant activities on *Salicornia herbacea* extracts. *Advances Materials Research*, **421**: 47-50.

Zhu, T., and Row, K.H. (2010). Extraction and determination of β-Sitosterol from *Salicornia herbacea* L. using monolithic cartridge. *Chromatographia*, **71**: 981-985.

Zhu, T., Li, S., and Row, K.H. (2011). Molecularly imprinted monolithic material for the extraction of three organic acids from *Salicornia herbacea* L. *Journal of Applied Polymer Science*, **121**: 1691-1696.