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Review

The Genus *Rumex*: Review of traditional uses, phytochemistry and pharmacology

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ABSTRACT

Ethnopharmacological relevance: The approximately 200 species of the genus *Rumex* (sorrel, Polygonaceae) are distributed worldwide (European, Asian, African and American countries). Some species have been used traditionally as vegetables and for their medicinal properties. Based on the traditional knowledge, different phytochemical and pharmacological activities have been at the focus of research. This review aims to provide an overview of the current state of knowledge of local and traditional medical uses, chemical constituents, pharmacological activities, toxicity, and safety of *Rumex* species, in order to identify the therapeutic potential of *Rumex* species and further directions of research.

Materials and methods: The selection of relevant data was made through a search using the keyword "Rumex" in "Scopus", "Google Scholar", "Web of Science", "PubMed", and "ScienceDirect" databases. Plant taxonomy was validated by the databases "The Plant List", and "*Mansfeld's Encyclopedia*". Additional information on traditional use and botany was obtained from published books and MSc dissertations.

Results: This review discusses the current knowledge of the chemistry, the *in vitro* and *in vivo* pharmacological studies carried out on the extracts, and the main active constituents, isolated from plants of genus *Rumex*. Although, there are about 200 species in this genus, most of the phytochemical and pharmacological studies were performed on up to 50 species. The aerial parts, leaves and roots of the plants are used as vegetables and for the treatment of several health disorders such as mild diabetes, constipation, infections, diarrhoea, oedema, jaundice, and as an antihypertensive, diuretic and analgesic and in case of skin, liver and gallbladder disorders, and inflammation. Many phytochemical investigations on this genus confirmed that *Rumex* species are rich in anthraquinones, naphthalenes, flavonoids, stilbenoids, triterpenes, carotenoids, and phenolic acids. Moreover, it draws the attention that high level of oxalic acid in some species can cause toxicity (kidney stones) if consumed large quantity.

Conclusions: This review confirms that some *Rumex* species have emerged as a good source of the traditional medicine for treatment of inflammation, cancer and different bacterial infections and provides new insights for further promising investigations on isolated compounds, especially quercetin 3-*O*-glucoside, emodin, nepodin, torachrysone, and trans-resveratrol to find novel therapeutics and aid drug discovery. In addition, hepatoprotective, antiviral and antidiabetic activities should have priority in future pharmacological studies. However, for applying species to prevent or treat various diseases, additional pharmacological studies are needed to find the mechanism of actions, safety and efficacy of them before starting clinical trials.

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1. Introduction

Local environmental resources derived from plants continue to play an important role in the provision of dietary and medical care for humans in many parts of the World. A very important factor turning to people's interest in wild plants as food are times of famine or food scarcity, but on the other hand eating wild products is becoming fashionable in our modern society (Schunko et al., 2015). The *Rumex* species, belonging in the Polygonaceae family, comprise about 200 species widely distributed around the World. The name *Rumex* originated from the Latin word for dart, alluding to the shape of the leaves (Saleh et al., 1993). There have been numerous ethnobotanical and ethnopharmacological literature reports dealing with the occurrence and traditional uses of *Rumex* species (Pardo-de-Santayana et al., 2005; Giday et al., 2009; Cakilcioglu and Türkoglu, 2010). In some regions, the leaves of *Rumex* species (e.g. *R. acetosa*, *R. acetosella*, *R. abyssinicus*, *R. crispus*, *R. sanguineus*, *R. tuberosus* and *R. thyrsiflorus*, *R. vesicarius*) are utilised as foods, mainly in the forms of sour soups (usually in milk), sauces and salads (Alfawaz 2006; Łuczaj and Szymański, 2007; Pardo-de-Santayana et al., 2007; Cakilcioglu and Türkoglu, 2009; Łuczaj, 2010; Polat et al., 2012a; Łuczaj et al., 2013; Sõukand and Kalle, 2015). Traditional names for several species used as food reflect their gustatory characteristics, taste and aroma, e.g. sour weed in the case of *Rumex*. The roots of many species belonging in the *Rumex* genus have been used in medicine from ancient times because of their gentle laxative effect. *R. acetosa* is officially listed in the Korean Food Code (Korea Food & Drug Administration) as one of the main food materials and has been used in folk medicine as a mild purgative and also for the treatment of cutaneous diseases (Lee et al., 2005). Some of the species are cultivated, e.g. *R. acetosa* and *R. vesicarius* (Bélanger et al., 2010). On the other hand, the members of this genus include many invasive weeds (e.g. *R. obtusifolius* and *R. crispus*) (Watanabe et al., 2011).

Plants belonging to the Polygonaceae are known to produce a large number of biologically important secondary metabolites, such as anthraquinones, naphthalenes, stilbenoids, steroids, flavonoid glycosides, leucoanthocyanidins and phenolic acids (Jang et al., 2005; Wegiera et al., 2007; Mei et al., 2009; Liang et al., 2010; Demirezer et al., 2001b; El-Hawary et al., 2011; Gescher et al., 2011). The aerial parts, leaves and roots of the plants are used in traditional medicine for the treatment of several health disorders such as infections, diarrhoea, constipation, mild diabetes, oedema, jaundice, and as an antihypertensive, diuretic and analgesic and in case of skin, liver and gallbladder disorders, and inflammation. The genus *Rumex* has attracted the attention of many researchers because of its phytoconstituents and medicinal properties. The extracts of these plants, and compounds isolated

from them, have been demonstrated to possess various pharmacological activities, including anti-inflammatory, antioxidant, antitumour, antibacterial, antiviral and antifungal properties *in vitro* and *in vivo* (Taylor et al., 1996; Demirezer et al., 2001; Lee et al., 2005; Rivero-Cruz et al., 2005; Kerem et al., 2006; Kisangau et al., 2009; Gautam et al., 2010; Liang et al., 2010; Yan et al., 2011).

Consumption of *Rumex* spp. seems to be safe, but they could contain high amount of oxalic acid. Oxalate can cause serious problems (calcium oxalate stone formation in kidneys, decrease iron absorption) in case of consuming them in large amount (Farré et al., 1989; Siener et al., 2006).

On the basis of 185 references, the present review provides a survey of the current state of knowledge of the ethnopharmacology, phytochemistry, pharmacological activities, toxicity, and safety of *Rumex* species, as well as their traditional uses which have been supported by pharmacological investigations in order to identify their relevance as food and potential therapeutic applications and to show further directions of research.

2. Taxonomy

Rumex is the second largest genus of family Polygonaceae with almost 200 species distributed in Europe, Asia, Africa and North America, mainly in the northern hemisphere. Among them 49 species listed in this article (see Table 1).

Plants belonging to the genus *Rumex* are annuals, biennials or perennials, mainly herbs, rarely shrubs. Usually they have long, stout roots, sometimes the roots are rhizomatous. Leaves are alternate, sometimes hastate or sagittate, and in subgenera Acetosella and Acetosa are acid-tasting. Flowers are hermaphrodite or unisexual, arranged in whorls on simple or branched inflorescences. In many species the flowers are green, but in some (such as sheep's sorrel, *R. acetosella*) the flowers and their stems may be brick-red. Valves are sometimes developing marginal teeth or dorsal tubercles as they mature. Fruits are trigonous nuts (Flora Europaea, 1993).

Although the names of some plants in this review have not been accepted by The Plant List (2013) database, the names reported by the authors in their original works were used and their taxonomic validation (scientific names, status and synonyms) were showed.

Table 1
Scientific names and synonym(s) of reported *Rumex* species in this article [according to The Plant List (2013) and †Hanelt (2001)].

Rumex species (Accepted names)	Synonyms used in referred articles
Rumex abyssinicus Jacq.	
Rumex acetosa L.	
Rumex acetosella L.	
Rumex aegyptiacus L.	
Rumex alpinus L.	
Rumex altissimus Alph. Wood	
Rumex alpestris Jacq.	*Rumex arifolius* All.
Rumex aquaticus L.	
Rumex brownii Campd.	
Rumex bucephalophorus L.	
Rumex chalepensis Mill.	
Rumex confertus Willd.	
Rumex conglomeratus Murray	
Rumex crispus L.	
Rumex cyprius Murb.	
Rumex dentatus L.	
Rumex gmelinii Turcz. ex Ledeb.	
Rumex hastatus D. Don	
Rumex hydrolapathum Huds.	
Rumex hymenosepalus Torr.	
Rumex japonicus Houtt.	
Rumex lanceolatus Thunb.	*Rumex ecklonianus* Meisn.
Rumex luminiastrum Jaub. & Spach	Probably misspelling of *R. limoniastrum* Jaub. & Spach accepted in The Plant List
Rumex maderensis Lowe	
Rumex maritimus L.	
Rumex nepalensis Spreng.	*Rumex bequaertii* De Wild.
Rumex nervosus Vahl	
Rumex obtusifolius L.	
Rumex palustris Sm.	
Rumex patientia L.	
Rumex pictus Forssk.	
Rumex pseudonatronatus (Borbás) Murb.	
Rumex pulcher L.	
Rumex rugosus Campd.	*Rumex acetosa* L. var. *hortensis* Dierb.†
Rumex sagittatus Thunb.	
Rumex sanguineus L.	
Rumex scutatus L.	
Rumex scutatus subsp. *induratus* (Boiss. & Reut.) Nyman	*Rumex induratus* Boiss. & Reut.
Rumex simpliciflorus Murb.	
Rumex stenophyllus Ledeb.	
Rumex steudelii Hochst. ex A. Rich.	
Rumex thyrsiflorus Fingerh.	
Rumex thyrsiflorus subsp. *papillaris* (Boiss. & Reut.) Sagredo & Malag.	*Rumex papillaris* Boiss. et Reut.
Rumex trisetifer Stokes	*Rumex chinensis* Campd.
Rumex tuberosus L.	*Rumex tuberosus* L. subsp. *horizontalis* (Koch) Rech.
Rumex usambarensis (Dammer) Dammer	
Rumex verticillatus L.	
Rumex vesicarius L.	
Rumex woodii N.E. Br.	

3. Traditional uses of *Rumex* species

Plants belonging in the genus *Rumex* have been used traditionally either as edible plants or for the treatment of several diseases in many parts of the World (Table 2).

3.1. *Rumex* species as foods and colouring agents

The aboveground parts of numerous species (e.g. *R. acetosa*, *R. acetosella*, *R. crispus*, *R. patientia* and *R. pseudonatronatus*) are gathered mainly during the spring and used as vegetables (Pardo-de Santayana et al., 2007; Dénes et al., 2013; Nedelcheva, 2013). In most cases, the roots are applied in therapy, but other plant parts, such as the leaves and fruits, or the seeds are also used. On occasion, leaves are used for sauces and soups or dressed with olive oil and sometimes mixed with boiled potatoes to mitigate their acidity (Łuczaj and Szymański, 2007; Guerra et al., 2008; Łuczaj, 2010; Łuczaj et al., 2013; Dénes et al., 2013). Some plants (e.g. *R. acetosa*, *R. acetosella*, *R. alpinus* and *R. nepalensis*) are consumed fried in olive oil or sautéed with butter or lard or are used as filling for pie (Moerman, 2003; Ali-Shtayeh et al., 2008; Misra et al., 2008; Dreon and Paoletti, 2009). The stems of *R. acetosa* and *R. alpinus* are consumed as raw snacks (Moerman, 2003; Łuczaj, 2010; Abbet et al., 2014), while the roots of *R. hymenosepalus* are used as chewing gum in North America (Lewis and Elvin-Lewis, 2003; Moerman, 2003). In some regions of India almost all parts of *R. crispus* are used either as food or as a medicine. The very young leaves of the plant are added to salads, cooked as a potherb or added to soups; stems are peeled and the inner parts eaten, and finally seeds are grounded into a powder and used as flour for making pancakes. The roasted seeds have been used as a coffee substitute (Pareek and Kumar, 2014). North-American Indians have also used the seeds of *R. hymenosepalus* for making cakes (Moerman, 2003). In Albania one of the most commonly quoted and used wild food plants are *Rumex* spp. (mainly *R. patientia* and *R.*

Table 2
Traditional medical uses and local names of *Rumex* species from different countries and regions.

Species	Syn	Plant part	Traditional uses	Dosage, application	Region	Ref
R. abyssinicus		Root	Stomach disorders		East Africa	Munavu et al. (1984)
		n.d.	Mild diabetes, antihypertensive, diuretic, analgesic, cancer		Ethiopia, Cameroon	Mekonnen et al. (2010) and Tamokou et al. (2013)
R. acetosa	Sorrel, Common sorrel, garden sorrel, Narrow-leaved dock, spinach dock,	n.d.	Mild purgative, cutaneous diseases, jaundice, sore throat, warts		Korea, Britain and Ireland	Lee et al. (2005) and Allen and Hatfield (2004)
		Root	Tenesmus, dysentery, gonorrhoea, fever, ulcer, scabies, skin itch, kidney diseases		Britain and Ireland	Committee on Chinese Medicine and Pharmacy (2009) and Allen and Hatfield (2004)
		Leaf	Fever, diarrhoea, lack of appetite, worm, "blood cleanser"		Hungary and Romania	Dénes et al. (2013), Butura, (1979) and Péntek and Szabó (1985)
	Sour dock, red sorrel,	Leaf	Abscesses		South Africa	Watt and Breyer-Brandwijk (1932)
	Réti/mezei sóska	Leaf	Diarrhoea, warts, bruises wounds	Decoctum	North America (Indians), Britain and Ireland	Moerman (2003) and Allen and Hatfield (2004)
R. acetosella	Sheep sorrel, common sheep sorrel,	Leaf	Analgesic, diuretic		Turkey	Cakilcioglu and Türkoglu (2010)
	Field sorrel, red sorrel, sour dock, juhsóska	Leaf	Warts, bruises	Poultice of steamed leaves	North America (Indians) and Romania	Moerman (2003) and Butura (1979)
			Stomach aid	Fresh leaves chewed	North America (Indians)	Moerman (2003)
		Aerial part, seed	Diarrhoea		Hungary	Erdei (2011)
		Aerial part	Jaundice, fever	Decoction, per os, 2–3 times daily from a week to month till the problem disappears	Iran	Amiri et al. (2014)
		Seed	Diarrhoea, dysentery		Hungary	Giovannini and Szathmáry (1961)
R. alpinus	Alpine dock, Monk's rhubarb	Root	Constipation		Hungary	Rácz et al. (1992)
		n.d.	Stomach problems		Bulgaria and Ukraine	Šťastná et al. (2010)
			Constipation, diarrhoea, eczema		Turkey	Šťastná et al. (2010)
R. aquaticus	Western dock	n.d.	Infections, diarrhoea, oedema, jaundice, constipation, fever		Far East	Jang et al. (2012)
R. bequaertii (syn. *Rumex nepalensis* Spreng.)		Root	Stomach disorders, cancer		East Africa and Cameroon	Munavu et al. (1984) and Tamokou et al. (2013)
R. chinensis (*R. trisetifer* Stokes)	Chinese dock	Root, leaf	Constipation, contusion, inflammation, acne, eczema, prurigo, scalp scabies, vulvitis	1–3 g daily in the form of a powder or decoction (constipation); a maceration in vinegar or alcohol of fresh roots or leaves for external use	Vietnam	Medicinal Plants in Viet Nam (1990)
R. confertus	Asiatic dock	Seed	Diarrhoea	3 g in 300 mL water (infusum), consume 50 mL hourly	Hungary	Rácz et al. (1992)
R. crispus	Curled dock, sour dock, narrow dock, yellow dock, curled dock, sour dock, fodros lórom	Root	Laxative, "blood cleanser", skin diseases, icterus, gastrointestinal tract ailments, bruises, burns, swellings, venereal diseases, sores, rashes, gonorrhoea		Hungary, Britain and Ireland, Turkey, Indian tribes (e.g. Paiutes, Shoshones, Zuni, Navajos)	Haraszti (1985), Allen and Hatfield (2004), Baskan et al. (2007), Shiwani et al. (2012), Steiner (1986) and Moerman (2003)
		Root	Swellings. sores	Mashed pulp	North America (Indians)	Moerman (2003)
		n.d.	Anthrax, purgative, astringent		South Africa	Watt and Breyer-Brandwijk (1932)
		n.d.	Dysentery	Infusion	North America (Indians e.g. Cherokees)	Moerman (2003)
		Leaf	Eye infections, antipyretic, expectorant, antitussive, vermicide, constipation, dizziness		Taiwan	Committee on Chinese Medicine and Pharmacy and Lin (2003)
		Fruit	Dysentery			Shiwani et al. (2012)
		Seed	Diarrhoea, wounds		Romania	Péntek and Szabó (1985)
		n.d.	Skin diseases, rheumatism, cough, constipation, tonic		Pakistan	Ahmed et al. (2014)
R. dentatus	toothed dock	Root	Bacterial and fungal infections (dysentery,		China	Zhang et al. (2012) and Zhu et al.

Table 2 (*continued*)

Species	Syn	Plant part	Traditional uses	Dosage, application	Region	Ref
			enteritis, acariasis), eczema, diarrhoea, constipation			(2010)
		n.d.	Astringent (cutaneous disorders)		India	Khare (2007)
R. ecklonianus	Smaller dock	Root	Sterility, washing wounds and bruises, purgative		Southern Africa (Sutos, Xosas, Zulus)	Watt and Breyer-Brandwijk (1932)
R. hastatus		Root, whole plant	Laxative, tonic agent, diuretic, against rheumatism, skin diseases, piles, bleeding of the lungs, cough, headache, fever, AIDS		China	Zhang et al. (2009) and Sahreen et al. (2014)
		n.d.	Astringent		India	Khare (2007)
R. hydrolapathum	Water dock	Root	Astringent, scurvy, "blood purifier"		Britain and Ireland	Allen and Hatfield (2004)
R. hymenosepalus	Canaigre, Canaigre dock	Leaf	Fever, gastrointestinal disturbances sore, cold			Rivero-Cruz et al. (2005) and Moerman (2003)
		Root	"Purify the blood", wounds, skin irritation, astringent, diarrhoea, cough			Rivero-Cruz et al. (2005), Tyler (1993) and Moerman (2003)
R. japonicus		n.d.	Constipation, jaundice, uterine haemorrhage, haematemesis		China	Zee et al. (1998)
R. madarensis		n.d.	Diuretic, "blood depurative", dermatosis			Tavares et al. (2010)
R. maritimus		Leaf	Burns			Rouf et al. (2003)
		n.d.	Purgative		India	Khare (2007)
		Seed	Tonic, analgetic for the back and the lumbar region, aphrodisiac		India	Rouf et al. (2003) and Khare (2007)
		Root	Purgative		India	Khare (2007)
R. nepalensis		Root	Stomach ache, haemostasis, tinea, dysentery, purgative		Ethiopia, China	Mei et al. (2009)
		Root	Purgative		South Africa, India	Watt and Breyer-Brandwijk (1932) and Khare (2007)
		Leaf	Colic, syphilic ulcers (externally), skin disorders	Infusum	India, Afghanistan, North India	Gautam et al. (2010), Khare (2007) and Gairola et al. (2014)
		Leaf	Bilharziasis	Strong decoction in tablespoon doses 3 times daily	South Africa	Watt and Breyer-Brandwijk (1932)
R. nervosus		n.d.	Acne, diabetes, ophthalmic antiseptic, wounds, eczema, typhus, rabies			Getie et al. (2003)
R. obtusifolius	Broad-leaved dock, Bitter dock, bluntleaf dock, butter dock	Aerial parts	Constipation		Hungary	Haraszti (1985)
		n.d.	Astringent, laxative, tonic, antidote to nettle, sores, blisters, burns, cancer, tumour		Ireland	Harshaw et al. (2010)
		Root	Skin eruption, blood purifier, jaundice, contraceptive	Infusum	North America, Britain and Ireland	Moerman (2003) and Allen and Hatfield (2004)
		Seed	Cough, colds, bronchitis		Britain and Ireland	Allen and Hatfield (2004)
R. patientia	lórom	Root	Constipation, dysentery		Hungary, Afghanistan, North India, North America (Indian tribes)	Haraszti (1985), Szalai (1991), Gairola et al. (2014) and Moerman (2003)
		Root	Skin problems	Juice, infusum	North America (Indian tribes, e.g. Cherokee)	Moerman (2003)
		Leaf	Wounds		Hungary	Szalai (1991) and Dénes et al. (2013)
		Leaf	Anaemia	Infusum	Serbia	Zlatković et al. (2014)
		Leaf	Backache, fever, respiratory disorders, rheumatism, skin diseases, throat sores		Afghanistan, North India, North America (Indian tribes, e.g. Cherokee)	Gairola et al. (2014) and Moerman (2003)
		Shoot	Backache, fever, rheumatism, skin diseases		Afghanistan, North India	Gairola et al. (2014)
R. scutatus	French sorrel, leaf-shield sorrel	n.d.	Antipyretic		Turkey	Cakilcioglu and Türkoglu (2010)
		Plant, leaf	Refrigerant, astringent (in case of dysentery), antiscorbutic	Juice	India	Khare (2007)

R. stenophyllus	Keskenylevelű lórom	Seed	Cough		Romania	Péntek and Szabó (1985)
R. steudelii		Root	Antifertility, rectal prolapse, haemorrhoids, wounds, eczema, swelling, leprosy, abdominal colic, tinea nigra		Ethiopia	Solomon et al. (2010)
R. tuberosus		Leaf	Antihypertensive, constipation, wound healing	Infusion, fresh leaves	Turkey	Polat et al. (2012b) and Cakilcioglu et al. (2010)
R. usambarensis		Root	Stomach disorders		East Africa	Munavu et al. (1984)
R. verticillatus	Swamp dock, water dock	n.d.	Jaundice		North America	Lewis and Elvin-Lewis (2003)
R. vesicarius	Bladder dock	n.d.	Tonic, analgesic, hepatic diseases, constipation, poor digestion, spleen disorders, flatulence, asthma, bronchitis, dyspepsia, vomiting, piles, alcoholism		Egypt, India	El-Hawary et al. (2011)
		n.d.	Antidote to scorpion stings		Saudi Arabia	Khan et al. (2014)
		Seed	Dysentery		India	Khare (2007)
R. woodii		n.d.	Diarrhoea		South Africa	Watt and Breyer-Brandwijk (1932)

n.d. no data

alpinus), which are used as vegetables mainly cooked with dairy products and rice or, more often, as filling for homemade savory pies (Pieroni and Quave, 2014). In alpine areas, *R. alpinus* was used in historical times for various purposes, e.g. leaves to surrogate of sauerkraut or spinach, stems were peeled and applied instead of rhubarb, or eaten fresh or put into cakes, biscuits, and puddings (Šťastná et al., 2010). The leaves of *Rumex* spp. (e.g. *R. acetosa*) use to make sarma, a traditional Middle Eastern and South-Eastern food (it roll around a filling made of rice, bulgur and/or minced meat and gently cooked) (Dogan et al., 2015).

Oxalic intoxication has at times been reported, mainly in children, due to the high oxalic acid content of the plants (Guerra et al., 2008).

The rhizomes of *R. abyssinicus* are used to refine butter and give it a yellow colour (Mekonnen et al., 2010). Moreover, the tuberous roots of some plants (e.g. *R. abyssinicus*, *R. hymenosepalus*) have been used in Kenya and North America as a source of a yellow dye which renders cellulose fibres red–brown when applied in the presence of sodium carbonate (Munavu et al., 1984; Moerman, 2003).

3.2. *Rumex* species in traditional medicines

For medicinal applications mainly decoctions or infusions are prepared from the plant parts, but there are other dosage forms too, e.g. the fresh young leaves of *R. nepalensis* are rubbed over the affected areas after injury from stinging nettles (Gautam et al., 2010). There is an old rhyme for *R. obtusifolius*: "Nettle in, dock out. Dock rub nettle out!" No objective evidence supports this claim aside from the fact that firm rubbing – by itself – was found to produce a short-lived lessening of the pain inflicted by nettle. It is also possible that the time and effort spent on finding a dock leaf is sufficient to distract the victim from the itching caused by nettle rash (Tyler, 1993; Grieve, 1995).

In Europe, mainly *R. acetosa*, *R. acetosella* (leaf, aerial parts, seeds), *R. alpinus* (root), *R. confertus* (seed), *R. crispus* (roots, seeds) and *R. obtusifolius* (aerial parts) are used for the treatment of different diseases. These plants are applied in Hungary and in Romania for constipation, diarrhoea, kidney disorders, swellings, sores, rashes and wounds, ringworm and as an astringent (Dénes et al., 2013; Butura, 1979). In Britain and Ireland *R. acetosa* is used for the treatment of scurvy, wounds, warts, bruises, jaundice and sore throat. Moreover, *R. hydrolapathum*, *R. conglomeratus* and *R. palustris* are also applied e.g. in case of scurvy, as "blood purifier", for bathing rashes and sunburn, and cancer cure. The decoction of the seeds of *R. obtusifolius* is used against coughs of all kinds, colds and bronchitis (Allen and Hatfield, 2004). *Rumex alpinus* was used as a laxative, and to treat stomach problems in Bulgaria and Ukraine, and in Turkey against diarrhoea, constipation and eczema (Šťastná et al., 2010). In Ireland, *R. obtusifolius* is used as astringent, laxative, tonic, antidote to nettle, and for the treatment of sores, blisters, burns and cancer (Harshaw et al., 2010). In traditional Austrian medicine *Rumex alpinus* leaves and roots have been used internally for treatment of viral infections (Bogl et al., 2013). *R. nervosus* is applied as a medicinal plant to cure acne, as a hypoglycaemic agent, and as an ophthalmic antiseptic agent. It is also used for the treatment of wounds, eczema, typhus and rabies (Getie et al., 2003).

An ethnobotanical survey of medicinal plants used in a small region in Turkey revealed that *R. acetosella* is used traditionally as an analgesic and diuretic, *R. scutatus* as an antipyretic, *R. tuberosus* as an antihypertensive and diuretic, and against constipation, and *R. tuberosus* subsp. *horizontalis* (syn. *R. tuberosus*) for wound healing (Cakilcioglu and Türkoglu, 2010; Cakilcioglu et al., 2010; Polat et al., 2012b; Kaval et al., 2014). The dried roots of *R. crispus* find use in traditional Turkish medicine for the promotion of

constipation and as a blood cleanser (Baskan et al., 2007). In other parts of the World, it has been used against skin diseases, icterus and gastrointestinal tract ailments. The fruits of the plant are used against dysentery, and the leaves as vegetables (Shiwani et al., 2012).

Several *Rumex* species have been used in traditional Chinese medicine (TCM) for the therapy of different diseases. *R. dentatus*, found almost everywhere in China, has been employed traditionally for the treatment of many kinds of bacterial and fungal infections, e.g. dysentery, enteritis and acariasis (Zhang et al., 2012). The use of *R. hastatus* has been reported for the healing of coughing, headache and fever (Zhang et al., 2009). The roots of *R. dentatus* are applied to treat acariasis, eczema, diarrhoea and constipation (Zhu et al., 2010). The roots of *R. nepalensis* find use as Tu-Da-Huang in TCM for the treatment of haemostasis and tinea (Mei et al., 2009). Moreover, it is used to cure dysentery and as a purgative. The fresh young leaves of the plant are rubbed over the affected areas after injury from stinging nettles, and are used to treat colic and syphilic ulcers (Gautam et al., 2010). *R. japonicus* has been used to promote constipation, and in healing jaundice, uterine haemorrhage and haematemesis (Zee et al., 1998). *R. aquaticus* apply as a drug against infections, diarrhoea, oedema, jaundice, constipation and fever in traditional oriental medicine (Jang et al., 2012). Moreover, it has been used as a substitute for rhubarb in Korea (Yoon et al., 2005). *R. acetosa* is officially listed in the Korean Food Code as one of the main food materials, and has been used in folk medicine as a mild purgative and for the treatment of cutaneous diseases (Lee et al., 2005). *R. maritimus* has also a number of ethnomedicinal uses; as examples, its leaves are applied against burns, while the seeds, which are tonic, are used to eliminate pain from the back and the lumbar region and as an aphrodisiac (Rouf et al., 2003). *Rumex crispus* has a long history of domestic herbal use in India and Pakistan. It is a gentle and safe laxative and useful for treating a wide range of skin problems (sores, ulcers and wounds). The root of the plant is alterative, mildly tonic, antiscorbutic, cholagogue and astringent, while the seeds effective in the treatment of diarrhoea (Pareek and Kumar, 2014; Ahmed et al. 2014). The roots and leaves of *R. dentatus* and *R. hastatus* are also used for the treatment of several diseases (foot and mouth infections, asthma, cough, jaundice, fever, weakness and scabies) by local communities in Pakistan (Abbasi et al., 2015).

In Africa, the aqueous root extracts of *R. abyssinicus*, *R. usambarensis* and *R. bequaertii* (syn. *Rumex nepalensis* Spreng.) have been utilised as remedies for various types of stomach disorder, while the extracts of *R. abyssinicus* are drunk to control mild diabetes, and as an antihypertensive, diuretic and analgesic (Munavu et al., 1984; Mekonnen et al., 2010). *R. steudelii* is one of the antifertility plants used in the folk medicine in Ethiopia. The roots of the plant, in combination with other medicinal plants, are additionally used in the treatment of rectal prolapse, haemorrhoids, wounds, eczema, swelling, leprosy, abdominal colic and tinea nigra (Solomon et al., 2010). *R. nepalensis* is applied to treat stomach ache in Ethiopian regions. *R. vesicarius* is a wild edible Egyptian herb. In folk medicine, it is used as a tonic and analgesic and for the treatment of hepatic diseases, constipation, poor digestion, spleen disorders, flatulence, asthma, bronchitis, dyspepsia, vomiting and piles, among others (El-Hawary et al., 2011).

In Australia *Rumex* spp. are used for the treatment of stings (Packer et al., 2012).

In 1970, Hartwell reviewed the plants used against cancer mainly in American traditional medicine. Among *Rumex* species *R. acetosa*, *R. acetosella*, *R. acutus*, *R. alpinus*, *R. aquaticus*, *R. britannica*, *R. crispus*, *R. hydrolapathum*, *R. hymenosepalus*, *R. obtusifolius*, *R. patientia*, *R. romassa*, *R. sanguineus* var. *rubrum* and *R. vesicarius* were applied for the treatment of different types of tumours. The preparation forms were very diverse, powder, cataplasm, decoction, infusion, poultice, ointment, plaster, and unguent were also applied, prepared from the roots, seeds, leaves, flowers and barks of the plants or the whole plants (Hartwell, 1970). In the Native American Ethnobotany (Moerman, 2003) several *Rumex* species (e.g. *R. acetosella*, *R. crispus*, *R. hymenosepalus*, *R. obtusifolius*, *R. patientia*) are listed as used Indian tribes for the treatment of different diseases (constipation, diarrhoea, dysentery, jaundice, skin problems, contraceptive, stomach aid and as a contraceptive).

The extracts of some *Rumex* species (*R. hymenosepalus* and *R. maderensis*) are used as a “blood depurative” or “blood purifier” (Rivero-Cruz et al., 2005; Tavares et al., 2010). *R. hastatus* is traditionally taken for the treatment of sexually transmitted diseases, including AIDS (Sahreen et al., 2014).

Finally, Canaigre, the root of *R. hymenosephalus*, has been marketed recently as red wild ginseng and recommended for a large number of maladies ranging from lack of vitality to leprosy, although it does not contain any of the active panaxoside-like saponin glycosides responsible for the physiological activities of ginseng (Tyler, 1993).

4. Phytochemistry of *Rumex* species

The genus *Rumex* is characterized by the accumulation of anthraquinones, naphthalene-1,8-diols, flavonoids and stilbenoids.

4.1. Anthraquinones

Rumex species are known to be rich in anthraquinones, particularly in the roots (Table 3). Emodin (**1**), perhaps the most ubiquitous natural anthraquinone, occurs in several higher plants, fungi and lichens. In higher plants, it is chiefly present in glycoconjugates. Emodin (**1**), chrysophanol (**2**) and physcion (**3**) are frequently found together in plants. The first comprehensive study of anthranoids that occur in *Rumex* species dates back to the 1970s, when Fairbairn et al. investigated the distribution of these compounds in all plant parts (roots, leaves and fruits) of 19 representatives of the *Rumex* genus [*R. hydrolapathum*, *R. scutatus*, *R. altissimus*, *R. crispus*, *R. stenophyllus*, *R. arifolius* (syn. *Rumex alpestris* Jacq.), *R. patientia*, *R. confertus*, *R. sanguineus*, *R. brownii*, *R. pulcher*, *R. acetosa*, *R. conglomeratus*, *R. acetosella*, *R. nepalensis*, *R. maritimus*, *R. alpinus*, *R. palustris*, and *R. obtusifolius*]. All these species proved to contain emodin (**1**), chrysophanol (**2**) and physcion (**3**) in all plant parts, in free, *O*- and/or *C*-glycosidic forms. The roots and fruits were the best sources of these anthraquinones (Fairbairn and El Muhtadi, 1972).

The occurrence of emodin (**1**), chrysophanol (**2**), physcion (**3**) and a nepodinglucoside has been described in the roots of *R. alpinus*, from which tissue cultures were set up by Berg et al., and emodin (**1**), chrysophanol (**2**), physcion (**3**), the dianthrones of chrysophanol (**32**) and physcion (**33**), their heterodianthrone (**34**) and the monoglucoside of chrysophanol (**10**) were identified (Berg and Labadie, 1981). The tuberous roots of *R. abyssinicus* were extracted with boiling petroleum ether and then with EtOAc. The EtOAc fraction was found to contain emodin (**1**), chrysophanol (**2**) and physcion (**3**) (Munavu et al., 1984). Emodin (**1**) has also been isolated from the EtOAc fraction of an aqueous ethanolic extract of the leaves of *R. chalepensis* (Hasan et al., 1995).

From the methanolic extract of the root tubers of *R. dentatus*, emodin (**1**), chrysophanol (**2**) and physcion (**3**) were identified by reverse-phase (RP) HPLC (Liu et al., 1997). Chrysophanol (**2**) and naphthalene derivatives (**43** and **49**) were isolated from the EtOAc extract of the roots by (Zhang et al., 2012). Three epimeric pairs of *C*-glucosyl anthrones [rumejaposides E (**20**), F (**25**), G (**26**), H (**27**), I (**28**) and cassialoin (**29**)] were produced from the roots of *R. dentatus* by on-line HPLC-UV-CD analysis (Zhu et al., 2010).

Table 3
Structures of anthraquinones and naphthalenes isolated from *Rumex* species.

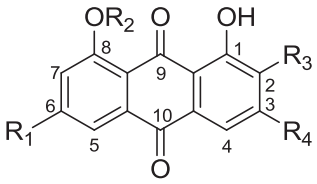
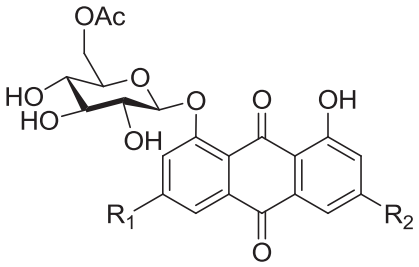
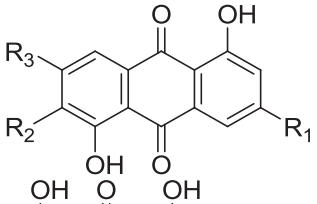
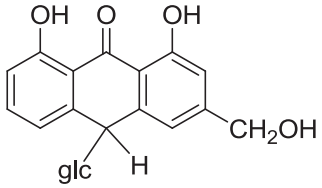
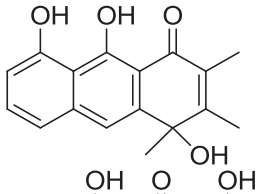
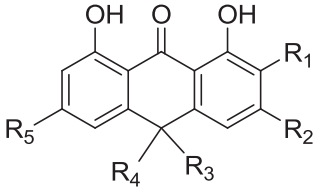
Compound	Substituents	Ref
Anthraquinones		
	**1.** R_1=OH, R_2=H, R_3=H, R_4=CH_3, emodin **2.** R_1=H, R_2=H, R_3=H, R_4=CH_3, chrysophanol **3.** R_1=OCH_3, R_2=H, R_3=H, R_4=CH_3, physcion **4.** R_1=H, R_2=H, R_3=H, R_4=CH_2OH, aloe-emodin **5.** R_1=OH, R_2=H, R_3=H, R_4=CH_2OH, citreoresin **6.** R_1=H, R_2=H, R_3=H, R_4=COOH, rhein **7.** R_1=OH, R_2=H, R_3=COOH, R_4=CH_3, endocrocin **8.** R_1=O-glc, R_2=H, R_3=H, R_4=CH_3 **9.** R_1=OH, R_2=glc, R_3=H, R_4=CH_3 **10.** R_1=H, R_2=glc, R_3=H, R_4=CH_3 **11.** R_1=OCH_3, R_2=glc, R_3=H, R_4=CH_3, reochrysin **12.** R_1=CH_3, R_2=glc, R_3=H, R_4=H, pulmatin	Munavu et al. (1984), Rivero-Cruz et al. (2005), Lee et al. (2005), Gautam et al. (2010), Berg and Labadie (1981) Liu et al. (1997), Hasan et al. (1995), Demirezer et al. (2001a) and El-Fattah et al. (1994) Zhang et al. (2012) Liang et al. (2010) Wegiera et al. (2007) Mei et al. (2009)
	**13.** R_1=H, R_2=CH_3 **14.** R_1=OH, R_2=CH_3	Liang et al. (2010)
	**15.** R_1=CH_3, R_2=H, R_3=H, ziganein **16.** R_1=OH, R_2=CH_2OH, R_3=H **17.** R_1=OCH_3, R_2=H, R_3=CH_3, przewalsquinone	Baskan et al. (2007) and Günaydin et al. (2002)
	**18.** Barbaloin	Wegiera et al. (2007)
	**19.** Rumexone	Günaydin et al. (2002)
	**20.** R_1=COOH, R_2=CH_3, R_3=OH, R_4=glc, R_5=H, rumejaposide A (10R) **21.** R_1=COOH, R_2=CH_3, R_3=OH, R_4=glc, R_5=H, rumejaposide B (10S) **22.** R_1=COOH, R_2=CH_3, R_3=OH, R_4=glc, R_5=OH, rumejaposide C (10R) **23.** R_1=H, R_2=CH_2OH, R_3=OH, R_4=glc, R_5=OH, rumejaposide D (10R) **24.** R_1=H, R_2=CH_3, R_3=OH, R_4=glc, R_5=OH, rumejaposide E **25.** R_1=H, R_2=CH_3, R_3=OH, R_4=glc, R_5=OH, rumejaposide F **26.** R_1=H, R_2=CH_3, R_3=H, R_4=glc, R_5=OH, rumejaposide G **27.** R_1=H, R_2=CH_3, R_3=H, R_4=glc, R_5=OH, rumejaposide H **28.** R_1=H, R_2=H, R_3=OH, R_4=glc, R_5=CH_3,(10R), rumejaposide I **29.** R_1=H, R_2=CH_3, R_3=OH, R_4=glc, R^5=H, cassialoin **30.** R_1=H, R_2=CH_3, R_3=OH, R_4=glc, R_5=OCH_3, (10S) patientoside A **31.** R_1=H, R_2=CH_3, R_3=OH, R_4=glc, R_5=OCH_3, (10R) patientoside B	Jiang et al. (2007) Zhu et al. (2010), Yang et al. (2013) and Jiang et al. (2007) Yang et al. (2013)

Table 3 (*continued*)

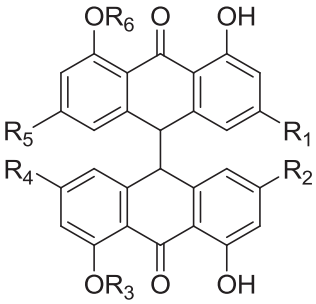
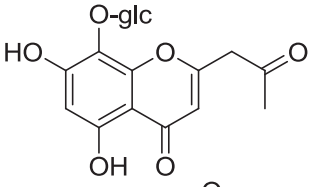
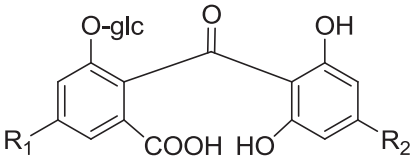
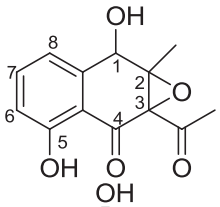
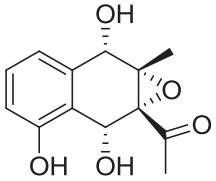
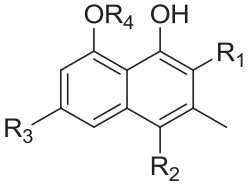
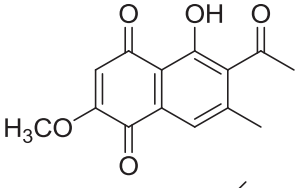
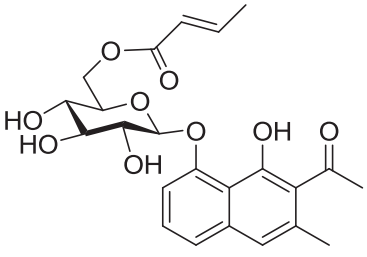
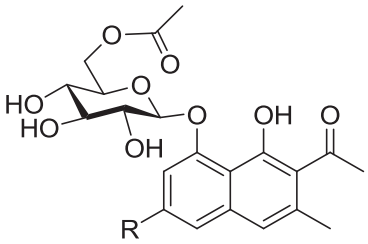
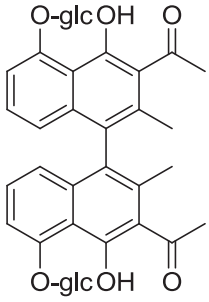
Compound	Substituents	Ref
	**32.** $R_1=R_2=CH_3$, $R_3=R_4=R_5=R_6=H$ Please move 32-34 to the next page (as well as the references), as the structure can be found there too in the pdf version. **33.** $R_1=R_2=CH_3$, $R_3=R_6=H$, $R_4=R_5=OCH_3$ **34.** $R_1=R_2=CH_3$, $R_4=OCH_3$, $R_3=R_5=R_6=H$ **35.** R_1=COOH, R_2=COOH, $R_3=R_6$=glc, $R_4=R_5=H$, (R+) sennoside A **36.** R_1=COOH, R_2=COOH, $R_3=R_6$=glc, $R_4=R_5=H$, (mezo) sennoside B	Berg et al. (1981) Wegiera et al. (2007)
	44. aloesin	Mei et al. (2009)
	**38.** $R_1=CH_3$, $R_2=H$, nepalenside A **39.** $R_1=H$, $R_2=CH_3$, nepalenside B	Mei et al. (2009)
Naphthalenes		
	**40.**	Zee et al. (1998)
	**41.**	Jiang et al. (2007)
	**42.** $R_1=COCH_3$, $R_2=H$, $R_3=H$, $R_4=H$, nepodin, musizin **43.** $R_1=COCH_3$, $R_2=H$, $R_3=H$, R_4=glc **44.** $R_1=COCH_3$, $R_2=Cl$, $R_3=H$, R_4=glc, patientoside A **45.** $R_1=R_2=Cl$, $R_3=H$, R_4=glc, patientoside B **46.** $R_1=COCH_3$, $R_2=H$, R_3=COOH, R_4=glc, rumexoside **47.** $R_1=COCH_3$, $R_2=H$, $R_3=H$, R_4=glc-glc, orientaloside **48.** $R_1=COCH_3$, $R_2=H$, $R_3=OCH_3$, $R_4=H$, torachrysone **49.** $R_1=COCH_3$, $R_2=H$, $R_3=OCH_3$, R_4=glc	Zhang et al. (2009); Gautam et al. (2010), Berg et al. (1981), Lee et al. (2013b) and Nishina et al. (1993) Zhang et al. (2012) and Demirezer et al. (2001b) Kuruüzüm et al. (2001) Mei et al. (2009) and Demirezer et al. (2001b) Zee et al. (1998)
	**50.** 2-methoxystypandrone	Nishina et al. (1993)
	**51.** Rumexneposide A	Liang et al. (2010)

Table 3 (*continued*)

Compound	Substituents	Ref
	**52.** R=OCH_3, rumexneposide **53.** R=H, hastatuside B	Liang et al. (2010) Zhang et al. (2009)
	**54.** Labadoside	Demirezer et al. (2001b)

From the roots of *R. patientia*, emodin (**1**), chrysophanol (**2**), physcion (**3**), emodin-6-*O*-*β*-D-glucopyranoside (**8**), emodin-8-*O*-*β*-D-glucopyranoside (**9**) and chrysophanol-8-*O*-*β*-D-glucopyranoside (**10**) were isolated by Demirezer et al. (2001). Oxanthrone-*C*-glycosides, patientosides A (**30**) and B (**31**), rumejaposides E (**20**) and I (**28**), and cassialoin (**29**) were later obtained from the roots of the plant (Yang et al., 2013). A phytochemical investigation of the aerial parts of *R. aquaticus* resulted in emodin-8-*O*-*β*-D-glucopyranoside (**9**) (Yoon et al., 2005).

From an aqueous acetone extract of *R. japonicus*, rumejaposides A–E (**20**–**24**) and emodin (**1**) were isolated (Jiang et al., 2007). Koyama et al. elaborated a simple and rapid cyclodextrin modified capillary zone electrophoresis method for the simultaneous separation and determination of the major anthraquinones emodin (**1**), chrysophanol (**2**) and their glucosides [emodin-8-*O*-*β*-D-glucoside (**9**) and chrysophanol-8-*O*-*β*-D-glucoside (**10**)] in *R. japonicus*, using 0.005 M α-cyclodextrin in 0.03 M borate buffer (pH 10.5) containing 10% acetonitrile (Koyama et al., 2003). Emodin (**1**), chrysophanol (**2**) and physcion (**3**) were later isolated from the dichloromethane extract of the plant by high-speed counter-current chromatography (Guo et al., 2011). Emodin (**1**) was also isolated from the ethyl acetate extract of *R. japonicus* fruits and stems (Jang et al., 2005; Jang et al., 2008).

From the CH_2Cl_2/MeOH (1:1) extract of *R. hymenosepalus* roots, emodin (**1**), chrysophanol (**2**), and physcion (**3**) were isolated (Rivero-Cruz et al., 2005). Bioactivity-guided fractionation of the CH_2Cl_2 fraction of the aerial parts of *R. acetosa* yielded four anthraquinones [emodin (**1**), chrysophanol (**2**), physcion (**3**) and emodin-8-*O*-*β*-D-glucopyranoside (**9**)] (Lee et al., 2005).

Investigation of the *n*-butanolic extract of the roots of *R. nepalensis* yielded two *seco*-anthraquinone glucosides, nepalensides A (**38**) and B (**39**), and the seconor derivative aloesin (**37**). The *seco*-anthraquinones are probably formed by the decomposition and oxidation of the anthraquinones chrysophanein (**10**) and pulmatin (**12**) (Mei et al., 2009). From the EtOAc extract of the roots, six anthraquinones [emodin (**1**), chrysophanol (**2**), physcion (**3**), endocrocin (**7**), emodin-8-*O*-*β*-D-glucopyranoside (**9**), and chrysophanol-8-*O*-*β*-D-glucopyranoside (**10**)] were isolated (Gautam et al., 2010). In the same year, emodin (**1**), chrysophanol (**2**), physcion (**3**), citreoresin (**5**), emodin-8-*O*-*β*-D-glucopyranoside (**9**), chrysophanol-8-*O*-*β*-D-glucopyranoside (**10**), chrysophanol-8-*O*-*β*-D-(6′-*O*-acetyl)glucopyranoside (**13**) and emodin-8-*O*-*β*-D-(6′-*O*-acetyl)glucopyranoside (**14**), were isolated from the roots of *R. nepalensis* (Liang et al., 2010). The anthraquinone (**1**–**3**, **9** and **10**), and naphthalene (**42** and **43**) contents of the plant were investigated by a validated HPLC method for their quantitative analysis. Three different extraction methods (refluxing, ultrasonication and pressurised liquid extraction) were used. The results showed that the refluxing method was the best technique for the extraction of the glycosides, while ultrasonication was found to be the most effective for the extraction of aglycones (Gautam et al., 2011).

From the roots of *R. crispus*, rare hydroxylated anthraquinones were isolated: 1,5-dihydroxy-3-methylanthraquinone (ziganein, **15**), 1,3,5-trihydroxy-6-hydroxymethylanthraquinone (**16**) and 1,5-dihydroxy-3-methoxy-7-methylanthraquinone (przewalsquinone, **17**), together with rumexone (**19**) (Günaydin et al., 2002). An analytical method based on micellar electrokinetic chromatography was later elaborated for the detection of compounds **15**–**17** in plant samples. The method did not require a pre-separation process and the silica capillaries were free of irreversible contamination of the plant matrix (Baskan et al., 2007).

A phytochemical investigation of different parts (leaves, stems, flowers and roots) of *R. luminiastrum* (*R. limoniastrum*) resulted in the isolation of emodin (**1**), chrysophanol (**2**), physcion (**3**), emodin-8-*O*-*β*-D-glucopyranoside (**9**), chrysophanein (**10**) and reochrysin (**11**) (El-Fattah et al., 1994).

Saleh et al. investigated the flavonoid and anthraquinone profiles of eight *Rumex* species [*R. aegyptiacus*, *R. crispus*, *R. pulcher*, *R. dentatus* ssp. *dentatus* (syn. *R. dentatus*), *R. vesicarius*, *R. pictus*, *R. simpliciflorus* and *R. cyprius*] native to Egypt. It was concluded that the anthraquinones are of low value as chemosystematic markers. All the aerial parts demonstrated the presence of emodin (**1**) in free form or as glucoside, while chrysophanol (**2**) was detected only in *R. pictus* (Saleh et al., 1993). Anthranoid derivatives [emodin (**1**), chrysophanol (**2**), physcion (**3**), aloe-emodin (**4**), rhein (**6**), barbaloin (**18**), and sennosides A (**35**) and B (**36**)] were analysed in the methanolic extracts of *R. acetosa*, *R. acetosella*, *R. confertus*, *R.*

Table 4
Structures of flavonoids and anthocyanins isolated from *Rumex* species.

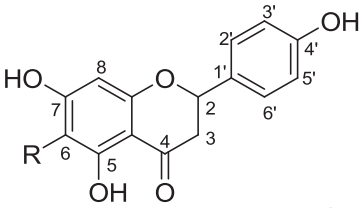
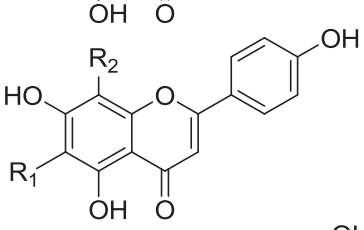
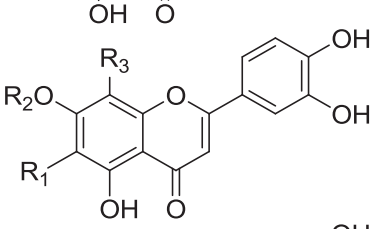
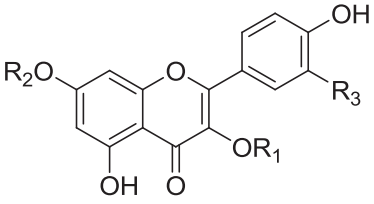
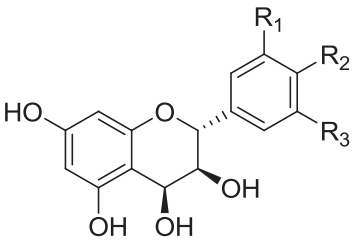
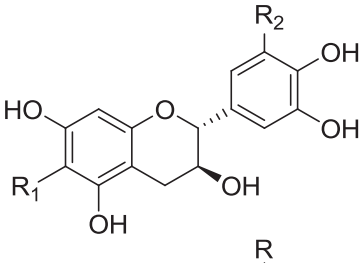
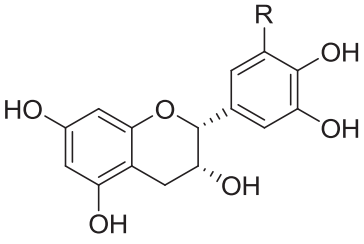
Compounds	Substituents	Ref
Flavonoids		
	**55.** R=glc	El-Hawary et al. (2011)
	**56.** R_1=H, R_2=H apigenin **57.** R_1=H, R_2=glc, vitexin **58.** R_1=glc, R_2=H, isovitexin	Saleh et al. (1993) Sahreen et al. (2014), El-Hawary et al. (2011) and Aritomi et al. (1965) El-Hawary et al. (2011)
	**59.** R_1=R_2=R_3=H, luteolin **60.** R_1=R_3=H, R_2=glc **61.** R_1=R_2=H, R_3=glc, orientin **62.** R_1=glc, R_2=R_3=H, isoorientin	Sahreen et al. (2014) El-Hawary et al. (2011), El-Fattah et al. (1994) and Saleh et al. (1993)
	**63.** R_1=H, R_2=H, R_3=OH, quercetin **64.** R_1=glc, R_2=H, R_3=H, astragalin **65.** R_1=glu, R_2=H, R_3=H **66.** R_1=gal, R_2=H, R_3=H, hyperoside **67.** R_1=ara, R_2=H, R_3=H **68.** R_1=rha-glc, R_2=R_3=H **69.** R_1=rha-gal, R_2=H, R_3=H **70.** R_1=rha, R_2=H, R_3=OH, quercitrin **71.** R_1=glc, R_2=H, R_3=OH, isoquercitrin **72.** R_1=H, R_2=glc, R_3=OH, quercimeritrin **73.** R_1=glu **74.** R^1=glc-gal, R_2=H, R_3=OH **75.** R_1=rha-glc, R_2=H, R_3=OH, rutin	Tavares et al. (2010) Saleh et al. (1993) El-Fattah et al. (1994) Orbán-Gyapai et al. (2014) Hasan et al. (1995) Aritomi et al. (1965) Tavares et al. (2010) El-Fattah et al. (1994) Yan et al. (2011) Sahreen et al. (2014), Zhang et al. (2009) and Hasan et al. (1995)
	**76.** R_1=H, R_2=OH, R_3=H, leucopelargonidine **77.** R_1=OH, R_2=OH, R_3=H, leucocyanidin **78.** R_1=OH, R_2=OH, R_3=OH, leucodelphinidin	Buchalter and Cole (1967)
	**79.** R_1=H, R_2=H, catechin **80.** R_1=H, R_2=OH, gallocatechin **81.** R_1=Cl, R_2=H, 6-chlorocatechin **82.** R_1=glc, R_2=H	Demirezer et al. (2001) and Stöggl et al. (2004) Gescher et al. (2011) Demirezer et al. (2001) El-Hawary et al. (2011)
	**83.** R=H, epicatechin **84.** R=OH, epigallocatechin	Rivero-Cruz et al. (2005), Stöggl et al. (2004) and Gescher et al. (2011)

Table 4 (*continued*)

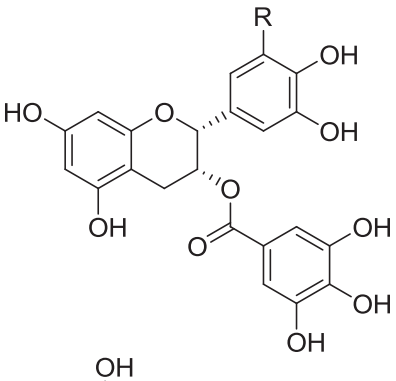
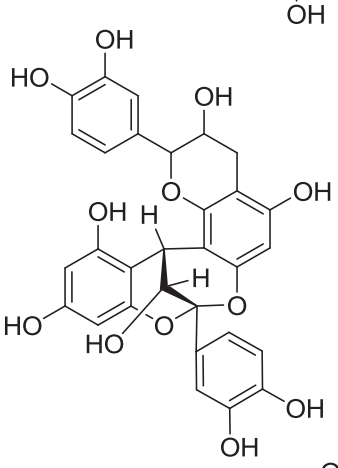
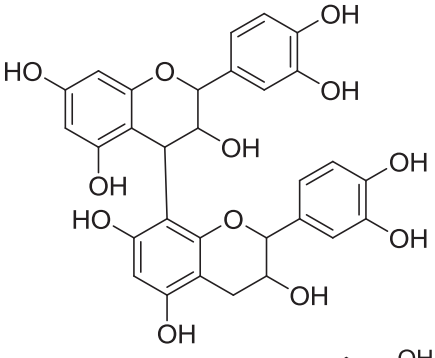
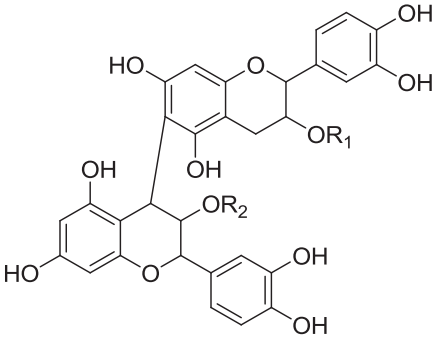
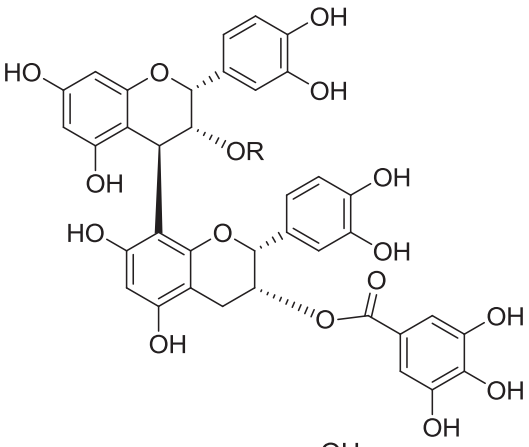
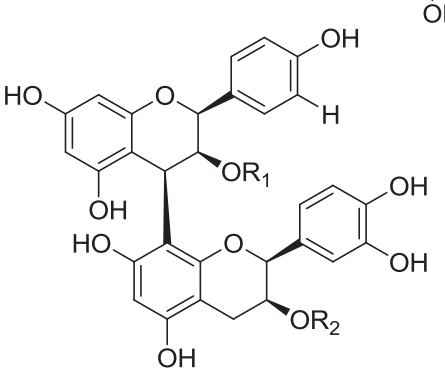
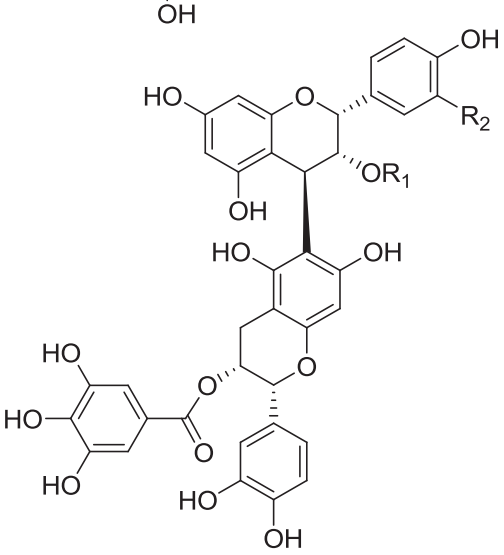
Compounds	Substituents	Ref
	**85.** R=H **86.** R=OH	Mei et al. (2009) and Gescher et al. (2011)
	**87.** (2R,3R,8S,14R,15R), procyanidin A2	Bicker et al. (2009)
	**88.** (2R,2′R,3R,3′S,4R), procyanidin B1 **89.** (2R,2′R,3R,3′R,4R), procyanidin B2 **90.** (2R,2′R,3S,3′S,4S), procyanidin B3 **91.** (2R,2′R,3S,3′R,4S), procyanidin B4	Gescher et al. (2011) and Bicker et al. (2009)
	**92.** $R_1=R_2=H$ (2R,2′R,3R,3′R,4S), procyanidin B5 **93.** $R_1=R_2=H$ (2R,2′R,3R,3′S,4S), procyanidin B7 **94.** $R_1=H$, $R_2=$gall **95.** $R_1=R_2=$gall	Bicker et al. (2009)

Table 4 (*continued*)

Compounds	Substituents	Ref
	**96.** R=H **97.** R=gallate	Gescher et al. (2011) Bicker et al. (2009)
	**98.** $R_1=R_2=H$ **99.** $R_1=H$, R_2=gallate **100.** $R_1=R_2$=gallate	Gescher et al. (2011)
	**101.** $R_1=H$, $R_2=H$ **102.** R_1=gallate, R_2=OH	Gescher et al. (2011)

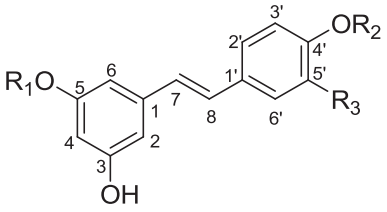
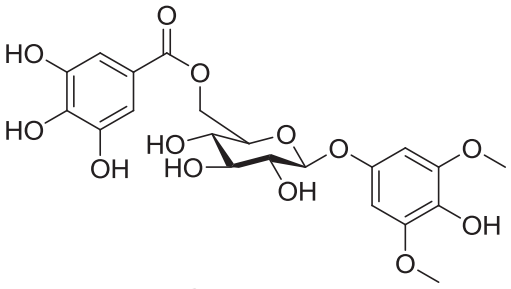
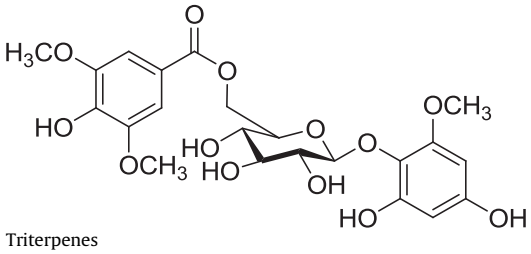
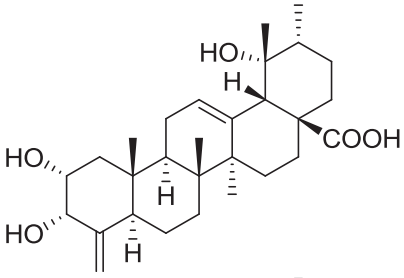
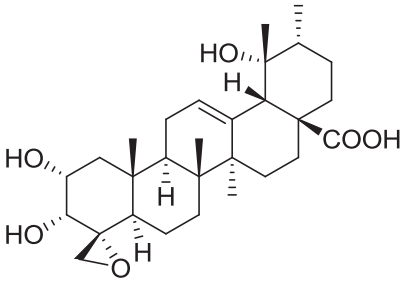
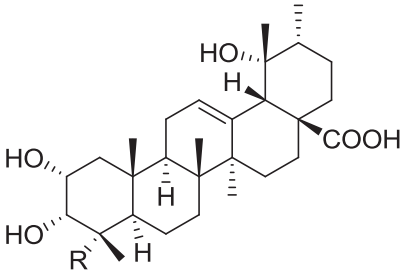
crispus, *R. hydrolapathum* and *R. obtusifolius* roots, leaves and fruits by RP-HPLC. The results showed that in most cases the roots were the richest in anthranoids, whereas the fruits were the poorest. The total content of the investigated compounds was the highest (164.01 mg/g) in *R. confertus* (Wegiera et al., 2007).

The *in vivo* pharmacokinetic properties of emodin (**1**) from Gan-kang granules was investigated by Li et al. The preparation contains *R. japonicus* among others, and is used for the treatment of hepatitis B. A simple, rapid, sensitive and accurate HPLC method was developed for the detection of **1** in rat plasma. It was observed that the emodin (**1**) in this preparation was absorbed faster than that in the *R. japonicus* root extract. The difference in the pharmacokinetic parameters of emodin (**1**) in rat between the root extract and the preparation was significant (Li et al., 2009).

4.2. Naphthalenes

A phytochemical investigation of the roots of *R. alpinus* resulted in the isolation of the naphthalene-1,8-diols nepodin (**42**), nepodin monoglucoside (**43**) and methoxynepodin (torachrysone, **48**) (Table 3) (Berg and Labadie, 1981). From the aerial parts of *R. aquaticus*, musizin-8-*O*-*β*-D-glucopyranoside (**43**) has been identified

Table 5
Structures of stilbenes, tannins and triterpenoids isolated from *Rumex* species.

Compounds	Substituents	Ref
Stilbenoids		
	**103.** $R_1=R_2=R_3=H$, *trans*-resveratrol **104.** $R_1=CH_3$, $R_2=R_3=H$, pinostilbene **105.** $R_1=H$, $R_2=CH_3$, $R_3=H$, deoxyrhapontigenin **106.** $R_1=R_2=H$, $R_3=OH$ **107.** $R_1=H$, $R_2=$glc, $R_3=H$ **108.** $R_1=H$, $R_2=$glc, $R_3=OH$ **109.** $R_1=$glc, $R_2=H$, $R_3=H$, piceid **110.** $R_1=$ara, $R_2=H$, $R_3=H$, rumexoid	Rivero-Cruz et al. (2005) and Kerem et al. (2003) Kerem et al. (2006)
Tannins		
	**111.**	Mei et al. (2009)
	**112.**	Bicker et al. (2009)
Triterpenes		
	**113.**	Jang et al. (2005)
	**114.**	Jang et al. (2005)
	**115.** $R=CH_3$, tormentic acid **116.** $R=CH_2OH$, myrianthic acid	Jang et al. (2005)

(Yoon et al., 2005). The bioassay-guided fractionation of an ethanolic extract of *R. crispus* afforded nepodin (**42**) (Lee et al., 2013c). From the roots of *R. japonicus*, an epoxynaphthoquinol derivative, 3-acetyl-2-methyl-1,5-dihydroxy-2,3-epoxynaphthoquinol (**40**), was isolated by Zee et al. in 1998. 3-Acetyl-2-methyl-1,4,5-trihydroxy-2,3-epoxynaphthoquinol (**41**) and 2-acetyl-1,8-dihydroxy-3-methyl-6-methoxynaphthalene (torachrysone, **48**) were subsequently isolated from the aqueous acetone extract of the roots (Jiang et al., 2007). Nishina et al. identified musizin (**42**), torachrysone (**48**) and 2-methoxystypandrone (**50**) from the roots of this plant (Nishina et al., 1993).

Two chlorinated naphthalene glycosides [patientosides A (**44**) and B (**45**)] were obtained from the roots of *R. patientia* by Kuruüzüm et al. in 2001. In the same year, five other naphthalene glycosides were reported from this plant. Three of them were new [rumexoside (**46**), orientaloside (**47**) and labadoside (**54**)], and two were known [nepodin-8-*O*-*β*-D-glucopyranoside (**43**) and torachrysone-8-*O*-*β*-D-glucopyranoside (**49**)] (Demirezer et al., 2001).

From the roots of *R. nepalensis*, aloesin (**37**), rumexoside (**46**), orientaloside (**47**) and torachrysone (**48**) were isolated by Mei et al. (2009). Later, Gautam et al. reported nepodin (**42**) and its glucoside (**43**) from the plant (Gautam et al., 2010). Liang et al. identified nepodin-8-*O*-β-D-glucopyranoside (**43**), torachrysone (**48**), torachrysone-8-*O*-β-D-glucopyranoside (**49**) and two naphthalene acylglucosides, rumexneposides A (**51**) and B (**52**), from the EtOAc fraction of the roots (Liang et al., 2010).

A phytochemical investigation of *R. hastatus* roots resulted in the isolation of nepodin (**42**), rumexoside (**46**), orientaloside (**47**), torachryson-8-yl β-D-glucopyranoside (**49**) and hastatuside B (**53**) (Zhang et al., 2009). From the EtOAc extract of *R. dentatus* roots, nepodin-8-*O*-*β*-D-glucopyranoside (**43**) and torachrysone-8-*O*-*β*-D-glucopyranoside (**49**) were described by Zhang et al. (2012).

4.3. Flavonoids

Besides anthraquinones, other main chemical constituents of the *Rumex* genus are flavonoids (Table 4). The flavonoids reported in the *Rumex* species were either flavonols or their *O*/*C*-glycosides. *R. acetosa* and *R. japonicus* are perennial herbs which are distributed throughout Japan, Korea and China (Elzaawely et al., 2005). Aritomi et al. isolated vitexin (**57**) from the leaves of *R. acetosa*, and quercitrin (**70**) from *R. japonicas* (Aritomi et al., 1965). From the EtOAc extract of *R. japonicus* fruits, quercetin (**63**), kaempferol-3-*O*-*β*-D-glucoside (astragalin, **64**), quercitrin (**70**), isoquercitrin (**71**) and (+)-catechin (**79**) were obtained (Tavares et al., 2010). Investigation of the aqueous acetone extract of the root resulted in rutin (**75**) and epicatechin (**83**) (Jiang et al., 2007). Chromatographic separation of the EtOAc extracts of an aqueous ethanolic extract of the leaves of *R. chalapensis* afforded three flavonol diglycosides [quercetin-3-*O*-*β*-D-glucopyranosyl (1→4)-*β*-D-galactoside (**74**), quercetin-3-rutinoside (rutin, **75**) and kaempferol-3-*O*-*α*-L-rhamnopyranosyl (1→6)-*β*-D-galactopyranoside (kaempferol 3-robinobioside, **69**)] and one flavonol monoglycoside, quercitrin (**70**). This was the first report of a (1→4)-linked disaccharide attached to quercetin instead of (1→2) or (1→6) (Hasan et al., 1995). From the aerial parts of *R. aquaticus*, kaempferol-3-*O*-*β*-D-glucuropyranoside (**65**), quercitrin (**70**) and quercetin-3-*O*-*β*-D-glucuropyranoside (**73**) were isolated (Yoon et al., 2005). Later, quercetin-3-*O*-galactoside (hiperoside, **66**) and quercetin-3-*O*-arabinoside (guaijaverin, **67**) were yielded from the plant (Orbán-Gyapai et al., 2014).

The investigation of *R. hastatus* roots resulted in the isolation of rutin (**75**) (Zhang et al., 2009). For the determination of four main flavonoids [vitexin (**57**), luteolin (**59**), luteolin-7-*O*-glucoside (**60**) and rutin (**75**)] in *R. hastatus*, a HPLC method was developed. This method demonstrated good linearity, precision, repeatability, accuracy and recovery, and was applicable for the quantitative analysis of *R. hastatus* roots (Sahreen et al., 2014). Phytochemical investigation of analcoholic extract of *R. luminiastrum* (*R. limoniastrum*) herb resulted in the isolation of kaempferol-7-*O*-rhamnoglucoside (**68**), quercimeritrin (**72**) and orientin (**61**). From the roots of *R. patientia*, catechin (**79**) and 6-chlorocatechin (**81**) were isolated (Demirezer et al., 2001).

Stöggl et al. developed a complex analytical method for the evaluation of catechin (**79**) and epicatechin (**83**) in *R. acetosa* leaf extracts. The methanolic extract was separated by RP LC. Identification of the compounds was carried out with diode array, fluorescence and MS detection. Additionally, HPLC–ESI-MS/MS was used to identify catechin (**79**) and epicatechin (**83**) in different phytopharmaceuticals (Stöggl et al., 2004). Gallocatechin (**80**), epicatechin (**83**), epigallocatechin (**84**), epicatechin-3-*O*-gallate (**85**), epigallocatechin-3-*O*-gallate (**86**), epicatechin-(4β→8)-epicatechin [procyanidin B2, (**89**)], epicatechin-3-*O*-gallate-(4β→8)-epicatechin-3-*O*-gallate [procyanidin B2-3,3′-di-*O*-gallate, (**97**)], and epicatechin-3-*O*-gallate-(4β→6)-epicatechin-3-*O*-gallate (**101**) were detected in the plant by RP-HPLC (Gescher et al., 2011). The phytochemical investigation of the EtOAc extract of the *R. acetosa* herb yielded numerous flavan derivatives [catechin (**79**), epicatechin (**83**), epicatechin-3-*O*-gallate (**85**)], propelargonidins, procyanidins, procyanidin dimers [procyanidin B1 (**88**), B2 (**89**), B3 (**90**), B4 (**91**), B5 (**92**), B7 (**93**) and A2 (**87**), epiafzelechin-(4β→8)-epicatechin (**98**), epiafzelechin-(4β→8)-epicatechin-3-*O*-gallate (**99**), epiafzelechin-(4β→6)-epicatechin-3-*O*-gallate (**101**), epiafzelechin-3-*O*-gallate-(4β→8)-epicatechin-3-*O*-gallate (**102**), procyanidin B2-3′-*O*-gallate (**96**), procyanidin B2-3,3′-di-*O*-gallate (**100**), procyanidin B5-3′-*O*-gallate (**94**) and procyanidin B5-3,3′-di-*O*-gallate (**95**)], trimers [procyanidin C1, epiafzelechin-(4β→8)-epicatechin-(4β→8)-epicatechin, epicatechin-(4β→8)-epicatechin-(4β→8)-catechin, cinnamtannin B1, cinnamtannin B1-*O*-gallate, epicatechin-(2β→7, 4β→8)-epiafzelechin-(4β→8)-epicatechin and epicatechin-3-*O*-gallate-(4β→8)-epicatechin-3-*O*-gallate-(4β→8) epicatechin-3-*O*-gallate] and tetramers (procyanidin D1 and parameritannin A1) and 1-*O*-β-D-(2,4-dihydroxy-6-methoxyphenyl)-6-*O*-(4-hydroxy-3,5-dimethoxybenzoyl-glucopyranoside) (**112**) (Bicker et al., 2009).

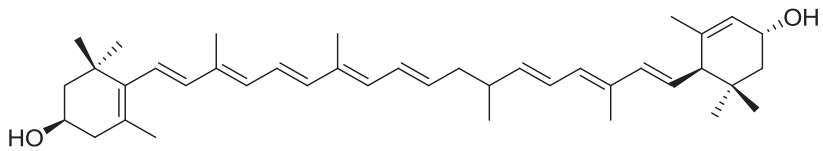
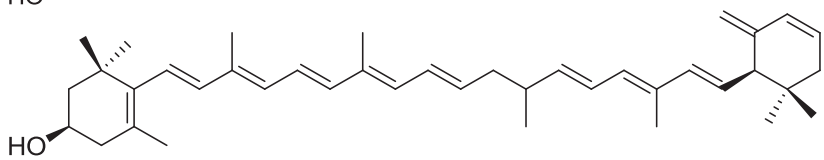
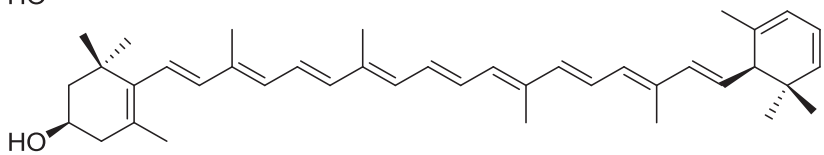
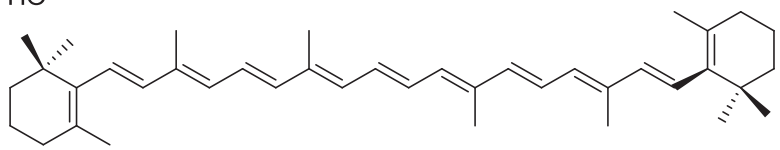
From the roots of *R. hymenosepalus*, epicatechin (**83**) and epigallocatechin (**84**) were isolated (Rivero-Cruz et al., 2005). Epicatechin (**83**) and epicatechin-3-*O*-gallate (**85**) were then detected in the roots of the plant by Mei et al. (2009).

Investigation of the bioactive compounds of *R. vesicarius* yielded flavonoids [naringenin-6-*C*-glucoside (**55**), apigenin-8-*C*-glucoside (vitexin, **57**), luteolin-8-*C*-glucoside (**61**), quercetin-6-*C*-hexoside, rutin (**75**), diosmetin-7-*O*-rhamnohexoside and diosmetin-7-*O*-rhamno-acetylhexoside, catechin (**79**), catechin-6-*C*-glucoside (**82**), epicatechin (**83**), epicatechin-3-*O*-gallate (**85**) and epigallocatechin-3-*O*-gallate (**86**)]. The phenolics in the EtOAc and *n*-butanolic fractions were analysed by means of HPLC-PDA-MS/MS-ESI. Quantification of the identified compounds revealed that naringenin-6-*C*-glucoside (**55**) was the major compound (El-Hawary et al., 2011).

From an acetone–water (7:3) extract of *R. obtusifolius* leaves, procyanidin dimers [B1 (**88**), B2 (**89**), B3 (**90**) and B7 (**93**)] and oligomers [epicatechin (4β→8, 2β→*O*→7)-epicatechin-(4β→8)-epicatechin and B2-3,3′-*O*-digallate (**96**)] were isolated through the use of Sephadex LH-20 gel chromatography followed by polyamide and C_{18} (RP-HPLC) chromatographies (Spencer et al., 2007).

An HPLC-DAD–MS/MS-ESI investigation of the methanolic extract of *R. induratus* leaves revealed the presence of flavonoids (6-*C*-hexosyl-quercetin, 8-*C*-hexosyl-luteolin, 6-*C*-hexosyl-luteolin, 6-*C*-hexosyl-apigenin, 3-*O*-hexosyl-quercetin, rutin (**75**), 7-*O*-hexosyl-diosmetin, 3-*O*-rutinosyl-isorhamnetin, 7-*O*-(acetyl)-pento-

Table 6
Structures of carotenoids isolated from *Rumex* species.

Carotenoids	Substituents	Ref
	**117.** Lutein	Bélanger et al. (2010) and Molnár et al. (2005)
	**118.** Anhydrolutein I	Molnár et al. (2005)
	**119.** Anhydrolutein II	Molnár et al. (2005)
	**120.** β-carotene	Bélanger et al. (2010)

hexosyl-diosmetin and 6-*C*-hexosyl-genkwanin) (Ferreres et al., 2006; Guerra et al., 2008). 6-*C*-Hexosyl-luteolin proved to be present in the highest amount in the extract, accounting for ca. 40.8% of the total phenolics (Ferreres et al., 2006). An investigation of the changes in the constituents in plants collected in different locations (among them greenhouse samples) and vegetation periods revealed that the total amount of phenolic compounds increased throughout the plant cycle, but was lower in the greenhouse samples than those observed in the field samples. The major compound in the greenhouse samples was 6-*C*-hexosyl-apigenin in all developmental stages (Guerra et al., 2008).

4.4. Stilbenoids

Hydroxylated stilbenes are among the most interesting and therapeutically important groups of plant-derived polyphenols. The most studied of them are *trans*-resveratrol (**103**) and its glycoside, piceid (**109**) (Table 5). Resveratrol (**103**) has been reported to provide protection against cardiovascular diseases through its lipid-lowering activity and by inhibiting lipid peroxidation in humans (Fremont et al., 1999). It has been found to be a potent inhibitor of tyrosine kinase (p56lck) and has been widely claimed to possess antifungal properties (Jayatilake et al., 1993; Gonzalez et al., 2003).

Kerem et al. reported the isolation and identification of *trans*-resveratrol (**103**) and two monomethylated stilbene derivatives [5,4′-dihydroxy-3-methoxystilbene (**104**) and 3,5-dihydroxy-4′-methoxystilbene (**105**)] from the EtOAc extract of the roots of *R. bucephalophorus* (Kerem et al., 2003). They later identified *trans*-resveratrol (**103**), piceid (5,4′dihydroxystilbene-3-*O*-β-D-glucopyranoside, **109**) and rumexoid (5,4′-dihydroxystilbene 3-*O*-α-arabinopyranoside, **110**) in the roots (Kerem et al., 2006). The level of resveratrol (**103**) was determined to be 165 ± 10 μg/g dry wt, and the levels of **104** and **105** were 204 ± 10 and 239 ± 10 μg/g dry wt. From the roots of *R. hymenosepalus*, four stilbenoids [resveratrol (**103**), 4-[(*E*)-2-(3,5-dihydroxyphenyl)ethenyl]-1,2-benzenediol (**106**), 4-[(*E*)-2-(3,5-dihydroxyphenyl)ethenyl]phenyl-hexopyranoside (**107**) and 4-[(*E*)-2-(3,5-dihydroxyphenyl)ethenyl]-2-hydroxyphenyl-hexopyranoside (**108**)] have been isolated (Rivero-Cruz et al., 2005).

An investigation of the EtOAc fraction of *R. nepalensis* roots and the ethanolic extract of *R. hastatus* roots also resulted in the isolation of resveratrol (**103**) (Zhang et al., 2009; Liang et al., 2010).

4.5. Tannins

Buchalter et al. investigated the antitumour activity of the tannin-rich extract of the roots and tubers of *R. hymenosepalus*. The extract demonstrated antitumour activity. Its further separation yielded polymeric leucoanthocyanidin units consisting of leucopelargonidin (**76**), leucodelphinidin (**78**) and leucocyanidin (**77**) (Table 5). The pharmacological investigation of these monomeric flavanoid units showed that they do not exhibit antitumour activity (Buchalter and Cole, 1967).

From the roots of *R. nepalensis*, (3,5-dimethoxy-4-hydroxyphenol)-1-*O*-β-D-(6-*O*-galloyl) glucose (**111**) was isolated by Mei et al. (2009).

4.6. Triterpenoids

Phytochemical investigation of the EtOAc extract of *R. japonicus* stems led to the isolation of four 24-norursane type triterpenoids: 2α,3α,19α-trihydroxy-24-norurs-4(23),12-dien-28-oic acid (**113**), 4(*R*), 23-epoxy-2α,3α,19α-trihydroxy-24-norurs-12-en-28-oic acid (**114**), myrianthic acid (**116**) and tormentic acid (**115**) (Table 5) (Jang et al., 2005).

4.7. Carotenoids

From steam-cooked *R. rugosus*, anhydroluteins I (**118**) and II (**119**) were isolated by Molnár et al. (Table 6). These compounds could be formed by the acid-catalysed dehydration of lutein (**117**) (Molnár et al., 2005).

In a comparative study, the lutein (**117**) and β-carotene (**120**) contents of frequently consumed uncultivated and cultivated leafy vegetables were investigated in India. One of them was *R. vesicarius*. Both fresh and cooked materials were analysed and it was observed that the lutein (**117**) content was 53 μg/g fresh weight,

Table 7
Other compounds isolated from *Rumex* species

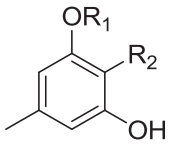
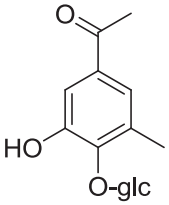
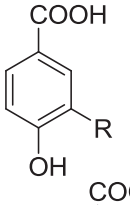
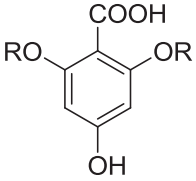
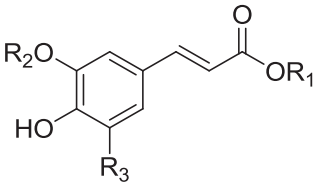
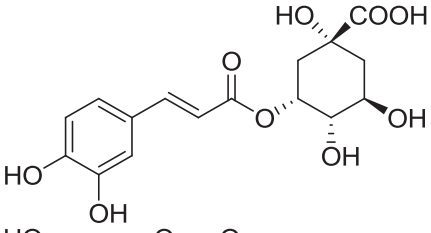
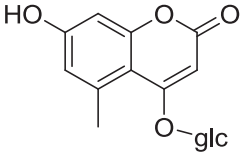
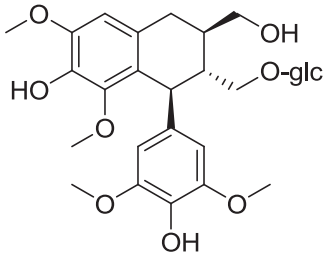
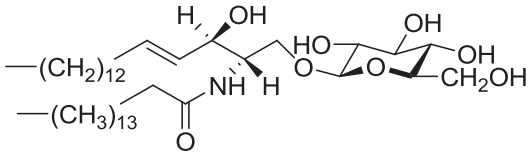
Other compounds	Substituents	Ref
	**121.** R_1=H, R_2=H orcinol **122.** R_1=H, R_2=Ac **123.** R_1=glc, R_2=H, sakakin **124.** R_1=glc, R_2=Ac	Demirezer et al. (2001) Berg and Labadie (1981) Mei et al. (2009) and Berg and Labadie (1981)
	**125.** Rumexin	Yoon et al. (2005)
	**126.** R=H, paraben-acid **127.** R=OCH_3, vanillic acid	Jiang et al. (2007) Kucekova et al. (2011)
	**128.** R=H **129.** R=CH_3	Jiang et al. (2007)
	**130.** R_1=H, R_2=H, R_3=H, caffeic acid **131.** R_1=CH_3, R_2=H, R_3=H **132.** R_1=glc, R_2=H, R_3=H **133.** R_1=H, R_2=CH_3, R_3=OCH_3, sinapic acid	Yoon et al. (2005) Lee et al. (2011) and Kucekova et al. (2011)
	**134.** Neochlorogenic acid	Tavares et al. (2010)
	**135.** Hastatuside A	Liang et al. (2010)
	**136.** Lyoniresinol glucoside	Mei et al. (2009)
	**137.** Glucosylceramide	Watanabe et al. (2011)

Table 8
Compounds of *Rumex* species.

Species	Plant part	Isolated compounds	Ref
R. abyssinicus	Root	**1–3**	Munavu et al. (1984)
R. acetosa	Leaf, root, flower	**1–3**, **9**, **35**, **36**, **57**, **79**, **80**, **83–86**, **89**, **97**, **101**, **103**, **127**, **133** polysaccharide RA-P	Aritomi et al. (1965), Stöggl et al. 2004; Gescher et al. 2011, Ito (1986), Lee et al. (2005) and Wegiera et al. (2007)
R. acetosella	Fruit, leaf	**1–4**, **35**, **36**	Wegiera et al. (2007)
R. aegyptiacus	Leaf	**1**, **73**	Saleh et al. (1993)
R. alpinus	Tissue cultures (root)	**1–3**, **10**, **32–34**, **42**, **43**, **48**, **124**	Berg and Labadie (1981)
R. aquaticus	Whole plant	**125**, **130–132**	Yoon et al. (2005)
R. bucephalophorus	Root	**103–105**, **109**, **110**	Kerem et al. (2003, 2006)
R. chalapensis	Leaf	**1**, **68**, **69**, **75**	Hasan et al. (1995)
R. confertus	Fruitleaf	**4**, **35**, **36**	Wegiera et al. (2007)
R. crispus	Leaf, whole plant, fruit, root	**1**, **4**, **35**, **36**, **42**, **71**, **73**	Saleh et al. (1993) and Wegiera et al. (2007)
R. cyprius	Leaf	**1**, **57**, **58**, **61**, **62**	Saleh et al. (1993)
R. dentatus	Root, tuber leaf	**1–3**, **43**, **49**, **65**, **73**	Liu et al. (1997), Zhang et al. (2012) and Saleh et al. (1993)
R. gmelinii	Aerial part	**132**	Lee et al. (2011)
R. hastatus	Root	**42**, **46**, **47**, **49**, **53**, **57**, **59**, **60**, **75**, **103**	Sahreen et al. (2014) and Zhang et al. (2009)
R. hydrolapathum	Fruit, leaf	**4**, **35**, **36**	Wegiera et al. (2007)
R. hymenosepalus	Root and tuber	**1–3**, **75–77**, **83**, **84**, **103**, 4-[(*E*)-2-(3,5-dihydroxyphenyl) ethenyl]-1,2-benzenediol, 4-[(*E*)-2-(3,5-dihydroxyphenyl) ethenyl]phenyl-hexopyranoside and 4-[(*E*)-2-(3,5-dihydroxyphenyl)ethenyl]-2-hydroxyphenyl hexopyranoside	Buchalter and Cole (1967) and Rivero-Cruz et al. (2005)
R. induratus	Leaf	75, 6-*C*-hexosyl-quercetin, 8-*C*-hexosyl-luteolin, 6-*C*-hexosyl-luteolin, 6-*C*-hexosyl-apigenin, 3-*O*-hexosyl-quercetin, 7-*O*-hexosyl-diosmetin, 3-*O*-rutinosyl-isorhamnetin, 7-*O*-(acetyl)-pento-hexosyl-diosmetin, 6-*C*-hexosyl-genkwanin, caffeoyl-hexoside, *p*-coumaroyl-hexoside isomers, feruloyl-hexoside, sinapoyl-hexoside, oxalic acid	Ferreres et al. (2006)
R. japonicus	Leaf, root, fruits, stem	**1**, **2**, **3**, **9**, **10**, **20–24**, **40–42**, **48**, **50**, **63**, **64**, **70**, **71**, **75**, **79**, **83**, **113–115**, **126**, **127**, **128**, **129**	Koyama et al. (2003), and Aritomi et al. (1965), Zee et al. (1998), Jiang et al. (2007), Nishina et al. (1993), Tavares et al. (2010), Jang et al. (2005) and Nishina et al. (1993)
R. luminiastrum (*R. limoniastrum*)	Fruit, leaf, stem, root	**1–3**, **9–11**, **61**, **68**, **72**,	El-Fattah et al. (1994)
R. maderensis	Leaf	**134**, ascorbic acid	Tavares et al. (2010)
R. nepalensis	Root	**1–3**, **5**, **7**, **9**, **10**, **13**, **14**, **37**, **38**, **39**, **42**, **43**, **46–49**, **51**, **52**, **83**, **85**, **103**, **111**, **123**, **136**	Mei et al. (2009), Gautam et al. (2010) and Liang et al. (2010)
R. obtusifolius	Leaf, fruit	**4**, **35**, **36**, **88**, **89**, **90**, **93**, **97**	Spencer et al. (2007) and Wegiera et al. (2007)
R. patientia	Root	**1–3**, **8–10**, **24**, **28–31**, **43–47**, **49**, **54**, **79**, **81**, **121**	Kuruüzüm et al. (2001), Demirezer et al. (2001a,b) and Yang et al. (2013)
R. pictus	Leaf	**1**, **2**, **56–59**, **61**, **62**	Saleh et al. (1993)
R. pulcher	Leaf	**1**, **73**	Saleh et al. (1993)
R. simpliciflorus	Leaf	**1**, **57**, **58**, **61**, **62**	Saleh et al. (1993)
R. vesicarius	Leaf	**1**, **55–59**, **61**, **62**, **75**, **79**, **83**, **85**, diosmetin-7-*O*-rhamno-hexoside and diosmetin-7-*O*-rhamno-acetylhexoside	El-Hawary et al. (2011) and Saleh et al. (1993)

and 127 μg/g cooked weight, while the β-carotene (**120**) content was 45 μg/g fresh weight, and 139 μg/g cooked weight (Bélanger et al., 2010).

4.8. Polysaccharides

From the root of *R. acetosa*, a polysaccharide (RA-P) was isolated. The plant material was extracted with boiling water. After filtration, the crude polysaccharide was obtained by precipitation with cold ethanol. Structure determination of the resulting white amorphous powder indicated a polymer with molecular weight in the region of 300 000, consisting of D-glucose in high and D-arabinose in low proportion (Ito, 1986).

4.9. Other compounds

From the roots of *R. patientia*, orcinol (**121**) was isolated (Table 7) (Demirezer et al., 2001). The occurrence of 2-acetylorcinol (**122**) and its monoglucoside (**123**) in the roots of *R. alpinus* was also established (Berg and Labadie, 1981). An acetophenone derivative, rumexin (**125**), was isolated from the methanolic extract of the aerial parts of *R. aquaticus*. Moreover, caffeic acid (**130**), 1-methylcaffeic acid (**131**) and 1-*O*-caffeoyl-β-D-glucopyranoside (**132**), were isolated from the plant (Yoon et al., 2005). From the fresh aerial parts of *R. gmelinii*, 1-*O*-caffeoyl glucoside (**132**) was identified (Lee et al., 2011). A phytochemical investigation of the aqueous acetone extract of *R. japonicus* roots resulted in the isolation of 2,6-dihydroxybenzoic acid (**128**), 4-hydroxybenzoic acid (**126**), 4-hydroxy-3-methoxybenzoic acid (vanillic acid, **127**) and 2,6-dimethoxy-4-hydroxybenzoic acid (**129**) (Jiang et al., 2007). Vanillic acid (**127**) and sinapic acid (**133**) were detected by HPLC in the flowers of *R. acetosa* (Kucekova et al., 2011). An HPLC-DAD–MS/MS-ESI analysis of the leaves of *R. induratus* revealed the presence of caffeoyl-hexoside, *p*-coumaroyl-hexoside isomers, feruloyl-hexoside and sinapoyl-hexoside (Ferreres et al., 2006).

The presence of ascorbic acid in a *R. maderensis* leaf extract was confirmed by an enzymatic method (9.00 mg/g). Neochlorogenic acid (**134**) was also found in this plant (Tavares et al., 2010). High level of vitamins C (115 mg/g) and A (11,700 IU/100 g) were reported from the leaves of *R. dentatus*, and also it was mentioned as a rich soruce of calcium and *β*-carotene (Khare, 2007).

Mei et al. isolated a lignan derivative, lyoniresinol 3α-*O*-β-D-glucopyranoside (**136**), and orcinol-glucoside (**123**) from the roots of *R. nepalensis* (Mei et al., 2009).

Qualitative and quantitative analysis of the hydro-ethanolic extract of *R. vesicarius* leaves demonstrated ascorbic acid and α-

tocopherol. Volatile constituents obtained from the fresh fruits of the plant were analysed by GC–MS. The 26 compounds identified (mono- and sesquiterpenes and long-chain hydrocarbons) accounted for 90.66% of the total sample. The lipid composition of the petroleum ether extract of the leaves was also investigated and 17 compounds were identified. The major hydrocarbons were docosane, nonacosane and dodecane (El-Hawary et al., 2011). The nutritional value (protein, lipid, mineral, organic acid, ascorbic acid and tocopherol content) of *R. vesicarius* was measured by Alfawaz. It was established that the leaves are a good source of minerals (calculated for 100 g dry weight: 2840 mg Ca, 2.5 mg Cu, 36.2 mg Fe, 1900 mg Mg, 2950 mg K, 1010 mg Na and 5.4 mg Zn), a moderate source of proteins (18.6 g/100 g) and ascorbic acid (253 mg/100 g), and high in oxalate (3060 mg/100 g) and low in lipids (3.4 g/100 g) and tocopherol (4.7 mg/100 g) (Alfawaz, 2006).

The dietary components of the New Nordic diet have been evaluated from the aspect of safety. One of the selected plants was *R. acetosa* (sorrel), a widely-used edible plant, whose leaves feature in soups and sauces or is added to salads. Sorrel is known to contain quite high levels of oxalic acid (300 mg/100 g), which can be lowered if the plant is cooked in hard water. The content of β-carotene (**120**) was quite low, up to 708 mg dw/kg (Mithril and Dragsted, 2012). The nutritional value of *R. acetosa* was investigated by Ladeji and Okoye. The amino acid composition, sodium, (5.0 mg/100 g) potassium (440.0 mg/100 g), magnesium (104.2 mg/100 g), calcium (1071.0 mg/100 g) and iron (15.0 mg/100 g) level were determined. All the essential amino acids were found to be present in the leaves of the plant (Ladeji and Okoye, 1993).

The oxalic acid content of the aqueous lyophilised extract of *R. induratus* was determined by an HPLC-UV method. This compound proved to be present in very high amount (51.7 ± 3.7 g/kg, dry basis) in the extract (Ferreres et al., 2006). Citric, malic, ascorbic and shikimic acids were also detected in the plant (Guerra et al., 2008). The oxalic acid and calcium content of *R. crispus* was measured by Guil et al. It was found that the plant contains 517–697 mg/100 g of oxalic acid and 15–29 mg/100 g of calcium. The oxalic acid/calcium ratio was the highest among the investigated plants; therefore the plant could have the highest adverse impact on dietary calcium bioavailability too (Guil et al., 1996). The oxalate and calcium level of sorrel (*R. acetosa* L. var. *hortensis*, syn. *R. rugosus*) leaves were also measured and 1391 mg/100 g of oxalate and 58 mg/100 g of calcium were found (Siener et al., 2006). In case of *R. papillaris* [*Rumex thyrsiflorus* subsp. *papillaris* (Boiss. & Reut.) Sagredo & Malag.] and *R. pulcher* the oxalate levels were 80.5–142.7 mg/100 g and 122.6–327.7, while the total vitamin C content 22.2–25.4 mg/100 g and 28.7–29.7 mg/100 g depending on the location. They also contain malic (9.9–11.4 mg/100 g and 3.2–5.1 mg/100 g) and citric (4.7 mg/100 g and 12.0–24.0 mg/100 g) acids (Sánchez-Mata et al., 2012).

The glucosylceramide (**137**) content of *R. obtusifolius* leaves was analysed by means of HPLC–MS. The observed high content of *n*-9 monoenoic 2-hydroxy fatty acids with 22 and 24 carbon-chain lengths is unique (Watanabe et al., 2011).

The fatty acid profiles of 20 Spanish wild vegetables [among them *R. pulcher* and *R. papillaris* (syn. *Rumex thyrsiflorus* subsp. *papillaris* (Boiss. & Reut.) Sagredo & Malag.)] were evaluated with GC-FID detection. It was observed that the samples in which the leaves predominated in their edible parts in general contained the highest amounts of polyunsaturated fatty acid, with *R. pulcher* outstanding as concerns its high polyunsaturated/saturated fatty acid ratio (Morales et al., 2012) (Table. 8).

5. Pharmacological activities of *Rumex* species

In the *Rumex* genus, 28 species, including *R. abyssinicus*, *R. acetosa*, *R. acetosella*, *R. alpinus*, *R. aquaticus*, *R. bequartii*, *R. chinensis* (syn. *Rumex trisetifer* Stokes), *R. confertus*, *R. crispus*, *R. dentatus*, *R. ecklonianus*, *R. hastatus*, *R. hymenosepalus*, *R. japonicus*, *R. madarensis*, *R. maritimus*, *R. nepalensis*, *R. nervosus*, *R. obtusifolius*, *R. patientia*, *R. pseudonatronatus*, *R. scutatus*, *R. stenophyllus*, *R. steudelii*, *R. usambarensis*, *R. verticillatus*, *R. vesicarius* and *R. woodii* are used in traditional medicine. Several extracts and isolated compounds have been evaluated for their antioxidant, anti-inflammatory, antitumour and antibacterial activities. The antiviral, antifungal, antiulcerogen, hepatoprotective, purgative, antidiabetic, antifertility, anthelminthic and antiplasmodial effects have also been studied. An overview of the modern pharmacological investigations performed on the mentioned species is described in detailed below.

5.1. Antioxidant activity

The antioxidant activities of 30 medicinal plants that are widely used in Mexico were tested by VanderJagt et al. The plant materials were dried, ground and extracted with H_2O by heating at 85 °C for 10 min. Analysis with a two-stage Trolox-based assay revealed that the extract of the stems of *R. hymenosepalus* had substantial activity (672 μmol Trolox equivalent/g dry wt) (VanderJagt et al., 2002). When the antioxidant effects of medicinal plants traditionally used in Cameroon were determined by means of the DPPH bleaching method, the Trolox equivalent antioxidant capacity (TEAC) and haemoglobin ascorbate peroxidase activity inhibition assays (HAPX), *R. abyssinicus* demonstrated the best activity in all these assays. In the case of DPPH, the area under the kinetic curve was ≈ 10. Gallic acid was used as standard in place of trolox in TEAC method. Gallic acid equivalent antioxidant capacity (GEAC) was ≈ 50 μg/mL in the case of *R. abyssinicus*. Finally, in HAPX method the inhibition of the ascorbic acid consumption (IAC in %) of *R. abyssinicus* was 100% (Tamokou et al., 2013). In this assay the antioxidant activity of emodin was also tested and the results detected were ≈ 8 in DPPH, ≈ 80 in TEAC and $T \approx 84\%$ in HAPX method. The antioxidant capacities (ORAC and EPR) of five Macronesian traditional medicinal plants (among them *R. maderensis*) were also evaluated, the H_2O–EtOH extracts of the leaves proving to contain the investigated compounds in highest quantities on HPLC-DAD-ED. The total phenol (9.9 mg GAE/g) and total flavonoid (5.23 mg CE/g) contents were measured. The peaks detected by the electrochemical detector corresponded to reactive species with a strong capacity to donate electrons. It was concluded that the antioxidant activity of *R. maderensis* is due to its ascorbic acid content (Tavares et al., 2010). The investigation of xanthine oxidase (XO) inhibitory activity of plants belonging to family Polygonaceae was resulted that especially the $CHCl_3$ extracts of the whole plant of *R. acetosella* ($IC_{50} = 19.3$ μg/mL), the $CHCl_3$ extract prepared from the flowers and fruits of *R. alpinus* ($IC_{50} = 23.4$ μg/mL), the herb extract of *R. conglomeratus* ($IC_{50} = 23.4$ μg/mL), the root extract of *R. hydrolapathum* ($IC_{50} = 25.4$ μg/mL), and the flowers and fruits extracts of *R. patientia* and *R. stenophyllus* ($IC_{50} = 27.6$ and 27.3 μg/mL) exhibited high activity against XO (Orbán-Gyapai et al., 2015).

An evaluation of the antioxidant potential of an EtOH extract of *R. patientia* revealed its potent activity. The extract significantly and dose-dependently scavenged DPPH radicals, O_2^- ($IC_{50} = 29$ μg/mL), OH radicals ($IC_{50} = 63$ μg/mL), and NO ($IC_{50} = 33$ μg/mL). Its total polyphenol content expressed in gallic acid equivalents was 315 mg/g (Lone et al., 2007). An antioxidant investigation of anthraquinones, flavans and orcinol (**121**) isolated from *R. patientia* indicated that only catechin (**79**) and 6-chlorocatechin (**81**) exhibited potent DPPH radical scavenging activity. After developing and drying, TLC plates were sprayed with a 0.2% DPPH solution in MeOH. Active compounds appeared as yellow

spots against a purple background. Quercetin was used as reference compound (Demirezer et al. 2001). The antioxidant properties of stilbenes isolated from *R. bucephalophorus* were assessed by using scavenging of the radical cation of ABTS relative to the water-soluble vitamin E analogue Trolox C. The TEAC values of resveratrol (**103**) and 5,4′-dihydroxy-3-methoxystilbene (**104**) were higher than that of 3,5-dihydroxy-4′-methoxystilbene (**105**) (represented by graphs). This was in agreement with the previous result that the 4′-hydroxy group of resveratrol (**103**) is usually the most reactive in scavenging free radicals (Kerem et al., 2003). The TEAC value of *trans*-resveratrol (**103**) (2.7) was higher than those of both piceid (**109**) (2.2) and rumexoid (**110**) (1.5). Each of the compounds was more potent than Trolox (Kerem et al., 2006).

The total phenolic contents, antioxidant activities and reducing powers of ethanol, hexane, $CHCl_3$, EtOAc and aqueous extracts of the aerial parts of *R. japonicus* were investigated by DPPH assay, β-carotene bleaching and superoxide radical methods. The EtOAc fraction possessed strong antioxidant activity (DPPH radical scavenging activity = 86.0 ± 0.20 μg/mL, EC_{50} = 0.04 ± 10.0001 μg/mL; superoxide radical scavenging activity = 16.4 ± 1.44 ppm), which correlated with the high levels of phenolic compounds, particularly pyrogallol and pyrocatechin (Elzaawely et al., 2005). A similar investigation was performed with *R. papillaris* [syn. *Rumex thyrsiflorus* subsp. *papillaris* (Boiss. & Reut.) Sagredo & Malag.] and *R. pulcher*, and established that the DPPH scavenging activity of the plants was EC_{50} = 2.45 mg/mL and 3.31 mg/mL, the reducing power developed as 0.6 mg/mL and 0.80 mg/mL and the β-carotene bleaching inhibition was 0.3 mg/mL and 0.34 mg/mL (Morales et al., 2014). In case of *R. vesicarius* the MeOH extract and its acetone, EtOAc and BuOH fractions were tested on different assays (lipid peroxidation and DNA–sugar damage inhibitory activities, DPPH radical and hydrogen peroxide scavenging effects). In each test system the MeOH extract of the whole plant showed the highest activity (inhibitions: 33.8% in case of lipid peroxidation, 66.3% in case of DNA–sugar damage, 96.6% in case of DPPH radical scavenging) (Khan et al., 2014). The antioxidant activity of different extracts (*n*-hexane, CH_2Cl_2 and MeOH) of *R. obtusifolius* was also investigated by DPPH assay. Methanol extract of the leaves showed the highest (RC_{50} = 0.08 mg/mL) activity, while its subfraction yielded by 50% MeOH on SPE resulted even higher activity (0.015 mg/mL) due to its phenolic content (Harshaw et al., 2010).

The antioxidant effects (DPPH and ABTS) of the chloroform and ethyl acetate extracts of *R. nepalensis* root were evaluated. Both fractions contained phenolic compounds, but their level was higher in the ethyl acetate extract (27.71%) than in the chloroform extract (8.20%). Trolox (IC_{50} = 15.7 μM in the case of DPPH, and 16.2 μM in the case of ABTS) and ascorbic acid (IC_{50} = 22.4 μM in the case of DPPH, and 25.5 μM in the case of ABTS) were used as positive controls. These extracts contained anthraquinones (**1**–**3**, **7**, **9** and **10**) and naphthalenes (**42** and **43**) too. None of the anthraquinones showed activity against the two radicals. Compounds **42** and **43** were found to scavenge both radicals strongly [IC_{50}s = 11.7 μM (**42**) and 40.1 μM (**43**) in the DPPH assay, and 13.5 μM (**42**) and 47.4 μM (**43**) in the ABTS assay]. The higher radical scavenging activity could be due to the phenolic content (in the case of the ethyl acetate extract) and the presence of nepodin (**42**) (in the case of the chloroform extract) (Gautam et al., 2010).

The HO-1 (haeme oxygenase) inducing ability and signalling mechanism of QGC (**73**) were studied in cultured feline oesophageal epithelial cells. HO-1 is one of the antioxidant enzymes which help protect against cellular damage. It was observed that QGC (**73**) possessed the ability to induce HO-1 protein and the ERK, PI3/Akt and PKC pathways (Kim et al., 2010).

The antioxidant activities of various extracts (methanol, *n*-hexane, ethyl acetate, chloroform, butanol and water) of *R. hastatus* were tested, and the total phenolic and flavonoid contents of the fractions were also determined. The butanol and methanol extracts exhibited the highest activities in all the assays (DPPH, ABTS, $^{\cdot}OH$, superoxide free radical scavenging, iron chelating, reducing and β-carotene bleaching power) with the exception of the H_2O_2 radical scavenging assay, where the chloroform extract proved to be the most active (Sahreen et al., 2014). The antioxidant activity of water and acetone extracts of *R. hastatus* was investigated with different methods (DPPH, OH^- radical scavenging, Fe^{3+} reducing power, and total antioxidant capacity). The result revealed that both extracts showed moderated activity (Abbasi et al., 2015).

In a pharmacological investigation of the ether, ethanol, and hot water extracts of the leaves and seeds of *R. crispus*, the water extracts of both plant parts displayed the highest antioxidant activities. The highest amount of total phenolic compounds was found in the ethanol extract of the seeds (220 μg/500 μg extract). As regards of the reducing power and DPPH scavenging activity, the ethanol extract of the seeds was the most effective (Yildirim et al., 2001). The abilities to quench singlet oxygen ($^1O_2$) and the protective effects of various extracts (hexane, chloroform, ethyl acetate and butanol) of *R. crispus* seeds against photodynamic damage were investigated in biological systems. Higher levels of total phenol content were observed for the ethyl acetate (EE) and butanol (BE) extracts. The values of QC_{50} (50% quenching concentration of $^1O_2$) detected for the EE (QC_{50} = 82 μg/mL) and the BE (QC_{50} = 116 μg/mL) were comparable to that of the positive control ascorbic acid (QC_{50} = 86 μg/mL) (Suh et al., 2011). The levels of *in vitro* antioxidant activity of the methanol extract of *R. crispus* fruits were tested by assay for ferric-reducing antioxidant power, DPPH-free radical scavenging activity and the ability to influence the lipid peroxidation (LP) in liposomes, and the *in vivo* effects on several hepatic antioxidant systems (LPx, GSH-Px, Px, CAT and XOD) in rats were studied. It was observed that the extract possessed direct antioxidant activity. On the basis of the *in vivo* experiments, it was concluded that the dosage regimen did not influence the levels of LP. The GSH-Px activity was increased moderately, while the GSH content was not influenced significantly by the extract. In the case of the XO inhibitory activity, a moderate increase was measured, but without a dose dependence (Maksimovic et al., 2011). The methanol extract of *R. crispus* roots exhibited strong DPPH radical scavenging (IC_{50} = 42.86 μg/mL). It exhibited a significant ability to protect against H_2O_2/Fe^{3+}/ascorbic acid-induced protein damage (Shiwani et al., 2012).

The ethanol extract of *R. dentatus* displayed a higher potential (96%) than that of the methanol extract (73%) to scavenge the free radical DPPH. The positive control ascorbic acid exhibited a 95% scavenging activity. The *in vitro* inhibition of LP was 86% in the case of the ethanol and 78% in the case of the methanol extract (Humeera et al., 2013). The antioxidant activity of water and acetone extracts of *R. dentatus* was investigated with different methods (DPPH, OH^- radical scavenging, Fe^{3+} reducing power, and total antioxidant capacity). The result revealed that both extracts showed moderated activity (Abbasi et al., 2015).

A lyophilised extract of *R. induratus* leaves exhibited a potent concentration-dependant antioxidant effect (IC_{50} = 149.9 μg/mL) through the reduction of DPPH. Moreover, the extract exerted an inhibitory effect on XO, with an IC_{25} of 708.8 μg/mL (Ferreres et al., 2006). In another investigation, a lyophilised aqueous extract of *R. induratus* leaves proved to have a concentration-dependant antioxidant potential (IC_{50} = 106.5 μg/mL). It also exhibited substantial scavenging activity against NO (IC_{50} = 92.7 μg/mL) (Guerra et al., 2008).

5.2. Antitumour activity

The *in vitro* cytotoxic properties of ethanol extracts of the fruits,

leaves and roots of *R. acetosa*, *R. acetosella*, *R. confertus*, *R. crispus*, *R. hydrolapathum* and *R. obtusifolius* were investigated against the two human leukaemic cell lines 1301 (human T lymphoblastic cells) and EOL-1 (human eosinophilic leukaemia) and the normal H9 (a clonal derivative of the T cell lines). The IC_{50} values revealed the highest activity for *R. confertus* [0.22 mg/mL (1301) and 0.23 mg/mL (EOL-1)] in the case of the roots, for *R. obtusifolius* [0.47 mg/mL (1301) and 0.44 mg/mL (EOL-1)] in the case of the leaves, and for *R. hydrolapathum* [0.42 mg/mL (1301) and 0.17 mg/mL (EOL-1)] in the case of the fruits (Wegiera et al., 2012). The methanol extract of *R. crispus* induced apoptosis on HT-29 cells in a dose-dependant manner, due to down-regulation of the expression of certain transcriptional factors (p53, caspase 3, -c-Myc and Bax). Moreover, it demonstrated a high potential in DNA protection (HEK 293 cellular DNA) (Shiwani et al., 2012).

The antiproliferative activities of aqueous and organic extracts of 27 species (*Rumex*, *Polygonum*, *Fallopia* and *Oxyria*) belonging in the Polygonaceae family that occur in the Carpathian Basin were tested against human tumour cell lines (HeLa, A431 and MCF7) by using the MTT assay. The *n*-hexane or chloroform extracts of *R. acetosa* (77.7% and 97.0% at 10 and 30 μg/mL, on HeLa cells), *R. aquaticus* (60.9% at 30 μg/mL on HeLa cells and 69.3% at 30 μg/mL on MCF7 cells), *R. scutatus* (51.2% at 30 μg/mL on HeLa cells and 56.2% at 30 μg/mL on MCF7 cells) and *R. thyrsiflorus* (96.2% at 30 μg/mL on A431 cells and 88.55% at 30 μg/mL on MCF7 cells) exerted substantial cell growth inhibitory activity against one or more cell lines (Lajter et al., 2013).

The anticancer effects of traditionally used Cameroonian medicinal plants were investigated on A431 (epidermal carcinoma), WM35 (melanoma), A2780 (ovary carcinoma) and cisplatin-resistant A2780cis cells. *Rumex abyssinicus* and *R. bequaertii* (syn. *R. nepalensis* Spreng.) showed only moderate [*R. abyssinicus*: 12.55 μg/mL (A2780), 8.014 μg/mL (A2780cis), 6.715 μg/mL (A431) and 4.615 μg/mL (WM35); *R. bequaertii*: 14.44 μg/mL (A2780), 29.31 (A2780cis), 3.615 μg/mL (A431) and 22.29 μg/mL (WM35)] activities (Tamokou et al., 2013). The alcoholic extract of *R. hymenosepalus* roots rich in tannins [leucopelargonidin (**76**), leucocyanidin (**77**) and leucodelphinidin (**78**)] exhibited antitumour activity in Walker 256 and sarcoma 180 test models in mice (data are not presented) (Cole and Buchalter, 1965; Buchalter and Cole, 1967).

Ito et al. investigated the antitumour action of *R. acetosa* polysaccharide (RA-P) on female ICR mice implanted with Sarcoma 180 solid tumour (inhibitory ratio 88.1% at 100 mg/kg). The antitumour activity of RA-P is due to the activation of the C3 (complement system), stimulation of the reticuloendothelial system and inhibition of the hepatic drug-metabolising enzymes (Ito, 1986). The methanol extract of *R. acetosa* flowers gave rise to a dose-dependant antiproliferative effect [average absorbances 0.5873 (25 μg/mL), 0.4472 (50 μg/mL), 0.2367 (75 μg/mL), and 0.1903 (100 μg/mL)] on HaCaT (human non-tumourigenic keratinocyte) cells using the MTT assay. As a control experiment, pure medium was used (absorbance 0.8187) (Kucekova et al., 2011). The CH_2Cl_2 extract of the aerial parts of *R. acetosa* exhibited antimutagenic and cytotoxic activities. The bioactivity-guided fractionation of the extract yielded four anthraquinones [emodin (**1**), chrysophanol (**2**), physcion (**3**) and emodin-8-*O*-*β*-D-glucopyranoside (**9**)]. The cytotoxic activities of the compounds and two synthetic derivatives were examined against A549 (non-small cell lung), SK-OV-3 (ovary), SK-MEL-2 (melanoma), XF498 (central nervous system) and HCY15 (colon) human tumour cell lines. Among the tested compounds, emodin (**1**) displayed a potent cytotoxic effect (IC_{50} = 3.32 μg/mL for A549; 2.94 μg/mL for SK-OV-3; 3.64 μg/mL for SK-MEL-2; 2.98 μg/mL for XF498; and 3.10 μg/mL for HCT15). The antimutagenic evaluation was performed with the Ames test and the SOS chromotest, using *Salmonella typhimurium* test strains. Emodin (**1**) had the strongest effect at a dose of 0.1 mg/plate, with 71.5% and 53.3% inhibition rates of revertant CFU (colony forming unit) per plate against NPD and NaN_3, respectively. As concerns antigenotoxic effects, emodin (**1**) revealed the highest activity against both mutagens used (19.6% in the case of methylnitronitrosoguanidine and 43.5% in the case of 4-nitroquinoline 1-oxide) (Lee et al., 2005).

Demirezer et al. carried out cytotoxicity tests on MCF (human breast carcinoma), HM02 (human melanoma) and HEPG2 (human epidermoid carcinoma) cell lines. In the course of their study, anthraquinones (**1**–**3**, **8**–**10**), flavans (**79**, **81**) and orcinol (**121**) isolated from *R. patientia* were tested. None of the investigated compounds inhibited the growth of the cell lines (Demirezer et al., 2001). In an earlier study, *R. patientia* was found to possess potent cytotoxic activity against brine shrimp (LC_{50} = 1.30 μg/mL) (Demirezer and Kuruüzüm, 1997). Whereas purified anthraquinone aglycones (**1**–**4**) from *R. scutatus* proved to have strong cytotoxic activity [LC_{50} = 0.05 μg/mL (**1**); 0.00 μg/mL (**2**); 0.15 μg/mL (**3**) and 0.01 μg/mL (**4**)], anthraquinone glycosides and catechin (**79**) were inactive (Demirezer et al., 2001).

When the antiproliferative activities of chrysophanol (**2**), nepodin-8-glucoside (**43**) and torachrysone-8-glucoside (**49**) were investigated on MCF-7, 7901 (gastric cancer), A375 (melanoma) and SKOV-3 (oophoroma) tumour cell lines, compound **2** showed higher activity (IC_{50} = 20.4 μM on MCF7, 513 μM on 7901, 83.1 μM on A375 and 5.62 μM on SKOV-3 cells), than the naphthalene derivatives (Zhang et al., 2012).

The cytotoxic activity of *R. obtusifolius* extract was investigated with brine shrimps lethality assay. The LD_{50} values of CH_2Cl_2 (1.00 mg/mL) and MeOH (> 1.00 mg/mL) extracts showed that the plant has low cytotoxic activity in compare with the positive control podophyllotoxin ($LD_{50} = 2.80 \times 10^{-3}$ mg/mL) (Harshaw et al., 2010).

Essiac tea, containing *R. acetosella*, was investigated for its ability to scavenge reactive oxygen species and for its effects on DNA damage. This preparation is used in homoeopathic cancer treatment and also to treat a variety of diverse allergies, hypertension and osteoporosis. *In vitro*, Essiac tea has been shown to inhibit cell proliferation and to induce differentiation in human prostate cancer cell lines (Ottenweller et al., 2004; Tai et al., 2004). It was found that Essiac tea effectively scavenges several types of radicals and possesses DNA-protective effects. In non-cellular systems, the tea effectively scavenged $^{\bullet}OH$ and $O_2^{\bullet-}$ radicals and prevented $^{\bullet}OH$-induced DNA damage. Radicals produced by the RAW 264.7 cellular reaction with Cr(VI) were also scavenged by the Essiac preparation. Moreover, the lipid peroxidation caused in cell membranes by exposure to $^{\bullet}OH$ radicals was inhibited by the tea (Leonard et al., 2006). Emodin (**1**) is known as a tyrosine kinase inhibitor (Jayasuriya et al., 1992). Its tumour inhibitory effect is based on the mammalian cell cycle modulation in specific oncogene-overexpressing cells (Zhang et al., 1995). Emodin (**1**) exerts therapeutic effects on pancreatic cancer through various antitumour mechanisms. The therapeutic efficacy of emodin in combination with chemotherapy was found to be higher than that of the corresponding single chemotherapeutic regime, and the combination therapy also exhibited fewer side-effects (Wei et al., 2013). A cytotoxic assay of emodin (**1**), chrysophanol (**2**), physcion (**3**), citreoresin (**5**), emodin-8-*O*-*β*-D-glucopyranoside (**9**), chrysophanol-8-*O*-*β*-D-glucopyranoside (**10**), chrysophanol-8-*O*-*β*-D-(6′O-acetyl)glucopyranoside (**13**), emodin-8-*O*-β-D-(6′-O-acetyl)glucopyranoside (**14**), aloesin (**37**), nepalensides A (**38**) and B (**39**), nepodin-8-*O*-β-D-glucopyranoside (**43**), orientaloside (**47**), torachrysone (**48**), torachrysone-8-*O*-β-D-glucopyranoside (**49**), rumexneposides A (**51**) and B (**52**), hastatuside B (**53**) (−)-epicatechin (**83**), (−)-epicatechin-3-*O*-gallate (**85**), resveratrol (**103**), orcinol glucoside (**123**), hastatuside A (**135**), lyoniresinol 3α-*O*-β-D-

glucopyranoside (**136**), and (3,5-dimethoxy-4-hydroxyphenol)-1-*O*-β-D-(6-O-galloyl)-glucose, isolated from *R. nepalensis* and *R. hastatus* was performed against A549, H522 (lung cancer), MCF-7, MCF-10A and SKBR3 cancer cell lines by using the MTT method, with cisplatin as positive control. Compounds **13**, **47**, **51**, and **103** exhibited marked activities, [**13**: 9.6 μM (MCF-10A); **47**: IC_{50} =29.0 μM (A549), 38.7 μM (H522), 7.6 μM (MCF-10A) and 19.9 μM (SKBR3); **51**: IC_{50}=31.0 μM (A549), 15.7 μM (H522), 21.8 μM (MCF-7), 22.8 μM (MCF-10A) and 20.7 μM (SKBR3); and **103**: IC_{50} 27.8 μM (A549), 29.4 μM (MCF-7) and 12.3 μM (MCF-10A)] (Liang et al., 2010).

5.3. Hepatoprotective activity

The antioxidant and hepatoprotective potential of ethanol extracts of *R. vesicarius* roots, leaves and fruits were investigated against carbon tetrachloride (0.5 mL/kg, orally, 3 times a week)-induced hepatotoxicity in comparison with silymarin (50 mg/kg, orally) in rats. Coadministration of the extracts or silymarin with carbon tetrachloride for 4 weeks revealed a marked hepatoprotective activity, with increased GSH content, and decreased liver index, MDA and hydroxyproline levels. The most pronounced activities were exhibited by the leaf extract (El-Hawary et al., 2011).

The ethanolic extract of *R. patientia* roots was significantly and dose dependently protective against the oxidative damage of lipids and DNA after treatment with ferric nitrilotriacetate (Fe-NTA). Prophylactic treatment with the *R. patientia* extract provided significant protection against LPO and H_2O_2 generation and also preserved quinone reductase activity after exposure to Fe-NTA. Moreover, it prevented the Fe-NTA-induced elevation in hepatic ornithine decarboxylase activity. The extract restored AST (aspartate amino transferase), ALT (alanine aminotransferase), ALP (alkaline phosphatase) and bilirubin levels to close to the control values, and preserved the hepatic architecture close to normal (Lone et al., 2007). The *in vivo* effects of an aqueous extract of *R. patientia* roots were investigated on drug-metabolizing enzymes in the rat liver. No significant alterations in NADPH cytochrome *c* reductase and NADH cytochrome b_5 reductase activities were observed compared to the control, but significant increases in the activities of cytochrome P4502E1 and GST were detected. The serum AST activity did not display a significant change. However, the serum ALT activity underwent a significant decrease compared to the control; the AST and ALT values were within the average normal laboratory range (Silig et al., 2004).

Various fractions (*n*-hexane, chloroform, ethyl acetate, *n*-butanol and residual aqueous) of *R. hastatus* roots led to reductions of elevated concentrations of AST, ALT, ALP and γGT generated by carbon tetrachloride. Moreover, the treatment maintained the structural consistency of the hepatocellular structure (Sahreen et al., 2013).

5.4. Anti-inflammatory and anti-ulcerogenic activities

Jäger et al. investigated plants used for headache or inflammatory ailments in traditional Zulu medicine by screening them for prostaglandin-synthesis inhibitory activity. Prostaglandins are involved in the complex processes of inflammation and are responsible for the sensation of pain. One of the highest inhibitions of cyclooxygenase (95%) was obtained with an ethanolic extract of *R. sagittatus* (Jäger et al., 1996).

Rumex patientia has been used extensively in traditional medicine in Turkey as a laxative, diuretic, antipyretic, wound cure and anti-inflammatory agent. The anti-inflammatory activity of an aqueous extract of the roots of the plant was investigated in carrageenan, histamine, dextran, serotonin and formaldehyde-induced oedema and cotton-pellet granuloma assays and in Kabak tests in rats. The extract was found to possess anti-inflammatory activity which could be attributed to the anthraquinones and tannins contained in the plant. Acute toxicity studies that were also performed revealed that the extract was non-toxic up to a dose of 3 mg/kg orally (Süleyman et al., 1999).

The chloroform and ethyl acetate extracts of *R. nepalensis* roots were investigated in an acute mouse inflammation model, based on the topical application of 12-*O*-tetradecanoylphorbol-13-acetate in a single-dose regimen. The extracts displayed significant activity when applied at 0.5 and 1.0 mg/ear. Indomethacin was used as positive control. From the EtOAc fraction, six anthraquinones (**1**, **2**, **3**, **7**, **9** and **16**) and two naphthalene derivatives (**42** and **43**) were isolated. Compounds **1**, **7** and **16** exhibited a 65.3%, 57.7% and 43.2% reduction in ear oedema, respectively. The COX-1 and COX-2 inhibitory activities of these compounds were also tested: they showed moderate to strong inhibitory effects on COX-1 [IC_{50}s=38.6 μM (**1**), 40.0 μM (**7**) and 27.4 μM (**16**), as compared with 0.18 μM in the case of the positive control indomethacin] and COX-2 [IC_{50}s=23.1 μM (**1**), 25.8 μM (**7**) and 32.3 μM (**16**), as compared with 0.15 μM in the case of the positive control celecoxib] activity. It was concluded that the anti-inflammatory effects of the extracts could be related to the presence of these anthraquinones and naphthalene derivatives (Gautam et al., 2010).

The anti-inflammatory activities of water and 70% ethanolic extracts of *R. acetosa* were tested in mice. Both extracts decreased the NO production in a murine macrophage cell line (RAW 267.4), in a dose-dependant manner. The higher activity of the ethanol extract was attributed to its higher emodin (**1**) content (Bae et al., 2012). An investigation of *R. abyssinicus* showed that the methanol extract of the plant inhibited the synthesis of PGE_2. *Rumex nervosus* and *R. abyssinicus* produced macrophage cell proliferation, too (Getie et al., 2003).

The pharmacological activities of quercetin-3-*O*-β-D-glucuronopyranoside (QGC) (**73**) isolated from *R. aquaticus* and the extract containing it (ECQ) have been investigated in numerous experimental models. The protective effect of QGC (**73**) on indomethacin-induced gastric damage in rats was evaluated. It was observed that QGC (**73**) enhanced the amount of mucus secretion in a dose-dependant manner, and inhibited neutrophil infiltration into the gastric mucosa and pro-inflammatory cytokine (TNF-α and IL-1β) production (Yan et al., 2011). The injury area, gastric lesion sizes, acid output and gastric pH were also decreased by QGC (**73**) (Min et al., 2009). In another experiment, superoxide dismutase (SOD), catalase (CAT) and myeloperoxidase (MPO) activities and malonaldehyde (MDA) levels were measured by ELISA after ECQ treatment. The results showed that it inhibited the reductions of SOD and CAT activities, and SOD expression. Further, ECQ suppressed the elevation of the MPO activity and the MDA levels (Jung et al., 2012). The cytoprotective effect of QGC (**73**) was also investigated against ethanol-induced cell damage. QGC (**73**) reduced the cytotoxicity induced by 10% ethanol, and inhibited the production of intracellular ROS and ERK ½ activation (Cho et al., 2011). Later, the action of the ethanol extract of the plant, containing QGC (**73**) (determined by HPLC as 10.78%), was evaluated on experimental reflux oesophagitis in rats. Omeprazole was used as positive control. The herbal extract (30 mg/kg) reduced the oesophagus lesions, acid output, MPO activity and MDA levels in a dose-dependant manner. The pH and GSH levels were also decreased, similarly as with omeprazole (30 mg/kg) (Jang et al., 2012). The same research group investigated the antioxidative and anti-inflammatory effects of QGC (**73**) on cultured feline oesophageal epithelial cells (EECs). QGC (**73**) administration led to potent ROS scavenger activity in the EECs, decreased the SOD and CAT activities, and inhibited acid-induced NF-κB nuclear translocation, COX-2 expression and PGE_2 secretion (Lee et al., 2013a). An evaluation of an *R. aquaticus* extract [containing 10.78% QGC (**73**)]

on iodoacetamide-induced chronic gastritis indicated that it significantly inhibited the elevation of the MDA level and MPO activity, and increased the level of glutathione, the SOD activity and the expression of SOD-2 (Lee et al. 2013c).

The antiulcerogenic effects of plant extracts used in Turkey for the treatment of peptic ulcer symptoms (e.g. stomach ache and heartburn) were investigated. When the extract prepared from the fruits of *R. patientia* was applied orally to rats, it afforded significant gastric protection (ulcer index = 27.0 ± 20.5; inhibition = 82.6%) at 440 mg/kg against an ethanol-induced gastric ulcer model. Healing effects were also confirmed in histopathological examinations (Gürbüz et al., 2005). The hot water extract of *R. acetosa* has been used in traditional medicine to treat gastritis and gastric ulcers. To confirm this observation, water and 70% ethanol extracts prepared from the whole plant were investigated in an HCl/ethanol-induced gastric ulcer model in mice. The protective effect was higher (90.9%) when the ethanol extract (100 mg/kg) was administered as pretreatment; in the case of the water extract, the inhibition was 41.2%. Sucralfate (100 mg/kg) used as a reference drug reduced the gastric lesions by 84.4%. Histological evaluation on the glandular stomach of the animals revealed that the extracts reversed the negative effects, e.g. inflammation, oedema, moderate haemorrhaging and loss of epithelial cells (Bae et al., 2012).

The methanolic extract of *R. acetosella* and its fractions (*n*-hexane, chloroform, ethyl acetate *n*-butanol and residual aqueous) exhibited strong urease inhibitory activity. Urease activity has been shown to be associated with numerous clinical conditions, including the development of gastrointestinal ulcers. The IC_{50} values of the residual aqueous (0.85 μg/mL) and *n*-butanol (0.91 μg/mL) fractions were lower than that of the positive control thiourea (0.97 μg/mL) (Ahmed et al., 2013).

5.5. Antimicrobial activity

5.5.1. Antibacterial activity

In an evaluation of the antibacterial activities of some edible plant ($n = 26$) extracts (buffered methanol and acetone) against common foodborne pathogens (*Bacillus cereus*, *Staphylococcus aureus*, *Listeria monocytogenes*, *Escherichia coli* and *Salmonella infantis*), the minimum inhibitory concentrations (MICs) of extracts were determined by the agar dilution method (800 μg/disc). One of the most effective extracts was that prepared from *R. nervosus*. The buffered methanolic extract of the plant inhibited Gram-positive bacteria (Alzoreky and Nakahara, 2003). The anti-mycobacterial activities of 15 plant extracts were tested against two strains (MTCC 6 and MTCC 994) of *Mycobacterium smegmatis* by the disk diffusion assay, with rifampicin as positive control [diameter of inhibition zones: 23.3 mm (MTCC 6) and 20.6 mm (MTCC 994)]. *Rumex hastatus* gave one of the highly active extracts [inhibition zone diameters of 13.6 mm (MTCC 6) and 11.3 mm (MTCC 994)]. Further evaluation of the extract against virulent and avirulent strains of *M. tuberculosis* using the BACTEC assay showed that it was inactive at 1.0 mg/mL (Gupta et al., 2010).

Rumex nervosus and *R. abyssinicus* exhibited antibacterial activity against *S. pyogenes* and *R. nervosus* against *S. aureus*. This and the anti-inflammatory effect of *R. abyssinicus* could justify its traditional use for the treatment of several skin diseases (Getie et al., 2003). In another assay, *R. abyssinicus* showed activity against *S. typhymurium*, *L. monocytogenes*, *E. coli* and *S. aureus* (Tamokou et al., 2013). The antimicrobial investigation of ether, ethanol, and hot water extracts of the leaves and seeds of *R. crispus* indicated that the ether extracts of both plant parts and the ethanol extract of the leaves possessed activities against *S. aureus* (diameter of inhibition zone: 8 mm) and *B. subtilis* (diameter of inhibition zone: 8 mm) (Yildirim et al., 2001). The antibacterial activity of *R. obtusifolius* extracts (*n*-hexane, CH_2Cl_2 and MeOH, and subfractions of MeOH extract) was tested against different bacterial strains by disc diffusion method. Ciprofloxacin was used as positive control (inhibition zones were 30 mm in all cases). The *n*-hexane extract did not show any activity at the test concentration, the CH_2Cl_2 extract was active only against *E. coli* (inhibition zone = 10 mm), and the MeOH extract was effective against all strains of bacteria tested (*B. cereus*, *B. subtilis*, *E. coli*, ampicillin-resistant *E. coli*, *S. aureus* and *S. typhii*). MIC values (1.56–25.0 mg/mL in case of MeOH extract and its fractions) were determined by resazurin assay (Harshaw et al., 2010).

The antibacterial activity of the methanol extract of *R. nepalensis* was evaluated against *B. subtilis*, *S. aureus*, *E. coli*, *Vibrio cholerae* and *Shigella dysenteriae*. The inhibitory effect of the root extract was found to be maximum against *S. dysenteriae* NCTC5 (diameter of zone of inhibition = 21.5 mm at 1000 μg/disc), and was comparable to that of chloramphenicol (22.0 mm at 10 μg/disc) (Ghosh et al., 2003a). The compounds isolated from *R. nepalensis* and *R. hastatus* were investigated against *Mycobacterium tuberculosis*; among them, rumexneposide A (**51**), torachrysone (**48**), nepodin-8-*O*-β-D-glucopyranoside (**43**), torachrysone-8-*O*-β-D-glucopyranoside (**49**), chrysophanol-8-*O*-β-D-(6′-*O*-acetyl)glucopyranoside (**13**), aloesin (**37**) and (−)-epicatechin-3-*O*-gallate (**85**) exhibited potent inhibitory activity, with MIC values of 20.7, 6.1, 26.6, 8.9, 4.1, 2.85 and 10.2 μM, respectively. Isoniazid was used as positive control (MIC: 2.04 μM). Moreover, torachrysone (**48**) displayed significant inhibitory activity against the *p*-aminobenzoic acid pathway, with an MIC value of 12.6 μM (Liang et al., 2010).

As part of a research programme (ICBG, Bioactive Agents from Dryland Biodiversity of Latin America), the possible anti-mycobacterial potential of compounds derived from selected Mexican medicinal plants was investigated. One of these plants was *R. hymenosepalus*, from which stilbenoids, flavan-3-ols and anthraquinones were isolated. All of the compounds were tested for their antimycobacterial activity by using the BACTEC 460 assay. On the basis of the MIC values, emodin (**1**), chrysophanol (**2**) and resveratrol (**103**) had marginal effects (with MIC 128 μg/mL). It was concluded that, although the individual substances had only modest activity, the original plant extract had a significant effect on the mycobacteria, thereby providing the rationale for the traditional use of the plant in the treatment of tuberculosis (Rivero-Cruz et al., 2005).

The antibacterial activities of different fractions of *R. japonicus* against *B. subtilis*, *B. cereus* and *E. coli* were investigated with ampicillin as positive control [zones of inhibition = 35 ± 0.50 mm (*B. subtilis*); 22 ± 0.88 mm (*B. cereus*); 33 ± 1.45 mm (*E. coli*)]. The ethyl acetate fraction showed the strongest antibacterial effect [zones of inhibition = 15 ± 0.33 mm (*B. subtilis*); 17 ± 0.33 mm (*B. cereus*); and 20 ± 0.88 mm (*E. coli*)] (Elzaawely et al., 2005). Nishina et al. tested the antimicrobial effects of 2-methoxystypandrone (**50**), musizin (**42**) and torachrysone (**48**). Compound **50** was the most active against *S. aureus*, *S. lutea* and *S. cerevisiae*. The only structural difference between compounds **48** and **42** is the presence of a methoxy group in the former instead of a hydroxy group, so the higher antimicrobial activity of **48** could be connected to the presence of the methoxy group (Nishina et al., 1993).

The antibacterial effects of alcoholic extracts of *R. dentatus* were tested against *Shigella flexneri*, *Klebsiella pneumoniae*, *E. coli*, *P. aeruginosa*, *Salmonella typhimurium* and *S. aureus* by means of the agar disk diffusion method. Gentamycin was used as positive control. The ethanol extract showed inhibitory effects against all of the tested bacterial strains except *S. flexneri* and *S. typhimurium*. The highest inhibition zone diameter (24 ± 0.57 mm) was detected for *P. aeruginosa* at 500 μg/mL (Humeera et al., 2013).

The antibacterial evaluation of protein extracts prepared from

the seeds of 6 medicinal plants with sodium phosphate–citrate buffer and sodium acetate buffer at different pH-s, demonstrated that *R. vesicarius* (at pH 7.6) was active against various bacterial strains with zones of inhibitions of 16 mm (*S. aureus*), 7.5 mm (*P. aeruginosa*) and 15 mm (*Proteus vulgaris*) at 2.73 μg/mL (Akeel et al., 2014).

5.5.2. Antiviral activity

Due to the high number of HIV infections and the rapid emergence of drug-resistant strains, the demand for new antiviral therapeutics against HIV-1 is increasing. Moreover, the standard antiviral therapies are too expensive for most Africans. In order to manage the AIDS epidemic in Africa, alternative treatments are clearly needed. One of the possible approaches is the screening of plants based on their ethnomedicinal data. In such a screening, 41 plant extracts were tested, and the methanol and water extracts of the fruits of *R. cyprius* were evaluated for their HIV-1 RT inhibitory effects. This plant has been used in Egyptian folk medicine. The water extract of the plant showed significant inhibitory effects, with an IC_{50} of 40 μg/mL (El-Mekkawy et al., 1995).

Selected plants used in Rwandan traditional medicine for the treatment of infections and/or rheumatoid diseases were investigated for their antiviral activity *in vitro* against the HIV-1 virus. Of the 38 tested 80% ethanolic extracts, prepared from plants of 21 different families, only two extracts gave promising selectivity indices (SI = ratio of the 50% cytotoxic concentration to the 50% effective antiviral concentration) higher than 1. One of them was the extract obtained from the leaves of *R. bequaertii* (syn. *Rumex nepalensis* Spreng.) ($SI > 11$; $EC_{50} = 17.7$ μg/mL; $CC_{50} > 200.0$; 89% protection against HIV-induced cytopathic effect) (Cos et al., 2002).

Medicinal plants that have been used to treat ailments of possible bacterial or viral origin, e.g. coughing and fever, were collected in the western Terai region of southern Nepal by Taylor et al. Methanol extracts ($n = 20$) were prepared and tested against poliovirus, Sindbis virus and herpes simplex virus. One of the investigated plants was *R. hastatus*. The root juice of this plant is used in traditional medicine for the treatment of tonsillitis and sore throat. The root is also chewed and a paste is applied externally. In this experiment, the extract of *R. hastatus* was one of the most active; at 50 μg/mL, it inactivated herpes simplex virus (in the dark) and partially inactivated this virus at 25 μg/mL (Taylor et al., 1996).

The acetone–water extract prepared from *R. acetosa*, enriched in oligomeric and polymeric proanthocyanidins, was tested against herpes simplex virus type1. It showed an IC_{50} of 0.8 μg/mL. The extract and its main compound, **96**, hindered virus entry into the host cell by blocking attachment to the cell surface, directly interacting with viral particles and leading to the oligomerization of envelope proteins (Gescher et al., 2011). *Rumex nervosus* demonstrated strong antiviral activity against Coxsackie virus B3 and influenza A virus at 100 μg/mL (Getie et al., 2003).

The *in vitro* antiviral activities of Sinupret® oral drops and a dry extract (containing Rumicis herba, *R. acetosa*) were investigated against a series of both enveloped and non-enveloped human pathogenic DNA and RNA viruses causing infections of the upper respiratory tract. Noteworthy concentration-dependant antiviral activity was recorded against Adeno 5, HRV 14 and RSV viruses. The inhibitory effect of the dry extract was higher than that of the oral drops (Glatthaar-Saalmüller et al., 2011).

5.5.3. Antifungal activity

Hexane fractions from hydroalcoholic extracts prepared from 10 plant species (among them *R. acetosa*) used in traditional Brazilian medicine were assayed against *Paracoccidioides brasiliensis* and murine macrophages. Unfortunately, the extract of *R. acetosa* did not display antifungal activity in this study (Johann et al., 2010). The antifungal activities of six Himalayan medicinal plants were tested against a number of fungal pathogens (*Aspergillus fumigatus*, *A. flavus*, *A. versicolor*, *A. niger*, *Blastoschizomyces capitatus*, *Fusarium oxysporum*, *F. moniliforme*, *F. semitectum*, *Pythium* sp., *Rhizopus* sp., *Sporotrichum* sp., *Thermomyces* sp.). The ethanol extract of *R. nepalensis* roots demonstrated activity against most of the investigated strains (except *A. fumigatus*, *A. niger* and *B. capitatus*) (Sharma et al., 2008). Screening of 9 traditionally used Tanzanian medicinal plants for antifungal activity resulted that CH_2Cl_2 extract prepared from the leaves of *R. usambarensis* inhibited the growth of *A. niger* (Inhibition zone was 17 mm by agar well method, and 12 mm by disk diffusion test at a concentration of 130 mg/mL). Fluconazole was used as positive control (32.5 and 27 mm inhibition zones at a concentration of 2 μg/mL) (Kisangau et al., 2009). The antifungal effects of *R. dentatus* alcoholic extracts were evaluated against *A. versicolor*, *A. flavus*, *Acremonium* spp., *Penicillium dimorphosporum*, *Candida albicans*, *C. kruesie* and *C. parapsilosis*. The highest effect was observed against *C. albicans* (14 ± 2.0 mm at 500 μg/mL) (Humeera et al., 2013).

5.6. Antidiabetic activity

Rumex patientia has been used as an antidiabetic in traditional Turkish medicine. Treatment with the extract of the plant can decrease the blood glucose level in streptozotocin (STZ)-induced diabetes in rats. In the experiments, it was observed that a 2% decoction of *R. patientia* grain decreased the glucose and HbA1c levels elevated by STZ. Morphologically, a mitochondrial vacuolization, swelling and dilatation of the endoplasmatic reticulum in the B cells was found (Degirmenci et al., 2005). In another study, feeding with *R. patientia* seeds for 4 weeks led to a hypoglycaemic effect and an improved serum lipid profile as regards HDL- and LDL-cholesterol in STZ-diabetic rats. However, the serum total cholesterol and triglyceride levels did not undergo a significant reduction in *R. patientia*-treated diabetics rats as compared with untreated diabetics. Moreover, the increased MDA content was attenuated and the activity of SOD (superoxide dismutase) was reduced in the hepatic tissue (Sedaghat et al., 2011).

The methanol and 80% methanol extracts of *R. crispus* brought about a significant ($p < 0.01$) inhibition of α-glucosidase and α-amylase as compared with the positive control acarbose (Shiwani et al., 2012). The methanol extract of *R. acetosella* and its fractions with various polarities (*n*-hexane, chloroform, ethyl acetate, *n*-butanol and residual water) possessed strong dose-dependant α-amylase inhibitory activity. The effect was comparable to that of the positive control acarbose. The activity of the residual aqueous fraction was the highest, with an IC_{50} value of 0.85 mg/mL (the IC_{50} of acarbose was 1.20 mg/mL) (Ahmed et al., 2013).

The protective activities of anthraquinones [emodin (**1**), chrysophanol (**2**), physcion (**3**), citreoresin (**5**), chrysophanol-8-*O*-glucoside (**10**), emodin-8-*O*-glucoside (**9**), nepalensides A (**38**) and B (**39**), patientosides A (**30**) and B (**31**), cassialoin (**29**), and rumejaposides E (**24**) and I (**28**)] isolated from *Rumex* species (*R. patientia*, *R. nepalensis* and *R. hastatus*) were investigated in diabetic nephropathy, as *Rumex* plants are traditionally used for the treatment of renal and urogenital disorders. The inhibitory effects on the secretion of IL-6 and the overproduction of extracellular matrix in high-glucose-induced mesangial cells were measured. All the compounds significantly inhibited the secretion of IL-6 at 10 μM, while **1**–**3**, **24**, **30** and **38** significantly decreased collagen IV and fibronectin production at 10 μM (Yang et al., 2013).

The preventive effect of *R. japonicus* against diabetic complications has been evaluated. The ethyl acetate extract of the fruits of the plant exerted significant *in vitro* inhibitory activity on the formation of advanced glycation end-products (AGEs). It is

believed that AGE cross-links play an important role in the arterial and myocardial stiffening that contributes to the increase in cardiac risk with aging and diabetes. The purification of the extract resulted in emodin (**1**) and the flavonoids quercetin (**63**), quercitrin (**70**), isoquercitrin (**71**), kaempferol-3-*O*-*β*-D-glucoside (**64**) and (+)-catechin (**79**). The evaluation of the compounds demonstrated that quercetin (**63**) and catechin (**79**) markedly reduced AGE-BSA cross-linking in a dose-dependant manner. Moreover, catechin (**79**) displayed dose-dependant breaking activity against preformed AGE-BSA cross-linking. In this experiment aminoguanidine was used as positive control (Tavares et al., 2010).

In a study of the α-glucosidase inhibitory activities of *trans*-resveratrol (**103**), piceid (**109**) and rumexoid (**110**), with acarbose as positive control, compound (**103**) showed 58% inhibition at 0.1 mM, while rumexoid (**110**) inhibited 57% of the enzyme activity at 0.5 mM. Both compounds were found to be more potent inhibitors of α-glucosidase than acarbose (35% at 0.5 mM). Piceid (**109**) did not display any activity (Kerem et al., 2006).

5.7. Immunomodulatory activity

The inhibitory effects of a water extract of *R. japonicus* roots were tested on atopic dermatitis (AD) -like skin lesions in NC/Nga mice. This plant is used in Eastern countries for the treatment of various skin diseases. AD-like skin lesions were induced with picryl chloride. Oral administration of the extract inhibited the development of lesions, and decreased the hypertrophy, hyperkeratosis and infiltration of inflammatory cells in the skin. Moreover, the IgE and IL-4 levels were significantly reduced by the *R. japonicus* extract. This was indicative of the suppression of the T-helper 2 cell response (Lee et al., 2006).

5.8. Psychopharmacological activity

The methanol extract of *R. nepalensis* was assessed for different psychopharmacological activities in rats and mice (Ghosh et al., 2002). This plant is widely distributed in the temperate region of the Himalayas. The roots of the plant have been used in folklore medicine to relieve mental tension and disturbance. The pharmacological results indicated that the methanol extract of *R. nepalensis* appears to have an influence on alterations in general behavioural profiles, including alertness, awareness, spontaneous activity, touch, pain and sound responses. The extract significantly potentiated the duration of phenobarbital sodium-induced sleeping time in mice at 200 and 400 mg/kg, suggesting probable tranquilising and CNS depressant action. Possible effects were examined on other test systems too, e.g. the exploratory behavioural pattern and muscle relaxant activity. Finally, it was concluded that the methanol extract of *R. nepalensis* possessed most of the pharmacological activities characteristic of minor tranquillisers (Ghosh et al., 2002).

5.9. Effects on the gastrointestinal tract

5.9.1. Antidiarrhoeal activity

Polygonaceae species are usually used as purgatives, but some species are utilised for the treatment of diarrhoea. One of them is *R. maritimus*, an annual herb widely distributed throughout Asia, North Africa and America. The antidiarrhoeal activities of different extracts (*n*-hexane, ethyl acetate and residual methanol) of its roots were evaluated in mice with castor oil and serotonin-induced diarrhoea and charcoal motility tests were performed at doses of 50, 100 and 200 mg/kg. The methanol extract showed the most promising and dose dependant activity against both castor oil and serotonin induced diarrhoea at 200 mg/kg. The methanol extract also significantly decreased the propulsion of a charcoal meal through the gastrointestinal tract (Rouf et al., 2003).

In an ethnobotanical study, the medicinal plants used in western Nepal were reviewed. One of the documented plants was *R. hastatus*, which has the highest fidelity level (100%), used for gastrointestinal ailments. The root powder or paste is used against diarrhoea and dysentery (Rokaya et al., 2010).

5.9.2. Purgative activity

The methanol extract of *R. nepalensis* root was investigated for its purgative effect in rats. Bisacodyl (3.5 mg/kg) was used as a standard. At oral doses of 100–400 mg/kg, the extract exhibited significant and dose-dependant purgative activity by increasing the intestinal peristalsis and gastrointestinal motility (Ghosh et al., 2003b).

5.10. Anti-asthmatic activity

The anti-asthmatic effect of 1-*O*-caffeoyl glucoside (**132**) from the *R. gmelinii* herb was investigated on the aerosolized ovalbumin challenge in ovalbumin-sensitised guinea-pigs, with measurement of the specific airway resistance and the recruitment of leucocytes and chemical mediators in the bronchoalveolar lavage fluid (BALF). 25 mg/kg of compound **132** significantly inhibited the specific airway resistance, by 26.79% in the immediate-phase response and by 52.94% in the late-phase response. The compound was less effective than the positive controls dexamethasone, disodium cromoglycate and salbutamol. The recruitments of neutrophils and eosinophils into the lung and the release of chemical mediators in the BALF were also significantly inhibited by **132** (Lee et al., 2011).

5.11. Antifertility activity

Rumex steudelii is one of the traditionally used antifertility plants in Ethiopia. An antifertility investigation of the methanolic extract prepared from the roots was performed in female rats, and the oral LD_{50} was determined in mice. Phytochemical characterisation of the extract showed that it contains phytosterols and polyphenols. It was observed that the methanol extract prolonged the oestrous cycle significantly and increased the length of the dioestrous phase. The weights of the ovary and uterus were decreased. The oral LD_{50} of the extract was found to be 5 g/kg (Gebrie et al., 2005a). In an investigation the possible mechanism of the antifertility action of the plant in rats, it was observed that the extract decreased the number of implantation sites. At a contraceptive dose, it had no oestrogenic activity in immature rats. The extract did not modify the serum oestrogen–progesterone ratio. It produced a concentration-dependant increase in uterine muscle contractions similar to that of the standard drug, oxytocin. It was concluded that this effect might evolve through the activation of muscarinic and/or histaminic receptors (Gebrie et al., 2005b). The effects of the extract on uterine histology and ovarian follicular growth were also determined after the administration of a *R. steudelii* root extract for 30 days. Significant decreases were observed in the uterine and ovarian wet weights. As concerns the uterine histology, the development of the endometrial epithelium, endometrial glands and stroma was inhibited, and dose-dependant decreases in the epithelial cell height and the stromal and myometrial thickness were also observed. Moreover, the number of active corpora lutea and healthy preantral and antral follicles decreased (Solomon et al., 2010).

5.12. Anthelminthic activity

Rumex abyssinicus is widely used in folk medicine for various ailments, e.g. the treatment of headache, haemorrhoids, ascariasis, scabies, fungal skin infections, wounds, eczema and sore throat,

and also to control mild forms of diabetes. Moreover, a decoction of the root and leaf powder of the plant is used as a vermifuge (Eguale et al., 2011). The aqueous and hydro-alcoholic extracts of the plant were investigated *in vitro* against the highly pathogenic and one of the most prevalent nematode parasites, *Haemonchus contortus*. The effective doses required to induce 50% inhibition of egg hatching (ED_{50}) were calculated. Both extracts of the aerial part of the plant demonstrated noteworthy dose-dependant inhibition (ED_{50}=0.11 for the aqueous extract, and 0.16 for the hydro-alcoholic extract) (Eguale et al., 2011).

In an ethnobotanical study, medicinal plants traditionally used as anthelminthics in Kenya were evaluated. One of the total 80 medicinal plants involved was *R. usambarensis*. This plant is used to treat worms and constipation. It is one of the most frequently used anthelminthic plants (Muthee et al., 2011).

5.13. Molluscicidal activity

A hot water extract of the root tubers of *R. dentatus* exerted molluscicidal activity against the snails *Oncomelania hupensis*, *Biomphalaria glabrata* and *Bulinus globosus*, which are vectors of *Schistosoma japonicum*, *S. mansoni* and *S. haematobium*. This molluscicidal activity was correlated with the anthraquinones, which were identified by HPLC. Nevertheless, the activity was moderate with respect to niclosamide, and too low to suggest further studies of this plant for snail control (Liu et al., 1997). The *n*-butanol and water extracts of *R. japonicus* roots were tested against *O. hupensis*. The reactions of the esterase isozyme, glycogen and total protein of the snails were also studied. The water extract of the root showed higher activity (LD_{50}=90.0 mg/L) than the *n*-butanol extract (LD_{50}=398.1 mg/L), but these activities were significantly lower than those of the synthetic molluscicides (the LD_{50} of sodium pentachlorophenate or niclosamide is around 0.1 mg/L) (Wang et al., 2006).

5.14. Antinematodal activity

The effects of condensed tannins (CTs) isolated from *R. obtusifolius* among others were evaluated on the egg hatching and larval development of the sheep nematode *Teladorsagia vitro*. 46% of the eggs hatched when 900 μg/mL of plant extract CTs was used (in the control group, 87% of the eggs hatched). In the larval development assay, only 4% of the eggs attained full development to L3 larvae in the case of 200 μg/mL CTs from *R. obtusifolius*, while 400 μg/mL killed 91% of the first-stage (L1) and the second-stage (L2) larvae. It was concluded that the CTs not only slow down the larval development, but also kill the undeveloped larvae (Molan and Faraj, 2010).

5.15. Antiplasmodial activity

An *in vitro* investigation of methanol, dichloromethane and aqueous extracts of 13 Rwandan medicinal plants (among them *R. abyssinicus* and *R. bequartii*) for antiplasmodial activity against a chloroquine-sensitive *Plasmodium falciparium* strain (3D7) indicated that the dichloromethane extract of *R. abyssinicus* roots showed high activity (IC_{50}=4.3 μg/mL). In tests against chloroquine-resistant *P. falciparium* strain W2, the IC_{50} of this extract was found to be 3.1 μg/mL. Nevertheless, the extract was cytotoxic (IC_{50}=13.3 μg/mL) on normal foetal lung fibroblasts (WI-38) (Muganga et al., 2010). The antiplasmodial activities of *R. crispus* extracts with various polarities (*n*-hexane, *n*-butanol, chloroform and ethyl acetate) were tested against chloroquine-sensitive (3D7) and -resistant (S20) *P. falciparium* strains in PfNDH2 assays. The chloroform and ethyl acetate extracts showed activity against both strains. The bioassay-guided fractionation of the combined extracts identified nepodin (**42**). The antiplasmodial investigation of the compound led to IC_{50} values of 0.70 μg/mL (3D7) and 0.79 μg/mL (S20), which were lower than those of the positive controls chloroquine and DPI. In the course of *in vivo* antimalarial assays, nepodin (**42**) was active in parasitaemia suppression in mice. Moreover, it prolonged the survival time in all of the tested groups (Lee et al., 2013b).

5.16. Diuretic effect

The aqueous and 80% methanol extracts of *R. abyssinicus* rhizomes were found to possess dose-dependant diuretic effects. Furosemide was used as positive control. The extracts significantly increased the urine volume and urinary electrolytes (Na^+, K^+ and Cl^-) (Mekonnen et al., 2010).

5.17. Analgesic activity

The highest doses (1000 mg/kg) of an 80% methanol extract of the *R. abyssinicus* rhizome reduced the number of writhings in mice by 67.6% and conferred more than 70% protection against thermally induced pain stimuli as compared with the positive controls aspirin and morphine (Mekonnen et al., 2010).

5.18. Neuroprotective effect

Two flavonoids [quercetin-3-galactoside (**66**) and quercetin-3-arabinoside (**67**)] isolated from *R. aquaticus* were investigated for neuroprotective activity. It was observed that at 10 μM concentration both compounds significantly improved cell survival in the oxygen–glucose deprivation model of ischaemia. Moreover, they also increased neurite outgrowth in differentiated PC12 cells subjected to ischaemic insult (Orbán-Gyapai et al., 2014).

5.19. Genotoxic effect

The potential genotoxic effect of plants used in traditional Ethiopian medicine was investigated. One of them was *R. steudelii*, used as an antifertility agent. The results showed that an extract of the roots induced significant DNA damage in mouse lymphoma L5178Y cells without inducing concomitant cytotoxicity, especially when the cells were exposed without metabolic activation (S9-mix) (Demma et al., 2009).

5.20. Clinical studies

BNO 1016 (Sinupret®, Bionorica SE, Neumarkt, Germany) is an extract of a fixed combination of five herbal drugs, among them *R. acetosa* [Gentian root (*Gentianae radix*), Primula flower *(Primulae flos*), Sorrel herb (*Rumicis herba*), Elder flower (*Sambuci flos*) and Verbena herb (*Verbenae herba*), in a ratio of 1:3:3:3:3] that has been developed for the treatment of sinusitis. *In vitro* and animal models have revealed that the preparation has antimicrobial and antiviral effects, and secretolytic and anti-inflammatory activity. Phase IIb/III studies indicated that 160 mg three times daily was the most effective dose. The efficacy and safety of this dosage for 15 days were studied in 2012 on symptoms of acute viral rhinosinusitis. It was observed that the herbal preparation is efficacious and well tolerated (Jund et al., 2012).

5.21. Toxicity of Rumex species

It is known that plants belonging in family Polygonaceae can contain high level of oxalic acid. Oxalic acid can cause serious problems in case of consuming them in large amount, e.g. a high dietary oxalate intake plays a key role in secondary hyperoxaluria,

a major risk factor for calcium oxalate stone formation. Dietary oxalate further reduces the intestinal absorption of calcium and other trace elements therefore impair the bioavailability of them due to the formation of insoluble complexes (Siener et al., 2006). The risk of poisoning could be decreased avoiding the ingestion of the cooking water of the plants.

There is a case report of fatal oxalic acid poisoning from eating sorrel soup (*R. crispus*). Oxalic acid has a corrosive action upon the digestive tract. Once it has been absorbed it reacts with calcium in plasma and insoluble calcium oxalate tends to precipitate in kidneys, blood vessels, heart, lungs, and liver; this reaction may also produce hypocalcaemia (Farré et al., 1989). In the few reported cases of oxalic acid intoxication, tubular oxalosis has been the main feature. Chronic intake of high oxalate containing herbs can impair iron absorption, too. Sorrel should be avoided by patients with kidney stones, rheumatism, arthritis, gout or hyperacidity since it can aggravate their conditions (Pareek and Kumar, 2014).

The mean lethal dose of oxalic acid for adult has been estimated as 15–30 g although amounts lower than 5 g can be fatal.

6. Discussion

The present review summarised the traditional medicine uses and phytochemical and pharmacological aspects of the genus *Rumex*. The species belonging to genus *Rumex* are widely distributed worldwide, mainly in Asia (China, India, Korea, Pakistan) and Turkey, but in the Eastern part of Europe (Poland, Hungary and Romania) too. The plants are frequently used either as vegetables or in traditional medicines. Present findings revealed that leaves are the most frequently utilised plant parts as foods (mainly fresh form), while leaves and roots are applied preferably for the treatment of different diseases. The most popular forms for consumption of *Rumex* sp. are salads, soups and snacks. Decoction, infusum, juice and powder from the plants are the major modes of preparations. Skin infections, sores and wounds are mostly treated by rubbing and pasting herbal preparations. However, for internal ailments, herbal preparations are administered mainly orally. Present survey reveals, that local inhabitants use plant based medications to treat different types of diseases, including gastrointestinal disorders (constipation, diarrhoea, ulcer), skin infections (eczema, wounds, sores and snake bites), respiratory diseases (cough, bronchitis, asthma), kidney and liver disorders (diuretic, jaundice), rheumatoid problems, fever, and reproductive problems. Constipation, diarrhoea and skin infections are the most common therapeutical areas in case of *Rumex* species. Roots are mainly used for the treatment of constipation, seeds in case of diarrhoea and leaves for the therapy of skin disorders.

To date over 130 molecules, including anthranoids, naphthalenes, flavonoids, stilbenes, terpenoids and phenolic compounds have been identified from *Rumex* plants. Anthraquinones are considered to be important taxonomic markers of the Polygonaceae family: especially emodin (**1**), chrysophanol (**2**) and physcion (**3**) have been isolated from many plants. Some *Rumex* species (*R. alpinus*, *R. nepalensis* and *R. patientia*) are especially rich in anthranoids. A series of glucosylated anthranoids, named rumejaposides (**20**–**28**), have been isolated from *R. dentatus* and *R. japonicus*. Dianthrones are detected in only few *Rumex* species. Another specific type of compounds isolated from this genus is the group of naphthalenes. Nepodin (musizin, **42**) and its glucoside (**43**), and torachrysone (**48**) and its glucoside (**49**) have been identified in several plants, especially from the roots. Among phenolic compounds flavonoids (kaempferol, quercetin and catechin derivatives), stilbenoids (*trans*-resveratrol, **103**) and tannins have been isolated from the members of the *Rumex* genus. Flavonoids have been detected in large quantities in *R. acetosa* roots, and in the leaves of *R. induratus* and *R. vesicarius*. Interestingly, two different structures have been reported for patientoside A in the literature. It has been isolated as an anthranoid (**30**) and also as naphthalene (**44**) from *R. patientia* (Kuruüzüm et al., 2001; Yang et al., 2013). In some cases, HPLC methods have been developed for the identification and measurement of compounds (Ferreres et al., 2006; El-Hawary et al., 2011). It can be stated that flavonoids have been valuable as chemotaxonomic markers, as they occur as flavon derivatives in *Rumex* species while flavans or chalcones are presented in other genus (e.g. *Polygonum*) of Polygonaceae family.

Pharmacological investigations have shown that the crude extracts and isolated compounds from *Rumex* species possess numerous kinds of biological activities, especially antioxidant, antitumour, anti-inflammatory, antiulcer, and antimicrobial effects. The most widely pharmacologically investigated plant is *R. abyssinicus*, which possesses anti-inflammatory, antioxidant, antibacterial, anthelminthic, antiplasmodial, diuretic and analgesic effects. It should be stated, however, that most of the pharmacological studies were conducted on crude and poorly characterized extracts. Throughout the present review it was found that some traditional medicinal uses of *Rumex* species have been validated and supported by pharmacological investigations. Some *Rumex* species usually associated with the presence of naphthalenes, flavonoids and other phenolic compounds have shown antioxidant property. The antioxidant activity of numerous *Rumex* species (*R. abyssinicus*, *R. acetosella*, *R. bucephalophorus*, *R. crispus*, *R. dentatus*, *R. hastatus*, *R. hymenosephalus*, *R. induratus R. japonicus*, *R. madarensis*, *R. nepalensis*, *R. patientia*) was investigated by different methods (DPPH, TEAC, superoxide free radical scavenging, iron chelating power, the abilities to quench singlet oxygen). Ethanol, hexane, chloroform, ethyl acetate, butanol, methanol and aqueous extracts of leaves, roots and seeds of the plants were tested. Trolox and ascorbic acid were used as positive controls. Mainly ethyl acetate extracts containing high level of phenolic compounds proved to be active. Flavonoids (**79**, **81**), stilbenoids (**103**–**105**, **109**, **110**) and naphthalenes (**42**, **43**) proved to be effective in antioxidant assays; the most active ones were **42**, **43** and **103** (IC_{50} = 11.7 μM (**42**), and 40.1 μM (**43**), in the DPPH assay, 13.5 μM (**42**) and 47.4 μM (**43**) in the ABTS assay, and TEAC value of **103** was 2.7) (Kerem et al., 2006; Gautam et al., 2010). None of the investigated anthraquinones showed activity against DPPH, Trolox and ABTS. There was only one *in vivo* study in the literature performed on rats, investigated the methanol extract of *R. crispus* on several hepatic antioxidant systems. Only moderate activity was observed in the case of GSH-Px and XOD (Maksimovic et al., 2011).

The investigation of the antiproliferative effect of different extracts of *Rumex* species and compounds (tannins, polysaccharides, anthraquinones, naphthalenes, stilbenoids and flavonoids) isolated from them resulted that the ethanol extract of *R. confertus*, *R. obtusifolius* and *R. hydrolapathum*, the methanol extract of *R. crispus* and the *n*-hexane or $CHCl_3$ extracts of *R. acetosa*, *R. aquaticus*, *R. scutatus* and *R. thyrsiflorus* proved to be the most active (Wegiera et al., 2012; Lajter et al., 2013). Among the tested compounds emodin (**1**, LC_{50} = 0.05 μg/mL), chrysophanol (**2** IC_{50} = 5.62 μM on SKOV-3 and 20.4 μM on MCF7 cells), its acetyl-glucoside (**13**, IC_{50} = 9.6 μM on MCF-10A), orientaloside (**47**, IC_{50} = 7.6 μM on MCF-10A) and resveratrol (**103**, IC_{50} = 12.3 μM on MCF-10A) showed remarkable cytotoxic or antiproliferative activity *in vitro* (Demirezer et al., 2001; Liang et al., 2010). The antimutagenic activity of the CH_2Cl_2 extract of *R. acetosa* and emodin (**1**) was also tested with the Ames test. Emodin (**1**) possessed strong inhibitory activity (75%) on revertant CFU (Lee et al., 2005).

In traditional medicines numerous *Rumex* species are used as anti-inflammatory agents. As a result of the pharmacological tests the antiulcerogen potential of *R. patientia* (at 440 mg/kg concentration), *R. acetosa* (at 100 mg/kg) and *R. acetosella* (IC_{50}

=0.85 μg/mL in case of residual aqueous fraction) seems to be promising as their healing effects were more effective than the positive controls sucralfate and thiourea (Gürbüz et al., 2005; Bae et al., 2012; Ahmed et al., 2013). The polar extracts of *R. patientia* also possessed hepatoprotective effect both *in vitro* and *in vivo* (Silig et al., 2004; Lone et al., 2007).

The antimicrobial potential of *Rumex* species and their compounds is the most researched area; extracts with different polarity were tested against various Gram positive and negative bacteria, fungi and viruses. In the case of antibacterial assays MIC values of aloesin (**37**, MIC=2.85 μM) and chrysophanol-8-*O*-(6′-acetyl)-glucoside (**13**, MIC=4.1 μM) are significant comparing to that of positive control isoniazid (MIC=2.04 μM) (Liang et al., 2010). It is known that polyphenol rich extracts are effective against viral infections by blocking attachment to the cell surface and directly interacting with viral particles. Among *Rumex* species *R. acetosa* proved to be active against herpes simplex virus 1 at an IC_{50} of 0.8 μg/mL (Gescher et al., 2011).

Anthracene derivatives, which occur in large quantities in *Rumex* species, seem to be the main biologically active compounds responsible for anti-inflammatory and anticancer properties. The flavonoid QGC (**73**) isolated in large amount from *R. aquaticus* and an extract containing quercetin-3-*O*-β-D-glucuronopyranoside (QGC, **73**) (ECQ) have been investigated in a number of experimental models. It exhibits pronounced anti-inflammatory and antioxidant activities (Min et al., 2009; Kim et al., 2010; Cho et al., 2011; Yan et al., 2011; Jang et al., 2012; Lee et al., 2013a).

Toxicological studies of *Rumex* species and their isolated compounds are limited. Most reports showed no toxicity or mortality at the effective doses (Süleyman et al., 1999). As concerns acute toxicity, *R. aquaticus* extract (ECQ) has been proven to be safe. The pharmacological effects of ECQ on general behaviour and on the central nervous, digestive, cardiovascular and respiratory systems and the smooth muscles were studied in order to search for any side effects in rats, mice, guinea pigs, and cats (Lee et al., 2012).

The measured activities compared with the ethnomedicinal uses of many species of *Rumex* genus are in agreement with the traditional uses of the plants. *Rumex patientia* and *R. acetosa* are used extensively in traditional medicine as an antipyretic, wound cure and anti-inflammatory agent. The anti-inflammatory activity of the aqueous extract of the plant was demonstrated *in vitro* (Süleyman et al., 1999; Bae et al., 2012). *Rumex abyssinicus*, *R. crispus* and *R. obtusifolius* exhibited antibacterial activity and it could justify its traditional use for the treatment of several skin diseases (Yildirim et al., 2001; Getie et al., 2003; Harshaw et al., 2010). The antibacterial activities observed in the case of *R. nepalensis* and *R. dentatus* confirmed their traditional use for the treatment of dysentery (Ghosh et al., 2003a; Humeera et al., 2013). Moreover, the antifungal effect of *R. dentatus* was also demonstrated *in vitro* (Humeera et al., 2013).

Because of the high tannin content of the roots of some *Rumex* species, they may have considerable carcinogenic potential.

7. Conclusions

In conclusion, numerous *Rumex* species are used worldwide either as food or for the treatment of several diseases. The present study indicates that the main traditional uses (antibacterial, purgative, antitumour and anti-inflammatory) of *Rumex* species have been validated by pharmacological studies. The most promising species for further investigations are *R. aquaticus* (anti-inflammatory and neuroprotective activites), *R. abyssinicus* (anti-inflammatory, antioxidant and antibacterial activities) *R. patientia* (antitumour, anti-inflammatory and antioxidant activities) and *R. acetosa* (anti-inflammatory and antioxidant activities). This review also highlights the importance of some anthraquinones (e.g. emodin, **1**), naphthalenes (nepodin, **42**) and flavonoids (e.g. quercetin-3-*O*-glucoside, **73**) for preventing or treating cancer, and some inflammatory diseases. However, ethnopharmacological studies are not exhausted, and clinical trials are missing. Current pharmacological data is in many cases limited to studies on plant extracts and hence, more bioactive components, and especially anti-inflammatory, antitumour and antimicrobial compounds should be identified by using bioactivity-guided isolation strategies. On the basis of this literature review it can be stated that hepatoprotective, antiviral and antidiabetic investigations may be promising in the future. The possible mechanisms of action and the potential synergistic or antagonistic effects of multi-component mixtures need to be evaluated through the integration of pharmacological, pharmacokinetic, bioavailability-centred and physiological approaches. In addition, more experiments, including *in vivo* and clinical studies, should be carried out in order to recognise any side effects or toxicity of purified extracts. Prolonged and high dose intake of traditional formulations containing *Rumex* should be avoided until more in-depth toxicity studies become available. The new findings may increase the present therapeutic importance of *Rumex* species and promote their future use in modern medicine.

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