

# 6

# A Review on Ethnomedicinal, Phytochemistry and Pharmacological Activities of *Rumex hastatus* D. Don

Iflah Hassan, Insha Mushtaq, Weekar Younus Raja, and Zulfiqar Ali Bhat

#### Abstract

This book chapter summarizes selected scientific evidence on phytochemistry and pharmacological potential of Rumex hastatus. This herb is a bushy shrub and is an annual, biennial and perennial herb. The edible parts of the plant are young leaves and shoots (Padulosi 1999) belonging to the family Polygonaceae, and it is commonly known as *khatimal*. R. hastatus is commonly found in northern Pakistan, southwest of China and northeast Afghanistan. In India, it is widely distributed in western Himalayas, Himachal Pradesh, Jammu and Kashmir and Uttaranchal. It has been reported to possess a wide range of traditional medicinal uses including in asthma, cancer, rheumatism, diuretic, diarrhoea, dysentery, toothache, gum healing, jaundice, hepatitis, cough, fever, piles, carminative, purgative, fungal infection, lungs, bleeding and as a flavouring agent. Preliminary phytochemical screening showed that this plant is rich in various chemical constituents which are medicinally important such as flavonoids, anthraquinones, cardiac glycosides, alkaloids, terpenoids, tannins, saponins, phenolic compounds and coumarins. It has anti-nociceptive, antipyretic, anti-inflammatory, hepatic protective, anticholinesterase, antioxidant, antiradical, cytotoxic, anti-tumour, and angiogenic potential. The objective of the present current chapter is to collect all the relevant research articles which give information regarding traditional uses, phytochemistry and therapeutic potential of R. hastatus. R. hastatus has potential for curing various diseases and has been well studied for its phytochemical properties. However, further scientific studies are needed to explore mechanisms of actions, adverse effects of the extracts, toxicity and the therapeutic effect of major secondary metabolites.

I. Hassan · Insha Mushtaq · W. Y. Raja · Z. A. Bhat ( $\boxtimes$ )

Pharmacognosy and Phytochemistry, School of Applied Sciences and Technology, Department of Pharmaceutical Sciences, University of Kashmir, Hazratbal, Srinagar, Jammu and Kashmir, India

M. H. Masoodi, M. U. Rehman (eds.), *Edible Plants in Health and Diseases*, https://doi.org/10.1007/978-981-16-4959-2\_6

# Keywords

 $Rumex hastatus \cdot Therapeutic potential \cdot Phytochemical properties \cdot Polygonaceae$ 

# Abbreviations

A. flavus	Aspergillus flavus
A. fumigatus	Aspergillus fumigatus
A. niger	Aspergillus Niger
ABTS	2,2'-Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)
AChE	Acetyl cholinesterase
AD	Alzheimer's disease
AIDS	Autoimmuno deficiency disease
BChE	Butyrylcholinesterase
ca.	Circa (approx.)
CAM	Chorioallantoic membrane assay
Cox-2	Cyclooxygenase-2
DNA	Deoxyribonucleic acid
DPPH	Diphenyl-1-picrylhydrazyl
E. coli	Escherichia coli
EtOH	Ethanol
F. solani	Fusarium solani
FID-MS	Flame ionization detector with mass spectrometer
$H_2O_2$	Hydrogen peroxide
HDL	High-density lipoproteins
IUCN	International Union for Conservation Research
LC50	Lethal concentration
LDL	Low-density lipoproteins
MeOH	Methanol
NSAIDs	Non-steroidal anti-inflammatory drugs
PFAF	Plants for a future
PHCs	Primary health Centre
R. hastatus	Rumex hastatus
STD	Sexually transmitted disease
TC	Total cholesterol
TLC	Thin layer chromatography
TNF	Tumour necrosis factor
Tsp	Teaspoon
UPLC-DAD	Ultra-performance liquid chromatography method with diode array
	detection

#### 6.1 Introduction

An examination is required to characterize and portray the future errands of phytochemical research in the new millennium and not just of the present status of improvement of phytochemical research yet in addition to chemosynthetic pharmaceutical exploration. Both end up in a race to grow new prescriptions, with less or no reactions, for restorative and preventive application in illnesses for which casualtybased treatment has been nonexistent or blemished (Yaniv and Bachrach 2005). Use of plants as drugs has started between 4500–1600 BC and 2500–600 BC in Rig-Veda and Ayurveda, respectively. Apart from this, they have been used by Greeks and Arabs in the history, which saw its rise to India and Europe as well (Jan et al. 2011). Different plant species are developed and utilized as vegetables and food, throughout the globe; however huge numbers of these are ignored and underutilized. These are labelled "dismissed or underutilized" on the grounds that they remain ineffectively described and abandoned by examination and protection. Likewise, they have been maintained by social tendencies and conventional framework. Continuous negligence of these vegetables implies that their potential centrality will be underestimated, henceforth underestimated at this point, yet a large number of them are light and versatile and bear unfavourable climatic conditions more than the fascinating ones. Extraordinary danger of delayed hereditary eroding and vanishing is put on them, which could additionally prevent opportunity choices for the country occupants (Padulosi et al. 1999; Johns and Eyzaguirre 2006; Mal 2007; Ghane et al. 2010). A portion of these disregarded and underutilized crop species might be wild, yet their jobs are indispensable in food security and nourishment and financially assist the people living below the poverty line in the provincial territories of the emergent nations (Magbagbeola et al. 2010). Vital medicinally important constituents are present in herbs producing distinct physiological activity on the human body. Alkaloids, tannins, flavonoids, terpenoids, saponins and phenols include the significant ones. Due to their therapeutic significance and low poisonousness, drug specialists are concerned about their exploration (Inayatullah et al. 2012). Isolation of many such entities has been established from different plants with perhaps novel mechanism of actions and negligible poisonousness to the host cell (Ahmad and Aqil 2007).

#### 6.1.1 Rumex and Polygonaceae

Ever since the time humans use plants and spices as cure against maladies and infirmities because of their healing benefits and different restorative focal points, *Rumex* L. (Dock) species have increased gigantic acknowledgement (Babulka 2004). Two huge clades were characterized after the atomic phylogenetic investigation by Navajas-Pérez et al. (2005) inside the variety *Rumex*, one framed by the species of subg. *Rumex* and the other made out of the species of subgenera Acetosa (includes

Rumex hastatus), acetosella and platypodium. Various Rumex species have been customarily utilized in various places of the world which in history have verifiable foundation. Propensities to utilize plants for various purposes, for example, medication, food, pharmaceuticals and so forth, are inculcated on the basis of interrelationship among the past, the present and what's to come, which is woven in human civilizations (Zhang et al. 2014). The two spheres of well-being which include ethnoveterinary and ethnomedicine are the main aspects in clinical practice where the plants have a great utility (Abbasi et al. 2013; Disler et al. 2014; Bartha et al. 2015; Hussain et al. 2015; Vogl et al. 2016). In the family Polygonaceae, Rumex is the second largest genus. It is widely distributed in most part of Europe, North America, Africa and Asia, predominantly in the northern half of the globe (Vasas et al. 2015). The family Polygonaceae generally known as the knotwood or smart weed family is a group of blooming or flowering plants (Uddin et al. 2014) and involves 56 plant genera with 5109 logical plant names of species, of these 1266 are acknowledged species names. A further of 1675 scientific plant names of intraspecific position for the family Polygonaceae are incorporated in the plant list (List 2010), among which Eriogonum (2410 species), Rumex (200 species), Coccoloba (120 species) and *Persicaria* (100 species) are the biggest ones (Uddin et al. 2014). Numerous types of this class are herbs; however some are bushes as well, and a couple are rhizomes. The genus Rumex is a commonly recognized name, represented by 25 perennial plant species in nations like Poland. In traditional medicine leaf, seeds, fresh plant juice, seeds, and aerial parts are the generally utilized. Rich hereditary diversity in a few wild plants of nutritional worth and potential therapeutic properties is mostly found in the West Himalayan biogeographic zone, which is known for it (Sinha and Sinha 2001; Singh et al. 2002). Asthma, bronchitis, cough, loose bowels, diarrhoea, dermatitis, ear infection, inflammatory conditions, jaundice, kidney disease, leprosy, toothache, ulcerative colitis and intestinal parasites are among the few medicinal properties credited to this family (Uddin et al. 2014).

#### 6.1.2 Rumex hastatus D. Don

*R. hastatus* belongs to the family Polygonaceae and is commonly called as "Khatimal". It is found in abundance in northern Pakistan, southwest China and northeast Afghanistan (Shinwari and Gilani 2003). The leaves and shoots are used in chutneys and pickles due to its pleasant acidic taste (Manan et al. 2007). It is reported that the whole plant is used as medicine. It is laxative, alterative and tonic (Shinwari and Gilani 2003) and used for treating sexually transmitted diseases like AIDS (Sahreen et al. 2011). The aqueous extract of the roots of *Rumex* is used traditionally for curing asthma (Abbasi et al. 2010, Abbasi et al. 2011). The leaves and young shoots are used as carminative, purgative, diuretic and in stomach problems (Murad et al. 2011). All the previous studies on *R. hastatus* leaves have proven them to be constituting righteous phenolic principles and are therefore verified antioxidant

sources. (Zhang et al. 2009; Sahreen et al. 2011) reported seven phenolic compounds from *R. hastatus* roots by referring the use in Chinese herbal system. The *R. hastatus* has been evaluated for various activities like antioxidant (Sahreen et al. 2011); antifungal (Hussain et al. 2010); antifungal and anti-bacterial (Hussain et al. 2010); antidiarrhoeal (Shakuntala et al. 2011) and anti-viral (Taylor et al. 1996).

#### 6.1.3 Review Methodology

There is no literature of review on *R*. *hast*atus that has been published yet; therefore the book chapter on the present topic was assembled with the goal of compiling the relevant data on the plant till date, this species being sparsely explored as compared to its other allies and species. The collection of selection of relevant data was made through a search using the keyword "Rumex," "R. hastatus". Pertinent data was collected from various major scientific databases including Medline, Scopus, ScienceDirect, Prota, SciFinder, PubMed, Google and Google Scholar, and plant taxonomy was validated by the databases *Mansfeld's Encyclopedia*, The Plant List, and PFAF. Various publication sites like Taylor and Francis, Elsevier and Springer used to collect the literature. Additional information on traditional use and botany was obtained from published books and MSc dissertation. A total of about 250 papers and articles were compiled which were published in different journals until May 2020. Data was analysed from different perspectives. All the literature was searched with the aim of obtaining data from different parts of the world and not specifically a particular region, thereby covering a vast and imperative field of knowledge. This was done to obtain the necessary data and research on the pertaining topic, until the present time. On the basis of 161 references, the present review was designed to provide a survey of the current state of knowledge of the phytochemistry and isolation; morphology and anatomy; nutritional importance; ethnobotany; and pharmacological activities of *R. hastatus*, as well as its traditional uses which have been supported by pharmacological investigations in order to identify its relevance as food and potential therapeutic applications and to show further directions of research (Table 6.1).

# 6.2 Ethnobotany

*R. hastatus* is quite rampant across the globe, and it is known by a variety of names in different languages.

Synonyms Rumex arifolius (List 2013) Rumex dissectus (Abbasi et al. 2011) Taxonomical Classification

Kingdom	Plantae
Subkingdom	Angiosperms
Division	Flowering plants
Class	Magnoliopsida
Subclass	Caryophyllidae
Order	Caryophyllales
Family	Polygonaceae
Genus	Rumex L.
Species	Hastatus D. Don

Conservation Status.

R. hastatus is included in IUCN Red List of threatened plants.

# 6.2.1 Habitat and Edible Part

Being a bushy shrub, *R. hastatus* is about 30–90 cm high (Singh et al. 2013a, b). The young shoots and leaves of this plant are edible (Sher et al. 2015; Seidemann 2005).

# 6.2.2 Ecology

## 6.2.2.1 Altitude

*R. hastatus* D. Don is mainly distributed at elevations of about 2400 m (Dutt et al. 2015). In Nepal, it however occurs at an elevation of 1000–2600 m (Manandhar 2002).

Country	Language	Name	References
India	Hindi	Kattameetha and almoru	Singh et al. (2014), Bisht and Sharma (2014)
India	Hindi	Khatapalak	Seidemann (2005),
India	Hindi	Churki, Bhilmora	Verma (2019), Dutt et al. (2015), Shedayi et al. (2014)
India	Hindi	Ammi, Khattiambi	Bhatia et al. (2018), Kumari et al. (2013)
India	Kumauni	Amlora, Chulmora	Verma (2019)
Pakistan	Hindko	Khitml	Abbasi et al. (2011)
Pakistan	Punjabi	Khattimal, Katamba	Verma (2019)
Pakistan	Urdu	KhattiButi	Verma (2019), Sher et al. (2015), Ullah
Pakistan	Pashto	Tarukay	et al. (2014)
Pakistan	Pashto	Teerwoki	Ullah et al. (2010)
Pakistan	Khowar	Sirkunzo	Ullah et al. (2014)
Nepal	Nepali	Kapu, Charimaal	Verma (2019)
Germany	German	Spiebigger, Ampfer	Seidemann (2005)
Europe	English	Arrowleaf dock, yellow sock, curled sock	Verma (2019)

**Table 6.1** Showing the different names of *Rumex hastatus* across the region

#### 6.2.2.2 Climate, Soil, pH and Lifespan

*R. hastatus* can grow in semi-shade (light woodland) or no shade. It can grow in wasteland, dry slopes and rocks (Dutt et al. 2015), shady slopes or dry streambeds (Manandhar 2002). The soil which is suitable for its growth includes light (sandy), medium (loamy) and heavy (clayey) soils and preferably well-drained soil. *R. hastatus* is an annual, biennial and perennial herb belonging to the family Polygonaceae. The common perennial herbs which grow in sour and acidic soils are members of this family (Zabta et al. 2003).

# 6.2.3 Distribution

*R. hastatus* is widely distributed in northeast Afghanistan, in north of Pakistan and southwest of China at an altitude of 700–2500 m (Qaiser 2001). In India the *Rumex* is widely distributed in Kumaun, Himachal Pradesh, Uttarakhand, Chandigarh, western Himalayas and Jammu and Kashmir (Zabta et al. 2003; Seidemann 2005; Paul and Chowdhury 2019). In Himachal Pradesh, the plant is found in Hamirpur, Lahual Chamba, Kullu and Spiti (Singh et al. 2014). It is also found in Mongolia, Russia, Tajikistan,Kazakhstan, Kyrgyzstan, Europe (Paul and Chowdhury 2019), Muree and Gilgit/Baltistan (Hameed et al. 2010).

#### 6.2.4 Phenology

Flowering time: May–June (Hameed et al. 2010). Fruiting time: March–November (Singh et al. 2014).

#### 6.2.5 Pollination

*R. hastatus* is a hermaphrodite (has both male and female organs), and it is mostly pollinated by wind.

# 6.2.6 Propagation

*R. hastatus* is propagated through seeds, which can be sown in spring. The seedlings are transferred in pots individually when they are large enough to handle and planted out in the summer. Division takes place in spring.

#### 6.2.7 Morphology and Description

Stem: The stem is herbaceous above and woody below and is erect and branched (Abbasi et al. 2011). The branches are finely grooved, purple-brown; branchlets are green and glabrous and about 50–90 cm tall (Anjen et al. 2003).

Leaves: The colour of the leaves is pale green with simple lobes which are directed outwards (Abbasi et al. 2011). The central lobe is narrowly triangular and linear. Leaves are solitary or fascicled; the blade is  $1.5-3 \text{ cm} \times 1.5-2 \text{ mm}$  and the petiole is 1.5-3.5 cm; apex is acute; basal lobes are curved; pedicel is slender and articulate below the middle; ocrea is fugacious and membranous (Anjen et al. 2003).

Roots: The roots are cylindrical, 0.5–0.9 cm wide and 3.5–6.5 cm long. The roots have transverse fissures and dark brown colour on upper surface. The inner surface is brown in colour and the fracture is short and mealy (Singh et al. 2013a, b).

Flowers: The flowers are numerous, small, pinkish in terminal paniculate clusters (Abbasi et al. 2011). They are polygamous. The petals of the male flowers are nearly uniform. In the female flowers, however, the outer petals are elliptic, and the inner ones are enlarged in fruit. Achenes are brown, ovoid, trigonous and shiny, ca. 2 mm. The valves are membranous, pinkish, orbicular or reniform, nearly pellucid, with small tubercle at the base; base is deeply cordate, apex is obtuse, and the margin is nearly entire (Anjen et al. 2003).

Fruits: *R. hastatus* bears one-seeded nutlet and fruit is pinkish (Abbasi et al. 2011).

# 6.3 Ethnomedicinal Importance

Traditional folk medical practices are empirical in nature; several million people with limited access to organized modern health-care centres depend on traditional systems of medicine to cater their primary health-care needs. Traditional systems of medicine are widely acknowledged to be effective and safe without any side effects (Farnsworth 1988). It has been ethnomedicinally used for various ailments. Various parts of the *R. hastatus* like leaves, roots, and stem are used in therapy. Different forms of preparation of this medicinal plant are employed (Table 6.2).

# 6.4 Nutritional Importance

In outlining the nutritional facts, the food quality and figures should be one of the major areas. *R. hastatus* is notable for its therapeutic importance; it is additionally utilized as nourishment for people. Leaves which are sour in taste are eaten raw as salad or made into chutney (Singh and Thakur 2014; Bhatia et al. 2018). To be concluded as a nutritional source and functional food, several authors assessed the nutritional and dietary properties of the plant and proved it as such (Ahmad et al. 2019). Many studies suggested that *R. hastatus* contains ample nutritional constituents and is a vital source of secondary metabolites, which can prove to be

Part used	Indication	Herbal preparation	Dosage form	References
Leaves	Toothache and gum healing	Dried powder	2 times a day	Rahman et al. (2016)
Stem, leaves, roots	Cancer	NAD <sup>a</sup>	NAD <sup>a</sup>	Alberto et al. (2016), Mishra et al. (2018)
Roots	Diarrhea and dysentery	Powder or paste or juice of root	2 tsp. 3 times a day (juice)	Coburn (1984), Pohle (1990), Manandhar (1995)
Roots and leaves	Wound healing in goats, cows and buffaloes	Powder	Given orally with flour for 4 days	Tariq et al. (2014)
Roots	Asthma	A sweet meal is made by mixing roots with <i>Quercus incana</i> and boiled with water. Sugar and semolina are added and cooked for 15 min	For children: 2–4 tsp., 2 times a day for 3–4 days. For adults: 8–10 tsp., 2–3 times a day, for 10–15 days	Abbasi et al. (2010)
Root	Rheumatism	Decoction	NAD <sup>a</sup>	Manandhar (2002), Abbasi et al. (2011), Shinwari and Gilani (2003)
Leaves and shoots	Diuretic	Leaves are directly eaten		Haq et al. (2011), Islam et al. (2006)
Roots, leaves	Jaundice and hepatitis	Root extract or fresh leaves are crushed along with water and sugar	One cup extract twice a day for 2 weeks	Haq et al. (2011), Singh and Thakur (2014), Singh and Attri (2014), Nadkarni and Nadkarni (1976)
Leaves	Appetizer	NAD <sup>a</sup>	NAD <sup>a</sup>	Sher et al. (2015)
Leaves	Blood purification	Leaves are directly eaten	NAD <sup>a</sup>	Ullah et al. (2010)
Root	Digestive ailments in cattle	Roots are taken and mixed with the powder of bark of <i>Quercus</i> <i>incana</i> and then boiled along with sugar and flour	Used for 10–15 days	Aziz et al. (2018)
Leaves	Blood pressure	Juice	NAD <sup>a</sup>	Singh and Thakur (2014)

**Table 6.2** Traditional therapeutic uses for *Rumex hastatus*

(continued)

Part used	Indication	Herbal preparation	Dosage form	References
Whole plant	STDs including AIDS	NAD <sup>a</sup>	NAD <sup>a</sup>	Vermani and Garg (2002), Zhang et al. (2009)
Roots	Cough and fever	Decoction	NAD <sup>a</sup>	Abbasi et al. (2010)
Leaves and young shoots	Carminative and purgative	NAD <sup>a</sup>	NAD <sup>a</sup>	Murad et al. (2011)
Roots	Piles	NAD <sup>a</sup>	NAD <sup>a</sup>	Gorsi and Miraj (2002)
Tuber	Tonsillitis and sore throat	Juice	Tuber is directly chewed	Ullah et al. (2014), Manandhar (2002)
Leaves	Giddiness and insanity	NAD <sup>a</sup>	NAD <sup>a</sup>	Pande et al. (2007)
Root	Skin disease	NAD <sup>a</sup>	NAD <sup>a</sup>	Manandhar (2002)
Leaves and shoots	Refrigerant and cooling agent	NAD <sup>a</sup>	NAD <sup>a</sup>	Hussain et al. (2006), Ahmad (2007).
Roots	Antiseptic	Root extract	NAD <sup>a</sup>	Singh and Attri (2014)
Roots	Headache	NAD <sup>a</sup>	NAD <sup>a</sup>	Kuete et al. (2013), Vasas et al. (2015)
Roots	Lungs bleeding	NAD <sup>a</sup>	NAD <sup>a</sup>	Gorsi and Miraj (2002)
Roots	Backache	Decoction of roots	NAD <sup>a</sup>	Abbasi et al. (2010)
Leaves and young shoots	Flavouring agent	Powder	NAD <sup>a</sup>	Murad et al. (2011), Ullah and Rashid (2007)
Roots	Bone fracture	NAD <sup>a</sup>	Orally	Ijaz et al. (2016)
Leaves	Irritation by stinging nettles, scorpion sting, snake bite	Paste	Paste is directly rubbed at the site	Khan et al. (2009), Shaheen et al. (2012)
Whole plant	Abortion			
Leaves	Cuts and wounds	Paste	Paste is directly applied	Bhatt and Negi (2006), Ahmad et al. 2016a, b
Whole plant	Bloody dysentery	Juice	NAD <sup>a</sup>	Manandhar (2002)
Leaves	Astringent	Juice	Leaves are directly eaten	Ali and Qaiser (2009)

Table 6.2 (continued)

(continued)

Part used	Indication	Herbal preparation	Dosage form	References
Leaf	Fungal	Paste	Leaf paste is	Uniyal and Shiva
	infection		applies at the	(2005)
			site	

Table 6.2 (continued)

<sup>a</sup>NAD not appropriately described

important for production of energy, growth and other functions. This plant is rich source of carbohydrates and fibre. Protein, moisture content, ash content and fats were also recorded (Hameed and Dastagir 2009; Singh et al. 2013a, b). Mineral elements though usually form a small portion of total composition of plant materials; they are nevertheless of great physiological importance particularly in the body metabolism (Bamiro et al. 1995). The elemental analysis in different parts of plant was carried out, and the concentrations are shown in Table 6.3 (Hameed et al. 2008).

# 6.5 Contraindication

Significant levels of oxalic acid are present in the plants, which gives the leaves of numerous individuals from this variety an acidic lemon flavour. Though completely alright in little amounts, the leaves ought not be eaten in huge amounts since the oxalic acid can secure up different supplements in the food, particularly calcium, along these lines causing mineral inadequacies. When the plant is cooked, the concentration of oxalic acid gets, however, decreased. Therefore, individuals with a propensity to rheumatism, arthritis, gout, kidney stones, or hyperacidity should take particular alert if considering this plant for their eating regimen, since it can bother their condition (Bown 1995).

# 6.6 Physicochemical Standardization

See Fig. 6.1 and Table 6.4.

#### 6.6.1 Macroscopical Characters

# 6.7 Phytochemistry

A comprehensive literature survey on phytochemical investigations of *R. hastatus* reveals that the chemical constituents reported from this plant are from different classes of secondary metabolites that include flavonoids, anthraquinones, phenolic

Plant part	C	0	Na	Mg	Al	Si	S	Р	CI	K	Ca	Fe
Root	44.78	44.78	0.38	0.55	0.44	1.20	0.33	0.27	0.95	3.21	2.77	0.52
Stem	42.48	42.48	0.59	0.46	0.20	1.32	0.45	0.27	1.61	6.10	1.51	0.58
Leaf	38.32	41.82	0.26	1.43	1.24	4.26	0.47	0.39	0.68	6.09	3.28	1.65
Petiole	36.11	50.34	1	1	2.12	4.56	1	1	1	3.17	3.70	1
Flower	47.57	48.00	1	0.77		0.79	1	1	1	1	2.87	1

Rumex hastatus
of
parts
different
of
ntal analysis e
Elemental
ble 6.3

Fig. 6.1 Aerial parts of Rumex hastatus at its flowering stage



Table 6.4 Physicocher	nic-Analytical parameter	Value (% W/W)
al determination of <i>Rum</i> hastatus	Ash values	
nusiulus	Total ash	13.78
	Water-soluble ash	0.58
	Acid-insoluble ash	0.77
	Sulphated ash	2.3
	Extractive values	
	Water soluble (hot)	12.6
	Ethanol soluble (hot)	4.90
	Water soluble (cold)	1.32
	Ethanol soluble (cold)	0.56
	Successive extractives	
	Petroleum ether	0.23
	Chloroform	0.38
	Ethyl acetate	2.2
	Methanol	14.3
	Aqueous	5.27
	Loss on drying	7.6
	Foaming index	<100
	Swelling index	5 mL
	Haemolytic value	10.48
	Crude fibre content	20.63

compounds, naphthalenes and various other constituents given in Table 6.5 (Zhang et al. 2009; Sahreen et al. 2014).

R. hastatus is differentiated by the presence of various secondary phytoconstituents. There are over 20 compounds which have been isolated from this plant. In roots the most abundant phytoconstituents are the anthraquinones and

Part used	Constituent	Extract	Reference
Bark	Tannins	Aqueous	Akhtar and Mirza (2018)
Bark	Coumarins	Methanol/ chloroform	Shafiq et al. (2017), Akhtar and Mirza (2018)
Bark	Alkaloids	Aqueous	Akhtar and Mirza (2018)
Bark	Saponins	Aqueous	Akhtar and Mirza (2018)
Whole plant	Steroid	Chloroform	Shafiq et al. (2017)
Whole plant	Flavonoid	Methanol	Shafiq et al. (2017)
Whole plant	Anthraquinone glycoside	Methanol	Shafiq et al. (2017)
Whole plant	Cardiac glycosides	Ethanol	Shafiq et al. (2017)
Root	Terpenoids	Methanol	Sahreen et al. (2015)
Root	Phlobatannin	Methanol	Sahreen et al. (2015)

Table 6.5 Qualitative phytochemical screening of Rumex hastatus

Table 6.6 Macroscopical characters

Characters	Observations	References
Taste	Leaves are sour in taste. The roots possess characteristic	Singh et al. 2013a, b,
	taste and odour	2014)
Size	Length 20-30 cm, diameter 2-5 mm	Wallis (1997)
Colour	Greenish yellow	
Shape	Regular branched	
Fracture	Short	
Odour	Characteristic	
Surface	Smooth	
characters		

their derivatives (Sharma et al. 2018). By UPLC-DAD method, various anthraquinone derivatives have been isolated from the methanol extract of aerial and root part. A phytochemical investigation on roots also led to the isolation of some naphthalenes by column chromatography as reported by Zhang et al. (2009). Apart from naphthalenes and anthraquinones, the other constituents isolated from *R. hastatus* are flavonoids. These are the polyphenolic compounds having potential antioxidant properties (Schlachterman et al. 2008). HPLC on the alcoholic extract of root and leaf and column chromatography of the root extract led to the isolation of some flavonoids (Zhang et al. 2009; Sahreen et al. 2011; Sahreen et al. 2014). Moreover, new fatty acid esters and phenolic glucosides were isolated and identified from the aerial parts of *R. hastatus* by column chromatography for the first time (Sultana et al. 2017). The isolated compounds and their nature are given in Tables 6.6 and 6.7, and their structures are shown in Figs. 6.2, 6.3, and 6.4.

Table 6.7 Chemi	Table 6.7 Chemical constituents isolated from Rumex hastatus			
Chemical class	Constituent	IUPAC	Extract	Reference
1. Flavanoids				
	(1a) Rutin	2-(3,4-Dihydroxyphenyl)-5,7-dihydroxy-3- [(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-	95% EtOH root extract	Zhang et al. (2009), Sahreen et al.
		[[(2R,3R,4R,5R,6S)-3,4,5-trihydroxy-6-		(2011)
		methyloxan-2-yl]oxymethyl]oxan-2-yl] oxychromen-4-one		
	(1b) Luteolin	2-(3,4-Dihydroxyphenyl)-5,7-	95% MeOH	Sahreen et al.
		dihydroxychromen-4-one	leaf and root	(2011, 2014)
			extract	
	(1c) Luteolin-7-O-glucoside	2-(3,4-Dihydroxyphenyl)-5-hydroxy-7-	95% MeOH	Sahreen et al.
		[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-	leaf and root	(2011, 2014)
		(hydroxymethyl)oxan-2-yl]oxychromen-4- one	extract	
	(1d) Kaempferol	3,5,7-Trihydroxy-2-(4-hydroxyphenyl)	95% MeOH	Sahreen (2011,
		chromen-4-one	leaf and root	2014)
			extract	
	(1e) Vitexin	5,7-Dihydroxy-2-(4-hydroxyphenyl)-8-	95% MeOH	Sahreen et al.
		[(2 <i>S</i> ,3 <i>R</i> ,4 <i>R</i> ,5 <i>S</i> ,6 <i>R</i> )-3,4,5-trihydroxy-6-	root extract	(2014)
		(hydroxymethyl)oxan-2-yl]chromen-4-one		
2. Anthraquinones		-	-	
	(2a) Emodin	1,3,8-Trihydroxy-6-methylanthracene-9,10-	80% MeOH	Liang et al. (2010),
		dione	root extract	Sharma et al.
				(0107)
	(2b) Physcion	1,8-Dihydroxy-3-methoxy-6-	95% MeOH	Liang et al. (2010),
		methylanthracene-9,10-dione	aerial extract	Sharma et al. (2018)
	(2c) Chrysophanol	1.8-Dihvdroxv-3-methvlanthracene-9.10-	80% MeOH	Sharma et al.
		dione	root extract	(2018)

6 A Review on Ethnomedicinal, Phytochemistry and Pharmacological Activities...

(continued)

	iacu)			
Chemical class	Constituent	IUPAC	Extract	Reference
	(2d) Emodin-8-Ο-β-D-glucopyranoside	<ol> <li>1,6-Dihydroxy-3-methyl-8-(((3R,5S,6R)- 3,4,5-trihydroxy-6- (hydroxymethyl)tetrahydro-2H-pyran-2-yl) oxy)anthracene-9,10-dione</li> </ol>	80% MeOH root extract	Sharma et al. (2018)
	(2e) Chrysophanol-8-O-β-D-glucopyranoside	1-Hydroxy-3-methyl-8-(((3R,5S,6R)-3,4,5- trihydroxy-6-(hydroxymethyl)tetrahydro-2H- pyran-2-yl)oxy)anthracene-9,10-dione	80% MeOH root extract	Sharma et al. (2018)
3. Phenolic glucosides	sides			
	( <b>3a</b> ) Hastatuside A	7-Hydroxy-5-methyl-4-[(2S,3R,4S,5S,6R)- 3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2- yl]oxychromen-2-one	95% EtOH root extract	Zhang et al. (2009)
	(3b) Hastatuside B	[(2R,3S,4S,5R,6S)-6-(7-acety]-8-hydroxy-6- methylnaphthalene-1-yl)oxy-3,4,5- trihydroxyoxan-2-yl]methyl acetate	95% EtOH root extract	Zhang et al. (2009)
4. Stilbenoids				
	Resveratrol	5-[( <i>E</i> )-2-(4-hydroxyphenyl)ethenyl]benzene- 1,3-diol	95% EtOH root extract	Zhang et al. (2009)
5. Napthalenes				
	(5a) Rumexoside	6-Acetyl-5-hydroxy-7-methyl-4- [(2S;3R,4S,5S,6R)-3,4,5-trihydroxy-6- (hydroxymethyl)oxan-2-yl]oxynaphthalene- 2-carboxylic acid	95% EtOH root extract	Zhang et al. (2009)
	(5b) Nepodin	1-(1,8-Dihydroxy-3-methylnaphthalen-2-yl) ethanone	95% EtOH root extract	Zhang et al. (2009)
	(5c) Torachryson-8-ylβ-D-glucopyranoside	1-(1-Hydroxy-6-methoxy-3-methyl-8- (((3R,5S,6R)-3,4,5-trihydroxy-6- (hydroxymethyl)tetrahydro-2H-pyran-2-yl) oxy)napthalen-2-yl)ethanone	95% EtOH root extract	Zhang et al. (2009)

Table 6.7 (continued)

		1-18-1(L3, 3K, 45, 3K, 45, 5K, 16, 2-3, -4, 10) droxymethyl)-4-1(25, 3R, 45, 55, 6R)-3, 4, 5- trihydroxy-6-(hydroxymethyl)oxan-2-yl] oxyoxan-2-yl]oxy-1-hydroxy-3- methylnaphthalen-2-yl]ethanone	95% EtOH root extract	Zhang et al. (2009)
6. Ester				
Fatty ester	(6a) Tridecyl oleate	Tridecyl (Z)-octadec-9-enoate	MeOH extract of aerial parts	Sultana et al. (2017)
Aromatic ester	(6b) 3',4'-Dihydroxybenzyl oleate	Heptadec-8-en-1-yl 2-(3,4-dihydroxyphenyl) acetate	MeOH extract of aerial parts	Sultana et al. (2017)
Sterol ester	(6c) β-Sitosteryl linoleate	[(35,85,95,10R,13R,145,17R)-17-[(2R,5R)-5- ethyl-6-methylheptan-2-yl]-10,13-dimethyl- 2,3,4,7,8,9,11,12,14,15,16,17-dodecahydro- 1H-cyclopenta[a]phenanthren-3-yl] (9Z,12Z,15Z)-octadeca-9,12,15-trienoate	MeOH extract of aerial parts	Sultana et al. (2017)
Steroidal ester	(6d) $\beta$ -Sitosterol 13-benzylether 3'-capriate	5-Ethyl-2-hydroxyphenyl deconate	MeOH extract of aerial parts	Sultana et al. (2017)
	(6e) $\beta$ -Sitosterol 3-benzyl ether 3'- oleate	5-Ethyl-2-hydroxyphenyl octadec-9-enoate	MeOH extract of aerial parts	Sultana et al. (2017)
	(6f) $\beta$ -Sitosterol 3-(3',4'-dihydroxybenzyl)eth er 3'-linoleate	$\beta$ -Sitosterol 3-(3',4'-dihydroxybenzyl)ether 3'-linoleate	MeOH extract of aerial parts	Sultana et al. (2017)
Steroidal tetragalactoside	(6g) $\beta$ -Sitosterol- $3\beta$ -benzyl $3'$ -oxy- $3'$ -O- $\beta$ -D-galactopyranosyl-(6a $\rightarrow$ 1b-)O- $\beta$ -D-galactopyranosyl-(6b $\rightarrow$ 1c)-O-D-galactopyranosyl-(6c $\rightarrow$ 1d)-O- $\beta$ -D-galactopyranosyl-2d-capriate	β-Sitosterol-3β-benzyl 3'-oxy-3'-O-β-D- galactopyranosyl-(6a $\rightarrow$ 1b-)O-β-D- galactopyranosyl-(6b $\rightarrow$ 1c)-O-D- galactopyranosyl-(6c $\rightarrow$ 1d)-O-β-D- galactopyranosyl- 2d-capriate	MeOH extract of aerial parts	Sultana et al. (2017)
7. Others				
Phenolic pentaxyloside	(7a) 1-Undecan oxy-3-phenol-3-O- $\beta$ -D- xylopyranosyl-(2a $\rightarrow$ 1b)-O- $\beta$ -D- -xylopyranosy 1-(2b $\rightarrow$ 1c)-O- $\beta$ -D-	$\begin{array}{l} 1 \text{-Undecan oxy-3-phenol-3-O-}\beta\text{-D-} \\ xylopyranosyl-(2a \rightarrow 1b)\text{-O-}\beta\text{-D-} \\ xylopyranosyl-(2b \rightarrow 1c)\text{-O-}\beta\text{-D-} \end{array}$	MeOH extract of aerial parts	Sultana et al. (2017)

(continued)
6.7
Table
Ë

Chemical class Constituent	Constituent	IUPAC	Extract	Reference
	xylopyranosyl-(2c $\rightarrow$ 1d)-O- $\beta$ -D- xylopyranosyl-(2d $\rightarrow$ 1e)-O- $\beta$ -D-	xylopyranosyl-( $2c \rightarrow 1d$ )-O- $\beta$ -D-xylopyranosyl-( $2d \rightarrow 1e$ )-O- $\beta$ -D-		
	xylopyranoside,			
α-Γ-	(7b) $\alpha$ -L-glucopyranosyl-(2a $\rightarrow$ 1b)-O- $\alpha$ -L-	$\alpha$ -L-glucopyranosyl-(2a $\rightarrow$ 1b)-O- $\alpha$ -L-	MeOH extract	Sultana et al.
Hexaglucoside	glucopyranosyl-(2b $\rightarrow$ 1c)-O- $\alpha$ -L-		of aerial parts	(2017)
derivative	glucopyranosyl-( $2c \rightarrow 1d$ )-O- $\alpha$ -L-			
	glucopyranosyl-(2d $\rightarrow$ 1e)O- $\alpha$ -L-	00		
	glucopyranosyl-(6e $\rightarrow$ 1f)-O- $\alpha$ -L-			
	glucopyranoside	glucopyranoside		



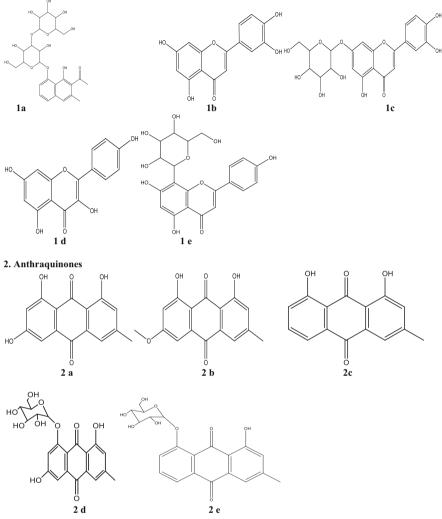
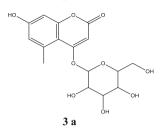
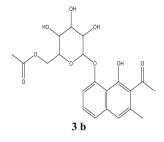


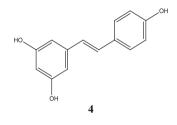
Fig. 6.2 Chemical structures of some isolated compounds from various extracts of R. hastatus

# 3. Phenolic glucosides

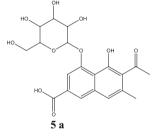


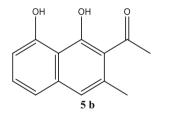


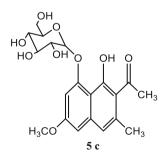




5. Napthalenes







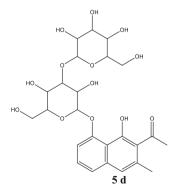
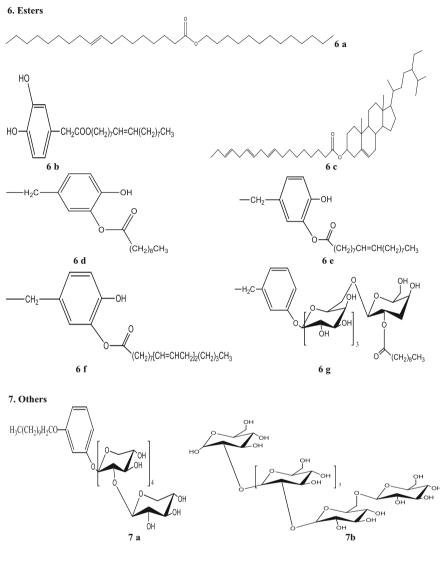


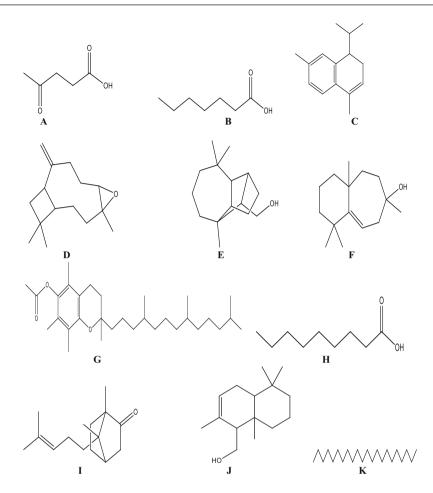
Fig. 6.2 (continued)





# 6.8 Pharmacology

Plants are well-known excellent perspectives for the discovery of new therapeutical products. The World Health Organization (WHO) estimates that 65–80% of the population of the developing countries depends on medicinal plants for basic pharmaceutical care (Singh et al. 2013c). The fact the plants are prominent origins



**Fig. 6.3** Chemical structures of some identified components of essential oil of *R. hastatus.* (a) Levulinic acid; (b) Enanthic acid; (c)  $\alpha$ -calcorene; (d) Caryophyllene oxide; (e) Isolongifol; (f) Widdrol; (g) Pelargonic acid; (h) Vitamin; (i) Campherenone; (j) Drimenol; (k) Docosane

for new bioactive principles is established and hence has wide utility in therapeutics (Kinghorn et al. 2011). Different parts of the medicinal plants have been utilized for various therapeutic purposes in folk medicine. Indeed, many of the plants and their preparations have been recorded to be used to treat different maladies and promote healing (Sen et al. 2010).

# 6.8.1 Anti-Nociceptive

The occurrence of tissue damage to the body is informed by means of a warning system called as pain (Nickel et al. 2012). Since pain modulation is an intricate

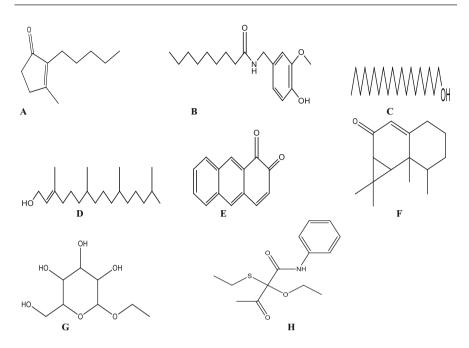


Fig. 6.4 Chemical structures of anticancer compounds identified in the GC-MS of chloroform fraction of *R. hastatus.* (a) Dihydrojasmone; (b) Nonivamide; (c) Eicosanol; (d) Phytol; (e) Anthracenedione; (f) Aristolone; (g) Ethyl alpha-d-glucopyranoside; (h) 2-Ethylthio-2-ethoxy-3-oxo-N-phenylbutanamide

process involving many mediators and receptors at the peripheral and central levels, its management using the available analgesics could not completely thrive well. Nociceptive neuron sensitivity is adjusted by a large variety of mediators in the extracellular space which either include neurotransmitters or neuromodulators in turn activating a large number of receptors and therefore a cascade of events controlling the perception of pain (Julius and Basbaum 2001; Scholz and Woolf 2002; Lewin et al. 2004; Hucho and Levine 2007; List 2010). Identification of the components involved in the complex process is undertaken worldwide, and attempts are being made to develop new agents that act on these components (Bektas et al. 2015). Analgesic drugs such as opiates that are currently available are not useful in all the cases as their beneficial effects are superseded by their various adverse effects (Zendehdel et al. 2011). Therefore, there is an urgent need of new analgesic drugs with promising pharmacological actions. In addition, the revelation of plant-based drugs with high restorative viability, however less or, perhaps, no toxicity, may be beneficial as substitutions to customary analgesics like narcotics and NSAIDs (Sen et al. 2010). Singh et al. (2013a, b) evaluated the anti-nociceptive potential of R. hastatus. The study involved the use of acetic acid-induced writhing method, tail flick model and formalin-induced pain model in mice, for establishing antinociceptive activity of the ethanol and aqueous extract of stem and root, using standard drugs. The study revealed that the minimum (200 mg/kg) and maximum (400 mg/kg) doses of the aqueous and ethanol extract of root and stem showed significant inhibition in mice in acetic acid-induced abdominal constrictions. Maximum inhibition was shown by the ethanolic extract (400 mg/kg) of root in abdominal constrictions in mice induced by acetic acid, and the effect was comparable to that produced by indomethacin. Taken together, the above results indicated that peripheral and central analgesic activity is exhibited by aqueous and ethanol extracts of both root and stem of *R. hastatus*. However, out of aqueous and ethanolic extracts, the former is more active. Both phases of the formalin-induced pain are inhibited with a more pronounced effect on the second than the first phase. Both central and peripheral effects are confirmed from the study. The results observed from both tail flick test and acetic acid-induced abdominal constrictions were found to be significant.

# 6.8.2 Antipyretic

When the body reaches to a temperature above normal, the condition is called as fever or pyrexia. An antipyretic is a kind of drug that will forestall or decrease fever by bringing down internal heat level from a raised state. Nonetheless, the "normal" temperature can fluctuate from individual to individual inside specific boundaries. By and large, most non-steroidal anti-inflammatory drugs (NSAIDs) work by repressing prostaglandin synthetase inside the nerve centre (Deshpande et al. 2003). Most of the antipyretic drugs cause inhibition of prostaglandin E2 (PGE2) biosynthesis and Cox-2 expression which in turn causes reduction in elevated body temperatures. Most of these agents are toxic to the hepatic cells, cortex of brain, glomeruli, and heart muscles, but they have high selectivity to inhibit Cox-2 in an irreversible manner, while the selectivity is lower for the natural Cox-2 inhibitors but with lesser toxic effects (Bouldin et al. 1999). Microbes including bacteria and viruses are the causative agents of fever setting off the body's defence system (Deshpande et al. 2003). Pain and pyrexia are frequently associated with infections and ailments. The drugs generally prescribed include the non-steroidal anti-inflammatory drugs (NSAIDs) which however have huge gastrointestinal side effects like peptic ulcer perforations, bleeding and obstructions restricting their uses in clinical settings (Ofman et al. 2002; Castellsague et al. 2012). Since there are fewer propensities for herbal drugs to cause any toxicity, therefore there is a huge demand of the same. Further there is an increase in the health-care costs which in turn influences people to find newer and natural low-cost alternatives (Bouldin et al. 1999).

Singh et al. (2013a, b) evaluated stem and roots of *R. hastatus* for its antipyretic activity using yeast-induced pyrexia in rats and was performed on the ethanolic and aqueous extracts of the plant. In hyperthermic rats, at the dosage of 400 mg/kg, the ethanolic extracts of both the parts produced a pronounced antipyretic effect in a dose-dependent manner when compared with untreated rats. The results were proportionate with the standard drug, paracetamol (150 mg/kg). This consequently confirmed that *R. hastatus* possessed significant antipyretic potential.

#### 6.8.3 Anti-Inflammatory

The act of utilizing plants, their parts, or concentrates as anti-inflammatory mixture is known since ancient times (Khalifa 2004). When infectious microorganisms, for example, viruses, fungi or bacteria, attack the body, dwell specifically in tissues and additionally flow in the blood, inflammation takes place (Artis and Spits 2015; Isailovic et al. 2015; Pedraza-Alva et al. 2015). There are two principal classes of inflammatory substances: anti-inflammatory mediators and pro-inflammatory mediators. Moreover, some mediators possess both properties of anti- and pro-inflammation (Vignali and Kuchroo 2012). Cytokines (e.g. tumour necrosis factor,  $\alpha$  interleukins and interferons), chemokines which include monocyte chemoattractant protein 1 and eicosanoids (e.g. leukotrienes and prostaglandins) are widely concentrated in relationship with the pathological states among the cellular pathways and inflammatory mediators. A significant pro-inflammatory cytokine which is discharged from different cells and applies numerous cell effects includes the tumour necrosis factor (TNF)- $\alpha$ , which is an effective inflammationregulating transcription factor (Montgomery and Bowers 2012; Zelová and Hošek 2013). Nevertheless anti-inflammatory medications are frequently connected with serious toxic effects, for example, peptic ulcers and gastrointestinal bleeding (Alwashli et al. 2012). Many natural drugs isolated from medicinal plants are considered as successful and more secure for the treatment of different ailments including inflammation (Stevenson and Hurst 2007).

The aqueous and ethanol extracts of roots and stem of *R*. hastatus were evaluated for anti-inflammatory activity (Singh et al. 2013a, b). This in vivo study made use of two common models cotton pellet-induced granuloma and carrageenan-induced paw oedema method at a dose of 400 mg/kg; the ethanolic concentrates of both root and stem (400 mg/kg) of *R. hastatus* happened to show more critical mitigating action than the lesser 200 mg dosages, in experimenting animals, following 3 hours of medication treatment. Dose-dependent anti-inflammatory action was prominent, which was comparable to the standard drug indomethacin, following 6 hours of drug treatment. Further, inhibition in rise of dry weight of cotton pellet-induced granuloma was shown by stem as well as root extracts of R. hastatus in the second method used. However, ethanol extract of the root showed the greatest per cent inhibition at 400 mg/kg of drug treatment, with the ethanol extract of the stem at the same dose trailing behind and the aqueous extract being least effective. The carrageenan-induced paw oedema method was used to evaluate the acute inflammatory activity. Carrageenan (a sulphated polysaccharide belonging to the family Rhodophyceae) is obtained from a seaweed and is most widely used to produce biphasic acute inflammation. The liberation of serotonin and histamine marks the first phase (about 1 hour), while the liberation of prostaglandin, bradykinin, lysosome and protease marks the second phase, which exceeds 1 hour. The second accelerating phase of swelling relation is measured after 3 hours, wherein prostaglandins play the significant role (Hernández-Pérez and Rabanal 2002). This study reveals that R. hastatus extracts exhibited inhibition of oedema, through all the phases of inflammation; nonetheless the effectiveness in the proliferative phase of inflammation was confirmed by the prominent contraction of cotton pellet granuloma by all the extracts. The outcome of this study strongly indicates the antiinflammatory potential of *R. hastatus* which however requires more exploration.

# 6.8.4 Antioxidant and Antiradical

Impressive consideration has been given to phenolics and flavonoids within enzymatic and non-enzymatic antioxidant components. Plants are expected to be a source of common antioxidant principles exhibiting significant antioxidant action and may assist with ensuring cells against the oxidative harm brought about by free radicals (Kähkönen et al. 1999). The hydroxyl and conjugated ring structures which are present in phenolic compounds have the ability of preventing oxidation through hydrogenation or complexing with oxidizing species and in turn scavenging free radicals (Shahidi et al. 1992). Along these lines, the medicinal plants have promising antioxidant compounds to be tried as antiradical drugs for the cure of illnesses arising because of oxidative pressure. The valuable impacts of antioxidant compounds have been confirmed in a few trial and epidemiological investigations (Ruch et al. 1989; Babu et al. 2001).

Sahreen et al. (2011) conducted a study to evaluate the antioxidant potential of different fractions of leaves of *R. hastatus*. The study found out that the ethyl acetate fraction of the plant contained high amount of total polyphenolics and exhibited promising potential of scavenging for ABTS radicals and hydroxyl radicals as well as prevention of  $\beta$ -carotene linoleic acid peroxidation, while butanolic fraction contained high flavonoid content and reflected most promising iron chelation, DPPH, and phospho-molybdate scavenging activity. However, scavenging of hydrogen peroxide by the chloroform fraction reflected its most potent antioxidant potential, although the antioxidant potential of methanolic and ethyl acetate fractions was found to be lower than that of standard.

Since no antioxidant studies had been conducted on the roots of *R. hastatus*, therefore (Sahreen et al. 2015) hypothesized that being an important ethnopharmacological part of the plant, the roots must have potential antioxidant activity, and henceforth designed an in vitro study on the same using different fractions. The results revealed that all the isolated fractions of the extract exhibited dose-dependent activity. The methanol and the butanol fractions showed the highest antioxidant potential, except hydrogen peroxide radical scavenging assay where highest scavenging activity was found in the chloroform fraction. Significant betacarotene linoleic acid was found in the aqueous fraction, with the least potential shown by ethyl acetate and n-hexane fractions. Further analysis in both the studies carried on by Sahreen et al. on the ethyl acetate fraction suggested the presence of kaempferol, luteolin, rutin and luteolin-7-O-glucoside and vitex might probably be the source of antioxidant potential of the plant (Sahreen et al. 2011; Sahreen et al. 2015).

Similar findings were found by Ahmad et al. (2015), when their study on the antioxidant potential of R. *hastatus* revealed strong antioxidant capability of crude

saponin and flavonoid extract obtained by fractionation of methanol extract of *R. hastatus*; ABTS free radical scavenging, DPPH, and hydrogen peroxide assays were used. Moreover the current study showed that the flavonoid fraction of the plant possessed highest antioxidant activity, and since the previous studies had revealed that the fractions exhibiting promising antioxidant potential contained flavonoids and phenols, it goes parallel with the fact that they may be credible for the drug possessing antioxidant potential, as reported (Sahreen et al. 2011; Afzal et al. 2014).

In one more investigational study executed by Ahmad et al. (2016a, b), the volatile oil of *R. hastatus* was put under surveillance, the results of which proved that the volatile oil of the plant was an antioxidant source in the free radical scavenging assay, which was significant and comparable with the positive control. Taken together, the results of all the studies clearly demonstrate the high antioxidant potential of *R. hastatus*, which after subjecting to development of new drug candidates can be helpful in numerous pathological states linked to oxidative stress and generation of free radicals.

#### 6.8.5 Hepatic Protective Effect

The liver plays out an assortment of significant host safeguard and metabolic activities that incorporate gluconeogenesis, detoxification, production of acute phase proteins, expulsion of endogenous mediators, emission of favourable pro-inflammatory cytokines, etc. (Pastor et al. 1995). It is a remarkable organ because of the fact that the loss of liver cells due to medication toxicity or different abuse can be overwhelmed by recovery (Mehendale 2005). Numerous reports uncovered that the free radicals created during hepatic damage exhausted the levels of the enzyme and non-enzyme framework which are connected to liver wounds (Liu et al. 2006).

A study was designed by Sahreen et al. (2013) on the leaves of *R. hastatus* to analyse their hepatoprotective activity, using methanol and its fractioned extracts hexane, butanol, chloroform, ethyl acetate and aqueous extract against carbon tetrachloride (CCl<sub>4</sub>), the agent causing hepatotoxicity in rats. The glutathione reserves as well as the activity of enzymes involved in oxidation were depleted, while the lipid peroxides, DNA and histopathological injuries were elevated by administration of CCl<sub>4</sub>. Moreover the hepatic damage like necrosis, fatty changes, Kupffer cell infiltration and cellular hypertrophy was also caused. When the different fractions of leaves of *R. hastatus* (200 mg/kg body weight) were supplemented, attenuation in the toxicity was noted in the liver tissues as the numerous parameters like enzymatic, histological and serological were normalized. Per cent DNA fragmentation and ladder assay were performed which clearly indicated the amelioration of hepatic damage and oxidative stress induced by CCl<sub>4</sub>.

Another similar study was undertaken by Sahreen et al. (2017) in order to explore the hepatoprotective nature of *R. hastatus* roots, using methanol and ethyl acetate extracts. Again,  $CCl_4$  was used as the agent to trigger hepatotoxicity which was checked over by different liver function markers including alkaline phosphatase,  $\gamma$ -glutamyltransferase, aspartate transaminase, alanine transaminase and lactate dehydrogenase. Also lipid profile was assessed by the amount of triglycerides, HDL, LDL and serum TC. Furthermore DNA and cell damages and enzyme activities were also assessed. After the co-administration of the different extracts of roots of *R. hastatus*, the lipid profile, liver function markers and cellular and DNA damages were restored in rats. The oxidation status was also improved revealing that the roots of *R. hastatus* are a strong source of antioxidant activity and have the capacity to restore liver from the toxicity and fibrosis caused by CCl<sub>4</sub>. This is a clear indication that the plant reflects promising treatment of ailments regulated by markers controlling oxidation as well as free radical-mediated pathological states and hence is a good drug candidate to be explored for hepatic ailments due to its hepatoprotective potential.

#### 6.8.6 Anticholinesterase

The most widely recognized neurological diseases are depression, Alzheimer's disease, epilepsy, anxiety, madness, susto (fear), numbness, insomnia, migraine, headache, stress, Parkinson's disease and so on (Bourbonnas-Spear et al. 2005; Aarsland et al. 2008). Depending on their traditional knowledge, large quantities of normal therapeutically active components have been extracted from different medicinal plants. For instance, the Ginkgo biloba was scientifically verified as anti-ageing and was customarily seen as memory enhancer, which however was established for treating Alzheimer's disease (mild or moderate) (Burkard and Lehrl 1991; Kanowski et al. 1996; Le Bars et al. 1997). Essential oils are comprehended to possess major significance as they can neutralize free radicals, which are produced in the process of metabolism of oxygen (Ruberto and Baratta 2000). ROS are liable for many ailing conditions which include nervous diseases and oxidative pressure (Kumar et al. 2012). They are also known for their scavenging potential and effectiveness in many cognitive conditions. Among the psychological issues, the disease called Alzheimer's disease (AD) is widely recognized in old individuals (Mukherjee et al. 2007). One helpful methodology for AD is to build the centralization of the synapse (acetylcholine) by hindering the protein (acetylcholinesterase) liable for its breakdown. Different medications of plant origin as well as chemical origin have been utilized for the regulation of Alzheimer's and different apprehensive diseases (Small et al. 1997).

Ahmad et al. (2015) conducted a study aiming to investigate the potential of *R. hastatus* using various fractions, viz. chloroform, n-hexane, ethyl acetate, crude saponins, aqueous fraction, methanol extract and flavonoids for acetylcholinesterase and butyrylcholinesterase inhibition at various concentrations (125, 250, 500, 1000  $\mu$ g/mL) in order to substantiate its traditional uses in neurological disorders, using Ellman's spectrophotometric analysis. Concentration-dependent cholinesterase inhibition was shown by all the extracts with radical scavenging potentiality. Saponins and flavonoids reflected the highest potential inhibition, while moderate to high potential inhibition was reflected by the subsequent fractions.

In the same manner, potential against butyrylcholinesterase inhibition of different plant extracts was also carried out. Therefore, the strong anticholinesterase potential of saponin and flavonoid extracts as well as the other fractions of R. hastatus confirmed claimed ethnomedicinal properties and established the potential of R. hastatus in the era of nervous disorders. Also the activity of extracts was comparable to that of positive control, galantamine. Furthermore, the study also revealed that the saponin and the flavonoid extracts exhibited the most prominent activity based on the enzyme (AChE, BChE) inhibition as well as radical scavenging potential, which also directed to the fact that the plant is a potent source of anticholinesterase compounds, which are most probably the saponins and flavonoids. This as well is supported by the fact that the saponins are also significant secondary metabolites, verified to be beneficial in different pharmacological activities. For example, traditional Chinese drugs are a source of saponins, demonstrating remarkable antioxidant potential (Xi et al. 2008). Also the saponins known as bacosides isolated from Bacopa monnieri and the flavonoids known as ginkgo flavon glycosides isolated from Ginkgo biloba possess the said activities (Das et al. 2002).

In another study conducted by Ahmad et al. (2016a, b), the isolation of essential oil from *R. hastatus* was done, which after assessment indicated that the plant is a potential source of significant volatile principles possessing anticholinesterase potential. The essential oil was subjected to the anticholinesterase assay performed against acetyl cholinesterase (AChE) and butyrylcholinesterase (BChE) at different concentrations ( $62.5-1000 \ \mu g/mL$ ). The results were however comparable with the positive control taken as galanthamine. Results of the study strongly indicate the anticholinesterase potential of essential oil. A clear conclusion could be drawn that *R. hastatus* as an important source of constituents may perhaps result in therapy development and neutralize free radicals as well as rehabilitate neurodegenerative disorders. The most common constituents isolated from *R. hastatus* during the study include the following: palmitic acid, methyl palmitate, myristic acid, capric acid, pelargonic acid, drimenol, cetane, docosane, velleral, isolongifolol, neophytadiene, acetone, widdrol and levulinic acid. After exploring the different constituents of essential oil obtained, it was concluded that the significant anticholinesterase activity of the volatile oil was due to the presence of various phytoconstituents present. It was also found that the prominent activity of R. hastatus might be attributed to its hydrophobic nature due to its significant affinity towards the hydrophobic site of AChE, which is also the active site (Steinberg et al. 1975; Loizzo et al. 2008). Various phytoconstituents of volatile oil have also been brought to light by other investigators previously, possessing antiradical and anticholinesterase activities (Yi and Kim 1982; Stamatis et al. 1999; Decker et al. 2005; Mehendale et al. 2008; Öztürk et al. 2011; Sengupta and Ghosh 2012).

#### 6.8.7 Anti-Tumour and Angiogenic Potential

Tumour is primarily described by unusual and unnecessary multiplication of cells, which dynamically disturb the cells in the neighbourhood. The formation of new blood vessels which is called the angiogenesis likewise happens alongside the multiplication of cells which happens in ordinary tissues very rarely, besides embryogenesis and wound repairing (Folkman 1992). It has been clearly showed that exorbitant angiogenesis prompts a few pathological states including ovarian cyst atherosclerosis, cancer, arthritis and osteomyelitis (Carmeliet and Jain 2000). Different chemotherapeutic substances are utilized against the pathophysiological conditions, which are angiogenesis dependent, particularly against tumour. Due to plenty of dangerous impacts of these agents, their use is discouraged, and the researchers are attempting to investigate bioactive substances obtained from medicinal plants which might be used in the management of tumour and other deadly disorders (Coats 1994; LaPoint et al. 2011; Ashton 2012). Plants, which are the most significant source of therapeutic substances, have been gaining substantially more consideration of the analysts for their great viability and low poisonousness (Shah et al. 2015). Potato tumour measure has been directed on a few plants of different families with remarkable outcomes (Hague et al. 2000; Hussain et al. 2007). High anti-angiogenic action has likewise been shown by a few species of plants using chorioallantoic membrane (CAM) assay (MiuRA et al. 2002; Wang et al. 2004). Numerous bioactive substances obtained from different plants have been assessed against tumour, showing great potential (Da Rocha et al. 2001).

Sahreen et al. (2015) conducted a study in order to evaluate the anti-tumour and anti-antigenic activities of different extracts of *R. hastatus* using potato tumour assay. The results simplified that the methanolic extract showed effective anti-tumour potential followed by n-butanol, aqueous and chloroform. Further ethyl acetate and n-hexane fraction showed the least potential. The outcome of this study was found to be in accordance to other studies (Fatima et al. 2009) establishing that it is the concentration of the samples on which the tumour inhibition rates depend upon. Findings of the study confirmed the preceding reports of (Islam et al. 2010; Ashraf et al. 2015) confirming that the anti-tumour potential is attributed to the bioactive principles of the plant as well as their strong solubility with appropriate solvent and also proving the statement of (Fatima et al. 2009) that tumour induction was changeable in case of different extracts of solvent.

In another study performed by Ahmad et al. (2016a, b), the anti-tumour and antiantigenic potential of crude saponins, methanol extract and various fractions of R. *hastatus* were evaluated, using potato tumour assay. The study found that the extracts exhibited notable potential in the assay. However the chloroform and saponin fractions exhibited the most prominent activities which lead to the conclusion that these might probably be potential targets for the isolation of bioactive compounds possessing anti-neoplastic action. It was noted that the anti-tumour activity possessed by some extracts of R. *hastatus* is more prominent than some previously known instances from various plants (Haque et al. 2000; Hussain et al. 2007). Similarly, the anti-antigenic potential of the plant is comparable with different plants with strong antiangiogenic activities (Wang et al. 2004) as well as higher than the formerly reported daidzein and genistein (Krenn and Paper 2009). Furthermore it is evident from the above discourse that saponin and the chloroform extracts being the most active might be the potential sources of active compounds, which can strongly ameliorate metastasis and neo-vascularization.

#### 6.8.8 Cytotoxic Activity

One of the most challenging diseases nowadays throughout the world is cancer which is one of the leading causes of mortality. A few variables have been accounted which cause hyperproliferation and malignancy (Borrego-Soto et al. 2015). The free radical-prompted lesions have been considered as one of the main sources of malignant growth (Valko et al. 2006). Different restorative systems are followed for the therapy of malignancy; however, chemotherapy has been considered as the most worthy and positive prognostic helpful methodology (Mohamed et al. 2015). Because of the useful and safe nature of all the medications from normal sources being biodegradable are favoured over the manufactured ones (Coats 1994). Different subsidiaries of natural anticancer medications are additionally being integrated and used against cancer (Jordan and Wilson 2004).

(Kamal et al. 2015) executed a study to establish the cytotoxic activity of crude saponins and methanolic extract as well as the subsequent fractions of R. hastatus against brine shrimps. Excellent activity was shown by the saponin extract at the concentration of 1000, 100 and 10  $\mu$ g/mL. Among the fractions, the chloroform fraction also showed prominent cytotoxicity. However, ethyl acetate and crude methanol extract showed similar lethality as LC50 of 90  $\mu$ g/mL. Further aqueous fraction and n-hexane fraction showed mediocre potential. The lethality caused in brine shrimps was notably highest in the case of the saponin extract, in which evidence is that anticancer properties might be attributed to these compounds. Moreover, it is also noted that the ethyl acetate and chloroform fraction showed remarkable cytotoxicity, which directs to the fact that the compounds (saponins and other components) responsible for the cytotoxicity are present in good amounts in these extracts. There is a positive correlation existing between the brine shrimp lethality assay and human nasopharyngeal carcinoma (KB cell line) as reported by Mclaughlin et al. (1998), Abdul et al. (2009), Fatima et al. (2009). All these results confirm the cytotoxic potential of different extracts of R. hastatus.

On the other hand, another study was conducted by Sahreen et al. (2015) to confirm the cytotoxic activities of *R. hastatus* roots, again using brine shrimp assay. Different fractions were evaluated for cytotoxicity, and the potential was found to be according to the following pattern: butanol > methanol > chloroform > aqueous > ethyl acetate > *n*-hexane. The earlier reports of (Hussain et al. 2010) were found in uniformity with the above findings, who also established that the methanol extracts

of *Rumex* species showed prominent cytotoxic potential and the plant was highly active against larvae of brine shrimp.

A more explained study was done by Ahmad et al. (2016a, b), to evaluate cytotoxic potential of this plant against NIH/3T3 and HeLa cell lines using different extracts of *R. hastatus*. It was aimed to find out the most active fraction of the plant, as well as the identification of bioactive constituents, causing cytotoxicity. It was found that all the solvent fractions were active against both cell lines but the chloroform fraction was prominent in activity against both cell lines. Furthermore the noted IC50 values along with the GC-MS analysis of chloroform fraction confirmed the presence of most of the active constituents in this fraction only, which also indicated the fact that this fraction should perhaps be the target for isolation of components useful in cytotoxic therapy to a large extent. The analysis of the chloroform extract also revealed some of the compounds possessing anticancer activities in *R. hastatus* including dihydrojasmone, phytol, anthracenedione, eicosanol, silane, aristolone, nonivamide, ar-tumerone, ethyl  $\alpha$ -d-glucopyranoside and sitostenone. (Komiya et al. 1999), for instance, reported that, in human lymphoid leukaemia Molt 4B cells, phytol has been known to induce programmed cell death. Similarly (Flescher 2005) reported dihydrojasmone, a new family of anticancer agents, which is also one of the member of jasmonate family. In nanoparticletype drug delivery system, silane has been confirmed as a remarkable agent, for anticancer compounds. Apart from anticancer activity, nonivamide a skin permeation enhancer used in various ointments etc. is also present in the chloroform fraction of the plant (Fang et al. 2001). Also, C20 aliphatic alcohols have been found useful in the management of hyperproliferative skin disorders, and eicosanol, present in R. hastatus, is also a C20 alcohol. Pope et al. (2001) and Firestone and Sundar (2009) also reported two sesquiterpenes, aristolone and Ar-tumerone, which show the cytotoxic potential. Similarly vitamin E, a phenolic compound with prominent free radical scavenging and cytotoxic activity, has also been reported (Baldioli et al. 1996; Yu et al. 2009; Salvador et al. 2013). The steroids extracted from plant extract were used against cancer cells. Therefore it shows that sitostenone, a natural steroid found in the plant extract after analysis, might also be responsible for the cytotoxic activity. Compiling all the results, it is very much evident that the chloroform fraction of R. hastatus possessed the most prominent activity against the two types of cell lines. Concluding from the above discourse, it's quite obvious that R. hastatus is a potent source of cytotoxic compounds, hence can be explored for the development of different drugs in this direction.

#### 6.8.9 Antidiarrhoeal Activity

High death rate in developing nations is due to diarrhoea where more than 5,000,000 children under 5 die yearly from serious diarrhoeal infections (Heinrich et al. 2005). It is described by frequent recurrence of solid discharge, stomachache and wet stool (Maiti et al. 2007). Diarrhoeal ailment is a main source of mortality and bleakness, particularly in kids in developing nations (Mani et al. 2010). A dominant part of

diarrhoeal cases are because of bacterial enteropathogens, diarrhoeagenic *Escherichia coli* being the most widely recognized reason in developing nations. The traveller's diarrhoea is caused by two important bacterial classes of diarrhoeagenic *E. coli*, mostly enteroaggregative and enterotoxigenic (Adachi et al. 2001) and intrusive bacterial microorganisms like *Campylobacter*, *Shigella* and *Salmonella* (Hoge et al. 1998). Thusly, there is a pressing requirement for the increase of research into plants claiming medicinal value in diarrhoeal infections (Mohammed et al. 2009). For the management of diarrhoeal infections, a large population of developing nations largely depend on natural medications. Considering this reality the World Health Organization has established a diarrhoeal disease control program, which incorporates investigations of conventional therapeutic practices, increasing health education and avoidance of the disease (Shaphiullah et al. 2003).

Very less research has been reported regarding the antidiarrhoeal activity of *R. hastatus*, though a study was undertaken by Shakuntala et al. (2011) to confirm the same using the ethanolic extract of the roots of *R. hastatus*. In normal gastrointestinal models of rats at 100, 150 and 200 mg/kg body weight, castor oil-induced diarrhoea was followed. The incidence, severity and the typical parameters of diarrhoea were reported to decrease with the increase in the doses of the ethanolic extract of the plant at 100, 150 and 200 mg/kg body weight. The prominent antimotility potential shown by the extract was comparable to the standard, atropine sulphate. This provides a basis to conclude that *R. hastatus* possesses some antidiarrhoeal potential, though more research and investigation are required in this direction.

#### 6.8.10 Antimicrobial

Nowadays, most of the nations use plants as the main source of potent and effective drugs to treat various diseases and ailments (Srivastava et al. 1996). Different diseases and infections are treated by potent therapeutic agents isolated from plants (Uniyal et al. 2006). As an integrative system of medicine, plants are being accessed to confirm their antimicrobial potential for the management and protection against pathogens in recent years because the plant extracts possessing antimicrobial properties can be very vital. Potent natural compounds obtained from plants possess an important role in the defence mechanism of plants as well as their physiological actions in the human body (Sahreen et al. 2010). Resistance is the major drawback with the commercial antibiotics which are being used for various infections. Moreover, a bunch of toxic effects like hypersensitivity, immune suppression, etc. are connected with the use of these drugs. As a matter of fact, the plants are not only being widely used as drugs but as cosmetics and nutritional food as well, further evaluation of which by in vitro methods has confirmed their utility as antimicrobials and in other diseases as well (Krishnaiah et al. 2007).

Vast antimicrobial activity studies have been carried out on *R. hastatus*. In one of the study carried out by Sahreen et al. (2015) on methanol extract of the plant as well

as its different fractionated extracts, numerous plant extracts reflected prominent antimicrobial potential, which is why they are being widely used in PHCs. All these results show that the plant has immense potential for antimicrobial activity.

#### 6.8.10.1 Antifungal

Sahreen et al. (2015) designed a study on *R. hastatus* roots using agar tube dilution method against *A. niger*, *A. flavus*, *A. fumigatus* and *F. solani*. Inhibition of all the fungi was observed which reflects the antifungal potential of *R. hastatus*, although it requires further research and investigation.

#### 6.8.10.2 Antibacterial Activity

Diverse antibacterial studies have been conducted on *R. hastatus*. Sahreen et al. (2015) performed a study on different root extracts of *R. hastatus* using agar well diffusion method. Crude methanol extract was fractioned with n-hexane, chloroform, n-butanol, ethyl acetate and residual aqueous fraction. Staphylococcus aureus which is a Gram-positive bacteria was inhibited by the extracts in the following order chloroform>n-hexane>methanol; however the other extracts had no effect on the growth of the respective bacteria. Besides, the chloroform fraction followed by methanol, butanol and ethyl acetate inhibited Bacillus subtilis, although the rest of the extracts didn't inhibit the growth of the respective bacteria. Similarly, the Gramnegative bacteria Klebsiella pneumonia's growth was inhibited in the order, viz. ethyl acetate, n-hexane>methanol, whereas other fractions did not inhibit its growth. Pseudomonas aeruginosa was also found to be inhibited by the plant. Moreover, growth of Salmonella typhi was inhibited in the order n-hexane>n-butanol>ethyl acetate, chloroform, methanol and aqueous. Furthermore, the growth of Enterobacter aerogenes was inhibited in the order aqueous>methanol and chloroform, and the remaining fractions did not show inhibition of the respective bacteria. Additionally, Micrococcus luteus and Escherichia coli reflected no antibacterial activity of any of the extracts. All the above results strongly indicate very potent activity of *R. hastatus* against different Gram-positive and Gram-negative bacteria.

Similar findings were found in the study conducted by Andleeb et al. (2018). Under this research, analysis of antibacterial potential of *R. hastatus* against various clinical pathogenic bacteria such **as** *Serratia marcescens*, *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Streptococcus pyogenes*, *Staphylococcus epidermidis* and *Pseudomonas aeruginosa* was performed using agar well diffusion method. The maximum inhibition of *S. pyogenes* was shown by the diethyl ether extract, while moderate inhibition was shown by chloroform fraction. Moderate inhibition of *K. pneumonia* and *S. aureus* was shown by diethyl ether and acetone fractions. Low or even no effect was shown by ethanol fraction on the growth of bacteria. Spot screening, TLC-bioautography and genomic DNA extraction (broth dilution method) also demonstrated the antibacterial effect of *R. hastatus*. Fine conclusion can be drawn from the above results that most of the extracts analysed were found to be promising source for the exploration of novel antimicrobials, thereby making it clear that *R. hastatus* could be successfully used as prominent antibacterial agent, as well as overcome the enigma of bacterial infections and multidrug-resistant microbial strains. (Ogram et al. 1987) further analysed the effect of the plant extracts on microbial DNA extracted from sediments and drew the same conclusion (Sahreen et al. 2011). The fall in DNA damages was exhibited by different root extracts of the plant. Lastly further establishment of the activity was reflected by spot screening results which is in accordance with the studies of (Oke and Hamburger 2002; Hussain et al. 2010).

One more study was conducted by Kamal et al. (2015) in the same direction. The analysis of crude flavonoids, saponins, crude methanolic extract and resultant fractions of R. hastatus by well diffusion method was carried out. The flavonoid fraction showed potent activity against all strains, which was however followed by the saponin extract, comparable to the positive control in the antibacterial assay. Similarly good zones of inhibition were shown by the ethyl acetate and chloroform fractions; the largest was however displayed by flavonoid extract against Bacillus cereus, while saponin was more effective against Escherichia coli. All the extracts were effective against Staphylococcus aureus, Klebsiella pneumoniae, Proteus mirabilis and Pseudomonas aeruginosa. Further analysis of various samples of *R. hastatus* revealed that this plant shows potent antibacterial activity; besides the flavonoid fraction was most active against different strains. It has already being established that this group of compounds is reported to possess remarkable antiinfective properties, and there are different compounds of flavonoids which have been discovered and identified, possessing potent antibacterial potential (Cushnie and Lamb 2005). Furthermore, it has been notified that synergistic effect is shown by numerous compounds of flavonoids when in combination, for instance, isorhamnetin-3-rutinoside, quercetin and rutin, present in the samples of Marrubium globosum, possess higher potential than the individual compound (Kimura and Yamada 1984). Moreover the saponins extracted from the plant also displayed prominent antibacterial potential against different bacterial strains which has also been reported by several investigators (Avato et al. 2006).

#### 6.8.11 Antidiabetic Activity

Diabetes mellitus is a metabolic issue described by increment in blood glucose level. It can influence people at any phase of life, yet the recurrence of diabetes is extensively high among the corpulent and matured individuals (Mellitus 2005). Various restorative measures are utilized to reduce the indications of this ailment. One of the powerful helpful measures is to diminish the absorption of glucose from the digestive system. Hence, the retention of glucose from the digestive system can be diminished viably by  $\alpha$ -glucosidase inhibition. Different plants have been accounted to have the  $\alpha$ -glucosidase restraint potential (Ha et al. 2014). Diabetes mellitus is one of the regular metabolic issues with micro- and macrovascular complexities that cause noteworthy dismalness and death. It is considered as one of the five driving reasons for death on the planet (Vats et al. 2004; Kumar et al. 2006). In the present-day medication, no agreeable powerful treatment is as yet accessible to cure the disease (Ghosh and Suryawanshi 2001). There is expanding

request by patients to utilize natural compounds with antidiabetic potential because of reactions and after-effects related with the utilization of insulin and oral hypoglycaemic agents (Holman and Turner 1991; Kameswrarao et al. 1997; Rao et al. 2001). These constraints have generally incited the investigation of the executives systems including the utilization of plant-based drugs which are as well low-cost antidiabetic drugs with less announced toxic symptoms (Atanasov et al. 2015).

This research was designed by Ahmad et al. (2019) on the different samples of *R. hastatus* for exploration of its in vitro antidiabetic activity. Further analysis of the extracts through GC (FID-MS) confirmed the presence of 120 compounds, among which, few antidiabetic agents were also identified, viz. guanidine, phytol, caryophyllene, anozol, nerolidol, ethylthreonine, butyl phthalate, indoline, myristic acid, dihydrobenzofuran and palmitic acid. It is a clear indication that the plant possesses antidiabetic potential. It may also be concluded that *R. hastatus* is among low-risk and nutritious plants based on the reported data. It can therefore be labelled as green functional food with antidiabetic activity, along with the source of different secondary metabolites. Growth, energy production and other vital functions of the body can be thereby met effectively along with the possible management of diabetes mellitus. Furthermore, when the traditional vegetables are unavailable, scarce or highly priced, it can also be used in this direction as well.

# 6.9 Conclusion

The medicinal plants are highest source of different phytoconstituents, possessing diverse pharmacological and ethnomedicinal activities. Medicinal plants have various properties for curing of various diseases for so many years. Currently an extensive research is going on worldwide to find novel phytoconstituents possessing novel pharmacological activities. In this book chapter, the facts reported are hard to clearly establish the structure-activity relationships and functionality regarding the pharmacological effects of various phytoconstituents.

In this chapter the data are collected from all the sources regarding ethnomedicinal uses, botanical description, pharmacology and phytochemistry of *R. hastatus* (Polygonaceae) a healing herb wildly grown in the areas of southwest China, northern Pakistan and northeast Afghanistan. Various phytoconstituents like quinones, terpenoids, coumarins, flavonoids, volatile oil and carotenoids have been reported in *R. hastatus*. It is noteworthy that *R. hastatus* has extensive medicinal uses, as ethnobotanical and ethnomedicinal data indicate. It exhibits several pharmacological activities such anti-inflammatory, hepatoprotective, antidiabetic and anti-tumour. It is potentially an important medicinal plant for mankind. So well-established use of *R. hastatus* medicinal plant preparations for the prevention and treatment of various ailments.

Acknowledgements Author Contributions: All authors had equally contributed to writing of this book chapter.

Conflict of Interest: There is no competing interests.

# References

Aarsland D et al (2008) Dementia in Parkinson's disease. Curr Opin Neurol 21(6):676-682

- Abbasi, A. M., et al. (2010). "Herbal medicines used to cure various ailments by the inhabitants of Abbottabad district, north west Frontier Province, Pakistan"
- Abbasi, A. M., et al. (2011). Medicinal plant biodiversity of lesser Himalayas-Pakistan., Springer Science & Business Media
- Abbasi AM et al (2013) Botanical ethnoveterinary therapies in three districts of the lesser Himalayas of Pakistan. J Ethnobiol Ethnomed 9(1):84
- Abdul M et al (2009) Biological evaluation of wild thyme (Thymus serpyllum). Pharm Biol 47(7): 628–633
- Adachi JA et al (2001) Enteroaggregative Escherichia coli as a major etiologic agent in traveler's diarrhea in 3 regions of the world. Clin Infect Dis 32(12):1706–1709
- Afzal S et al (2014) Total phenolic content, in vitro radical scavenging and antimicrobial activities of whole plant Rumex hastatus. Sci Int 26(2):102–107
- Ahmad SS (2007) Medicinal wild plants from Lahore-Islamabad motorway (M-2). Pak J Bot 39(2):355
- Ahmad I, Aqil F (2007) In vitro efficacy of bioactive extracts of 15 medicinal plants against ESβLproducing multidrug-resistant enteric bacteria. Microbiol Res 162(3):264–275
- Ahmad S et al (2015) Antioxidant and anticholinesterase investigations of Rumex hastatus D. Don: potential effectiveness in oxidative stress and neurological disorders. Biol Res 48(1):20
- Ahmad S et al (2016a) Antitumor and anti-angiogenic potentials of isolated crude saponins and various fractions of Rumex hastatus D. Don. Biol Res 49(1):18
- Ahmad S et al (2016b) Evaluation of Rumex hastatus D. Don for cytotoxic potential against HeLa and NIH/3 T3 cell lines: chemical characterization of chloroform fraction and identification of bioactive compounds. BMC Complement Alternat Med 16(1):308
- Ahmad S et al (2019) Nutritional and medicinal aspects of Rumex hastatus D. Don along with in vitro anti-diabetic activity. Int J Food Prop 22(1):1733–1748
- Akhtar N, Mirza B (2018) Phytochemical analysis and comprehensive evaluation of antimicrobial and antioxidant properties of 61 medicinal plant species. Arab J Chem 11(8):1223–1235
- Alberto J et al (2016) Some traditional medicinal plants of north region from Puebla, Mexico: uses and potential pharmacological activity of Rumex spp. Nat Prod Chem Res 4(223):2
- Ali H, Qaiser M (2009) The ethnobotany of Chitral valley, Pakistan with particular reference to medicinal plants. Pak J Bot 41(4):2009–2041
- Alwashli A et al (2012) Analgesic and anti-inflammatory activities of Boswellia elongata Balf Methanolic extracts, as endemic plants in Yemen. J Biol Active Prod Nat 2(2):90–98
- Andleeb S et al (2018) Biological activities and secondary metabolite screening of rumex hastatus extract through Fourier transform infrared and Raman spectroscopy. Infect Disord Drug Targets 18(2):164–176
- Anjen L et al (2003) 1a. Shrub, rarely a subshrub. Flora China 5:277-350
- Artis D, Spits H (2015) The biology of innate lymphoid cells. Nature 517(7534):293-301
- Ashraf A et al (2015) Antioxidant, antimicrobial, antitumor, and cytotoxic activities of an important medicinal plant (Euphorbia royleana) from Pakistan. J Food Drug Anal 23(1):109–115
- Ashton C, J. (2012) Synthetic cannabinoids as drugs of abuse. Curr Drug Abuse Rev 5(2):158-168
- Atanasov AG et al (2015) Discovery and resupply of pharmacologically active plant-derived natural products: a review. Biotechnol Adv 33(8):1582–1614
- Avato P et al (2006) Antimicrobial activity of saponins from Medicago sp.: structure-activity relationship. Phytother Res 20(6):454–457

- Aziz MA et al (2018) Traditional uses of medicinal plants used by indigenous communities for veterinary practices at Bajaur agency, Pakistan. J Ethnobiol Ethnomed 14(1):11
- Babu B et al (2001) Antioxidant and hepatoprotective effect of Acanthus ilicifolius. Fitoterapia 72(3):272–277
- Babulka P (2004) Les rumex, de l'ethnobotanique à la phytothérapie moderne (Rumex spp.). Phytothérapie 2(5):153–156
- Baldioli M et al (1996) Antioxidant activity of tocopherols and phenolic compounds of virgin olive oil. J Am Oil Chem Soc 73(11):1589–1593
- Bamiro F et al (1995) Comparative elemental contents (Cu, Ca, Zn, K, Mg, Ni, Fe and Cd) of seven various edible tubers in Nigeria. Pak J Sci Ind Res 38:316–318
- Bartha SG et al (2015) Ethnoveterinary practices of Covasna County, Transylvania, Romania. J Ethnobiol Ethnomed 11(1):35
- Bektas N et al (2015) The role of muscarinic receptors in pain modulation. World J Pharmaceut Med Res 1(1):40–49
- Bhatia H et al (2018) Traditionally used wild edible plants of district Udhampur, J&K, India. J Ethnobiol Ethnomed 14(1):73
- Bhatt V, Negi G (2006) Ethnomedicinal plant resources of Jaunsari tribe of Garhwal Himalaya, Uttaranchal. Indian J Tradit Knowl 5(3):331–335
- Bisht AS, Sharma DK (2014) Plants utilization by the communities of Bharsar and adjoining area of Pauri Garhwal District, Uttarakhand, India. Biodiversitas J Biol Diversity 15(1):94–100
- Borrego-Soto G et al (2015) Ionizing radiation-induced DNA injury and damage detection in patients with breast cancer. Genet Mol Biol 38(4):420–432
- Bouldin AS et al (1999) Pharmacy and herbal medicine in the US. Soc Sci Med 49(2):279-289
- Bourbonnas-Spear N et al (2005) Plant use by the Q'eqchi'Maya of Belize in ethnopsychiatry and neurological pathology. Econ Bot 59(4):326–336
- Bown D (1995) The Royal Horticultural Society encyclopedia of herbs and their uses. Dorling Kindersley Limited
- Burkard G, Lehrl S (1991) Verhältnis von Demenzen vom Multiinfarkt-und vom Alzheimertyp in ärztlichen Praxen. Münch Med Wschr1 33(Suppl 1):38–43
- Carmeliet P, Jain RK (2000) Angiogenesis in cancer and other diseases. Nature 407(6801):249-257
- Castellsague J et al (2012) Safety of non-steroidal anti-inflammatory drugs (SOS) project individual NSAIDs and upper gastrointestinal complications: a systematic review and metaanalysis of observational studies (the SOS project). Drug Saf 35(12):1127
- Coats JR (1994) Risks from natural versus synthetic insecticides. Annu Rev. Entomol 39(1): 489–515
- Coburn B (1984) Some native medicinal plants of the western Gurung. Kailash 1(1-2):55-88
- Cushnie TT, Lamb AJ (2005) Antimicrobial activity of flavonoids. Int J Antimicrob Agents 26(5): 343–356
- Da Rocha AB et al (2001) Natural products in anticancer therapy. Curr Opin Pharmacol 1(4): 364–369
- Das A et al (2002) A comparative study in rodents of standardized extracts of Bacopa monniera and Ginkgo biloba: anticholinesterase and cognitive enhancing activities. Pharmacol Biochem Behav 73(4):893–900
- Decker EA et al (2005) Measuring antioxidant effectiveness in food. J Agric Food Chem 53(10): 4303–4310
- Deshpande S et al (2003) Antiulcer activity of Tephrosia purpurea in rats. Indian J Pharmacol 35(3): 168–172
- Disler M et al (2014) Ethnoveterinary herbal remedies used by farmers in four north-eastern Swiss cantons (St. Gallen, Thurgau, Appenzell Innerrhoden and Appenzell Ausserrhoden). J Ethnobiol Ethnomed 10(1):32
- Dutt HC et al (2015) Oral traditional knowledge on medicinal plants in jeopardy among Gaddi shepherds in hills of northwestern Himalaya, J&K, India. J Ethnopharmacol 168:337–348

- Fang J-Y et al (2001) Capsaicin and nonivamide as novel skin permeation enhancers for indomethacin. Eur J Pharm Sci 12(3):195–203
- Farnsworth NR (1988) Screening plants for new medicines. Biodiversity 15(3):81-99
- Fatima N et al (2009) Biological activities of Rumex dentatus L: evaluation of methanol and hexane extracts. Afr J Biotechnol 8(24):6945–6951
- Firestone GL, Sundar SN (2009) Anticancer activities of artemisinin and its bioactive derivatives. Expert Rev. Mol Med 11:e32
- Flescher E (2005) Jasmonates—a new family of anti-cancer agents. Anti-Cancer Drugs 16(9): 911–916
- Folkman J (1992) The role of angiogenesis in tumor growth. Semin Cancer Biol 3(2):65-71
- Ghane SG et al (2010) Indigofera glandulosa Wendl.(Barbada) a potential source of nutritious food: underutilized and neglected legume in India. Genet Resour Crop Evol 57(1):147–153
- Ghosh S, Suryawanshi S (2001) Effect of Vinca rosea extracts in treatment of alloxan diabetes in male albino rats. Indian J Exp Biol 39(8):748–759
- Gorsi MS, Miraj S (2002) Ethenomedicinal survey of plants of Khanabad village and its allied areas, District Gilgit. Asian J Plant Sci 1(5):604–615
- Ha BG et al (2014) Antidiabetic effect of nepodin, a component of Rumex roots, and its modes of action in vitro and in vivo. Biofactors 40(4):436-447
- Hameed I, Dastagir G (2009) Nutritional analyses of Rumex hastatus D. Don, Rumex dentatus Linn and Rumex nepalensis Spreng. Afr J Biotechnol 8(17):4131–4133
- Hameed I et al (2008) Nutritional and elemental analyses of some selected medicinal plants of the family Polygonaceae. Pak J Bot 40(6):2493–2502
- Hameed I et al (2010) Anatomical studies of some medicinal plants of family Polygonaceae. Pak J Bot 42(5):2975–2983
- Haq F et al (2011) Traditional uses of medicinal plants of Nandiar Khuwarr catchment (District Battagram), Pakistan. Pak J Med Plant Res 5(1):39–48
- Haque N et al (2000) Evaluation of antitumor activity of some medicinal plants of Bangladesh by potato disk bioassay. Fitoterapia 71(5):547–552
- Heinrich M et al (2005) Spasmolytic and antidiarrhoeal properties of the Yucatec Mayan medicinal plant Casimiroa tetrameria. J Pharm Pharmacol 57(9):1081–1085
- Hernández-Pérez M, Rabanal RM (2002) Evaluation of the antiinflammatory and analgesic activity of Sideritis canariensis var. pannosa in mice. J Ethnopharmacol 81(1):43–47
- Hoge CW et al (1998) Trends in antibiotic resistance among diarrheal pathogens isolated in Thailand over 15 years. Clin Infect Dis 26(2):341–345
- Holman R, Turner R (1991) Oral agents and insulin in the treatment of NIDDM. Textbook of diabetes. Blackwell, Oxford, vol 9, p 467
- Hucho T, Levine JD (2007) Signaling pathways in sensitization: toward a nociceptor cell biology. Neuron 55(3):365–376
- Hussain F et al (2006) Ethnobotanical profile of plants of Shawar Valley, District Swat, Pakistan. Int J Biol Biotechnol 3(2):301–307
- Hussain A et al (2007) Cytotoxic and antitumor potential of Fagonia cretica L. Turk J Biol 31(1): 19–24
- Hussain F et al (2010) Antibacterial, antifungal and insecticidal activities of some selected medicinal plants of Polygonaceae. Afr J Biotechnol 9(31):5032–5036
- Hussain SA et al (2015) Potential herbs and herbal nutraceuticals: food applications and their interactions with food components. Crit Rev Food Sci Nutr 55(1):94–122
- Inayatullah S et al (2012) Bioprospecting traditional Pakistani medicinal plants for potent antioxidants. Food Chem 132(1):222–229
- Ijaz F et al (2016) Investigation of traditional medicinal floral knowledge of Sarban Hills, Abbottabad, KP, Pakistan. J Ethnopharmacol 179:208–233
- Isailovic N et al (2015) Interleukin-17 and innate immunity in infections and chronic inflammation. J Autoimmun 60:1–11

- Islam M et al (2006) Weeds and medicinal plants of Shawar valley, District Swat. Pak J Weed Sci Res 12(1–2):83–88
- Islam M et al (2010) In vitro evaluation of Croton bonplandianum Baill. As potential antitumor properties using Agrobacterium tumefaciens. J Agric Technol 6(1):79–86
- Jan G et al (2011) Indigenous medicinal plants used by local people of Shahi, lower Dir (Khyber Pakhtunkhwa), southern Himalayan regions of Pakistan. Int J Biol Biotechnol 8(2):345–353
- Johns T, Eyzaguirre PB (2006) Linking biodiversity, diet and health in policy and practice. Proc Nutr Soc 65(2):182–189
- Jordan MA, Wilson L (2004) Microtubules as a target for anticancer drugs. Nat Rev. Cancer 4(4): 253–265
- Julius D, Basbaum AI (2001) Molecular mechanisms of nociception. Nature 413(6852):203-210
- Kähkönen MP et al (1999) Antioxidant activity of plant extracts containing phenolic compounds. J Agric Food Chem 47(10):3954–3962
- Kamal Z et al (2015) Ex vivo antibacterial, phytotoxic and cytotoxic, potential in the crude natural phytoconstituents of Rumex hastatus D. Don. Pak J Bot 47(SI):293–299
- Kameswrarao B, et al (1997) Herbal medicine. In The management by indigenous resources, pp 375–377
- Kanowski S et al (1996) Proof of efficacy of the ginkgo biloba special extract EGb 761 in outpatients suffering from mild to moderate primary degenerative dementia of the Alzheimer type or multi-infarct dementia. Pharmacopsychiatry 29(02):47–56
- Khalifa A (2004) Herbs: nature's pharmacy. Casablanca, Arab Cultural Center
- Khan M et al (2009) Medicinal plants of Sewa river catchment area in the Northwest Himalaya and its implication for conservation. Ethnobot Leafl 2009(9):5
- Kimura M, Yamada H (1984) Interaction in the antibacterial activity of flavonoids from Sophora japonica L. to Propionibacterium. Yakugaku Zasshi 104(4):340–346
- Kinghorn AD et al (2011) The relevance of higher plants in lead compound discovery programs. J Nat Prod 74(6):1539–1555
- Komiya T et al (1999) Phytol induces programmed cell death in human lymphoid leukemia molt 4B cells. Int J Mol Med 4(4):377–457
- Krenn L, Paper D (2009) Inhibition of angiogenesis and inflammation by an extract of red clover (Trifolium pratense L.). Phytomedicine 16(12):1083–1088
- Krishnaiah D et al (2007) Phytochemical antioxidants for health and medicine a move towards nature. Biotechnol Mol Biol Rev 2(4):97–104
- Kuete V et al (2013) Cytotoxicity, mode of action and antibacterial activities of selected Saudi Arabian medicinal plants. BMC Complement Altern Med 13(1):354
- Kumar GPS et al (2006) Anti-diabetic activity of fruits of Terminalia chebula on streptozotocin induced diabetic rats. J Health Sci 52(3):283–291
- Kumar H et al (2012) The role of free radicals in the aging brain and Parkinson's disease: convergence and parallelism. Int J Mol Sci 13(8):10478–10504
- Kumari S et al (2013) An ethnobotanical survey of medicinal plants used by Gujjar Community of Trikuta Hills in Jammu and Kashmir, India. J Med Plant Res 7(28):2111–2121
- LaPoint J et al (2011) Severe toxicity following synthetic cannabinoid ingestion. Clin Toxicol 49(8):760–764
- Le Bars PL et al (1997) A placebo-controlled, double-blind, randomized trial of an extract of Ginkgo biloba for dementia. JAMA 278(16):1327–1332
- Lewin GR et al (2004) A plethora of painful molecules. Curr Opin Neurobiol 14(4):443-449
- Liang HX et al (2010) Bioactive compounds from Rumex plants. Phytochem Lett 3(4):181–184 List P (2010) The plant list, Version
- List P (2013) The Plantlist working list of all plant species, version 1.1 September 2013, [cited 2015 Jan 26]
- Liu J-Y et al (2006) The protective effects of Hibiscus sabdariffa extract on CCl4-induced liver fibrosis in rats. Food Chem Toxicol 44(3):336–343

- Loizzo MR et al (2008) Natural products and their derivatives as cholinesterase inhibitors in the treatment of neurodegenerative disorders: an update. Curr Med Chem 15(12):1209–1228
- Magbagbeola J et al (2010) Neglected and underutilized species (NUS): a panacea for community focused development to poverty alleviation/poverty reduction in Nigeria. J Econ Int Finan 2(10):208–211
- Maiti A et al (2007) In vivo evaluation of antidiarrhoeal activity of the seed of Swietenia macrophylla king (Meliaceae). Trop J Pharm Res 6(2):711–716
- Mal B (2007) Neglected and underutilized crop genetic resources for sustainable agriculture. Indian J Plant Genet Resour 20(1):1–14
- Manan Z et al (2007) Diversity of medicinal plants in Wari subdivision District Upper Dir, Pakistan. Pak J Plant Sci (Pakistan) 13(1):19–26
- Manandhar NP (1995) A survey of medicinal plants of Jajarkot District, Nepal. J Ethnopharmacol 48(1):1–6
- Manandhar NP (2002) Plants and people of Nepal. Timber Press, Portland
- Mani M et al (2010) Anti-diarrhoeal activity of methanolic extract of root bark of Ailanthus altissima Swingle (family: Simaroubaceae) on experimental animals. Int J Pharm Sci Res 1: 197–202
- Mclaughlin JL et al (1998) The use of biological assays to evaluate botanicals. Drug Inf J 32(2): 513–524
- Mehendale HM (2005) Tissue repair: an important determinant of final outcome of toxicantinduced injury. Toxicol Pathol 33(1):41–51
- Mehendale S et al (2008) Fatty acids, antioxidants, and oxidative stress in pre-eclampsia. Int J Gynecol Obstet 100(3):234–238
- Mellitus D (2005) Diagnosis and classification of diabetes mellitus. Diabetes Care 28(S37):S5-S10
- Mishra AP et al (2018) Bioactive compounds and health benefits of edible Rumex species-a review. Cell Mol Biol 64(8):27–34
- MiuRA T et al (2002) Isoflavone aglycon produced by culture of soybean extracts with basidiomycetes and its anti-angiogenic activity. Biosci Biotechnol Biochem 66(12):2626–2631
- Mohamed AF et al (2015) Patient benefit-risk tradeoffs for radioactive iodine-refractory differentiated thyroid cancer treatments. J Thyroid Res 2015:438235
- Mohammed A et al (2009) Preliminary anti-diarrhoeal activity of hydromethanolic extract of aerial part of Indigofera pulchra in rodents. Asian J Med Sci 1(2):22–25
- Montgomery SL, Bowers WJ (2012) Tumor necrosis factor-alpha and the roles it plays in homeostatic and degenerative processes within the central nervous system. J Neuroimmune Pharmacol 7(1):42–59
- Mukherjee PK et al (2007) In vitro acetylcholinesterase inhibitory activity of the essential oil from Acorus calamus and its main constituents. Planta Med 73(3):283
- Murad W et al (2011) Indigenous knowledge and folk use of medicinal plants by the tribal communities of Hazar Nao Forest, Malakand District, North Pakistan. J Med Plant Res 5(7): 1072–1086
- Nadkarni K, Nadkarni AK (1976) Indian Materia Medica, vol 1. Popular Prakashan Pvt. Ltd., Bombay, p 799
- Navajas-Pérez R et al (2005) The evolution of reproductive systems and sex-determining mechanisms within Rumex (Polygonaceae) inferred from nuclear and chloroplastidial sequence data. Mol Biol Evol 22(9):1929–1939
- Nickel FT et al (2012) Mechanisms of neuropathic pain. Eur Neuropsychopharmacol 22(2):81-91
- Ofman JJ et al (2002) A metaanalysis of severe upper gastrointestinal complications of nonsteroidal antiinflammatory drugs. J Rheumatol 29(4):804–812
- Ogram A et al (1987) The extraction and purification of microbial DNA from sediments. J Microbiol Methods 7(2–3):57–66
- Oke J, Hamburger M (2002) Screening of some Nigerian medicinal plants for antioxidant activity using 2, 2, diphenyl-picrylhydrazyl radical. Afr J Biomed Res 5(1–2):77–79

- Öztürk M et al (2011) In vitro antioxidant, anticholinesterase and antimicrobial activity studies on three Agaricus species with fatty acid compositions and iron contents: a comparative study on the three most edible mushrooms. Food Chem Toxicol 49(6):1353–1360
- Padulosi S, Eyzaquirre P, Hodgkin T (1999) Challenges and strategies in promoting conservation and use of neglected and underutilized crop species. In Perspectives on new crops and new uses, pp 140–145
- Pande P et al (2007) Ethno veterinary plants of Uttaranchal-a review. IJTK 6(3):444-458
- Pastor C et al (1995) Liver injury during sepsis. J Crit Care 10(4):183-197
- Paul P, Chowdhury M (2019) Diversity of members of Polygonaceae from West Bengal, India. Plant Arch 19(2):157–164
- Pedraza-Alva G et al (2015) Negative regulation of the inflammasome: keeping inflammation under control. Immunol Rev 265(1):231–257
- Pohle P (1990) Useful plants of Manang district: a contribution to the ethnobotany of the Nepal Himalaya. Nepal Research Centre, Nepal
- Pope LE et al (2001) Treatment of hyperproliferative skin disorders with C18 to C20 aliphatic alcohols. Google Patents
- Qaiser M (2001) Polygonaceae in Flora of Pakistan. No. 205, Karachi
- Rahman IU et al (2016) A novel survey of the ethno medicinal knowledge of dental problems in Manoor Valley (Northern Himalaya), Pakistan. J Ethnopharmacol 194:877–894
- Rao BK et al (2001) Antihyperglycemic activity of Momordica cymbalaria in alloxan diabetic rats. J Ethnopharmacol 78(1):67–71
- Ruberto G, Baratta MT (2000) Antioxidant activity of selected essential oil components in two lipid model systems. Food Chem 69(2):167–174
- Ruch RJ et al (1989) Prevention of cytotoxicity and inhibition of intercellular communication by antioxidant catechins isolated from Chinese green tea. Carcinogenesis 10(6):1003–1008
- Sahreen S et al (2010) Evaluation of antioxidant activities of various solvent extracts of Carissa opaca fruits. Food Chem 122(4):1205–1211
- Sahreen S et al (2011) Phenolic compounds and antioxidant activities of Rumex hastatus D. Don. Leaves. J Med Plant Res 5(13):2755–2765
- Sahreen S et al (2013) Ameliorating effect of various fractions of Rumex hastatus roots against hepato-and testicular toxicity caused by CCl 4. Oxid Med Cell Longev 2013:325406
- Sahreen S et al (2014) Comprehensive assessment of phenolics and antiradical potential of Rumex hastatus D. Don. roots. BMC Complement Altern Med 14(1):47
- Sahreen S et al (2015) Evaluation of phytochemical content, antimicrobial, cytotoxic and antitumor activities of extract from Rumex hastatus D. Don roots. BMC Complement Altern Med 15(1): 211
- Sahreen S et al (2017) Evaluation of Rumex hastatus leaves against hepatic fibrosis: a rat model. BMC Complement Altern Med 17(1):435
- Salvador JA et al (2013) Anticancer steroids: linking natural and semi-synthetic compounds. Nat Prod Rep 30(2):324–374
- Schlachterman A et al (2008) Combined resveratrol, quercetin, and catechin treatment reduces breast tumor growth in a nude mouse model. Transl Oncol 1(1):19
- Scholz J, Woolf CJ (2002) Can we conquer pain? Nat Neurosci 5(11):1062-1067
- Seidemann J (2005) World spice plants: economic usage, botany, taxonomy. Springer Science & Business Media
- Sen S et al (2010) Analgesic and anti-inflammatory herbs: a potential source of modern medicine. Int J Pharm Sci Res 1(11):32
- Sengupta A, Ghosh M (2012) Comparison of native and capric acid-enriched mustard oil effects on oxidative stress and antioxidant protection in rats. Br J Nutr 107(6):845–849
- Shafiq N et al (2017) Chemical and biological analysis of the extract from the plant Rumex hastatus for its secondary metabolites. Res J Life Sci Bioinf Pharm Chem Sci 3:40–44
- Shah S et al (2015) Phytochemicals, in vitro antioxidant, total phenolic contents and phytotoxic activity of Cornus macrophylla Wall bark collected from the North-West of Pakistan. Pak J Pharm Sci 28(1):23–28

Shaheen H et al (2012) Indigenous plant resources and their utilization practices in village populations of Kashmir Himalayas. Pak J Bot 44(2):739–745

Shahidi F et al (1992) Phenolic antioxidants. Crit Rev Food Sci Nutr 32(1):67-103

- Shakuntala BP et al (2011) Evaluation of antidiarrhoeal activity of extract from roots of Rumex hastatus (family: Polygonaceae) on experimental animals. J Appl Pharm Sci 1(6):182–185
- Shaphiullah M et al (2003) Antidiarrheal activity of the methanol extract of Ludwigia hyssopifolia Linn. Pak J Pharm Sci 16(1):7–11
- Sharma R et al (2018) Comprehensive metabolomics study of traditionally important Rumex species found in Western Himalayan region. Nat Prod Commun 13(2):1934578X1801300219
- Shedayi AA et al (2014) Traditional medicinal uses of plants in Gilgit-Baltistan, Pakistan. J Med Plant Res 8(30):992–1004
- Sher H et al (2015) Indigenous knowledge of folk medicines among tribal minorities in Khyber Pakhtunkhwa, northwestern Pakistan. J Ethnopharmacol 166:157–167
- Shinwari ZK, Gilani SS (2003) Sustainable harvest of medicinal plants at Bulashbar Nullah, Astore (northern Pakistan). J Ethnopharmacol 84(2–3):289–298
- Singh P, Attri BL (2014) Survey on traditional uses of medicinal plants of Bageshwar Valley (Kumaun Himalaya) of Uttarakhand, India. Int J Conserv Sci 5(2):223–234
- Singh KJ, Thakur AK (2014) Medicinal plants of the Shimla hills, Himachal Pradesh: a survey. Int J Herb Med 2(2):118–127
- Singh MP et al (2002) Plant biodiversity and taxonomy. Daya Books
- Singh S et al (2013a) Antinociceptive, antiinflammatory and antipyretic activities of Rumex hastatus D. don stem and roots. Der Pharmacia Sinica 4(3):95–102
- Singh S et al (2013b) Pharmacognostical standardization of the roots of Rumex hastatus D. Don Asian J Pharm Clin Res 6:126–128
- Singh S et al (2013c) A review on Cassia species: pharmacological, traditional and medicinal aspects in various countries. Am J Phytomedicine and Clin Ther 1(3):291–312
- Singh J et al (2014) Wild vegetable plants used by tribal people of Kinnaur district, Himachal Pradesh, India. Int J Usuf Mngt 15(2):47–56
- Sinha RK, Sinha S (2001) Ethnobiology: role of indigenous and ethnic societies in biodiversity conservation, human health protection and sustainable development. Surabhi Publications
- Small GW et al (1997) Diagnosis and treatment of Alzheimer disease and related disorders: consensus statement of the American Association for Geriatric Psychiatry, the Alzheimer's Association, and the American Geriatrics Society. JAMA 278(16):1363–1371
- Srivastava JP et al (1996) Medicinal plants: an expanding role in development. The World Bank
- Stamatis H et al (1999) Studies on the enzymatic synthesis of lipophilic derivatives of natural antioxidants. J Am Oil Chem Soc 76(12):1505
- Steinberg GM et al (1975) Hydrophobic binding site in acetylcholinesterase. J Med Chem 18(11): 1056–1061
- Stevenson D, Hurst R (2007) Polyphenolic phytochemicals—just antioxidants or much more? Cell Mol Life Sci 64(22):2900–2916
- Sultana S et al (2017) Chemical constituents from the aerial parts of Rumex hastatus D. Don. J Pharm Biol Sci 5(5):179–187
- Tariq A et al (2014) Ethnoveterinary study of medicinal plants in a tribal society of Sulaiman range. Sci World J 2014:10
- Taylor R et al (1996) Antiviral activities of medicinal plants of southern Nepal. J Ethnopharmacol 53(2):105–110
- Uddin K et al (2014) Taxonomy and traditional medicine practices of Polygonaceae (smartweed) family at Rajshahi, Bangladesh. Int J Adv Res 2(11):459–469
- Uniyal SK et al (2006) Traditional use of medicinal plants among the tribal communities of Chhota Bhangal, Western Himalaya. J Ethnobiol Ethnomed 2(1):14
- Ullah A, Rashid A (2007) Valley, Hindukush range, Pakistan. Pak J Weed Sci Res 13(1–2):27–32
- Ullah R et al (2010) Traditional uses of medicinal plants in Darra Adam Khel NWFP Pakistan. J Med Plant Res 4(17):1815–1821

- Ullah A et al (2014) Medicinal plants used in the isolated region of Bumburet, Kalash Valley, District Chitral, Pakistan. Pak J Weed Sci Res 20(3):359–373
- Uniyal B, Shiva V (2005) Traditional knowledge on medicinal plants among rural women of the Garhwal Himalaya, Uttaranchal. Indian J Tradit Knowl 4(3):259–266
- Valko M et al (2006) Free radicals, metals and antioxidants in oxidative stress-induced cancer. Chem Biol Interact 160(1):1–40
- Vasas A et al (2015) The genus Rumex: review of traditional uses, phytochemistry and pharmacology. J Ethnopharmacol 175:198–228
- Vats V et al (2004) Ethanolic extract of Ocimum sanctum leaves partially attenuates streptozotocininduced alterations in glycogen content and carbohydrate metabolism in rats. J Ethnopharmacol 90(1):155–160
- Verma KK (2019) Protective effect of Rumex hastatus leaves extract against hepatic and cognitive decline in animal models of liver cirrhosis
- Vermani K, Garg S (2002) Herbal medicines for sexually transmitted diseases and AIDS. J Ethnopharmacol 80(1):49–66
- Vignali DA, Kuchroo VK (2012) IL-12 family cytokines: immunological playmakers. Nat Immunol 13(8):722
- Vogl CR et al (2016) Local knowledge held by farmers in eastern Tyrol (Austria) about the use of plants to maintain and improve animal health and welfare. J Ethnobiol Ethnomed 12(1):40
- Wallis, T. E. (1997). Delhi, CBS publishers
- Wang S et al (2004) Angiogenesis and anti-angiogenesis activity of Chinese medicinal herbal extracts. Life Sci 74(20):2467–2478
- Xi M et al (2008) Antioxidant and antiglycation properties of total saponins extracted from traditional Chinese medicine used to treat diabetes mellitus. Phytother Res 22(2):228–237
- Yaniv Z, Bachrach U (2005) Handbook of medicinal plants. CRC Press, Boca Raton
- Yi B-H, Kim D-H (1982) Antioxidant activity of maltol, kojic acid, levulinic acid, furfural, 5-hydroxymethyl furfural, and pyrazine. Korean J Food Sci Technol 14(3):265–270
- Yu W et al (2009) Anticancer actions of natural and synthetic vitamin E forms: RRR-α-tocopherol blocks the anticancer actions of γ-tocopherol. Mol Nutr Food Res 53(12):1573–1581
- Zabta K et al (2003) Medicinal plants and other useful plants of District Swat, Pakistan. Al Aziz Press, Peshawar, p 79
- Zelová H, Hošek J (2013) TNF- $\alpha$  signalling and inflammation: interactions between old acquaintances. Inflamm Res 62(7):641–651
- Zendehdel, M., et al. (2011). "Evaluation of pharmacological mechanisms of antinociceptive effect of Teucrium polium on visceral pain in mice"
- Zhang LS et al (2009) Hastatusides a and B: two new phenolic glucosides from Rumex hastatus. Helv Chim Acta 92(4):774–778
- Zhang Y et al (2014) Diversity of wetland plants used traditionally in China: a literature review. J Ethnobiol Ethnomed 10(1):72