Heliyon 9 (2023) e14159

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Review article

Critical review on Rumex dentatus L. a strong pharmacophore and the future medicine: Pharmacology, phytochemical analysis and traditional uses

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ARTICLE INFO

Keywords:
Rumex dentatus
Flavonoids
Anthraquinones
Endocrocin
Allelochemicals
Strong biological significance

ABSTRACT

Objectives: Rumex dentatus L. (polygonaceae) is one of the most important species of genus *Rumex* widely utilized for the treatment of various human diseases. Most parts of the plant species like leaves, shoots and roots are found to be rich in many pharmacologically important bioactive constituents that are useful against many diseases like acariasis, eczema, diarrhea, constipation, diuretic, astringent, refrigerants and various types of skin diseases. The main aim of the presented review is to highlight and document research findings carried out by different research groups on *Rumex dentatus,* like pharmacological potential, phytochemistry investigations based on presence of phytoconstituents, traditional uses and economic importance till date. The information so collected and documented will become available to researchers, scientists and botanists to explore the medicinal benefits of this prized herb for the assistance of mankind which in turn will open up new opportunities for more organized and collective research efforts towards utilization and scientific validation of its pharmacological potential.

Methods: In-vitro and in-vivo preclinical animal studies have been included in detail. The reports and results have been taken from Scopus, Google Scholar, Web of Science, PubMed and Science Direct, Research gate, Articles & Advice, databases. Plant taxonomy studies were taken and confirmed from the available databases. "The Plant List", and "Mansfeld's Encyclopedia". Additional information on traditional uses, botany were obtained from published books.

Key findings: From results and findings, it has been concluded that *Rumex dentatus* is a rich source of secondary metabolites such as flavonoids, anthraquinones, phenolics, phytosterols, phytoesteryl esters etc. The bactericidal, anti-inflammatory, antimicrobial, anti-tumor and anti-dermatitis properties of *Rumex dentatus* have been attributed due to the presence of these phytochemicals. In this review, we present a critical account of its habitat, morphology, phyto-constituent profile, pharmacology and traditional uses, which will provide a source of information to the researchers for further studies.

Conclusions: The disclosed review endorses that *Rumex dentatus* emerged a unique source of Endocrocin, Emodin, Emodin-glycoside, Chrysophenol-glycoside, Quercetin, Helonioside-A and a number of other important bioactive compounds. These isolated compounds have been found to be active against cancer, inflammation, tumor, dermatitis, acariasis, eczema and various bacterial

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https://doi.org/10.1016/j.heliyon.2023.e14159
Received 25 March 2022; Received in revised form 13 February 2023; Accepted 22 February 2023
Available online 5 March 2023

infections, thus providing new insights for further promising investigations on isolated compounds. In addition, *Rumex dentatus* was found as an excellent traditional medicine against many cutaneous disorders. Taking into account the astounding pharmacological properties of *Rumex dentatus* in consideration, the plant species is a library of bio-active compounds with a strong biological profile, therefore needs an attention of botanical community around the globe to improve its growth for medicinal uses and commit to broaden research in this field for its proper utilization and scientific exploitation.

1. Introduction

Drug discovery and development is one of the complex phenomena which needs high thought put research and very high financial assistance with modern instrumentation. This can be understood here as one of the leading company 'Merck' which established a data that for every 10000 molecules given for drug analysis for efficient biological assays, 20 are selected for animal testing, ironically from these 20 only 10 are being used for human testing the more surprise come as at the end only 1 drug will be approved for the sale by food and drug administration (FDA) of united states [1]. Not only that, Merck also claims that 1 drug takes a minimum of 12 years at the cost of 231 million USDs. This reflects that the drug development via classical methods is a time consuming and very expensive process [2]. However the rise of natural product derived molecules as drugs have historically made a major contribution in drug discovery and pharmacology, especially against all microbial and infectious diseases [3]. Earlier when science was in its infancy people were using herbs as medications to cure disease. With the advancement of science particularly towards drug discovery, a large number of drugs were isolated and tested successfully against numerous diseases [4]. Thus the plant derived molecules become a center of interest among the scientific community as the isolation to testing process seems more promising and feasible than synthetic drug designs [5]. Consequently, interest in natural products as drug leads is being revitalized, for tackling most of the diseases like (asthma, jaundice, bacterial to viral infections, even hereditary related diseases were successfully treated using naturally isolated compounds [6]. Preclinical research and clinical trials on natural products across the world revolutionized the subject [7]. Natural products have given excellent results against chronic inflammation associated diseases, atherosclerosis and ischemia. The therapeutic or preventative utilities of natural products in chronic inflammatory diseases have solved major problems in drug development institutions [8]. In this review we precisely added useful technological developments that are enabling natural product-based drug discovery from *Rumex dentatus* and highlight all its applications and its key opportunities.

At present, around half of the drugs currently in clinical use are of plant origin [9]. Natural products possess extraordinary specificity and potency compared to artificially designed molecules as drugs [10]. These characteristics of natural products are due to nature's own high-throughput screening process for the optimization of bioactive compounds. Plant secondary metabolites are the highest paragon of nature which serves as the lead structures for the development of new therapeutics owing to their interesting structural features and intriguing biological profiles [11]. The plant flora showed numerous assays with each part of the plant where found to act against particular disease [12]. The advancement of research work on natural product extraction with some outstanding natural isolates like penicillin, nicotine, morphine, codeine, ephedrine, quinines, anthraquinones, benzofurans, furans, imidazopyridines, harmaline, harmole, tubocurarine, atropine, hyoscyamine, scopolamine, strychnine Podophyllotoxin, tryptamine, bufotenin, cinnamons etc, has been isolated [13]. Apart from that, the plants were also used to treat diseases like Alzheimer's disease (AD), Parkinson's disease, epilepsy, schizophrenia, neuro regeneration, leukemia, typhoid and influenza etc are being addressed using plant medications [14,15]. Further anti-tumor, antibacterial, antifungal, antiviral, anti-inflammatory, and antimicrobial, anti-depressant, anti-allergic, vasoconstrictor, vasodilator and anti-diabetic drugs are also obtained from plants. Thus plants are ultimate reservoirs of drugs and are considered as a backbone in drug industries [16]. Keeping in mind the abundant biological applications of plants and plant derived compounds, in this review, we have chosen *Rumex dentatus* for identification, pharmacology, phytochemistry, traditional uses and allelopathic analysis. The presented review provides an assessment of the current state of knowledge of the ethnopharmacology, phytochemistry, pharmacology and safety of *Rumex dentatus*. Further the strong accord on its traditional uses supported by pharmacological investigations in order to identify its relevance as a potential therapeutic plant and as source of food have been entirely collected and discussed in this review.

1.1. Pharmacological evidences of polygonaceae family

Various medicinal benefits are credited to this family, especially for bronchitis, cough, asthma, dysentery, diarrhea, earache, eczema, inflammatory, kidney disease, jaundice, paralysis, leprosy, toothache, colitis, intestinal parasites, ulcerative and money more, among polygonaceae species *Rumex* is famous and interesting which is discussed as under.

Rumex, a genus of polygonaceae family, is very predominant worldwide. There are about 200 species of this genus known, many of which are useful and traditionally used for medicinal practices [17]. All parts of the plant were found useful and have a number of health benefits. Literature studies revealed that genus *Rumex* possess diverse pharmacological assays like, antioxidant, anti-inflammatory, antifertility, cytotoxic, purgative, antibacterial, antifungal, antidiarrheal, antiviral and antipyretic assays [18]. It

was found that plant parts (root, stem leafs) of *Rumex hastatus*, are shown various bioassays such as antioxidant, anti-nociceptive, anti-diarrheal, and cytotoxic potential [19]. The plant also showed efficient antibacterial and diuretic properties [20]. *Rumex abyssinicus*, were traditionally used to cure hypertension and for relieving pain. A large number of important chemical constituents were found in *Rumex* which includes anthraquinones, naphthalene's, tannins, flavonoids, phenolic acids, stilbenoids, triterpenes, carotenoids, etc [21]. *Rumex hymenosepalus* contains Leucodelphinidin and Leucopelargonidin which are antitumor substituents [22] Neopodin, a substance found in *Rumex japonicus*, has an inhibitory effect of osteoclast [23]. *Rumex nepalensis Spreng*, is another species that is widely used for various actions like antifungal, antibacterial, purgative. This species has moderate cytotoxicity and high phytotoxic activity [24]. *Rumex dentatus, Rumex acetosa, Rumex crispus, Rumex patientia* and *Rumex obtusifolius* are some of the plants highly used for various pharmacological actions [25].

1.2. Taxonomic position

The importance of plants, especially medicinally active plants are in demand for the pharmacological studies in order to overcome the stress of medicinal needs. Among the largely existing traditionally valued plants known, the*Rumex dentatus* has its place on top. The genus *Rumex* is the second major family of Polygonaceae with approximately more than 200 species spread in Europe, Asia, Africa and North America, largely in the northern hemisphere [26]. *Rumex dentatus* is a species of flowering plant of family polygonaceae known by the common names like toothed dock, Indian dock or aegean dock. It is native to parts of Eurasia, North Africa, and Asia. It is commonly known as Abuj in Kashmir and widely distributed all over Jammu & Kashmir region. *Rumex dentatus* has therefore been chosen for the investigation due to its simplicity of access and strong traditional and pharmacological values.

2. Classification

Kingdom: Plantae.
Subkingdom: Tracheobionta (vascular plant).
Super division: Spermatophyta (seed plant).
Division: Magnoliophyta– Flowering plants.
Class: Magnoliopsida– Dicotyledons.
Subclass: Caryophyllidae
Order: Polygonales
Family: Polygonaceae– Buckwheat family.
Genus: Rumex L.– *dock*.
Species: *dentatus*.

3. Distribution around the globe

Literature analysis revealed that *Rumex* is the second major genus of family polygonaceae having more than two hundred species spread all around the world mostly in the northern hemisphere [27–29]. In China, *Rumex dentatus* could be found almost everywhere [30–33]. In India, *Rumex dentatus* L. is found in the plains, from Assam, Sylhet to the Indus ascending the Himalayas 300 m 1000 ft [34]. Pakistan and Egypt have found larger sources of distribution. In Kashmir *Rumex dentatus* is found everywhere from cities and urban to mountainous regions. It has almost 22 species in Jammu and Kashmir [35]. We collected the plant at different locations such as RS Pora Jammu, Srinagar, Budgam, Beerwah, Tangmarg, Pattan, Baramulla, Pahalgam, Drang, Gulmarg, Affarvat, Anantnag, Shopian, Leh, Kargil and Mansar Lake of Jammu and Kashmir etc.

4. General morphology

In Kashmir valley*Rumex dentatus* is known by its local name Abuj and its leaves have been used as a source of vegetable from time immemorial. *Rumex dentatus* belongs to the family Polygonaceae and is found throughout temperate western Himalayas from Kashmir to Kumaon, 8000–12000 feet. It is a seasonal flowering plant and grows in distraught areas, often in moist regions, such as lakeshores and the edges of cultivated fields. It is biennial with a cylinder, erect stem up to 70 or 80 cm in maximum height, grooved, branched from base, glabrous, branches ascending to almost divaricated [36]. The leaves are lance-shaped to oval with slightly wavy edges, growing to a maximum length around 12 cm. The inflorescence is an interrupted series of clusters of flowers, with 10–20 flowers per cluster and each flower hanging on a pedicel [37]. Flowers are bisexual. Outer tepals are elliptic 2 mm, inner petals enlarged in fruit, valves triangular ovate, 4–5 × 2.5–3 mm, all valves with tubercles 1.5–2 mm, visibly net veined, base rounded, each margin with 2–4 teeth, apex acute to subacute. Achenes yellowish brown, shiny, ovoid, sharply trigonous, 2–2.5 mm, base narrow, apex acute [38]. The variations in physical appearance of *Rumex dentatus* at different times in a year are shown in photographs taken below (Fig. 1) stage 1 stage 2 and stage 3.

Fig. 1. Different growth stages of *Rumex dentatus*.

5. Flowering stage and pollination

The flowering period of plant is May to June; its seeds ripen from July to August. The species is a hermaphrodite. The pollination generally occurs via anemophily or entomophily. *Rumex dentatus* mostly grows healthy in light (sandy), medium (loamy) and heavy (clay) soils. The tested soil of the plant is well-drained with neutral and alkaline in nature. Also, the plant favors mostly semi-shade, semi sunny light with moist soil [39]. Since *Rumex dentatus* can be easily found growing wild in Kashmir, thus researchers have easy access to use it for detailed phytochemical analysis and further evaluation. In view of the literature survey, it was found that all the parts of the plant are important and was found active against various diseases.

6. Traditional uses

The *Rumex* plant as mentioned above has vast traditional uses [40]. The plant was timely monitored and scientists brought it to light in order to help the common people in various ways, food and medicine in particular [41]. In the year 2001, *Rumex* plant was proven to have anti-bactericidal activity [42]. The plant species also showed anti-inflammatory, astringent, antitumor, diuretic and anti-dermatitis assays. The presence of cholagogu, tonic and laxative agents were also found in the plant [43,44]. All parts of the plant (leaves, stem and roots) have been used to treat pneumonia, cough, stomach-ache, smallpox and abscesses [45]. The given references

Table 1
Traditional uses of different parts (leaves, stem and roots) of *Rumex dentatus* from different places.

Species	Plant Part	Traditional uses	Region	References
Rumex dentatus	Leaves, Roots and stem	Pneumonia, cough, stomach-ache, smallpox and abscesses	Pakistan	Munir et al., 2016 [58]
	Leaves	Diuretic, refrigerant and cooling agent	Peshawar	Hameed and Dastagir 2009 [59], Fatima et al., 2009 [47].
	Roots	Acariasis, purgative, eczema, and dysentery	Pakistan	Saleem et al., 2014 [49]
	Roots	Acariasis, eczema, diarrhea and constipation	China	Zhu et al., 2010 [60]
	Leaves and shoots	Diuretic, refrigerant and cooling agents	Peshawar	Islam et al., 2006. [55], Hussain et al., 2006 [48].
	Roots	Used for treating astringent, cutaneous and purgative disorders		Chopra et al., 1986. [53], Manandhar et al., 2002 [54]
	Root Paste	Used to relieve headache		Manandhar, 2002 [54]
	Roots and Leaves	Used to treat asthma, jaundice, foot and mouth infections, fever, cough, weakness and scabies	Pakistan	Sing et al., 2023 [61]
	Whole plant	Anti-inflammatory, astringent, antitumor, and diuretic, antidermatitis, cholagogue, tonic and laxative agents		Suleyman et al., 1999 [62]., Litvinenko and Muzych Kina, 2003 [63], Demirezer, 1993 [64]
	Roots	Used as a folk medicine for treating ascariasis, eczema, diarrhea and constipation.		Olowokudejo et al., 2008 [65]
Rumex dentatus	Roots and leaves	bactericidal, anti-inflammatory, antitumor, anthelmintic, astringent, and anti-dermatitis, its roots are also used in folk medicine for treating acariasis, eczema, diarrhea, and constipation	Egypt	Abou et al., 2013 [66]
	Roots and leaves	Bactericidal, astringent, anti-dermatitis, diuretic, cholagogue, tonic and laxative agents	India	Humeera et al., 2013 [50]

provide us the record of traditional uses of *Rumex* species. But to our surprise, among them *Rumex dentatus* have the best accord of traditional uses. It has been observed that each part of *Rumex dentatus* is useful and important for medicinal purposes. The leaves of the plant were used traditionally as diuretic, refrigerant and cooling agents [46,47,48]. The roots of *Rumex dentatus* were used as an anti acariasis, purgative, eczema, and dysentery purposes [49]. *Rumex dentatus* were found to have broad spectrum of assays, such as antimicrobial and antioxidant assays and could be used as a possible alternative for treating above mentioned ailments [50]. The plant has been also employed traditionally for the treatment of various bacterial and fungal infections, e.g. enteritis, ascariasis and dysentery [51]. The roots were also used to treat diarrhea and constipation [52]. Further the roots of *Rumex dentatus* were also used as an astringent, curing cutaneous disorders and producing purgative effects [53,54]. Areal parts like leaves and shoots were used as diuretic, refrigerant and cooling agents [55]. *Rumex dentatus* is known to play a major role in bone and pain related disorders. Thus the plant is applied for strong decoction to dislocated bones and is used to ease body pain. Root pastes of the plant were applied externally to relieve headache [56]. Literature reports also revealed that the plant is a traditional herb in countries like Pakistan. Its roots and leaves were also used in treating diseases like foot and mouth infections, asthma, cough, jaundice, fever, weakness and scabies) [57]. Thus from the above discussion it is clear that the plant has an inordinate traditional importance and has a wide scope of being used as a traditional herb in India (Table 1).

7. General pharmacology of *Rumex dentatus*

The presented review summarized*in vitro* and *in vivo* biological properties carried out on the extracts of *Rumex dentatus* till date. Our efforts to summarize the comprehensive research work carried on phytochemistry, pharmacology, allelopathy and economic importance of *Rumex dentatus* can be a productive for researchers. The diverse extracts like methanol, hexane, ethyl acetate, chloroform, DCM, and H_2O have been evaluated for various biological assays such as antibacterial, antifungal, cytotoxic, antitumor, hepatoprotective, and skin disorders [67]. It is important to note that extracts of different parts of "*Rumex dentatus*" like, leaf, stem and roots showed predominantly different biological assays with respective extracts and provide clear evidences of variable phytochemicals present in the plant [68]. Researchers also found that, the mixtures of solvent extractions of *Rumex dentatus* were found to be active against variety of diseases than their individual ones. Literature precedents also showed that the methanolic extracts of roots and shoots of *Rumex dentatus* were found to be effective against all the bacterial strains tested, however the hexane extract inhibited fungal growth (up to 80%) more efficiently than the methanolic extracts [69]. Concentration of different extracts of *Rumex dentatus* effectively inhibited tumor induction on the potato discs produced by wild type agrobacterium strains. It was also reported that the methanolic extracts of leaf and stem inhibited radish seed germination (70 and 61% respectively) and root length more than the hexane extracts [70]. Also the extracts of *Rumex dentatus* were found active against various diseases [71]. Researchers then tried to isolate phytochemicals responsible for these assays of the plant. Some outstanding molecules have been isolated using HPLC analysis and normal column chromatography. All the isolates were characterized by spectral analysis like (IR, ^{1}HNMR, ^{13}CNMR, MS and X-ray crystallography) [72]. The various kinds of molecules like alkaloids, saponins, anthraquinones, tannins and flavonoids were found in the plant [73]. Moreover, various important bioactive compounds, such as chlorogenic acid, quercetin, myricetin, vitamin C, and kaempferol, have been identified in roots [74]. Previous phytochemical studies on *Rumex dentatus* have demonstrated the presence of anthraquinones, flavonoids, phytosterols, phytosteryl esters, fatty acids, chromones and anthrones [75]. The reported assays of solvent extracts of *Rumex dentatus* till date have been summarized in the presented review discussed as under.

7.1. Antioxidant assay

Nature has glorified the plants with some special agents for protection of their cells from the damage caused by free radicals (unstable molecules made during the process of oxidation in normal metabolic reactions). But for animals free radicals may play a part in cancer, heart disease, stroke, and other diseases of aging. Plants are considered a rich source of antioxidants and*Rumex dentatus* is one among them proven to have strong antioxidant properties [76]. It was observed that the total phenolic content and antioxidant capacities assayed by 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical scavenging and β-carotene bleaching methods on *Rumex dentatus* [77]. The results showed that the total phenolic content in the ethyl acetate fractions of leaves and roots were high and measured at 169.5 and 257.4 mg. The ethyl acetate fractions of leaves and roots exhibited strong DPPH activity and the DPPH IC50 values were 0.021 and 0.012 mg/mL of leaves and roots respectively. Furthermore, the ethyl acetate fractions of leaves and roots showed high reducing power and antioxidant activity assayed by β-carotene bleaching method. GC-MS and HPLC analyses indicated that these fractions contained a variety of phenolic compounds including *p*-hydroxybenzoic acid, syringic acid, vanillin, benzoic acid, ferulic acid, and cinnamic acid, used the plant for antioxidant activity [78]. Different extracts used, which revealed that the extracts exhibited scavenging effects in concentration-dependent manner on superoxide anion radicals and hydroxyl radicals. The phytochemical tests carried out with the crude extracts of Rumex dentatus showed the presence of flavonoids, terpenoids, alkaloids, saponins, tannins, anthraquinones and cardiac glycosides in it. The total phenolic content of these extracts was estimated quantitatively from standard calibration curve of gallic acid and it varied from 145 μg/mg in butanol extract to 45 μg/mg in petroleum ether extract [79]. The standardization of Rumex dentatus by performing the investigations and estimation of sugar, starch, tannins, phenolics and flavonoids is very important research finding. The sugar and starch content in powdered leaves of Rumex dentatus was found to be 0.037% & 5.78%. The UV spectroscopic estimation of tannins, phenolics, and flavonoid content in powdered leaves of Rumex dentatus was found to be 1.15%, 56.008%, 0.353% [80]. evaluated the antioxidant properties by 2, 2-diphenyl-1-picrylhydrazyl (DPPH) free radical using a slightly modified method. Each extract sample was initially analyzed spectrophotometrically at 513 nm using a concentration of 200 μg/mL and the extracts revealed worthy antiradical activity (≥50%). The extract was further examined to find IC50

values at lower concentrations. The % antiradical activity of test extract = (1-Aab/Bab) × 100Aab is the absorbance of the extract sample. Bab is the absorbance of reagent with negative control. Ascorbic acid served as positive control. Thus from above discussion the plant was found to be good in compounds having antioxidant activity.

7.2. Antibacterial assays

Antibacterial agents obliterate bacteria or subdue their growth or to stop the faster reproducing properties. The worldwide problem of antibiotic resistance is becoming one of the foremost scientific issues of current times [81]. The progress of new antibiotics is slow and complex process. However the bacterial resistance is decreasing and our arsenal of existing drugs posing a catastrophic threat as ordinary infections become untreatable. Preventative action is needed to help in reducing resistance. Now the aim of the world scientific community is to improve the ability to target infections more precisely by encouraging the development of new tools. As of now synthetic drugs are time consuming and difficult to produce on time, therefore the search for plant derived drugs have accelerated in recent years [82]. Ethno pharmacologists, botanists, microbiologists, and natural-product chemists are working on plants and trying to explore phytochemicals for probing and generating library of medications which "leads" for treatment of infectious diseases on timely basis [83]. The antibacterial cure by scientific community using *Rumex dentatus* marked strong impact discussed as under [84] investigated the antimicrobial assays of *Rumex dentatus* L., and used Agar disk diffusion method for antimicrobial activity. *Rumex dentatus* extracts were tested against different clinical bacterial strains (*Shigella flexneri, Klebsiella pneumoniae, Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus and Salmonella typhimurium*). Among all extracts, the butanol extract showed strong antibacterial activity against *Klebsiella pneumoniae* (inhibition zone diameter of 20 mm) [85]. presented the study to investigate the antibacterial activity of the stem extract of *Rumex dentatus* against bacterial pathogenic strains (*Bacillus subtilis, Escherichia coli, S. aureus and Micrococcus lutes P. aeruginosa*). The result of the extracts in methanol and cold water were found to be effective against all the tested bacterial strains. Then minimum inhibitory concentration (MIC), of the extracts against these bacterial strains were found to be in the range of 0.10 mg/ml. The research reported that *Rumex dentatus* is a potential plant against bacterial pathogenic strains [86]. Studied the effect of different extracts of *Rumex dentatus* on harmful bacterial strains and observed that ethanol and hexane extracts have the potential to inhibit most of the tested multi-drug resistant bacterial strains [87]. Prepared leaf, stem and root extracts in methanol and hexane by simple maceration. The methanol extracts of root and shoot were found effective against all the bacterial strains tested. Zone of inhibition ranged between 9.7 and 12.1 mm. They reported that *Rumex dentatus*methanol extract showed presence of alkaloids, saponins, anthrax quinones and tannins while flavonoids were also found in both methanol as well as hexane extract were mainly responsible for bacterial inhibition. Thus with the given evidence the plant has strong potential to be used as an antibacterial phytomedicine. If the plant is given clinical priority it can better replace synthetic medication for various bacterial infections.

7.3. Antiviral assays

Viruses are microscopic organisms found everywhere on earth. They have the potential to infect every living organism even bacteria can't be spared [88]. Sometimes viruses are so deadly and can be fatal. Some viral infections trigger no noticeable reaction till death of an infected person. A virus has the potential to have particular effect on individual and the same virus can affect human but not animals or vice versa or both. Viruses vary in complexity. They consist of genetic material, RNA or DNA, surrounded by a coat of protein, lipid (fat), or glycoprotein. Viruses cannot replicate without a host, so they are classified as parasitic [89]. Viral infections are thought to be one of the most serious threats to human life. It is now widely acknowledged that natural products (NPs) are the single most important source of antiviral agents for the treatment of COVID-19 [90]. In order to overcome viral infections both synthetic and plant medications have been immensely used. Herein we report *Rumex dentatus* as an antiviral medication, the research team investigated the inhibitory effects against dengue virus serotype 2 (DENV-2) by using five different solvent fractions (extracted by methanol, ethanol, benzene, chloroform and n-hexane) of *Rumex dentatus* [91]. The study finds that the methanolic extract of *Rumex dentatus* demonstrated the highest antiviral efficacy by inhibiting DENV-2 replication, with IC_{50} of 0.154 μg/mL and 0.234 μg/mL. Not much work on *Rumex dentatus* against viruses has been done, the plant has the potential if given priority in this field of research and can act as potential medication against different viruses like found active against dengue virus.

7.4. Antifungal assays

[92] Studied antifungal activity of various extracts of *Rumex dentatus* on various fungal strains. The study revealed that the tested fungal species *Fusarium solani*, *Aspergillus flavus* and *Aspergillus niger* were more susceptible to crude extracts of *Rumex dentatus* with MICs 0.75, 2.15, and 1.75 μg/ml, respectively [93] used *Rumex dentatus* extracts and evaluated it for antifungal activity. Leaf, stem and root extracts of *Rumex dentatus* were made in methanol and hexane by simple maceration. The methanol and hexane extracts of root and shoot were tested on various fungal strains and the hexane extracts inhibited fungal growth (up to 80%) more efficiently than the methanol extracts. The more work in this filed needs to be done and plant must be thoroughly used on different fungal strains to explore it as medicinal herb for fungal diseases.

7.5. Anticancer assays

Cancer refers to any one of a large number of diseases categorized by the uncontrolled and abnormal growth of cells with the aptitude to penetrate and terminate normal body tissue. The disease often has the ability to spread throughout the body. Cancer is the second-leading cause ofdeath in the world and needs strong and viable medication [94]. *Rumex dentatus* has been evaluated against various cancer cell lines successfully [95]. used methanolic and hexane extracts of *Rumex dentatus* and evaluated them for cytotoxicity and antitumor assays. The positive results were observed with the inhibition of tumor induction on the potato discs produced by wild type *Agrobacterium* strains At10 and At6. The root extracts either in methanol or hexane showed LD50 values below 1000 ppm in brine shrimp mortality assay. The *Rumex dentatus* methanol extract showed presence of alkaloids, saponins, anthraquinones and tannins while flavonoids were also found in both methanol as well as hexane extract. [96], evaluated *Rumex dentatus* against breast cancer MDA-MB-231 cell line, a triple negative human breast cancer cell line with invasive properties and to identify the molecular targets underlying its mechanism of action. Cytotoxicity of plant extracts was determined against breast cancer cells, using the MTT assay. Flow cytometry was performed to analyze the changes in cell cycle and apoptotic effect, if any. Cells were also studied for their wound healing and invasive potential as well as for Western blotting of apoptotic genes and nuclear factor-kappa B (NF-κB) pathway [97] used different concentrations of the extracts and dose-dependent growth inhibition of treated cancerous cells was observed at 48 h treatment. Maximum anti-proliferative activity was obtained by ethanol, benzene and chloroform extracts against breast cancer MCF-7 cell line with lowest IC50 at almost equal concentrations as 47.3, 49 and 48 μg/mL respectively. Benzene and chloroform extracts also inhibited prostate cancer cells (DU-145) proliferation at relatively lower IC50 as 94 μg/mL and 99 μg/mL respectively while methanol (123 μg/mL) and ethanol (128 μg/mL) extracts were more potent to inhibit proliferation of hep-2 cells. All the extracts were non-cytotoxic for HCEC normal cell line. Overall, MCF-7 cell line showed most sensitivity among all tested cancerous cell lines to extracts of *Rumex dentatus* with lowest IC50 values. Proving to have anticancer effects the plant needs attention as there is evidence of having anticancer molecules which are responsible for its anticancer activity.

7.6. Anti-diabetic assay

Diabetes is a disease, occurs when your blood glucose, also called blood sugar, is too high [98]. Blood glucose is central source of energy which comes from the food. Insulin, a hormone made by the pancreas, helps glucose from food to get into cells to be used for energy [99]. The other complications caused by this disease are heart disease, heart attack, stroke, neuropathy, nephropathy, retinopathy and vision loss, hearing loss, foot damage such as infections and sores, that don't heal, skin conditions such as bacterial and fungal infections, depression and dementia, thus we can say that the diabetes is very dangerous and needs immediate cure [100]. Scientists are trying to get medication for the disease both via synthesis and using natural products. The ant-diabetic effects of polyphenol-rich *Rumex dentatus* extract (RDE) were investigated in type 2 diabetic rats. Phytochemical investigation of the aerial parts of *Rumex dentatus* resulted in the isolation of one new and seven known compounds isolated for the first time from this species. In diabetic rats, RDE attenuated hyperglycemia, insulin resistance and liver injury and improved carbohydrate metabolism. RDE suppressed oxidative stress and inflammation and upregulated PPARγ. In silico molecular docking analysis revealed the binding affinity of the isolated compounds toward PPARγ and decreased glucose level in cells. This proved that the plant can prove natural diabetic healer [101]. We must treat the plant as one of the useful anti-diabetic herb and should work on it for further exploration.

7.7. Anti-inflammatory assay

The inflammatory response (inflammation) occurs when tissues are injured by bacteria, trauma, toxins, heat, or any other cause. The damaged cells release chemicals including histamine, bradykinin, and prostaglandins [102]. These chemicals cause blood vessels to leak fluid into the tissues, causing swelling, the inflammation is sometimes dangerous and need immediate antidote [103]. Chronic inflammation frequently involves dysregulation of a wide range of intracellular signalling pathways, including transcription factors, kinases, and cell surface receptors. In a normal situation, inflammation activates a variety of protein kinases, including AKT/PI3K, MAPK, and JAK, as well as the families of protein kinases associated with the members of these protein kinase families, with the goal of modifying metastasis progression [104]. Several *Rumex* species, including *R. vesicarius, R. nepalensis*, and *R. patientia*, have been reported to have anti-inflammatory properties [105–108]. A study found that *R. dentatus* polyphenol-rich extract increased PPARc expression while suppressing inflammation and oxidative stress [109]. Another study found that *R. dentatus* methanolic extract has an anti-inflammatory effect in mice at a dose of 500 mg/kg (p.o) [110]. However, the precise compound responsible for such activities is still unknown [111]. investigated the gastroprotective and other biological effects of *Rumex dentatus* crude extract. According to this study, immunohistochemistry, ELISA, and Western blot techniques revealed improved cellular architecture and decreased expression of inflammatory markers such as cyclooxygenase (COX2), tumour necrosis factor (TNF-), and phosphorylated nuclear factor kappa B (*p*-NFB). In RT-PCR, it lowers H+/K + -ATPase mRNA levels. To summarize, *Rumex dentatus* extracts and phytoconstituents have the potential to be effective anti-inflammatory drug candidates with anti-diarrheal, anti-secretary, antispasmodic, anti-H. pylori, and anti-ulcer properties. The detailed biological significance of different extracts of *Rumex dentatus* with year wise progress is shown via graphical representation in Fig. 2. It was clear from the literature that plant has been studied extensively since 1950 to 2020.

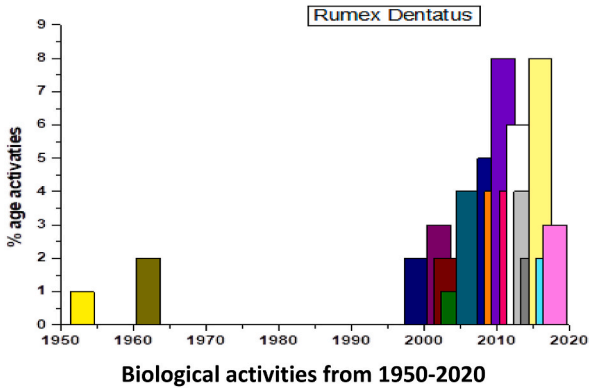


Fig. 2. The enhanced biological significance of extracts of *Rumex dentatus* since 1950–2020.

8. Phytochemicals isolated from *Rumex dentatus* and their observed biological assays

Phytochemicals are the substances of plant origin whichprovides health and medicinal benefits including preclusion and treatment of diseases. They are naturally present in foods and acting in synergy, bestow potential on different infections. The present review describes the structural representation of isolated phytochemicals from *Rumex dentatus* and their biological assays done till date. Researchers all over the world worked on *Rumex dentatus* and isolated number of phytochemicals and performed their biological assays. Compounds isolated [112,113] from *Rumex dentatus* till date are summarized in Table 2.

The research in the field of isolation of bioactive molecules continues and every year compounds are being added herein more compounds have been isolated during the time from *Rumex dentatus* and identified by spectroscopic data. The compounds are chrysophanol, 6 methyl 7 acetyl 1,8dihydroxy 3 methoxy naphthalene-1-O-β-D(L)-glucoside, and 6-methyl-7-acetyl-1,8-dihydroxy naphthalene-1-Oβ D(L) glucoside [114,115]. The compounds were screened for biological assays and showed antiproliferation assays, using the MTT assay in four cell lines (breast cancer MCF 7, gastric cancer 7901, melanoma A375 and oophoroma SKOV 3) [116] Team of scientists isolated novel, eight anthraquinone derivatives from *Rumex dentatus*, compounds were found as emodin, physcion, chrysophanol, physcion glucoside, endocrocin, emodin glucoside, chrysophanol, chromone derivatives and monoterpenes [117]. Then further ten compounds have been isolated which were identified as helonioside A, gallic acid, isovanillic acid, p hydroxycinnamic acid, succinic acid, n butyl beta D fructopyranoside, quercetin, hexadecanoic acid 2, 3 dihydroxy propyl ester, beta sitosterol and daucosterol [118,119]. The conformation of three epimeric pair of new C glucosyl anthrones from *Rumex dentatus* by on line high performance liquid chromatography circular dichroism (HPLC CD) analysis were also reported. All the mentioned compounds were isolated from the roots of *Rumex dentatus* by column chromatography. Their structures were elucidated by mass spectrometry, nuclear magnetic spectroscopy and HPLC CD analysis. The structural names of the compounds isolated areas under, 10R C d glucosyl 10 hydroxyemodin 9 anthrone (rumejaposide E, 1) and 10S C d glucosyl 10 hydroxyemodin 9 anthrone (rumejaposide F, 2), 10R C d glucosylemodin 9 anthrone (rumejaposide G, 3) and 10S C d glucosylemodin 9 anthrone (rumejaposide H, 4), 10S C d glucosyl 10 hydroxy chrysophanol 9 anthrone (cassialoin, 5) and 10R C d glucosyl 10 hydroxy chrysophanol 9 anthrone (rumejaposide I, 6). Rumejaposides F I (24 and 6) was new C glucosyl anthrones. Rumejaposide E (1) and cassialoin (5) [120–123] have been already reported in literature. Structurally all the compounds are shown in section 2 and well mentioned in the given summery. The summarized compounds will be helpful to researchers and ease their work for new isolation.

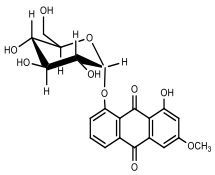
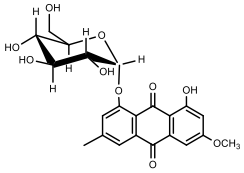
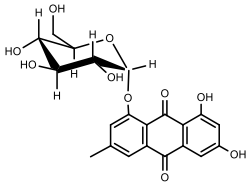
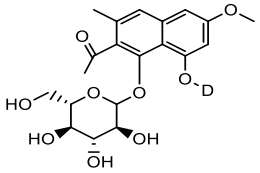
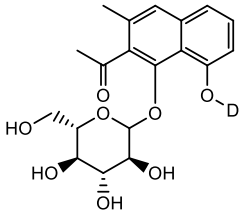
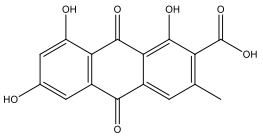
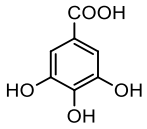
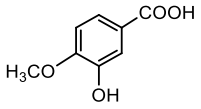
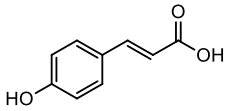
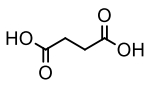
Section 2: The isolated anthraquinone glycoside derivatives from *Rumex dentatus*.

With the advancement of molecular isolation technique, plants were extensity studied. The isolation of compounds from*Rumex dentatus* has started in 2002, since then more than 41 compounds have been isolated. It can be easily accessed from graph in Fig. 3 that the isolation since 2002 till 2019 has paced up the work and need further exploration due to the presence of biologically potent drugs like quinones, isoquinones, flavonoids, etc. in the plant skeleton.

9. Economic importance of *Rumex dentatus*

Plants as a source of food and medicine reveal their importance and impact on economic potential. Traditionally*Rumex* species as source of medicine has marked its place around the globe [124]. Plants with strong historical background of service and their potential to continue contributing in the future by supporting sustainable development of societies and economies, attracted scientists towards such fields of research [125]. The dependence of humans from past, the present and the future is woven in human cultures and their habits to use plants as medicine, food, pharmaceuticals and energy. According to the traditional knowledge, *Rumex dentatus* has a strong record of medicinal value for improving health and welfare [126]. Usefulness for human diet is documented in numerous studies. The presence of bioactive compounds in *Rumex dentatus* and the uses of its extract for curing number of diseases add wide scope of the plant [127]. Thus from vegetation to the medicinal importance *Rumex dentatus* plant will act as an alternate food and strong solution to various deadly diseases [128]. Economic importance might be well correlated with increasing interest for functional food area worldwide, which further may lead to intensify the production of *Rumex dentatus* and its presence in market stands [129].

Table 2
Compounds isolated from *Rumex dentatus*.

S·NO.	Name	Structure	Reported Activity	Year
1	Chrysophenol-glycoside		Antiproliferation Assays in Four Cell Lines	Zhang et al., 2012. [30], Jan et al., 2012 [135].
2	Physcion-glycoside			Jan et al., 2016 [117].
3	Emodin-glycoside		Anti proliferative assay	Jan et al., 2012 [135].
4	6-methyl-7-acetyl-1,8-dihydroxy-3-methoxy naphthalene-1-O-D(L)-glucoside		Anti proliferative Assay	Zhang et al., 2012 [116].
5	6-methyl-7-acetyl-1,8-dihydroxy naphthalene-1-O-D(L)-glucoside		Anti proliferative Assay	Jan et al., 2012., Zhang et al., 2012 [116,135].
6	Endocrocin		Anti-Cancer	Jan et al., 2012., Zhan et al., 2006 [51,135].
7	Gallic acid		Anti histamine, Antifungal	Zhu et al., 2006 [133].
8	Isovanillic acid		Antioxidant	Zhu et al., 2006 [133].
9	*p*-hydroxycinnamic acid		Antioxidant	Zhu et al., 2006 [133].
10	Succinic acid		Arthritis and joint pain	Zhu et al., 2006 [133].

(*continued on next page*)

Table 2 (*continued*)

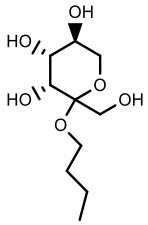
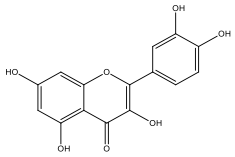
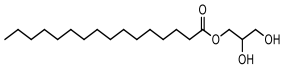
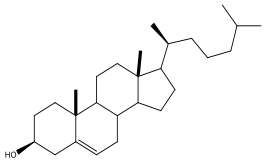
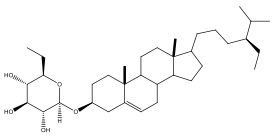
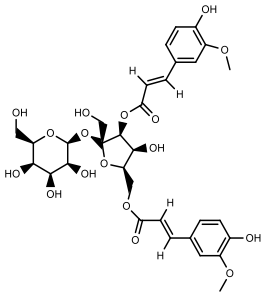
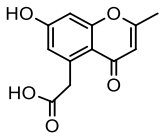
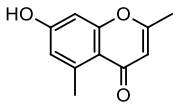
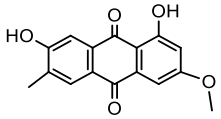
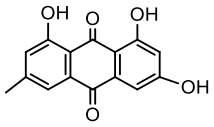
S·NO.	Name	Structure	Reported Activity	Year
11	n-butyl-beta-D-fructopyranoside		Antiproliferative effects	Zhu et al., 2006 [133].
12	Quercetin		Anti-inflammatory and anti hypertension	Zhu et al., 2006 [133].
13	hexadecanoic acid 2, 3-dihydroxy propyl ester		Disruptive effect on membranes	Zhu et al., 2006 [133].
14	beta-sitosterol			Zhu et al., 2006 [133].
15	Daucosterol		Inactivation of PI3K/Akt pathway and upregulation of*PTEN*gene	Zhu et al., 2006 [133].
16	Helonioside A		Anti proliferative assay	Zhu et al., 2006 [133].
17	2-(7-hydroxy-2-methyl-4-oxo-4H-chromen-5-yl) acetic acid		Antitumor, antibacterial, antifungal, anticoagulant, and CNS assay	Zhu et al., 2006 [133].
18	7-hydroxy-2, 5-dimethyl-4H-chromen-4-one		CNS active, anti-inflammatory	Zhu et al., 2006 [133].
19	Physcion		Antimicrobial Assay	Khalil et al., 2022 [109]
20	Emodin		Antimicrobial Assay	Khalil et al., 2022 [109]

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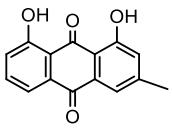
Table 2 (*continued*)

S·NO.	Name	Structure	Reported Activity	Year
21	Chrysophenol		Anti proliferative	Zhang et al., 2012 [30].

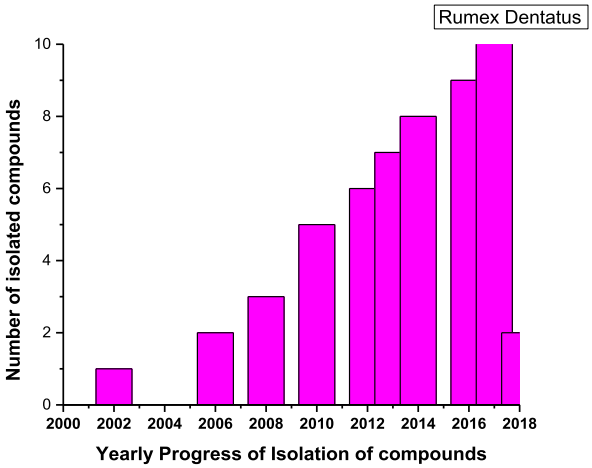


Fig. 3. Rate of isolation of biologically active molecules from *Rumex dentatus*.

10. Techniques used to isolate and identify compounds from *R dentatus*

There are several methods used to isolate different chemicals from *R. dentatus*, including HPLC-PD, HPLC, column chromatography, GC/MS, and GLC [130–132]. By using ^{1}HNMR, ^{13}CBNMR, MS, and IR spectroscopy, the compounds have been characterized [133–135]. Compounds isolated and identified via above given techniques are Rumejaposide E, Rumejaposide F, Rumejaposide G, Rumejaposide H, cassialoin, rumejaposide, quercetin, avicularin, quercitrin, rutin, myricetin, and kaempfero, as well as vitamin C, vitamin A, *p*-hydroxybenzoic acid, cinnamic acid, syringic acid, ferulichave been detected in *R. dentatus*.

11. Conclusion

As a result, among the many therapeutic plants that are currently available, Rumex dentatus, a traditional pharmacophore that is extensively used in traditional medicine, occupies a significant position. Traditionally leaves of this plant are used for abscesses, diuretic, refrigerant and as cooling agent, while shoots and roots are used to cure pneumonia, cough, stomach-ache, small pox, asthma, jaundice, fever etc. The plant has been found rich in large number of high valued bioactive compounds. Among these, anthraquinones, naphthalene, flavonoids, phenols and acids are the main classes of bioactive compounds. More than forty one (41) bioactive compounds have been isolated till date from this plant species and all of these compounds were found active against various diseases. The broad spectrums of diseases were treated by using raw parts of *Rumex dentatus* or its extracts. The plant showed antimicrobial and antioxidant activity, it was also found effective for inflammation and showed potential hepato-protective, anti-helminthic, insecticidal, antimicrobial, antitumor, antiviral and anticancer properties. As from the literature reports, extracts prepared from different parts of *Rumex dentatus* using different solvent systems showed variable biological assays. Apart from its strong bioactive accord, the plant was also found to be allopathic in nature which adds further to its pharmacological importance. Thus the plant can be used as a selective weedicide as it is having great scope in replacing chemical weedicides which have proven harmful for the environment as well as for plants and animals leaving heavy metals and other toxic chemical in the environment. Therefore the concluding remarks of *Rumex dentatus* in terms of traditional uses, isolated phytochemicals and phytochemistry done till date placed it on top of researcher's choice as a strong herbal base formulations to be used against these many diseases for better and benefit of mankind. The plant holds unique place among the various medicinal plants available around us. The present review highlight and document the research findings carried out on this plant species by different researchers to bring light on the work done till date on *Rumex dentatus* and make it available to the students, researchers for more scientific studies to bridge the gap in better utilization and validation of its pharmacological potential. The present review has been drafted and documented such that the complied data can be easily accessed to broaden its future research prospects and made it available to scientific community with easy access.

Author contribution statement

All authors listed have significantly contributed to the development and the writing of this article.

Funding statement

This work was supported by UGC-MANF [F1-17.1/2013-14/MANF-2013-14-MUS-JAM-26374].

Data availability statement

Data will be made available on request.

Declaration of interest's statement

The authors declare no conflict of interest.

Ethical statement

This article does not contain any studies with human participants or animals performed by any of the authors.

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