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INVESTIGATION OF GENUS RUMEX FOR THEIR BIOLOGICALLY ACTIVE CONSTITUENTS

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ABSTRACT: The Potential of natural products to serve as effective and safe pharmaceutical agents have been increased due to the growing need of anti-inflammatory, anti-cancer and anti-biotic agents. Rural areas population of the Afro-Asian countries rely on the traditional medicinal systems to cure their ailments and largely based on the use of roots, leaves, fruits and flowers of different medicinal plant. A large number of sources of natural products, including plants, animals and minerals, have been found to be the basis of treatment of human diseases and have been explored to use by human for thousands of years. Pharmaceutical significance of the genus *Rumex* depends upon the occurrence of the chemical constituents which are found to have biological activities like anti-malarial, anti-inflammatory, anti-diarrheal, anti-viral activities and many other activities. Latest research was carried out on *Rumex* for its antioxidants, antibacterial, antiviral, antifungal, anti-mutagenic, anti-tumor and anti-suppressive activities The genus *Rumex* has attracted the attention of many investigators to isolate and analyze secondary metabolites due to its medicinal properties. This review article emphasized on the medicinally and biologically active secondary metabolites isolated from the various species of the genus *Rumex*. This genus is a rich source of the chemical compounds acting as drugs like anti-viral, anti-fungal, anti-bacterial, anti-inflammatory, anti-pyretic, anti-tumor, anti-aging agents. Different classes of compounds occurring in various species of the genus *Rumex* such as quinines, anthraquinones, naphthalene, flavonoids, chromones, steroids, terpenoids etc. play a vital role in drug discovery.

KEYWORDS: *Rumex species*, Chemical constituents, Biological activities

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1.INTRODUCTION

The presence of large number of biologically active compounds in different species of the Genus *Rumex* made it significant in medicine as well as pharmaceutical industry. These active compounds are called as secondary metabolites like flavonoid glycosides, anthraquinones, steroids, proanthocyanidins and phenolic compound [1]. The genus *Rumex* belonging to family polygonaceae [2] which consists of more than 200 species that are of worldwide in distribution. The plants belong to this genus flowers from April to May and their seeds ripen from May to June. Botanically it have been identified that the plants belong to this genus are perennial herbs [3]. The species of the genus *Rumex* are of wide occurrence and 25 of them grow in Poland [4]. The species occurring in this genus are very difficult to distinguish from each other due to similarity in their morphology. The original importance and significant of the genus *Rumex* was based on the chemical constituents present that show biological activities like anti-malarial, anti-inflammatory [5], anti-diarrheal [6], anti-viral activities [7] and many other activities. Latest research carried out on *Rumex* has proved its significance acting as anti-oxidants, anti-bacterial, anti-viral, anti-fungal, anti-mutagenic, anti-tumor and anti-suppressive agents [8-10]. The genus *Rumex* has attracted attention of researchers to investigate its different species for their chemical constituents due to their medicinal properties. Different classes of the chemical compounds occurring in different species belong to genus *Rumex*.

Chemical Constituents

Acids*:* Acids acting as both essential and non-essential to living organisms even human. A number of acids have been isolated from different species of the genus *Rumex*. The acids are very important from biological point of view. Among acids isolated from different species of the genus *Rumex* are mostly fatty acids e.g.; Lenoleic acid (1), palmitic acids (2), steric acids (3) have been isolated from the species *R. induratus*. Among these, Linoleic acid (1) is acting as essential to human, but the saturated acids like palmitic acids (2), steric acids (3) are acting as non-essential. Similarly, benzoic acid (4), has been isolated from the species *R. induratus* [11,12] benzoic acid (4) occurs naturally free or in esterified form as methyl-ester or ethyl-ester. It is used to preserve food [13], as antibacterial and antifungal agent [14]. Oxalic acid (5) was isolated from *R. abyssinicus* while tartaric acid (6) and citric acid (7) were obtained from *R. nervosus*. Due to the presence of oxalic acid (5), tartaric acid (6) and citric acid (7), crude extracts of these plants were tested against anti-bacterial activity. Chrysophanic acid (8) was isolated from *R. abissinicus* and *R. nepalensis* [15]. Due to the

presence of chrysophanic acid (8) in *R. nepalensis* showed the antifungal activity. Moreover leaves of *R. nepalensis* are cooked as food, infusion given in dysmenorrhoea and in stomach to patient [16]. Moreover, Chrysophanic acid (8) was also isolated from roots of *R. japonicus* and used to cure acute and chronic cutaneous diseases [17]. Ferulic acid (9) was identified in leaves of *R. induratus*. 4-vinylguaiacol was obtained from the decarboxylation of ferulic acid (9) [18] and the ferulic acid (9) acts as anti-aging and anti-cancer agents. Likewise, the roots of *R. crispus* contains erulic acid (10) and leaves of the *R. crispus* contain ascorbic acids (11), both these (10) and (11) acting as anti-tumor agents and (11) is also acting as anti-oxidant [19].

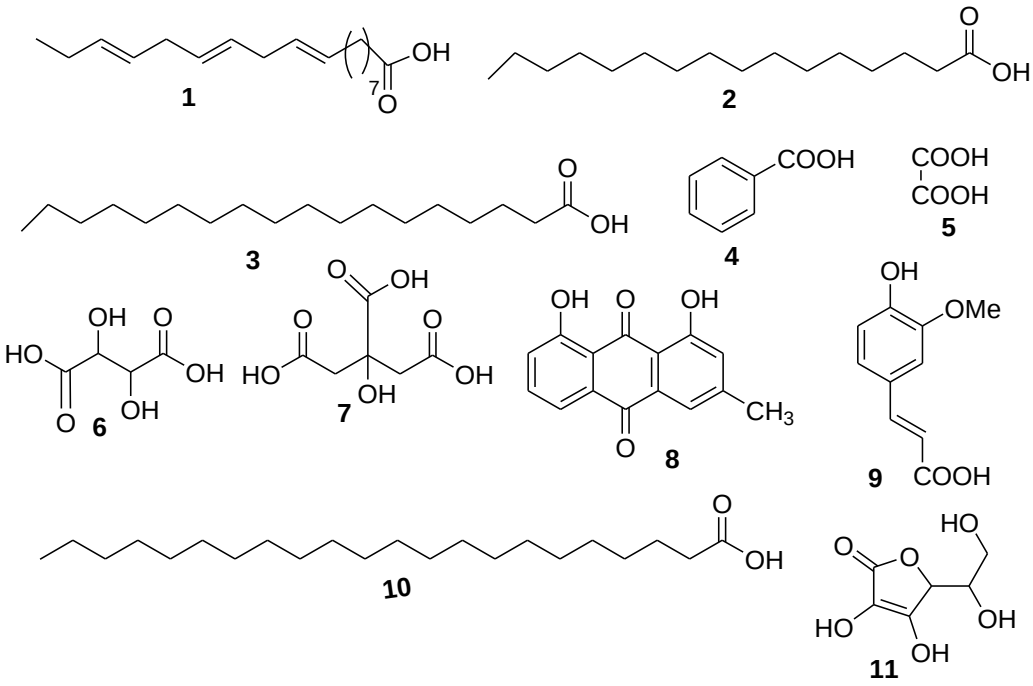


Figure 1: Structures of Acids (**1-11**)

Alcohols and aldehydes

Alcohols and aldehydes especially the saturated and unsaturated are much important. They were also isolated from some species of the genus *Rumex*. For example, (E)-4-hexen-1-ol (12) and 2,4-hexadiene-1-ol (13) were detected in *R. induratus* and derived from fatty acid metabolism [15] while on the other hand concerning to aldehydes, the presence of (E)-cinnamaldehyde (14) was noticed [15] and it is responsible for inhibition of the growth of *E. coli* [20]. Similarly, Retinal (15) was also isolated from the *R. induratus* and also derived from central cleavage of β-carotene [15] which is a chromophore and provide all visual pigments [21]. Aldehydes and alcohols are very important due to their property which is responsible for imparting green color to leaves and constituent a defense mechanism to mechanical damage [22].

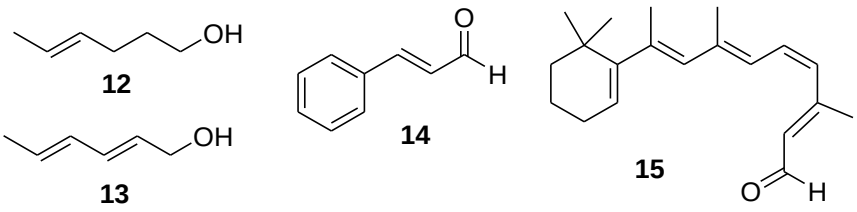


Figure 2: Structures of the Alcohols (**12, 13**) and Aldehydes (**14, 15**)

Anthraquinones and their derivatives

A large number of species belong to the genus *Rumex* are the rich sources of hydroxy-anthraquinones. The type and level of hydroxy-anthraquinones in plants widely varies depending upon the genetic factors and environmental conditions [23]. Chemical analysis of pharmaceutically important anthraquinonoes lead to the isolation of three important anthraquinones from roots of *R. crispus* which are 1,5-dihydroxy-3-methylanthraquinone(16),1,3,5-trihydroxy-6-hydroxymethylanthraquino ne (17) and 1,5-dihydroxy-3-methoxy-7-methylanthraquinone (18). These compounds (16-18) make the use of deride roots of *R. crispus* to cure constipation, to purify the blood in skin complaints in Turkish traditional medicine, the leaves of plants are used as food. Recently, research showed that anthraquinones contribute to bioactivities within this genus especially as to the anti-micro-organic, purgative, anti-inflammatory activities [24, 25]. The anthraquinone derivatives used as secondary metabolites important for plants have been detected and isolated chromatographically. For example, physcion(**20**), physcion-1-O-β-D-glycopyranoside (21), nepodine (22), rhein (23), physcion-8-O-β-D-glycopyranoside (24) were isolated from the *R. acetosa, R. acetosella, R. confertus, R .crispus, R. hydrolapathum, R. obtusifolius and R. nepalensis* [7] and all these compounds (19-24) delivered a material called *radix lapathi* to these plants which is used in phytotherapy due to their laxative properties. Furthermore, it was noticed that *R. acetosa* and *R. acetosella* are used in our diet [26,12]. Presence of Nepodin (22), in the roots of *R. nepalensis* make its use as anti-fungal while due to the presences of the emodine (19) &physcion (20) the extract from roots of *R. abssinicus* were reported to use as antibacterial against a large number of bacteria [27]. Moreover, *R. abyssinicus* play an important role in improving the immune system of the body [8] and in process of wound healing, regeneration of epithelial cells [8]. Likewise, Rhein-dianthrone-D-glycoside (25) was identified in leaves, roots and fruits of *R. crispus* and *R. obtusifolus*and use as sennoside [7]. Similarly, 3-acetyl-5-hyroxy-7-methoxy-2-methyl-1,4-naphthaquinone (26) was reported in *R. japonicus* and is utilized as antimicrobial agent. On the same way, Aloe-emodine acetate (27), which is an anthraquinone derivative was reported in *R. acetosa* [28], acting as a starting material for synthesis of anthracyclin anti-biotics, as cathartic agent, anti-septic and anti-microbial, anti-mutagenic, antibacterial and anti-leukamic agents. Another derivative of anthraquinone, Emodine (19) was also reported in *R .japonicus*& it is used to cure acute & chormic cutaneous disease [23]. Similarly,

another species of the genus *Rumex*, *R. mantimus* on analysis was found to contain anthraquinone which are responsible to remove pain from back and also used as tonic to burns. It has been investigated that the dried roots of *R. patientia* are used as purgative, constipative, deporative and tonic in Turkish medicine because of the presence of anthraquinone glycoside like emodine-6-O-β-D-glucopyranoside (28), chrysophanol-8-O-β-D-glycopyranoside (29), emodine-8-O-β-D-glycopyranoside (30) [29]. The anthraquinone present in extract of *R. nepalesis* are responsible for its purgative activity because it has been found that these anthraquinones increase the intestinal peristalsis & gastro-intestinal motility and also provide support to traditional medicine system [24].

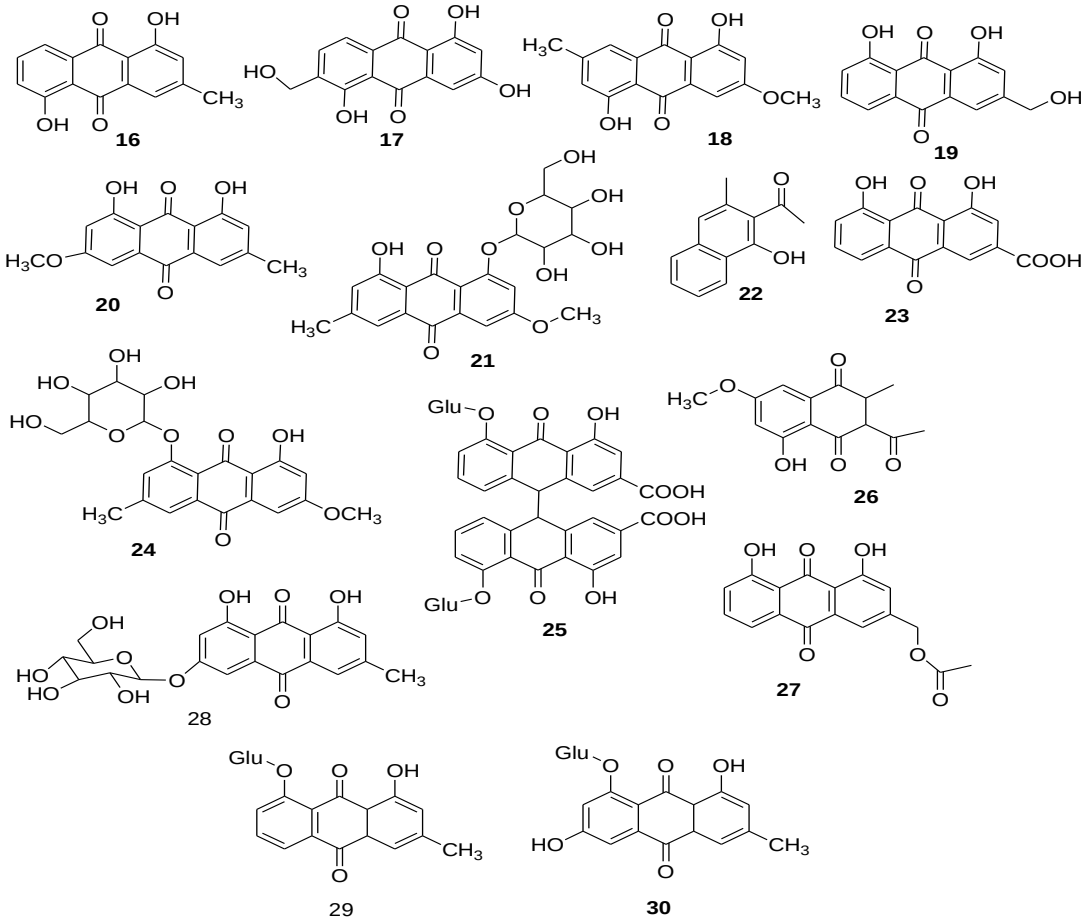
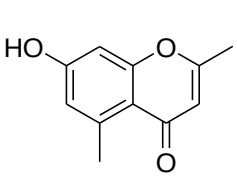


Figure 3: Structures of Anthraquinones and their derivatives (**16-30**)

Chromones

Another class of chemical compounds known as chromes occur in the different species of the genus *Rumex*. e.g.; 7-hydroxy-2,5-dimethyl chromone (31) & 2-methyl-5-carboxy methyl-7-hydroxychro mone (32) [30] (Zhu et al., 2006). Due to the presence of these compounds some species like *R. maritimus* is used in diarrhoed [9].



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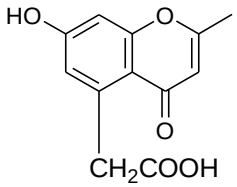

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Figure 4: Structures of Chromones (**31, 32**)

Flavonnoids

An important class of secondary metabolites also called as bio Flavonoids also occur in the genus *Rumex*. These were discovered as vitamin p by a biochemist Albert Szent-Gyorgi who was awarded nobel prize [31-33]. Flavonoids are polyphenolic compounds occurring in plants [34]. These are derivatives of a large heterogenous group of benzo-γ-pyron and are present in fruits, vegetables and medicinal plants. These have attracted the attention of the researchers over the last several decades and their biological activities like anti-oxidant, apoptosis-induction and anti-inflammatory activity have been noticed [35-37]. These activities show the beneficial effects of flavonoids in different human pathologies, including hypertension, inflammatory conditions even cancer [38]. The flavonoids obtained from plants are highly gastro-protective against gastric mucosal lesions induced by ethanol in rats in vivo [39]. The aerial parts of *R. acetosa* have been investigated to contain flavonoids like rutin (**33**), hyproside (34), quercetin (35), quercitrin (36), avicularin (37), vitexin (38), Orientin (39), and iso-orientin (40). Similarly, *R. japonicus* have been investigated to contain querctin (35), quercitrin (36), iso-quercitrin (41) [40] along with kaempferol-3-O-β-D-glucoside (42) and catechin (43) and all these compounds are found to act as therapeutic agents for diabetic complication and related disease.

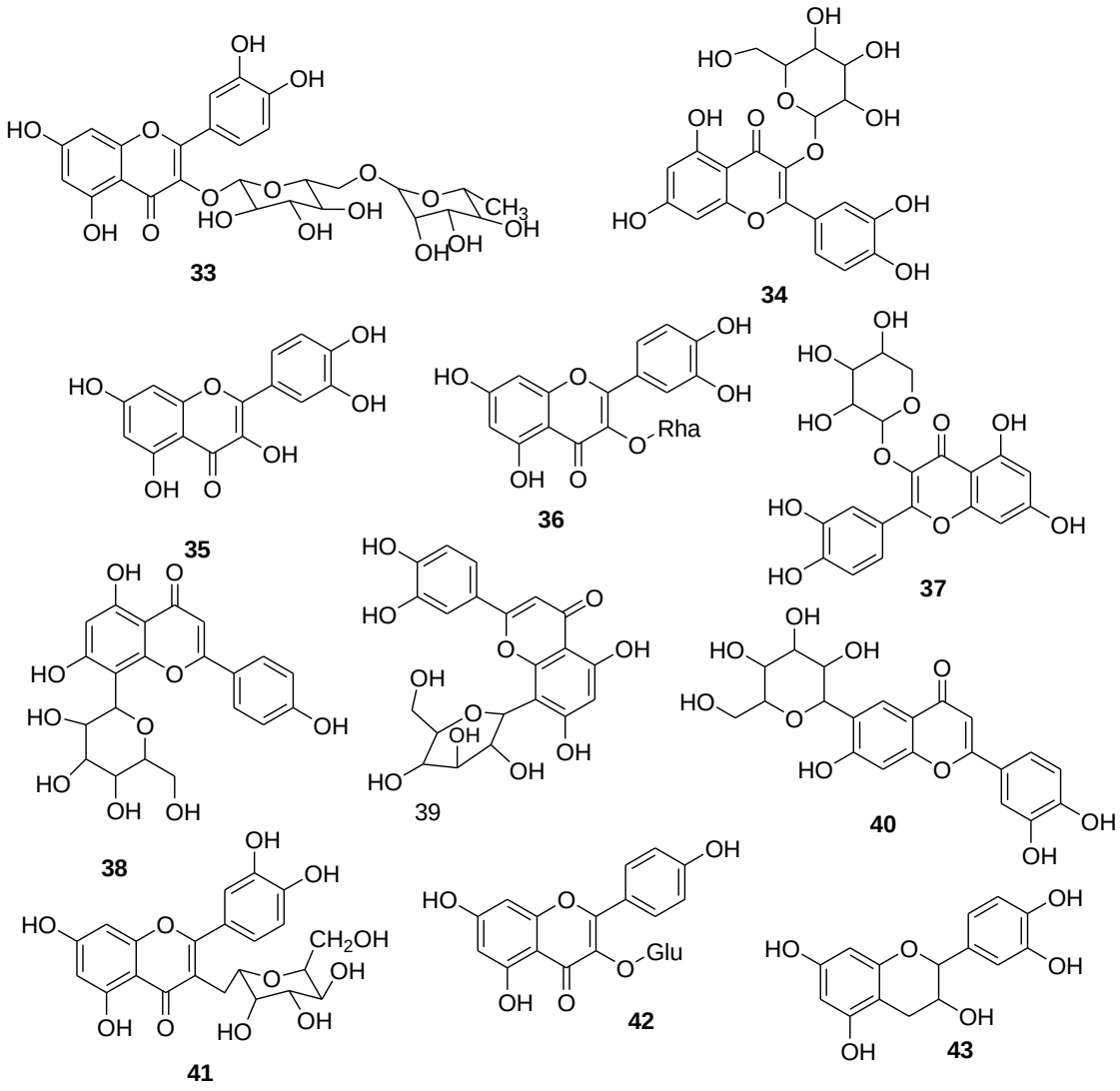

Figure 5: Structures of the Flavonoids (**33-43**)

Moreover, Rutin (33) has beneficial effects on capillary permeability and flow. The leaves of species *R. crispus* contain flavonoids like quercetin (35), quercitrin (36), rutin (33) and due to presence of these compounds in these plants, their leaves are used to treat skin, ailments like biols, hives, ring worms, itch, jaundice, acne scabies, psoriasis, eczema and other skin diseases. Both quercitrin (36) and rutin (33) are utilized as anti-tumor agents and quercetin (35) as anti-carcinogenic for breast cancer. Antioxidant activity of *R. Crispus* is found to occur due to the presence of flavonoids. Likewise Catechin (42) was isolated from the plant *R. patientia* along with some of simple haloginated flavan-3-ol, called as 6-chloro catechin (44) showing cytotoxic effects as well as radical scavenging properties [38].

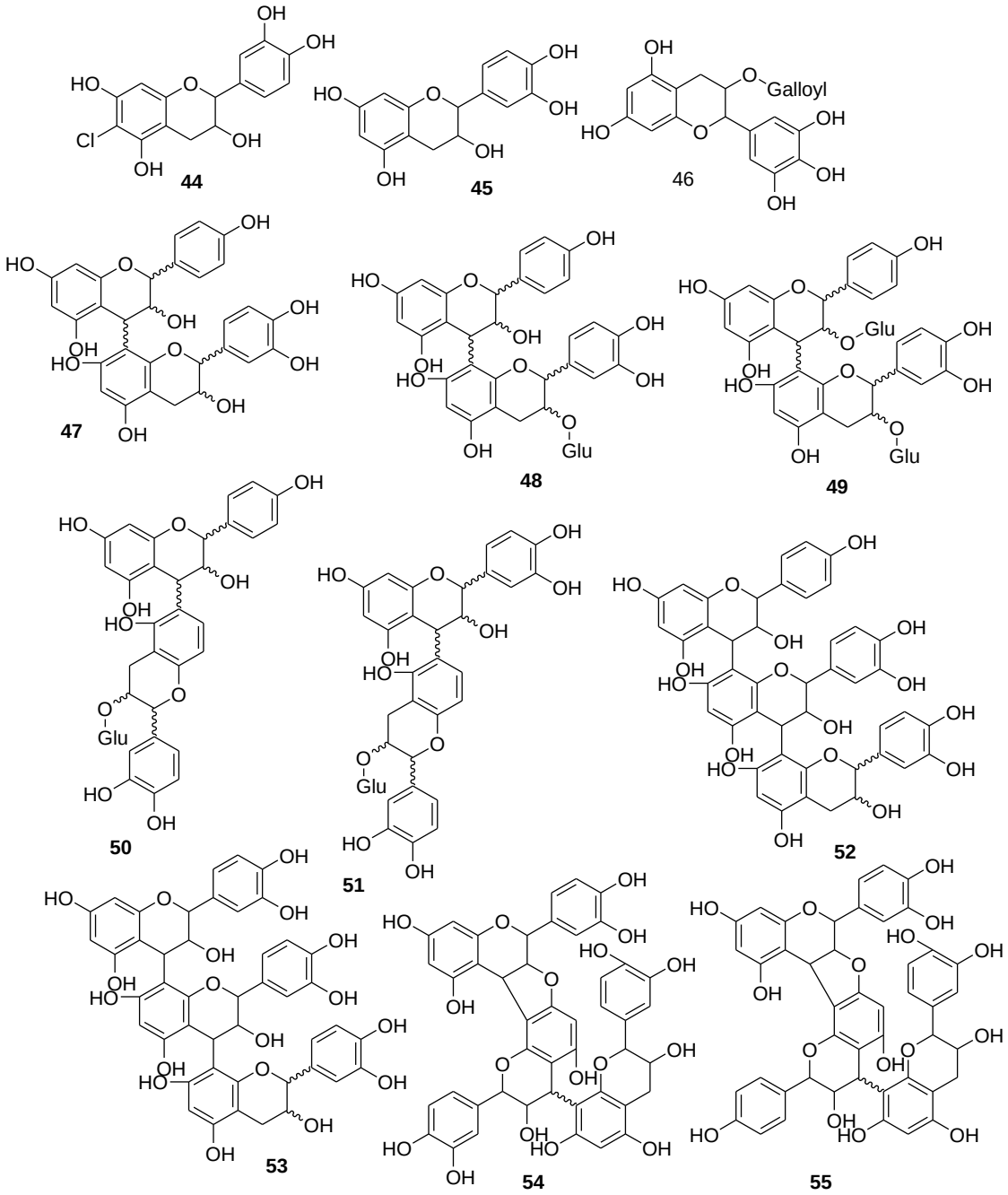

Figure 6: Structures of Flavonoids (**44-55**)

Recently, the extraction of aerial parts of *R. acetosa* was carried out and from ethyl acetate fraction, the flavan-3-ol like catechin (45), epicatechin-3-O-gallate (46) were isolated. Similarly Epiafzelechin-(4β→8)-epicatechin (47), Epiafzelechin-(4β→8)-epicatechin-3-O-gallate (48), epiafz elechin-3-O-gallate-(4β→8)-epicatechin-3-O-gallate (49), epiafzelechin-(4β→6)-epicatechin-3-O-g allate (50) were found the constituents of the plant *R. acetosa*. Likewise, some other flavonoids e.g; Epicatechin-(4β→6)-epicatechin-3-O-gallate (51), epiafzelechin-(4β→8)-epicatechin-(4β→8)-epica techin (52), epicatechin(4β→8)-epicatechin-(4β→8)-catechin (53), Epicatechin-(2β→7,4β→8)-epic atechin-(4β→8)-epicatechin (54),epicatechin-(2β→7,4β→8)-epiafzelechin-(4α→8)-epicatechin(55)

epicatechin-3-O-gallate-(2β→7,4β→8)-epicatechin(4β→8)Epicatechin (56), epicatechin-(2β→7,4β →8)-[epicatechin-(4β→6)]-epicatechin (57), 1-O-β-D-(2,4-dihydrobenzoyl)-glycopyranoside (58), epicatechin-(2β→7,4β→8)-epicatechin(4β→8)-phloroglucinol (59), epicatechin-3-O-gallate(4β→8) -epicatechin-3-O-gallate-phloroglycinal (60) were also isolated from *R. acetosa* [41].

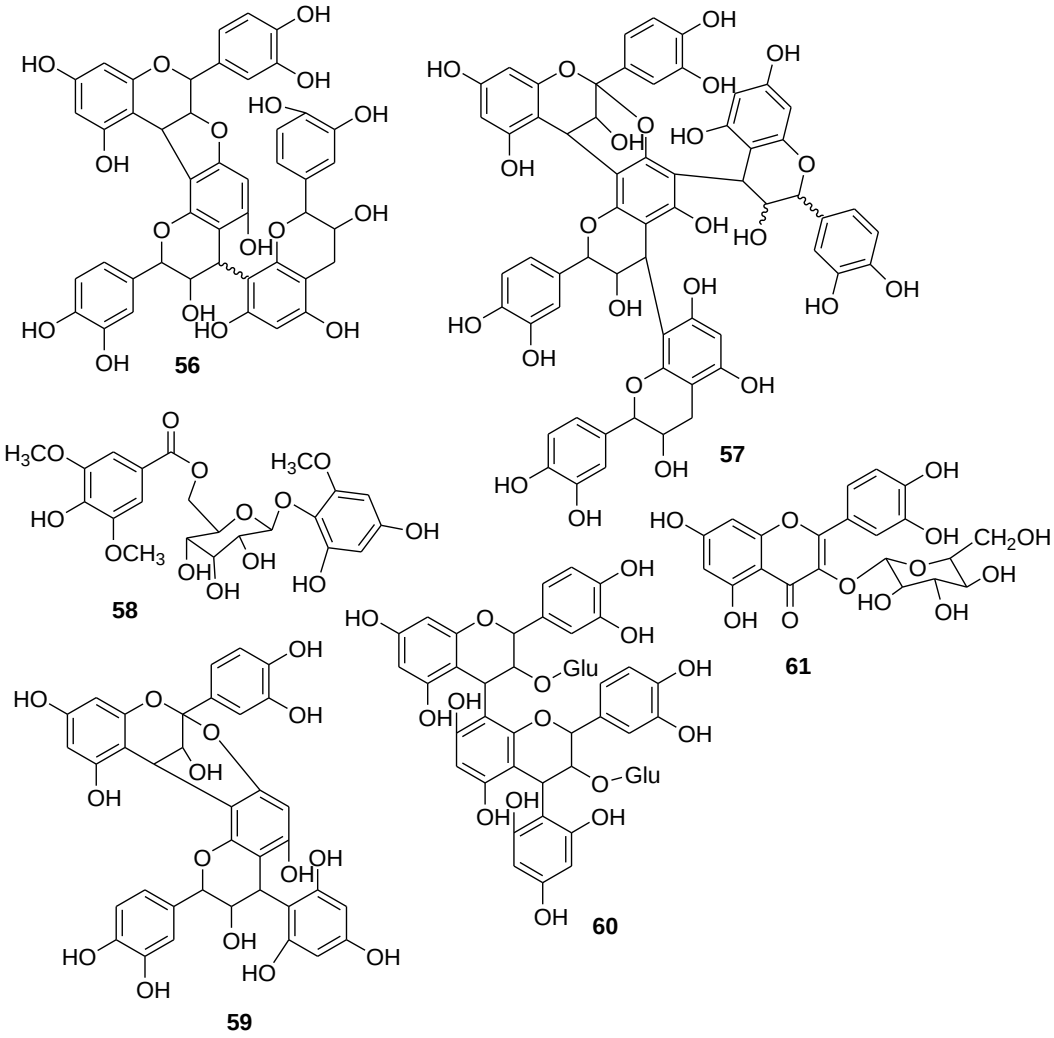

Figure7: Structures of the Flavonoids (**56**-**61**)

All these compounds (45-60) show immuno-stimulating and anti-phlogistic activities. A large number of flavonoids were also identified in *R. nervosus* [19, 20] and these are responsible for treatment of acne, a hypoglycemic agent and an ophthalmic anti-septic and is also used to cure the wounds, eczema, typhus and rabies [8]. Moreover, a flavonoid glycoside Quercitin-3-O-*β*-D-glucur onopyranoside (61) was isolated from *R. aquaticus*herba [42] and is found to act as potent protective on oesophagitis and gastritis and it induce HO-1 function as a part of cyto-protective mechanism related to anti-oxidant activities [43, 44] anti-inflammatory [45,46] anti-proliferative [47] and anti-apopototic properties [48]. The anti-oxidant activities, reducing power of 2, 2-diphenyl-1-picrylhydrazyl (DPPH) scavenging activities, anti-microbial activities of seeds and leaves of *R. crispus* are due to presence of flavonoids [13].

Ketones

Related to ketones, four compounds were isolated from *R. induratus*. Among these four compounds, hexahydrofernesylacetone (62) is the main compound occurring in large amount [15] and used as anti-microbial agent against a number of fungi and bacteria [49]. Similarly, acetovanilone (63) and jasmine (64) were also reported [15]. Acetovanilone (63) is used as therapeutic agent for treatment of inflammatory diseases and as inhibition of NADPH-oxidase which reduce the production of superoxide radical (O-2) [50]. Jasmine (64) is used as an indicator of jasmonate pathway in damaged leaves and regulate the behavior of some insects [51].

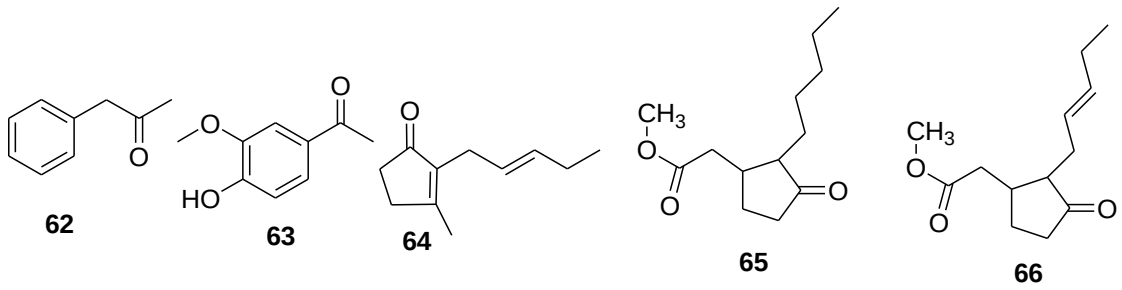

Figure 8: Structure of Ketones (**62-66**)

Moreover, dihydrojasmonate acid methyl ester (65) and jasmonate methyl ester (66) were also isolated from *R. induratus* [15] and these are used as potent lipid regulators in plants that response to mechanical trauma and pathogenesis. Methyl jasmonate (66) cause death in leukemia, lymphoma and melanoma cells in breast and prostate carcinoma [52].

Naphthalene Derivatives

Naphthalene derivatives were also pointed out to occur in genus *Rumex*. e.g. rumexoside (67), labadoside (68) and orientaloside (69) have been also isolated from *R. patientia* [29] and these compounds (67-69) are acting as purgative, constipative, depurative and tonic agents. 1,1,6-trimethyl-1,2-dihydronaphthalene (70), 1,2-dihydroxy-2,5,8-trimethylnahthalene (71), 1,1,6,8-tetramethyl-1,2-dihydronaphthalene (72) and 2,6-diisopropylnaphthalene (73) were obtained from *R. induratus* [15] and all these compounds (70-73) were utilized as protecting agents against insects and marking agents for attraction by their UV-absorption [53].

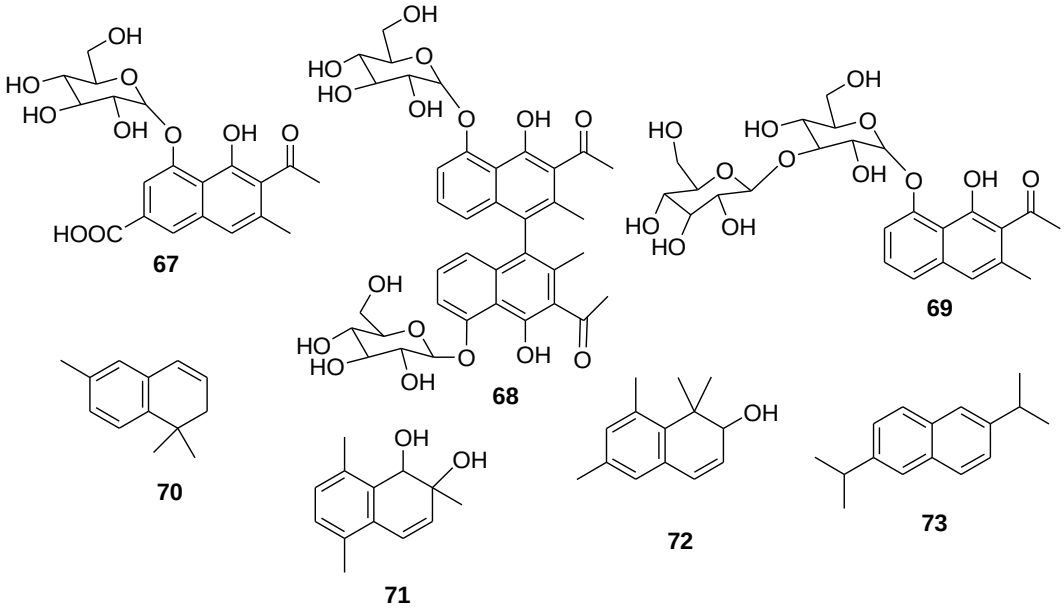

Figure 9: Structures of Naphthalene Derivatives (**67-73**)

Nor-isoprenoids

Nor–isoprenoids are obtained from degradation of carotenoids like carotene. A number of nor-isoprenoids are obtained from Rumex species like safranal (74), β-cyclocitral (75), homocyclocitral (76), β-demascenone (77), E-geranylacetone (78), β-ionone (79), β-ionone methyl (80) were isolated from R. induratus [15] and all these (74-80) are much important due to their low threshold values and characteristic aroma and they also used in flavoring [54]. β-ionone (79) has many biological activities like anti-bacterial and anti-fungal.

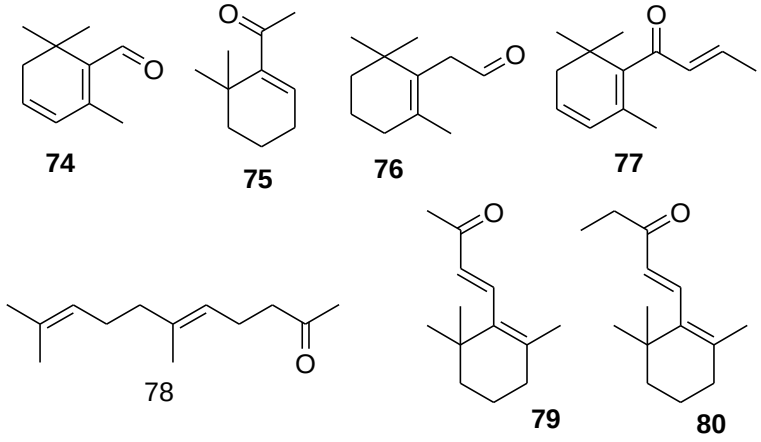

Figure 10: Structures of Nor-ioprenoids (**74-80**)

Polyphenolic compounds

Some species of the genus *Rumex* have been investigated to contain polyphenolic compounds. e. g. *R. ecklonianus* have been investigated to contain polyphenolic compounds due to its purgative, anti-oxidant, anti-bacterial activities. Moreover, this species is used in treatment of chloresis and

anemia due to presence of polyphenolic contents [55]. A biologically important phenol derivative, Orcinol (81) has been isolated from *R. patientia* which is used as anti-oxidant [37]. Another species known as *R. steudelii* is responsible for the anti-fertility effect due to the presence of the phenolic compounds in it [56].

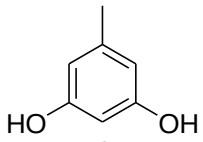

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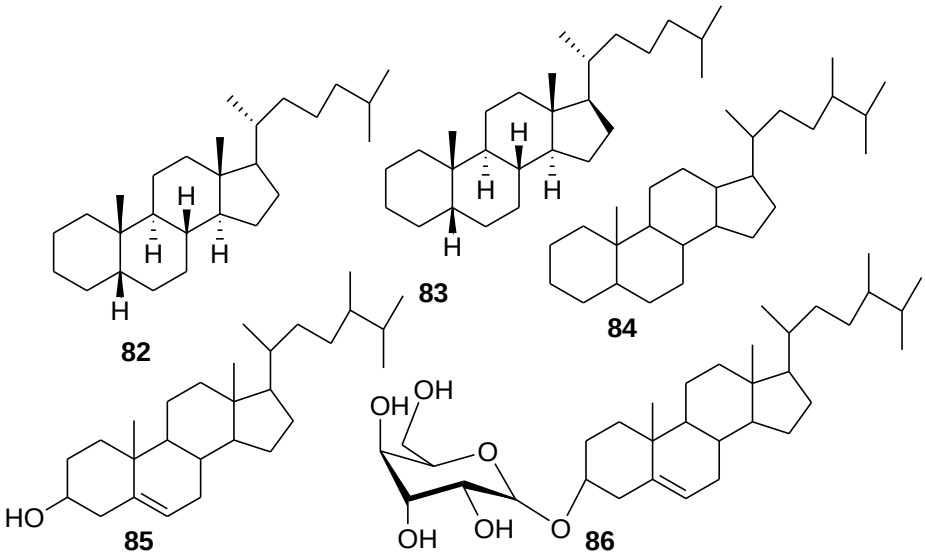
Figure 11: Structures of Polyphenolic Compound (**81**)

Steroids

Steroids have also been reported in some species of *Rumex* [38]. For example, β-cholestan (82), α-cholestan (83) and stigmastane (84) were isolated from *R. induratus* [15]. Similarly, *β*-sitosterol (85) and *β*-sitosterol-3-O-*β*-D-glycoside (86) were isolated from *R. patientia* [57].



82 **83** **84** **85** **86**

Figure 12: Structures of the Steroids (**82-86**)

Terpenes

Another class of naturally occurring medicinally and economically important compounds is the terpenes, have been isolated from leaves of *R. induratus* and some other species of the genus *Rumex*. For example, *β*-carotene (87) occurs in leaves of *R. crispus* and is used as anti-tumour agent. Likewise, Squalene (88) a tritepene has been isolated from the extract of *R. induratus*. It has pleasant and bland taste. Squalene is used as tumor inhibitor [58], anti-oxidant, anti-aging in sun blocks etc. [59].

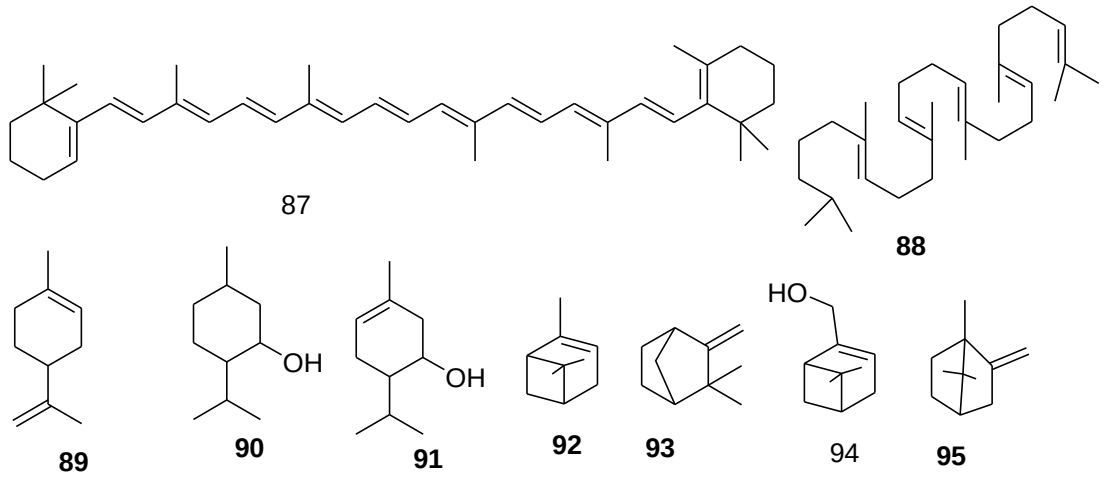


Figure 13: Structures of Terpenes (**87-95**)

Similarly, some other terpenoids like Limonene (89), menthol (90) and (E)-piperitol (91) were obtained from *R. induratus.* Limonene (89) is used to prevent mammary, liver, lung and other cancers [60] (Gould, 1997). Moreover, menthol (90) and (E)-piperitol (91) are used in flavoring industries and pharmaceuticals, cosmetics, agrochemicals and cooling substances. Menthol (90) also contains anti-microbial activity [61]. Furthermore, leaves of *R. induratus* have been investigated to contain α–pinene (92), camphene (93), myrtenol (94), camphor (95) [15].

4. CONCLUSION

There are a large number of species belong to the genus *Rumex* have been concluded to have a great significance in medicine, pharmaceuticals and economics, as these contain number of biologically important chemical compounds in them. A large number of species of this genus have been characterized by the presence of c-glycosylflavonoids, anthraquinones, naphthalene derivatives, essential oils, terpenoids, steroids, phenolic compounds, proanthocyanins and many other volatile compounds. The presence of these compounds proved the genus important as anti-malarial, anti-inflammatory, antidiarrheal, anti-viral, anti-acne, pain killer, skin ointment used by community as plant pasted form and in pharmaceutics as chemical constituents. Much of work was done on this genus due to its phenolic and organic acid composition and anti-oxidant potential [62-64], mercury bio accumulation capacity, its pollen's allergic action [65] and the characterization of DNA in its chromosomes. Thus, reviews indicated that mostly occurring constituents of the different species of the *Rumex* are the flavonoids and anthraquinones which are responsible of pharmacological actions of this genus.

CONFLICT OF INTEREST

The authors have no conflict of interest.

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