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Investigations on Kaempferol, Quercetin and other flavonoids in aquatic plants of Iraqi marshlands-II

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Abstract
Nasturtium officinale also commonly known as watercress is one of the famous Iraqi marshlands aquatic plants that is rich in flavonoids aglycones as well as their glycosidic derivatives particularly that quercetin, kaempferol, rutin, and isorhmnatin identified in all plant parts primarly contributing to their biological influences besides other uses as reducing agent for nanopartilces preparation. Watercress flavonoids participate in many plant's biological activities including antioxidant, DNA repair, lymphocytes p-glycoprotiens functiuons modulation, antihyperlipidemic, hypoglycemic, anti-inflammatory, antimicrobial, antitumor, antimetastatic, antiaging, organ-protection influences…etc. by mean of diverse molecular mechanisms. In this survey, we have summarized the reported flavonoids types, content and factors affecting their extracts contents of three aquatic plant Nasturtium officinale detected in the Iraqi central marshlands, in provenance of Thi-Qar. Surveying the phytochemical investigations regarding Nasturtium officinale of reported abundance of polyphenolic compounds content including flavonoids like flavonols and flavonones, particularly, in different plant parts.the total flavonoids content of R. nasturtium-aquaticum hydroalcoholic extract is 62–63 mg catechin equivelant /g extract while, in other contry is 35.17 mg catechin equivelant/g of the extract. However, the total phenolic compounds contents in the extraction solvent follows the order of order leaves aqueous extract> Leaves methanolic extract> Seeds methanolic extract> Roots methanol extract> Seeds aqueous extract> Roots aqueous extract that justify the extracts order of radical scavenging order of Leaves aqueous extract> Leaves methanolic extract> Seeds methanolic extract> Roots aqueous extract> Roots methanolic extract> Seed aqueous extract. The total phenolic and flavonoids content varies in different plant parts, however, the total phenolic compounds content follows the order of roots ≤ stem < leaves. Meanwhile, the rhamnose glycosides content in the leaves mostly C7-O-rhamnose glycoside is higher than both stems and roots. While, the total flavonoid content aglycone as well as glycosides follows the order of ethyl acetate > n-hexane > n-butanol fractions. Several factors affecting the content of flavonoids in different plant parts besides various flavoinoids compounds number/contents are summarized in this survey which contribute to formerly mentioned biological influences.

Key words: *Nastrium officinale, marshlands, Aquatic, Plants, Quercetin, Kaempferol.*

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I.INTRODUCTION

The plant flavonoids occur as colorful substances that exhibit broad spectrum of antimicrobial influences [1-3], besides, protecting the lipophilic cellular organelles against oxidative stress destruction via their antioxidant activity [4], however, antioxidant polyphenolic compounds anthocyanins as well as flavonoids are much abundant in flowers, to which their color is attributed, than in leaves and fruits [5-8]. One of their outstanding characteristics that has gained overwhelming attention by researchers is their powerful antioxidant characteristic to which their remarkable cancer as well as heart preventing influences are awed. In this context, their redox reaction antioxidant action is a chemical structure related property as they can capture as well as neutralizing the reactive oxygen species, singlet and triplet oxygen reactions quenching in addition to peroxide decomposing effect explaining their chronic human diseases protecting influence especially related to the low density lipoprotein oxidation such as atherosclerosis [9]. Human pharmacokinetics have revealed that flavonoids are quickly metabolized into glucuronide, sulfate, as well as O-methyl ether metabolites, yet, the later one is flavonoids solubility dependent [10, 11]. Nevertheless, any chemical alteration that may enhance their solubility may reduce metabolic rate resulting in declined bioavailability [12-15]. Furthermore, as the water media salinity increases flavonoids levels declines,

however, less than ascorbic acid, tannins and total phenolics that demonstrate an extensive non-linear decline [16]. Moreover, cocking as well as thermal processing such as blanching, canning, sterilizing and freezing influence on the total flavonoids levels as well as antioxidant effects varies according to their type/chemical structure, yet, influences their bioavailability as well as redox potential [17], although most of flavonoids are fairly stable at relatively elevated temperatures as well as prolonged storage intervals, yet, flavonol glycosides[18, 19]. In general polyphenolics loses some of their antioxidant effect after cooking in boiling water, however, microwave assisted cooking/extraction cause 97% of the flavonoids antioxidant activity while 74-87% of that of phenolic acids [18]. One of the fundamental class of the flavonoids is the flavonol (3-hydroxy-flavonol) characterized with hydroxylation at the C3 basic flavonoid nucleus structure at ring C. However, O-glycosylation metabolites at C3, C5, C7, C3‘, C4‘, C5‘ hydroxyls are encountered in this class as in cases of the major flavonls of Brassica crops and other plants such as quercetin, kaempferol, myricetin and isorhamnetin, besides their glycosides mainly found in various parts of the plants particularly, the fruits and flowers [20, 21, 22-27]. Thus, in edible plants flavonols mostly available as glycosides, although, the sugar part of these glycosides may be conjugated to hydroxycinnamic moiety [28-30]. In general, these compounds are powerful antioxidant agents in higher plants, yet, the pattern of hydroxylation as well as glycosylation quietly reduce their antioxidant potential [31] beside, exhibiting antimicrobial, light screeners..etc[32]. Hence, for such broad spectrum of biological influences they are extensively investigated for potential therapeutic lead drug molecule invention as well as exploring their metabolic profile since they are much safer than chemical drugs as well [22]. Another class of flavonoids are flavones like apigenin, luteolin identified in edible flowers [33]. In general, flavonoids aglycones are freely soluble in alcohols such as methanol as well as ethanol therefore their extraction concentration is greater than acetone. However, their water soluble glycosides are rich in aqueous extracts [4, 34-36], although flavonoids extraction levels is in the following order flavonols in alcoholic extract> total phenolics in water extract> total flavonoids in aqueous extract> total flavonoids in alcoholic extract> total flavonols in aqueous extract> total phenolics in alcoholic extract [37]. As a widely distributed phytochemicals in the plant kingdom, these plant metabolites cannot be synthesized by the animal kingdom being such as human being [38, 39], despite their crucial health benefits. However, within their sun light induced photosynthesis biosynthetic pathways in the plants [40] from corresponding chalcone, the plant‘s chalcone isomerase mediates the conversion of naringenin chalcone into naringenin followed by the naringenin into dihydrokaempferol by mean of flavone 3-hydroxylase enzyme. The later metabolite is subsequently converted into dihydroquercetin or dihydromyricetin by the mean of flavonoid 3′-hydroxylase or flavonoid 3′5′-hydroxylase enzyme, respectively. The final step of flavonoids biosynthesis involves the production of flavonols: kaempferol, quercetin, and myricetin from dihydroflavonols via flavonol synthase catalysis. However, a subsequent glycosylation reactions convert quercetin into rutin by mean of flavonol 3-O-glucosyltransferase and flavonol 3-O-glucoside Lrhamnosyltransferase enzymes activities [41-43]. Finally, within the last decade, flavonoids/polyphenolic compounds extracts finds their way as a low-coast and ecofriendly efficient reducing and stabilizing agents for nanoparticles synthesis [44-47].

II.SOME SPECIFIC QUERCETIN DERVIATIVES BIOLOGICAL INFLUENCES:

There are several natural analogues of Quercertin which products of either alkylation (mostly methylation) or glycosylation of one of its phenolic hydroxyl groups (Quercetin O-glycosides) mostly, C3 and C7 phenolic functionalities. The Quercetin glycosides occurs single or two sugar residues of mono saccharides including glucose, galactose, rhamnose, as well as xylose, however, C3-O glycosides are the most commonly glycoside encountered in the plants [48]. The 3-O-glucoside as well as 7-O-β-D-glucopyranoside have been reported to exploit various biological influences including antioxidant, wound healing besides, antiinflammatory effects [49, 50]. The quercetin-3-O-β-d-glucopyranoside isomer of the quercetin C3-O glycosides is also known as Isoquercitrin in vitro, oncolon cancer HCT-116 and DLD-1 at concentration of 75-150 μM for
24h, as well as in vivo, on SW-480 *Xenopus*embryos at concentration of 150 μM, induces its antineoplastic influence via arresting tumor cells proliferation throughWnt/β-catenin signaling pathway suppression by mean of targeting the nuclear translocation of β-catenin [51].

The third quercetin glycosidic derivative is Quercitrin (quercetin-3-O-α-L-rhamnopyranoside) that exhibits powerful antileishmanial influence with IC_{50} of approximately 2.23 μM along with low toxicity [52, 53], meanwhile, it glucopryanoside analogue Quercetin-3-O-α-L-rhamnopyranosyl-β-D-glucopyranoside exhibits antifungal as well as antibacterial influences at MIC ranges of 10.5-21.1 μM and 212–423 μM respectively [54]. However, the advantages of skin allergic eruption condition known as prurigo nodularis management of Isoquercetin, besides, its procallagen production rate enhancement by 70% at 5 μg/mL concentration while declining the production of MMP-1 protein by 41% make beneficial to be used for topical applications and cosmetology as anti-wrinkle agent [55, 56]. In addition, quercetin-3-O-rhanmnside and quercetin-3neohesperidoside known as rutin are reported to exploit antidiabetic influence [53], however, (Pollini, et al., 2019) have reported the significance of quercetin-3-O-rutinoside-7-O-glucoside as a therapeutic agent [57]. Antioxidant, apoptotic, Anti-

inflammatory as well as cardiovascular protective influences are reported to isorhamnetin and Quercetin-3-O-rutinoside glycosides of quercetin [53, 58].

Regarding alkylated quercetin derivatives and their glycosides, the monomethyl ether derivative of quercetin, Isorhamnetin (3′-methoxy-3,4′,5,7-tetrahydroxyflavone) and rhamnetin (7-O-Methylquercetin) widely distributed in plant kingdom [59] are also been reported to exploit various biological effects. Isorhamnetin have reported to exploit a meaningful promising therapeutic influences in cases of cardiovascular as well as hemorrhagic conditions, besides, an and anti-inflammatory and anticancer influence [60-62]. However, isorhamnetin exhibits its cardiovasacular protective effect in rats model via aortic vasodilatation, portal veins, and mesenteric arteries by endotherial-independent manner [63], yet its anti-inflammatory influence via modulating the expression of pro-inflammatory markers particularly prohibiting the NF-kappa B [64]. In addition, other biological activities including estrogen stimulatory influence via estrogen receptor interaction [66], anti-adipogenic activity make it useful for obesity counteraction via Wnt signaling pathway as well as β-catenin stabilization [66]. In case of skin cancer, isorhamnetin elicits its antineoplastic effect via blocking its epidermal growth factor (EGF) by mean of suppressing of COX-2 protein expression, yet it also exhibits its anticancer influences against the human epithelial A431 cancer cell line via negative impact on the growth of anchorage-dependent and independent cells [58], hence, it is reported to reduce the size as well as weight of tumors [61, 67]. Other anticancer modes of action are also reported for isorhamnetin including farnesyl protein transferase (FPTase) inhibition, hence, arresting[68] cell cycle as well as promoting necrosis/apoptosis in human colon HCT-116 cancer cell line [69], besides, inducing apoptosis along with arresting cell proliferation of gastric tumors. isorhamnetin have been reported to exert better hepatoprotive effect than quercertin against aflatoxin B1 induced oxidative stress dependent liver cancer [70], by mean of inhibition of the carcinogenesis factor, peroxisome proliferator-activated receptors (PPAR-γ) prohibition [71]. Nevertheless, rhamnetin, the quercetin 3-O-methyl ether glycoside (3-O-[3‴-O-(p-coumaroyl)-alpha-l-rhamnopyranosyl(1→3)-alpha-l-rhamnopyranosyl(1→6)]-beta-dgalactopyranoside) and rhamnazin dimethyl ether of quercetin glycoside known as (3,5-dihydroxy-2-(4hydroxy-3-methoxyphenyl)-7-methoxychromen-4-one) as a 3′,7-dimethyl quercetin analogue [72-75] distributed in various plant parts including leaves and fruits that exhibit antioxidant [76], anticancer [77, 78], antimicrobial effects [79].

Remarkably, *Nymphoides indica* aquatic plant leaves have been reported to contain Quercetin-3,7-dimethyl ether 4‘-glucoside which exhibits antidiabetic via α-glucosidase inhibitory influence as well as antiglycation effect [80]. This compound at concentration of 10 μg/mL exhibits its skin-moisturizing influence via enhancing the synthesis of filaggrin, involucrin, loricrin, and hyaluronic acid synthase 1 by 78%, 85%, 93%, and 95%, respectively in a dose dependent manner. However, it maintain its anti-inflammatory effect via decline the upstream inflammatory cytokines as well as their signaling factors p38, JNK, and ERK phosphorylation by 57%, 47%, and 35%, respectively, besides, enhancement the expression of nuclear factor-kB as along with inhibitory kappa B alpha (IkB). In fact, Quercetin-3,7-dimethyl ether 4‘-glucoside at concentrations of 1, 5, and
10 μg/mL inhibits the NF-kB translocation promoted by UVB radiation by 57%, 65% and 83%, respectively, in addition to dose dependent prohibition of NF-kB activation, TNF-alpha, IL-1, IL-6, and IL-8, the expression of UVB radiation induced TARC and MDC expression in the keratinocytes. Thus, Quercetin-3,7-dimethyl ether 4‘-glucoside is a useful natural anti-inflammatory agent to counteract skin chronic inflammatory conditions associated with UVB irradiation[81]. Other isorhamnetin derivative, isorhamnetin 3-O neohesperidoside protects the cells DNA against hydroxyl free radical deleterious influence via its antioxidant potential [82].

Moreover, 3-O-methylquercetin has been reported to inhibit phaosphodiesterase enzyme isomers 3 and 4 (PDE3, PDE4) [83, 84], however, 8-C-(Ephenylethenyl) derivative of quercetin have been found to exhibit in vitro anticancer activity at concentration of 15 μM for 24h on SW-620 andHCT-116 through inducing cell arrest at G2/M phase, autophagy, as well as arresting cellcycle via inclining LC-I/II, Atg7,p-Erk1/2, p-JNK, pp38MAPK, while, declining Beclin andSQSTM1/p62 expressions [84, 85].Nevertheless, the semisynthetic analogue of quercetin, 3,7-dihydroxy-2-[4-(2-chloro-1,4-naphthoquinone-3-yloxy)-3-hydroxyphenyl]-5hydroxychromen-4-one have been reported to exploit curative influences against acute colitis as well as cancer through its anti-inflammatory influences, yet, it anticancer effect mechanism on HCT-116 and HT-29 colorectal cell lines is based on first; induction of oxidative stress, second; accumulation of acidic and autophagic vessels/vacuoles, third; inclining LC3-I and LC3-II along with declining SQSTM1/p62, p-Akt/PI3K, p-Erk1/2, p-p38 MAPK and p-JNK expressions [86].Furthermore, the other O-alkylated derivative of quercetin 5,3‘dihydroxy-3,7,4‘-triethoxyflavone (TEF) have been reported to exhibit its antineoplastic effect against colon caner HCT-116 cell line via promoting apoptotic events particularly in the endoplasmic reticulum along with declining the endoplasmic reticulum stress through inclining intracellular calcium ion and reactive oxygen species expressions along with promoting the inositol requiring kinase 1-α (IRE1-α), lymphoma 2 associated X (Bax), and X-box-binding protein 1 (XBP-1) expressions, whereas declining Bcl-2 levels. ER stress cause modulation (ATF)-6, (PERK), (CHOP), (GRP78) and (p-eIF2α/ eIF2α) while, promoting the JNK as well as p38 signaling pathways [87]. Finally, rutin isolated from *Nasturtium officinale*is reported to exhibit anti-inflammatory potential via indirect IkB protein degradation/phosphorylation suppression [88, 89].

III. SOME SPECIFIC KAEMPFEROL AND MYRICETIN/ THIER DETIVATIVES BIOLOGICAL INFLUENCES:

Kaempferol is a second significantly important flavonol widely distributed in plant particularly the edible ones as aglycon as well as various glycoside type derivatives of commonly known antioxidant influence [90-92]. Kaempreol glycosides include kaempferol 7-O-glucoside [93], kaempferol 3,7-dirhamnoside known as kaempferitrin [94], kaempferol 3-rhamnoside knowen as afzelin [95], kaempferol-3-O-robinoside-7-O-rhamnoside known as robinin [96], kaempferol 3-O-sophoroside known as sophoraflavonoloside [97], kaempferol-3-Ogalactoside known as trifolin [98], kaempferol-3-O-β-d-glucoside known as astragalin [99], Kaempferol-3-O-β-dglucopyranoside-7-O-α-l-rhamnopyranoside[100, 101], and 4′-O-methylkaempferol known as Kaempferide[102]. Like other flavonoids both of Kaempferol as well as kaempferide are reported to be useful for management of several health anomalies [103]. Whereas, kaempferol and its analogous alkylated in addition to glycosides have been reported to exploit antimicrobial [104], antioxidant, antiinflammatory[105], antineoplastic [106], neuroprotection against neurodegenerative conditions like Parkinson disease[107], antihyperglycemic [108], immunomodulatory [103], antiosteoporotic, antiestrongenic [109], anxiolytic [110], analgesic [111], and antihypersensitivity influences [103]. In addition, both Kaempferol and Kaempferol Rhamnosides are reported to elicit antiwrinkle influence beside, kaemperol reported antimicrobial influences [112] against various microbes including fungal and parasitic infections including *Plasmodium falciparum*[102, 113], besides exhibiting anti-wrinkle influences[114].However, its anti-inflammatory influence is maintained via inflammatory/pro-inflammatory factors, mediators and inflammatory proteins expression [105] including those in activated macrophages as what other flavonols, quercetin and isorhamnetin do [115]. However, antiatherosclerotic effect is mediated via its potent antioxidant influence, antihyperlipidmeic effect, prohibition of the aggregation of foam-producing cells that promotes LDL oxidation, and maintaining the elimination of cholesterol and other cells out of these macrophages [116, 117]. Remarkably, the chemical structure plays a determinant role of kaempferol derivatives antioxidant effect particularly those isolated from Brassica species which are caffeic acid acylated derivatives with two additional caffeic acid moiety of caticholic hydroxyl groups that enhance its radical scavenging structural stability [118, 119].

Although its derivative, kaempferide possesses antiestrogenic useful for its breast cancer directed antitumor effect and liver P450 targeted antioxidant characteristics[121, 122]. Furthermore, both of kaempferol as well as its analogous glycosidic metabolite, kaempferoid exert chemo-/radio-rotective, antineoplastic, and antiglycine effects [123, 124], however, kaempferol exploits its ovarian cancer targeting antineoplastic effect via down regulation of vascular endothelial growth factor receptors [125, 126]. In addition, both of kaempferol and quercetin have been reported to act synergistically to arrest cell proliferation of human gut cancer cell lines [127], whereas, like genistien, luteolin, quercetin and apigenin it exhibits powerful DPP-4 inhibitory influence [128]. Kaempferol at dose of 60 μmol/L for 24h exhibits its in vitro antitumor against HT-29 via prohibition of cell proliferation through declining the IGF-IR, ErbB3, p-PI3K/Akt, p-Erk/12 expression along with induction of apoptosis [129]. In another study, at 60 μmol/L for 24-48h, kaempferol in vitro exerts its antineoplastic influence against HT-29 and SW-480 through induction of apoptosis via inclining c-Caspase-3, -7, -9, PARP, Bik, Bad, FasL and cyto-c along with declining the Bcl-xL expression [130]. In a third study, kaempferol at 20-60 μmol/L for 6h concentration exhibits its in vitro antineoplastic influence against HT-29 cell line via suppressing cell cycle At G1 and G2/M phases through declining the expression of CDK2, CDK4, Cdc25C, Cdc2, cyclin B1, cyclins D1, cyclin E, cyclin A and p-Rb [131]. In a forth study, kaempferol has been reported to elicit its in vitro antineoplastic influences at 20-60 μmol/L for 6h concentration against HT-29 cell line through its antioxidant potential that prevent DNA/cellular damage through declining lipid peroxidation along with inclining CAT, SOD and GPx expressions [132]. In a fifth study, kaempferol has been reported to exhibit its in vitro antineoplastic influence at concentration 5-100 μM for 10h against HCT-116 via induction epigenetic modification through inclining the hyperacetylation of histone complex H3 [133].

Furthermore, Keamferol as well as quercetin besides their derivatives rich phenolic fraction of Brassica oleraceae L. var. acephala DC have been reported to exhibit antibacterial influence against Staphylococcus aureus, Enterobacter faecalis and Bacillus subtilis, gram positive bacterial as well as against Moraxella catarrhalis, gram negative one [134], yet, its derivative, Kaempferol-3-O-α-L-(2″,4″-di-E-p-coumaroyl)rhamnoside and kaempferol-3-O-a-L-(2″-E-pcoumaroyl-4″-Z-p-coumaroyl)-rhamnoside have been reported to possess antibacterial effect against MRSA [135].Moreover; kaempferol-7-O-glucoside isolated from Securigera securidaca (L.) Degen & Dorfl. as well as *Dryopteris crassirhizoma* are reported to exploit anti-HIV influences [136, 137]. Finally, the watercress radio-protective influence is attributed to its kaempherol glycosides, isothiocyanate as well as other phytochemicals via free radical scavenging protects the DNA [138]. Regarding kaempferol biosynthesis in *Saccharomyces cerevisiae* microorganism happens via phenylalanine pathway via converting the first substrate, phenalanine into p-coumaryl-CoA via 4-coumaric acid ligase followed by condensation of one of this p-coumaryl-CoA molecules with three malonyl-CoA molecules into naringenin which is in turn converted into kaempferol through dihydrokaempferol by flavanone 3β-hydroxylase [139].

The flavonoid, 3,5,7-trihydroxy-2-(3,4,5-trihydroxyphenyl)chromen-4-one known as myricetin widely distributed as a one of the major flavonoids in the plants including the edible plants reported to exploit wide range of biological influences including; Antioxidant, Antibacterial, Antiviral, Anti-gingivitic, Antihistaminic, Antiallergenic, Anti-gastric, Anti-gonadotrophic, Anti-inflammatory, Anti-mutagenic, anticancer, Hypoglycemic, Vasodilator, and Diuretic effects. However, these influences of them maintained via various enzymes inhibitory influence such as Topoisomerase-I, Topoisomerase-II, COMP, Lipoxygenase, Oxidase, Quinone-Reductase, and Tyrosine-Kinase Inhibition. Remarkably, it is found that the antiproliferative influence of previously discussed flavonoids is in the following order isorhamnetin > kaempferol > myricetin > rutin, while their antioxidant influence is in the following order rutin > myricetin > kaempferol > isorhamnetin [22]. Nevertheless, myricetin induce apoptosis via counteracting signaling pathways [140], besides, damaging DNA via oxidizing its pyrimidines/purines leading to its cleavage in case of exhibiting its antineoplastic influence against the hepatocellular carcinoma (HepG2) cell line [141]. In addition, myricetin-isorhamnetin- kaempferol combination synergistically promotes the anticancer drug cytarabine apoptosis mediated antiproliferative effect [141]. Besides, it exploits its characteristically powerful chemopreventive influence against UVB induced skin cancers via direct counteracting the Fyn kinase enzyme followed by UVB-induced COX2 inhibition [142].

Interestingly, besides myricetin antimicrobial influence [143], it is reported to inhibit the helicase protein (nsP13) of the SARS-CoV virus, hence, exploiting antiviral activity [144]. Nevertheless, its neurological and neuro-protective influences are paradoxic, since it cause muscles paralysis at toxic dose via attenuating acetylcholine release in the neuromuscular junction [145], however, its combination with rosmarinic acid counteracts Parkinson‘s disease via prohibiting amyloid-β (Aβ) protein oxidation/aggregation, synaptic function impairment by mean of site specific interaction [146], glutamate-induced excite-toxicity in discrete as well as multiple pathways including inhibiting caspase-3 pathway [147]. Furthermore, although myricetin enhances the metabolic of carvedilol via inhibiting the liver metabolic enzymes CYP2C9 or CYP2D6 along with blocking Pgp-mediated efflux of this drug in the gut and the liver [148], at 20 μM concentration, myrecetin significantly prohibits the mRNA and surface protein CD36 in U937 derived macrophages contributing to its anti-atherosclerosis effect [149]. In addition, it is reported that the myricetin glycoside derivative, myricetin-3-Orhamnoside like ruin and quercetin elicits antidiabetic influence [53]. It is worthy to note that myricetin has poor oral bioavailablity as the largest part of the dose is majorly trapped in the gut mucosa although the absorbed amount is supposed to exhibit a considerable influence at the cellular level that controls cell cycle [22]. However, catechin is reported to exhibit hepato-protection via prohibiting NF-jB expression [150], while, luteolin is reported to exploit its antitumor effect against hepatocarcinoma HepG2 cell line via modulating AMPK-NF-jB signaling through induction of intracellular reactive oxygen species generation [151]. Nevertheless, apigenin is reported to elicit antineoplastic influence against ovarian as well as colon cancer [152, 153], besides, interfering with Leydig cells testosterone biosynthesis/secretion [154]. Finally, the flavonone, naringenin, a citrus fruits characteristic flavonoids has been reported to exhibit a bunch of biological influences including aortic cAMP and cGMP mediated smooth muscle vaso-relaxation effect in rat aorta model along with phosphodiestrase enzyme inhibitory influences targeting isomers 1, 4 and 5 explaining its cardiovascular conditions therapeutic potential [155]. In addition, reactive oxygen species production down-regulation along with NFjB action by mean of EGFRPI3KAkt/ERK MAPKinase signaling pathway may contribute to naringenin anti-inflammatory as well lung mucous secretion [156]. Furthermore, Naringenin-7-O-glucoside is found to counteract Adriamycin developed oxidative stress in H9C2 cardiomyocytes, besides, the doxorubicin promoted cardiomyopathy due to induction of apoptosis explaining its anticancer drug related cardiomyopathy prevention effect [157]. One of the naringenin derivatives, pectolinarigenin has been reported to elicit antimicrobial influences against *Staphylococcus aureus*, *Plasmodium falciparum* K1, and *Trypanosoma cruzi* at IC_{50} values of 49.8 μM, 41.8 μM, and 32.0 μM respectively along with cytotoxic influence against PMM cell line [158].

IV. NASTIRITIUM OFFICINALE AQUATIC PLANT POLYPHENOLIC AND FLAVONOIDS CONTENTS

Nasturtium officinale commonly known as watercress, contains several biologically effective phytochemicals including phenolic compounds such as flavonoids, proanthocyanidins, and phenolic acids, in various plant parts which are reported as the major identified class of its phytochemicals [88, 159-166]. However, quercetin, kaempferol as well as rutin are the fundamental flavonoids in its flavonoid profile [167] explaining the plant diaetray and pharmaceutical significance as antioxidant agents as the plant is rich in phenolic, proanthocyanidins, as well as flavonoinds, particularly, quercetin and rutin in addition to other bio-reductive molecules[88, 159, 168-179]. Besides, being useful as capping, stabilizing and reducing agent for nanoparticles synthesis particularly the plant methanolic and water extracts rich in these phytochemicals especially rutin as encountered in manganese oxide as well as goldium nanoparticles synthesis [180].In addition, *N. officinale* phenolic compounds including flavonoids contributes to the plant potential of DNA damage repair along with modulating the p-glycoprotiens in the lymphopcytes, in addition to blood antioxidant status modulation in the healthy

individuals [159, 161] since these plant's polyphenolic compounds scavange the reactive oxygen species that protects the tissues against this oxidative damage as a part of its antioxidant mechanism [177, 178, 181, 182] particularly those in the aquesous extract besides reported antihyperglycemic influence [183]. Nevertheless, the elevated total phenolic content explains the plant's potent antioxidant influence as other bio-reductant *Nasturtium officinale* R. Br do particularly the plant microshoots [184] that could be also mediated through its phytochemicals, particularly the phenolic ones, free radicals trapping, reducing power as well as metal chelation [178], hence, declining the superoxide anion, cellular lipid peroxidation. Studies have speculated that the plant's flowers polyphenolic compounds is significantly correlated to the to its antioxidant potential which confers the plant DNA damage counteraction as well as health beinificial influences [185]. The phenolic/flavonoids and their glycosides besides other *N. officinale* phytochemicals such as tannins contributed antioxidant as well as other antimicrobial influences renders this plant a promising candidate for cosmetology issue use/production as anti-aging, antiacni as well as skin-lightening agent[186, 187]. In addition, quercetin glycoside, hydroxycinnamic acids enahces the isomer 2 of the antioxidant enzyme superoxide dismutase by two folds [176].

Furthermore, these phenolic/flavonoids contributes to watercress anti-genotoxic, anti-proliferative, as well as anti-metastatic influences against human colon cancer cell lines [176] conforming the *N. officinalis* leaves as well as flowers methanolic extract anticancer influence [188]. However, both of polyphenolic compounds (flavonoids) as well as glucosinolates via their anti-inflammatory and powerful antioxidant influence also contributes to their cancer preventive influence of the plant in highly cancer development risk individuals [36, 159, 175, 189-193]. Moreover, in vitro attenuation of IκB -Kinase β mediated anti-Osteoclastogenesis in RAW 264 Cells as well as dental anticandidial influences are reported to its extract and oil (rich in flavonoids and tannins) respectively [194, 195]. Furthermore, *N. officinali* hexane as well as chloroform extracts have been reported to exhibit potent bacteriostatic influence against *Pseudomonas aeruginosa* at MIC of 0.02 mg/ml while broad bactericidal influence against a wide range of bacteria species at MIC values range of 0.02-2.5 mg/ml [196]. Thus, watercress, richness in phenolics (including flavonoids and tannins) as well as glucosinolates are characteristics health promotors of the plant particularly as antioxidant, anticancer, antimicrobial, anti-inflammatory, antipsoriatic, as well as cardioprotective [159, 177,197-202], although they are exist in a declined level in the hydroalcoholic extracts. In this context, the phenolic, flavonoids as well as glycosides rich watercress rich extract have been reported to exhibit hypocholesterolemia and hypolipidemic influences via declining the serum levels of total as well as the low-density lipoprotein cholesterols in streptozotocin induced diabetic rat model post oral administration [202]. In fact, the elevated content of total phenolic and flavonoids contents of these antioxidants in *N. officinale* extract explains the plant's hypolipidemic-dependent cardioprotective influence as they cause dramatic deciline in the LDL/HDL in high-fat diet rat model [204]. Later on, (Karami, et al., 2018) have reported the effectiveness of phenolic compounds/flavonoids rich *N. officinale* methanolic extract hepato-protective as well as nephron-protective influences against the γ-radiation induced hepatotoxicity and vancomycin-induced nephrotoxicity respectively via their antioxidant potential [205]. Furthermore, a 200 mg/Kg dose of *N. officinale* hydroalcoholic extract rich in polyphenols and glycosides exploits hypolipidemic as well as hypoglycemic influences in diabetic rats model [206]. In addition, (Hoseini, et al., 2009) have reported the *N. officinale* methanolic extract at a dose of 0.8-1 gm/kg considerably decline the glucose blood level one weak post treatment beginning in rat model [207]. In this respect, it is reported that the secondary metabolites of *N. officinale* such as flavonols/their glycosides (like quercetin, kaempferol and rutin), other flavonoids, as well as and glucosinolate (like gluconasturtiin) confers the plant's extracts their anti-hyperglycemic influence particularly its alcoholic extracts [208], although, (Qeini, et al., 2008) have reported no such influences to watercress [209]. Moreover, both of the *N. officinale* phenolic phytochemicals/flavonoids rich extracts antioxidant as well as anti-inflammatory influences explains these extracts protective influences such as lung protection [193] and kidney protection, however, the later is reported to *the N. officinale* hydroalcoholic extract against gentamycin-induced [190]. In addition, N. officinale phenolic and other phytochemicals have been exhibits antiinflammatory as well as immune-modulatory influences [210, 211]via inhibiting and/or amelroiting various proinflammatory mediators [212].

Furthermore, the phenolic compounds, flavonoids, anthocyanin and other antioxidant phytochemical rich *N. officinale* hydroalcoholic which are of anticancer potential as well as other complex array of activities confers the extract antineoplastic influence that is reported to prohibit Hella cells as well as fibroblasts growth [213]. In addition, besides the high phenolic/flavonoid compounds containing N. officinale water extract antioxidant influence [214, 215], it is reported that this extract high rutin and other flavonoids content may explains its proliferation as well as osteosblastic differentiation of the bone marrow mesenchymal stem cells in murine model [216]. In addition, it is reported that *N. officinale* phenolic compounds (including flavonols and other flavonoids) as well as sulfur containing phytochemicals like glucosinolates mostly exists in its methanolic extract confer its remarkable antimicrobial influence against wide range of bacterial pathogens as compared to the plant low antimicrobial influence of these low phytochemical content water extract [217]. However, the

polyphenolic compounds of the watercrees flowers are reported to be susceptible to GIT chemical modification when orally administered [218].

The complex phytochemical profile of N. officinale enrcuhed with of carotenoids, phenolic compounds, flavonoids as well as glucosinolates are participants in the plant antioxidant profile [36, 214, 219, 220]. Several watercress extracts are reported to contain high phenolic as well as flavonoids, particularly quercetin, contents as in case of ethanolic [176], methanolic and ethyl acetate [206, 221, 222] extracts, although, the hydroalcoholic extracts exhibit weak antioxidant influence encountered in FRAP assay due to their low phenolic and flavonoids content [193]. Remarkably, methanolic extract exhibits better antioxidant activity than ethyl acetate or hexane extracts [223], thus much better antioxidant influence encountered with the polar solvent extracts like that of methanol as compared to non-polar solvent extract such hexane[206] can be explained by their phenolic compounds/flavonoids content. Nevertheless, the phenolic/flavonoid compounds profile varies with the plant part, where in wild type of *N. officinale* L. the total phenolic content is in the order of roots ≤ stem < leaves explained by the same order of antioxidant influence profile in both methanoluc and aqueous extract, although, the antioxidant influence is greater than with aqueous extract due to the greater total phenolic content [36]. In this respect, (Amiri, 2012) also has reported that the leaves methanolic extract exhibits greater antioxidant influence than both of the methanolic stem and flowers extract and plant oil due to greater total phenolic content [224]. Furthermore, (Martínez-Sánchez, et al., 2008) have demonstrated that the flavonoids content, which mostly rhamnose glycosides, in the leaves of *N. officinale* is greater than that in the stem and roots [175], yet, a resembling higher phenolic compoundsdependent antioxidant potential of the plant leaves as compared to the roots is reported by (Aires, et al., 2013) [190]. Similarly, (Abdul, et al., 2018) have reported elevated total phenolic content in the methanolic extract of *N. officinale* from Kurdistan, Iraq as compared to chloroform that exhibits low total phenolic content. Besides, they have reported significant correlation between the methanolic total phenolic content and the total antioxidant capacity of 649.3 μmol/g [225]. However, (Hassimotto et al., 2009) have related the soil grown *N. officinale* antioxidant effect (9.6 μmol BHT equiv/g) to lipophic caratinoide compounds, polyphenolic compounds as well as phenolic acids demonstrated by the β-carotene bleaching assay, although, the polyphenolic compounds in vivo antioxidant influence is tissues/organs dependent issue [226]. In addition, it is reported that the antioxidant influence (IC50 = 932–1494 μg/mL) of the watercress, grown at different altitudes and periods, aerial part extract is positively correlated to the its phytochemicals content particularly the total phenolic content that approaches optimum level within the vegetative period as detected in TAC assay [160].

Moreover, (Boligon, et al., 2013) have reported that the radical scavenging-dependent antioxidant influence of *N. officinale* crude extracts as well as its fractionation solvents is in the following order butanolic fraction > ethyl acetate fraction > dichloromethane fraction > crude extract corresponding to their total phenolic and flavonoids contents, although the ethyl acetate fraction exhibits the highest total flavonoids content. The butanol fraction exhibits radical scavenging 23.6% higher influence than ethyl acetate, 50% higher than CH_2Cl_2 fraction while, 69.1% higher than the crud extract beside, exploiting 2 folds greater radical scavenging IC50 value than that of ascorbic acid due to its highest total phenolic content which is strongly correlated to its antioxidant effect. Hence, explaining the plant's cells, lipids, proteins and DNA protective effect. The iron-induced TBARS production inhibition of the plant extract fraction is in the following order ethyl acetate > butanolic > dichloromethane > crude extract as investigated in brain preparations. The superiority of ethyl acetate inhibitory influence is attributed to its high antioxidant phytochemicals rutin (1.92%), chlorogenic, and caffeic acids content [88]as what is reported by (Yazdanparast, et al, 2008) [119].

Similarly, (Yaricsha, 2017) also has reported greatest total flavonoids, as aglycone or one-two sugar residues flavonoids glycosides, content in the ethyl acetate fraction of the crude *N. officnale* R. Br. extract where the order of flavonoids content is ethyl acetate > n-hexane > n-butanol fractions. This indicate that the order of total flavonoids content in different solvents is not necessary to be similar to that of total phenolic (phenolic acids + flavonoid + tannin + anthocyanin + others) content, thus, the butanol fraction exploits the greatest total phenolic content along with lowest total flavonoids content [227]. Furthermore, (Iseri, et al., 2014) have demonstrated that the total phenolic contents in *N. officinale*, leaves, roots and seeds, aquesous and methanolic extracts is in the following order leaves aqueous extract> Leaves methanolic extract> Seeds methanolic extract> Roots methanol extract> Seeds aqueous extract> Roots aqueous extract that justify the extracts order of radical scavenging order of Leaves aqueous extract> Leaves methanolic extract> Seeds methanolic extract> Roots aqueous extract> Roots methanolic extract> Seed aqueous extract due to mutual correlation between the total phenolic content/phytochemical proton donating capablity and radical scavenging effect. However, the extracts' antibacterial effect is dependent on the phenolic and glucosinolate compounds content in the methanolic/aqueous extracts which exhibit the following order Leavs methanolic extract> Roots methanolic extract>L and Roots aqueous extract> Seeds methanolic and aqueous extracts. Generally leaves as well as methanolic extracts exploit greater antibacterial influences [228]. In addition, (Meriem, et al., 2017) have reported moderate radical scavenging antioxidant influence of the leaves and stems combination ethanolic extract due to moderate phenolic phytochemicals content attributed to the destruction of some of these compound during heating-based extraction

process, although flavonoids of C7-O-rhamnose residue glycosylation is identified in greatest amount in the leaves [229] on one hand. On the other hand, (Fenton-Navarro, et al., 2018) have reported that *N. officinale* leaves alcoholic extracts contains elevated levels of phenolic, polyphenolic and flavonoids phytochemicals conferring elevated radical scavenging capacity of the plant [208]. This enhanced radical scavenging antioxidant influence of *N. officinale* explains its protein protective potential against oxidative damage [215].

In contrast to previous studies, edible watercress have been reported to exploit elevated polyphenolic/flavonoid phytochemicals in its hexane fraction of its fruits hydroalcoholic extract as compared to the wild non-edible variant of the plant, containing less total phenolic and total flavonoids content post hydrolysis, conferring them potent antioxidant influence, although, different plant phytochemicals synergistically contribute to the plant antioxidant influence. However, heat-based reflux extraction of the plant material contributes to the elevated total phenolic and flavonoids contents particularly in the hexane fraction of the non-edible variant on one hand. On the other hand, methanol as well as hydroalcoholic extraction system is reported to be the best extraction solvent for phenolic and flavonoid phytochemicals as compared to the other less polar extraction solvents including ethyl acetate, chloroform and hexane. High correlation is observed between the extract fraction antioxidant influence as indicated by FRAP/ABTS assays and the extract fraction phenolic and flavonoids compounds content, particularly with the total phenolic content, besides, similar correlation is observed with the extract potent cytotoxic anticancer influence of both edible and non-edible variant of watercress in human malignant melanoma cell line model as the extract is rich in isothiocyanates, polyphenols, phenolics compounds [230]. In addition, (Rawal, et al., 2021) have reported that the hydroalcoholic extract of *N. officinale* exploits greatest total tannins, flavonoids and phenolic contents as compared to other extracts explaining its highest antioxidant influence which also conforms the role of extraction solvent polarity on the total contents of these phytochemicals although their content is significant in all type of extracts [231]. Furthermore, (Moradi, et al., 2017) have reported higher total phenolic and flavonoid contents contributed antioxidant influence is encountered with soxhelt extraction method as compared to the incubation method of *Rorippa nasturtium aquaticum* hydroalcoholic extract although significant difference is in the total phenolic content that are both confers the extract its anticancer potential on hella cell line [213].

Interestingly, microshoot cultures of *N. officinale* cultivated in a bioreactor with phenylalanine and/or tryptophan bioprecursors supplementation have demonstrated elevated total polyphenolic, flavonoids as well as glucosinolates production upon phenylalamine supplementation along with enhanced CUPRAC and FRAP assays conformed antioxidant influence,besides, the bacteriostatic influence against skin bacterial pathogens [232]. In this context, both of watercress hydroalcoholic extract (with major quercetin content) as well as quercetin counteracts oxidative stress based kidney as well as liver damages caused by arsenic and lead toxicities post 3-7 days management via inclining glutathione peroxidase alongwith declining malonyl dialdehyde levels in rat models [233, 234] via quercetin‘s enhanced glutathione peroxidase gene expression, hence, declining the free radicals accumulation [235, 236]. In addition, (Moskaug, et al., 2005) have related a γ-glutamylcysteine synthetase expression enhancement to flavonoids influence hence inclining the glutathione level [218]. However, (Pereira, et al., 2011) have reported that wild *N. officianle* radical scavenging influence is significantly correlated to the flavonols, the reducing power to the phenolics and flavonols, while the β-carotene bleaching and TBARS formation inhibition assays to phenolic compounds [237], while, others related the watercress extract radical scavenging influence to the plant‘s phenolic/flavonoid content [178]. The electron donating/accepting as well as chelating capabilities of the phenolic/flavonoids plant metabolites lies behind its free radicals scavenging hence terminating free radicals chain reaction, reducing and metal ions sequestering mediated mechanisms of antioxidant effect [178]. The total phenolic and flavonoids contents in various plant parts and extracts are listed in table (4). However, (Klimek-Szczykutowicz, et al., 2022) have reported that cultured *N. officinale* microshoots demonstrates total polyphenolic content range of 131.89-336.89 mg gallic acid equivalent /100 g dry weight, while, total flavonoids content range of 305.86 to 1131.33 mg rutoside equivalent/100 g dry weight that contributes to both antioxidant as well as tyrosinase enzyme inhibitory influences [238]. While, the total phenolic as well as flavonoids contents of different samples from different regions of Kumaun region, Uttarakhand varies between three extraction solvents aqueous, hydro-alcoholic and ethanolic in ranges of 0.266 to 4.842 mg catechin equivalent/g dry weight and from 3.849 to 7.509 mg quercetin equivalent/g dry weight for total phenolic content and total flavonoids content respectively [231].

Moreover, (Zeb, 2015) have reported 70.0, 78.0, and 81.6% radical scavenging influence for *N. officinale* root, stem, and leaves methanolic extracts attributed to their phenolic/flavonoids content [36]. In addition, (Aguiar, et al., 2020) have reported that total phenolic content of *Rorippa nasturtium-aquaticum* is 1.1 ± 0.03 mg gallic acid equivalent per gram of the plant while the total flavonoids content is 2.55 ± 0.04 mg quercetin equivalence per gram of the plant [178]. Reports from Iran have demonstrated that the various *N. officinale* and *R. nasturtium-aquaticum* hydroalcoholic extracts exploit very close total phenolic contents of 9697 mg GAE/g extract range, yet with higher total flavonoids content of 62–63 mg catechin equivalent /g extract [119, 178]. Whereas, other country study have exploited less total phenolic content of 50.42 mg gallic acid equivalent/g

of the extract, while, similar flavonoids content of approximately 35.17 mg catechin equivalent/g of the extract [237]. However, the total phenolic content of watercress is affected by the heating temperature of air-drying as it leads to the decline of the total phenolic content to 80.4 ± 4.8, 51.6 ± 3.6, 51.1 ± 3.3% corresponding to drying heat of 40, 55 and 70 ^{0}C, respectively. Thermal chemical modifications/degradation of polyphenolic compounds such as auto-oxidation, or addition reactions, thus, affecting the plant antioxidant influence [239].

Table (4): reported total phenolic compounds, flavonoids and flavonoles in *N officinale*:

Part used	Type of extract	Total phenolic content	Total flavonoids content	Flavonols/polyphenolic/ tannins content	Ref.
Part used	**Type of extract**	**Total phenolic content**	**Total flavonoids**	**Flavonols/polyphenolic/**	**Ref.**
Leaves	Methanolic extract: polar sub-fraction	198.7 ± 1.6 μg GAE/mg	13.2 ± 0.2 μg QE/mg	---------	[224]
Leaves	Methanolic extract: polar sub-fraction	46.6 ± 0.5 μg GAE/mg	22.3 ± 0.5 μg QE/mg	---------	[224]
Leaves	Aqueous extract	61.46 ± 8.47 mg GAE/ g	773 ± 64.38 mg QE/ g	Polyphenols: 568.5 ± 50.13 mg PE/ml	[208]
Leaves	Acetone extract	112 ± 9.45 mg GAE/ g	1400 ± 207 mg QE/ g	Polyphenols: 812.75 ± 6.7 mg PE/ml	[208]
Leaves	Ethanolic extract	552.5 ± 39.12 mg GAE/ g	5067 ± 116.83 mg QE/ g	Polyphenols: 1680.25 ± 168.37 mg PE/ml	[208]
Leaves	Aqueous extract	88.60 ± 2.41 µg PCE/ g extract	--------	--------	[240]
Leaves	Ethanolic extract	74.18 ± 1.72 µg PCE/ g extract	-------	-------	[240]
Leaves	Methanolic extract	51.9 ± 2.3 mg GAE/ g extract	-------	--------	[36]
Leaves	Aqueous extract	60.9 ± 5.5 mg GAE/ g extract	-------	-------	[36]
Leaves	Methanolic extract	52.06 ± 3.82 μg GAE/mg of extract	3.32 ± 0.47 μg QE/mg of extract	-------	[242]
Leaves	Ethyl acetate extract	32.76 ± 0.66 μg GAE/mg of extract	5.02 ± 0.1 μg QE/mg of extract	--------	[242]
Leaves	Hexane extract	25.4 ± 3.33 μg GAE/mg of extract	7.32 ± 0.32 μg QE/mg of extract	-------	[242]
Leaves	Aqueous juice	285 ± 20 μg TAE/g of material	146 ± 3.54 μg RE/g of material	Tannins: 82 ± 14 μg TAE/g of material	[161]
Leaves	Methanolic extract	27.35 ± 0.90 mg GAE/g fresh weight	-------	-------	[243]
Leaves and branches	Hydro-ethanolic crude extract	104.41 ± 1.34 mg GAE/ g	71.83 ± 1.54 mg RUE/ g	--------	[88]
Leaves and branches	Hydro-ethanolic extract: butanolic fraction	337.6 ± 0.91 mg of GAE/ g	148.12 ± 0.52 mg RUE/ g	---------	[88]
Leaves and branches	Hydro-ethanolic extract: ethyl acetate fraction	257.92 ± 0.36 mg of GAE/ g	147.74 ± 0.66 mg RUE/ g	--------	[88]
Leaves and branches	Hydro-ethanolic extract: CH_2Cl_2 fraction	168.68 ± 0.67 mg of GAE/ g	95.18 ± 0.87 mg RUE/ g	--------	[88]
Stem	Methanolic extract: polar sub-fraction	59.8±0.2 μg GAE/mg	9.5 ± 0.1 μg QE/mg	---------	[224]
Stem	Methanolic extract: non-polar sub-fraction	12.6 ± 0.3 μg GAE/mg	34.6 ± 0.6 μg QE/mg	---------	[224]
Flowers	Methanolic extract: polar sub-fraction	84.5±0.9 μg GAE/mg	16.2 ± 0.4 μg QE/mg	---------	[224]

			content	tannins content	
Flowers	Methanolic extract: non-polar sub-fraction	20.7± 0.2μg GAE/mg	52.1±0.9 μg QE/mg	---------	[224]
Aerial parts	Hydro-ethanolic extract	35.86 ± 2.2 mg GAE/g of dry plant	29.00 ± 3.74mg QE/g of dry plant	-------	[193]
Aerial parts	Hydro-ethanolic extract	96.2 mg GAE/g of the extract	63.2 mgmg CE/g dry extract	-------	[176]
Aerial parts	Methanolic extract	Range: 8.03-9.35 mg GAE/g plant in vegetative period Range: 6.5-7.65 mg GAE/g plant in generative period	Range: 26.5-31.11 mg QE/g of plant in vegetative period Range: 36.89-42.65 mg QE/ g of plant in generative period	-------	[160]
Aerial parts	Hydroalcohlic extract	4.842 mg CE/g dry weight	7.509 mg QE/g dry weight	-------	[231]
Aerial parts	Ethanolic extract	0.266 mg CE/g dry weight	5.136 mg QE/g dry weight	-------	[231]
Aerial parts	Aqueous extract	2.287 mg CE/g dry weight	3.849 mg QE/g dry weight	-------	[231]
Aerial parts	Methanolic crude extract	121.4 ± 2.6 mg GAE/g of the extract	-------	-------	[225]
Aerial parts	Aqueous solution of the extract	99.2 ± 1.8 mg GAE/g of the extract	-------	-------	[225]
Aerial parts	Methanolic extract: ethyl acetate fraction	83.3 ± 0.8 mg GAE/g of the extract	-------	-------	[225]
Aerial parts	Methanolic extract: chloroform fraction	34.5 ± 0.8 mg GAE/g of the extract	-------	-------	[225]
Aerial parts	Methanolic extract	Edible: 47.66 ± 0.63 mg GAE/g of the extract Non-edible: 9.31 ± 1.51 mg GAE/g of the extract	**Edible:** 64.52 ± 2.69 mg RUE/g of the extract 13.55 ± 2.28 mg CE/g of the extract **Non-edible:** 12.94 ± 0.91 mg RUE/g of the extract 19.29 ± 1.88 mg CE/g of the extract	-------	[230]
Aerial parts	Hydroalcoholic extract	78 ± 6.32 mg GAE/g dry extract	96.46 ± 8.11 mg RUE/g dry extract	-------	[205]
Aerial parts	Hydroethanolic extract	97.2 ± 3.5 mg GAE/g dry extract	49.2 ± 2.4 mg CE/g dry extract	-------	[215]

Continue table (4)…..

Continue table (4)….

Part used	Type of extract	Total phenolic content	Total flavonoids content	Flavonols/polyphenolic/ tannins content	Ref.
Aerial parts	Methanolic extract of of wild R. nasturtituim-aquaticum	50.42 ± 2.77 mg GAE/g extract	35.17 ± 3.36 CE/ g extract	32.76 ± 0.67 mg QE/g of the extract	[237]
Whole plant	Hydro-ethanolic extract	96.2 ± 3.5 mg GAE/g of dry plant	63.2 ± 2.4 mg CE/g dry plant	--------	[119]
Whole plant	Hydro-ethanolic extract: n-butanol fraction	3.624 ± 0.13 mg GAE/g of the extract	1.462 ± 0.101 mg QE/gof the extract	--------	[237]
Whole plant	Hydro-ethanolic extract: ethyl acetate fraction	1.469 ± 0.01 mg GAE/g of the extract	2.701 ± 0.013 mg QE/g of the extract	---------	[237]
Whole plant	Hydro-ethanolic extract: n-hexane fraction	0.739 ± 0.14 mg GAE/g of the extract	2.011 ± 0.023 mg QE/g of the extract	---------	[237]
Whole plant Rorippa nasturtium-aquaticum	hydroalcoholic extract	**Incubation method:** 16.8 ± 0.96 mg GAE/g of the extract **Soxhlet method:** 23.53 ± 0.61 mg GAE/g of the extract	**Incubation method:** 11.69 ± 0.74 mg QE/g of the extract **Soxhlet method:** 13.51 ± 1.17 mg QE/g of the extract	---------	[213]
Whole plant	Methanolic extract	4.5mg GAE/g of the dry plant	--------	Polyphenolic: 5.12 mg GAE/g of the dry plant	[244]
Whole plant	acetone/water/acetic acid (70:29.5:0.5)	1.86-1.71 mg/ g fresh weight	--------	--------	[245]
Seeds	Methanolic extract	43.7 ± 6.2 mg GAE/g of extract	-------	-------	[36]
Seeds	Aqueous extract	14.8 ± 1.1 mg GAE/g of extract	-------	-------	[36]
Roots	Methanolic extract	20.2 ± 1.5 mg GAE/g of extract	-------	-------	[36]
Roots	Aqueous extract	12.3 ± 1.2 mg GAE/g of extract	-------	-------	[36]
Leaves	Aqueous juice	2.89 ± 0.08 mg GAE/ml of juice	1.26 ± 0.04 mg RUE/ ml of juice	------	[246]
Aerial parts	Ethanolic	0.39-0.6 mg GAE/100 g plant material	2.93-5.39 mg QE/100 g plant material	------	[247]
Baby-leaves	Methanol/water and ethanol/water mixtures in pressurized liquid extraction method	From 20152.7 ± 830 to 21047.3 ± 1900.4 7 μg GAE/g dry weight	------	**Total flavonols**: From 12692.6 ±652.2 to 13697.5 ± 13967 μg/g dry weight **Total flavon-3-ols:** From 280.9 ± 13.2 to 478.1 ± 17.6μg/g dry weight	[189]
Stems and leaves	Hydro-methanolic	28 ± 2 g/kg extract	22 ± 1 g QE/kg extract	----------	[248]
Microshoots and its culture of watercress	Methanolic extract	**Culture:** 3.1 ± 0.19-3.74 ± 0.25 mmol TE/100 g dry weight **Plant material:** 2.7 ± 0.31mmol TE/100 g dry weight	**Culture:** 1.6 ± 0.08 -0.95 ± 0.03 mmol RE/100 g dry weight **Plant material:** 1.89 ± 0.2mmol RE/100 g dry weight = 64.43 mg/100 g dry material	----------	[249]

Continue table (4)….

Part used	Type of extract	Total phenolic content	Total flavonoids content	Flavonols/polyphenolic/tannins content	Ref.
Leaves and stem	Methanolic/chloroform	27.9 ± 2.5 mg GAE/g dry weight	9.3 ± 3.0 mg QE/g dry weight	----------	[250]
	Aqueous	25.7 ± 2.5 mg GAE/g dry weight	5.4 ± 1.6 mg QE/g dry weight		
Aerial parts	Hydro-alcoholic high pressure extraction at (35-40% ethanol)	48.9-53.0 mg/g extract	38.2-42.1 mg QE/g extract	**Total kaempferol glycoside derivatives**: 6.27-6.51 mg/g extract **Total isorhamnetin glycoside derivatives**: 16.8519.36 mg/g extract **Total quercetin glycoside derivatives:** 15.09-16.2 mg/g extract	[251]

* GAE: gallic acid equivalent, ** RUT: rutin equivalent, *** GE: quercetin equivalent, **** DW : dry weight, ***** PE :phloroglucinol equivelant, ******RE: rutinoside extract, ******* CE: catechin equivelant, ********PCE: pyrocatechol equivalent, *********TAE: tannic acid equvelant, **********TE: trolox equivalent.

In addition, the method heating used for cooking/extraction also affects the plant phenolic content of watercress, hence, the plant antioxidant potential. The fresh plant material possess optimum phenolic content of (14.86 ± 2.02 mg GAE/g plant dry weight), however, boiling of watercress for 2-10 minutes reduces the total phenolic content by 49% to 71%. While, microwave and steaming of watercress for 5 minutes have harmless effect on its total phenolic content, although, blending and chopping along with 120 minutes storage at room temperature causes considerable declining of the total phenolic content to 10.76 ± 1.15 mg GAE/g and 8.65 ± 2.29 mg GAE/g dry weight. In addition, the processing of the fresh watercress considerably affects the total flavonoids content which is 10.70 ± 1.07mg/g dry weight, where 10 minutes of boiling is enough to destroy all of the flavonoids content in the sample. Nevertheless, blending besides chopping brings about the rapid destruction of the chemically liable nature flavonols of total flavonoids contents of 3.42 ± 0.32 and 4.11 ± 0.36 mg/ g dry weight respectively on one hand. On the other hand, microwave and steaming types of heating greatly preserve watercress flavonols content. Therefore, boiling of watercress for 10 minutes causes extensive declining (67% loss) of the antioxidant influence from 74.54 ± 10.81 µmol AAE/g to 46,03 ± 9.42 µmol AAE/g dry weight. Resembling results is observed, 120 minutes post blending and chopping to antioxidant effect of 42.84 ± 8.00 and 48.47 ± 9.63 µmol AAE/g dry weight respectively. However, no significant influence is observed with steaming or microwave heating, besides, similar heating effect is observed on both carotenoids and glucosinolate levels that also significantly affects the plant antioxidant potential [496]. The heating influence on flavonols is also reported by (Martinez-Sanchez, et al., 2008) and (Aires, et al., 2013), however, the later authors reported total phenolic content of fresh plant of 14.00 ± 0.03 mg GAE/g dry weight [458, 473]. Interestingly, post harvesting treatment and storage conditions also affect the total phenolic (87 ± 2 mg GAE/g of extract) as well as flavonoids (36 ± 1 mg catechin equivalent/g of extract) contents of the fresh watercress, hence, the plant's antioxidant potential (according to TBARS inhibition assay). Cold storage maintains the total phenolic content at higher level of 7 days of storage, yet, 5 kGy gamma radiation dose treatment of the harvested watercress alongwith cold storage conditions also maintains its total flavonoids level at 34 ± 2 mg catechin equivalent/g of extract as well as antioxidant potential, while inclines the total phenolic content inclines 98 ± 1 mg GAE/g of extract 252, 253.

The extraction solvent as well as extraction method also influenced the total phenolics and flavonoids content in the fresh as well as freeze dried *N. officinale* samples extracts. Utilization of pressurized fluid extraction with various mixing ratio of CO_2-ethanol mixture solvent system of 50:50, 60:40 leads to 10.1±0.8 mg GAE/g with antioxidant capacity of 204.4±21.5 µmol TE/g, 70.8±10.7 µmol CAE/g, and 189.5±22.9 µmol TE/g for ORAC, HORAC, and HOSC assays. Remarkably as the ratio of ethanol increases within the limit of 40-50% optimum total phenolic compounds extraction is obtained including phenolic acids as well as flavonoids such as rutin, while, at 90% non-phenolic as well as non-polar phenolic phytochemicals are extracted. However, the demonstrated significant correlation of the total phenolic content to the antioxidant potential of the plant, the radical scavenging effect is directly determined by the total phenolic content of the plant[254]. Moreover, the growth period of plant harvesting also determines the level of the total phenolic content, where the greatest total phenolic content value in watercress aerial parts collected from different altitudes, in Mazandaran, Iranian, is obtained within the vegetative period, from 8.03 ± 1.01 GAE/g in Nosrat abad to 9.35 ± 1.14 mg GAE/g in Touska cheshme, while, the lowest value is obtained in samples collected within the generative period, from 6.5 ± 0.3 GAE/g in Nosrat abad to 7.65 ± 0.39 mg GAE/g in Touska cheshme. The opposite is for the total flavonoids content, greatest value is obtained at the generative period, from 36.89 ± 2.23 GAE/g in Nosrat abad

to 42.65 ± 1.09 mg GAE/g in Touska cheshme, while, lowest value is obtained at the vegetative period, from 26.57 ± 1.16 GAE/g in Nosrat abad to 31.11 ± 1.45 mg GAE/g in Touska cheshme. However, the higher altitude growing plant have higher contents of total phenolic and total flavonoids content in either cases [160]. Nevertheless, (Ninirola, et al., 2014) have reported that the total phenolic content is independent to watercress life cycle as well as aeration circumstances; 47.3-51.7 mg catechin equivalent/g fresh weight in spring at all aeriation conditions, while, 42-50.6 mg catechin equivalent/g fresh weight in winter at all aeriation conditions. Besides, any alteration in the plant antioxidant potential is related to other phytochemicals levels[255].

In addition, the cultivation model of *N. officinale* in a hydroponic system type greenhouse, have revealed that the total phenolics and flavonoids content inclines with plant age, from 832 ± 41 ng catechin equivalent/g in the fisrt day to 1178 ± 128 ng catechin equivalent/g fresh weight in the fourth day of cultivation and from 415 ± 20 ng catechin equivalent/g in the fisrt day to 529 ± 46 ng catechin equivalent/g fresh weight in the fourth day of cultivation day respectively [211]. Furthermore, the degree of watercress growth media also affects the polyphenolic, flavonoids and tannins content, where inclining the water NaCl level from 100 mM to 150 mM declines the watercress leaves content of these phytochemicals attributed to the Na^+ and Cl^- ions plant toxicity [16] on one hand. On the other hand, at hypotonic 10 mM saline concentration in water, the total phenolic content inclines by 33% while the optimum level of 134 mg catchin equivalent/g is obtained at spring, while no obvious change is observed at winter [256].

Remarkably, the strength of light also influences the total flavonoids content in watercress. LED light of various strength used in watercress microshots culture leads to total flavonoids content range of 546.791149.45 mg rutin equivalent/100 g dry weight, while the total polyphenolic content range of 190-226 mg GAE/100 g dry weight contributing to the variation of the plant antioxidant potential [257].Finally, the availability of the biosynthesis precursors such as phenylalanine and tryptophan also affects the total phenolics and flavonoids content, where the level of total flavonoids content at 3.0 mM of phenylalanine concentration inclines from 565.16 ± 14.32 mg rutin equivalent/g dry weight to 1364.38 ± 80.14 mg rutin equivalent /g dry weight at first day of phenylalanine supplementation, while, inclines from 863.71 ± 49.96 mg rutin equivalent/g dry weight to 1016.75 ± 23.76 mg rutin equivalent/g dry weight at tenth day of phenylalanine supplementation on one hand. On the other hand, the level of total flavonoids content at 3.0 mM tryptophan concentration inclines from565.16 ± 14.32 mg rutin equivalent /g dry weight to1241.89 ± 74.62 mg rutin equivalent /g dry weight at first day of tryptophan supplementation, while, inclines from 863.71 ± 49.96 mg rutin equivalent /g dry weight to 964.93 ± 142.40 at tenth day of tryptophan supplementation. Furthermore, the level of total polyphenolics content at 3.0 mM phenylalanine concentration inclines from189.61 ± 25.82 mg GAE/g dry weight to 282.68 ± 7.75 mg GAE/g dry weight at first day of phenylalanine supplementation, while, unaffected after 10 days of supplementation.However, the level of total polyphenolics content at 3.0 mM tryptophan concentration inclines from 189.61 ± 25.82 mg GAE/g dry weight at first day of tryptophan supplementation, while, inclines from248.02 ± 4.55 mg GAE/g dry weight to 1062.76 ± 28.77 mg GAE/g dry weight at the tenth day of tryptophan supplementation. Thus, tryptophan supplementation is critical for dramatic incline of polyphenolic compounds biosynthesis while phenylalanine supplementation is critical for dramatic incline of flavonoids compounds biosynthesis. In this context, (Klimek-Szczykutowicz, et al., 2021) have reported that rutinosides level at 3.0 mM of phenylalanine concentration inclines from 3.82 ± 0.60 mg/100 g of dry weight to 9.50 ± 1.14 mg/100 g of dry weight at first day of tryptophan supplementation, while, inclines from 2.94 ± 0.52 mg/100 g of dry weight to 9.94 ± 0.89 mg/100 g of dry weight to at tenth day of phenylalanine supplementation on one hand. On the other hand, the level of rutinosides at 3.0 mM of tryptophan concentration is not affected at first day of tryptophan supplementation, while, at the tenth day of tryptophan supplementation the rutinosides level inclines from 2.94 ± 0.52 mg/100 g of dry weight to 7.55 ± 0.66 mg/100 g of dry weight [232].

N. officinale extracts are rich in quercetin, kaempferol, isorhamnetin as well as their derivatives such as rutin are reported to be the major flavonoids/secondary metabolits exist the plant [9, 168, 88, 175,189, 190, 200,259-261], although, quercetin as well as its derivatives are more abundant/dominant than kaempferol and its glycosides [168]. Hydrolytic extraction of fresh freeze dried plant material with 1.2M HCl containing 50% hydromethanolic extract contains 1 mg/100 g and 4 mg/100 g fresh plant of kaempferol and quercetin respectively [168]. However, (Syamsianah, Anggraini, 2016) have reported 107.11 mg/kg plant material contributing its reported antihyperlipidemic potential in diabetic rats model [262],while, the roots of watercress from New zaeland also contains apigenin and quercetin as quercetin 3 (cafferoyldiglucoside) 7 glucoside [36]. In addition, rutinosides at are also identified in watercress at concentration of 21.17 ± 2.67 mg/100g dry weight in the cultivated microshoots after 8 days of cultivation, while, 17.00 ±1.45 mg/100g dry weight in the adult plant extract [218]. Nevertheless, quercetin glucosides such as rutin is reported to confer the plant its antineoplastic potential against HT115 colon cancer cell line [174]as what is reported to other quercetin as well as kaempferol flavonols, besides, the antioxidant

influences cytoprotective effect[36].In addition, leaves extract of *N. officinale* reveals the existence of isorhamnetin and quercetin-3-O-rutinoside that confer the extract its antioxidant influence [190, 238,241], yet, similar quercetin, Kawmpferol and rutinoside flavonoids profile is reported by (Bong, et al., 2020) in various parts of watercress [263]. Moreover, (Pinela, et al., 2018) have reported that the level of quercetin and isorhamnetin derivatives, quercetin-3-O-sophoroside and isorhamnetin-Ohydroxyferuloylhexoside-O-hexoside is more abundant in wild *N. officinale* than the edible variant [248]. However, (Aires, et al., 2013) have demonstrated that, quercetin-3-O-rutinoside as well as isorhamnetin are of the major phenolics member flavonol type constituents contributing to the watercress fresh baby leaves antioxidant potential [190], as well as for mature plant beside exploiting anti-inflammatory influence [181].Nevertheless, three major types of flavonols as well as their derivatives are also identified kaempferol, quercetin and isorhamnetin, particularly, Kampferol-3,7-diglucoside as the major flavonol with 3.76 ± 0.09 mg/g dry weigh estimated level. Moreover, rutoside, isoquercitrin, and kaempferol O-rhamnohexoside are also identified, in addition to detecting feruloyl, ceffeoyl, p-coumaroyl and sinapoyl glucoside type derivatives, while boiling/maturation in general reduces their total phenolics content as 1.5 fold lower flavonoids content is estimated as compared to the fresh young-baby leaves [168, 190]. Various flavonoids contents in different watercress parts and extracts are listed in table (5).

Furthermore (Akbari Bazm, et al., 2019) have reported that *N. officinale* antioxidant influence also apignine beside quercetin and kaempferol compounds [264]. Whereas, kaempherol glycosides in watercress confers the plant radio-protective/free radicals scavenging influences that protects the DNA alongwith enhancing DNA synthesis [137]. In addition, watercress aerial parts aqueous extract is rich in carationoids, hydroxycinammic acid and flavonoids including isorhamnetin, apigenin, luteolin, and rutin are reported to participate in goldium nanoparticles synthesis as reducing as well as stabilising agents [169]. However, isorhamnetin-O-sophoroside-Omalonyl(hexoside) (0.38 mg/mL) have been identified as the major flavonol in watercress leaves and stalk juice, while, quercetine and its glycoside derivative are dominant in the hydromethanolic extract of the plant‘s leaves and roots contributing to the extract‘s radical scavenging influence [36]. It is necessary to note that watercress aerial parts hydroalcoholic extract quercetin glycoside derivative contributes to the extract antineoplastic influences as well as plant‘s cancer-preventive potential [174].

Table (5): Reported *Nasturtium officinale* isolated flavonoids in different parts various extraction solvents.

Plant part	Extraction solvent	Isolated flavonoids	Quantity of each flavonoid	Ref.
Baby-leaves	Methanol/water and ethanol/water mixtures in pressurized liquid extraction method	- Catechin derivative.	From 280.9 ± 13.2 to 478.1 ± 17.6 μg/g dry weight	[189]
		- Quercetin-7-O-sophoroside	From 68.2 ± 1.5 to 80.3 ± 12.2 μg/g dry weight	
		- Quercetin-3-O-rutinoside-7-O-glucoside	From 335.6 ± 14.1 to 447.5 ± 62.8 μg/g dry weight	
		- Quercetin-3-(caffeoyl-diglucoside)-7-O-rhamnosyl	From 834.9 ± 40.2 to 966.3 ± 137.1μg/g dry weight	
		- Quercetin-3-caffeoylglucoside-6”-malonylglucose	From 2597.2 ± 110.9 to 3202 ± 690.8 μg/g dry weight	
		- Disinapolgentiobiose	From 465.2±76.9 to 512.6 ± 38.5μg/g dry weight	
		- Isorhamnetin-3-hydroxyferuloylglucoside-7-glucoside	From 938.8 ± 153.2 to 987.9±142.3 μg/g dry weight	
		- Isorhamnetin-3-caffeoyl-diglucoside-7-rhmnosyl	From 3260.8 ± 262.9 to 3513.2 ± 329.7 μg/g dry weight	
Leaves and stalks	hydroethanolic	- Rutin	48.4 ± 2.4 mg/Kg crud extract	[259]

Continue table (5)….

Plant part	Extraction solvent	Isolated flavonoids	Quantity of each flavonoid	Ref.
Leaves and stalks	Aqueous juice	- Quercetin-O-hexoside-O-(malonyl)hexoside	0.091 ± 0.005 mg/ml juice	[246]
		- Protocatechuic acid-O-hexoside	0.097 ± 0.005 mg/ml juce	
		- Quercetin-O-sophoroside-O-rutinoside	0.142 ± 0.001 mg/ml juice	
		- Quercetin-O-(coumaroyl) sophoroside	0.034 ± 0.002 mg/ml juice	
		- Quercetin-O-rutinoside (rutin)	0.129 ± 0.007 mg/ml juice	
		- Quercetin-O-(sinapoyl)hexoside-O-rutinoside	-------	
		- Quercetin-O-sophoroside-O-(malonyl)hexoside	0.121 ± 0.004 mg/ml juice	
		- Isorhanmetin-O-hydroxyferuloyl hexoside-O-hexoside	-------	
		- Quercetin-O-hexoside	0.141 ± 0.008 mg/ml juice	
		- Isorhamnetin-O-sophoroside-O-rutinoside	------	
		- Rutin-O-hexoside	0.088 ± 0.003 mg/ml juice	
		- Isorhamnetin-O-sophoroside-O-hexoside	0.085 ± 0.005 mg/ml juice	
		- Isorhamnetin-O-hydroxyferuloylhexoside-O-malonyl(hexoside)	0.013 ± 0.001 mg/ml juice	
		- Isorhamnetin-O-sophoroside-O-malonyl(hexoside)	0.38 ± 0.016 mg/ml juice	
		- Kaempferol.	-------	
		- Isorhamnetin-O-rutinoside-O-(malonyl)hexoside	-------	
		- Isorhamnetin-O-(acetyl)hexoside	-------	
young baby-leaves	Aqueous	- Quercetin. - Kaempferol and Catechin **(their level not detected)**	0.4± 0.03μ g/g fresh weight	[178]
Oil of the leaves	Hydrodistilation	- Myristicin	57.6%	[224]
Leaves	Hydro-methanolic	- Apigenin. - Quercetin-3-O-(caffeoyldiglucoside)-O-7glucoside. - Kaempferol-3-O-(caffeoyldiglucoside)-7-Orhamnoside.	-------	[36]
Leaves and stem	Hydroalcoholic extract	- Quercetin 3-O-D-galactoside. - Quercetin 3-O rutinoside. - Kaempferol. - Apigenin. - Kaempferol-3-O-coumaroylglucoside.	--------	[262]
Leaves	70% acetonitrile	- Quercetin-3-O-sophoroside-7-O-glucoside.	**Fresh:** 0.09 ± 0.02μ mol/g **Dry:** 1.0 ±0.2μ mol/g	[159]
		- Quercetin-3-O-glucoside-(6″-malonylglucoside).	**Fresh:** 0.13 ± 0.029 μmol/g **Dry:** 1.43 ±0.295 μmol/g	
		- Quercetin-3-O-sophoroside.	**Fresh:** 0.05 ± 0.005 μmol/g **Dry:** 0.5 ±0.05 μmol/g	
		- Quercetin-3-O-rutinoside (Rutin).	**Fresh:** 0.05 ± 0.004 μmol/g **Dry:** 0.6 ±0.017 μmol/g	
Leaves	Hydro-methanolic extract	- Quercetin-3-O-Sophoroside, 7-O-Rhamnside	**Fresh:** 0.088 ± 0.021 μmol/g **Dry:** 1.006 ±0.223 μmol/g	[174]
		- Quercetin -3-*O*-Glc-Glc-Malonyl (Quercetin-3-O-Glc- (6″-Malonyl-Glc))	**Fresh:** 0.125 ± 0.029 μmol/g **Dry:** 1.340 ±0.295 μmol/g	
		- Quercetin -3-*O*-Sophoroside.	**Fresh:** 0.05 ± 0.005 μmol/g **Dry:** 0.585 ±0.051 μmol/g	
		- Quercetin -3-*O*-Rutinoside (Rutin).	**Fresh:** 0.052 ± 0.004 μmol/g **Dry:** 0.602 ±0.017 μmol/g	

Continue table (5)….

Plant part	Extraction solvent	Isolated flavonoids	Quantity of each flavonoid	Ref.
Aerial parts	Hydroalcoholic extract	- Quercetin 3-*O*-Rutinoside Rhamnoglucoside (Rutin) - Quercetin 3-*O*-Glucoside (Isoquercitrin) - Quercetin-3-O-Sophoroside, 7-O-Rhamnoside - Quercetin -3-*O*-Sophoroside - Quercetin-3-O-Glc- (6″-Malonyl-Glc)	---------	[174]
Aerial parts	1.2m HCl containing 50% MeOH extract	- Myricetin (2 mg/kg of plant). - Quercetin (83 mg/kg of plant). - Kampferol (15 mg/kg of plant). - Luteolin (<0.3 mg/kg of plant). - Apigenin (<0.1 mg/kg of plant).	**Total flavonoids:** 98 mg/kg of plant	[264]
Microshoots and its culture	Methanolic extract	- Rutoside	**Culture:** 3.06± 0.28 - 23.24 ±1.98 mg/ 100 g dry weight **Plant material:** 7.20± 0.67 mg/ 100 g dry weight	[249]
		- Isoquercitrin	**Plant material:** 57.05± 5.11 mg/ 100 g dry weight	
		- Kaempferol O-rhamnohexoside	**Plant material:** 0.18 ± 0.02 mg/ 100 g dry weight	
Roots	Hydro-methanolic	- Dihydro kaempferol hexoside - Kaempferol-3-O-(caffeoyldiglucoside)-7-Orhamnoside. - Quercetin-3,7-O-diglucoside. - Quercetin-3-O-rutinoside 7-O-glucoside. - Quercetin-3-O-triglucoside.	---------	[36]
Leaves and stem	Hydro-ethanolic	- Quercetin_3_O-d_galactoside. - Quercetin_3_O_rutinoside. - Kaempferol_3_coumaroylglucoside. - Kaempferol. - Apigenin.	--------	[265]
Aerial parts	Hydro-alcoholic high pressure extraction at (35-40% ethanol)	- Quercetin-3-O-sophoroside	1.21-1.25 mg/g extract	[251]
		- Quercetin-3-O-manolylglucoside-7-Oglucoside	1.93-2.13 mg/g extract	
		- Quercetin-3-O-rutinoside-7-O-glucoside	0.92-0.93 mg/g extract	
		- Quercetin-O-sophoroside-O-malonylhexoside	5.13-6.09 mg/g extract	
		- Quercetin-O-dihexosyl-O-malonylhexoside	1.01-1.05 mg/g extract	
		- Quercetin-O-sinapoylhexoside-O-rutinoside	1.32-1.35 mg/g extract	
		- Kaempferol-O-feruloylhexoside-Omalonylhexoside	1.81-1.92 mg/g extract	
		- Kaempferol-O-hydroxyferuloylglucuronide-Omalonylhexoside	2.12-2.24 mg/g extract	
		- Kaempferol-O-feruloylhexoside-O-hexoside	1.13-1.14 mg/g extract	
		- Kaempferol-O-feruloylhexoside-O-rutinoside	1.20-1.21 mg/g extract	
		- Isorhamnetin-O-sophoroside-Omalonylhexoside	6.25-7.35 mg/g extract	
		- Isorhamnetin-O-hydroxyferuloylhexoside-Omalonylhexoside	7.88-9.22 mg/g extract	
		- Isorhamnetin-O-hydroxyferuloylhexoside-Ohexoside	2.72-2.79 mg/g extract	
		- Kaempferol-O-feruloylhexoside-O-hexoside	1.13-1.14 mg/g extract	

Continue table (5)….

Plant part	Extraction solvent	Isolated flavonoids	Quantity of each flavonoid	Ref.

Aerial parts	Hydro-alcoholic high pressure extraction at (95-100% ethanol)	- Quercetin-O-coumaroylsophoroside	1.3-1.51 mg/g extract	[251]
		- Quercetin-O-sophoroside-O-rutinoside	1.15-1.16 mg/g extract	
		- Quercetin-3-O-rutinoside (rutin)	1.19-1.20 mg/g extract	
Stems andleaves	Hydro-methanolic	- Quercetin-3-*O*-rutinoside (rutin)	1.0 ± 0.1 g/ kg of extract	[248]
		- Quercetin-*O*-sophoroside-*O*-rutinoside	1.1 ± 0.1 g/ kg of extract	
		- Quercetin-*O*-coumaroylsophoroside	1.4 ± 0.1 g/ kg of extract	
		- Quercetin-*O*-sophoroside-*O*-malonylhexoside	1.5 ± 0.1 g/ kg of extract	
		- Quercetin-O-dihexosyl-O-malonylhexoside	0.9 ± 0.2 g/ kg of extract	
		- Quercetin-*O*-sinapoylhexoside-*O*-rutinoside	1.0 ± 0.2 g/ kg of extract	
		- Isorhamnetin-*O*-hydroxyferuloylhexoside-*O*hexoside	1.9 ± 0.1 g/ kg of extract	
		- Isorhamnetin-*O*-hydroxyferuloylhexoside-*O*-malonylhexoside	1.5 ± 0.1 g/ kg of extract	
		- Isorhamnetin-*O*-sophoroside-*O*malonylhexoside	1.9 ± 0.1 g/ kg of extract	
		- Kaempferol-*O*-feruloylhexoside-*O*-rutinoside	1.7 ± 0.2 g/ kg of extract	
		- Kaempferol-*O*-feruloylhexoside-*O*-hexoside	0.9 ± 0.2 g/ kg of extract	
		- Kaempferol-*O*-hydroxyferuloylglucuronide-*O*malonylhexoside	0.9 ± 0.1 g/ kg of extract	
		- Kaempferol-*O*-feruloylhexoside-*O*malonylhexoside	0.9 ± 0.1 g/ kg of extract	
Aerial parts of watercress of Guangdong China of characteristics flavonoids	Hydro-methanolic	- Kaempferide, Rhamnetin. - Azaleatin. - Kaempferol-3-O-glucoside - Apigenin-6-C-(2Ⅱ-xylosyl)glucoside. - Isosaponarin (Isovitexin-4'-O-glucoside). - Quercetin-3-O-xylosyl(1→2)glucoside. - Quercetin-3-O-(2Ⅱ-O-rhamnosyl)galactoside. - 2'-Hydoxy,5-methoxyGenistein-4',7-Odiglucoside. - Luteolin-6-C-glucoside-7-O-(6Ⅱ-p coumaroyl)glucoside. - Quercetin-3-O-rutinoside-7-O-glucoside. - Luteolin-6-C-glucoside-7-O-(6Ⅱferuloyl)glucoside.	--------	[32]
Leaves 2 month age plant	80% hydromethanolic extract	- Rutin	1090± 2.41μ g/ g dry weight	[263]
		- Kaempferol.	7.63± 0.19μ g/ g dry weight	
		- Quercetin.	-----	
Stem 2 month age plant	80% hydromethanolic extract	- Rutin	45.25± 1.62μ g/ g dry weight	
		- Kaempferol.	3.13± 0.18μ g/ g dry weight	
		- Quercetin.	-----	
Roots 2 month age plant	80% hydromethanolic extract	- Rutin	64.95± 4.32μ g/ g dry weight	
		- Kaempferol.	3.58± 0.41μ g/ g dry weight	
		- Quercetin.	0.38± 0.19μ g/ g dry weight	

-- Continue table (5)….

Plant part	Extraction solvent	Isolated flavonoids	Quantity of each flavonoid	Ref.

Flower 2 month age plant	80% hydro-methanolic extract	- Rutin	1324.55± 10.29μ g/ g dry weight	[263]
		- Kaempferol.	103.15± 3.93μ g/ g dry weight	
		- Quercetin.	28.91± 0.28μ g/ g dry weight	
Seeds 2 month age plant	80% hydromethanolic extract	- Rutin	47.15 ± 0.94μ g/ g dry weight	[263]
		- Kaempferol.	56.3± 0.2μ g/ g dry weight	
		- Quercetin.	-------	
Aerial parts	70% hydromethanolic	- Kaempferol-3-O-diglucoside-7-O-glucoside.	3.76±0.09 mg/g dry weight	[214]
		- Isorhamnetin-3-O-glucoside.	1.18±0.03 mg/g dry weight	
		- Kaempferol-3-O-(feruloyl-triglucoside)-7-Oglucoside.	1.73±0.06 mg/g dry weight	
		-Quercetin-3-O-(feruloyl-glucoside)-3'-O(sinpoyl-glucoside)-4'-O-glucoside + Quercetin-3-Op.coumaroyl-glucoside.	0.52±0.01 mg/g dry weight	
		- Quercetin-3,4'-O-diglucoside-3'-O-(p.coumaroyl-glucoside) + Kaempferol-3,4'-Odiglucoside	0.35±0.02 mg/g dry weight	
		- Quercetin-3-O-(cafeioyl-glucoside)-3'-O(sinpoyl-glucoside)-4'-glucoside.	1.35±0.26 mg/g dry weight	
		- Quercetin-3,4'-O-diglucoside-3'-O-(cafeioylglucoside)	0.76±0.02 mg/g dry weight	
		- Kaempferol-3-(sinpoyl-triglucoside)-7-Oglucoside.	0.68±0.14 mg/g dry weight	
		- Kaempferol-3-O-(sinpoyl-glucoside)-4'-Oglucoside.	0.36±0.05 mg/g dry weight	
Leaves	80% hydromethanolic extraction	- Quercetin-3-O-triglucoside-7-O-Rhmnoside.	7.8 ± 2.9 mg/100 g fresh weight	[175]
		- Quercetin-3-O-diglucoside-7-O-Rhmnoside.	7.3 ± 1.4 mg/100 g fresh weight	
		- Kaempferol-3-O-triglucoside-7-O-Rhmnoside	18.4 ± 3.7 mg/100 g fresh weight	
		- Kaempferol-3-O-diglucoside-7-O-Rhmnoside	8.3 ±1.9 mg/100 g fresh weight	
		- Quercetin-3-O-(Cafeioyl-triglucoside)-7-O-Rhmnoside	10.1±2.4 mg/100 g fresh weight	
		- Quercetin-3-O-(Cafeioyl-triglucoside)-7-ORhmnoside (isomer) + Quercetin-3-O-(Cafeioyldiglucoside)-7-O-Rhmnoside.	19.7 ±4.0 mg/100 g fresh weight	
		- Kaempferol-3-O-(Cafeioyl-triglucoside)-7-ORhmnoside + Quercetin-3-diglucoside-7-ORhmnoside + Kaempferol-3-O-(Cafeioyl-diglucoside)-7-O-Rhmnosiode	13.1 ±3.0 mg/100 g fresh weight	
		- Quercetin-3-O-(Sinpoyl-triglucoside)-7-O-Rhmnoside	14.1 ±3.0 mg/100 g fresh weight	
		- Quercetin-3-O-(Sinpoyl-diglucoside)-7-ORhmnoside (isomer)+Quercetin-3-O-(Feruloyltriglucoside)-7-Rhmnoside	29.3 ±6.3 mg/100 g fresh weight	

-- Continue table (5)….

Plant part	Extraction solvent	Isolated flavonoids	Quantity of each flavonoid	Ref.
Leaves	80% hydromethanolic extraction	- Keampferol-3-O-(Sinpoyl-triglucoside)-7-O-Rhmnosdie	10.2 ± 2.2 mg/100 g fresh weight	[175]

		- Kaempferol-3-O-(Feruloyl-triglucoside)-7-ORhmnoside +Quercetin-3-O-(*p*.Coumaroyl-triglucoside)-7-O-Rhmnoside	35.7 ± 7.5 mg/100 g fresh weight	
		- Quercetin-3-O-(Feruloyl-triglucoside)-7-O-Rhmnoside (isomer)	14.8 ±3.0 mg/100 g fresh weight	
		- Quercetin-3-O-(*p*.Coumaroyl-triglucoside)-7-O-Rhmnoside (isomer)	10.9 ±2.2 mg/100 g fresh weight	
		- Kaempferol-3-O-(*p*.Coumaroyl-triglucoside)-7-O-Rhmnoside + Kaempferol-3-O-(*p*.Coumaroyltriglucoside)-7-O-Rhmnoside (isomer) + Kaempferol-3-O-(*p*.Coumaroyl/Cafeioyltriglucoside)-7-O-Rhmnoside	19.6 ±4.4 mg/100 g fresh weight	
		- Kaempferol-3-O-(*p*.Coumaroyl/Cafeioyltriglucoside)-7-O-Rhmnoside (isomer)	16.7 ±3.4 mg/100 g fresh weight	
		- Quercetin-3-O-(*p*.Coumaroyl/Sinpoyltriglucoside)-7-O-Rhmnoside	9.9 ± 2.7 mg/100 g fresh weight	
		- Quercetin-3-O-(Feruloyl/Feruloyltriglucoside)-7-O-Rhmnoside	3.8 ±1.2 mg/100 g fresh weight	
		- Quercetin-3-O-(*p*.Coumaroyl/Feruloyltriglucoside)-7-O-Rhmnoside	4.2 ±1.4 mg/100 g fresh weight	
		- Quercetin-3-O-(*p*.Coumaroyl/Feruloyltriglucoside)-7-O-Rhmnoside (isomer)	4.6 ±2.4 mg/100 g fresh weight	
		- Kaempferol-3-O-(*p*.Coumaroyl/Feruloyltriglucoside)-7-O-Rhmnoside	2.3 ±0.7 mg/100 g fresh weight	
		- Kaempferol-3-O-(*p*.Coumaroyl/Feruloyltriglucoside)-7-O-Rhmnoside (isomer)	1.7 ±0.8 mg/100 g fresh weight	
Aerial parts	Aqueous juice and ethanolic extract	- Rhmnazin. - Rhmnazin-3-O-glucoside. - Rhmnazin-3-O-sophoroside. - Rhamnetin. - Rhamnetin-3-O-glucoside. - Rhamnetin3-O-sophoroside. - Isoquercetin (quercetin-3glucoside). - Quercetitrin-3-O-sophoroside-7O-glucoside. - Kaempferol-3-O-glucoside. Isorhamnetin-3-O-glucoside.	--------	[173]

Sixteen quercetin, kaempferol as well as isorhamnetin glycoside derivatives have been identified in the aerial parts of watercress using hydroalcoholic cold high pressure extraction method at different water:ethanol mixture and pressures, yet, optimum isolated amount obtained for quercetin, kaempferol as well as isorhamnetin compounds occur at highest pressure as well as 35-40% hydro-ethanolic solvent system, although some quercetin glycosides optimum isolation occur at 80% mixture [251].However, (Pinela, et al., 2018) else where have reported slightly less amount /close number (18) of quercetin, kaempferol and isorhamnetin glycosides derivatives that is negatively influenced by the post-harvesting treatments gamma radiation at 5kGy> nitrogen atmosphere> vaccum packing> air packing, although the isolated phytochemicals have been demonstrated to contribute the plant‘s radical scavenging as well as beta-carotene bleaching inhibition antioxidant mechanisms, DNA protecting and antineoplastic influences. The flavonoid compound was dominant over other phenolic phytochemicals, yet, quercetin-3-O-sophoroside, isorhamnetin-Ohydroxyferuloylhexoside-O-hexoside, isorhamnetin-O-hydroxyferuloylhexoside-Omalonylhexoside, and isorhamnetin-O-sophoroside-O-malonylhexoside are of the highest levels while kaempferol (4) derivatives are of least number and levels among the identified flavonoids. Inversely, gamma radiation post-harvesting treatment incline the levels of quercetin-3O-sophoroside, p-coumaric acid, quercetin-Ocoumaroylsophoroside, isorhamnetin-O-hydroxyferuloylhexosideO-hexoside and isorhamnetin-O-sophoroside-O-hexoside[248].

Furthermore, several flavonoids are identified in four varieties of *N. officinale* one from Untied States of America and three from China incliding eight anthocyanins, twenty two flavones, two isoflavones, two three dihydroflavonol, one flavanols (naringenin-7-O-glucoside), one flavones, and other flavonoids derivative of genisten, nargingenin, luteolin, cyaniding, ehamnetin, quercetin, and kaempferol. However, the highest total flavonoids content is obtained from the chines variety (14.1 mg/ g of extract). Isoflavones isolated from watercress are mostely genistein and its derivatives, while, one of the characteristics flavones is 6-Cmethylkaempferol-3-glycosides, yet, the anthocyanine are mostly delphilinium derivatives including delphinidin-3,5,30-Tri-O-glucoside and cyanidin-3-O-(6‖-O-p-coumaroyl)sophoroside-7-O-glucoside. Besides, identifying thirteen characteristics flavonoids of kaempferol, quercetine and luteoline dertivative …etc. [32].

Moreover, (Giallourou, et. al, 2016) have reported the influence of watercress plant material processing, heating, steaming, copping, blending and microwaving irradiation influences on the flavonoids type phytochemicals content. They have demonstrated that all of the processing types negatively affect the phytochemicals levels, yet, Quercetin-3,4'-diglucoside-3'-(p.coumaryl-glucoside and Kaempderol - 3,4'diglucoside seems to be the most resistant phytochemical among all flavonols to domestic processing including boiling. The total flavonoids content of the row plant material is 10.70±1.07 mg/g dry weight, besides plenty of flavonoids phytochemicals are identified as shown in table (6) adapted from (Giallourou, et al., 2016) report[214]. In addition, most of the identified flavonols are feruloly, ceffeoyl, p-coumaroyl and sinapoyl glucosides of kaempferol, quercetin and isorhamnetin, of which Kampferol-3-O-diglucoside-7-glycoside (3.76 ± 0.09 mg/g dry weight), quercetin-3-O-sophoroside and isorhamnetin-O-hydroxyferuloylhexoside-O-hexoside are the most abundant ones [214]. Moreover, (Asfaram, et al., 2018) have reported the utilization of SnO2-nanoparticles (Cu and S-@SnO2-NPs) sorbent for low cost and best enrichment capacity for the ultrasound assisted dispersive micro solid phase extraction of quercetin from watercress with optimum sorption capacity of 39.37 mg/g of sorbent and 85% recovery using methanol solvent and of detection sensitivity of 4.35-14.97 ng/ml. The extraction capacity is reported to be influenced by the ultrasound time, pH of the media, eluent volume and sorbent mass where the best values of pH of extraction, sorbent mass, sonication time, elution volume are 3.5, 16 mg, 8 min, and 0.2 ml respectively that leads to 92.9% [266].

In addition, (Bong, et al., 2020) have demonstrated that watercress flowers possesses the greatest levels of rutin, quercetin and kaempferol as compared to other parts of the plant, however, rutin level in the flowers is greater than stem, seed, root, and leaves by 29.27, 28.09, 20.39, and 1.21 folds respectively, while, kaempferol by 32.96, 28.81, 13.52, and 1.83 folds respectively depending on the biosynthetic enzyme gene availability/expression. Whereas, despite quercetin is detected in the flowers and root, yet, its level in the flowers is 76.08 folds of that in the roots which is awed to the biosynthetic enzyme gene availability/expression [263]. Interstingely, (Martínez-Sánchez et al., 2008) have reported the identification of quercetin and kaempferol glycosides/acyl derivatives in N. officinale leaves, while, rhamnetin is not detected. However, antioxidant influences is signifncantly correlated to the quercetin rather than kaempferol glycosides. Remarkably, they have also reported remarkable glycosylation pattern where glucoside glycosylation is characteristic to C3 hydroxyl group while glycosylation at C7 position mostly happens with rhamnose residues in these flavonols in addition to ferulic acid as well as coumaric acid acylation at C3 position glucosides [175]. Nevertheless, (Aires, et al., 2013) have demonstrated that the antoixdant properties of N. officinale roots and baby-leaves is mostly related to their quercetin-3-O-rutinoside, isorhamnetin as well as caffeic acid content which are of the major phenolic compounds constituents as total flavonoids content represent 40% of the total phenolic compounds content, whereas, quercetin-3-O-rutinoside and isorhamnetin represent 79% of the total flavonoids content [190].

Table (6): flavonoids content in N. officinale plant material after various processings [214].

Flavonoid compound	**Quantity**				
	Boiling at 90 ^{0}C 210 min	**Microwaving at 1400W 1-3 min**	**Steaming at 100 ^{0}C 5-15 min**	**Chopping at 21 ^{0}C After 0-120 min**	**Blending at 21 ^{0}C After 0-120 min**

Kaempferol-3-Odiglucoside-7-Oglucoside.	0.58±0.16 - 1.09±0.16 mg/g of dry material	1.31±0.22 - 2.25±0.33 mg/g dry material	1.25±0.19 - 1.50±0.28 mg/g dry material	0.72±0.14 - 1.12±0.17 mg/g dry material	1.13±0.20 - 1.31±0.01 mg/g dry material
Isorhamnetin-3-Oglucoside.	0.26±0.06 - 0.46±0.04 mg/g of dry material	0.44±0.09 - 0.76±0.06 mg/g of dry material	0.45±0.06 - 0.53±0.11 mg/g of dry material	0.38±0.11 - 0.42±0.07 mg/g dry material	0.42±0.06 - 0.47±0.02 mg/g dry material
Kaempferol-3-O-(feruloyltriglucoside)-7-Oglucoside.	0.35±0.08 - 0.62±0.08 mg/g of dry material	0.57±0.10 - 0.99±0.20 mg/g of dry material	0.59±0.11 - 0.68±0.13 mg/g of dry material	0.49±0.14 - 0.58±0.09 mg/g dry material	0.64±0.12 - 0.66±0.01 mg/g dry material
Quercetin-3-O-(feruloyl-glucoside)-3'-O-(sinpoylglucoside)-4'-Oglucoside + Quercetin-3-O-p.coumaroylglucoside.	0.16±0.03 - 0.28±0.01 mg/g of dry material	0.20±0.04 - 0.36±0.09 mg/g of dry material	0.22±0.07 - 0.27±0.10 mg/g of dry material	0.06±0.03 - 0.15±0.04 mg/g of dry material	0.23±0.07 - 0.26±0.02 mg/g of dry material
Quercetin-3,4'-Odiglucoside-3'-O-(p.coumaroylglucoside) + Kaempferol-3,4'-Odiglucoside	0.06±0.03 - 0.21±0.04 mg/g of dry material	0.25±0.04 - 0.37±0.09 mg/g of dry material	0.19±0.06 - 0.28±0.10 mg/g of dry material	0.11±0.08 - 0.17±0.10 mg/g of dry material	0.19±0.02 - 0.27±0.07 mg/g of dry material
Quercetin-3-O-(cafeioyl-glucoside)3'-O-(sinpoylglucoside)-4'glucoside.	0.12±0.07 - 0.29±0.09 mg/g of dry material	0.29±0.01 - 0.63±0.42 mg/g of dry material	0.32±0.10 - 0.40±0.08 mg/g of dry material	0.34±0.17 - 0.41±0.14 mg/g of dry material	0.26±0.11 - 0.44±0.26 mg/g of dry material
Quercetin-3,4‘-Odiglucoside-3‘-O(cafeioyl-glucoside)	0.13±0.02 - 0.36±0.08 mg/g of dry material	0.44±0.01 - 0.61±0.08 mg/g of dry material	0.36±0.08 - 0.44±0.16 mg/g of dry material	0.26±0.09 - 0.30±0.11 mg/g of dry material	0.29±0.10 - 0.37±0.06 mg/g of dry material
Kaempferol-3(sinpoyl-	0.13±0.15 - 0.20±0.02 mg/g of	0.23±0.01 - 0.36±0.05 mg/g of	0.16±0.03 - 0.23±0.05 mg/g of	0.11±0.02 - 0.16±0.03 mg/g of	0.11±0.06 - 0.21±0.05 mg/g of
triglucoside)-7-Oglucoside.	dry material	dry material	dry material	dry material	dry material
Kaempferol-3-O-(sinpoyl-glucoside)4‘-O-glucoside.	0.08±0.02 - 0.15±0.05 mg/g of dry material	0.14±0.01 - 0.20±0.04 mg/g of dry material	0.15±0.02 - 0.16±0.03 mg/g of dry material	0.08±0.03 - 0.11±0.01 mg/g of dry material	0.06±0.03 - 0.11±0.04 mg/g of dry material

Furthermore, (Goda, et al., 1999) have reported the identification of eleven flavonoids of quercetin, rhamnazin as well as rhamnetin flavonols besides their glycosides that exhibit antihistaminic influence via intracellular calcium release independent mechanism from RBL-2H3 cells, particularly, Rhamnetin and rhamnazin methoxyflavonol that exploit their influence at IC_{50} value and potency very close to that of ketofine fumarate [173]. In other study, (Santos, et al., 2014) have reported the identification of eleven flavonoid and their glycosides derivatives of quercetin, kaempferol and isorhamnetin in the baby-leaves that belongs to flava-3-ol, flavonol and flavone classes. In addition, they have demonstrated that their level varies after 10 days storage, however, no significant difference between the extraction capacity of these flavonoids between methanol and ethanol [189]. Finally, (Rodrigues, et al., 2016) have reported the best recovery of flavonoids in watercress, particularly, rutin using CO_2:ethanol solvent system in cold highly pressurized extract at ethanol concentration of 40-60% [254].

V.CONCLUSIONS

Nasturtium officinale also commonly known as watercress is one of the famous Iraqi marshlands aquatic plants that is rich in flavonoids aglycones as well as their glycosidic derivatives particularly that quercetin, kaempferol, rutin, and isorhmnatin identified in all plant parts primarily contributing to their biological influences besides other uses as reducing agent for nanoparticles preparation. Watercress flavonoids participate in many plant‘s biological activities including antioxidant, DNA repair, lymphocytes p-glycoprotiens functiuons modulation, antihyperlipidemic, hypoglycemic, anti-inflammatory, antimicrobial, antitumor, antimetastatic, antiaging, organ-protection influences…etc. by mean of diverse molecular mechanisms. In this survey, we have summarized the reported flavonoids types, content and factors affecting their extracts contents of three aquatic plant *Nasturtium officinale* detected in the Iraqi central marshlands, in provenance of Thi-Qar. Surveying the phytochemical investigations regarding *Nasturtium officinale* of reported abundance of

polyphenolic compounds content including flavonoids like flavonols and flavonones, particularly, in different plant parts. Both of sulfer containing phytochemicals, glucosinolates and phenolic phytochemicals including flavonoids are efficiently extracted with polar organic solvents mostly methanol, ethanol as well as their hydroalcoholic mixtures as compared to the non-polar solvents such as hexane besides, the reported variation among the different variants of watercress. In addition, habitation conditions plays role in determining the total flavonoids content of watercress . For example, the total flavonoids content of R. nasturtium-aquaticum hydroalcoholic extract is 62–63 mg catechin equivalent /g extract while, in other country is 35.17 mg catechin equivalent/g of the extract. However, the total phenolic compounds contents in the extraction solvent follows the order of order leaves aqueous extract> Leaves methanolic extract> Seeds methanolic extract> Roots methanol extract> Seeds aqueous extract> Roots aqueous extract that justify the extracts order of radical scavenging order of Leaves aqueous extract> Leaves methanolic extract> Seeds methanolic extract> Roots aqueous extract> Roots methanolic extract> Seed aqueous extract. The total phenolic and flavonoids content varies in different plant parts, however, the total phenolic compounds content follows the order of roots ≤ stem < leaves. Meanwhile, the rhamnose glycosides content in the leaves mostly C7-O-rhamnose glycoside is higher than both stems and roots. While, the total flavonoid content aglycone as well as glycosides follows the order of ethyl acetate > n-hexane > n-butanol fractions. The reported leaves extracts total phenolic content ranges from 27.35 mg to 552.5 mg GAE/g, while, the total flavonoids content ranges from 132 mg-7320 mg QE/g. The leaves and stem extracts total phenolic content ranges from 25.7 mg to 337.6 mg GAE/g, while, the total flavonoids content ranges from 5.4-147.12 mg QE/g. Whereas, the baby leaves extracts contains total phenolic compounds of 2.015 mg to 2.105 mg GAE/ g dry weight, while, the total flavonols content ranges from 1.269 mg to 1.3697 mg/g dry weight, yet the total flavon-3-ol total content of 280.9 to 478.1μg/g dry weight. The stem extracts total phenolic content ranges from 12.6-59.8 mg GAE/g, while, the total flavonoids content ranges from 9.5-34.6 mg QE/g. The flowers extracts total phenolic content ranges from 20.7 mg to 84.5 mg GAE/g, while, the total flavonoids content ranges from 16.2 mg to 52.1 mg QE/g. The aerial extracts total phenolic content ranges from 0.2664.842 mg CE/g or 0.39-121.4 mg GAE/g, while, the total flavonoids content ranges from 35.17 mg to 63.2 mg CE/g or 2.93 mg to 29 mg QE/g or 96.46 mg RUE/g. However, whole plant extracts total phenolic content is 0.39 mg GAE/g of dry plant, while, the total flavonoids content is 2.93 mg CE/g dry plant. The whole plant extracts total phenolic content ranges from 0.739 mg to 4.5 mg GAE/g while, the total flavonoids content ranges from 1.462 mg to 2.011 mg QE/g. However, whole plant extracts total phenolic content is 96.2 mg GAE/g of dry plant, while, the total flavonoids content is 63.2 mg CE/g dry plant. The seeds and roots extracts total phenolic content ranges from 14.8 mg to 43.7 mg GAE/g and 12.3 mg to 20.2 mg GAE/g respectively while, their total flavonoids content are not determined to our knowledge. Moreover, the aerial parts extract content of the total kaempferol glycoside derivatives: 6.27-6.51 mg/g extract, the total isorhamnetin glycoside derivatives: 16.85-19.36 mg/g extract, while, the total quercetin glycoside derivatives: 15.09-16.2 mg/g extract. Furthermore, method of extraction plays role in determining the total phenolic and flavonoids compounds contents, besides, the individual quercetin, kaempferol and isorhamnetin glycosides levels in the extracts where the microwaving has the least negative impact followed by blending while chopping, steaming and boiling even for short time not exceeding 10 minutes cuases decline in the level of these constituents. Yet, utilization of the modern methods of extraction like freez drying and utilization of pressurized fluid extraction with various mixing ratio of CO_2-ethanol mixture solvent system of 50:50, 60:40 leads to total phenolic content of 10.1±0.8 mg GAE/g. Furthermore, seasonal effect as well as cultivation conditions, like dgree of water salinity, expression degree to light and supplementation with the biosynthetic precursors greatly influences the total phenolic compounds, total flavonoids, and individual flavonoids content of the plant. The total flavonoids and polyphenolic compounds contents inclines at 3.0 mM concentration supplementation of phenylalanine and tryptophane dramatically to arround two folds of its original level, while, rutinosides level inclines to around 3 folds and 4 folds of its original level upon 3.0 mM phenylalanine and tryptophane supplementation respectively. Isorhamnetin-O-sophoroside-O-malonyl(hexoside) is the major flavonol in watercress leaves and stalk juice, while quercetine and its glycoside derivative such as rutin/rutinosides are dominant in the hydromethanolic extract of the plant‘s leaves and roots to which cancer preventive influence of the plant is attributed. Moreover, kaempferol and isorhamnetin glycosides of leaves as well as baby leaves are also related to the plant‘s antineoplastic influence. In addition, quercetin and isorhamnetin derivatives, quercetin-3-O-sophoroside and isorhamnetin-O-hydroxyferuloylhexoside-O-hexoside is more abundant in wild *N. officinale* than the edible variant, while, Kampferol-3,7-diglucoside as the major flavonol quantified in the leaves 3.76 ± 0.09 mg/g dry weight. Remarkably, over twenty four flavonoids, aglycones, glycosides (3-O-glucosides and 7-O-rhamnosides) as well as their 3-O- glycosides, ferulic, sinpoic, caffeic and P-coumaric acids acyl derviatives of quercetin and keampferol. In addition, 3-O-di and tri-glucosides as well as their phenolic acids/malonyl acyl derivatives are reported. However, rutin (3-O-rutinosides) and quercetin-3-O-sophorosides and apigenin are also identified in the hydroalcoholic leaves extracts. The dominant flavonoids of the greatest determined levels of flavonoids/their derivatives is Kaempferol-3-O-triglucoside-7-O-Rhmnoside, Quercetin-3-O-(Feruloyltriglucoside)-7-O-

Rhmnoside and Quercetin-3-O-(Sinpoyl-triglucoside)-7-O-Rhmnoside of reported contents of 18.4 ± 3.7 mg, 14.1 ± 3.0 mg and 14.1 ± 3.0 mg/100 g fresh weight respectively. However, the dominant flavonoindes glycosides phenolic acid acylated derivative identified combinations are (Kaempferol-3-O(Feruloyl-triglucoside)-7-O-Rhmnoside and Quercetin-3-O-(*p*.Coumaroyl-triglucoside)-7-O-Rhmnoside), (Quercetin-3-O-(Sinpoyl-diglucoside)-7-O-Rhmnoside (isomer) and Quercetin-3-O-(Feruloyl-triglucoside)-7Rhmnoside), (Quercetin-3-O-(Cafeioyl-triglucoside)-7-O-Rhmnoside (isomer) and Quercetin-3-O-(Cafeioyldiglucoside)-7-O-Rhmnoside) and (Kaempferol-3-O-(*p*.Coumaroyl-triglucoside)-7-O-Rhmnoside + Kaempferol-3-O-(*p*.Coumaroyl-triglucoside)-7-O-Rhmnoside (isomer) + Kaempferol-3-O-(*p*.Coumaroyl/Cafeioyl-triglucoside)-7-O-Rhmnoside) of reported contents of 35.7 ± 7.5 mg, 29.3 ± 6.3 mg, 19.7 ± 4.0 mg, and 19.6 ± 4.4 mg/100 g fresh weight. While, the leaves oil contains Myristicin, besides, Catechin and isorhmnatine derivatives are identified in the baby leaves extract. Whereas, around twenty three flavonoids are identified in the leaves and stalk/stem extracts which are mostly quercetin, isorhamnetin and kaempferol aglycones, 3-O-hexoside (glucoside, galactoside and sophoroside) glycosides, rutinosides (rutin) besides their 3-O-glycosides ferulic and coumaric acids derivatives alongwith 7-O-glucoside malonic acid derivatives. In addition, apigenin, isorhamnetin-3-O-glycoside acetyl derivative, besides, quercetin, kaempferol and isorhamnetin-3-O-sophoroside-7-rutinosides are also detected. Yet, the most dominant phytochemicals are isorhamnetin-*O*-hydroxyferuloylhexoside-*O*-hexoside and isorhamnetin-*O*-sophoroside-*O*-malonylhexoside which are of 1.9 ± 0.1 g/ kg of extract conent of each. Moreover, around sixty various flavonoids are isolated from the aerial parts of watercress which are mostly, 3-O-, 3,4‘-O- and 3,7-O-; mono-, di- and tri-glucoside, sophoroside, rutinosides rhamnosides of quercetin, isoquercetrin, kaempferol, isorhamnetin, rhamnetin, rhamnazin, and leuteolin besides, their aglycones of quercetin, isoquercetrin, kaempferol, isorhamnetin, rhamnetin, rhamnazin, leuteolin, myristin, azaleatin, and apigenin. In addition, a very complex pattern of phenolic acids (ferulicm, comaric and sinpoic) and malonic acids derivatives of their 3-O-, 3,4‘-O- and 3,7-O mono-, di- and tri-glucoside, sophoroside, rutinosides rhamnosides of quercetin, kaempferol and isorhamnetin flavonoids. Meanwhile, the dominant flavonoids of the greatest determined levels of flavonoinds/their derivatives is isorhamnetin-O-hydroxyferuloylhexoside-O-malonylhexoside, Isorhamnetin-O-sophoroside-Omalonylhexoside, Quercetin-O-sophoroside-O-malonylhexoside of concentrations of 7.88-9.22 mg, 6.25-7.35 mg, and 5.13-6.09 mg/g extract respectively. Furthermore, around eight flavonoids are identified in the roots extracts of watercress which are mostly quercetin and kaempferol aglycones as well as 3-O- and 3,7-O-monoglycosides including rutin. Secondly, 3-O- di- and tri-glucosides besides their ferulic acid derivatives. However, dihydrokaempferol glycoside si also identified in the roots extracts although non of the reported compounds is quantified. Finally, quercetin, kaempferol and rutin are also detected in the seeds and flowers of watercress, yet, individual flavonoids are not identified or quantified to our knowledge. Nevertheless, some have reported that rutin level in the flowers is greater than stem, seed, root, and leaves by 29.27, 28.09, 20.39, and 1.21 folds respectively, while, kaempferol by 32.96, 28.81, 13.52, and 1.83 folds respectively depending on the biosynthetic enzyme gene availability/expression, while, yet, quercetin level in the flowers is 76.08 folds of that in the roots. Isoflavones are also isolated from watercress including genistein and its derivatives, while, one of the characteristics flavones is 6-C-methylkaempferol-3-glycosides.

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