Healing capacities

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Review article

Healing capacities of nettles: Dendrocnide, Girardinia, Laportea, and Urtica

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ABSTRACT

Introduction: Dendrocnide, Girardinia, Laportea, and Urtica are members of the stinging nettle family (Urticaceae) that have fine stinging needles on their aerial parts. Particular members of the first three genera are endemic to Indonesia and known as itchy leaves (local name: daun gatal or jelatang). However, Urtica is not endemic and widespread in many countries. This review aims to decipher the bioactive compounds and healing capacity properties of Dendrocnide, Laportea, and Girardinia compared with Urtica.

Methods: Scientific articles were searched and screened from PubMed, Science Direct, Google Scholar, and the scientific repository collection of several Indonesian Universities.

Results: Dendrocnide is the only reported genus that produced pain-causing peptides, namely moroidin and gympietides. In addition, *Urtica ferox* also produces pain-causing peptides, namely Δ-Uf1a and β/δ-Uf2a. These peptides determine the pain level of the contacted tissue. All genera possess various phenolic acids and flavonoids, with Urtica being the most reported. Limited reports on alkaloids, steroids, saponin, and fatty acids are available for Laportea and Urtica. The healing capacity properties of the four genera include antidiabetic, antiulcer, antibacterial, cardiovascular-related activities, brain disorder, allergic rhinitis-related activities, and anticancer activities.

Conclusion/discussion: Learning from Urtica, three endemic species of Dendrocnide, Laportea, and Girardinia are excellent herbal materials that may mimic the healing capacity of Urtica.

1. Introduction

The stinging nettle family (Urticaceae) is a distinctive herbaceous plant with stinging hairs. Dendrocnide, Girardinia, Laportea, and Urtica are the stinging nettle family members. The first three are endemic and found in Indonesia, particularly in the eastern part, particularly Ambon and Papua (Thalib et al., 2021), and have the same local name, "daun gatal" (itchy leaf). These different scientific names are called "daun gatal". They are probably either different or synonymic species of the stinging netty family, even though their leaf extracts are one of the herbal remedies (Dhouibi et al., 2020). Urtica is a commensal stinging herb widespread in many countries, especially in the tropical and subtropical regions (Mueen, 2016).

Moreover, the scientific information available on the first three genera is less than Urtica. Because of their diverse and remarkable morphological diversity, the conventional approach or morphological study may not be enough to be applied for the proper identification of species. Therefore, molecular identification of the stinging nettle family is needed before research is done (Grosse-Veldmann et al., 2016; Huang et al., 2019; Kang et al., 2008; Wu et al., 2013).

The aerial parts of most nettle species have stinging trichomes that can inflict a painful sting. Two species known for their painful solid sting are Dendrocnide (Australian stinging trees) and Laportea (wood nettles). However, many nettles are potential traditional medicine (Otles and Yalcin, 2012). The community uses itchy leaves as a remedy for pain, stiffness or aches, headaches, stomach aches, muscle and joint pain, and bruises. When applied to the whole body, itchy leaves will cause a very itchy effect, which the community believes to be an antipain medicine (Simaremare et al., 2019). In addition, itchy leaves have antioxidant, antibacterial, analgesic, and anticancer activity (Thalib et al., 2021) and

Abbreviation: ALP, Alkaline phosphatase; AST, Alanine transaminase; Bcl2, B-cell lymphoma 2; BDNF, *Brain-Derived Neurotrophic Factor*; BT-474, A human breast tumor cell line; CUS, Chronic unpredictable stress; DM, Diabetes Mellitus; FIRI, Last fasting insulin resistance index; GLUT4, Glucose transporter-4; GSH, Glutathione; HDL, High-density lipoprotein; IL-6, Interleukin-6; iNOS, *Inducible nitric oxide synthase*; ITS, Internal transcribed spacer; LDL, Low-density lipoprotein; NRF2, NF-E2 p45-Related Factor 2; PPAR, Peroxisome Proliferator-activated Receptors; PGC1α, Peroxisome proliferator-activated receptor Gamma Coactivator 1 alpha; PIO, Pioglitazone; SOD, Super oxidant dismutase.

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are helpful in the control of hypertension and diabetes and prevent prostatic hyperplasia, rheumatoid arthritis, and cancer (Dhouibi et al., 2020).

Three genera of stinging netty grow endemically in Indonesia. They are Dendrocnide (local name: kemaduh), Laportea (local name: daun gatal), and Girardinia (local name: bedor) (Fig. 1) (DeVore et al., 2020; Simaremare et al., 2019). This review compares these three endemic genera with *Urtica dioica* (UD) regarding their bioactive compounds and healing capacity properties (Dhouibi et al., 2020). The objectives of this review were to find comparative profiles of the bioactive compounds and the healing capacity properties of Dendrocnide, Laportea, Girardinia, compared with Urtica

2. Methodology

For this narrative review, we searched scientific articles from PubMed, Sciencedirect, Google Scholar, and the Indonesian university repository. With this comparative study, the significance and novelty of the results can guide further research activities of the three endemic species to mimic Urtica's research progress.

3. Bioactive compounds of Dendrocnide, Girardinia, Laportea, and Urtica

A broad range of bioactive compounds has been reported, including peptides, phenolic compounds (phenolic acids and flavonoids) (Table 1), alkaloids, steroids, lignans, and fatty acids (Ibrahim et al., 2018; Taheri et al., 2022).

3.1. Pain-causing peptides

Among stinging nettle, Dendrocnide is well known for its most violently stinging Nettle. *Dendrocnide moroides* and *Laportea moroides* can produce moroidin, a unique bicyclic peptide (Fig. 1) with tryptophan side-chain cross-links. It was isolated initially as a pain-causing agent from the Australian stinging tree (*Dendrocnide moro*[74]), which can strongly inhibit the polymerization of tubulin (Gilding et al., 2020; Kersten et al., 2022; Morita et al., 2000).

Dendrocnide (Australian stinging nettles), well known for its most violently stinging nettle, also produces other ultra-stable mini prote[14] dubbed "gympietides" that are highly neurotoxic (Fig. 2) (Ensi[13] et al., 2021). In vitro and in vivo studies of gympietides suggest that Nav channel blockers can clinically deliver pain relief to stinging nettle sufferers. The gympietides can affect channel inactivation or V[13] activation, which may stimulate enhanced neuronal excitability. The stinging hairs of *D. excelsa* and *D. moroides* produce ultra-stable mini proteins that cause pain and stimulate nociceptors by altering the deactivation of voltage-gated sodium channels conveyed on sensory neurons (Gilding et al., 2020).

To date, there have been no reports for moroidin from Girardinia, Laportea, and Urtica. Nevertheless, two peptide toxins reported from *Urtica ferox* (New Zealand tree nettle) have r[5]tly been identified. They are Δ-Uf1a and β/δ-Uf2a that dependable for the signs of *U.ferox* tingles. Δ-Uf1a is a cytotoxic thionin that produces pain via disturbance of cell membranes, while β/δ-Uf2a defines a new neurotoxin that triggers pain and systemic symptoms via alteration[5] voltage-gated sodium (Na(V)) channels. Both toxins are common among members of the Urticaceae, suggesting that they are probably pain-causing agents underlying the stings of other Urtica species (Xie et al., 2022).

3.2. Nettle' phenolic acids and flavonoids

No plant leave has no flavonoids. Without flavonoids, no plant can survive and maintain its life. The issue is not whether nettle leaves have flavonoid but what are their major flavonoids. The four genera studied here have flavonoids (Table 1). Limited scientific report on the flavonoid of Dendrocnide.

The major flavon[67] in the nettle aerial part are quercetin, rutin, kaempferol (Devkota et al., 2022; Farag et al., 2013), chlorogenic acid, isorhamnetin, 5-O-caffeoylquinic acid, and Vicenin-2 (Table 1). Several compounds are only found in[14]aportea, not in Urtica. Particular phenolic compounds genistein; 5,7,4-trihydroxyisoflavone- 5-O-*β*-D-gluco pyranoside; 5,7,3′-trihydroxy-4-methoxyisoflavone-7-O-*β*-lucopyranoside; and *a*-ionol, can serve as fingerprint compounds to differentiate L. *bulbifera* from Urtica. Several isoflavones can be detected and isolated from Laportea but not from Urtica. Isoflavones content can discriminate L.*bulbifera* from Urtica. It is considered that isoflavones are a specific compound in the Laportea genus (Lu et al., 2022).

3.3. Nettle alkaloids

Alkaloids are abundant in the methanolic extract of the old leave of *Dendrocnide stimulans, Laportea decumana*, and *Girardinia palmata* (Liswandari, 2020; Taheri et al., 2022). Thirteen (Feng et al., 2022) plus three alkaloids (Lu et al., 2022) can be identified from the leave of *Laportea bulbifera* (Table 2). They may serve as fingerprint compounds to distinguish *L.bulbifera* from Urtica (Lu et al., 2022).

Nettle alkaloids have reno-hepatoprotective and antidiabetic potentials (Adetunji et al., 2021; Taheri et al., 2022) and function as analgesic substances commonly used to treat rheumatoid and rhe[15]atic arthritis (Feng et al., 2022; Han et al., 2020). Particular alkaloids may be responsible for the anti-mycobacterial activity (Singh et al., 2013;

Fig. 1. Nettle leaf from Indonesia. A: Specimen from Ambon; B: Specimen from Yakuhimo, Papua.

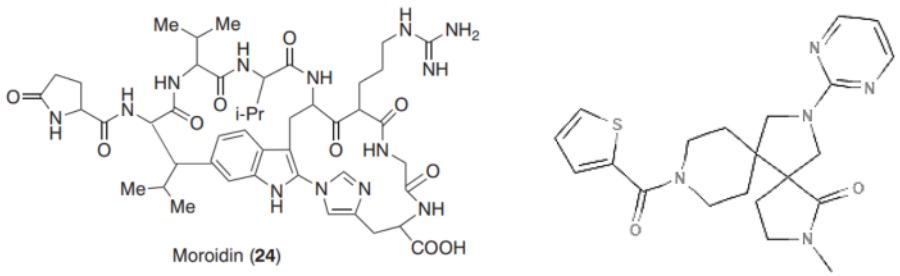

Fig. 2. Chemical structure of moroidin (La Regina et al., 2019) and gympietides (PubChem).

Table 1
Phenolic compounds of stinging nettles.

Species	Bioactive compound	Solvent	Bioactivity	Ref.
Girardinia				
G. palmata	p-Cumaric acid			(Yuan et al., 1999)
G. diversifolia	5-O-feruloyl quinic acid trans syringin, phytol		Anticancer	(Sharan Shrestha et al., 2020)
Laportea				
L.*bulbifera*	Kaempferol 3-O-rutinoside, Quercetin Isoquercetin Chlorogenic acid Galuteolin, Rutin		Rheumatoid arthritis	(Li et al., 2020)
	Coumarins			(Zhang et al., 2013)
Urtica				
U.cannabina	Isoquercitrin			(Aishan et al., 2010)
U.circularis	Vanillic acid, Ferulic acid, p-Cumaric acid Caffeic acid, vicenin-2, vitexin, isovitexin Chlorogenic acid	Hydroethanolic	sedative	(Anzoise et al., 2013)
U.dioica	Caffeic acid	Aquaous	Nettle tea	(Kregiel et al., 2020)
	Caffeoylmalic acid	Ethanolic	Antidiabetic Antibacterial	(Dar et al., 2013; Sternša et al., 2020)
	Kaempferol 3-O-glucoside	Ethanolic, Methanolic	Antiendometriosis Antibacterial Antiurolithiatic	(Ilhan et al., 2019; Sternša et al., 2020; Zhang et al., 2014)
	Trans-ferulic acid			(Ji et al., 2007)
	Quercetin			(Ji et al., 2007)
	Isoquercetin	Ethanolic	Antiendometriosis Antibacterial	(Ilhan et al., 2019; Sternša et al., 2020)
	Quercetin p-coumaroyl glucoside		Antidiabetic, Antibacterial	(Dar et al., 2013)
	Isorhamnetin-3-O-glucoside, Isorhamnetin 3-O-rutinoside	Ethanolic	Antiendometriosis Antibacterial	(Ilhan et al., 2019; Sternša et al., 2020)
	Scopoletin			(Ji et al., 2007)
	Ursolic acid			(Ji et al., 2007)
	Rutin	Ethanolic	Anxiolytic Antidiabetic, Antibacteria Antiendometriosis	(Dar et al., 2013; Ilhan et al., 2019; Parashar et al., 2017; Sternša et al., 2020)
	Chlorogenic acid		Antidiabetic, Antibacterial	(Dar et al., 2013)
U. fissa	Urticaside	Alcohol-EtOAc fraction	Antirheumatic	(Wang et al., 2018)
	Kaempferol 3-O-rutinoside, luteolin		Antiurolithiatic	(Zhang et al., 2014)
	Coumarins		Anticancer	(Lin et al., 2008)

Taheri et al., 2022). The molecular docking method showed that these alkaloids have an inhibitory effect on human steroid 5α-reductase 2 (SRD5α2) which is associated with prostate cancer (Lu et al., 2022). In vivo studies proved that nettle pyrrole alkaloids (Fig. 3) possess significant analgesic activities (Feng et al., 2022).

3.4. Nettle steroids, saponins, lignan, fatty acids, and other compounds

Steroids are reported as bioactive compounds in *G.diversifolia* (Sharan Shrestha et al., 2020), *G.palmata* (Yuan et al., 1999), L.*bulbifera* (Zhu et al., 2011), L.*crenalata* (Khan et al., 2007), and *U.dioica* (Ji et al., 2007). Several steroids are present in these nettle extracts, i.e., β-sitosterol, γ-sitosterol, sitostanol, campesterol, and fucosterol. Several steroids, namely β-sitosterol, 3-hydroxysitosterol and 3-hydroxystigmast-5-en-7-one, γ-sitosterol, and ursolic acid can be isolated from the petroleum ether root extract of *Girardinia diversifolia* (Njogu et al., 2011). Most of them are associated with the anticancer activity of the extract and can reduce the symptoms of Benign Prostatic Hyperplasia (BPH). β-sitosterol and γ-sitosterol also have an antidiabetic activity and an anti-inflammatory agent. Its ursolic acid is a promising drug for treating various diseases, such as cancer, ulcer, hypoglycaemic, hyperlipidemic, bacterial and viral infections, inflammation, allergy, CNS depression, hepatoprotection, and cardioprotection (Tripathi et al., 2013).

Secondary metabolites like nettle saponin have antibacterial, antiviral, and antifungal properties. The sapogenins are hydrolyzed products from saponins. The highest content from the isolation and separation of

Table 2
List of alkaloids in *Laportea bulbifera* and *Urtica dioica*.

Nettle plant	Alkaloid	Ref.
Laportea bulbifera	Uracil 6-hydroxypurine 3-bofuranosyladenine	(Lu et al., 2022)
UD	Butyl (2S)-[2-formyl-5-(butoxymethyl)−1H-pyrrol-1-yl] propanoate 2-[formyl-5- (methoxymethyl) _1-hydro-pyrrol-1- 3-butyric acid butyrate 2-[formyl-5- (b 3 methyl ether) _1- 3-drogenpyrrol-1-yl] butyric acid butyl ester 4- [formy-5- (methoxymethyl) _1H-pyrrol-1-yl] butanoic acid, 3-formyl-5- (methoxymethyl) _1-hydro-pyrrol-1-yl] butyric acid methyl ester 2-[formyl-5- (butyl methyl ether) _1- 3-drogenpyrrol- 1-yl] butyric acid methyl ester Crinumaquine Capparisine A 5-hydroxyl-2- hydroxymethyl pyridine Berberine Cordyrrole A Lobechine Capparisine B	(Feng et al., 2022)

sapogenins from *Urtica dioica* are hederagenin and oleanolic acid (Ligor et al., 2021).

Analysis of fatty acids of ethanolic extract of *Urtica dioica* shows the existence of unsaturated fatty acids involved in reepithelization. This reepithelization capacity is essential in wound healing (Zouari Bouassida et al., 2017), especially hydroxy fatty acids (Farag et al., 2013). Extracts from non-polar solvents compose mainly of palmitic, stearic, and oleic acids (Grauso et al., 2019) and ceremide, such as urticamide, with antiurolithiatic activity (Zhang et al., 2014).

Several lignans from *Urtica fissa* are neourticol A and B, urticalactone III. neoolivil tetraacetate 16 nd urticalactones I and II. They have an antirheumatic capacity (Wang et al., 2019; Zhang et al., 2019). Other compounds in nettle are histamine, organic acids, and terpenes. Histamine has an analgesic effect (Fu et al., 2006). Organic acids, like formic acid, oxalic acid, tartaric and salicylic acids, are found in nettle extracts with analgesic and antiurolithiatic effects (Fu et al., 2006; Zhang et al., 2014). Terpenes like dotriaoctane, octadecane, nonadecane, and megastigmanes are found in *G.palmata* 52 *crenulata, U.dioica.* They are known for their analgesic (Dhouibi et al., 2018; Ji et al., 2007; Khan et al., 2014; Yuan et al., 1999). Several derivates of terpene have antidiabetic, anti-inflammatory, and antibacterial (Dar et al., 2013).

4. Healing capacity properties of Dendrocnide, Laportea, Girardinia, and Urtica

Stinging Nettle possesses many phytochemicals that determine excellent pharmacological activities (Taheri et al., 2022). In this review, a wide range of healing capacity properties of the four stinging Nettle is listed in Table 3. Besides their itchy sensation, this review deciphers several healing capacities using categories introduced by Devkota et al. (2022) that focus on antidiabetic, antiulcer activities, antibacterial, cardiovascular, brain disorder, allergic rhinitis, reno-hepatic protective, and anticancer activities.

4.1. Antioxidant of nettle extracts

A list of information on DPPH scavenging activities is in Table 4. Various extracts of *Laportea alatipes* are known for their potent antioxidant activity (Mahlangeni et al., 2020). Hydro methanolic and ethyl acetate extracts of UD and *Urtica parviflora* hav 1 ubstantial antioxidant effects (Salmi et al., 2021) that protect against cell injury caused by the reactive oxygen species (Pandey et al., 2010). *Dendrocnide sinuate* has antioxidant properties but is not very strong (Subba et al., 2016). Girardinia has the most potent antioxidants compared with the other three nettles. *Laportea aestuans* has also antioxidant activity (Table 4) (Oloyede and Oyelola, 2013).

4.2. Anti-inflammatory and immunostimulatory properties of nettle extracts

Various UD extracts have anti-inflammatory activities. Their polar extracts (water, ethanolic, methanolic) display moderate anti-inflammatory activities. Nevertheless, their non-polar extracts (dichloromethane, hexane) also exhibit potent anti-inflammatory effects. Their non-polar UD extracts are more effective than polar extracts (water, methanol, ethanol) for treating inflammatory disorders (Johnson et al., 2013), such as in treating rheumatoid arthritis (Dhouibi et al., 2020).

Chlorogenic is available in large amounts in stinging nettle extracts (Pinelli et al., 2008). In addition, chlorogenic acid containing hydroalcoholic extract from various nettle possesses sedative activity (Anzoise et al., 2013), anti-dengue activity (Flores-Ocelotl et al., 2018), positive effects on rheumatoid arthritis (A 16 Nikfarjam et al., 2022; Li et al., 2020), and antinociceptive and anti-inflammatory activities (Marrassini et al., 2010). Vicenin-2, a flavonoid glycoside, is found as an ethanolic extract of *Urtica circularis* and pos 8 ses significant anti-inflammatory 8 tivity. This glycoside modifies LPS-induced total nitrite, TNF-α, and translocation of the nuclear factor NF-κB (Marrassini et al., 2011).

The leaves of *Urtica fissa*, a folk medicine for rheumatism arthritis in

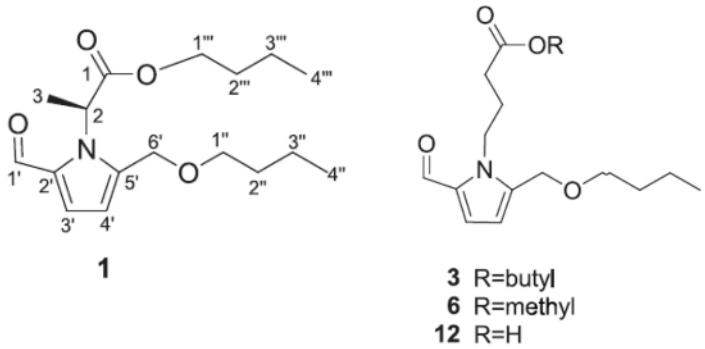

Fig. 3. Nettle pyrrole alkaloids (Feng et al., 2022).

Table 3
Healing capacities of Dendrocnide, Girardinia, Laportea and Urtica.

Bioactivity	Species	Extract	Ref.
1 ***Hypoglycemic property***			
Antidiabetic	*L. aestuans*	Methanolic	(Adetunji et al., 2021)
	L. aestuans	Aqueous/tea	(Lans, 2006)
	L. alatipes	Aqueous	(Mahlangeni et al., 2020)
	L. bulbifera	Total caumarin	(Wang et al., 2013)
	L. ovalifolia	Aqueous	(Momo et al., 2006; Tsabang et al., 2015)
	U. dioica	Hydroethanolic	(Ghafari et al., 2011; Golalipour et al., 2010)
2 ***Antiulcer activities***			
Antiulcer	*U. dioica*	Water extract	(Gülçin et al., 2004)
		Hydromethanolic	(Sisay et al., 2021)
3 ***Antibacterial Activities and wound healing***			
Antimicrobial	*D. sinuate*	Methanolic	(Subba et al., 2016)
	L. aestuans	Methanolic	(Mambe et al., 2016)
		Hydrodistillation, essential oils	(Oloyede, 2016; Oloyede and Oyelola, 2013)
		Hexane	(Oloyede and Oyelola, 2013)
	L. crenulata	Petroleum ether, chloroform, methanol	(Khan et al., 2007; Rahman et al., 2008)
	L. ovalifolia	Methanolic	(Tchinda et al., 2017)
	U. dioica	Aqueous, methanolic	(Körpe et al., 2013)
		Ethanolic	(Maimunah, 2021)
		Butanol, ethyl acetate, hexane	(Modarresi-Chahardehi et al., 2012)
	U. fissa	Aqueous, ethanolic, methanolic, EtOAc	(Kregiel et al., 2018)
	U. pilulifera	Aqueous, methanolic	(Körpe et al., 2013)
4 ***Cardiovascular-related activities***			
Antihypertension	*U. dioica*	Aqueous, methanolic	(Testai et al., 2002; Vajic et al., 2018)
5 ***Activities related to brain disorders: analgesic, anti-anxiolytic and antidepressant effects***			
Analgesic	*D. moroides*	lyophilized crude trichome extract in 50% acetonitrile	(Gilding et al., 2020)
	L. decumana	Aqueous	(Simaremare et al., 2015)
	L. bulbifera		(Li et al., 2020)
	U. thunbergiana		(Fu et al., 2006)
	U. fissa	Ethanolic (neourticol A and B)	(Wang et al., 2018, 2019)
Anxiolytic	*U. urens*	Methanolic	(Doukkali et al., 2015)
	U. circularis	Hydroethanolic	(Anzoise et al., 2013)
6 ***Activities Related to Allergic Rhinitis and Itchy sensing***			
Allergic rhinitis	*U. dioica*	Hydroethanolic	(Roschek et al., 2009)
Pollen allergy	*U. dioica*	Pollen	(Tiotiu et al., 2016)
7 **Reno-hepato protective effects**			
Reno-hepato protective	*L. aestuans*	Methanolic	(Adetunji et al., 2021)
	U. dioica	Hydroethanolic	(Golalipour et al., 2010)
	L. aestuans		(Lans, 2006)
8 ***Anticancer effects***			
Anticancer	*D. moroides*	Moroidin	(Kersten et al., 2022)
	G. diversifolia	Methanolic	(Sharan Shrestha et al., 2020)
	L. aestuans	Hydroethanolic	(Omolola et al., 2018)
	L. crenulata	Petroleum ether, chloroform, methanolic	(Rahman et al., 2008)
	U. dioica	Aqueous	(Hodroj et al., 2020)
		Ethanolic	(Brahmi-Chendouh et al., 2021)
	U. fissa	Ethanolic, successively partitioned of Petroleum ether, dichlormethane, and ethyl acetate from the residue,-suspended water	(Zhang et al., 2019)
	U. hyperborea	Ethanolic, ethyl acetate	(Su et al., 2019)
9 ***Others***			
Stamina booster	*D. peltata*		(Mom et al., 2015; Simaremare et al., 2019)
Antacid	*L. aestuans*	Aqueous	(Christensen et al., 2015)

Table 4
The antioxidant activity (DPPH radical scavenging activity) of nettle studied.

Species	Extract	DPPH	Ref.
Dendrocnide sinuata	Methanolic	No activity	(Subba et al., 2016)
Girardinia diversifolia	Methanolic	14.37 ± 0.7 mgTE/g	(Sharan Shrestha et al., 2020)
Girardinia heterophylla	Ethanolic	IC50: 3.21 μg/mL	(Myint et al., 2019)
Laportea aestuans	Hexane, chrysen-2-ol	0.0625 mg/ml in the DPPH (64.73%)	(Oloyede and Oyelola, 2013)
Urtica dioica	Hydroethanolic	IC50: 88.33 ± 2.88 μg/mL.	(Khare et al., 2012)
	Crude saponins	IC50: 0.159 mg/ml	(Razika et al., 2017)
	Distilled water	IC50: 152.34 ± 0.37 μg/mL	(Zemmouri et al., 2017)
	EtOAc fraction after hydro-alcoholic	IC50: 78.99 ± 0.17 μg/ml	(Joshi et al., 2015)
	Petroleum ether	IC50: 167.54 ± 1.97, μg/ml	(Loshali et al., 2021)
	Chloroform	IC50: 134.41 ± 0.82, μg/ml	
	EtOAc	IC50: 88.15 ± 1.39 μg/ml	
	Ethanolic	IC50: 186.38 ± 1.91 μg/ml	
U. parviflora	Hydromethanolic	IC50: 808 μg/ml	(Pandey et al., 2010)
	Ascorbic acid.	IC50: 22.43 μg/ml for	
Urtica urens	Acetone	60.8% (at 1 mg/ml)	(Jimoh et al., 2010)
	Methanolic	91.2% (at 1 mg/ml)	
	Water	63.5%(at 1 mg/ml)	
	Ascorbic acid	100% (at 1 mg/ml)	

China A, possess a ceramide urticamide, two secolignans urticalactones I and II, and a flavonoid glycoside urticaside. They possess an anti-inflammatory potential that can inhibit the release of NO and TNF-α in vivo study using lipopolysaccharide (LPS) stimulated RAW 264.7 cells, with IC(50) values less than 4.0 μM (Wang et al., 2018).

Polar extract, such as methanolic extract of UD contain flavonoid glucosides, such as quercetin-3-O-rutinoside, kaempferol-3-O-rutinoside, and kaempferol-3-O-glucoside. Quercetin-3-O-rutinoside has immunostimulatory activity. Kaempferol-3-O-rutinoside and Kaempferrol-3-O-glucoside have a role in treating T2DM, rheumatism, and inflammatory muscle. Additionally, UD kaempferol-rich extract helps treat virus infection, antiurolithiasis, and endometriosis (Akbay

et al., 2003). Other flavonoid glycosides also exhibit immunostimulatory activity. Isorhamnetin-3-O-glucoside are glycosides that can be isolated from the methanolic extract of UD. Its fraction has immunostimulatory activity (Akbay et al., 2003) and exhibits promising activity in endometriosis (Ilhan et al., 2019).

4.3. Hypoglycemic properties, diabetic and hypolipidemic effects

Extracts of *Laportea ovalifolia*, *Urtica dioica*, and *U. dentata* have hypoglycemic effects. A decoction of the leaves of *Laportea ovalifolia* is widely used to treat diabetes mellitus (Momo et al., 2006). The leaf extract of *Urtica dioica* been reported to improve glucose homeostasis in vivo. (Dhouibi et al., 2020) It has also been reported that the total coumarin content of *Urtica dentata* exhibits significant defense against the increase of autoimmune diabetes. Total coumarins can decrease blood levels of glucose. Whole coumarins inhibit high glucose-induced HBZY-1 cell proliferation and hypertrophy, down-regulating transforming growth factor-β1, connective tissue growth factor and toll-like receptor 4 activation (Cao et al., 2015). Nettle tea may improve glycaemic control in T2DM patients needing insulin therapy (Kianbakht et al., 2013).

Nettle tea is recommended for adjuvant therapy for diabetic patients and their antidiabetic drugs (Otoom et al., 2006). Infusion UD either as a sole agent or herbal mixture can reduce the blood sugar level of T2DM (Fodor and Keve, 2006). UD distillate is prepared and consumed as a traditional herbal drink or nettle tea. This nettle tea has protective effects on diabetes recovery by controlling the serum insulin, blood glucose, pancreatic islets, and β-cells in diabetic rats. It has been proved that treating hyperglycemic rats with UD dramatically decreased blood glucose and significantly enhanced serum insulin. Therapy with UD does not change the mean β-cell volumes, but the islet volumes and β-cell numbers can be significantly recovered. UD treatment improves hyperglycemia by partially restoring plasma insulin levels. UD avoids islet atrophy and regenerates β-cells (Gohari et al., 2018). UD extract or fraction can decline blood glucose upon oral delivery. The particular fraction can stimulate insulin secretion in glucose-responsive MIN6 clonal beta-cells and improve glucose uptake (approximately 1.5-fold) in L6-GLUT4myc myoblast cells. UD fraction probably has cyclical peptides that facilitate glucose uptake (Domola et al., 2010).

There are several molecular mechanisms of nettle in diabetic metabolism (Table 6). UD is attributed to different compounds, such as polyphenols, triterpenes, sterols, flavonoids, and lectins. This extract reduces blood glucose and the risk of CVD. Antioxidant and anti-inflammatory properties interfere with different cellular signalization pathways, increase NO, inhibition of α-amylase and α-glycosidase, modulation of GLUT4, and protection of pancreatic β-cells, among others (El Haouari and Rosado, 2019). UD has benefits in diabetic encephalopathy. UD extract balances the granule cell loss in the diabetic rat dentate gyrus, which can enhance cognitive loss in diabetes (Fazeli et al., 2008). UD is known as an antihyperglycemic plant. The UD-containing formula has a potential antihyperglycemic and triglyceride-lowering effect (Khalili et al., 2017). The antidiabetic effects of the extract of the stinging nettle are associated with cardiovascular effects (El Haouari and Rosado, 2019) and diabetic encephalopathy (Fazeli et al., 2008), and hypolipidemic effects (Momo et al., 2006). Moreover, nettle is responsible for antidiabetic effects, such as increasing insulin secretion and proliferation of pancreatic β-cells (Samakar et al., 2022).

4.4. Antiulcer activities

UD (Devkota et al., 2022; Gülçin et al., 2004) and *Urtica simensis* (Sisay et al., 2021) have antiulcer activity. So far, no report is available for Dendrocnide, Girardinia, and Laportea. UD water extract can decrease mucosal injury. Its extract can protect the stomach mucous membrane. This extract also hinders the excess acid secretion and diminishes the acidity of stomach liquid in ulcers (Burkova et al., 2011;

Table 6
Antidiabetic activity of various extracts of Urtica dioica.

Extract	Model	Increasing effects on	Ref.
Ethanol/water (70/30)	Clinic	Insulin secretagogue	Kianbakht et al., 2013)
Ethanol/water (70/30)	In vitro	Inhibitory effects on alpha-glucosidase activity	(Onal et al., 2005) (Kianbakht et al., 2013)
Distilled water	In vitro	Pancreatic α- amylase	(Rahimzadeh et al., 2014)
	Docking analysis	Dipeptidyl peptidase 4, Alpha-amylase and beta-glucosidase activities	(Salim et al., 2020)
Ethanol/water (50/50)	In vivo	Regulating glucose transporter-4 (GLUT4) translocation toward the plasma membrane	(Kadan et al., 2013)
Hydroethanolic	In vivo	Expression of hypothalamic neuropeptides and hippocampal astrogliosis. (The astrocyte number in the dentate gyrus of diabetic rats after treatment with Nettle is increased)	(Jahanshahi et al., 2009)
Methanol/water (50/50)	In vivo	Associative and spatial memory deficit	(Patel et al., 2015)
Hydroethanolic	In vivo	Attenuate diabetic neuropathy (memory dysfunction and hyperalgesia), either in the peripheral nervous system or in the central nervous system	(Patel and Udayabanu, 2013)
Methanol/water (50/50)	In vivo	Attenuating diabetes mediates neuronal destruction and DNA disintegration in the hippocampus, upregulation BDNF, TrKB, Cyclin D1, Bcl2, autophagy5 and autophagy7, and downregulation iNOS mRNA expression and TNF-α in hippocampal regions	(Patel et al., 2018)
Ethanol/water (30/70)	In vivo	Ameliorating hippocampal insulin signaling, oxidative stress, neuroinflammation, and cognitive impairment	(Rahmati et al., 2021)
Ethanol/water (50/50)	In vivo	Ameliorating the undesirable effect of glucose on cell feasibility and functionality of beta-RINm5F cells, either separately or in combination	(Pérez Gutiérrez et al., 2021)
Ethanol/water (80/20)	In vivo	Influencing nuclear receptor signaling e.g., the PPARs (peroxisome proliferator-activated receptors) that play an essential part in glucose homeostasis. Imitation activators of PPARalpha (fibrates) are commonly used for the therapy of diabetes. Natural products, such as carnosic acid and carnosol, are known as activators of PPARgamma	(Rau et al., 2006)
Ethanol/water (70/30)	Clinic	Agonistic effects on PPARgamma	(Kianbakht et al., 2013)
	In vivo	Improving the expression of the levels of proteins (PGC1α and NRF2) which are involved in mitochondrial biogenesis and its function	(Seyydi et al., 2022)
	In vivo	Decreasing levels of fasting blood glucose (FBG), hemoglobin A1c (HbA1c), C-reactive protein (CRP), systolic blood pressure (SBP)	(Tabrizi et al., 2022)

Devkota et al., 2022). UD water extract has analgesic and antiulcer properties, besides its antioxidant, antimicrobial, and analgesic properties (Gülçin et al., 2004).

The juice of the semi-crushed leaf of *Urtica simensis* has been used to treat peptic ulcer disease. In vivo study with rats proved that hydro-ethanolic leave extract of *U. simensis* has antisecretory activity, an ulcer-protective, and ulcer-healing activity. Its methanolic extract (400 mg/kg/day dose of 80% extract) can achieve the highest gastroprotective effect. In vivo studies confirmed the ulcer healing and antiulcerogenic activity of *U. simensis*, thus following the traditional claim (Sisay et al., 2021).

4.5. Antibacterial activities and wound healing

Stinging nettle is known as herbal medicine for wound healing (Zouari Bouassida et al., 2017) and acne vulgaris (Kılıç et al., 2019). Various extracts of Girardinia, Leportea, particularly Urtica, can inhibit many microorganisms, including Gram-positive bacteria, Gram-negative bacteria, pathogenic yeasts, and fungi (Table 7). Most of the extracts have a broad spectrum of antibiotic activities. They are rich in flavonoids and polyphenols. Limited information is available on the antibacterial activity of nettle essential oils. Nevertheless, essential oils from L. *aestuans* have antimicrobial activities (Oloyede, 2016; Oloyede and Oyelola, 2013).

The UD hydro-ethanolic extract has been used for wound healing activities. This extract is efficient in wound healing support. Additionally, the extract has not only antibacterial capacity but also an ability to stimulate epidermal regeneration. It has unsaturated fatty acids, and a high quantity of lupeol is identified for its contribution to reepithelialization (Zouari Bouassida et al., 2017). For wound healing, extract-containing ointments can be created and used to accelerate the therapy of infected wounds. Additionally, the topical use of nanoparticles with the help of UD extract can accelerate the methicillin-resistant *Staphylococcus aureus* (MRSA)-infected wound healing (Chood Gharehpapagh et al., 2021).

UD extracts have been reported for their solid antibacterial activity in acne vulgaris. Acne vulgaris is a common skin disease characterized by increased sebum production, inflammation, and colonization of *Cutibacterium (Propionibacterium) acnes* on pilosebaceous follicles. The topical application of UD extracts can be a good candidate for local acne treatment (Kılıç et al., 2019).

UD also has an anti-mycobacterial potential against multi-drug resistant (MDR) strain of *Mycobacterium tuberculosis*. Hexane extract of UD can produce an inhibition zone of 20 mm in disk diffusion assay and MIC of 250 μg/mL. Phytochemical analysis indicated that this anti-mycobacterial activity is due to terpenoids (Singh et al., 2013).

The polyphenol and flavonoids from UD extracts are antibacterial agents and antioxidants. Their hydroethanolic extract has the most potent antibacterial and antioxidant activities that are good for wound healing. Histopathological and biochemical explorations show that the hydroethanolic extract of UD can complete epidermal regeneration. For this re-epithelium process, unsaturated fatty acids and a high concentration of lupeol are known for their involvement (Zouari Bouassida et al., 2017). The antioxidant capacity of UD is found to exhibit a potent neuroprotective effect. UD keeps the dopaminergic neurons by lowering mito-oxidative impairment, neuroinflammation, and cellular revision

Table 7
List of microorganisms inhibited by Laportea and Girardinia.

Plant	Extract	Species	Ref.
Dendrocnide stimulans		*Tuberculosis*	(Grosvenor et al., 1995)
G.diversifolia	Petroleum ether	*Bacillus pumilus Staphylococcus aureus Escherichia coli Aspergillus niger Saccharomyces cerevisiae Candida albicans*	(Njogu et al., 2011)
	Polar fractions	*B. pumilus, S.aureus E.coli*	(Njogu, 2007)
	Ethyl acetate	*A.niger S.cerevisiae C.albicans*	(Njogu, 2007)
	Oil extraction	Ringworm	(Bhat et al., 2014)
	Zinc oxide nanoparticles	*Streptococcus pneumoniae S.aureus, E.coli Klebsiella pneumoniae Pseudomonas aeruginosa C.albicans A. niger*	(Negi et al., 2022)
G.heterophylla	Aqueous, ethanolic, petroleum ether	*Bacillus subtilis. E.coli Pneumoniae, A. niger*	(Bedi et al., 2013)
L.aestuans	Oils and essential oils	*B.subtilis, S.aureus, E. coli K.pneumoniae, A.niger P. aeruginosa, Salmonella typhi, Penicillium notatum C.albicans*	(Mambe et al., 2016; Oloyede, 2016)
L.decumana	Aqueous	Wound healing	(Prabawati et al., 2021)
	Ethanolic	*C.albicans*	(Simaremare et al., 2020)
L.interupta	Ethanolic, hydroethanolic	*S.aureus, E.coli*	(Pertiwi and Fernanda, 2019)
U.dioica	Aqueous	*P. aeruginosa*	(Alp and Aksu, 2010)
	Aqueous, methanolic	*Bacillus, Shigella* spp.	(Körpe et al., 2013)
	Hydroalcoholic, ethanolic, methanolic	*S.aureus, Staphylococcus epidermidis, E.coli, Bacillus cereus*	(Motamedi et al., 2014)
	Ethanolic	*Klebsiella pneumoniae P. aeruginosa, Serratia marcescens, Shewanella*	(Batool et al., 2017; Stemiša et al., 2020)
	Methanolic, butanol, ethyl acetate, hexane, ethanolic	MRSA	(Batool et al., 2017; Modarresi-Chahardehi et al., 2012; Salehzadeh et al., 2014)
	Butanol, ethyl acetate, hexane	*B. cereus Vibrio parahaemolyticus*	(Modarresi-Chahardehi et al., 2012)
	Selenium nanoparticles	*B.subtilis, Mycobacterium tuberculosis, S. aureus, Propionibacterium acne, E.coli, P.aeruginosa, C.albicans, Aspergillus flavus, A.niger*	(Deveci et al., 2013; Hashem and Salem, 2022; Kılıç et al., 2019; Singh et al., 2013; Stanciuc et al., 2011; Turker and Usta, 2008)

Table 8
List of cancer inhibited by nettle plants.

Type of cancer	Plant extract	Molecular mechanism	Ref.
Breast cancer	Dichloromethane extract of *Urtica dioica*	Inhibit proliferation Inhibit migration or metastasis	(Asoori et al., 2017)
Breast adenocarcinoma	Ethanolic extract of *Urtica membranacea*	Induce apoptosis	(Solowey et al., 2014)
Human breast adenocarcinoma cells MDA-MB-468	Dichloromethane extract of *Urtica dioica*	Inhibit proliferation upregulate caspase-3, caspase-9, Downregulate bcl2 Induce apoptosis	(Mohammadi et al., 2016)
Human breast cancer cell line (MCF-7)	Aqueous extract of *Urtica dioica*	Inhibit proliferation induce apoptosis	(Fattahi et al., 2013)
Prostate cancer cell lines (PC-3)	Hydroethanolic extract of *Urtica*	Inhibit proliferation	(Asadi-Samani et al., 2018)
Acute myeloid leukemia (AML) cell lines (U-937 and KG-1)	Aqueous extract of *Urtica dioica* (nettle tea)	Inhibit proliferation, Induce apoptosis Downregulate Bax and Bcl-2 Arrest cell-cycle	(Hodroj et al., 2020)
Colorectal cancer: cancer cells HCT-116.	Dichloromethane extract *of Urtica dioica*	Induce apoptosis Upregulate Caspase-3 and Caspase-9 Downregulate Bcl-2 Arrest cell cycle at the G2 phase	(Mohammadi et al., 2016)
Benign prostatic hyperplasia	theoretical evidence of *L.bulbifera*	inhibitory effect on human steroid 5α-reductase 2	(Lu et al., 2022)
Benign prostatic hyperplasia	Ethyl acetate and alcohol-soluble extract of *Urtica hyperborean*	Inhibit proliferation Induce apoptosis Reduce the prostate index, Reduce the serum DHT and EGF levels Downregulate EGF and Bcl-2 genes	(Su et al., 2019)
Vero normal-cell line CCL-81	Aqueous extract of *Urtica dioica* as Selenium nanoparticles	Cytotoxicity	(Hashem and Salem, 2022)
Several cancer types	Moroidin	Inhibit tubulin proliferation	(Regina et al., 2019)
Non-small cell lung cancer (NSCLC)	Hydroethanolic extract of *Urtica dioica*	Inhibit proliferation Arrest growth Induce apoptosis	(D'Abrosca et al., 2019)
Benign prostatic hyperplasia (BPH)	Hydroethanolic extract of *Laportea aestuans*	Antioxidant	(Omolola et al., 2018)
Tumor cells HeLa and CCRF-CEM cells	Hydroethanolic extract of *Urtica fissa*	Inhibit proliferation	(Zhang et al., 2019)
Gastrointestinal cancer HepG2 and HTC116	Methanolic extract of *Urtica dioica*	Inhibits proliferation Induces apoptosis	(Kardan et al., 2020)

and enhancing neurotrophic potential (Bisht et al., 2017).

4.6. Cardiovascular-related activities

UD has traditionally been used to control cardiovascular disorders, especially hypertension (Dhouibi et al., 2020). UD is considered a valuable plant due to bioactive compounds such as formic acid and rich sources of flavonoids. The role of nettle in metabolic syndrome has several mechanisms, such as alterations in potassium and calcium channels which improve hypertension (Samakar et al., 2022). UD can be used to remedy hypertension. Its aqueous extract has a hypotensive potential in the rat in vivo. Study with the isolated Langendorff-perfused rat heart, this extract (1 and 2 g/l) can markedly decrease heart rate and increase left ventricular pressure. Nevertheless, a higher concentration (5 g/l) can trigger cardiac arrest. The extract produces aorta vasoconstriction owing to the activation of alpha1-adrenergic receptors (Legssyer et al., 2002).

UD has antihyperlipidemic properties that are mediated by inhibiting HMGCoA reductase and ameliorating lipid peroxidation via antioxidant effects. Quercetin, one of the flavonoids in UD, is responsible for decreasing total cholesterol (Samakar et al., 2022). UD also has an antiplatelet action in which flavonoids are mainly implicated. Its flavonoids also markedly inhibit platelet aggregation. Aqueous and ethyl acetate extracts of UD inhibit thrombin-induced platelet aggregation and exhibits the most antiaggregant effect (El Haouari et al., 2006).

4.7. Brain disorders related activities: analgesic, anti-anxiolytic and antidepressant effects

Stinging nettle has analgesic, anti-anxiolytic, and antidepressant effects. *Laportea decumana* leaf is enormously beneficial for pain and muscle aches relief. It is a stamina booster and can reduce fatigue and stiffness. Local people in Papua pick the itchy leaf and apply it to the painful body part. This leaf gives an itching sensation as a marker that the drug works according to public belief but can relieve pain in the area that is applied after a few minutes. Modern use of itchy leaf has been developed in the form of topical ointment or cream (Gilding et al., 2020; Hole et al., 2016; Mom et al., 2015; Rayburn et al., 2009; Simaremare et al., 2019; Sjakoer and Liswandari, 2020). It is also applied to chronic low back and musculoskeletal pain patients. It is applied gently, flicking the lower half of the back with its leafed end. The musculoskeletal pain is relieved by incorporating stinging nettle (Alford, 2007).

Laportea and Urtica possesses quercetin and rutin. They have a neuroprotective effect on chronic stress. Chronic stress results in neurological complications like depression, cognitive dysfunction, anxiety disorders, and a decline in locomotion and muscle coordination abilities (Parashar et al., 2017). Stinging nettle, particularly UD, possesses an abundance of quercetin that may benefit in treating chronic stress. Quercetin has a good effect on behavioral dysfunction, oxidative pressure, and hippocampal neuroinflammation. Treatment with quercetin can reduce anxiety, attenuate depression, improve cognitive dysfunction and normalize locomotor activity. Quercetin can efficiently prevent neurological complications by rescuing the brain from oxidative and inflammatory stress (Mehta et al., 2017). Rutin in stinging nettle extract can also rescue behavioral insufficiencies by declining depression and anxiety, recovering cognition, and locomotor & muscle coordination skills. Treatment with rutin can protect the hippocampal neuronal loss. The hippocampal dysfunction is associated with T2DM. Then, hippocampal dysfunction results in depression, anxiety, and cognitive decline. Treatment with UD hydroalcoholic leaf extract is applicable for diabetes with anxiety and depression (Patel et al., 2018; Patel and Udayabanu, 2014).

UD extracts are also a therapeutic alternative for relieving pain. Its ethanol extract has analgesic properties (Dhouibi et al., 2018). UD has strong anti-inflammatory and anti-arthritic effects (Yang et al., 2013). UD-herbal antirheumatics are indicated in painful inflammatory and degenerative rheumatic diseases (Chrubasik and Pollak, 2002). A leaf extract of UD is an excellent adjuvant drug for rheumatic diseases. The UD extract can stimulate the secretion of proinflammatory cytokines (Obertreis et al., 1996; Rayburn et al., 2009) and can be an excellent genuine painkiller source (Dhouibi et al., 2018). The abundance of

quercetin and rutin in UD extract can also attenuate stress-related complications. Quercetin can alleviate behavioral dysfunction. Anxiety, depression, cognitive dysfunction, and locomotor activity can improve with quercetin. Quercetin treatment can significantly lower oxidative, inflammatory, and neural damage (Mehta et al., 2017). Rutin has a neuroprotective effect on chronic stress. It rescues chronic unpredictable stress (CUS)-caused behavioral insufficiencies by minimizing depression, and anxiety, improving cognition and locomotor & muscle coordination skills. Rutin guarded the CUS-induced hippocampal neuronal loss (Parashar et al., 2017). Rutin from UD's aerial parts exhibits promising endometriosis activity (Ilhan et al., 2019).

UD extract has protective effects on the activity of acetylcholinesterase (AChE), and can AChE activity. UD extract also has protective effects on the oxidative damage of brain tissues. It can increase the malondialdehyde (MDA) concentration in the hippocampal and cortical tissues while decrease thiols content and superoxide dismutase (SOD) and catalase (CAT) activities in the brain. Treatment with the extract reverse all the effects of scopolamine-induced memory impairment model. The beneficial effects of UD on memory can be attributed to its protective effects on AChE activity and oxidative damage of brain tissue (Ghasemi et al., 2019). Therefore, UD extract can be used in the treatment of epilepsy. The EAE was effective and significant in an experimental study against MES and PTZ-induced seizures. The potent antioxidant extract of UD root has an antiepileptic effect (Loshali et al., 2021).

Potential therapeutic agent for oxidative stress associated with neurodegenerative diseases such as Alzheimer's, Huntington's, and Parkinson's disease. They are characterized by a generalized systemic neurological defect, loss of neuromuscular connection, and memory dysfunction. Antioxidant-rich extract of UD can improve behavioral performance and motor coordination. Additionally, it also lessens pro-inflammatory cytokines and restore the glutathione and catalase levels. UD extract has a significant role in the modulation of the antioxidant system and ameliorates the damage caused by inflammatory cytokines (Dhouibi et al., 2021).

4.8. Allergic rhinitis-related activity and itchy sensing

In vitro study shows that UD leaf extracts exhibit inhibition of histamine H1 receptor, cyclooxygenase 1 (COX-1), cyclooxygenase 2 (COX-2), and hematopoietic prostaglandin D2 synthase (HPDS). COX-1, COX-2, and HPDS are enzymes related to the stimulating allergic rhinitis (Devkota et al., 2022). No information is available for Dendrocnide, Girardinia, and Laportea.

Itchy sensing can be stimulated by *Dendrocnide meyeniana*. *D. meyeniana* can induce severe acute dermatitis during outdoor activities. The aerial part of *D. meyeniana* can cause auto-sensitization dermatitis. It has erythematous papules accompanied by itching and stinging sensations over the left inner elbow and then extended to the trunk and limbs (Chang et al., 2009; Gilding et al., 2020). The itchy effect is probably not a benefit, but applying the leaf by scrubbing it to the body will create itchy sensing before other benefits come. The causes for itchy sensing and other benefits are probably not coming from the same phytochemical substances. The chemical causes are different or attributed to different classes of compounds. Their stinging hairs or trichomes are nearly unseeable to the bare eye. Once touched by the skin, the trichome tips crack off. This event injects fluid containing substances and can hurt the skin (Otles and Yalcin, 2012). The skin-painful itching and burning sensations may last up to 12 h. The acid fluid from trichomes is acetylcholine, histamine, formic acid, silica, serotonin, and 5-hydroxy tryptamine. These compounds are smooth muscle stimulants (Otles and Yalcin, 2012).

4.9. Reno-hepatoprotective effects

The methanolic leaf extract of *Laportea aestuans* potential in managing the reno-hepatoprotective potentials (Adetunji et al., 2021). A methanolic extract of UD has anti-urolithiatic activity. Treatment with the methanolic extract of UD can decline the raised of urinary calcium, oxalate, and creatinine, and calcium and oxalate. Furthermore, renal histological studies show a significant decline in calcium oxalate crystal. Because of its intense anti-urolithiatic activity, UD extract may have the potential as a natural therapeutic agent for various urological disorders (Zhang et al., 2014).

Urtica dioica has hepatoprotective potential. In vivo studies with CCl (4)-induced hepatotoxicity in-vitro (HepG2 cells) show that the most potent fraction is ethyl acetate fraction from hydroethanolic extract (Joshi et al., 2015).

4.10. Anticancer effects

The moroidin-rich extract is promising for anticancer medicine. Moroidin is an inhibitor of tubulin polymerization that leads structures for cancer therapy (Gilding et al., 2020; Kersten et al., 2022). Tubulin is the primary target of potential anticancer agents (Kobayashi et al., 2001; La Regina et al., 2019). Moroidin is found in Dendrocnide. Nevertheless, there is evidence that *Laportea bulbifera* may have the potential to inhibit benign prostatic hyperplasia (BPH) (Lu et al., 2022).

Among the member of stinging nettle, UD is frequently reported as a promising chemotherapeutic agent for breast cancer, prostate cancer, lung cancer, and leukemia. UD polar extracts can inhibit proliferation and metastasis, induce apoptosis, upregulate caspase, arrest the cell cycle, and inhibit tubulin proliferation (Table 8). Polar or nonpolar extracts of UD have anticancer activities. UD significantly inhibits breast cancer cell proliferation and the migration of breast cancer cell lines (Thalib et al., 2021; Yoshikawa et al., 2000).

4.11. Other healing capacity properties

Other than the healing capacities, as mentioned earlier, there are additional properties that have not yet been intensively explored. Some of them are virus infection, photoprotection, osteoporosis, and inhibition of medically relevant enzymes. UD extracts have been introduced for an acute respiratory infection caused by COVID-19. UD is a potent inhibitor of the ACE-2 receptor. Several bioactive compounds, such as quercetin, β-sitosterol, luteoxanthin, violaxanthin, and rutin, are potential candidates for developing target-specific therapeutic drugs against COVID-19 (Flores-Ocelotl et al., 2018; Moslemifard et al., 2020; Pan et al., 2020; Rakshit et al., 2021; Rivero-Segura and Gomez-Verjan, 2021; Upreti et al., 2021; Yildirim et al., 2013).

Ethanolic extract of *Girardinia diversifolia* is good phototherapeutic or skin UV protector. Its ethanolic extract contains many UV protectors, such as 2-methyltetradecane dodecane, 2,6,11-trimethyl-; 2,6,11-trimethyldodecane, and trimethylhexane (Bhat et al., 2014; Dhouibi et al., 2018). Aqueous extract of L.*aestuans* can prevent osteoporosis (de Oliveira et al., 2012). Many extracts have inhibitory activity against acetylcholinesterase, butyrilcholinesterase, tyrosinase, α-amylase and α-glucosidase (Jang et al., 2018; Sharan Shrestha et al., 2020), and downregulate adenosine deaminase and ornithine decarboxylase gene expression (Fattahi et al., 2018).

5. Drug delivery: administration and preparation of itchy leave ailments

Administration of itchy leave extracts can be an oral and topical ailment. Oral administration can be in the form of nutraceutical food or herbal tea alone or as a formula that is prepared from fresh or dry leaves. As a topical ailment, itchy leaves can be prepared as gel, cream, or ointment for topical ailments as transdermal administration.

Nettle leaves can be consumed as nutraceuticals. As a nutraceutical, the nettle leaf can be consumed for treating diabetes. Its antidiabetic activity better than acarbose (Mahlangeni et al., 2020). Recently, UD

leave also belongs to highly nutritious food. (Devkota et al., 2022). Nettle leaves and their extracts can be added to the bread's formulation. This addition can improve the bread's composition in phenolic acids, flavonoids, microelements, and macro elements. This bread shows significant antioxidant activity (Durović et al., 2020).

Nettle leaves can become an ingredient of loloh. Loloh is an herbal drink that is produced and consumed exclusively in Bali (Indonesia) to prevent and treat different health problems. Nettle plants, such as *Dendrocnide stimulans*, are used to prepare loloh to treat heartburn, fever, diarrhea, hypertension, and other minor health problems. The leave decoctions and juice can be simply added to the preparation. The Balinese communities preserve this ethnobotanical knowledge. Even, *Dendrocnide stimulans* are understudied. It can be a promising herbal material for further research (Sujarwo et al., 2015).

As an herbal tea, the most promising extraction methods of the leave are decoction and tincture (*U. dioica*) (Mihaylova et al., 2018). Nettle tea of itchy leave is the easiest way of aqueous preparation that the community can do. It can be prepared by cooking, decoction, infusion, maceration, and water-based ointment.

The ointment has been used to relieve pain in Papua. Ointment of itchy leaves can be prepared with a water-soluble base ointment. So far, this ointment has no maximal effectiveness if it is compared with its leaves. It must be developed continuously. Its organoleptic, pH, homogeneity, stinky, effectiveness, and dispersive power should be standardized (Simaremare et al., 2015).

The use of topical ointment can support the skin route of drug delivery. But, the permeability barrier in the skin is challenging for drug molecules to pass through. Fortunately, extract from *Dendrocnide meyeniana, Urtica thunbergiana* can enhance penetration (Fuh et al., 2019). It has been proved that this extract-penetration enhancer can enhance insulin and insulin sensitizers (curcumin and rutin) through mouse skin. Therefore, the percutaneous route is an exciting and inventive investigation field of drug delivery. However, it is challenging for drug molecules to pass through the skin's surface, which is characterized by its permeability barrier. Sting crude extracts of *Dendrocnide meyeniana, Urtica thunbergiana* were used as the penetration enhancers. Generally, natural plant extracts can be preferred over chemically synthesized molecules and are safe and potent penetration enhancers for stimulating the transdermal absorption of drugs (Fuh et al., 2019).

6. Conclusions and prospects

Overall, we revealed the dominance of Urtica in stinging nettle studies. This study assists in future research on bioactive compounds and healing capacities of the Indonesian endemic genus Dendrocnide, Girardinia, and Laportea.

- Bioactive compounds of four nettle genera are dominant in phenolic compounds. Polar extracts of the aerial part are rich in phenolic acids and flavonoids. Moroidin is present in the most violently stinging nettle, Dendrocnide. Nettle alkaloids are essential not only for a fingerprint that differentiates nettle species but also in association with their healing capacities.
- Medicinally, the four genera have broad healing capacities, such as in treating ulcers, diabetes, cancer, rheumatoid arthritis, bacterial infection, diarrhea, sprains, kidney stones, urinary tract infection, high blood pressure, hemorrhoids, flu, cough, fever, and pain (as analgesic drug), etc.
- The preparation of extracts can be tailored according to the allotment, and mainly polar extracts can be delivered as nettle tea or herbal drink, cream or ointment, or as concentrated extract containing capsules/tablets.

Recommendation for the future direction

- Research on Dendrocnide, Laportea, and Girardinia needed to be developed to mimic Urtica
- The possible application for the treatment of rheumatic arthritis, diabetes, heartburn, cancer, and wound healing needs to be explored.
- Standardized quality in preparing the extract of stinging Nettle is needed.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

Abd-Nikfarjam, B., Abbasi, M., Memarzadeh, M., Farzam, S.-A., Jamshidian, A., Dolati-Somarin, A., 2022. Therapeutic efficacy of Urtica dioica and evening primrose in patients with rheumatoid arthritis: a randomized double-blind, placebo-controlled clinical trial. J. Herb. Med. 32, 100556 https://doi.org/10.1016/j.hermed.2022.100556.

Adetunji, O.A., Olugbami, J.O., Adegoke, A.M., Gbadegesin, M.A., Odunola, O.A., 2021. Reno-Hepatoprotective and Antidiabetic Properties of Methanol Leaf Extract of *Laportea aestuans* in Wistar Rats. J. Evid. Based Integr. Med. 26 https://doi.org/10.1177/2515690x211017464.

Aishan, H., Baba, M., Iwasaki, N., Kuang, H., Okuyama, T., 2010. The constituents of *Urtica cannabina* used in Uighur medicine. Pharm. Biol. 48 (5), 577–583. https://doi.org/10.3109/13880200903214215.

Akbay, P., Basaran, A.A., Undeger, U., Basaran, N., 2003. In vitro immunomodulatory activity of flavonoid glycosides from *Urtica dioica* L. Phytother. Res. 17 (1), 34–37. https://doi.org/10.1002/ptr.1068.

Alford, L., 2007. The use of nettle stings for pain. Altern. Ther. Health. Med. 13 (6), 58.

Alp, E., Aksu, M.I., 2010. Effects of water extract of *Urtica dioica* L. and modified atmosphere packaging on the shelf life of ground beef. Meat Sci. 86 (2), 468–473. https://doi.org/10.1016/j.meatsci.2010.05.036.

Anzoise, M.L., Marrassini, C., Ferraro, G., Gorzalczany, S., 2013. Hydroalcoholic extract of *Urtica circularis*: a neuropharmacological profile. Pharm. Biol. 51 (10), 1236–1242. https://doi.org/10.3109/13880209.2013.785574.

Asadi-Samani, M., Rafieian-Kopaei, M., Lorigooini, Z., Shirzad, H., 2018. A screening of growth inhibitory activity of Iranian medicinal plants on prostate cancer cell lines. Biomedicine (Taipei) 8 (2), 8. https://doi.org/10.1051/bmdcn/2018080208.

Batool, R., Salahuddin, H., Mahmood, T., Ismail, M., 2017. Study of anticancer and antibacterial activities of *Foeniculum vulgare, Justicia adhatoda* and *Urtica dioica* as natural curatives. Cell. Mol. Biol. (Noisy-le-grand) 63 (9), 109–114. https://doi.org/10.14715/cmb/2017.63.9.19.

Bedi, P., Thakur, N., Singh, B., 2013. Antimicrobial activity of *Girardinia heterophylla*. Int. J. Medical Health Biomed. Bioeng. Pharmaceut. Eng. 7 (11), 724–728.

Bhat, P., Hegde, G.R., Hegde, G., Mulgund, G.S., 2014. Ethnomedicinal plants to cure skin diseases-an account of the traditional knowledge in the coastal parts of Central Western Ghats, Karnataka, India. J. Ethnopharmacol. 151 (1), 493–502. https://doi.org/10.1016/j.jep.2013.10.062.

Bisht, R., Joshi, B.C., Kalia, A.N., Prakash, A., 2017. Antioxidant-Rich Fraction of *Urtica dioica* Mediated Rescue of Striatal Mito-Oxidative Damage in MPTP-Induced Behavioral, Cellular, and Neurochemical Alterations in Rats. Mol. Neurobiol. 54 (7), 5632–5645. https://doi.org/10.1007/s12035-016-0084-z.

Brahmi-Chendouh, N., Piccolella, S., Nigro, E., Hamri-Zeghichi, S., Madani, K., Daniele, A., Pacifico, S., 2021. *Urtica dioica* L. leaf chemical composition: a never-ending disclosure by means of HR-MS/MS techniques. J. Pharm. Biomed. Anal. 195, 113892 https://doi.org/10.1016/j.jpba.2021.113892.

Burkova, V.N., Boev, S.G., Vengerovskiĭ, A.I., Iudina, N.V., Arbuzov, A.G., 2011. [Gastroprotective action of the nettle extract in experimental peptic ulcer]. Eksp. Klin. Farmakol. 74 (1), 24–27.

Cao, H., Ji, Y., Li, W., Liu, Y., Fu, R., Xiang, M., 2015. Protective effects of the total coumarin fraction of *Urtica dentata* on experimental diabetic nephropathy in vitro and in vivo. Planta Med. 81 (15), 1353–1360. https://doi.org/10.1055/s-0035-1557866.

Chang, Y.T., Shen, J.J., Wong, W.R., Yen, H.R., 2009. Alternative therapy for autosensitization dermatitis. Chang Gung Med. J. 32 (6), 668–673.

Choodari Gharehpapagh, A., Farahpour, M.R., Jafarirad, S, 2021. The biological synthesis of gold/perlite nanocomposite using *Urtica dioica* extract and its chitosan-capped derivative for healing wounds infected with methicillin-resistant *Staphylococcus aureus*. Int. J. Biol. Macromol. 183, 447–456. https://doi.org/10.1016/j.ijbiomac.2021.04.150.

Christensen, C.B., Soelberg, J., Jäger, A.K., 2015. Antacid activity of Laportea aestuans (L.) Chew. J. Ethnopharmacol. 171, 1–3. https://doi.org/10.1016/j.jep.2015.05.026.

Chrubasik, S., Pollak, S., 2002. [Pain management with herbal antirheumatic drugs]. Wien. Med. Wochenschr. 152 (7–8), 198–203. https://doi.org/10.1046/j.1563-258x.2002.11115.x.

D'Abrosca, B., Ciaramella, V., Graziani, V., Papaccio, F., Della Corte, C.M., Potenza, N., Morgillo, F., 2019. *Urtica dioica* L. inhibits proliferation and enhances cisplatin

cytotoxicity in NSCLC cells via Endoplasmic Reticulum-stress mediated apoptosis. Sci. Rep. 9 (1), 4986. https://doi.org/10.1038/s41598-019-41372-1.
Dar, S.A., Ganai, F.A., Yousuf, A.R., Balkhi, M.U., Bhat, T.M., Sharma, P., 2013. Pharmacological and toxicological evaluation of *Urtica dioica*. Pharm. Biol. 51 (2), 170–180. https://doi.org/10.3109/13880209.2012.715172.
de Oliveira, G.L., Holanda Cavalcanti Andrade, L., Morais de Oliveira, A.F., 2012. Xanthosoma sagittifolium and Laportea aestuans: species used to prevent osteoporosis in Brazilian traditional medicine. Pharm. Biol. 50 (7), 930–932. https://doi.org/10.3109/13880209.2011.637054.
Deveci, A., Coban, A.Y., Tanrıverdi Çaycı, Y., Acicbe, O., Taşdelen Fışgın, N., Akgüneş, A., Durupınar, B., 2013. [In Vitro effect of ankaferd blood stopper®, a plant extract against *Mycobacterium tuberculosis* Isolates]. Mikrobiyol Bul. 47 (1), 71–78. https://doi.org/10.5578/mb.4264.
Devkota, H.P., Paudel, K.R., Khanal, S., Baral, A., Panth, N., Adhikari-Devkota, A., Hansbro, P.M., 2022. Stinging nettle (Urtica dioica L.): nutritional composition, bioactive compounds, and food functional properties. Molecules 27 (16). https://doi.org/10.3390/molecules27165219.
DeVore, M.L., Nyandwi, A., Eckardt, W., Bizuru, E., Mujawamariya, M., Pigg, K.B., 2020. Urticaceae leaves with stinging trichomes were already present in latest early Eocene Okanogan Highlands, British Columbia, Canada. Am. J. Bot. 107 (10), 1449–1456. https://doi.org/10.1002/ajb2.1548.
Dhouibi, R., Affes, H., Ben Salem, M., Charfi, S., Marekchi, R., Hammami, S., Ksouda, K., 2021. Protective effect of *Urtica dioica* in induced neurobehavioral changes, nephrotoxicity and hepatotoxicity after chronic exposure to potassium bromate in rats. Environ. Pollut. 287, 117657 https://doi.org/10.1016/j.envpol.2021.117657.
Dhouibi, R., Affes, H., Ben Salem, M., Hammami, S., Sahnoun, Z., Zeghal, K.M., Ksouda, K., 2020. Screening of pharmacological uses of *Urtica dioica* and others benefits. Prog. Biophys. Mol. Biol. 150, 67–77. https://doi.org/10.1016/j.pbiomolbio.2019.05.008.
Dhouibi, R., Moalla, D., Ksouda, K., Ben Salem, M., Hammami, S., Sahnoun, Z., Affes, H., 2018. Screening of analgesic activity of Tunisian *Urtica dioica* and analysis of its major bioactive compounds by GCMS. Arch. Physiol. Biochem. 124 (4), 335–343. https://doi.org/10.1080/13813455.2017.1402352.
Domola, M.S., Vu, V., Robson-Doucette, C.A., Sweeney, G., Wheeler, M.B., 2010. Insulin mimetics in Urtica dioica: structural and computational analyses of *Urtica dioica* extracts. Phytother. Res. 24 (Suppl 2), S175–S182. https://doi.org/10.1002/ptr.3062.
Doukkali, Z., Taghzouti, K., Bouidida, E.L., Nadjmouddine, M., Cherrah, Y., Alaoui, K., 2015. Evaluation of anxiolytic activity of methanolic extract of *Urtica urens* in a mice model. Behav. Brain Funct. 11, 19. https://doi.org/10.1186/s12993-015-0063-y.
Đurović, S., Vujanović, M., Radojković, M., Filipović, J., Filipović, V., Gašić, U., Zeković, Z., 2020. The functional food production: application of stinging nettle leaves and its extracts in the baking of a bread. Food Chem. 312, 126091 https://doi.org/10.1016/j.foodchem.2019.126091.
El Haouari, M., Bnouham, M., Bendahou, M., Aziz, M., Ziyyat, A., Legssyer, A., Mekhfi, H., 2006. Inhibition of rat platelet aggregation by *Urtica dioica* leaves extracts. Phytother. Res. 20 (7), 568–572. https://doi.org/10.1002/ptr.1906.
El Haouari, M., Rosado, J.A., 2019. Phytochemical, anti-diabetic and cardiovascular properties of *Urtica dioica* L. (Urticaceae): a review. Mini Rev. Med. Chem. 19 (1), 63–71. https://doi.org/10.2174/1389557518666180924121528.
Ensikat, H.J., Wessely, H., Engeser, M., Weigend, M., 2021. Distribution, ecology, chemistry and toxicology of plant stinging hairs. Toxins (Basel) 13 (2). https://doi.org/10.3390/toxins13020141.
Farag, M.A., Weigend, M., Luebert, F., Brokamp, G., Wessjohann, L.A., 2013. Phytochemical, phylogenetic, and anti-inflammatory evaluation of 43 Urtica accessions (stinging nettle) based on UPLC-Q-TOF-MS metabolomic profiles. Phytochemistry 96, 170–183. https://doi.org/10.1016/j.phytochem.2013.09.016.
Fattahi, S., Ardekani, A.M., Zabihi, E., Abedian, Z., Mostafazadeh, A., Pourbagher, R., Akhavan-Niaki, H., 2013. Antioxidant and apoptotic effects of an aqueous extract of *Urtica dioica* on the MCF-7 human breast cancer cell line. Asian Pac. J. Cancer Prev. 14 (9), 5317–5323. https://doi.org/10.7314/apjcp.2013.14.9.5317.
Fattahi, S., Ghadami, E., Asouri, M., Motevalizadeh Ardekanid, A., Akhavan-Niaki, H., 2018. Urtica dioica inhibits cell growth and induces apoptosis by targeting Ornithine decarboxylase and Adenosine deaminase as key regulatory enzymes in adenosine and polyamines homeostasis in human breast cancer cell lines. Cell. Mol. Biol. (Noisy-le-grand) 64 (3), 97–102. https://doi.org/10.14715/cmb/2018.64.3.16.
Fazeli, S.A., Gharravi, A.M., Ghafari, S., Jahanshahi, M., Golalipour, M.J., 2008. The granule cell density of the dentate gyrus following administration of *Urtica dioica* extract to young diabetic rats. Folia Morphol. (Warsz) 67 (3), 196–204.
Feng, X., Ju, P., Chen, Y., Li, X., Wang, M., 2022. Analgesic alkaloids from Urticae Fissae Herba. Chin. Herb. Med. 14 (1), 125–129. https://doi.org/10.1016/j.chmed.2021.09.008.
Flores-Ocelotl, M.R., Rosas-Murrieta, N.H., Moreno, D.A., Vallejo-Ruiz, V., Reyes-Leyva, J., Domínguez, F., Santos-López, G., 2018. *Taraxacum officinale* and *Urtica dioica* extracts inhibit dengue virus serotype 2 replication in vitro. BMC Complement. Altern. Med. 18 (1), 95. https://doi.org/10.1186/s12906-018-2163-3.
Fodor, J.I., Keve, T., 2006. [New phytotherapical opportunity in the prevention and treatment of 2-type of diabetes mellitus]. Acta Pharm. Hung. 76 (4), 200–207.
Fu, H.Y., Chen, S.J., Chen, R.F., Ding, W.H., Kuo-Huang, L.L., Huang, R.N., 2006. Identification of oxalic acid and tartaric acid as major persistent pain-inducing toxins in the stinging hairs of the nettle, *Urtica thunbergiana*. Ann. Bot. 98 (1), 57–65. https://doi.org/10.1093/aob/mcl089.
Fuh, Y.M., Pham, D.C., Weng, C.F., 2019. Effects of sting plant extracts as penetration enhancers on transdermal delivery of hypoglycemic compounds. Medicina (Kaunas). 55 (5) https://doi.org/10.3390/medicina55050121.
Ghafari, S., Balajadeh, B.K., Golalipour, M.J., 2011. Effect of *Urtica dioica* L. (Urticaceae) on testicular tissue in STZ-induced diabetic rats. Pak. J. Biol. Sci. 14 (16), 798–804. https://doi.org/10.3923/pjbs.2011.798.804.
Ghasemi, S., Moradzadeh, M., Hosseini, M., Beheshti, F., Sadeghnia, H.R., 2019. Beneficial effects of Urtica dioica on scopolamine-induced memory impairment in rats: protection against acetylcholinesterase activity and neuronal oxidative damage. Drug Chem. Toxicol. 42 (2), 167–175. https://doi.org/10.1080/01480545.2018.1463238.
Gilding, E.K., Jami, S., Deuis, J.R., Israel, M.R., Harvey, P.J., Poth, A.G., Durek, T., 2020. Neurotoxic peptides from the venom of the giant Australian stinging tree. Sci. Adv. 6 (38) https://doi.org/10.1126/sciadv.abb8828.
Gohari, A., Noorafshan, A., Akmali, M., Zamani-Garmsiri, F., Seghatoleslam, A., 2018. *Urtica dioica* distillate regenerates pancreatic beta cells in streptozotocin-induced diabetic rats. Iran J. Med. Sci. 43 (2), 174–183.
Golalipour, M.J., Ghafari, S., Afshar, M., 2010. Protective role of *Urtica dioica* L. (Urticaceae) extract on hepatocytes morphometric changes in STZ diabetic Wistar rats. Turk. J. Gastroenterol. 21 (3), 262–269. https://doi.org/10.4318/tjg.2010.0098.
Grauso, L., Emrick, S., Bonanomi, G., Lanzotti, V., 2019. Metabolomics of the alimurgic plants Taraxacum officinale, Papaver rhoeas and Urtica dioica by combined NMR and GC–MS analysis. Phytochem. Anal. 30 (5), 535–546. https://doi.org/10.1002/pca.2845.
Grosse-Veldmann, B., Nürk, N.M., Smissen, R., Breitwieser, I., Quandt, D., Weigend, M., 2016. Pulling the sting out of nettle systematics - A comprehensive phylogeny of the genus Urtica L. (Urticaceae). Mol. Phylogenet. Evol. 102, 9–19. https://doi.org/10.1016/j.ympev.2016.05.019.
Grosvenor, P.W., Supriono, A., Gray, D.O., 1995. Medicinal plants from Riau Province, Sumatra, Indonesia. Part 2: antibacterial and antifungal activity. J. Ethnopharmacol. 45 (2), 97–111. https://doi.org/10.1016/0378-8741(94)01210-Q.
Gülçin, I., Küfrevioglu, O.I., Oktay, M., Büyükokuroglu, M.E., 2004. Antioxidant, antimicrobial, antiulcer and analgesic activities of nettle (Urtica dioica L.). J. Ethnopharmacol. 90 (2–3), 205–215. https://doi.org/10.1016/j.jep.2003.09.028.
Han, S., Wei, R., Han, D., Zhu, J., Luo, W., Ao, W., Zhong, G., 2020. Hypouricemic effects of extracts from urtica hyperborea jacq. ex wedd. in hyperuricemia mice through XOD, URAT1, and OAT1. In: Biomed. Res. Int., 2020, 2968135 https://doi.org/10.1155/2020/2968135.
Hashem, A.H., Salem, S.S., 2022. Green and ecofriendly biosynthesis of selenium nanoparticles using *Urtica dioica* (stinging nettle) leaf extract: antimicrobial and anticancer activity. Biotechnol. J. 17 (2), e2100432 https://doi.org/10.1002/biot.202100432.
Hodroj, M.H., Al Bast, N.A.H., Taleb, R.I., Borjac, J., Rizk, S, 2020. Nettle tea inhibits growth of acute myeloid leukemia cells in vitro by promoting apoptosis. Nutrients 12 (9). https://doi.org/10.3390/nu12092629.
Hole, E., Simaremare, E.S., Yabansabra, Y.Y., Gunawan, E., & Ruban, A.J.J.F.G. (2016). Uji Mutu Fisik Formulasi Salep Daun Gatal (*Laportea decumana* (Roxb.) Wedd.). 3(2), 55–60.
Huang, X., Deng, T., Moore, M.J., Wang, H., Li, Z., Lin, N., Sun, H., 2019. Tropical Asian Origin, boreotropical migration and long-distance dispersal in Nettles (Urticeae, Urticaceae). Mol. Phylogenet. Evol. 137, 190–199. https://doi.org/10.1016/j.ympev.2019.05.007.
Ibrahim, M., Rehman, K., Razzaq, A., Hussain, I., Farooq, T., Hussain, A., Akash, M.S.H., 2018. Investigations of phytochemical constituents and their pharmacological properties isolated from the genus Urtica: critical review and analysis. Crit. Rev. Eukaryot. Gene Expr. 28 (1), 25–66. https://doi.org/10.1615/CritRevEukaryotGeneExpr.2018020389.
Ilhan, M., Ali, Z., Khan, I.A., Taştan, H., Küpeli Akkol, E., 2019. Bioactivity-guided isolation of flavonoids from Urtica dioica L. and their effect on endometriosis rat model. J. Ethnopharmacol. 243, 112100 https://doi.org/10.1016/j.jep.2019.112100.
Jahanshahi, M., Golalipour, M.J., Afshar, M., 2009. The effect of *Urtica dioica* extract on the number of astrocytes in the dentate gyrus of diabetic rats. Folia Morphol. (Warsz) 68 (2), 93–97.
Jang, C., Yadav, D.K., Subedi, L., Venkatesan, R., Venkanna, A., Afzal, S., Kim, M.H., 2018. Identification of novel acetylcholinesterase inhibitors designed by pharmacophore-based virtual screening, molecular docking and bioassay. Sci. Rep. 8 (1), 14921. https://doi.org/10.1038/s41598-018-33354-6.
Ji, T.F., Liu, C.H., Wang, A.G., Yang, J.B., Su, Y.L., Yuan, L., Feng, X.Z., 2007. [Studies on the chemical constituents of *Urtica dioica* L. grown in Tibet Autonomous Region]. Zhong Yao Cai 30 (6), 662–664.
Jimoh, F., Adedapo, A., Aliero, A., Afolayan, A., 2010. Polyphenolic and biological activities of leaves extracts of *Argemone subfusiformis* (Papaveraceae) and *Urtica urens* (Urticaceae). Rev. Biol. Trop. 58 (4), 1517–1531. https://doi.org/10.15517/rbt.v58i4.5428.
Johnson, T.A., Sohn, J., Inman, W.D., Bjeldanes, L.F., Rayburn, K., 2013. Lipophilic stinging nettle extracts possess potent anti-inflammatory activity, are not cytotoxic and may be superior to traditional tinctures for treating inflammatory disorders. Phytomedicine 20 (2), 143–147. https://doi.org/10.1016/j.phymed.2012.09.016.
Joshi, B.C., Prakash, A., Kalia, A.N., 2015. Hepatoprotective potential of antioxidant potent fraction from Urtica dioica Linn. (whole plant) in CCl(4) challenged rats. Toxicol. Rep. 2, 1101–1110. https://doi.org/10.1016/j.toxrep.2015.07.020.
Kadan, S., Saad, B., Sasson, Y., Zaid, H., 2013. In Vitro Evaluations of Cytotoxicity of Eight Antidiabetic Medicinal Plants and Their Effect on GLUT4 Translocation. Evid. Based Complement. Alternat. Med. 2013, 549345 https://doi.org/10.1155/2013/549345.

Kang, D.L., Pan, Q.H., Yi, Z.L., Jiang, J.X., 2008. [Study on phylogenetic relationships of urticaceae based on rbcL sequence]. Fen Zi Xi Bao Sheng Wu Xue Bao 41 (4), 255–264.

Kardan, M., Rafiei, A., Golpour, M., Ebrahimzadeh, M.A., Akhavan-Niaki, H., Fattahi, S., 2020. *Urtica dioica* extract inhibits cell proliferation and induces apoptosis in HepG2 and HTC116 as gastrointestinal cancer cell lines. Anticancer Agents Med. Chem. 20 (8), 963–969. https://doi.org/10.2174/1871520620666200311095836.

Kersten, R.D., Mydy, L.S., Fallon, T.R., de Waal, F., Shafiq, K., Wotring, J.W., Weng, J.K., 2022. Gene-guided discovery and ribosomal biosynthesis of moroidin peptides. J. Am. Chem. Soc. 144 (17), 7686–7692. https://doi.org/10.1021/jacs.2c00014.

Khalili, N., Fereydoonzadeh, R., Mohtashami, R., Mehrzadi, S., Heydari, M., Huseini, H. F., 2017. Silymarin, olibanum, and nettle, a mixed herbal formulation in the treatment of type II diabetes: a randomized, double-blind, placebo-controlled, clinical trial. J. Evid. Based Complem. Altern. Med. 22 (4), 603–608. https://doi.org/10.1177/2156587217696929.

Khan, A., Haque, E., Rahman, M.M., Mosaddik, A., Rahman, M., Sultana, N., 2007. A new triterpenoid from roots of Laportea crenulata and its antifungal activity. Nat. Prod. Res. 21 (11), 959–966. https://doi.org/10.1080/14786410701371470.

Khan, A., Islam, M.S., Rahman, M., Zaman, T., Haque, M.E., 2014. Pesticidal and pest repellency activities of a plant derived triterpenoid 2α,3β,21β,23,28-penta hydroxyl 12-oleanene against Tribolium castaneum. Biol. Res. 47 (1), 68. https://doi.org/10.1186/0717-6287-47-68.

Khare, V., Kushwaha, P., Verma, S., Gupta, A., Srivastava, S., & Rawat, A.K.S. (2012). Pharmacognostic evaluation and antioxidant activity of Urtica dioica L.

Kianbakht, S., Khalighi-Sigaroodi, F., Dabaghian, F.H., 2013. Improved glycemic control in patients with advanced type 2 diabetes mellitus taking *Urtica dioica* leaf extract: a randomized double-blind placebo-controlled clinical trial. Clin. Lab. 59 (9–10), 1071–1076. https://doi.org/10.7754/clin.lab.2012.121019.

Kılıç, S., Okullu, S., Kurt, Ö., Sevinç, H., Dündar, C., Altınordu, F., Türkoğlu, M., 2019. Efficacy of two plant extracts against acne vulgaris: initial results of microbiological tests and cell culture studies. J. Cosmet. Dermatol. 18 (4), 1061–1065. https://doi.org/10.1111/jocd.12814.

Kobayashi, J., Suzuki, H., Shimbo, K., Takeya, K., Morita, H., 2001. Celogentins A-C, new antimitotic bicyclic peptides from the seeds of *Celosia argentea*. J. Org. Chem. 66 (20), 6626–6633. https://doi.org/10.1021/jo0103423.

Körpe, D.A., İşeri, Ö.D., Sahin, F.I., Cabi, E., Haberal, M, 2013. High-antibacterial activity of Urtica spp. seed extracts on food and plant pathogenic bacteria. Int. J. Food Sci. Nutr. 64 (3), 355–362. https://doi.org/10.3109/09637486.2012.734290.

Kregiel, D., Pawlikowska, E., Antolak, H., 2018. Urtica spp.: ordinary plants with extraordinary properties. Molecules 23 (7). https://doi.org/10.3390/molecules23071664.

La Regina, G., Coluccia, A., Naccarato, V., Silvestri, R, 2019. Towards modern anticancer agents that interact with tubulin. Eur. J. Pharm. Sci. 131, 58–68. https://doi.org/10.1016/j.ejps.2019.01.028.

Lans, C.A., 2006. Ethnomedicines used in Trinidad and Tobago for urinary problems and diabetes mellitus. J. Ethnobiol. Ethnomed. 2, 45. https://doi.org/10.1186/1746-4269-2-45.

Legssyer, A., Ziyyat, A., Mekhfi, H., Bnouham, M., Tahri, A., Serhrouchni, M., Fischmeister, R., 2002. Cardiovascular effects of Urtica dioica L. in isolated rat heart and aorta. Phytother. Res. 16 (6), 503–507. https://doi.org/10.1002/ptr.1087.

Li, Y., Chen, S.Y., Gong, Z.P., Kang, N.F., Wu, D., Tang, J., Wang, Y.L., 2020. [Differences in intestinal absorption characteristics of Laportea bulbifera extract in normal and rheumatoid arthritis model rats by isolated everted intestine model]. Zhongguo Zhong Yao Za Zhi 45 (2), 405–411. https://doi.org/10.19540/j.cnki.cjcmm.20190821.201.

Ligor, M., Kiełbasa, A., Ratiu, I.A., Buszewski, B., 2021. Separation and quantification of selected sapogenins extracted from nettle, white dead-nettle, common soapwort and washnut. Molecules 26 (24). https://doi.org/10.3390/molecules26247705.

Lin, Y., Shi, R., Wang, X., Shen, H.M., 2008. Luteolin, a flavonoid with potential for cancer prevention and therapy. Curr. Cancer Drug Targets 8 (7), 634–646. https://doi.org/10.2174/156800908786241050.

Liswandari, A.V., 2020. Kajian Bioprospeksi Zat Aktif Daun Gatal (*Laportea decumana*), Kemaduh (*Dendrocnide stimulans* (Lf) Chew) Dan Bedor (*Girardinia palmata* Gaud) (Bioprospective Study On Active Compounds of Itchy Leave (*Laportea decumana*), Kemaduh (*Dendrocnide Stimulans* Lf. Chew) and Bedor (*Girardinia Palmata* Gaud). Universitas Islam Malang. http://repository.unisma.ac.id/handle/123456789/505.

Loshali, A., Joshi, B.C., Sundriyal, A., Uniyal, S., 2021. Antiepileptic effects of antioxidant potent extract from Urtica dioica Linn. root on pentylenetetrazole and maximal electroshock induced seizure models. Heliyon 7 (2), e06195. https://doi.org/10.1016/j.heliyon.2021.e06195.

Lu, X., Zhao, Y., Li, B., Feng, W., Qi, J., Feng, B., 2022. Phytochemical, chemotaxonomic and bioinformatics study on Laportea bulbifera (Urticaceae). Chem. Biodivers. 19 (7), e202200070 https://doi.org/10.1002/cbdv.202200070.

Mahlangeni, N.T., Moodley, R., Jonnalagadda, S.B., 2020. Nutritional value, antioxidant and antidiabetic properties of nettles (Laportea alatipes and Obetia tenax). Sci. Rep. 10 (1), 9762. https://doi.org/10.1038/s41598-020-67055-w.

Maimunah, S., 2021. Uji aktivitas antibakteri ekstrak etanol daun jelatang (*Urtica dioica* L.) terhadap *Escherichia coli* (Antibacterial activity of ethanolic extract from jelatang leave (*Urtica dioica* L.) against *Escherichia coli*). Jurnal Kimia Saintek dan Pendidikan 5 (1), 23–30.

Mambe, F.T., Voukeng, I.K., Beng, V.P., Kuete, V., 2016. Antibacterial activities of methanol extracts from Alchornea cordifolia and four other Cameroonian plants against MDR phenotypes. J. Taibah Univ. Med. Sci. 11 (2), 121–127. https://doi.org/10.1016/j.jtumed.2015.12.001.

Mansoori, B., Mohammadi, A., Hashemzadeh, S., Shirjang, S., Baradaran, A., Asadi, M., Baradaran, B., 2017. *Urtica dioica* extract suppresses miR-21 and metastasis-related genes in breast cancer. Biomed. Pharmacother. 93, 95–102. https://doi.org/10.1016/j.biopha.2017.06.021.

Marrassini, C., Acevedo, C., Miño, J., Ferraro, G., Gorzalczany, S., 2010. Evaluation of antinociceptive, antinflammatory activities and phytochemical analysis of aerial parts of *Urtica urens* L. Phytother. Res. 24 (12), 1807–1812. https://doi.org/10.1002/ptr.3188.

Marrassini, C., Davicino, R., Acevedo, C., Anesini, C., Gorzalczany, S., Ferraro, G., 2011. Vicenin-2, a potential anti-inflammatory constituent of Urtica circularis. J. Nat. Prod. 74 (6), 1503–1507. https://doi.org/10.1021/np100937e.

Mehta, V., Parashar, A., Udayabanu, M., 2017. Quercetin prevents chronic unpredictable stress induced behavioral dysfunction in mice by alleviating hippocampal oxidative and inflammatory stress. Physiol. Behav. 171, 69–78. https://doi.org/10.1016/j.physbeh.2017.01.006.

Mihaylova, D., Vrancheva, R., Desseva, I., Ivanov, I., Dincheva, I., Popova, M., Popova, A., 2018. Analysis of the GC-MS of volatile compounds and the phytochemical profile and antioxidant activities of some Bulgarian medicinal plants. Z. Naturforsch. C. J. Biosci. 74 (1–2), 45–54. https://doi.org/10.1515/znc-2018-0122.

Modarresi-Chahardehi, A., Ibrahim, D., Fariza-Sulaiman, S., Mousavi, L., 2012. Screening antimicrobial activity of various extracts of *Urtica dioica*. Rev. Biol. Trop. 60 (4), 1567–1576. https://doi.org/10.15517/rbt.v60i4.2074.

Mohammadi, A., Mansoori, B., Aghapour, M., Baradaran, P.C., Shajari, N., Davudian, S., Baradaran, B., 2016a. The herbal medicine *Urtica dioica* inhibits proliferation of colorectal cancer cell line by inducing apoptosis and arrest at the G2/M phase. J. Gastrointest Cancer 47 (2), 187–195. https://doi.org/10.1007/s12029-016-9819-3.

Mohammadi, A., Mansoori, B., Goldar, S., Shanehbandi, D., Khaze, V., Mohammadnejad, L., Baradaran, B., 2016b. Effects of *Urtica dioica* dichloromethane extract on cell apoptosis and related gene expression in human breast cancer cell line (MDA-MB-468). Cell. Mol. Biol. (Noisy-le-grand) 62 (2), 62–67.

Mom, S.A., Langi, M.A., Kainde, R.P., Nurmawan, W., 2015. Studi etnobotani tumbuhan daun gatal di kecamatan kwamkilama kabupaten mimika (Ethnobotanical study of itchy leave from district Kwamkilama, Mimika). In: Paper presented at the COCOS E Journal Univerrsity of Sam Ratulangi. Manado.

Momo, C.E., Oben, J.E., Tazoo, D., Dongo, E., 2006. Antidiabetic and hypolipidaemic effects of a methanol/methylene-chloride extract of Laportea ovalifolia (Urticaceae), measured in rats with alloxan-induced diabetes. Ann. Trop. Med. Parasitol. 100 (1), 69–74. https://doi.org/10.1179/136485906x78517.

Morita, H., Shimbo, K., Shigemori, H., Kobayashi, J., 2000. Antimitotic activity of moroidin, a bicyclic peptide from the seeds of Celosia argentea. Bioorg. Med. Chem. Lett. 10 (5), 469–471. https://doi.org/10.1016/s0960-894x(00)00029-9.

Moslemifard, M., Gorji, N., Ghadimi, R., Kamalinejad, M., Shirafkan, H., Mozaffarpur, S. A., 2020. Hospital diet for COVID-19, an acute respiratory infectious disease: an evidence-based protocol of a clinical trial. Caspian J. Intern. Med. 11 (Suppl 1), 466–478. https://doi.org/10.22088/cjim.11.0.466.

Motamedi, H., Seyyednejad, S.M., Bakhtiari, A., Vafaei, M., 2014. Introducing *Urtica dioica*, a native plant of Khuzestan, as an antibacterial medicinal plant. Jundishapur J. Nat. Pharm. Prod. 9 (4), e15904. https://doi.org/10.17795/jjnpp-15904.

Mueen, K., Parasuraman, Subramani, 2016. *Urtica dioica* L., (Urticaceae): a stinging nettle. System. Rev. Pharm. 5, 6–8. https://doi.org/10.5530/srp.2014.1.3.

Myint, A.A., Shwe, H.H., Khaing, A.A., Moe, T.T., & Pe, N.N. (2019). Studies on phytochemicals screening, antimicrobial activities and antioxidant acivities from the roots of *Girardinia heterophylla* Dene.

Negi, A., Gangwar, R., Vishwakarma, R.K., Negi, D.S., 2022. Biogenic zinc oxide nanoparticles as an antibacterial, antifungal, and photocatalytic tool mediated via leaves of *Girardinia diversifolia*. J. Nanotechnol. Environ. Eng. 7 (1), 223–233.

Njogu, P., Thoithi, G., Mwangi, J., Kamau, F., Kibwage, I.O., Kariuki, S., Sciences, C.A.J. o.P., 2011. Phytochemical and antimicrobial investigation of *Girardinia diversifolia* (Link) Friis (Urticaceae). East Central African J. Pharmaceut. Sci. 14 (3).

Njogu, P.M., 2007. Phytochemical Investigation and Antimicrobial Activity of Girardinia diversifolia (link) Friis (urticaceae). University of NAIROBI.

Obertreis, B., Ruttkowski, T., Teucher, T., Behnke, B., Schmitz, H., 1996. Ex-vivo in-vitro inhibition of lipopolysaccharide stimulated tumor necrosis factor-alpha and interleukin-1 beta secretion in human whole blood by extractum urticae dioicae foliorum. Arzneimittelforschung 46 (4), 389–394.

Oloyede, G.K., 2016. Toxicity, antimicrobial and antioxidant activities of methyl salicylate dominated essential oils of *Laportea aestuans* (Gaud). Arab. J. Chem. 9, S840–S845. https://doi.org/10.1016/j.arabjc.2011.09.019.

Oloyede, G.K., Oyelola, M.S., 2013. Chrysen-2-ol derivative from West Indian Wood Nettle Laportea aestuans (L.) Chew inhibits oxidation and microbial growth in vitro. Excli J. 12, 894–906.

O. Omolola, E., Ogunlade, O.O., Salako, A.O, 2018. Phytochemical screening and antioxidant parameters data in prostatic rats fed with *Laportea aestuans* leaves Data Brief 20, 577–581. https://doi.org/10.1016/j.dib.2018.08.020.

Onal, S., Timur, S., Okutucu, B., Zihnioğlu, F., 2005. Inhibition of alpha-glucosidase by aqueous extracts of some potent antidiabetic medicinal herbs. Prep. Biochem. Biotechnol. 35 (1), 29–36. https://doi.org/10.1081/pb-200041438.

Otles, S., Yalcin, B., 2012. Phenolic compounds analysis of root, stalk, and leaves of nettle. ScientificWorldJournal 2012, 564367. https://doi.org/10.1100/2012/564367.

Otoom, S.A., Al-Safi, S.A., Kerem, Z.K., Alkofahi, A., 2006. The use of medicinal herbs by diabetic Jordanian patients. J. Herb. Pharmacother. 6 (2), 31–41.

Pan, B., Fang, S., Zhang, J., Pan, Y., Liu, H., Wang, Y., Liu, L., 2020. Chinese herbal compounds against SARS-CoV-2: puerarin and quercetin impair the binding of viral S-protein to ACE2 receptor. Comput. Struct. Biotechnol. J. 18, 3518–3527. https://doi.org/10.1016/j.csbj.2020.11.010.

Pandey, S., Sah, S.P., Sah, M.L., Mishra, D., 2010. An antioxidant potential of hydromethanolic extract of *Urtica parviflora* Roxb. J. Basic Clin. Pharm. 1 (3), 191–195.

Parashar, A., Mehta, V., Udayabanu, M., 2017. Rutin alleviates chronic unpredictable stress-induced behavioral alterations and hippocampal damage in mice. Neurosci. Lett. 656, 65–71. https://doi.org/10.1016/j.neulet.2017.04.058.

Patel, S.S., Parashar, A., Udayabanu, M., 2015. *Urtica dioica* leaves modulates muscarinic cholinergic system in the hippocampus of streptozotocin-induced diabetic mice. Metab. Brain Dis. 30 (3), 803–811. https://doi.org/10.1007/s11011-014-9646-9.

Patel, S.S., Ray, R.S., Sharma, A., Mehta, V., Katyal, A., Udayabanu, M., 2018. Antidepressant and anxiolytic like effects of *Urtica dioica* leaves in streptozotocin induced diabetic mice. Metab. Brain Dis. 33 (4), 1281–1292. https://doi.org/10.1007/s11011-018-0243-1.

Patel, S.S., Udayabanu, M., 2013. Effect of *Urtica dioica* on memory dysfunction and hypoalgesia in an experimental model of diabetic neuropathy. Neurosci. Lett. 552, 114–119. https://doi.org/10.1016/j.neulet.2013.07.029.

Patel, S.S., Udayabanu, M., 2014. *Urtica dioica* extract attenuates depressive like behavior and associative memory dysfunction in dexamethasone induced diabetic mice. Metab. Brain Dis. 29 (1), 121–130. https://doi.org/10.1007/s11011-014-9480-0.

Pérez Gutiérrez, R.M., Muñiz-Ramirez, A., Garcia-Campoy, A.H., Mota Flores, J.M., 2021. Evaluation of the antidiabetic potential of extracts of *Urtica dioica, Apium graveolens,* and *Zingiber officinale* in mice, zebrafish, and pancreatic β-Cell. Plants (Basel) 10 (7). https://doi.org/10.3390/plants10071438.

Pertiwi, K.K., Fernanda, S.D., 2019. Aktivitas Antibakteri Herba Daun Gatal (*Laportea interupta* L. Chew) terhadap *Staphylococcus aureus* dan *Escherichia coli* (Antibacterial activity of itchy leave (*Laportea interupta* L.Chew) on *Staphylococcus aureus* and *Escherichia coli*). J. Educ. Sci. Technol. 2 (1) https://doi.org/10.25139/htc.v2i1.1558.

Pinelli, P., Leri, F., Vignolini, P., Bacci, L., Baronti, S., Romani, A., 2008. Extraction and HPLC analysis of phenolic compounds in leaves, stalks, and textile fibers of *Urtica dioica* L. J. Agric. Food Chem. 56 (19), 9127–9132. https://doi.org/10.1021/jf801552d.

Prabawati, R., Putro, W.A.S., La Goa, Y., Hardia, L., Utami, D.P., 2021. The effectiveness test of wound healing daun gatal (*Laportea decumana*) against mice (*Mus musculus* L). In: Proceedings of the International Colloqium on Environmental Education, Istanbul, September 25-26, 2021.

Rahimzadeh, M., Jahanshahi, S., Moein, S., Moein, M.R., 2014. Evaluation of alpha-amylase inhibition by *Urtica dioica* and *Juglans regia* extracts. Iran. J. Basic Med. Sci. 17 (6), 465–469.

Rahman, M.M., Khan, A., Haque, M.E., Rahman, M.M., 2008. Antimicrobial and cytotoxic activities of Laportea crenulata. Fitoterapia 79 (7–8), 584–586. https://doi.org/10.1016/j.fitote.2008.04.007.

Rahmati, M., Keshvari, M., Mirnasouri, R., Chehelcheraghi, F., 2021. Exercise and *Urtica dioica* extract ameliorate hippocampal insulin signaling, oxidative stress, neuroinflammation, and cognitive function in STZ-induced diabetic rats. Biomed. Pharmacother. 139, 111577 https://doi.org/10.1016/j.biopha.2021.111577.

Rakshit, G., Dagur, P., Satpathy, S., Patra, A., Jain, A., Ghosh, M., 2021. Flavonoids as potential therapeutics against novel coronavirus disease-2019 (nCOVID-19). J. Biomol. Struct. Dyn. 1–13. https://doi.org/10.1080/07391102.2021.1892529.

Rau, O., Wurglics, M., Dingermann, T., Abdel-Tawab, M., Schubert-Zsilavecz, M., 2006. Screening of herbal extracts for activation of the human peroxisome proliferator-activated receptor. Pharmazie 61 (11), 952–956.

Rayburn, K., Fleischbein, E., Song, J., Allen, B., Kundert, M., Leiter, C., Bush, T., 2009. Stinging nettle cream for osteoarthritis. Altern. Ther. Health. Med. 15 (4), 60–61.

Razika, L., Thanina, A.C., Nadjiba, C.M., Narimen, B., Mahdi, D.M., Karim, A., 2017. Antioxidant and wound healing potential of saponins extracted from the leaves of Algerian Urtica dioica L. Pak. J. Pharm. Sci. 30 (3(Suppl)), 1023–1029.

Rivero-Segura, N.A., Gomez-Verjan, J.C., 2021. In silico screening of natural products isolated from Mexican herbal medicines against COVID-19. Biomolecules 11 (2). https://doi.org/10.3390/biom11020216.

Roschek Jr., B., Fink, R.C., McMichael, M., Alberte, R.S, 2009. Nettle extract (Urtica dioica) affects key receptors and enzymes associated with allergic rhinitis. Phytother. Res. 23 (7), 920–926. https://doi.org/10.1002/ptr.2763.

Salehzadeh, A., Asadpour, L., Naeemi, A.S., Houshmand, E., 2014. Antimicrobial activity of methanolic extracts of *Sambucus ebulus* and *Urtica dioica* against clinical isolates of methicillin resistant *Staphylococcus aureus*. Afr. J. Tradit. Complement. Altern. Med. 11 (5), 38–40. https://doi.org/10.4314/ajtcam.v11i5.6.

Salim, B., Said, G., Kambouche, N., Kress, S., 2020. Identification of phenolic compounds from nettle as new candidate inhibitors of main enzymes responsible on type-II diabetes. Curr. Drug Discov. Technol. 17 (2), 197–202. https://doi.org/10.2174/1570163815666180829094831.

Salmi, D., Riou, C., Issawi, M., Titouche, Y., Ambrosini, V., Smail-Saadoun, N., Houali, K., 2021. Antibacterial and antioxidant activities of endophytic fungi and nettle (*Urtica dioica* L.) leaves as their host. Cell. Mol. Biol. (Noisy-le-grand) 67 (3), 204–211. https://doi.org/10.14715/cmb/2021.67.3.33.

Samakar, B., Mehri, S., Hosseinzadeh, H., 2022. A review of the effects of Urtica dioica (nettle) in metabolic syndrome. Iran. J. Basic Med. Sci. 25 (5), 543–553. https://doi.org/10.22038/ijbms.2022.58892.13079.

Seyydi, S.M., Tofighi, A., Rahmati, M., Tolouei Azar, J., 2022. Exercise and *Urtica dioica* extract ameliorate mitochondrial function and the expression of cardiac muscle Nuclear Respiratory Factor 2 and Peroxisome proliferator-activated receptor Gamma Coactivator 1-alpha in STZ-induced diabetic rats. Gene 822, 146351. https://doi.org/10.1016/j.gene.2022.146351.

Sharan Shrestha, S., Sut, S., Ferrarese, I., Barbon Di Marco, S., Zengin, G., De Franco, M., Rajbhandary, S., 2020. Himalayan nettle girardinia diversifolia as a candidate ingredient for pharmaceutical and nutraceutical applications-phytochemical analysis and in vitro bioassays. Molecules 25 (7). https://doi.org/10.3390/molecules25071563.

Simaremare, E., Sawaki, Y., Pratiwi, R.D., Gunawan, E., 2020. Uji antifungi ekstrak etanol daun gatal [*Laportea decumana* (Roxb.) Wedd] terhadap *Candida albicans* (Antifunfal test of ethanolic extract of itchy leave (*Laportea decumana* (Roxb.)Wedd) on *Candida albicans*). Jurnal Farmasi Galenika 7 (2), 108–119.

Simaremare, E.S., Holle, E., Budi, M., 2015. Perbandingan Efektifitas Antinyeri Salep Daun Gatal Dari Simplisia *Laportea decumana* dan *Laportea sp* (A comparative study on analgesic ointment of itchy leave *Laportea decumana* and *Laportea* Sp.). Jurnal Farmasi Indonesia 12 (1), 1–10.

Simaremare, E.S., Pratiwi, R.D., Rusnaeni, R., Gunawan, E., Dirgantara, S., 2019a. Pemanfaatan tanaman daun gatal (*Laportea decumana*) Sebagai obat anti capek (The use of itchy leave (*Laportea decumana*) as anti tired drug). Jurnal Pengabdian dan Pemberdayaan Masyarakat 3 (1), 97–103.

Simaremare, E.S., Uopmbin, E., Gunawan, E., 2019b. Studi etnobotani daun gatal oleh masyarakat Kiwirok Papua (Ethnobotanical study of itchy leave in Kiwirok society, Papua). Jurnal Farmasi Indonesia 16 (1), 45–58.

Singh, R., Hussain, S., Verma, R., Sharma, P., 2013. Anti-mycobacterial screening of five Indian medicinal plants and partial purification of active extracts of *Cassia sophera* and *Urtica dioica*. Asian Pac. J. Trop. Med. 6 (5), 366–371. https://doi.org/10.1016/s1995-7645(13)60040-1.

Sisay, W., Andargie, Y., Molla, M., Norahun, A., 2021. Hydromethanolic Crude Extract of the Leaf of Urtica simensis Hochst. ex. A. Rich. (Urticaceae) acquires appreciable antiulcer effect: validation for in vivo antiulcer activity. Evid. Based Complement. Alternat. Med. 2021, 6591070 https://doi.org/10.1155/2021/6591070.

Sjakoer, N.A.A., Liswandari, A.V., 2020. Bioprospeksi Daun Gatal (Laportea decumana) Di Desa Ngadas Ponconcokusumo (Bioprospection of itchy leave (Laportea decumana) in village Ngadas Ponconcokusumo). In: Paper presented at the National Conference of Life Science dan Teknologi. Indonesia, 2020. Universitas Negeri Malang.

Solowey, E., Lichtenstein, M., Sallon, S., Paavilainen, H., Solowey, E., Lorberboum-Galski, H., 2014. Evaluating medicinal plants for anticancer activity. ScientificWorldJournal 2014, 721402. https://doi.org/10.1155/2014/721402.

Stanciuc, A.M., Gaspar, A., Moldovan, L., Saviuc, C., Popa, M., Măruțescu, L., 2011. In vitro antimicrobial activity of Romanian medicinal plants hydroalcoholic extracts on planktonic and adhered cells. Roum. Arch. Microbiol. Immunol. 70 (1), 11–14.

Sterniša, M., Bucar, F., Kunert, O., Smole Možina, S., 2020. Targeting fish spoilers Pseudomonas and Shewanella with oregano and nettle extracts. Int. J. Food Microbiol. 328, 108664 https://doi.org/10.1016/j.ijfoodmicro.2020.108664.

Su, R.N., Wei, R.R., Luo, W.Z., Zhu, J.X., Wang, L., Zhong, G.Y., 2019. [Study on effect of extract from Tibetan medicine Urtica hyperborean on anti-prostatic hyperplasia]. Zhongguo Zhong Yao Za Zhi 44 (9), 1953–1959. https://doi.org/10.19540/j.cnki.cjcmm.20190304.004.

Subba, B., Srivastav, C., Kandel, R.C., 2016. Scientific validation of medicinal plants used by Yakkha community of Chanuwa VDC, Dhankuta, Nepal. Springerplus 5, 155. https://doi.org/10.1186/s40064-016-1821-5.

Sujarwo, W., Keim, A.P., Savo, V., Guarrera, P.M., Caneva, G., 2015. Ethnobotanical study of Loloh: traditional herbal drinks from Bali (Indonesia). J. Ethnopharmacol. 169, 34–48. https://doi.org/10.1016/j.jep.2015.03.079.

Tabrizi, R., Sekhavati, E., Nowrouzi-Sohrabi, P., Rezaei, S., Tabari, P., Ghoran, S.H., Safiri, S., 2022. Effects of *Urtica dioica* on metabolic profiles in type 2 diabetes: a systematic review and meta-analysis of clinical trials. Mini Rev. Med. Chem. 22 (3), 550–563. https://doi.org/10.2174/1389557521666210929143112.

Taheri, Y., Quispe, C., Herrera-Bravo, J., Sharifi-Rad, J., Ezzat, S.M., Merghany, R.M., Cho, W.C., 2022. *Urtica dioica*-derived phytochemicals for pharmacological and therapeutic applications. Evid. Based Complement. Alternat. Med. 2022, 4024331 https://doi.org/10.1155/2022/4024331.

Tchinda, C.F., Voukeng, I.K., Beng, V.P., Kuete, V., 2017. Antibacterial activities of the methanol extracts of Albizia adianthifolia, Alchornea laxiflora, Laportea ovalifolia and three other Cameroonian plants against multi-drug resistant Gram-negative bacteria. Saudi J. Biol. Sci. 24 (4), 950–955. https://doi.org/10.1016/j.sjbs.2016.01.033.

Testai, L., Chericoni, S., Calderone, V., Nencioni, G., Nieri, P., Morelli, I., Martinotti, E., 2002. Cardiovascular effects of *Urtica dioica* L. (Urticaceae) roots extracts: in vitro and in vivo pharmacological studies. J. Ethnopharmacol. 81 (1), 105–109. https://doi.org/10.1016/s0378-8741(02)00055-7.

Thalib, A., Masadah, R., Prihartono, P., Hamid, F., Hasan, H., Keliwawa, S., Labulawa, I., 2021. *Laportea decumana* (Robx) Wedd. Herbal endemic potential from Indonesia: a literature review. J. Open Access Macedonian J. Medic. Sci. 9 (F), 639–643. https://doi.org/10.3889/oamjms.2021.7759.

Tiotiu, A., Brazdova, A., Longé, C., Gallet, P., Morisset, M., Leduc, V., Poncet, P., 2016. Urtica dioica pollen allergy: clinical, biological, and allergomics analysis. Ann. Allergy Asthma Immunol. 117 (5), 527–534. https://doi.org/10.1016/j.anai.2016.09.426.

Tripathi, N., Kumari, S., Singh, R., Singh, C., Singh, P., & Varshney, V.J.O.J.o.C. (2013). Phytochemical studies from the roots of Girardinia heterophylla. 29(3), 1143–1148.

Tsabang, N., Kadjob, S., Mballa, R.N., Yedjou, C.G., Nnanga, N., Donfagsiteli, N.T., Tchounwou, P.B., 2015. New approach for the development of improved traditional medicine: case of a preparation of an oral hypoglycemic medicine from Laportea ovalifolia (Schumach. & Thonn.) Chew. (Urticaceae). J. Mol. Pharm. Org. Process. Res. 3 (2) https://doi.org/10.4172/2329-9053.1000125.

Turker, A.U., Usta, C., 2008. Biological screening of some Turkish medicinal plant extracts for antimicrobial and toxicity activities. Nat. Prod. Res. 22 (2), 136–146. https://doi.org/10.1080/14786410701591663.

Upreti, S., Prusty, J.S., Pandey, S.C., Kumar, A., Samant, M., 2021. Identification of novel inhibitors of angiotensin-converting enzyme 2 (ACE-2) receptor from *Urtica dioica* to combat coronavirus disease 2019 (COVID-19). Mol. Divers 25 (3), 1795–1809. https://doi.org/10.1007/s11030-020-10159-2.

Vajic, U.J., Grujic-Milanovic, J., Miloradovic, Z., Jovovic, D., Ivanov, M., Karanovic, D., Mihailovic-Stanojevic, N., 2018. *Urtica dioica* L. leaf extract modulates blood pressure and oxidative stress in spontaneously hypertensive rats. Phytomedicine 46, 39–45. https://doi.org/10.1016/j.phymed.2018.04.037.

Wang, J., Lu, J., Lan, Y., Zhou, H., Li, W., Xiang, M., 2013. Total coumarins from Urtica dentata Hand prevent murine autoimmune diabetes via suppression of the TLR4-signaling pathways. J. Ethnopharmacol. 146 (1), 379–392. https://doi.org/10.1016/j.jep.2013.01.009.

Wang, M.Y., Yang, Y., Zhou, X.Y., Wang, S.S., Duan, S.X., Li, X.B., 2018. The chemical constituents from *Urtica fissa* leaves. J. Asian Nat. Prod. Res. 20 (8), 709–718. https://doi.org/10.1080/10286020.2017.1383397.

Wang, M.Y., Zhang, Y., Zhang, H., Feng, X.R., Li, X.B., 2019. New lignans from urticae fissae herba. J. Asian Nat. Prod. Res. 21 (6), 516–521. https://doi.org/10.1080/10286020.2018.1457652.

Wu, Z.-Y., Monro, A.K., Milne, R.I., Wang, H., Yi, T.-S., Liu, J., Li, D.-Z., 2013. Molecular phylogeny of the nettle family (Urticaceae) inferred from multiple loci of three genomes and extensive generic sampling. Mol. Phylogenet. Evol. 69 (3), 814–827. https://doi.org/10.1016/j.ympev.2013.06.022.

Xie, J., Robinson, S.D., Gilding, E.K., Jami, S., Deuis, J.R., Rehm, F.B.H., Durek, T., 2022. Neurotoxic and cytotoxic peptides underlie the painful stings of the tree nettle Urtica ferox. J. Biol. Chem. 298 (8), 102218 https://doi.org/10.1016/j.jbc.2022.102218.

Yang, C.L., Or, T.C., Ho, M.H., Lau, A.S., 2013. Scientific basis of botanical medicine as alternative remedies for rheumatoid arthritis. Clin. Rev. Allergy Immunol. 44 (3), 284–300. https://doi.org/10.1007/s12016-012-8329-8.

Yildirim, N.C., Turkoglu, S., Ince, O.K., Ince, M., 2013. Evaluation of antioxidant properties, elemental and phenolic contents composition of wild nettle (*Urtica dioica* L.) from Tunceli in Turkey. Cell. Mol. Biol. (Noisy-le-grand) (Suppl 59), Ol1882–Ol1888.

Yoshikawa, K., Tao, S., Arihara, S., 2000. Stephanotic acid, a novel cyclic pentapeptide from the stem of Stephanotis floribunda. J. Nat. Prod. 63 (4), 540–542. https://doi.org/10.1021/np990532x.

Yuan, Y., Ai, K., Chen, G., 1999. [Chemical constituents of Girardinia palmata ssp ciliata]. Zhong Yao Cai 22 (4), 191–193.

Zemmouri, H., Sekiou, O., Ammar, S., El Feki, A., Bouaziz, M., Messarah, M., Boumendjel, A., 2017. Urtica dioica attenuates ovalbumin-induced inflammation and lipid peroxidation of lung tissues in rat asthma model. Pharm. Biol. 55 (1), 1561–1568. https://doi.org/10.1080/13880209.2017.1310905.

Zhang, H., Li, N., Li, K., Li, P., 2014. Protective effect of *Urtica dioica* methanol extract against experimentally induced urinary calculi in rats. Mol. Med. Rep. 10 (6), 3157–3162. https://doi.org/10.3892/mmr.2014.2610.

Zhang, H., Zhang, Y., Wang, M.Y., Chen, S., Li, X.B., 2019. The chemical constituents with cytotoxicity from *Urtica fissa* seed. J. Asian Nat. Prod. Res. 21 (11), 1068–1074. https://doi.org/10.1080/10286020.2018.1563074.

Zhang, S.S., Zhou, H., Li, L.L., Lu, J.L., Yin, G.X., Xiang, M., 2013. [Preparation technology of total coumarins from Laportea bulbifera]. Zhong Yao Cai 36 (4), 636–639.

Zhu, Z., Ma, L., Zhu, H.Y., Yang, X.S., Hao, X.J., 2011. [Studies on the chemical constituents of Laportea bulbifera]. Zhong Yao Cai 34 (2), 223–225.

Zouari Bouassida, K., Bardaa, S., Khimiri, M., Rebaii, T., Tounsi, S., Jlaiel, L., Trigui, M, 2017. Exploring the *Urtica dioica* leaves hemostatic and wound-healing potential. Biomed. Res. Int. 2017, 1047523 https://doi.org/10.1155/2017/1047523.

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