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Review Article

Ethnomedicinal uses, phytochemistry, pharmacology and toxicological aspects of genus *Wendlandia*: an overview

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ABSTRACT

The genus *Wendlandia* includes around 70 species and is native to southeast Asia, northeast Africa, China, Australia, and Turkey. Mnay plant species of this genus have ethnomedicinal properties, which are used to deal various health complications, including dysentery, severe fever, cough, diabetes, hypertension, hyperlipidemia, constipation, and inflammation. This review sought to summarize details on the ethnomedicinal uses, phytochemical composition, safety aspects, and toxicology of *Wendlandia* species. Additionally, it covered the nomenclature, distribution, taxonomy, and botanical characteristics of this genus. Several electronic databases were used to retrieve the information, including Google Scholar, PubMed, Web of Science, Scopus, Science Direct, and Springer Link. The Plant List (www.theplantlist.org) was used for taxonomical authentications. SciFinder and PubChem were utilized for the verification of chemical structures and IUPAC (International Union of Pure and Applied Chemistry) name of the compounds. Numerous examinations of chemical constituents of the *Wendlandia* genus have identified approximately 60 essential plant compounds, such as iridoid glycosides, flavonoids, flavonoid glycosides, carotenoids, and triterpenes. Various research studies have showcased the therapeutic potential of *Wendlandia* species, highlighting their abilities in treating diabetes, combating oxidation, reducing inflammation, fighting microbes, lowering blood pressure, and potentially hindering cancer growth. The significance of *Wendlandia* in traditional medicine systems and its role as a valuable origin of impactful natural compounds are evident. This review provided scientific basis for future endeavors, including chemical investigations into already studied species and other less studied species of *Wendlandia* for finding future lead compounds.

Introduction

Currently, approximately 350,000 vascular plant species and 325,000 flowering plant species exist worldwide. However, only a tiny fraction, precisely 25,791 plants, less than 8% of the total, have been formally studied for their potential therapeutic uses (Antonelli et al., 2020). It is important to note that medicinal plants contain diverse bioactive phytochemicals, which can serve as valuable foundations for creating innovative medications (Bari et al., 2021). In recent times, synthetic chemical sources have taken over the pharmaceutical sector, and thus, the consumption of chemicals is rising at an alarming rate (Brishty et al., 2021). For ameliorating one disease, maybe today's functional chemical analog can create a dormant home for tomorrow's unknown illness. To escape this problem, using

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herbal medicine is a better choice. Herbal drugs derived from plant sources are being tremendously exploited to deal with various human diseases (Maryam et al., 2018; Rashid et al., 2023; Mitra et al., 2022). The genus *Wendlandia* is such an exclusive source of phytochemical value. This genus belongs to a widely distributed tropical family called Rubiaceae, encompassing around 13,200 species spread across 615 different genera. *Wendlandia* has different life forms: trees, shrubs, and herbaceous plants with annual and perennial life cycles (Xie et al., 2010). Approximately 50-70 species of this genus are located in the Indo-Malayan region (Choze et al., 2010). In the past, various mountain communities noticed that by using traditional medicinal practices, plants could effectively treat conditions such as ulcers, dysentery, athlete's foot, diabetes, whooping cough, bronchitis, asthma, migraines, and more. Further, researchers have an extensive focus on this genus. Some species of this genus *Wendlandia* are of miraculous importance and are used in the treatment of snake bites, scorpion stings, regulation of menses, securing the birth of male children, diarrhea and intestinal parasites, hypertension, cardiovascular dysfunctions, mental disturbs and alimentary disorders (Sindhe et al., 2015).

Wendlandia has bioactive molecules and the presence of diversified phytoconstituents such as; Ixoxide, Iridoid glycosides, diphenylpicrylhydrazyl (DPPH), hydroxyl radical, flavonoid, terpenes, triterpenes, beta carotene, lycopene, caffeic acid, rutin, procyanidin, catechin, myricyl stearate, stearic acid, D-mannitol, b -sitosterol, stigmasterol, and geniposidic acid etc. make this genus a tremendous medicinal value (Raju et al., 2014; Dinda et al., 2011; Inouye et al., 1988). These phytochemical molecules give a large variety of pharmacological activities like antimicrobial, antioxidant, antidiabetic, anticancer, anti-inflammatory, analgesic, antinociceptive, anti-asthmatic, insecticidal, and anti-mutagenic activity (Sindhe et al., 2015).

Considering the various activities of the genus *Wendlandia*, this review aimed to provide a comprehensive profile of the genus *Wendlandia*, focusing on its traditional uses, phytochemistry, pharmacological and toxicological properties.

Methodology

To acquire evidence for this review, we did a thorough literature search utilizing the Google Scholar and PubMed databases. The leading search terms were "*Wendlandia*," "*Wendlandia* species," "ethnopharmacology," "ethnobotany," "chemical constituents," "phytoconstituents," "biological activity," "pharmacological activity," "toxicology," and "safety." We also used additional academic platforms such as Google Scholar, PubMed, Web of Science, Scopus, Science Direct, and Springer Link to get the essential information. During the compilation and synthesis of material, the downloaded papers were thoroughly examined to determine the legitimacy and usefulness of their data. Information gathered from the chosen articles encompassed the names of reported plant species, the specific parts of plants examined, isolated phytochemicals from these species, pharmacological studies on each plant extract, the kinds of experiments conducted, the dosage or concentration used in these experiments, and relevant details on toxicity studies. The material retrieved was classified and reported in detail for each category. To authenticate the identity of the Gynura species mentioned in this review, the Plant List (ww.theplantlist.org) was employed. ChemDraw Ultra 7.0 was used to draw all the chemical structures, which were validated using SciFinder and PubChem.

Taxonomy and Distribution

Wendlandia genus comprises approximately 50-70 species, ranging from south-east Asia to north-east Africa, China, Australia and Turkey. Some representative species are shown in the Fig. 1. It is under the rubiaceae family, rubiaceae is the fourth largest angiosperm family in the world. Rubiaceae plants typically stand out due to their simple, opposite, or whorled leaves, paired interpetiolar stipules, and an ovary situated inferiorly (Ranjan and

Kumar, 2015). Schumann (1891) was the first to suggest the intragenic categorization of *Wendlandia*. He divided the genus into two sets based on the varying lengths of its species. This division failed to reflect the true relationship of the species of *Wendlandia*. Furthermore, Cowan (1932) divided *Wendlandia* by the characters of stigma, stamens and the feature of the stipules. The genus *Wendlandia* is popular in the hilly regions among the tribes of tropical & sub-tropical areas. As it is a forestry flowering plant, its culinary and medicinal uses make this genus significant from the Rubiaceae family (Choze et al., 2010). The scientific name, synonyms and distribution of the species have already been established with different previously accepted name within the genus. Notably, the original author names, original publication resources, accepted or synonymous plant name and the International Plant

Name Index (IPNI) identifier by the plant list (www.theplantlist.org). Raju et al., (2012) reported its tubular flower, evergreen woody trees protect the hilly soil from erosion and similarly useful for pollination by a wide array of pollinators including butterflies, beees, flies, wasps, moth etc (Xie et al., 2010). Because of the similarity of some species of *Wendlandia* like *Wendlandia formosana* is closely related to some phytoconstituents derived from *Angustifolia* (Choze et al., 2010). The complete taxonomical classification of the genus is given below:

Kingdom	**Plantae**
Subkingdom	**Viridiplantae**
Infrakingdom	**Streptophyta**
Division	**Embryophyta**
Subdivision	**Tracheophyta**
Division	**Spermatophytina**
Order	**Gentianales**
Family	**Rubiaceae**
Subfamily	**Ixoroideae**
Tribe	**Gardenieae**
Genus	***Wendlandia***

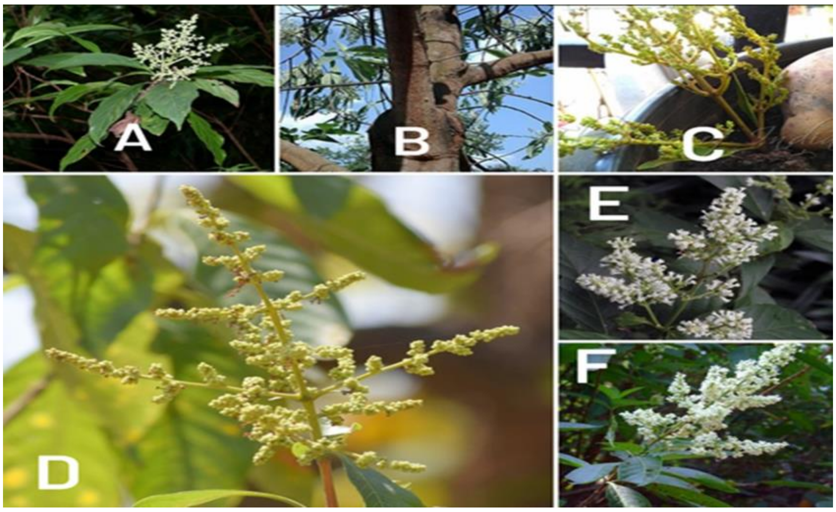

Fig. 1. (A) Wendlandia formosana, (B) Wendlandia heynei (C) Wendlandia glabrata (D) Wendlandia tinctoria (E) Wendlandia wallachii (F) Wendlandia thyrosoidea.

Ethnomedicinal Uses

Several *Wendlandia* species have a long history of use in traditional ethnomedicine to treat a range of ailment in India, Pakistan, Australia, Srilanka, Bangladesh, Japan, China, Turkey and the Southeast Asian regions including Vietnam, Malaysia, Thailand. A brief description about *Wendlandia* species and its reported activity is given below:

Wendlandia heyenei: The Rubiaceae family plant *W. heynei* (Schult.) Santapau and Merchant, popularly known as "Ukan Pansara," is abundantly spread in Rawalpindi, Kahuta, Panjar district, Pakistan (Maryam et al., 2018). Local populations utilize this plant to cure ulcers, swellings, wounds, diarrhoea, fever, urinary problems, skin illnesses, colds and coughs, and body pains (Khatoon and Irshad, 2016). The tree's fruits and barks are used to cure piles (Rawat et al., 2009). Furuncles and urinary diseases are treated with a bark paste. The powdered leaf extract has wound-healing effects, and the leaves and fruits' decoction are effective in amenorrhea, as an antispasmodic, and as a febrifuge (Ajaib et al., 2018). Its roots are utilized as an antidote to snake bite (Murthy et al., 1986). In India, *W. heynei's* bark is used to treat colds and high fevers.

Wendlandia exserta: *W. exserta* Roxb. DC., a member of the Rubiaceae family known regionally as chila/ratela/tikli, is widely distributed in the sub-Himalayan region, particularly in areas prone to landslides. It serves as a valuable source of fuelwood and yields small timber. This plant can potentially cover expansive areas, especially in regions susceptible to soil erosion (Dhiman and Gupta, 2009). The bark displays a reddish-brown hue. Its leathery leaves are arranged oppositely, broadly oval or lanceolate. The flowers, which are white and minute, grow in sessile clusters at the apex, forming pyramidal structures around 25cm long (Praveen et al., 2007). The leaves and fruit decoctions of Wendlandia exserta are utilized in treating conditions like amenorrhea, fever, spasms, and skin ailments such as eczema and scabies. Moreover, the flowers possess properties beneficial for purifying blood and are employed in managing joint infections (Shahzadi et al., 2018)

Wendlandia glabrata: Young sprouts of *Wendlandia glabrata* DC are used as functional foods in India's north-eastern region. This blooming plant from the Rubiaceae family is used to make the traditional salad Singju. The plant has qualities such as lowering obesity and managing blood sugar. It is also used to treat dysentery in addition to serving as an expectorant (Meetei and Singh, 2007). In hepatocytes and myoblast cells, extracts of *W. glabrata* suppress G-6-Pase and glucose absorption. This study revealed procyanidin A2 (PCA2) as a powerful anti-diabetic drug with significant aglucosidase inhibition. It has been shown that PCA2 lowers the amount of G-6-Pase protein and mRNA in diabetic mice while increasing glucose absorption in CC1 hepatocytes and C2 C12 myoblast cells (Sheikh et al., 2019). The fraction extracted from *W. glabrata*, rich in novel iridoid compounds, exhibited noteworthy potential in reducing blood glucose levels. It also effectively prevented hepatic gluconeogenesis conditions by significantly increasing the phosphorylation of AMP-activated protein kinase (AMPK) by approximately 1.4 to 1.7 times and downregulated key enzymes involved in gluconeogenesis, such as glucose-6-phosphatase (G6Pase) and phosphoenolpyruvate carboxykinase (PEPCK) (Sarma et al., 2022).

Wendlandia paniculata: *Wendlandia paniculata* (Roxb.) DC is an exceedingly uncommon species in Bangladesh, utilised by the Chakmas tribe in mountains regions. It is commonly used as a treatment for chest pain by rubbing the crushed leaves on the chest. The plant family Rubiaceae encompasses the flowering plant genus *Wendlanda*, distributed across regions spanning from tropical and subtropical Asia to Queensland and the northern parts of Africa. According to Hasan et al., 2021, these plants could serve as a promising source for hypoglycemic medications and possess anthelmintic properties, given the historical use of various plants and plant-derived substances in diabetes treatment. Herbs having hypoglycemic qualities promote insulin release, enhance glucose uptake by adipose or muscle tissues, and inhibit glucose absorption from the digestive tract as well as hepatic glucose synthesis (Hui et al., 2009). Acute, chronic, visceral, inflammatory, and neuropathic pain are all possible (Masuda et al., 2017; Tamba et al., 2013). A quarter of all Americans, for example, suffer from chronic discomfort. With these numbers in its favour, pain has emerged as a global health problem and the leading cause of disability globally (Gedin et al., 2017).

Plants have long been used as analgesic agents in folk medicine (Ullah et al., 2015; Ayaz et al., 2016). The search for new bioactive molecules with analgesic effects in medicinal plants is intensifying. Diarrhoea is defined as a gastrointestinal disorder characterised by a rapid flow of gastric material through the gastrointestinal tract, leading to abnormal and frequent semi-solid or watery faecal discharge that occurs on average three times per day (Yakubu and Salimon, 2015; Vickers, 2017; Singh et al., 2012). Enteric pathogenic bacteria such as *Salmonella typhi*, *Shigella flexneri*, *Escherichia coli*, *Staphylococcus aureus*, *Vibrio cholerae*, and *Candida albicans* are common causes of diarrhoea in humans (Akinboro et al., 2007; Kitaoka et al., 2011).

Wendlandia tinctori: *Wendlandia tinctoria* var. *grandis* (Roxb.) DC. is a flowering plant that exhibits characteristics of both evergreen and deciduous plants. In the summer season, *W. tinctoria* plays a vital role by providing butterflies with an important nectar supply and serving as a pollen source for honey bees. *W. tinctoria* is commonly used by tribal communities to treat snakebite. It is also utilized to alleviate cramps in cholera patients. Previous research found that the stem of *W. tinctoria* contains stearic acid, geniposidic acid, d-mannitol, -sitosterol, myricyl stearate, and stigmasterol. According to earlier findings, the root of W. tinctoria contains a variety of iridoid glucosides, including 5-dehydro-8-epi-mussaenoside, 5-dehydro-8-epi-adoxosidic acid, wendoside, 8-epi-mussaenoside, and 10-O-dihydro feruloyldeacetyldaphylloside (Dinda et al., 2006; Dinda et al., 2011). Farzana et al. (2022) recently conducted a study where they identified a total of eight phenolic compounds in W. tinctoria. These compounds include liquiritigenin (1), naringenin (2), apigenin (3), kaempferol (4), glabridin (5), ferulic acid (6), 4-hydroxybenzoic acid (7), and 4-hydroxybenzaldehyde (8). Additionally, the study demonstrated that the stem extract of this plant species has antioxidant, hypoglycemic, and antidiarrheal properties (Farzana et al., 2022). The individual ethnomedicinal uses of the main *Wendlandia* species are summarized in Table 1.

Iridoid Glycoside

Iridoids are cyclopentanopyran-like monoterpenoids that exist in a broad range of animals and plants. They are generated biosynthetically from 8-oxogeranial. Iridoids are most often found in plants as glycosides, most of which are linked to glucose (Tundis et al., 2008). It has been regarded as defense chemicals against pathogens. Majority of *Wendlandia* species contain iridoid glycoside. From *Wendlandia formosana* this iridoid glycosides are elucidated Methyl deacetyl asperulosidate, 10-O-caffeoyl scandoside methyl ester, 6-methoxy scandoside methyl ester, 10-O-caffeoyl deacetyl dephylloside, 6-beta methoxy geniposide, 6-beta hydroxyl geniposide (Raju et al., 2011). In 2006 and 2011, Dinda et al. depicted the following compounds like: 8-epi-deoxyloganic acid, Deacetyl – daphylloside, Caffeoylmussaenosidic acid, Caffeoylmussaenosidic acid hexaacetate, Ixoside, Ixoside tetraacetate, 5-Dehydro-8-epi-adoxasidic Acid pentaacetate, 8-epi-mussaenoside, 8-epi-mussaenoside tetraacetate, 5-dehydro-8-epi-mussaenoside, 5-dehydro-8-epi-mussaenoside tetraacetate, 10-O-Dihydroferuloyldeaxetyldaphylloside, 10-O-

Table 1. General information, taxonomical distribution and ethnomedicinal uses of Genus *Wendlandia.*

Species (Accepted Name)	Synonyms	Plant Part Used	Geographical Locations	Ethnomedicinal Uses	References
Wendlandia paniculata (Roxb.) DC.	*Gardenia* burha Buch. -Ham. ex Wall. *Rondeletia paniculata* Roxb. *Wendlandia paniculata* var. genuina Valeton	Leaves	Northwestern Vietnam, western Africa, Southeast Asia, subtropical countries of East Asia and northern Australia.	Anti-diabetic property, anti-diarrheal effect, antinociceptive activity	Hasan et al., 2021
Wendlandia formosana Cowan	*Wendlandia formosana* subsp. *formosana*	Leaves, stem bark & wood	Indo Malayan region to China	Antioxidant, analgesic property	Delprete, 1999
Wendlandia tinctoria (Roxb.) DC.	*Wendlandia tinctoria* subsp. *Callitricha* (Cowan) W.C. Chen *Wendlandia tinctoria* subsp. *Floribunda* (Craib) Cowan *Wendlandia tinctoria* subsp. *Handelii* Cowan *Wendlandia tinctoria* subsp. *Intermedia* (F.C.How) W.C.Chen *Wendlandia tinctoria* subsp. *Orientalis* Cowan *Wendlandia tinctoria* var. *grandis* (Roxb.) DC.	Stem, root and bark	North-eastern states of India	Antidote to snakebite, antibacterial activity, antioxidant, hypoglycemic, and antidiarrheal properties	Raju et al., 2014; Farzana et al., 2022
Wendlandia glabrata DC.	*Rhombospora sumatrana* (Miq.) Miq. *Wendlandia glabrata* var. *glabrata* *Wendlandia sumatrana* Miq. *Wendlandia tenuiflora* Miq. Ex Hook.f.	Tender shoot	North-eastern states of India	Anti-hypoglycemic activity, reduce obesity, anti-diarrheal effect used in dysentery, act as expectorant	Sheikh et al., 2019
Wendlandia heynei (Schult). Santapau and Merchant	*Rodeletia cinerea* Wall. *Rodeletia exserta* Roxb. *Rodeletia heynei* Schult. *Rodeletia orissensis* Roth *Rodeletia thyrsiflora* Roth *Wendlanida cinerea* DC. *Wendlandia exserta* (Roxb.) DC.	Bark, leaves, root	Panjar, Kahuta, Rawalpindi district, Pakistan	Treatment of piles, furuncles, urinary infections, amenorrhea, febrifuge, antispasmodic activity, antioxidant, anti-inflammatory activity, antidote to snake bite, used in cold & high fever	Maryam et al., 2018
Wendlandia ligutroides (Boiss. & Hohen.) Blakelock	*Sestina kotschyi* (Boiss. & Hohen.) Chiov. *Sestina ligustroides* Boiss. & Hohen *Wendlandia Kotschyi* Boiss. & Hohen.	aerial parts (stems, leaves, and flowers)	North Iraq, Turkey	Antiprotozoal activity	Çalış et al., 2020
Wendlandia thyrosoidea (Roth) Steud.	*Canthium thyrsoidea* Roem. & Schult. *Canthium thyrsoideum* Schult. *Cupia thyrsoidea (Roth)* DC. *Ixora montana* Miq. ex Hook. f *Webera thyrsoidea* Roth *Wendlandia lawii* Hook.f. *Wendlandia montana* K. Schum. *Wendlandia notoniana* Wall. ex Wright & Arn. *Wendlandia thyrsoidea* var. lawii (Hook.f.) Cowan	Leaves	Central Western Ghats region of Chikkamagaluru, Karnataka, India	Antimicrobial, analgesic property	Vinu et al., 2021
Wendlandia wallichii (Wight and Arn)	*Wendlandia wallachii* var. *wallachii*	Leaves	North-eastern region in tropical Africa and Asia	Fat and fiber content used as common vegetable. Decrease the risk of constipation, lower diabetes, serum cholesterol level, heart diseases, breast and colon cancer, hypertension etc. High protein source used as a dietary element.	Chaudhuri et al., 2018
Wendlandia bicuspudata Wight & Arn	*Wendlandia notoniana* var. *bicuspudata* (Wight & Arn.) Hook.f. *Wendlandia notoniana* var. *zeylanica* Hook.f.	Wood	Hilly regions of Srilanka	Antioxidant activity	De Silva et al., 1987
Wendlandia exerta (Roxb.) DC.	Not available	Leaves	Pakistan Nepal, Indian	Antibacterial, anti-fungal, analgesic activity	Ajaib et al., 2018

Table 2. Phytoconstituents of Genus *Wendlandia*

Comp. No	Phytochemical class	Compounds	Sources	Plant part	Reference
1	Iridoid glycoside	Scandoside methyl ester	*W. formosana, W. bicuspudata W. ligustroides*	Stem, leaves & flowers	De silva et al., 1987, Moreina et al., 2010
2	Iridoid glycoside	Methyl deacetyl asperulosidate	*W. formosana*	Leaves	Raju et al., 2011
3	Iridoid glycoside	10-O-caffeoyl scandoside methyl ester	*W. formosana, W. tinctoria*	Leaves	Raju et al., 2011
4	Iridoid glycoside	6-methoxy scandoside methyl ester	*W. formosana*	Leaves	Raju et al., 2011
5	Iridoid glycoside	10-O-caffeoyl deacetyl dephylloside	*W. formosana*	Leaves	Raju et al., 2011
6	Diterpene alkaloid	Phytol	*W. formosana*	Leaves	Massey and Burton, 1990
7	Pentacyclic triterpenoid	Ursolic acid	*W. formosana*	Leaves	Raju et al., 2014
8	Iridoid glycoside	Gardenoside	*W. formosana W. ligustroides*	Stem, leaves & flowers	Inouye et al., 1988
9	Iridoid glycoside	Geniposidic Acid	*W. formosana, W. ligustroides*	Stem, leaves & flowers	Çalış et al., 2020; Tzakon et al., 2007
10	Iridoid glycoside	10-Deoxyloganic acid	*W. formosana, W. ligustroides*	Stem, leaves & flowers	Inoue et al., 1992; Takeda et al., 1996
11	Iridoid glycoside	6-beta methoxy geniposide	*W. formosana, W. ligustroides*	Stem, leaves & flowers	Raju et al., 2014
12	Iridoid glycoside	6-beta hydroxyl geniposide	*W. formosana, W. ligustroides*	Stem, leaves & flowers	Raju et al., 2014
13	Flavonoid glycoside	Rutin	*W. heynei*	Leaves	Maryam et al., 2018
14	Polyphenolic flavonoid	Catechin	*W. heynei*	Leaves	Maryam et al., 2018
15	Prsotacyanidin flavonoid	Procyanidin A2	*W. glabrata*	Tender shoot	Sheikh et al., 2019
16	Retinol	Beta carotene	*W. heynei*	Bark & leaves	Maryam et al., 2018
17	Flavonoid	Lycopene	*W. heynei*	Bark & leaves	Maryam et al., 2018
18	Polyphenolic flavonoid	7-Deoxygardoside	*W. formosana, W. ligustroides*	Stem, leaves & flowers	Bianco et al., 1986
19	Iridoid glycoside	8-epi-deoxyloganic acid	*W. ligustroides*	Stem, leaves & flowers	Nakamura et al., 2000; Murai et al., 1984; Teng et al., 2005
20	Iridoid glycoside	Deacetyl - daphylloside	*W. ligustroides*	Stem, leaves & flowers	Tzakou et al., 2007
21	Iridoid glycoside	8-epi-deoxyloganic acid deacetyl - daphylloside	*W. ligustroides*	Stem, leaves & flowers	Dinda et al., 2011
22	Iridoid glycoside	Caffeoylmussaenosidic acid	*W. tinctoria*	Stem	Dinda et al., 2011
23	Iridoid glycoside	Caffeoylmussaenosidic acid hexaacetate	*W. tinctoria*	Stem	Dinda et al., 2011
24	Iridoid glycoside	Ixoside	*W. formosana*	Leaves	Dinda et al., 2011
25	Iridoid glycoside	Ixoside tetraacetate	*W. formosana*	Leaves	Dinda et al., 2011
26	Iridoid glycoside	5-Dehydro-8-epi-adoxasidic Acid	*W. tinctoria*	Stem	Inouye et al., 1988
27	Iridoid glycoside	5-Dehydro-8-epi-adoxasidic Acid pentaacetate	*W. tinctoria*	Stem	Dinda et al., 2006
28	Iridoid glycoside	8-epi-mussaenoside	*W. tinctoria*	Stem	Dinda et al., 2006
29	Iridoid glycoside	8-epi-mussaenoside tetraacetate	*W. tinctoria*	Stem	Dinda et al., 2006
30	Iridoid glycoside	5-dehydro-8-epi-mussaenoside	*W. tinctoria*	Stem	Dinda et al., 2006

31	Iridoid glycoside	5-dehydro-8-epi-mussaenoside tetraacetate	*W. tinctoria*	Stem	Dinda et al., 2006
32	Iridoid glycoside	10-O-Dihydroferuloyldeaxetyldaphylloside	*W. tinctoria*	Stem	Dinda et al., 2006
33	Iridoid glycoside	10-O-Dihydroferuloyldeaxetyldaphylloside hexaacetate	*W. tinctoria*	Stem	Dinda et al., 2006
34	Iridoid glycoside	Wendoside	*W. tinctoria*	Stem	Dinda et al., 2006
35	Iridoid glycoside	Wendoside pentaacetate	*W. tinctoria*	Stem	Dinda et al., 2006
36	Iridoid glycoside	Aglucone Wendoside pentaacetate	*W. tinctoria*	Stem	Dinda et al., 2006
37	Iridoid glycoside	10-O-Caffeoyldeacetyldaphylloside	*W. tinctoria*	Stem	Dinda et al., 2006
38	Iridoid glycoside	8-α-dihydrogeniposide	*W. tinctoria*	Stem	Inouye et al., 1988
39	Iridoid glycoside	Semperoside	*W. tinctoria*	Stem	Dinda et al., 2006
40	Iridoid glycoside	10-O-Veratroyleranthemoside	*W. tinctoria*	Root	Dinda et al., 2011
41	Iridoid glycoside	10-O-Veratroyleranthemoside tetraacetate	*W. tinctoria*	Root	Dinda et al., 2011
42	Iridoid glycoside	Eranthemoside	*W. tinctoria*	Root	Dinda et al., 2011
43	Iridoid glycoside	10-O-trans-coumaroyleranthemoside	*W. tinctoria*	Root	Dinda et al., 2011
44	Terpene	Octa acyl lupeols	*W. formosana*	Stem	Delprete, 1999; Raju et al., 2004
45	Terpene	Deca acyl lupeols	*W. formosana*	Stem	Delprete, 1999; Raju et al., 2004
46	Coumarin	Coumarin	*W. formosana*	Stem	Canuto and Silveira, 2006
47	Flavonoid	Scopoletin	*W. formosana*	Stem	Ribeiro and Kaplan, 2002
48	Flavonoid	Kaempferol	*W. formosana*	Stem bark & Wood	Delprete, 1999
49	Flavonoid	Quercetin	*W. formosana*	Stem bark & Wood	Delprete, 1999
50	Flavonoid	Flavonol rutin	*W. formosana*	Stem bark & Wood	Delprete, 1999
51	Flavonoid	Myricitrin	*W. formosana*	Stem bark & Wood	Choze et al., 2010; Delprete, 1999
52	Triterpene	Pentacyclic triterpenes ursolic acid	*W. formosana*	Stem	Delprete, 1999; Raju et al., 2004
53	Phenolic compound	2-Methoxy-4-hydroxy-benzoic acid	*W. formosana*	Stem	Berretta, 2007
54	Flavonoid	Naringenin	*W. formosana*	Stem	Delprete, 1999
55	Iridoid Glycoside	6-O-methyl-Scandoside methyl ester	*W. ligustroides*	Stem, leaves & flowers	Machida et al., 2003
56	Iridoid Glycoside	6-O-methyl deacetyl–daphylloside	*W. ligustroides*	Stem, leaves & flowers	Machida et al., 2003
57	Iridoid Glycoside	Ixoroside	*W. tinctoria*	Stem	Inouye et al., 1988
58	Iridoid Glycoside	Iridodial	*W. tinctoria*	Stem	Inouye et al., 1988
59	Iridoid Glycoside	Gardenosidic acid	*W. tinctoria*	Stem	Inouye et al., 1988
60	Iridoid Glycoside	Ixoside 11-methyl ester	*W. tinctoria*	Stem	Inouye et al., 1988

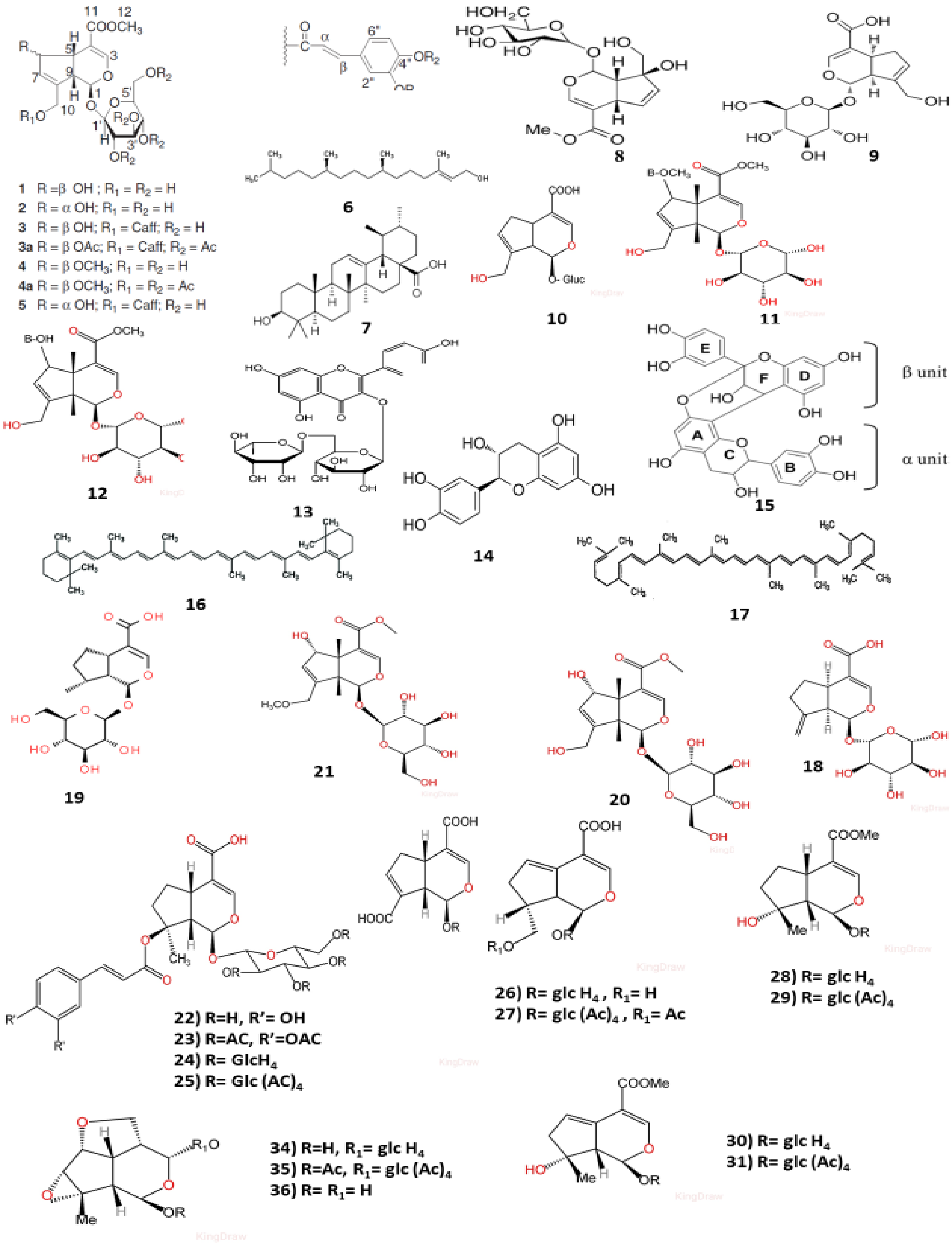

Fig. 2. The chemical structures of 60 phytocompounds of Genus *Wendlandia* listed in Table 2

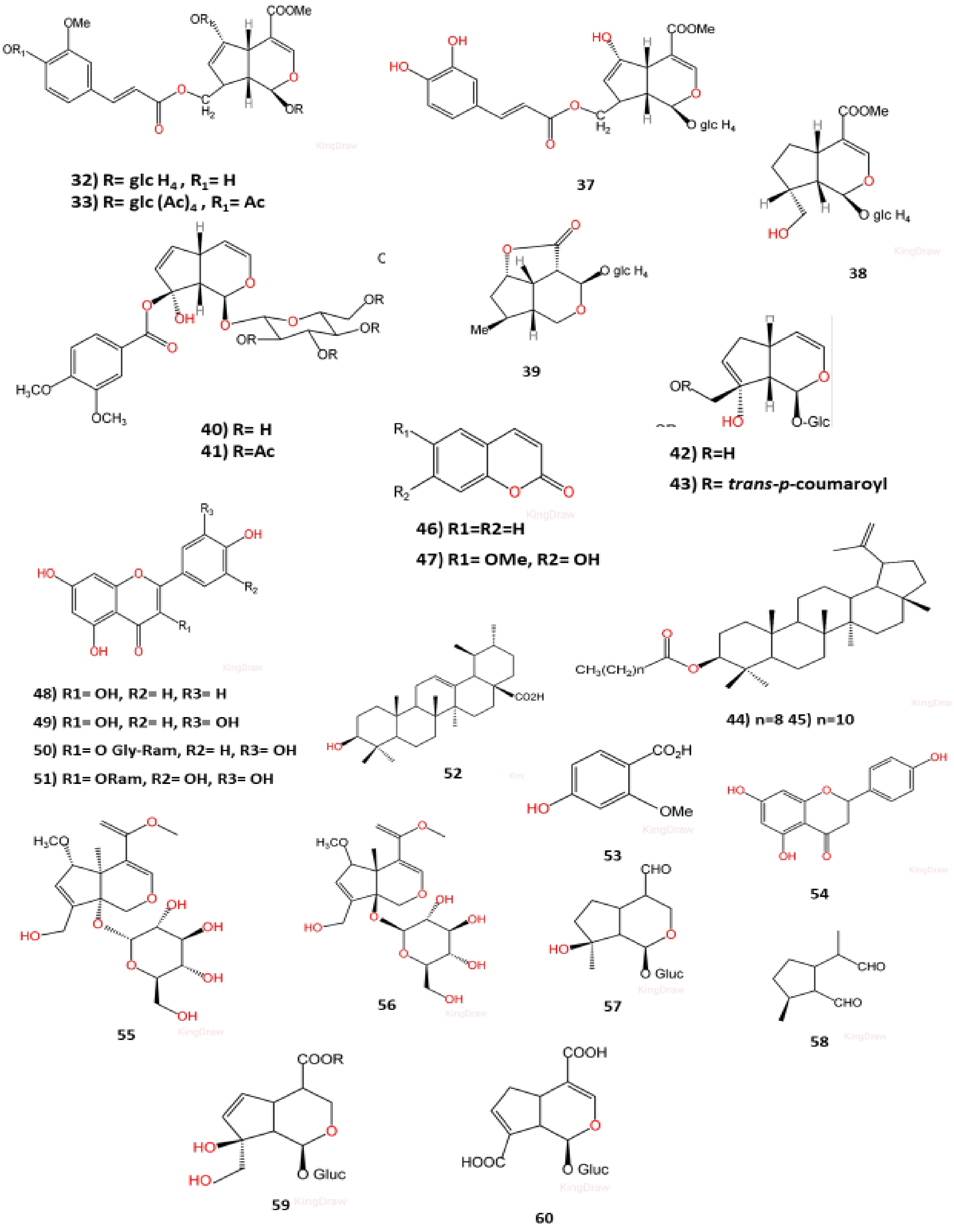

Fig. 2. The chemical structures of 60 phytocompounds of Genus *Wendlandia* listed in Table 2 (Continued)

Dihydroferuloyldeaxetyldaphylloside hexaacetate, Wendoside, Wendoside pentaacetate, Aglucone Wendoside pentaacetate, 10-O-Caffeoyldeacetyldaphylloside, Semperoside, 10-O-Veratroyleranthemoside, 10-O-Veratroyleranthemoside tetraacetate, Eranthemoside, 10-O-trans-coumaroyleranthemoside from *Wendlandia tinctoria* (Dinda et al., 2006; Dinda et al., 2011). Despite the inherent biological capability, the specific molecular mechanisms behind the impactful effects of iridoid glycosides remain unexplained. It is hypothesized that due to the presence of unstable aglycones resembling glutaraldehyde structures and possessing alkylating properties against nucleophilic residues in biomolecules, particularly amino acids, these compounds might induce protein denaturation in the cell wall of pathogens (Dinda et al., 2006; Dinda et al., 2011).

The main pharmacological effects of iridoid glycosides are antioxidant, anti-diabetic, anti-inflammatory, anti-obesity activities. Sheikh et al., (2019) reported α-glucosidase inhibitory activities of the methanol extract of shoots of *Wendlandia glabrata*. Alpha-glucosidase is considered for future lead molecules for type 2 diabetes. *Wendlandia* species have plenty source of α-glucosidase. That is why it has promising potential for postprandial management of DM type 2. Diabetes mellitus stems from irregular sugar metabolism due to insufficient insulin production or the body's resistance to insulin in target organs (Maiti et al., 2004). Despite the recognized therapeutic benefits of fruit-based remedies in traditional medicine for diabetes, developing economically viable natural treatments lags behind modern pharmaceuticals (Wadkar et al., 2008).

Dietary polysaccharides play a crucial role in generating blood glucose (Ghani, 2015). α-glucosidase, a key enzyme, is pivotal in transforming polysaccharides into monosaccharides. Hence, there's a pressing need to create food or herbal solutions and inhibitors that can slow down α-glucosidase activity, thereby managing post-meal blood sugar levels. Additionally, targeting glucose-6-phosphatase (G-6-Pase) holds promise in treating type 2 diabetes. G-6-Pase oversees the final step in generating glucose from gluconeogenesis and glycogenolysis. Studies suggest that reducing blood glucose involves curtailing hepatic glucose production by regulating G-6-Pase. Diabetic animals show elevated protein content and mRNA levels of G-6-Pase, contributing to heightened blood sugar. Therefore, G-6-Pase inhibitors are seen as potential means to lessen hepatic glucose output, making them an appealing therapeutic option for type 2 diabetes treatment.

Flavonoid

Flavonoids, a type of polyphenolic compounds present in plants, are frequently part of human diets. Chemically, they feature a basic structure composed of a 15-carbon skeleton comprising two phenyl rings and a heterocyclic ring (Mitra et al., 2022).

Wendlandia species are flowering plant, their leaves, root juice, flowers contain a rich source of flavonoid. *Wendlandia formosana* has rutin, catechin, procyanidin A2, lycopene, beta carotene, scopoletin, quercetin, myricitrin, naringenin flavonoids. Among these some are polyphenolic flavonoid, flavanone, carotenoids type. Flavonoids are thought to offer health advantages by affecting different cell pathways and acting as antioxidants. Rutin and catechins, among flavonoids, are the prevalent polyphenolic compounds in our diet and are widespread in plants (Spencer, 2008; Maryam et al., 2018; Sheikh et al., 2019; Bianco et al., 1986).

Flavonols, like quercetin, are the primary bioflavonoids and are also present everywhere, albeit in smaller amounts. Flavonoids are widely spread, diverse, and generally less toxic compared to other plant compounds like alkaloids (Eumkeb et al., 2010, Kumar et al., 2010). That is the reason for showing antioxidant and dietary supplement for mankind.

Flavonoids and saponins prevent the creation or release of prostaglandins, autocoids, and contractions caused by spasm-inducing agents, similarly affecting movement and the release of fluids and electrolytes (Eumkeb et al., 2010, Kumar et al., 2010) while saponins may forestall the arrival of histamine (Wang et al., 2010). Polyphenols and tannins help fortify the lining of the intestines, reducing intestinal leakage, speeding up intestinal transit, and promoting a better equilibrium in water movement across the mucosal cells (Phoem et al., 2013).

Terpene

A terpene molecule is made up of 10 carbon atoms and must have a double bond. Terpene hydrocarbons are sensitive to heat and readily undergo oxidation. This is why citrus oils, rich in terpenes, are prone to these changes. *Wendlandia* have a small range of terpene like phytol, ursolic acid, acyl lupeol found in stem, bark of *Wendlandia formosana.* Ursolic acid is a substance with various chemical, biological, and physiological impacts. With the recent discovery of ursolic acid's anti-inflammation and anti-cancer effects via targeting signal pathways, particularly in preventing breast cancer, ursolic acid has gained attention (Venugopal and Liu, 2012). Ursolic acid is presently being tested on humans to treat cancer, tumors, and wrinkles (Sultana, 2011). Certain terpenes are believed to possess anti-inflammatory, antiseptic, antiviral, and antibacterial qualities. However, the essential oil's impact results from the collective physiological actions of its various components. Specific terpenes might exhibit analgesic effects or serve as stimulants. Some are known to prompt mucous secretion, making them effective decongestants. Throughout history, essential oils have found widespread use in medicinal practices (Nuutinen, 2018)

Toxicological profile

W. heynei methanol extract was found to protect the liver from damage caused by bisphenol A (BPA), suggesting its potential as a supportive treatment for drug-induced liver injury (Maryam et al., 2018). Conversely, a flavonoid called catechin from *W. formosana* was associated with the development of autoantibodies, leading to conditions like haemolytic anaemia and renal failure. This led to the removal of Catergen, a drug containing catechin used for treating viral hepatitis, from the market in 1985 (Mazuz wt al., 2023).

Future Perspective

There are available chemical substances in *Wendlandia* species that have biological properties for lowering serum glucose, controlling lipid profile, skin diseases, and regulating the menstruation cycle. Nowadays, convenient drugs are present in the market, but these drugs produce a wide range of cytotoxic side effects. In this review, *Wendlandia* species showed different phytoconstituents that can be used as drugs and dietary supplements. The presence of flavonoids and glycosides exerts antioxidant, anti-diabetic, and anti-inflammatory activities, making this genus a combined source of safe medicinal value. This review also manifested that screened phytochemicals and isolated compounds will be potential sources of the drug industry in the future to treat multiple diseases if analyzed.

Limitations

There are some limitations of the review. The review did not pay close attention to the stated phytoconstituents of the genus or their detailed mechanisms of action due to lack of enough evidences of exact mechanistic information.

Conclusion

Wendlandia, a genus with a rich traditional medicinal background, exerts diverse biological effects that align with its various therapeutic applications. Among *Wendlandia* species, certain species have broad spectrum of phyto-constituents and other reported as effective pharmacological effect. Behind in depth mechanism align with their pharmacokinetic profile study may be clarified further about it vast pharmacological action. Analyzing the chemicals in these compounds might lead to exciting possibilities for new medicines. Given the global revival of interest in herbal remedies, *Wendlandia* species offer a compelling option for various conditions like diabetes, obesity, hypertension, inflammation, cancer, menstrual irregularities, skin issues, and related disorders. Moreover, some *Wendlandia* species are utilized as dietary supplements and are considered safe for occasional consumption. However, more research is needed to determine how effective and safe it is to consume these plants long-term.

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