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The antibacterial potential and effects of *Rhodiola* sp. on gut microbiota

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Abstract The challenge of antimicrobial resistance requires new solutions, and *Rhodiola* sp. is a promising candidate due to its rich medicinal history. This review focuses on *Rhodiola* sp., especially *R. rosea*, highlighting its phytochemical constituents, such as salidroside, rosavins, and other phenolics, and their antimicrobial potential. We investigate the efficacy of *Rhodiola* sp. against various pathogenic bacteria, suggesting their value in combating antimicrobial resistance. Additionally, *Rhodiola* compounds are being investigated both as direct antimicrobials and as resistance modifiers that increase the efficacy of antibiotics. *Rhodiola* extracts and salidroside modulate gut microbiota, thereby affecting health and physiological and metabolic disorders. This illustrates the comprehensive therapeutic potential of *Rhodiola* sp. We emphasize the importance of understanding the complex interactions between *Rhodiola* phytochemicals, their antimicrobial effects, and their effects on gut microbiota as well as the need for in-depth research. Further studies will be crucial for the development of holistic treatment approaches. Finally, *Rhodiola* sp. is highlighted as an important natural resource in the fight against microbial pathogens and antibiotic resistance. Research on *Rhodiola* sp. should continue to further unravel pharmacological and health-promoting potential and thus address an important public health challenge.

Keywords *Rhodiola* sp. · Phytochemicals · Antimicrobial activity · Antimicrobial resistance · Gut microbiota · Herbal medicine

Introduction

During the last decade, *Rhodiola* plants have gained much attention, illustrated by around 150 publications every year (CAS SciFinder^{n} 2023). Species of the genus *Rhodiola* L. (Crassulaceae) are characterized as perennial herbs with rhizomes and usually fleshy persistent leaves (WFO 2023a). Their natural habitat spreads over the subarctic and subalpine northern hemisphere (PWO 2023). The number of reported species varies between 53 (WFO 2023a) and 72 (IPNI

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2023), and this variability is due to numerous species names being mentioned in the literature that are not accepted species names anymore. Several *Rhodiola* species have been reported for their traditional medicinal uses, including *R. rosea* L. (roseroot, golden rod), *R. kirilowii* (Regel) Maxim., *R. algida* (Ledeb.) Fisch. & C.A.Mey., *R. wallichiana* (Hook.) Fu, and *R. crenulata* (Hook.f. & Thomson) H.Ohba (Tao et al. 2019). The frequently mentioned species *R. sachalinensis* Boriss. and *R. imbricata* Edgew. are regarded as synonyms for *R. rosea* L. (WFO 2023b) and are thus not mentioned separately in this review. Similarly, *R. sacra* (Raym.-Hamet) Fu is a synonym for *R. chrysanthemifolia* subsp. *sacra* (Raym.-Hamet) H.Ohba, and thus the currently accepted name is used (WFO 2023c). The most well-known is roseroot, *R. rosea*; its rhizomes and roots are used as traditional herbal medicinal products to relieve symptoms of stress, such as fatigue and exhaustion (EMA 2023). Aside from these traditional uses, the chemistry (see "The phytochemistry of Rhodiola sp." section) of *Rhodiola* compounds implies potential antibacterial effects.

The worldwide spread of antibiotic resistance represents an alarming situation that calls for immediate action (WHO 2023). Natural plant products, including those discovered in *Rhodiola*, are increasingly recognized as promising agents to fight antibacterial resistance (Klančnik et al. 2021; Waditzer und Bucar 2021; Abdallah et al. 2023; Goncalves et al. 2023; Liu et al. 2023a). The antimicrobial activities of *Rhodiola* sp. should also be discussed in light of their impact on the complex microbial ecosystem in the digestive tract, i.e., gut microbiota (GM). The crucial role of GM in various physiological and immunological functions is being increasingly recognized, and thus the reported activities of *Rhodiola* sp. in this complex relationship between GM, health, and disease are covered by this review. Overall, the present review provides an overview of the current knowledge on *Rhodiola* extracts and compounds as antibacterials, research gaps, and perspectives for future developments towards *Rhodiola* antibacterial preparations.

The phytochemistry of *Rhodiola* sp.

The chemistry of *Rhodiola* species has been extensively studied in the last years (Chiang et al. 2015; Dong et al. 2023; Marchev et al. 2016, 2020; Michels et al. 2020; Langeder und Grienke 2021; Kunčič et al. 2022; Kosakowska et al. 2018; Tao et al. 2019; Olennikov et al. 2020). Quality control of *Rhodiola* roots and herbal medicinal products is still based on phenylethanoids (mainly salidroside) and phenylpropanoids (rosavins) (Marchev et al. 2020; Dimpfel et al. 2018). However, attempts are being made to expand the range of marker compounds by including flavonoids (Zomborszki et al. 2019). Additionally, the monoterpene alcohol glycoside rosiridin was shown to be present in significant amounts in *Rhodiola* plant material and medicinal products on the market (Langeder und Grienke 2021). Tang et al. (2023) revealed that rosiridin naturally occurs as two C-4 epimers based on one enantiomeric aglycone. The spectrum of activity of relevant *Rhodiola* phytochemicals is even wider, illustrated by recent studies on the memory-enhancing effect of long-chain feruloyl fatty alcohol esters such as ferulic acid eicosyl ester (FAE-20) (Michels et al. 2020, 2018). Kunčič et al. (2022) revealed that proanthocyanidins (including catechins such as epigallocatechin gallate (EGCG)) and flavonoid glycosides obtained from *R. rosea* crude ethanolic extracts exert inhibitory effects on *Campylobacter* intercellular signaling. This clearly indicates that several *Rhodiola* sp. phytochemicals are of relevance for quality control of *Rhodiola* plant material and products, and that current strategies focusing on only salidroside and rosavins should be re-evaluated. A list of the most frequently reported compound classes is provided in Table 1, and characteristic compounds of each class are presented in Fig. 1.

Medicinal uses of *Rhodiola* sp.

Among *Rhodiola* species, *R. rosea* has been most extensively studied in the context of traditional medicine. Detailed outlines of the long history of *R. rosea* in European and Asian materia medica have been presented by Anheyer et al. (2021) and Pannossian et al. (2010). The first written reports of medicinal uses of *R. rosea* even date back to ancient Greece. *Rhodiolae radix* ("*Rodia riza*") was mentioned by Dioscurides as an externally applied remedy against headache, an indication which is later frequently mentioned in herbal books of the Middle Ages and early modern age (Anheyer et al. 2021). Further

Table 1 Major compound classes identified in *Rhodiola* species

Compound class	Representative compounds	*Rhodiola* sp.	References
Phenylpropanoid glycosides	Cinnamyl alcohol glycosides (e.g., rosavin)	*R. crenulata, R. rosea, R. quadrifida*	Tao et al. (2019)
Phenylethanoids	Tyrosol glycosides (e.g., salidroside)	*R. crenulata, R. rosea, R. kirilowii, R. chrysanthemifolia* subsp. *sacra, R. quadrifida*	Tao et al. (2019)
Phenylmethanoids	Benzyl-*O*-β-D-glucopyranoside	*R. rosea*	Marchev et al. (2016)
Phenolic acids/ esters	Ferulic acid eicosyl ester	*R. rosea*	Michels et al. (2020)
Flavonoids—flavones	Herbacetin-, gossypetin-, kaempferol-, quercetin-, tricin-, hibiscetin-*O*-glycosides	*R. crenulata, R. rosea, R. quadrifida*	Tao et al. (2019), Kunčič et al. (2022), Langeder and Grienke (2021), Olennikov (2023), Olennikov et al. (2020)
Flavonoids—catechins	Epigallocatechin, epigallocatechin gallate	*R. crenulata, R. rosea, R. kirilowii, R. chrysanthemifolia* subsp. *sacra*	Kosakowska et al. (2018), Kunčič et al. (2022), Tao et al. (2019)
Oligomeric/ polymeric proanthocyanidins	Oligomers/polymers of epigallocatechin and its gallate esters	*R. crenulata, R. rosea, R. heterodonta, R. semenovii, R. kirilowii*	Kosakowska et al. (2018), Kunčič et al. (2022), Yousef et al. (2006)
Lignans/ flavonolignans	Aryl tetralin type lignans, dihydrobenzofuran neolignans, flavonolignans (rhodiolin)	*R. crenulata, R. rosea*	Yang et al. (2012), Zapesochnaya und Kurkin (1983)
Coumarins	Umbelliferone, scopoletin, 7-methoxycoumarin-6-aldehyde	*R. rosea, R. crenulata, R. chrysanthemifolia* subsp. *sacra, R. quadrifida*	Tao et al. (2019)
Cyanogenic glycosides	Lotaustralin, rhodiocyanoside A	*R. rosea*	Marchev et al. (2016)
Acyclic alcohol glycosides	Rhodiolosides A–F, geraniol-derived glycosides (e.g., (*4R*)/(*4S*)-rosiridin)	*R. rosea, R. renulata, R. chrysanthemifolia* subsp. *sacra*	Tao et al. (2019), Tang et al. (2023), Ma et al. (2006)
Essential oils	Geraniol, myrtenol, n-octanol, n-decanol, tetrahydronootkatone, *trans*-pinocarveol, linalool, phenylethanol, linalool oxide, cymene	*R. rosea*	Rohloff (2002), Galambosi et al. (2010), Evstatieva et al. (2010), Kosakowska et al. (2018), Michels et al. (2020), Jin et al. (2010)
	2-Methyl-3-buten-2-ol, n-octanol, geraniol	*R. crenulata*	Lei et al. (2004), Lei et al. (2003)

traditional indications include tumors, mental conditions ("hysteria"), liver disease, swellings, edema, hernias, discharges, and skin disorders, and the use of *R. rosea* as a stimulant and astringent (Panossian et al. 2010; Anheyer et al. 2021; Chiang et al. 2015). In the European Union, herbal medicinal products containing a dry extract (DER 1.5–5:1) of *R. rosea* rhizomes and roots (extracted by 67–70% ethanol (*v/v*)), are used to relieve symptoms of stress (e.g., fatigue and exhaustion) (EMA 2023). This indicates adaptogenic and stress-protective effects.

Recently, the pharmacological activities and mechanisms of action of *R. rosea* in chronic diseases have been reviewed (Bernatoniene et al. 2023). Furthermore, a critical review of the effectivity of *Rhodiola* preparations in enhancing exercise performance was

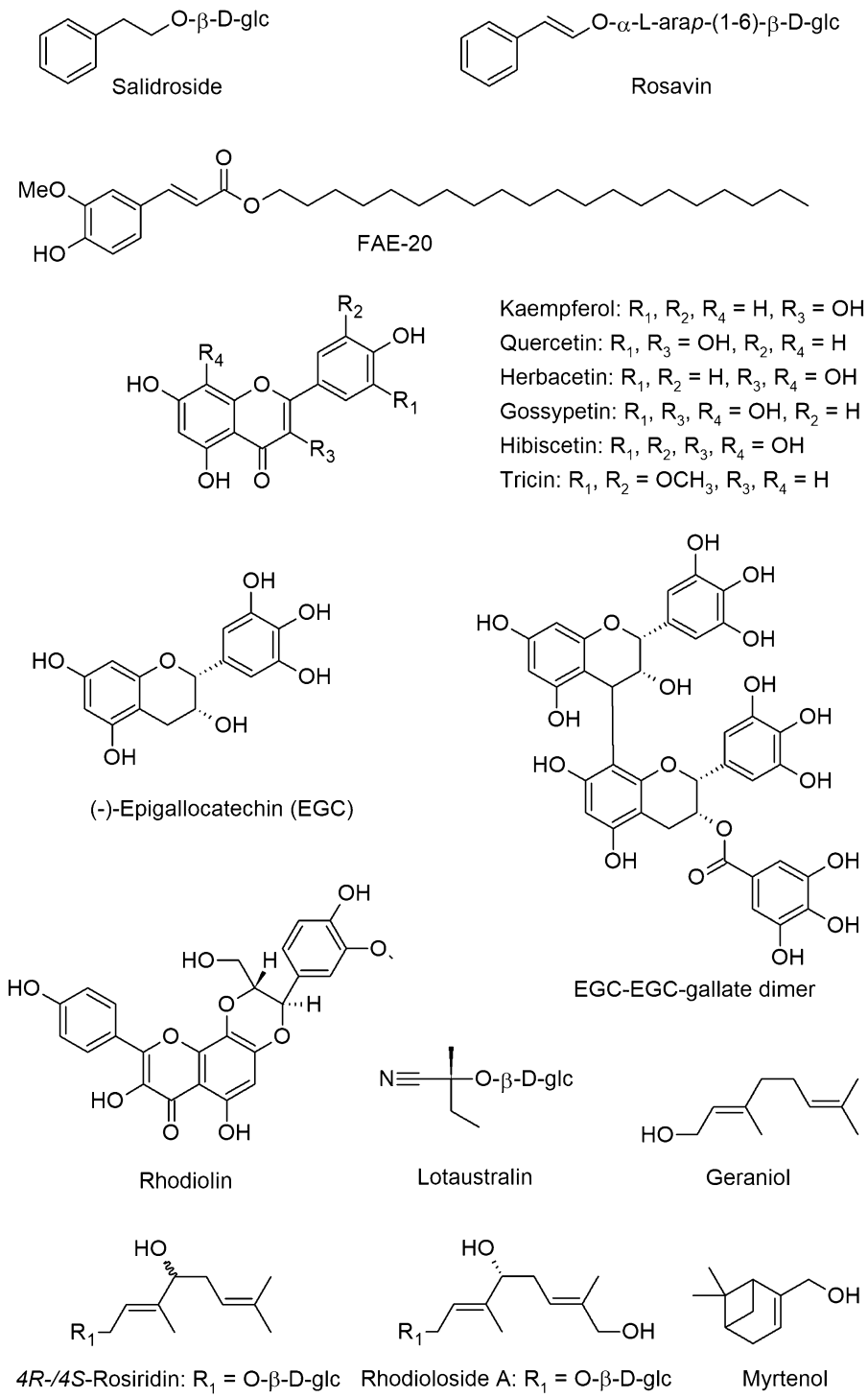

Fig. 1 Structures of *Rhodiola* sp. compounds. FAE-20: ferulic acid eicosyl ester

published (Tinsley et al. 2024). It concluded that they exhibit potential to enhance performance and performance-related outcomes for several types of exercise but that the findings were inconsistent, possibly due to variable preparations, doses, durations of administration, and patient cohorts (Tinsley et al. 2024). The

dose–response action of *Rhodiola* extracts and compounds was demonstrated to exhibit hormesis, i.e., a relationship in which low doses are beneficial, whereas high doses can even be toxic (Calabrese et al. 2023).

Key compounds for activities

Salidroside is considered a key *Rhodiola* compound that acts on the central nervous system (affecting Parkinson's disease and Alzheimer's disease) and heart (affecting atrial fibrosis and coronary heart disease) and attenuates hepatotoxic effects and oxidative stress (Jin et al. 2022; Hai et al. 2023; Gao et al. 2023; Li and Yao 2023; Liang et al. 2023a; Zhang et al. 2023; Tao et al. 2023). Additionally, rosavin (a cinnamyl alcohol glycoside) is regarded as a quality-determining compound, and its activities have been discussed by Wang et al. (2023). Another study identified FAE-20 and β-sitosterol glucoside as important *R. rosea* compounds for learning in *Drosophila melanogaster* larvae (Michels et al. 2020). The exhibited learning effect does not require known dopaminergic reward neurons and was also shown for synthetic FAE-20, not only in *Drosophila* but also in mouse models (Michels et al. 2018).

Aside from *R. rosea*, *R. crenulata* (used in traditional Tibetan medicine) has gained recent attention because of its pharmacological and medicinal effects. A 70% ethanolic extract of *R. crenulata* dried roots exhibited better regulating effects on senescence, which was correlated with antioxidant activities, in assays of senescence-associated β-galactosidase staining and lifespan in LO2 cells (Liang et al. 2023b). The strongest antibacterial effects were found for an ethyl acetate extract of *R. crenulata* roots; the ethyl acetate and crude ethanolic extract exhibited the highest antioxidant activities (Zhong et al. 2020).

Antibacterial activity of *Rhodiola* sp.

A variety of high-quality herbal medicines from *Rhodiola*, such as capsules, tablets, and oral liquids, are commercially available, reflecting the worldwide popularity of *Rhodiola* products (Furmanowa et al. 2002). Furthermore, *Rhodiola* root extracts are widely used in food additives and other commercial pharmaceutical preparations. This use indicates various potential applications of the plant, ranging from traditional medicine to modern pharmacology and the food industry (Nikoo et al. 2018). Numerous studies have investigated *Rhodiola* sp. bioactivity, each describing different potential beneficial effects, such as controlling microorganisms or influencing microbiota. The widespread use of *Rhodiola* sp. has led to the discovery of its numerous bioactive compounds. For example, Rattan et al. (2020) investigated the cultivation of *Rhodiola* sp. (e.g., *R. rosea*) in bioreactors to obtain higher metabolite yields and thus enable industrial applications. However, wild samples generally contain higher concentrations of bioactive compounds (Rattan et al. 2020).

Increasing antimicrobial resistance, fueled by the (over)use of antibiotics and the slow development of new antimicrobials, is emerging as a major global threat to healthcare, agriculture, food production, and environment. The World Health Organization (WHO) predicts that antibiotic resistance will be the leading cause of death worldwide by 2050, especially as the (over)use of antibiotics in human and veterinary medicine contributes to the spread of resistant pathogens (WHO 2023). Therefore, the urgency to find innovative alternative strategies has led to the exploration of natural alternatives, such as extracts and secondary metabolites from various plants, including *Rhodiola* sp., as potential antimicrobial agents (Zhong et al. 2020).

Rhodiola sp. are known for their diverse bioactive compounds, including phenols, phenylpropanoids, and flavonoids, as described in the previous section. The most studied compounds include salidroside, rosavin, and tyrosol, which are predominantly found in roots and rhizomes (Furmanowa et al. 2002; Peschel et al. 2013; Nikoo et al. 2018). Due to their unique bioactive profiles, *Rhodiola* sp. are promising candidates for developing novel antimicrobials and thereby addressing the challenges of antimicrobial resistance. Additionally, their bioactive compounds act as resistance-modifying agents that increase the efficacy of existing antibiotics. In the context of food safety, the antioxidant and antimicrobial properties of bioactive *Rhodiola* compounds may represent natural preservatives in the food industry, which is in line with the growing consumer preference for natural additives (Nikoo et al. 2018). Studies such as that by Kosakowska et al. (2018) have highlighted the antioxidant and antibacterial activities of *R. rosea*

ethanolic extracts, which are rich in phenolic compounds such as salidroside, tyrosol, and rosavin derivatives.

This review highlights the diverse research on antibacterial effects of *Rhodiola* sp., emphasizing the different species, plant parts, solvents, extracts, bioactive constituents, methods for determining antimicrobial activity, and target microorganisms (Table 2). The use of different parts of the *Rhodiola* plant, such as roots, rhizomes, and stems, has been a focus of research. For example, Furmanowa et al. (2002) investigated ethanolic extracts from *R. rosea* roots and rhizomes, whereas Ming et al. (2005) from dried stems.

Various solvents are used for extraction, including ethanol, water, n-hexane, ethyl acetate, and n-butanol. The choice of solvent influences the efficiency of the extraction and the resulting bioactivity of the compounds (Ming et al. 2005). Research has investigated both total extracts and specific fractions of *Rhodiola*. For example, fractions from ethanolic extracts, which are rich in distinctive bioactive compounds, have been investigated for their antibacterial properties (Kunčič et al. 2022). Various bioactive components in *Rhodiola* extracts, such as salidroside, rosavin, tyrosol, gossypetin-7-*O*-L-rhamnopyranoside, and rhodioflavonoside, have been identified and exhibit different levels of activity against microorganisms (Zaushintsena et al. 2020; Ming et al. 2005).

Methods such as liquid–liquid partitioning, disk diffusion tests, and minimum inhibitory concentration measurements, have been used to determine antimicrobial activity. These methods have provided insights into the efficacy of *Rhodiola* extracts against various microorganisms (Ming et al. 2005; Tsvetov et al. 2023), including the bacteria *Staphylococcus aureus* and *Acinetobacter baumannii* and fungi (Zaushintsena et al. 2020; Tsvetov et al. 2023). *R. rosea* extracts have been found to inhibit biofilm formation and extracellular polysaccharide synthesis in *Streptococcus mutans* and affect intercellular signaling in *Campylobacter jejuni* (Zhang et al. 2020; Šimunović et al. 2020). NADES-based *R. rosea* extracts showed bactericidal activity against cultures of *Micrococcus luteus, Pseudomonas fluorescens*, and *Bacillus subtilis*, highlighting the broad-spectrum antimicrobial potential of *Rhodiola* (Tsvetov et al. 2023). *Rhodiola* bioactive compounds have shown not only direct antimicrobial effects but also properties that alter resistance and increase the efficacy of existing antibiotics. Additionally, their antioxidant properties have potential applications in food safety as natural preservatives (Nikoo et al. 2018).

Mechanism of antibacterial action

Research on bioactive compounds from natural sources has uncovered a variety of substances with antimicrobial properties and has thus enabled decisive advances in combating microbes. However, these compounds exhibit diverse mechanisms of action, ranging from disruption of bacterial cell walls and microbial metabolism to interactions with microbial cell membranes and intracellular processes. This diversity in their modes of action underlines their potential for developing new approaches against microbial resistance and infection.

For example, certain *Rhodiola* compounds can disrupt bacterial cell walls and alter microbial metabolism, and thereby contributing to their antimicrobial efficacy. These compounds include salidroside and rosavin from *R. rosea* and *R. crenulata,* which showed antibacterial activity against *Propionibacterium acnes* and improved the survival rate of *D. melanogaster* by affecting the expression of antimicrobial peptide genes and decreasing the levels of reactive oxygen species (Ioset et al. 2011; Chiang et al. 2015). Other research has identified compounds with a broad spectrum of pharmacological activities, such as anti-inflammatory, antioxidant, and immunostimulatory effects, which are particularly effective against pathogens such as *Aeromonas hydrophila* by destroying bacterial cell walls and reducing virulence (Chiang et al. 2015; Chung et al. 2017; Zhang et al. 2021; Zhao et al. 2022a). In addition, some *Rhodiola* compounds have been shown to interfere with microbial cell processes and have improved antibacterial properties compared to conventional agents such as ferulic acid. This leads to the disruption of cell walls and biofilms, resulting in membrane hyperpolarization and leakage of cell contents (Chiang et al. 2015; Song et al. 2023). Their efficacy against multidrug-resistant strains is remarkable, particularly due to their ability to interact with microbial cell membranes, trigger cell lysis, and disrupt cytoplasmic membranes, thereby altering membrane permeability and stability (Chiang et al. 2015; Tagousop et al. 2018; Strugała et al. 2017).

Table 2 Antibacterial activity identified in *Rhodiola* species

Plant species	Plant material	Bioactive compounds	Effect (MIC/inhibition zone method)	Bacteria	Results (MIC/inhibition zone)	Broader spectrum of antibacterial actions	References
R. rosea	Ethanolic (96% *v/v*) extract of air-dried and powdered roots and rhizomes (E1) and callus from the 72nd (E2) and 97th passage (E3)	Salidroside, cinnamyl alcohol, rosavine	Growth inhibition (MIC/inhibition zone)	*Staphylococcus aureus*	E1: 100–150 μg/mL 11–15 mm E2: 100 μg/mL 10 mm E3: inactive	Not specified	Furmanowa et al. (2002)
R. rosea	Methanol extract of underground part; 95% ethanol extract of stems	Gossypetin-7-*O*-L-rhamnopyranoside (C1), rhodioflavonoside (C2), gallic acid, *trans-p*-hydroxycinnamic acid, *p*-tyrosol	Growth inhibition (MIC)	*Staphylococcus aureus*	C1: 50 μg/mL C2: 100 μg/mL	C1 and C2 exhibited activity against *S. aureus*	Ming et al. (2005)
R. rosea	Dried powdered underground organs, aqueous and ethanolic (60% *v/v*) dry extracts	Salidroside, tyrosol, rosarin, rosavins, rosin, *trans*-cinnamic alcohol, EO components	Broth microdilution method, MIC, minimum bactericidal concentration	*Staphylococcus aureus* *Bacillus subtilis* *Pseudomonas aeruginosa* *Escherichia coli* *Candida albicans* *Staphylococcus epidermidis* *Klebsiella pneumoniae* *Yersinia enterocolitica* *Shigella sonnei* *Proteus mirabilis* *Listeria monocytogenes* *Enterobacter aerogenes* *Salmonella* Enteritidis *Salmonella* Typhimurium	1–2 mg/mL 1–8 mg/mL 4–32 mg/mL 2–32 mg/mL 4–32 mg/mL 1–2 mg/mL 4 mg/mL 4–8 mg/mL 4–8 mg/mL 8–32 mg/mL 16–32 mg/mL 8–32 mg/mL 32 mg/mL 32–64 mg/mL	Antioxidant and antibacterial activity	Kosakowska et al. (2018)
R. rosea	Ethanolic extract (96% *v/v*) of dried powdered underground organs	Not specified	Antibacterial activity (MIC), QS reduction, decreased motility, adhesion to polystyrene surfaces, and adhesion and invasion reduction rates (%) of INT407 cells	*Campylobacter jejuni*	500 mg/L	Reduced QS by 96 ± 16% Decreased motility by 35 ± 8% Decreased adhesion to polystyrene by 96 ± 4% Decreased invasion of INT407 cells by 82 ± 7%	Šimunović et al. (2020)

Table 2 continued

Plant species	Plant material	Bioactive compounds	Effect (MIC/inhibition zone method)	Bacteria	Results (MIC/inhibition zone)	Broader spectrum of antibacterial actions	References
R. rosea	Ethanolic extract (75% *v/v*) of dried root	Not specified	Confocal laser scanning microscopy, crystal violet staining, CFU counting, SEM, qRT-PCR, and zymogram assay. Antibiofilm activity (/) inhibition of virulence genes	*Streptococcus mutans*	0.50 μg/μL and 0.25 μg/μL	Suppressed expression of gtf genes and QS, inhibited enzymatic activity of Gtf proteins, good biocompatibility with human cells, and inhibition of biofilm formation and extracellular polysaccharide synthesis	Zhang et al. (2020)
R. crenulata	Fresh rhizomes, dried powdered rhizomes, EO, and crude extracts (95% EE, PE, EA, BE, and WE extracts)	Major EO components: 1-octanol, geraniol, 6-methyl-5-hepten-2-ol BE: rich in phenols and flavonoids Identified EE compounds: gallic acid, ethyl gallate, rosavin, herbacetin	Antibacterial and antioxidant activities Hydrodistillation, GC–MS, solvent extraction, fractionation, micro-broth-dilution-colorimetric assay, DPPH radical scavenging, Fe^{2+} reducing power tests	*Shigella dysenteriae* *Escherichia coli* *Salmonella* Typhimurium *Staphylococcus aureus* *Streptomyces albus*	1.25 (EE)– > 5 mg/mL (PE/WE) 2.5 (EE, BE, CE)– > 5 mg/mL (PE/WE) 2.5 (EE)– > 5 mg/mL (PE, BE, WE, EO) 1.25 (EE)– > 5 mg/mL (PE, WE, EO) 1.25 (EE)– > 5 mg/mL (PE, WE, EO)	EO showed moderate inhibitory activity, and EE exhibited the strongest antibacterial activity among the extracts	Zhong et al. (2020)
R. rosea	Ethanolic extract (96% *v/v*) of roots and rhizomes. Two plant materials: "Rosavine" (R) and "Mattmark" (M)	Gallic acid, salidroside, rosavins, PACs, flavonoids (herbacetin glycosides)	Antibacterial activity (MIC), reduced intercellular signaling (%)	*Campylobacter jejuni*	Reduced autoinducer-2-mediated signaling R: 125–500 mg/L M: 62.5– > 1000 mg/L	R: 59% M: 48%	Kunčič et al. (2022)
	Fractions 1–5: F1 0%, F2 20%, F3 40%, F4 70% MeOH, F5 PVP + 50% MeOH	The fractions are rich in the following: gallic acid (F1); salidroside (F2); salidroside, rosavins, and PACs (F3); rosavins and flavonoids (F4); salidroside and rosavins with almost no PACs or flavonoids (F5)			Reduced autoinducer-2-mediated signaling and antimicrobial activity F1: 250– > 1000 mg/L F2: 125– > 1000 mg/L F3: 62.5–250 mg/L F4: 125–250 mg/L F5: 250–1000 mg/L	F3: 72–65% F4: 70–68% F5: 43–27%	

Table 2 continued

Plant species	Plant material	Bioactive compounds	Effect (MIC/inhibition zone method)	Bacteria	Results (MIC/inhibition zone)	Broader spectrum of antibacterial actions	References
R. rosea	NADES-based extracts of powdered rhizomes (choline chloride:malonic acid 1:1, choline chloride:malic acid 1:1, choline chloride:citric acid 1:1, and choline chloride:tartaric acid 2:1	Polyphenols (flavonoids and polyphenolic acids) including rosavin	Antibacterial activity studied using disc diffusion method and bacterial cultures Growth inhibition (inhibition zone, reduction of cell number)	*Micrococcus luteus* *Pseudomonas fluorescens* *Bacillus subtilis*	Not specifically quantified in the text; however, extracts showed significant bactericidal activity even at 0.5% concentration for most bacteria. Complete cell inhibition of *Micrococcus* sp. with 0.5% solution of all studied extracts	*M. luteus*: complete inhibition at low concentration *P. fluorescens*: bactericidal growth inhibition at low concentration *B. subtilis*: bactericidal activity observed for non-spore-forming bacteria at low concentration	Tsvetov et al. (2023)

MIC, minimum inhibitory concentration; QS, *quorum sensing*; EO, essential oil; EE, ethanol extract; PE, petroleum ether extract; EA, ethyl acetate extract; BE, n-butanol extract; WE, water extract; PACs, proanthocyanidins; NADES, Natural Deep Eutectic Solvents

Proanthocyanidins, which belong to the class of condensed tannins, have a sophisticated mode of action against microorganisms, primarily due to their structure as oligomers or polymers of monomeric flavan-3-ols, products of the flavonoid biosynthesis pathway. These phytochemicals, known for their potent antimicrobial properties, also provide a wide range of health benefits that include antioxidant, anticancer, antidiabetic, and neuroprotective effects, as detailed by Rauf et al. (2019).

Similarly, EGCG, a prominent component of *R. rosea*, is known for its versatile bioactive properties, which are particularly effective in combating bacterial growth and resistance. Its importance extends beyond microbial control to crucial aspects of food safety and preservation. EGCG shares its beneficial properties with other phenolic compounds such as epigallocatechin, gallic acid, and catechin (Zhang et al. 2022; Nikoo et al. 2018). These properties make EGCG and similar compounds valuable agents for addressing current public health and food safety challenges. The antibacterial effects of EGCG include binding to the peptidoglycan layers of Gram-positive bacteria and inducing oxidative stress in Gram-negative bacteria. It inhibits microbial efflux pumps, such as CmeABC and CmeDEF, in *Campylobacter*, which can restore the efficacy of macrolides in resistant strains (Nikoo et al. 2018; Smole Možina et al. 2011; Kurinčič et al. 2012). This aspect is particularly important as *C. jejuni* has shown resistance in food processing plants, leading to bacterial gastroenteritis and posing a challenge due to antibiotic resistance (Smole Možina et al. 2018; Taha-Abdelaziz et al. 2023). The potential of EGCG as a resistance-modifying agent, particularly in combination with novel antibiotics against *Campylobacter* strains, indicates new possibilities for its application in vitro and in vivo. This multi-faceted approach, ranging from direct interactions with bacteria to inhibition of efflux pumps, underlines the value of EGCG as an alternative to conventional antibiotics and requires further research to explore its full potential (Taha-Abdelaziz et al. 2023).

Recent advances in the fight against pathogens emphasize the effectiveness of natural antimicrobial formulations, particularly those combining organic acids and plant extracts. Studies such as those by Balta et al. (2021) and Kunčič et al. (2022) have highlighted the significant effect of such extracts on inhibiting *quorum sensing* in bacterial pathogens, particularly *C.*

jejuni. The ethanolic extract of *R. rosea* effectively disrupts autoinducer-2-mediated intercellular signaling in *C. jejuni*, a crucial pathway for bacterial communication and pathogenicity. This finding indicates the potential of *R. rosea* extracts as antimicrobial agents that can attenuate bacterial virulence. The study by Šimunović et al. (2020) further supports this idea, demonstrating that natural (including *R. rosea*) extracts reduce *quorum sensing* in *C. jejuni*, leading to reduced surface adhesion and invasion of host cells. A luxS-deficient *C. jejuni* mutant exhibited reduced biofilm formation, motility, and virulence, underscoring the critical role of *quorum sensing*, particularly autoinducer-2 signaling, in the pathogenicity of the bacterium. In addition, EGCG has been recognized as an effective modulator of antibiotic resistance (Klančnik et al. 2012) and inhibitor of *quorum sensing*. EGCG also inhibits biofilm formation and thus further enhances the antimicrobial potential of these natural extracts.

Overall, these studies suggest a comprehensive approach to combating microbial threats, utilizing compounds such as EGCG and the inhibitory effects of *R. rosea* extracts on *quorum sensing*. Despite promising results, further extensive research is needed to fully understand the therapeutic potential and specific antimicrobial actions of these compounds (Elgamoudi and Korolik 2021; Castillo et al. 2015; Klančnik et al. 2021). This line of research provides promising opportunities for developing innovative antimicrobial strategies using natural extracts.

Rhodiola sp. and the gut microbiota (GM)

The complex ecosystem of microbes in the digestive tract, known as GM, plays a crucial role in various physiological and immunological functions, and GM imbalance is associated with numerous diseases. This complex relationship between GM and health is reflected in the effects of natural compounds such as *Rhodiola* extracts and salidroside. Recent studies (summarized in Table 3) show that these compounds can significantly affect the composition and metabolism of GM, with implications for health and disease management.

For example, *R. crenulata* and *R. rosea* have been observed to alter GM in mice and *D. melanogaster*, leading to more favorable bacterial profiles and potential anti-ageing benefits. The effects of salidroside on GM in various disease models have been associated with improved gut health and decreased inflammation. These changes in GM composition correlate with improved physical performance and alleviated memory impairment in certain experimental models. Beyond the specific changes in GM, the broader pharmacological effects of *Rhodiola* extracts and salidroside include roles in metabolic, cardiovascular, and neurological disorders, which are often mediated by GM. The evidence for these interactions and their effects are briefly outlined in Table 3, which provides an overview of the current state of knowledge on how *Rhodiola* and salidroside affect GM and contribute to health and disease management.

The roles of GM in both health and disease have been extensively studied in recent decades. GM is instrumental in the digestion and absorption of nutrients, especially indigestible carbohydrates, the synthesis of short-chain fatty acids, vitamins, amino acids, and secondary bile acids; and many other physiological and immune functions. It is an essential component of the host's immune system and prevents pathogen colonization and allergy development. GM organisms can also significantly alter certain medications once ingested (Bull and Plummer 2014; Lynch and Pedersen 2016).

Aside from various phenolic compounds, *Rhodiola* sp. also contains cyanogenic glycosides, like lotaustralin (see Table 1). The mode of action of cyanogenic glycosides on microorganisms is closely linked to their enzymatic degradation, a process that mainly occurs in the human colon, an environment rich in GM. In this part of the digestive system, bacterial hydrolysis plays a crucial role in the degradation of cyanogenic glycosides and leads to the formation of hydrocyanic acid, which is known for its potential toxicity. This degradation involves two important steps: initial hydrolysis of cyanogenic glycosides to cyanohydrin and subsequent degradation to cyanide. Several factors influence the rate of cyanide production, including the presence of specific enzymes such as β-glucosidase, the sugar content in the glycoside molecule, and the stability of the cyanohydrin intermediate. Some cyanogenic glycosides (e.g., amygdalin, linustatin, and neolinustatin) are first hydrolyzed to simpler sugars (e.g., glucose), which then form compounds such as prunasin, linamarin, and lotaustralin. This process of hydrolysis and subsequent

Table 3 Review of recent studies of *Rhodiola* sp. extracts or its active compound salidroside (SAL) with evidenced effects on gut microbiota (GM)

The aim of the study	Effects on GM	Other proposed (potentially GM-mediated) effects	References
Effects of *Rhodiolae crenulatae radix et rhizoma* on the GM of mice	Increased abundance of *Lactobacillus* and *Bifidobacterium*; decreased pathogenic *Enterococcus* and *Escherichia coli*	Regulation of the digestive tract and stabilization of the GM community	Yang et al. (2015)
Effects and anti-ageing properties of *R. rosea* on the GM of *Drosophila melanogaster*	Altered microbial composition, including an increased and decreased abundance of *Acetobacter* and *Lactobacillales*, respectively	Potential anti-ageing mechanism that is related to GM composition, including changes in total culturable and quantifiable bacterial load	Labachyan et al. (2018)
Effects of *R. rosea* on the GM of diabetic (leptin receptor knockout (db/db)) mice and their influence on type 2 diabetes	Modest GM modulation with an increase in *Desulfovibrionales*; improved integrity of the intestinal barrier	Decreased LPS levels and inflammatory markers, improved fasting blood glucose levels, and altered insulin response	Jafari et al. (2022)
Effects and protective role of *R. crenulata* extract on DSS-induced colitis in mice	Prevention of intestinal dysbiosis; restoration of microbial richness and diversity; increase in *Lactobacillus* and *Bifidobacterium*; decrease in *Proteobacteria*, *Parasutterella*, and *Staphylococcus*	Alleviated pathological abnormalities in colonic mice, including increased colon length, improved colonic injury, reduced pro-inflammatory factors, and maintained intestinal barrier function by upregulating tight junction proteins (ZO-1 and occludin)	Wang et al. (2021)
Effects of *R. rosea* SAL on the GM of mice with furan-induced liver injury and its ameliorative effect on liver injury	Improved GM balance with more Bacteroidetes and LPS-suppressing genera (*Akkermansia, Roseburia*) and less LPS-producing *Proteobacteria* and pathogenic bacteria (*Blautia, Desulfovibrio, Sporobacter, Anaerofustis, Olsenella*)	Decreased systemic low-grade inflammation and LPS levels, protection against liver injury, attenuated hepatic oxidative injury, and regulated oxidative indices and cytokine levels	Yuan et al. (2019)
Effects of SAL on high-fat-diet-induced non-alcoholic steatohepatitis and its mechanism with a focus on the GM–bile acid–farnesoid X receptor (FXR) axis	Improved GM dysbiosis in mice, with an increase in norank_f_*Lachnospiraceae* and *Ruminiclostridium* spp. and a decrease in *Lactobacillus* and *Alloprevotella* spp.	Improved bile acid regulation, liver steatosis, triglyceride content, and serum inflammatory factors; reduced oxidative stress, inflammatory damage, and serum liver enzyme levels; and activation of FXR (which influences lipid metabolism and inflammation via the GM–bile acid–FXR axis)	Li et al. (2020)
Effects of SAL and TCM on AD in the SAMP8 mouse model and the role of the microbiota–gut–brain axis	Inverted ratio of Bacteroidetes to Firmicutes; decreased pathogenic groups (*Clostridiales_vadinBB60*, *Peptococcus*, *Streptococcus*, *Ruminococcaceae_UCG_009*). SAL improved intestinal barrier integrity, altered GM, and eliminated *Clostridiales* and *Streptococcaceae* (Xie et al. 2020). Evidence of gut dysbiosis compromising host immune responses, indicating the importance of GM in AD (Ma et al. 2023)	Reduced (hippocampus-dependent) memory impairment, toxic Aβ1 peptide deposition, microglial activation, and proinflammatory factor levels in the brain (Xie et al. 2020). Reference to GM as a target for the efficacy of TCM in treating AD (Ma et al. 2023)	Xie et al. (2020), Ma et al. (2023)

Table 3 continued

The aim of the study	Effects on GM	Other proposed (potentially GM-mediated) effects	References
Effects of SAL on GM disorders caused by excessive antibiotic intake and their regulation with different doses and durations	Improved GM recovery, richness, diversity, and community structure; increase in *Bacteroides*, *Actinobacteria*, *Parabacteroides*, *Dubosiella*, *Lactobacillus,* and *Bifidobacterium*; decrease in disease-related bacteria (norank_f_*Muribaculaceae*, *Helicobacter,* and *Ruminococcus*_torques_group)	SAL reshaped the GM and increased production of SCFAs, which correlated with improved intestinal health, decreased inflammatory cytokine levels, and restored intestinal barrier function. SAL at low doses was particularly effective in promoting probiotic proliferation and SCFA production	Sun et al. (2022)
Effects of SAL on the GM and iron metabolism of diabetic mice and its potential as an alternative therapy for diabetes	Altered GM composition, including an increased proportion of Bacteroidetes (*Bacteroides, Alistipes*) and a decreased proportion of *Lactobacillus* and pathogenic bacteria (*Enterobacter*)	Decreased blood glucose levels and amelioration of diabetic cardiomyopathy in diabetic db/db mice, with inhibited ferroptosis and iron accumulation. Regulation of glucose and iron metabolism by influencing the GM. *Lactobacillus* is associated with iron metabolism, indicating a potential therapeutic target	Shi et al. (2022)
Effects of SAL on the GM of diabetic mice (with type 2 diabetes) and its protective effects in the body	Altered GM composition and decreased abundances of *Candidatus arthromitus* and *Odoribacter* in diabetic mice; these genera were found to be potential targets for treating diabetes. SAL altered the diversity and function of the GM in db/db mice. It attenuated inflammatory damage, lipid accumulation, and inflammatory changes in diabetic liver	Decreased blood sugar levels; improved insulin sensitivity, body weight, and kidney, liver, and pancreas damage; attenuated inflammatory damage, lipid accumulation, and inflammatory changes in diabetic liver. *Candidatus arthromitus* and *Odoribacter*, important GM species in diabetes, could serve as potential therapeutic targets	Zhao et al. (2022b)
Effects of SAL on the GM of obese mice (high-fat-diet-induced obesity) and its role in alleviating obesity	SAL modulated intestinal dysbiosis; restored microbial community structure and diversity; decreased *Lachnospiraceae bacterium 28–4*, *Alistipes finegoldii*, and *Bacteroides sartorii*; alleviated high-fat-diet-induced obesity; reduced fat accumulation, liver inflammation, and metabolic endotoxemia; improved intestinal damage; and increased the expressions of mucin and tight junction proteins	Decreased weight gain and fat accumulation in the body and alleviated pathological intestinal damage, indicating that the beneficial effects of SAL on obese mice are related to GM regulation. The GM is partially improved by restoring the structure and diversity of the microbial community. A study on fecal microbiota transplantation confirmed the role of SAL in alleviating obesity symptoms	Liu et al. (2023c)

Table 3 continued

The aim of the study	Effects on GM	Other proposed (potentially GM-mediated) effects	References
Effects of SAL on the GM of colitic mice and its role in the alleviation of DSS-induced colitis	Improved GM structure; increased *Lactobacillus*; decreased *Dubosiella*, *Turicibacter*, *Alistipes,* and *Romboutsia*. SAL inhibited DSS-induced colitis in mice as evidenced by improvement in colon length, histology, and DAI score. SAL partially restored the GM of colitic mice	Inhibited intestinal damage and reduced pro-inflammatory macrophages, colitis, and intestinal inflammation in a GM-dependent manner. Both SAL and fecal microbiota transplantation affected the GM community by decreasing the abundance of certain bacteria (e.g., *Turicibacter, Alistipes,* and *Romboutsia*) and increasing the abundance of *Lactobacillus*. The anti-inflammatory effect of SAL was GM-dependent, as evidenced by its disappearance after applying antibiotics	Liu et al. (2023b)
Effects of SAL on the GM of colonic (DSS-induced) mice and its role in combating intestinal macrophage pyroptosis and dysbacteriosis-induced colonic Th17/Treg imbalance	Improved GM diversity and Th17/Treg ratio in DSS-induced mice, increased Firmicutes, inhibited upregulation of TREM1 and pyroptosis-related proteins in inflamed colons, suppressed LPS/ATP-induced pyroptosis of BMDMs, and downregulated TREM1 even when NLRP3 was inhibited	SAL protected against colitis by disrupting macrophage pyroptosis and Th17/Treg balance. SAL improved GM diversity and the Th17/Treg ratio, particularly increasing the abundance of Firmicutes. Transplantation of SAL-treated fecal bacteria into mice with depleted GM reproduced resistance to intestinal inflammation	Liu et al. (2023d)
Effects of SAL on the GM of mice during exercise (weight-bearing swimming) and its role in combating fatigue symptoms	Altered GM composition with increases in *Alistipes, Rikenellaceae, Parabacteroides,* and *Lactobacillus*. SAL-treated mice showed prolonged swimming time and increased respiratory enzyme activity after training, as well as higher species diversity and abundance in the Ex + SAL group, i.e., mice exposed to exercises and SAL	Improved physical performance, reduced fatigue, and prevented exercise-induced injuries in mice. Analysis of microbial function suggests that SAL may improve exercise-induced fatigue by modulating processes related to energy metabolism and GM composition	Zhu et al. (2023)
Rhodiola and SAL in the treatment of metabolic disorders	Not directly mentioned, focuses on the treatment of metabolic disorders	Multi-target effects on oxidative stress, inflammation, mitochondria, autophagy, cell death, and AMPK signaling in metabolic disorders	Bai et al. (2019)
Pharmacological advances of SAL in the treatment of metabolic and cardiovascular diseases	Not directly mentioned, focuses on metabolic and cardiovascular diseases	Improved glucose tolerance, insulin sensitivity, β-cells, and liver function and inhibited adipogenesis, inflammation, and oxidative stress	Zhao et al. (2021)
Pharmacological activities of *R. rosea* extracts and SAL	Not directly mentioned, focuses on stress-protective, anti-ageing, anti-inflammatory, and anti-cancer effects	Inhibited/activated the mTOR pathway, decreased angiogenesis, and increased neovascularization	Li et al. (2017)

Table 3 continued

The aim of the study	Effects on GM	Other proposed (potentially GM-mediated) effects	References
Understanding the enzymatic degradation of cyanogenic glycosides in the colon and its effects on intestinal microflora	Glycoside degradation leads to the formation of hydrocyanic acid by hydrolysis of the glycosides to cyanohydrin and then to cyanide, predominantly by the GM	Altered rate of cyanide production, depending on the presence of β-glucosidase enzymes, the sugar content in the glycoside molecule, and the stability of cyanohydrin. May have less severe effects on microorganisms than the theoretical toxicity of hydrocyanic acid	Cressey and Reeve (2019)
Pharmacological properties and synthesis of SAL	Not directly mentioned, focuses on a broad spectrum of pharmacological properties	Effects on the cardiovascular and central nervous system; anti-hypoxia, anti-fatigue, anti-ageing, anti-cancer, anti-inflammatory, anti-oxidant, anti-viral, anti-diabetic, anti-osteoporotic, and immunostimulant effects	Zhang et al. (2021)
Overview of the positive effects of *R. rosea* extract and its use in chronic diseases	Not directly mentioned	Potential in treating diabetes, cancer, cardiovascular, and neurological disorders	Bernatoniene et al. (2023)
Effects of SAL on memory impairment induced by long-term ethanol consumption in rats	Improved GM composition and diversity and increased abundance of *Actinobacteria*, *Bifidobacterium*, *Ligilactobacillus*, *Adlercreutzia,* and *Lactobacillus*	Improved memory in alcoholics possibly related to regulation of gut dysbiosis and hippocampal dysfunction	Jiao et al. (2023)

AD, Alzheimer's disease; DSS, dextran sulfate sodium; TCM, Traditional Chinese Medicine; LPS, Lipopolysaccharide; DAI, disease activity index; BMDMs, bone marrow-derived macrophages; SCFAs, short-chain fatty acids

cyanide production is inevitably associated with interactions with GM. Although the formation of hydrocyanic acid suggests high toxicity, the actual effects of cyanogenic glycosides on GM are generally less severe than theoretically predicted. This is due to the complex interplay of metabolic factors within the colon, highlighting the nuanced relationship between these glycosides and the GM environment (Cressey and Reeve 2019).

Moreover, imbalanced GM has been associated with pathological gastrointestinal conditions (e.g., inflammatory bowel disease and irritable bowel syndrome), colorectal cancer, systemic disease manifestations (e.g., type 2 diabetes and obesity), and chronic diseases (e.g., gastrointestinal, respiratory, liver, and cardiovascular diseases) (Fan and Pedersen 2021). Owing to complex bidirectional communication along the microbiota–gut–brain axis, GM is also crucial for brain function. In addition to physiological disorders, GM dysbiosis can also cause mental illness. Studies suggest that abnormal microbiota and microbiota–gut–brain dysfunction may directly cause mental disorders, as treating GM can alleviate anxiety/depression (Liang et al. 2018). The research gap is highlighted in recent reviews on the interactions between natural products and GM microorganisms, particularly in relation to mood disorders (Korczak et al. 2023; Pferschy-Wenzig et al. 2022). Future studies evaluating the efficacy of medicinal plants (known as adaptogens, e.g., *R. rosea*), their isolated compounds, or the postbiotic metabolites formed from them in the treatment of disease symptoms should consider the bidirectional interaction between phyto-constituents and GM microorganisms. This well-established bidirectional interaction can influence the efficacy of natural products in the treatment of various diseases (Wilson and Nicholson 2017). The proven examples of *R. rosea* and *R. crenulata* extracts and salidroside modulating host GM are listed in Table 3. These studies suggest that GM may mediate the therapeutic activity of *Rhodiola* preparations in alleviating disease symptoms as diverse as intestinal inflammation, metabolic syndromes, and neurodegenerative diseases and in exerting anti-fat effects.

Potential applications and future perspectives

The increasing resistance of bacteria to conventional antibiotics has drawn scientific attention to the potential of *Rhodiola* sp. extracts and their bioactive components as antibacterial agents. This line of research, underscored by studies by Altantsetseg et al. (2007), Kurinčič et al. (2012), Klančnik et al. (2021), and Zhang et al. (2022), is becoming increasingly important in addressing the challenges posed by antimicrobial resistance. A major advantage of using *Rhodiola* sp. or their derivatives lies in their natural origin, which represents a more organic and potentially safer alternative to synthetic additives, especially in the context of food safety and preservation. These natural antimicrobials improve the efficacy of existing antibiotics and provide a crucial solution to the problem of bacterial multidrug resistance. In addition, the use of *Rhodiola* sp. as additives in animal feed, disinfectants in packaging, and inhibitors of bacterial growth is becoming a promising strategy. As Elgamoudi and Korolik (2021) suggest, this approach not only ensures safer food production "from farm to fork" but can also improve the effectiveness of antibiotics in treating foodborne infections. However, despite these promising developments, more extensive research is still needed to fully understand the antibacterial mechanisms of *Rhodiola* sp. extracts and their active compounds, as emphasized by Zhang et al. (2022). Such further research is essential for maximizing the potential of *Rhodiola* sp. to combat bacterial resistance and improve food safety.

Recent research has investigated the use of plant-based nanoparticles as an innovative alternative to conventional antibiotics, particularly in the treatment of multi-drug-resistant bacterial infections. These nanoparticles, especially when derived from plants, have the advantage of being less toxic and more effective against bacterial pathogens. The development of antimicrobial nanotherapeutics using plant-derived nanoparticles has been characterized by their lower toxicity and environmental impact (Anand et al. 2022). A notable study by Singh et al. (2018) investigated the use of *R. rosea* extracts for the synthesis of gold and silver nanoparticles. These nanoparticles could inhibit the formation of biofilms by bacteria such as *Pseudomonas aeruginosa* and *Escherichia coli*. This research not only presents an environmentally friendly method of synthesizing nanoparticles but also highlights the stability and antimicrobial efficacy of these nanoparticles. The presence of bioactive *R. rosea* compounds on nanoparticle surfaces significantly enhances antimicrobial functionality and shows much promise for medical applications (Singh et al. 2018; Anand et al. 2022).

The further development of in vitro systems and bioreactor cultures for *Rhodiola* sp., as demonstrated in the work of Rattan et al. (2020) and Marchev et al. (2016), represents a sustainable and feasible method for improving the production of bioactive substances. This approach particularly focuses on *R. rosea* and the production of secondary metabolites with pharmaceutical value. Supported by an improved understanding of *R. rosea* biosynthetic pathways and enzymes involved in metabolite production, these biotechnological methods are very promising for the sustainable production of secondary metabolites. Furthermore, Chiang et al. (2015) underscore the anti-ageing and antioxidant properties of *Rhodiola* sp. and emphasize its potential for developing treatments or supplements that promote longevity and combat age-related diseases. This is consistent with research into in vitro *R. rosea* cultivation as a means of providing sustainable sources of these valuable secondary metabolites. The prospect of creating green cell factories for *Rhodiola* compounds not only promotes pharmaceutical development but is also in line with environmentally friendly practices in the cultivation and use of medicinal plants.

Furthermore, ongoing research highlights the need to further explore the antibacterial mechanisms of *Rhodiola* extracts and their active compounds, while emphasizing the need for safe and environmentally friendly methods for their use (Anand et al. 2022). Given that *Rhodiola* sp. often grow slowly and are endangered in their natural habitats, there is a growing need for alternative sustainable sources of important phytochemicals. This need can be met through bioengineering and sustainable production techniques, as proposed by Kasprzyk et al. (2022). For example, a study by Nikoo et al. (2018) investigated a modified EGCG molecule with improved solubility and antioxidant activity achieved by methods such as nano-encapsulation and spray drying.

Conducting toxicity studies in vitro and in animal models is essential to demonstrate the safety of *Rhodiola* products, especially when considering their

use in dietary supplements, food ingredients, and pharmaceuticals. As Nikoo et al. (2018) and Kasprzyk et al. (2022) emphasize, this research is crucial for ensuring the safe use of these compounds in human nutrition and therapy. These extracts are promising for the development of new drugs and dietary supplements, especially those with antitumor, antimicrobial, and antioxidant properties, thus expanding the scope of *Rhodiola* in health and medicine. The growing interest in *Rhodiola* sp. and promising results underline the need for continued research and development in this area. Such sustained efforts are crucial to fully exploit the potential of *Rhodiola* sp. in medicine and biotechnology.

Conclusions

Our research on *Rhodiola* sp. shows a unique integration of traditional herbal knowledge and advanced pharmacological research. Species such as *R. rosea* and *R. imbricata* are rich sources of bioactive compounds, particularly salidrosides, rosavins, and phenolics, which have significant antimicrobial potential. These phytochemicals are effective against a broad spectrum of pathogenic microorganisms and thus importantly contribute to global efforts to combat antibiotic resistance. Additionally, these compounds are not only potent antimicrobials but also serve as resistance-modifying agents that can increase the efficacy of existing antibiotics. This dual role of *Rhodiola* compounds offers promising opportunities for developing innovative antimicrobial strategies and therapies. In addition to their antimicrobial properties, a key aspect of the therapeutic potential of *Rhodiola* sp. lies in their effects on GM. The modulation of GM by *Rhodiola* extracts and their active constituents (e.g., salidroside) affects health in general. Changes in GM composition correlate with improved physiological and metabolic conditions, underlining the comprehensive health benefits of *Rhodiola* sp.

This review has revealed a clear need for more in-depth research. Future studies should explore the complex interactions between the antimicrobial effects and effects on GM of *Rhodiola* phytochemical constituents. This research is crucial for the development of holistic treatment approaches that fully utilize the phytochemical spectrum of *Rhodiola* sp. Overall, *Rhodiola* sp. represents a significant natural resource in the ongoing fight against microbial pathogens and antimicrobial resistance, offering a versatile approach to health and well-being. Its rich phytochemical profile combined with its effect on GM makes it a valuable candidate for future pharmacological applications and health management strategies.

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References

Abdallah EM, Alhatlani BY, de Paula Menezes R, Martins CHG (2023) Back to nature: medicinal plants as promising sources for antibacterial drugs in the post-antibiotic era. Plants (basel) 12(17):3077. https://doi.org/10.3390/plants12173077

Altantsetseg K, Przybyl JL, Weglarz Z, Geszprych A (2007) Content of biologically active compounds in roseroot (*Rhodiola* sp.) raw material of different derivation. Herba Pol 53(4):20–26

Anand U, Carpena M, Kowalska-Góralska M, Garcia-Perez P, Sunita K, Bontempi E et al (2022) Safer plant-based nanoparticles for combating antibiotic resistance in bacteria: a comprehensive review on its potential applications, recent advances, and future perspective. Sci Total Environ 821:153472. https://doi.org/10.1016/j.scitotenv.2022.153472

Anheyer D, Schröter M, Dobos G, Cramer H (2021) Traditionelle nutzung von Arzneimitteln aus *Rhodiola rosea* (Rosenwurz). Z Phytother 42(06):280–291. https://doi.org/10.1055/a-1540-9820

Bai X-L, Deng X-L, Wu G-J, Li W-J, Jin S (2019) *Rhodiola* and salidroside in the treatment of metabolic disorders. Mini Rev Med Chem 19(19):1611–1626. https://doi.org/10.2174/1389557519666190903115424

Balta I, Linton M, Pinkerton L, Kelly C, Stef L, Pet I et al (2021) (2021) The effect of natural antimicrobials against *Campylobacter* spp. and its similarities to *Salmonella* spp., *Listeria* spp., *Escherichia coli*, *Vibrio* spp., *Clostridium* spp. and *Staphylococcus* spp. Food Control 121:107745. https://doi.org/10.1016/j.foodcont.2020.107745

Bernatoniene J, Jakstas V, Kopustinskiene DM (2023) Phenolic compounds of *Rhodiola rosea* L. as the potential alternative therapy in the treatment of chronic diseases. Int J Mol Sci 24(15):12293. https://doi.org/10.3390/ijms241512293

Bull MJ, Plummer NT (2014) Part 1: the human gut microbiome in health and disease. Integr Med (encinitas) 13(6):17–22

Calabrese EJ, Dhawan G, Kapoor R, Agathokleous E, Calabrese V (2023) *Rhodiola rosea* and salidroside commonly induce hormesis, with particular focus on longevity and neuroprotection. Chem Biol Interact 380:110540. https://doi.org/10.1016/j.cbi.2023.110540

Castillo S, Heredia N, García S (2015) 2(5H)-Furanone, epigallocatechin gallate, and a citric-based disinfectant disturb quorum-sensing activity and reduce motility and biofilm formation of *Campylobacter jejuni*. Folia Microbiol (praha) 60(1):89–95. https://doi.org/10.1007/s12223-014-0344-0

Chiang H-M, Chen H-C, Wu C-S, Wu P-Y, Wen K-C (2015) *Rhodiola* plants: chemistry and biological activity. J Food Drug Anal 23(3):359–369. https://doi.org/10.1016/j.jfda.2015.04.007

Chung D, Kim SY, Ahn J-H (2017) Production of three phenylethanoids, tyrosol, hydroxytyrosol, and salidroside, using plant genes expressing in *Escherichia coli*. Sci Rep 7(1):2578. https://doi.org/10.1038/s41598-017-02042-2

Cressey P, Reeve J (2019) Metabolism of cyanogenic glycosides: a review. Food Chem Toxicol 125:225–232. https://doi.org/10.1016/j.fct.2019.01.002

Dimpfel W, Schombert L, Panossian AG (2018) Assessing the quality and potential efficacy of commercial extracts of *Rhodiola rosea* L. by analyzing the salidroside and rosavin content and the electrophysiological activity in hippocampal long-term potentiation, a synaptic model of memory. Front Pharmacol 9:425. https://doi.org/10.3389/fphar.2018.00425

Dong T, Liu H, Sha Y, Sun L (2023) A comparative study of phytochemical metabolites and antioxidant properties of *Rhodiola*. Arab J Chem 16(1):104420. https://doi.org/10.1016/j.arabjc.2022.104420

Elgamoudi BA, Korolik V (2021) *Campylobacter* biofilms: potential of natural compounds to disrupt *Campylobacter jejuni* transmission. Int J Mol Sci 22(22):12159. https://doi.org/10.3390/ijms222212159

EMA (2023) European Union herbal monograph on *Rhodiola rosea* L., rhizoma et radix. https://www.ema.europa.eu/en/medicines/herbal/rhodiolae-roseae-rhizoma-et-radix

Evstatieva L, Todorova M, Antonova D, Staneva J (2010) Chemical composition of the essential oils of *Rhodiola rosea* L. of three different origins. Pharmacogn Mag 6(24):256–258. https://doi.org/10.4103/0973-1296.71782

Fan Y, Pedersen O (2021) Gut microbiota in human metabolic health and disease. Nat Rev Microbiol 19(1):55–71. https://doi.org/10.1038/s41579-020-0433-9

Furmanowa M, Starosciak B, Lutomski J, Kozlowski J, Urbanska N, Krajewska-Patan A et al (2002) Antimicrobial effect of *Rhodiola rosea* L. roots and callus extracts on some strains of *Staphylococcus aureus*. Herba Pol 48(1):23–31

Galambosi B, Galambosi Z, Hethelyi E, Szoke E, Volodin V, Poletaeva I, Iljina I (2010) Importance and quality of roseroot (*Rhodiola rosea* L.) growing in the European North. Z Arznei- Gewuerzpflanzen 15(4):160–169

Gao Z, Zhan H, Zong W, Sun M, Linghu L, Wang G et al (2023) Salidroside alleviates acetaminophen-induced hepatotoxicity via Sirt1-mediated activation of Akt/Nrf2 pathway and suppression of NF-κB/NLRP3 inflammasome axis. Life Sci 327:121793. https://doi.org/10.1016/j.lfs.2023.121793

Gonçalves ASC, Leitão MM, Simões M, Borges A (2023) The action of phytochemicals in biofilm control. Nat Prod Rep 40(3):595–627. https://doi.org/10.1039/D2NP00053A

Hai Z, Wu Y, Ning Z (2023) Salidroside attenuates atrial fibrosis and atrial fibrillation vulnerability induced by angiotensin-II through inhibition of LOXL2-TGF-β1-Smad2/3 pathway. Heliyon 9(11):e21220. https://doi.org/10.1016/j.heliyon.2023.e21220

Ioset KN, Nyberg NT, van Diermen D, Malnoe P, Hostettmann K, Shikov AN, Jaroszewski JW (2011) Metabolic profiling of *Rhodiola rosea* rhizomes by ^{1}H NMR spectroscopy. Phytochem Anal 22(2):158–165. https://doi.org/10.1002/pca.1262

IPNI (2023) The international plant names index and world checklist of vascular plants. http://www.ipni.org and https://powo.science.kew.org/

Jafari M, Juanson Arabit JG, Courville R, Kiani D, Chaston JM, Nguyen CD et al (2022) The impact of *Rhodiola rosea* on biomarkers of diabetes, inflammation, and microbiota in a leptin receptor-knockout mouse model. Sci Rep 12(1):10581. https://doi.org/10.1038/s41598-022-14241-7

Jiao Y, Zhao Z, Li X, Li L, Xiao D, Wan S et al (2023) Salidroside ameliorates memory impairment following long-term ethanol intake in rats by modulating the altered intestinal microbiota content and hippocampal gene expression. Front Microbiol 14:1172936. https://doi.org/10.3389/fmicb.2023.1172936

Jin Y, Park DW, Li X, Li D, Row KH (2010) Primary study of volatiles composition of *Rhodiola sachalinensis* by using gas chromatography and mass spectrometry (GC/MS). Korean J Chem Eng 27(4):1262–1268. https://doi.org/10.1007/s11814-010-0170-2

Jin M, Wang C, Xu Y, Zhang Z, Wu X, Ye R et al (2022) Pharmacological effects of salidroside on central nervous system diseases. Biomed Pharmacother 156:113746. https://doi.org/10.1016/j.biopha.2022.113746

Kasprzyk PG, Vickery C, Ye M, Sewastianik M, Gong W, Ding S et al (2022) Safety of a sustainably produced, bioengineered, nature-identical salidroside compound. Nutrients 14(11):2330. https://doi.org/10.3390/nu14112330

Klančnik A, Možina SS, Zhang Q (2012) Anti-*Campylobacter* activities and resistance mechanisms of natural phenolic compounds in *Campylobacter*. PLoS ONE 7(12):e51800. https://doi.org/10.1371/journal.pone.0051800

Klančnik A, Šimunović K, Sterniša M, Ramić D, Smole Možina S, Bucar F (2021) Anti-adhesion activity of phytochemicals to prevent *Campylobacter jejuni* biofilm formation on abiotic surfaces. Phytochem Rev 20(1):55–84. https://doi.org/10.1007/s11101-020-09669-6

Korczak M, Pilecki M, Granica S, Gorczynska A, Pawłowska KA, Piwowarski JP (2023) Phytotherapy of mood disorders in the light of microbiota-gut-brain axis. Phytomedicine 111:154642. https://doi.org/10.1016/j.phymed.2023.154642

Kosakowska O, Bączek K, Przybył JL, Pióro-Jabrucka E, Czupa W, Synowiec A et al (2018) Antioxidant and antibacterial activity of roseroot (*Rhodiola rosea* L.) dry extracts. Molecules 23(7):1767. https://doi.org/10.3390/molecules23071767

Kunčič A, Bucar F, Smole Možina S (2022) *Rhodiola rosea* reduces intercellular signaling in *Campylobacter jejuni*. Antibiotics (basel) 11(9):1220. https://doi.org/10.3390/antibiotics11091220

Kurinčič M, Klančnik A, Smole Možina S (2012) Epigallocatechin gallate as a modulator of *Campylobacter* resistance to macrolide antibiotics. Int J Antimicrob Agents 40(5):467–471. https://doi.org/10.1016/j.ijantimicag.2012.07.015

Labachyan KE, Kiani D, Sevrioukov EA, Schriner SE, Jafari M (2018) The impact of *Rhodiola rosea* on the gut microbial community of *Drosophila melanogaster*. Gut Pathog 10:12. https://doi.org/10.1186/s13099-018-0239-8

Langeder J, Grienke U (2021) A supercritical fluid workflow for the quality assessment of herbal drugs and commercial preparations from *Rhodiola rosea*. Phytochem Anal 32(6):982–991. https://doi.org/10.1002/pca.3040

Lei Y, Nan P, Tsering T, Bai Z, Tian C, Zhong Y (2003) Chemical composition of the essential oils of two *Rhodiola* species from Tibet. Z Naturforsch C J Biosci 58(3–4):161–164. https://doi.org/10.1515/znc-2003-3-402

Lei Y, Peng N, Tsering T, Wang L, Liu S, Zhong Y (2004) Interpopulation variability of rhizome essential oils in *Rhodiola crenulata* from Tibet and Yunnan. China Biochem Syst Ecol 32(6):611–614. https://doi.org/10.1016/j.bse.2003.10.007

Li L, Yao W (2023) The therapeutic potential of salidroside for Parkinson's disease. Planta Med 89(4):353–363. https://doi.org/10.1055/a-1948-3179

Li Y, Pham V, Bui M, Di Song L, Wu C, Walia A et al (2017) *Rhodiola rosea* L: an herb with anti-stress, anti-aging, and immunostimulating properties for cancer chemoprevention. Curr Pharmacol Rep 3(6):384–395. https://doi.org/10.1007/s40495-017-0106-1

Li H, Xi Y, Xin X, Tian H, Hu Y (2020) Salidroside improves high-fat diet-induced non-alcoholic steatohepatitis by regulating the gut microbiota-bile acid-farnesoid X receptor axis. Biomed Pharmacother 124:109915. https://doi.org/10.1016/j.biopha.2020.109915

Liang S, Wu X, Hu X, Wang T, Jin F (2018) Recognizing depression from the microbiota-gut-brain axis. Int J Mol Sci 19(6):1592. https://doi.org/10.3390/ijms19061592

Liang Q, Guo R, Tsao J-R, He Y, Wang C, Jiang J et al (2023a) Salidroside alleviates oxidative stress in dry eye disease by activating autophagy through AMPK-Sirt1 pathway. Int Immunopharmacol 121:110397. https://doi.org/10.1016/j.intimp.2023.110397

Liang T, Zhou J, Jing P, He Z, Jiao S, Zhao W et al (2023b) Anti-senescence effects of *Rhodiola crenulata* extracts on LO2 cells and bioactive compounds. J Ethnopharmacol 306:116179. https://doi.org/10.1016/j.jep.2023.116179

Liu C, Dong S, Wang X, Xu H, Yang X, Wu S et al (2023a) Research progress of polyphenols in nanoformulations for antibacterial application. Mater Today Bio 21:100729. https://doi.org/10.1016/j.mtbio.2023.100729

Liu J, Cai J, Fan P, Dong X, Zhang N, Tai J, Cao Y (2023b) Salidroside alleviates dextran sulfate sodium-induced colitis in mice by modulating the gut microbiota. Food Funct 14(16):7506–7519. https://doi.org/10.1039/d3fo01929b

Liu J, Cai J, Fan P, Dong X, Zhang N, Tai J, Cao Y (2023c) Salidroside protects mice from high-fat diet-induced obesity by modulating the gut microbiota. Int Immunopharmacol 120:110278. https://doi.org/10.1016/j.intimp.2023.110278

Liu X, Zhou M, Dai Z, Luo S, Shi Y, He Z, Chen Y (2023d) Salidroside alleviates ulcerative colitis via inhibiting macrophage pyroptosis and repairing the dysbacteriosis-associated Th17/Treg imbalance. Phytother Res 37(2):367–382. https://doi.org/10.1002/ptr.7636

Lynch SV, Pedersen O (2016) The human intestinal microbiome in health and disease. N Engl J Med 375(24):2369–2379. https://doi.org/10.1056/NEJMra1600266

Ma G, Li W, Dou D, Chang X, Bai H, Satou T et al (2006) Rhodiolosides A-E, monoterpene glycosides from *Rhodiola rosea*. Chem Pharm Bull (tokyo) 54(8):1229–1233. https://doi.org/10.1248/cpb.54.1229

Ma L, Jiang X, Huang Q, Chen W, Zhang H, Pei H et al (2023) Traditional Chinese medicine for the treatment of Alzheimer's disease: a focus on the microbiota–gut–brain axis. Biomed Pharmacother 165:115244. https://doi.org/10.1016/j.biopha.2023.115244

Marchev AS, Dinkova-Kostova AT, György Z, Mirmazloum I, Aneva IY, Georgiev MI (2016) *Rhodiola rosea* L.: from golden root to green cell factories. Phytochem Rev 15(4):515–536. https://doi.org/10.1007/s11101-016-9453-5

Marchev AS, Koycheva IK, Aneva IY, Georgiev MI (2020) Authenticity and quality evaluation of different *Rhodiola* species and commercial products based on NMR-spectroscopy and HPLC. Phytochem Anal 31(6):756–769. https://doi.org/10.1002/pca.2940

Michels B, Zwaka H, Bartels R, Lushchak O, Franke K, Endres T et al (2018) Memory enhancement by ferulic acid ester across species. Sci Adv 4(10):eaat6994. https://doi.org/10.1126/sciadv.aat6994

Michels B, Franke K, Weiglein A, Sultani H, Gerber B, Wessjohann LA (2020) Rewarding compounds identified from the medicinal plant *Rhodiola rosea*. J Exp Biol 223(16):jeb223982. https://doi.org/10.1242/jeb.223982

Ming DS, Hillhouse BJ, Guns ES, Eberding A, Xie S, Vimalanathan S, Towers GHN (2005) Bioactive compounds from *Rhodiola rosea* (Crassulaceae). Phytother Res 19(9):740–743. https://doi.org/10.1002/ptr.1597

Nikoo M, Regenstein JM, Ahmadi Gavlighi H (2018) Antioxidant and antimicrobial activities of (-)-epigallocatechin-3-gallate (EGCG) and its potential to preserve the quality and

safety of foods. Compr Rev Food Sci Food Saf 17(3):732–753. https://doi.org/10.1111/1541-4337.12346

Olennikov DN (2023) New metabolites of *Rhodiola rosea*. II. Hibiscetin glycosides. Chem Nat Compd 59(2):254–258. https://doi.org/10.1007/s10600-023-03969-x

Olennikov DN, Chirikova NK, Vasilieva AG, Fedorov IA (2020) LC-MS profile, gastrointestinal and gut microbiota stability and antioxidant activity of *Rhodiola rosea* herb metabolites: a comparative study with subterranean organs. Antioxidants (basel) 9(6):526. https://doi.org/10.3390/antiox9060526

Panossian A, Wikman G, Sarris J (2010) Rosenroot (*Rhodiola rosea*): traditional use, chemical composition, pharmacology and clinical efficacy. Phytomedicine 17(7):481–493. https://doi.org/10.1016/j.phymed.2010.02.002

Peschel W, Prieto JM, Karkour C, Williamson EM (2013) Effect of provenance, plant part and processing on extract profiles from cultivated European *Rhodiola rosea* L. for medicinal use. Phytochemistry 86:92–102. https://doi.org/10.1016/j.phytochem.2012.10.005

Pferschy-Wenzig E-M, Pausan MR, Ardjomand-Woelkart K, Röck S, Ammar RM, Kelber O et al (2022) Medicinal plants and their impact on the gut microbiome in mental health: a systematic review. Nutrients 14(10):2111. https://doi.org/10.3390/nu14102111

PWO (2023) Plants of the World online. https://powo.science.kew.org/taxon/urn:lsid:ipni.org:names:30061153-2

Rattan S, Sood A, Kumar P, Kumar A, Kumar D, Warghat AR (2020) Phenylethanoids, phenylpropanoids, and phenolic acids quantification vis-à-vis gene expression profiling in leaf and root derived callus lines of *Rhodiola imbricata* (Edgew.). Ind Crops Prod 154:112708. https://doi.org/10.1016/j.indcrop.2020.112708

Rauf A, Imran M, Abu-Izneid T, Iahtisham-Ul-Haq PS, Pan X et al (2019) Proanthocyanidins: a comprehensive review. Biomed Pharmacother 116:108999. https://doi.org/10.1016/j.biopha.2019.108999

Rohloff J (2002) Volatiles from rhizomes of *Rhodiola rosea* L. Phytochemistry 59(6):655–661. https://doi.org/10.1016/s0031-9422(02)00004-3

CAS SciFinder^{n} (2023) CAS, American Chemical Society. https://scifinder-n.cas.org/

Shi J, Zhao Q, Hao DD, Miao HX, Wan S, Zhou CH et al (2022) Gut microbiota profiling revealed the regulating effects of salidroside on iron metabolism in diabetic mice. Front Endocrinol (lausanne) 13:1014577. https://doi.org/10.3389/fendo.2022.1014577

Šimunović K, Ramić D, Xu C, Smole Možina S (2020) Modulation of *Campylobacter jejuni* motility, adhesion to polystyrene surfaces, and invasion of INT407 cells by *quorum-sensing* inhibition. Microorganisms 8(1):104. https://doi.org/10.3390/microorganisms8010104

Singh P, Pandit S, Beshay M, Mokkapati VRSS, Garnaes J, Olsson ME et al (2018) Anti-biofilm effects of gold and silver nanoparticles synthesized by the *Rhodiola rosea* rhizome extracts. Artif Cells Nanomed Biotechnol 46(-sup3):S886–S899. https://doi.org/10.1080/21691401.2018.1518909

Smole Možina S, Kurinčič M, Klančnik A, Mavri A (2011) *Campylobacter* and its multi-resistance in the food chain. Trends Food Sci Technol 22(2):91–98. https://doi.org/10.1016/j.tifs.2010.09.003

Smole Možina S, Klančnik A, Kovac J, Jeršek B, Bucar F (2018) Antimicrobial natural products against *Campylobacter*. In: Mérillon J-M, Riviere C (eds) Natural antimicrobial agents. Springer, Cham, pp 3–30. https://doi.org/10.1007/978-3-319-67045-4_1

Song W, Xin J, Yu C, Xia C, Pan Y (2023) Alkyl ferulic acid esters: evaluating their structure and antibacterial properties. Front Microbiol 14:1135308. https://doi.org/10.3389/fmicb.2023.1135308

Strugała P, Tronina T, Huszcza E, Gabrielska J (2017) Bioactivity in vitro of quercetin glycoside obtained in *Beauveria bassiana* culture and its interaction with liposome membranes. Molecules 22(9):1520. https://doi.org/10.3390/molecules22091520

Sun T, Yang J, Lu L (2022) Salidroside improves antibiotic-induced gut microbiota disturbance and low levels of short-chain fatty acids in mice. Foods 11(19):3073. https://doi.org/10.3390/foods11193073

Tagousop CN, Tamokou J-D, Ekom SE, Ngnokam D, Voutquenne-Nazabadioko L (2018) Antimicrobial activities of flavonoid glycosides from *Graptophyllum grandulosum* and their mechanism of antibacterial action. BMC Complement Altern Med 18(1):252. https://doi.org/10.1186/s12906-018-2321-7

Taha-Abdelaziz K, Singh M, Sharif S, Sharma S, Kulkarni RR, Alizadeh M et al (2023) Intervention strategies to control *Campylobacter* at different stages of the food chain. Microorganisms 11(1):113. https://doi.org/10.3390/microorganisms11010113

Tang Y, Friesen JB, Lankin DC, McAlpine JB, Nikolić D, Chen S-N, Pauli GF (2023) Geraniol-derived monoterpenoid glucosides from *Rhodiola rosea*: resolving structures by QM-HifSA methodology. J Nat Prod 86(2):256–263. https://doi.org/10.1021/acs.jnatprod.2c00836

Tao H, Wu X, Cao J, Peng Y, Wang A, Pei J et al (2019) Rhodiola species: a comprehensive review of traditional use, phytochemistry, pharmacology, toxicity, and clinical study. Med Res Rev 39(5):1779–1850. https://doi.org/10.1002/med.21564

Tao L, Liang Z-F, Miao L, Guo Y-J, Li Y, Liu Y-L et al (2023) Mechanism of salidroside against coronary artery disease by network pharmacology analysis. BMC Complement Med Ther 23(1):194. https://doi.org/10.1186/s12906-023-04027-3

Tinsley GM, Jagim AR, Potter GDM, Garner D, Galpin AJ (2024) *Rhodiola rosea* as an adaptogen to enhance exercise performance: a review of the literature. Br J Nutr 131(3):461–473. https://doi.org/10.1017/S0007114523001988

Tsvetov N, Paukshta O, Fokina N, Volodina N, Samarov A (2023) Application of natural deep eutectic solvents for extraction of bioactive components from *Rhodiola rosea* (L.). Molecules 28(2):912. https://doi.org/10.3390/molecules28020912

Waditzer M, Bucar F (2021) Flavonoids as inhibitors of bacterial efflux pumps. Molecules 26(22):6904. https://doi.org/10.3390/molecules26226904

Wang Y, Tao H, Huang H, Xiao Y, Wu X, Li M et al (2021) The dietary supplement *Rhodiola crenulata* extract alleviates

dextran sulfate sodium-induced colitis in mice through anti-inflammation, mediating gut barrier integrity and reshaping the gut microbiome. Food Funct 12(7):3142–3158. https://doi.org/10.1039/d0fo03061a

Wang S, Feng Y, Zheng L, He P, Tan J, Cai J et al (2023) Rosavin: research advances in extraction and synthesis, pharmacological activities and therapeutic effects on diseases of the characteristic active ingredients of *Rhodiola rosea* L. Molecules 28(21):7412. https://doi.org/10.3390/molecules28217412

WFO (2023a) World Flora Online, *Rhodiola* L. http://www.worldfloraonline.org/taxon/wfo-4000033013

WFO (2023b) World Flora Online, *Rhodiola sachalinensis* Boriss. http://www.worldfloraonline.org/taxon/wfo-0000399409

WFO (2023c) World Flora Online, *Rhodiola sacra* (Raym.-Hamet) Fu. http://www.worldfloraonline.org/taxon/wfo-0001300649

WHO (2023) World Health Organization, Antimicrobial resistance. https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance

Wilson ID, Nicholson JK (2017) Gut microbiome interactions with drug metabolism, efficacy, and toxicity. Transl Res 179:204–222. https://doi.org/10.1016/j.trsl.2016.08.002

Xie Z, Lu H, Yang S, Zeng Y, Li W, Wang L et al (2020) Salidroside attenuates cognitive dysfunction in senescence-accelerated mouse prone 8 (SAMP8) mice and modulates inflammation of the gut-brain axis. Front Pharmacol 11:568423. https://doi.org/10.3389/fphar.2020.568423

Yang Y, Liu Z, Feng Z, Jiang J, Zhang P (2012) Lignans from the root of *Rhodiola crenulata*. J Agric Food Chem 60(4):964–972. https://doi.org/10.1021/jf204660c

Yang Z, Zeng G, Peng L, Zhang M, Cheng J, Zhan R (2015) Preliminary study on effect of *Rhodiolae crenulatae radix et rhizoma* cell wall-broken decoction pieces on intestinal flora of mice. Zhongguo Zhong Yao Za Zhi 40(15):3053–3058

Yousef GG, Grace MH, Cheng DM, Belolipov IV, Raskin I, Lila MA (2006) Comparative phytochemical characterization of three *Rhodiola* species. Phytochemistry 67(21):2380–2391. https://doi.org/10.1016/j.phytochem.2006.07.026

Yuan Y, Wu X, Zhang X, Hong Y, Yan H (2019) Ameliorative effect of salidroside from *Rhodiola rosea* L. on the gut microbiota subject to furan-induced liver injury in a mouse model. Food Chem Toxicol 125:333–340. https://doi.org/10.1016/j.fct.2019.01.007

Zapesochnaya GG, Kurkin VA (1983) The flavonoids of the rhizomes of *Rhodiola rosea* II. *A. flavonolignan* and glycosides of herbacetin. Chem Nat Compd 19(1):21–29. https://doi.org/10.1007/BF00579955

Zaushintsena A, Babich O, Bryukhachev E, Milenteva I, Starcev A (2020) Opportunities for using biologically active substances *Rhodiola rosea* L. in the production of functional food with consideration for antimicrobial activity. E3S Web Conf 176:1011. https://doi.org/10.1051/e3sconf/202017601011

Zhang Z, Liu Y, Lu M, Lyu X, Gong T, Tang B et al (2020) *Rhodiola rosea* extract inhibits the biofilm formation and the expression of virulence genes of cariogenic oral pathogen *Streptococcus mutans*. Arch Oral Biol 116:104762. https://doi.org/10.1016/j.archoralbio.2020.104762

Zhang X, Xie L, Long J, Xie Q, Zheng Y, Liu K, Li X (2021) Salidroside: a review of its recent advances in synthetic pathways and pharmacological properties. Chem Biol Interact 339:109268. https://doi.org/10.1016/j.cbi.2020.109268

Zhang S, Jiang S, Deng N, Zheng B, Li T, Liu RH (2022) Phytochemical profiles, antioxidant activity and antiproliferative mechanism of *Rhodiola rosea* L. phenolic extract. Nutrients 14(17):3602. https://doi.org/10.3390/nu14173602

Zhang N, Nao J, Dong X (2023) Neuroprotective mechanisms of salidroside in Alzheimer′s disease: a systematic review and meta-analysis of preclinical studies. J Agric Food Chem 71(46):17597–17614. https://doi.org/10.1021/acs.jafc.3c06672

Zhao C-C, Wu X-Y, Yi H, Chen R, Fan G (2021) The therapeutic effects and mechanisms of salidroside on cardiovascular and metabolic diseases: an updated review. Chem Biodivers 18(7):e2100033. https://doi.org/10.1002/cbdv.202100033

Zhao L, Jin X, Xiong Z, Tang H, Guo H, Ye G et al (2022a) The antivirulence activity of umbelliferone and its protective effect against *A. hydrophila*-infected grass carp. Int J Mol Sci 23(19):11119. https://doi.org/10.3390/ijms231911119

Zhao Q, Shi J, Chen S, Hao D, Wan S, Niu H, Zhang Y (2022b) Salidroside affects gut microbiota structure in db/db mice by affecting insulin, blood glucose and body weight. Diabetes Metab Syndr Obes 15:2619–2631. https://doi.org/10.2147/DMSO.S372192

Zhong L, Peng L, Fu J, Zou L, Zhao G, Zhao J (2020) Phytochemical, antibacterial and antioxidant activity evaluation of *Rhodiola crenulata*. Molecules 25(16):3664. https://doi.org/10.3390/molecules25163664

Zhu H, Shen F, Wang X, Cheng Y, Guo Y, Qian H, Liu Y (2023) Reshaped gut microbial composition and functions associated with the antifatigue effect of salidroside in exercise mice. Mol Nutr Food Res 67(12):e2300015. https://doi.org/10.1002/mnfr.202300015

Zomborszki PZ, Kúsz N, Csupor D, Peschel W (2019) Rhodiosin and herbacetin in *Rhodiola rosea* preparations: additional markers for quality control? Pharm Biol 57(1):295–305. https://doi.org/10.1080/13880209.2019.1577460