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Medicinal Marvels: A Comprehensive Study at the Nutritional and Therapeutic Potential of *Russula* Mushrooms

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Abstract

Russula, is a prominent genus in mycological study, emphasizing its scientific, ecological, and human dimensions. Originating with Christian Hendrik Persoon's recognition in 1796, the genus now comprises 1428 accepted species, renowned for its aesthetic allure and ecological significance. *Russula* is the second most diverse ectomycorrhizal genus, and plays a pivotal role in sustaining forest ecosystems through mutualistic symbioses with various plant hosts, adapting to diverse environments globally. Beyond its ecological role, *Russula* reveals a dual identity as an ecological cornerstone and a culinary treasure, with numerous species prized for their culinary excellence, contributing to various cuisines globally. Moreover, the genus holds untapped potential as a reservoir of medicinal and nutraceutical compounds, opening avenues for interdisciplinary research. The article highlights the widespread distribution and diverse host preferences of *Russula*, emphasizing its significant role in global forest ecosystems. The pharmacological potential of *Russula* mushrooms has been explored, revealing their antioxidant, anticancer, antimicrobial, anti–inflammatory, antiviral, antidiabetic, and immunomodulatory activities. This study identified specific bioactive compounds within *Russula* species that exhibit therapeutic potential, supporting their role in natural healthcare. In conclusion, the article underscores the profound implications of *Russula*, ranging from ecological significance to potential contributions to human health and nutrition.

Keywords – Ectomycorrhiza – Edible Mushroom – Medicinal Mushroom – Mycochemicals – Pharmacological studies

Introduction

Russula, a venerable subject of mycological inquiry, commands both scientific curiosity and ecological importance. Christian Hendrik Persoon's landmark work in 1796 introduced this genus, which has since burgeoned into a repository of biodiversity, boasting an astounding 1428 taxonomically accepted species (Mycobank 2023, Catalogue of Life 2024). Its defining features, including resplendent pigmented caps, spore prints varying from pale white to deep yellow, and distinct amyloid spore ornamentation, render *Russula* an object of enduring fascination. Beyond its aesthetic allure, *Russula*'s unique morphological traits, such as the brittle context, attached gills, and the conspicuous absence of latex or volva on the stipe, have contributed to its distinct

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taxonomic characterization (Ghosh & Das 2017). *Russula* ranks as the second most diverse ectomycorrhizal genus following *Cortinarius*. Ectomycorrhizal associations, a hallmark of the genus, establish mutualistic symbioses with diverse plant hosts spanning a gamut of ecosystems, ranging from arid scrublands to verdant coniferous woodlands (Sharma 2017). This ecological role is pivotal in sustaining forest ecosystems through nutrient exchange and promoting plant growth and health (Trappe 1962, Wang et al. 2015). This has bestowed upon *Russula* a truly global presence, adapting and thriving in ecosystems as diverse as the arctic tundra and the tropical rainforests (Looney et al. 2018, Adamčík et al. 2019, Ghosh et al. 2021). The evocative sobriquet "brittle gills mushrooms" encapsulates the intriguing gill structure of *Russula* species, which conspicuously fragment upon maturation, setting them apart from the latex–exuding *Lactarius* genus. However, the macro–morphological features such as cap color can be highly variable within a species and there are relatively few features to distinguish many closely related species within this genus. Given its specious nature, *Russula* has been one of the most difficult genera for fungal systematics and taxonomy (Singer 1986, Miller & Buyck 2002, Wang et al. 2015, Looney et al. 2018). Notably, the enigmatic crumbly texture of these mushrooms, attributed to the presence of sphaerocysts adds to their mystique and allure (Woo 1989, Marley 2010). The etymology of the genus name, "*Russula*" derived from the diminutive form of "*rússa*," denoting "red" or "reddish" underscores the striking coloration that characterizes many *Russula* species (Acta Plantarum 2023).

However, the resonance of *Russula* extends beyond its aesthetic and ecological dimensions. Its obligate root–mutualistic nature positions it as a keystone in ecosystem dynamics, fostering crucial symbiotic relationships that have far–reaching impacts on nutrient cycling and plant health (Wang et al. 2015, Jabeen et al. 2017, Kiran et al. 2021) Recent molecular investigations, including advancements in classification methodologies and anatomical scrutiny, have unveiled the previously hidden intricacies of the taxonomic diversity of *Russula*. All members of *Russula* are obligatory root mutualistic species that can form ectomycorrhizae with diverse plants and play important ecological roles in sustaining forest biodiversity and as nutrient sources for some animals (Yuan et al. 2019). Buyck et al. (2018) demonstrated that the anatomy of ectomycorrhiza added support to a new infrageneric classification system of the genus based on a new multi–locus analysis of five housekeeping genes.

Amidst its ecological importance, *Russula* embraces a nuanced relationship with human livelihoods. The dual identity of *Russula* is an ecological cornerstone and culinary treasure trove. Many species within this genus are prized for their culinary excellence, contributing both palatability and nutritional value to various cuisines (Li et al. 2010, Khatua et al. 2015, Khatua et al. 2019, Li et al. 2021). Beneath the surface lies the untapped potential of *Russula* species as reservoirs of medicinal and nutraceutical compounds, which opens avenues for interdisciplinary research and biotechnological exploration.

This review delves into the diverse landscape of the *Russula* genus, examining its numerous species, their ecological roles, and their potential benefits. By analyzing their medicinal, nutritional, and nutraceutical properties, this exploration aims to highlight the significant implications of this genus, underscoring its importance in science, nature, and human health.

Geographic Diversity of *Russula*

Russula stands out as one of the largest and most morphologically diverse genera among basidiomycetes worldwide (Zhou et al. 2022). Geographically and ecologically, these fungi are widely distributed, establishing ectomycorrhizal relationships with various plant species. Beyond their ecological significance, certain *Russula* species are sought after for culinary purposes. Within the realm of ectomycorrhizal fungi, *Russula* is notably prevalent across different regions (Wang et al. 2020, Zhou et al. 2022). Recent research indicates that *Russula* spp., form ectomycorrhizal associations with a variety of plant species spanning diverse plant families, including Leguminosae, Fagaceae, Dipterocarpaceae, and Pinaceae (Wang et al. 2015, van Der Heijden 2015, Hackel et al. 2022). These findings highlight the widespread distribution, abundance, and diverse host preferences of *Russula*, suggesting a significant role for this genus in global forest ecosystems. The geographical distribution of the *Russula* is given in Fig. 1, offering a comprehensive visual insight into the global spread of this fungal taxon. Several *Russula* species, such as *R. atropurpurea*, *R. nigricans*, *R. pectinatoides*, and *R. sororia* have been found on multiple continents of the Northern hemispheres (Chou & Wang, 2005, Adamčík & Buyck 2011, Wang et al. 2015). Conversely, certain species exhibit specific geographic distributions; for example, *Russula brevipes* is predominantly found in North America (Bergemann & Miller 2002, Buyck & Adamčík 2013), *R. ochroleuca*, *R. nana* in Europe (Eberhardt 2002, Miller & Buyck 2002) while *Russula discopus*, *R. pseudocarmecina* and *R. ochraceorivulosa* in tropical regions (Riviere et al. 2007, Kleine et al. 2013). In the last decade, biodiversity surveys employing advanced molecular techniques and exploring previously overlooked regions and ecological niches have led to the identification of numerous new *Russula* species. Examples include *R. changbaiensis* (northeast China), *R. caeruleoanulata* (west Africa), *R. galbana* (Australasia), *R. tsokae* (Sikkim, Himalayas), *R. purpureozonata*, and *R. adwanitekae* (Indian Himalaya) (Lebel & Tonkin 2007, Douanla–Meli & Langer 2009, Das et al. 2010, Li et al. 2013, Ghosh et al. 2021).

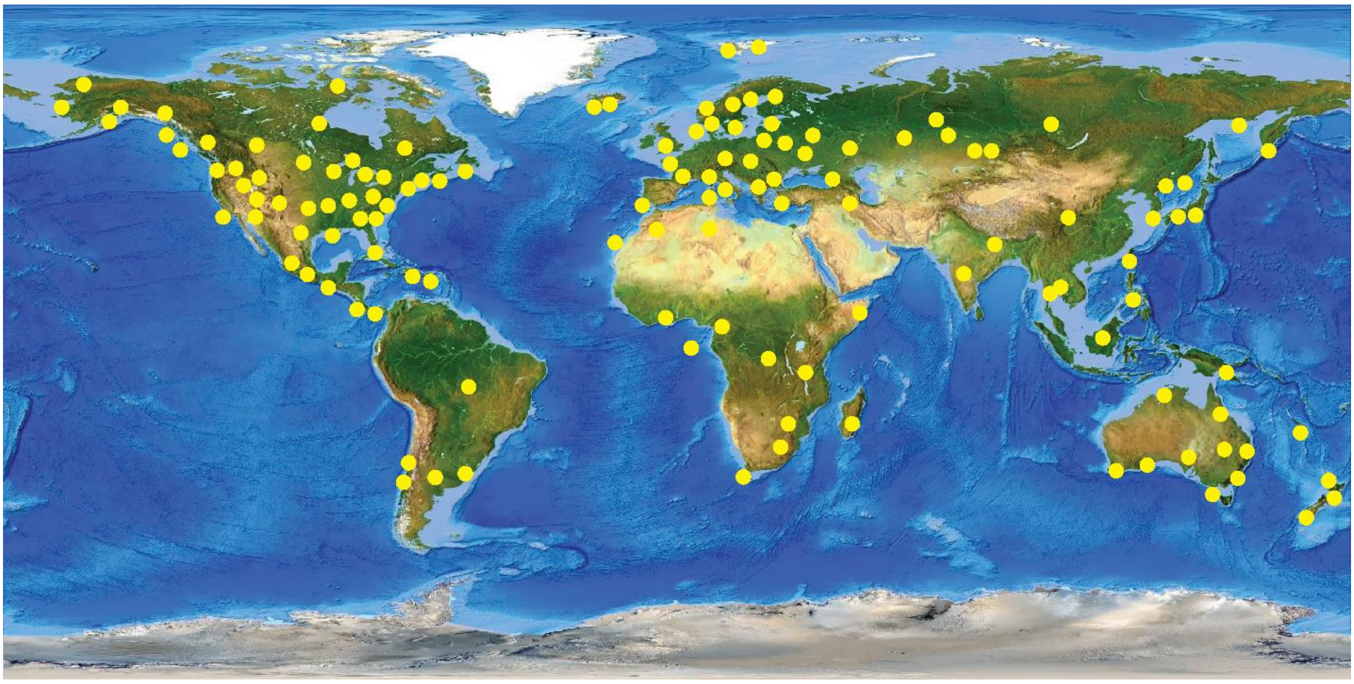

Fig. 1 – Geographical distribution of *Russula* species

***Russula*: Harnessing its Functional Food Potential**

Individuals within diverse geographic regions engage in the foraging of various *Russula* mushroom species for culinary purposes. There exists a cultural disparity in the assessment of the edibility of *Russula*, with North American field guides generally cautioning against the consumption of most species within the genus and highlighting their non–edible nature. In contrast, European field guides present a more favorable perspective, identifying a greater number of edible species (Marley 2010). *Russula* mushrooms display a diverse range of edibles, with some species considered excellent choices for consumption, whereas others are deemed inedible or even toxic (Nieminen & Mustonen 2020). *Russula virescens* stands out as a particularly fine edible fungus, possessing an excellent flavor both in its raw and cooked forms. The nutty taste is notably enhanced when the mushroom is dried (Boa 2004, Russell 2006). Fresh *R. virescens* mushrooms, weighing 100 g, contain approximately 92.5% moisture and provide 365 kcal. The nutritional composition per 100 g of dry mushroom includes 62.27 g of carbohydrates, 21.85 g of proteins, and about 1.85 g of fat (Leal et al. 2013). Additionally, it contains phosphorus, calcium, and various other compounds (Zhu et al. 2013). Another edible species, *Russula brevipes*, achieves its best culinary potential when parasitized by the ascomycete *Hypomyces lactifluorum*, transforming it into a highly sought–after edible form known as a lobster mushroom. In this state, the fruit body's surface develops into a hard, thin crust with a cooked lobster color, while the gills are reduced to blunt ridges, and the flesh becomes compacted and less brittle (Spahr 2009, French Hill Pond Fungi 2013). *Russula heterophylla* is also considered edible of the highest quality and is known for its delicious taste (Boa 2004). *Russula vesca* is appreciated as another edible wild mushroom (Boa 2004, Dahlberg 2019). Among the tribal communities of West Bengal, *Russula senecis* is exclusively popular for culinary purposes. The fruiting body is typically cooked with mustard oil and spices (Khatua et al. 2015, Dutta & Acharya 2014). Several other *Russula* species, are edible including *R. alutacea* (Li et al. 2020), *R. alatoreticula* (Khatua et al. 2019), *R. aeruginea* (Kumar et al. 2014, Boa 2004), *R. crustose* (Boa 2004, Bessette et al. 2007, Bhatt & Lakhanpal 1988), *R. cyanoxantha* (Pacioni & Lincoff 1981, Boa 2004, Desjardin et al. 2015), *R. griseocarnosa (*Wang et al. 2009), *R. furcate* (Hard 2019, Atkinson 1901), *R. lilacea* (Boa 2004), and *R. ochroleuca* (Boa 2004, Kumar et al. 2014). While *R. delica* is indeed an edible species, it is not widely appreciated due to its unpleasant taste (Phillips 2013). Additionally, "The Edible Fungi of Tropical Africa" annotated database (Degreef & de Kesel 2023) records 14 *Russula* species as edible, including *R. acuminata, R. cellulata, R. ciliata, R. compressa, R. congoana, R. hiemisilvae, R. meleagris, R. ochrocephala, R. phaeocephala, R. roseoviolacea, R. sejuncta, R. sese, R. sesemoindu*, and *R. striatoviridis*.

Beneficial effects of *Russula* on human health

Mushrooms, with a rich history steeped in traditional medicinal practices, have emerged as a valuable resource in the realm of natural healthcare. Harnessing their therapeutic potential, various mushroom species have been employed for centuries, contributing to diverse traditional medicinal systems globally. Several species within the *Russula* exhibit noteworthy medicinal properties. In homeopathy, a tincture derived from fresh *Russula foetens* proved effective against chorea, accompanied by complications such as unconsciousness, muscular spasms, anxiety, dyspnea, nausea, colic, vomiting, diarrhea, cold extremities, pseudo–erysipelas on elbows, and painless furuncles distributed across the entire body (Clarke 1902, Patil 2012). *Russula rosea* is employed as a medicinal agent in China (Jian–Wen et al. 2000), while *R. virens* has historical significance in traditional Chinese medicine for treating liver diseases, eye disorders, and chest distress (Zhu et al. 2013). Lectins isolated from *R. delica* exhibit inhibitory effects against HIV–1 reverse transcriptase, suggesting their potential as drugs for AIDS treatment (Lam & Ng 2011). Moreover, *R. delica* Fr. (RD) extracts display antioxidant and antimicrobial activities, making them suitable for applications in the food industry (Türkoğlu et al. 2007). The separate analysis of the chemical composition and antioxidant activities of the pileus and stipe of *R. griseocarnosa* further underscores the antioxidant properties of this species (Chen et al. 2010), offering promising avenues for exploration in the treatment of diverse diseases. In conclusion, the scientifically validated medicinal attributes of *Russula* mushrooms underscore their potential as valuable contributors to human health and well–being.

Composition and Structural Characteristics of Mycochemicals in *Russula*

Mycochemistry is a new field of study that focuses on the vast array of compounds produced and collected from mushrooms. These chemicals are referred to as “mycochemicals” and are of interest to scientists. *Russula* species produce diverse secondary metabolites with various biological activities. These compounds, found in diverse repertoires of fungi, hold promise for innovative applications in medicine, biotechnology, and environmental solutions, adding a fascinating dimension to our understanding of the symbiotic relationships that fungi maintain in various ecosystems. In the last several decades, a large number of chemical constituents have been isolated from the fruiting bodies and mycelial culture of the fungi of the genus *Russula*. As previously reported, polysaccharides, terpenoids, phenolic acids, and sesquiterpenes are the main bio–active secondary metabolites found in this genus (Clericuzio et al. 2012, Panda et al. 2020, Cheng et al. 2024). Thus, the isolation, characterization, chemistry, and related bioactivities of these compounds will be highlighted based on their chemical categorization. It focuses on isolating and elucidating the chemical structures of these chemicals, as well as their biosynthesis, metabolism, turnover, natural distribution, and biological characteristics (Dewick 2009). The health, nutrition, and use of mycochemicals as functional foods for both people and animals are significant (Cateni et al. 2022, Khatua & Acharya 2022). Table 1 & Fig. 2 presents a comprehensive overview of mycochemical compounds identified in the *Russula* genus, along with their associated pharmacological activities. The data highlights the diverse chemical profile of *Russula* species and provides insights into potential therapeutic applications associated with these compounds.

Table 1 An overview of mycochemicals and their pharmacological activities in the *Russula*.

Plant	**Myochemical**	**Pharmacological activity**	**References**
Russula alatoreticula	Ascorbic acid, Β–Carotene, Cinnamic acid, Lycopene, Phenols, Pyrogallol, Rusalan	Anti–Bacterial, Anti–Cancer, Anti–Microbial, Anti–Oxidant	Khatua et al. 2017, Khatua et al. 2019, Khatua et al. 2021
Russula albonigra	Β–Glucan, Heteroglycan	Antioxidant, and Immunostimulant	Nandi et al. 2012
Russula alutacea	Polysaccharide (Rap–1)	Antioxidant, Anti–inflammatory	Li et al. 2020
Russula brevipes	Lactarorufin A, Russulactarorufin	–	Suri et al. 1997
Russula chloroides	Ferulic Acid, Gallic Acid, Myricetin	GST activity	Shomali et al. 2019
Russula cyanoxantha	(22E,24R) –Ergosta–7,22–Dien–3β,5α,6α–Triol, (24S) –Ergosta–7–Ene–3β,5α,6α–Triol, (2S,3S,4R,2′R) –2– (2′–Hydroxytetracosanoylamino) 5α,8α–Epidioxy– (22E,24R) –Ergosta–6,22–Dien–3β–Ol, 5α,8α–Epidioxy– (24S) –Ergosta–6–En–3β–Ol, Adenine, Allitol, D–Allitol, Ergone, Ergosterols, Fumaric acid, Inosine, Octadecane–1,3,4–Triol, Pyroglutamic acid, Stearic acid	Antibacterial, Antioxidant, Anti–proliferative	Zhao et al. 2011, Gao et al. 2001a
Russula delica	9,11–Cis–Octadecenic acid, 9–Cis–Octadecenoic acid, Caffeic acid, Dodecanoic acid, Doeicosanoic acid, Eicosanoic acid, Gallic acid, Hexadecanoic acid, Octadecanoic acid, Pentadecanoic acid, Russulanorol, Tetradecanoic acid, Tetraeicosanoic acid, Glycoproteins	Antioxidant, Cell Proliferation and Phagocytic Activity; Anti–viral and Anti–cancer	Yaoita et al. 2003, Yaltirak et al. 2009, Zhao et al. 2010

Table 1 Continued

Plant	Myochemical	Pharmacological activity	References
Russula foetens	Lactapiperanol A & E, Marasmane sesquiterpene lactones such as marasmoic and russulfoen acid derivatives, Russulfoen	Anti–cancer	Wang et al. 2006, Kim et al. 2010
Russula griseocarnosa	Ascorbic acid, Caffeic acid, Carotene, Ergosterol, Lycopene, Phenolics, Protocatechuic acid, B–Carotene	Antioxidant, Antitumor, Immunostimulatory	Chen et al. 2010
Russula japonica	Russujaponol A–L plorantinone B and its derivative Russujaponol A (Sesquiterpene)	Neurite Outgrowth Promoting Activity; Anticancer	Yoshikawa et al. 2006, Yoshikawa et al. 2009
Russula lepida	(24E) –3β–hydroxycucurbita–5,24–diene–26–oic acid, (24E) –3,4–secocucurbita–4,24–diene–3,26–dioic acid, (24E) –3,4–secocucurbita–4,24–diene–3,26,29–trioic acid, rulepidadiol, and rulepidatriol, Lectin, Lepidolide, rulepidol	Anti–inflammatory, Cytotoxic activity	Jian–Wen et al. 1999, Jian–Wen et al. 2000, Jian–Wen et al. 2002, Zhang et al. 2010
Russula nigricans	Nigricanin (Ellagic Acid)	–	Jian–Wen Tan et al. 2004
Russula nobilis	Russulanobilines A–C	–	Malagòn et al. 2014
Russula ochroleuca	Ochroleucin A1, Adenine, D–allitol, Cerebroside B & D, Ergostaol and its derivatives, Stearic acid, Uracil, thioacetic anhydride and ochroleucin A1–2 & B	Antioxidant, Immune–stimulatory effect	Gao et al. 2001b, Sontag et al. 2006, Zhou et al. 2011
Russula pseudocyanoxantha	Ascorbic Acid, Chlorogenic Acid, Cinnamic Acid, Gallic Acid, Lycopene, P–Coumaric Acid, Pyrogallol, Salicylic Acid, B–Carotene	Antioxidant, Antiinflammatory, Antiproliferative, Antibacterial	Khatua & Acharya 2022
Russula queletii	Piperalol and Piperdial		Zhou et al. 2011

Table 1 Continued

Plant	**Myochemical**	**Pharmacological activity**	**References**
Russula rosea	Aristolane sesquiterpenoids (rulepidadiol, rulepidatriol), triterpenoids, Aristolane sesquiterpenes, secocucurbitane triterpenes	Anti–diabetic	Jian–Wen et al. 2000, Lee et al. 2016
Russula sanguinaria	15–Hydroxyblennin A, Blennin A, C & D, Lactarorufin A, Piperalol, Vellerolactone	–	Gilardoni et al. 2014
Russula senecis	Benzoic acid derivative (Vanillic Acid, Salicylic Acid, Gallic Acid), Cinnamic acid and its derivatives (Chlorogenic Acid, Ferulic Acid, Cinnamic Acid, P–Coumaric Acid), Pyrogallol, Rusenan, RuseCap	Antioxidant, antimicrobial, Cytotoxic activity	Khatua et al. 2015, Khatua & Acharya, 2017, Khatua, & Acharya, 2018
Russula subnigricans	Cyclopropylacetyl– (R) – carnitine, Cycloprop–2–ene carboxylic acid, Russuphelin A–E	–	Takahashi et al. 1992, Matsuura et al. 2009;
Russula vesca	Triyne acid and Triynol	–	Hearn et al. 1973
Russula virescens	Cinnamic Acid, Citric Acid, Fumaric Acid, Malic Acid, Oxalic Acid, P–Hydroxybenzoic Acid, and Β–Tocopherol	Anti–oxidant	Sun et al. 2010, Leal et al. 2013
Russula vinosa	(24E) –3,4–Seco–cucurbita–4,24–diene–26,29–dioic acid–3–methyl ester, (24E) –3,4–Seco–cucurbita–4,24–diene–26–oic acid–3–ethyl ester, (24E) –3β–Hydroxycucurbita–5,24–diene–26,29–dioic acid, (2S,3S,4R,20R) –2– (20) –Hydroxydocosanoylamino) eicosane–1,3,4–triol, 7α,8α,13–trihydroxy–marasm–5–oic acid γ–lactone, Aristolone, Rosacea acid A & B, Rulepidadione C, Triterpenes, Vinosane	Immunostimulant	Zhang et al. 2019, Zhang et al. 2021
Russula viscida	Ochroleucins A1 & A2	–	Sontag et al. 2006

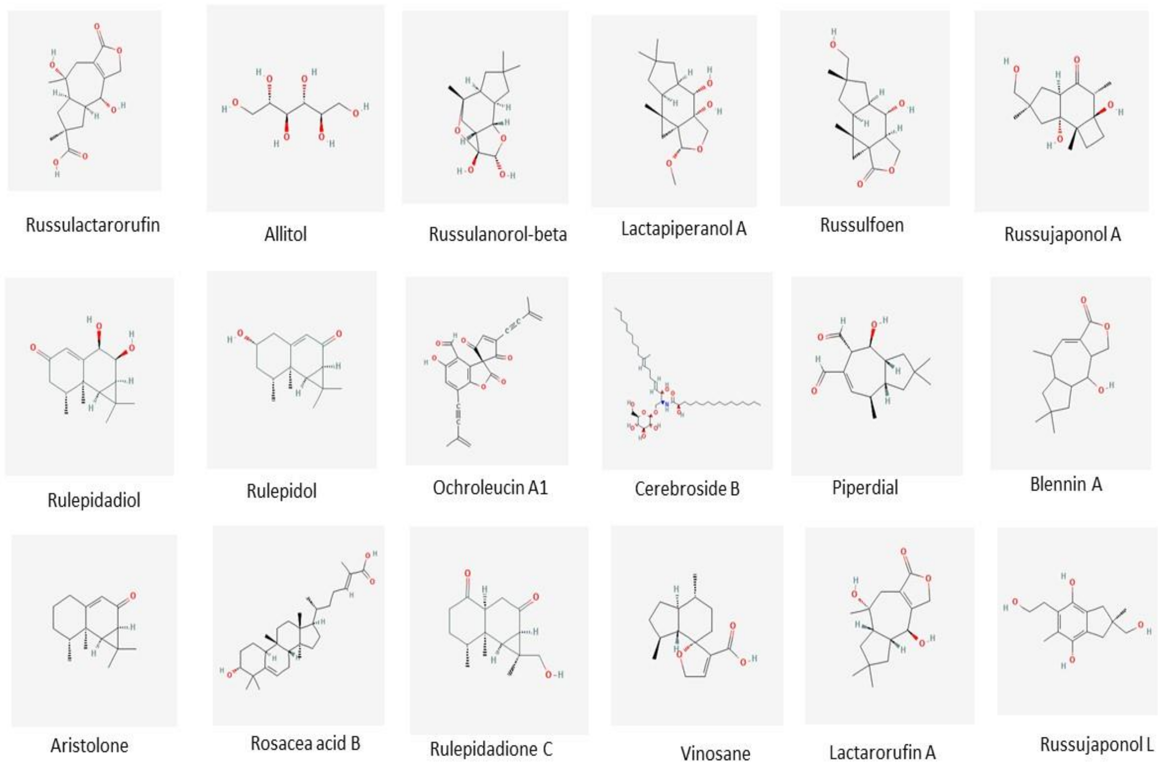

Fig. 2 – Chemical structures of some isolated chemicals of the *Russula*. (Source: https://pubchem.ncbi.nlm.nih.gov/)

Pharmacological Potential of *Russula* Mushrooms

Anti–oxidant activity

The intricate balance within the human body is continually challenged by free radicals and oxidants, which are the reactive entities generated during metabolic processes. When in excess, these species can induce significant cellular and tissue damage, leading to the accumulation of pro–oxidant factors and oxidative stress (Manisha et al. 2017). Prolonged exposure contributes to the development of chronic conditions, including cancer, diabetes, ageing, cardiovascular, and neurological diseases (Gulcin et al. 2004, Sachindra et al. 2010, Sharifi–Rad et al. 2020). Recognizing mushrooms as reservoirs of bioconstituents with high curative potential, researchers have delved into their beneficial aspects for treating various human pathologies. Prasad et al. (2015), reported the anti–oxidant activity of methanol extract of *Russula brevipes* fruiting bodies and mycelia with EC_{50} 0.89 and 7.08 mg/ml, respectively in 2,2–diphenyl–1–picrylhydrazyl (DPPH) assay. In another study, it's methanol and water extract showed reducing power ability with 3.60 and 0.95 mg of GAE/g, respectively. In Ferredoxin–reducing substance (FRS) assay, IC_{50} values of 1.60 and 1.80 mg/ml were observed while 271 and 705% inhibition shown in lipid peroxidation, respectively (Puttaraju et al. 2006). Notably, *Russula delica* exhibited a noteworthy IC_{50} value of 4 mg/ml in the ferrozine assay (Yaltirak et al. 2009). Similarly, *Russula densifolia*, *R. violeipes*, and *R. cyanoxantha* demonstrated robust ABTS, DPPH, superoxide scavenging, and metal–chelating activities, accompanied by varying total phenolic and flavonoid content (Panda et al. 2020). The antioxidant activity of *Russula nigricans* was evident, inhibiting lipid peroxidation with IC_{50} values of 17 ± 2 and 120 ± 22 µg/mL for its ethanol and methanol extracts, respectively (Kostić et al. 2020).

Fungal polysaccharides have also been reputed to exhibit potent anti–oxidant activity. The water–soluble polysaccharide rusenan, from *Russula senecis* showed anti–oxidant activity in superoxide, hydroxyl, DPPH, ABTS, β–carotene, ferrous ion chelating and reducing power assay with EC_{50} values of 360, 403, 1387, 638, 488, 80, 3885 µg/ml, respectively (Khatua & Acharya 2018). Additionally, Khatua et al. reported good antioxidant activity of rusalan (polysaccharide isolated from *R. alatoreticula* basidiocarps) (Khatua et al. 2017). Crude polysaccharide fraction, RuseCap from *Russula senecis* also displayed potent scavenging action in superoxide, hydroxyl, DPPH, ABTS, ferrous ion chelating and reducing power assays with EC_{50} values of 872, 892, 1960, 712, 257, 4068 µg/ml, respectively (Khatua & Acharya 2017). RVP–1 and RVP–2, crude polysaccharides from *Russula virescens,* evaluated for antioxidant activity by using hydroxyl, superoxide radical, self–oxidation of 1,2,3–phentriol, reducing power and metal chelating assay. RVP–1 & 2 showed 67.3 and 98 % hydroxyl radical inhibition, respectively, at 0.01–5.0 mg concentration. At 0.15–5 mg, RVP–1 exhibits stronger scavenging activity with 2.4–88.1% superoxide inhibition compared to vitamin C (0–83.1%). The reducing and chelating abilities of RVP–1 & 2 were recorded as 0.77, 0.96 and 93.3, 51.2%, respectively at 20 and 10 mg/ml concentration. RVP–1 acted as a better antioxidant in a self–oxidation assay (Sun et al. 2010). Besides, ploysachharides, mushrooms are well known for their phenolic content. Phenol rich extract RusePre, from *R. senecis* evinced to be a strong hydroxyl radical scavenger and ferrous chelator with EC_{50} 5 and 158 µg/ml, respectively. In DPPH assay, it was found to be quite effective with just 1.34 ± 0.07 mg/ml, EC_{50} value (Khatua et al. 2015). In conclusion, the multifaceted antioxidant activities of various *Russula* species underscore their pharmaceutical potential and position them as promising natural sources for combating oxidative stress–related health issues.

Anti–cancer activity

Cancer, a formidable and widespread disease, continues to pose a significant threat to global health. Researchers have diligently explored the potential of various mushroom species to combat this deadly ailment (Greenwell & Rahman 2015). In a study, ethanol extracts of *R. violeipes*, *R. cyanoxantha* and *R. densifolia* expressed an IC_{50} value of 56.66, 65.95 and 73.48 mg/ ml at 72 h against human cancer cell line (HeLa) (Panda et al. 2020). Similarly, methanolic extracts of *R. rosea*, *R. nigricans, and R. integra showed activity against the human tumor cell line HepG2 (*Kostić et al. 2020*).* In different studies conducted by Khatua et al. (2019, 2021), ethanol and methanol extracts from *R. alatoreticula* were evaluated for their anticancer efficacy against Hep3B liver cancer cells. The ethanol extract significantly reduced cell number by 19, 51 and 75% at 100, 300 and 500 µg/ml concentration with GI_{50} 300 µg/ml. It was found to be 358.57 µg/ml for methanol extract (Khatua et.al 2019, Khatua et.al 2021). A bioactive steroid, ergone, from *R. cyanoxantha* has also been shown to induce apoptosis in hepatocellular carcinoma HepG2 cells by arresting the cell cycle at the G2/M phase, as assessed by MTT and staining assays. The IC_{50} values were 15.6, 11.8 and 10.0 µg/ml when calculated at intervals of 6 h (Zhao et al. 2011).

Lectin, isolated from *Russula delica* fruiting bodies was evaluated for anti–proliferation against two human cell lines including HepG2 and MCF7 (hepatoma and breast cancer) by using MTT assay. Results revealed the strong potency of lectin as it inhibits the growth of HepG2 and MCF 7 cells with an inhibitory concentration of 0.88 and 0.52 µM, respectively (Zhao et al. 2010). In another study, a ribonuclease derived from *Russula delica* also inhibits the proliferation of these two cancer cell lines at a concentration of 8.6 and 7.2 µM, respectively (Zhao et al. 2010b). Russujaponol A, isolated from *Russula japonica* was evaluated for cytotoxic activity on human HT1080 fibrosarcoma cells *in vitro* and results were compared with the standard drug doxorubicin. Results showed that russujaponols A, suppressed the growth of human fibrosarcoma (HT1080) cells upto 63% at 3.73 µM as compared with the standard which showed 52% inhibition at 0.17 µM (Yoshikawa et al. 2006). Russulfoen and other Marasmane sesquiterpene lactones isolated from *Russula foetens* were evaluated for cytostatic activity against A549, SK–OV–3, SK–MEL–2 and HCT–15 human tumor cell lines *in vitro* by using sulforhodamine B assay and results compared with standard drug doxorubicin. The lactones exhibit strong anti–cancerous action against the cell lines and IC_{50} values were recorded from 15.4 to >30 µM, maximally by russulfoen against SK–MEL–2 (Kim et al. 2010). The diverse *Russula* species unveil a rich reservoir of bioactive compounds, showcasing significant potential in the realm of cancer treatment, thus positioning them as promising candidates for further exploration in oncological research.

Anti–microbial activity

Russula delica extract was evaluated for its antimicrobial activity against *Bacillus cereus, Escherichia coli, Listeria monocytogenes, Pseudomonas aeruginosa, Proteus vulgaris RSKK, Staphylococcus aureus, Salmonella enteritidis, Yersinia enterocolitica, and Shigella sonnei*. Results showed that. The ethanol extract exhibited antimicrobial activity against specific microbes with an inhibitory diameter of 7–17 mm. Maximum inhibition was observed against *S. sonnei* (Yaltirak et al. 2009).

The antimicrobial activity of the methanol/water (80:20) extract of *Russula delica* was evaluated against clinical isolates using a microdilution assay. Results showed that the extract exhibited anti–microbial activity against tested microbes with MIC values ranging from 5 to 20 mg/ml, with potent activity against *Streptococcus agalactiae and S. pyogenes* with MIC value of 5 mg/ml each (Alves et al. 2012).

The anti–microbial activity of ethanol and aqueous extract (hot and cold) of *R. vesca* was evaluated against *Streptococcus pneumoniae, Klebsiella pneumoniae, Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Proteus mirabilis, Salmonella typhi, Bacillus cereus* and *Candida albicans* by using disc diffusion assay. The hot water extract showed potent activity against *S. typhi and P. mirabilis* with the zone of inhibition 7.41 and 7.11 mm, respectively, while ethanolic extract showed potent activity against *C. albicans* with the zone of inhibition 10.44 mm (Nwachukwu & Uzoeto 2010). In a similar study, ethanol and methanol fractions of *R. alatoreticula* were shown to inhibit the growth of six pathogenic microbial strains with 88–2673 μg/ml MIC values, lowest against *S. aureus* (Khatua et.al 2019, Khatua et.al 2021).

The mushrooms, *R. violeipes*, *R. cyanoxantha* and *R. densifolia* also showed moderate inhibitory response against human pathogenic microorganisms with zone of inhibition ranging from 16.25 to 25.50 mm (Panda et al. 2020). Similarly, alcoholic extract of *R. nigricans*, *R. integra* and *R. rosea* inhibits more than 80% formation of *S. aureus* biofilms (Kostić et al. 2020).

Anti–inflammatory activity

In the exploration of the medicinal potential of *Russula* mushrooms, the study delves into the anti–inflammatory prowess of *Russula virescens*, particularly highlighting the significant impact of its ethanol extract (RVE) on mitigating nitric oxide production in RAW 264.7 cells. The test results were systematically compared to the control at concentrations of 0.5, 1, 2.5, and 5 mg/ml. At the highest concentration (5 mg), the RVE–treated sample exhibited a considerable reduction in TNF–α mRNA expression (Hur et al. 2012). In a parallel investigation, an aqueous extract of *R. violeipes* showed anti–inflammatory activity by denaturing albumin at an IC_{50} of 73 μg/ml, surpassing the effectiveness of aspirin, a standard anti–inflammatory drug, with an IC_{50} of 411 μg/ml (Panda et al. 2020). In summary, the ethanol extract from *Russula virescens* and the aqueous extract from *R. violeipes* manifest pronounced anti–inflammatory effects, presenting promising avenues for further exploration in the development of anti–inflammatory interventions.

Anti–viral activity

In the ongoing battle against infectious diseases, viruses stand as prominent adversaries, posing a substantial threat to global health. This study investigated the antiviral potential of various *Russula* species, focusing on a novel homodimeric lectin derived from *Russula delica* fruiting bodies. This homodimeric lectin was rigorously evaluated for its anti–HIV potential using ELISA techniques. The findings revealed its robust inhibition against HIV–1 reverse transcriptase, showcasing a remarkable IC_{50} value of 0.26 μM (Zhao et al. 2010). These preliminary results illuminate the promising anti–viral activity within *Russula* mushrooms, emphasizing the potential significance of their bioactive compounds in the ongoing efforts to combat viral infections and improve global health.

Anti–diabetic activity

In the complex realm of metabolic disorders, diabetes emerges as a prevalent condition characterized by abnormal elevations in blood sugar levels. This disorder, rooted in the malfunction of insulin, necessitates effective approaches to mitigate elevated glucose levels. One promising avenue involves inhibiting the enzymatic action of α–amylase and α–glucosidase enzymes. Several investigations have scrutinized the anti–diabetic activity inherent in various *Russula* species, shedding light on their potential as promising therapeutic agents in the effective management of diabetes. Panda et al. (2020) conducted a study anticipating the suppression of glucosidase enzyme activity through *in vitro* evaluations of *Russula densifolia*, *Russula violeipes*, and *Russula cyanoxantha* extracts. Notably, the water extracts of *R. violeipes* exhibited superior activity with an IC_{50} potency of 83 µg/ml, outperforming the standard Acarbose (IC_{50}, 97 µg/ml). Additionally, the chloroform extract of *R. violeipes* displayed an IC_{50} of 98 µg/ml, showing its effectiveness in α–amylase enzyme inhibition compared to other studied mushroom extracts (standard drug Acarbose, IC_{50}, 146 µg/ml). In another study, aristolane sesquiterpenes and seco–cucurbitane triterpenes from *Russula rosea* underwent assessment for anti–diabetic activity using the protein tyrosine phosphatase 1B (PTP1B) inhibitory assay. The results highlighted the potent PTP1B inhibitory activity of (24E) –3,4–secocucurbita–4,24–diene–3,26,29–trioic acid, with an impressive IC_{50} value of 0.4 µM compared to the positive control oleanolic acid (IC_{50}=1.1 µM) (Lee et al. 2016). These findings unravel the anti–diabetic potential within select *Russula* species, suggesting a nuanced approach in diabetes management by targeting key enzymes. The bioactive compounds present in these mushrooms showcase promising, encouraging further exploration for their role in innovative therapeutic strategies against diabetes.

Immunomodulatory activity

Given the intricate network of immune responses, the immunomodulatory potential of natural compounds is significant. A study conducted by Khatua & Acharya (2018) investigates Rusenan, a polysaccharide derived from *Russula senecis*, evaluating its immunomodulatory effects on LPS–stimulated RAW 264.7 murine macrophage cells *in vitro*. The results reveal compelling evidence of Rusenan's immunostimulatory prowess at a concentration of 50 µg/ml. It induces innate immunity by enhancing phagocytosis, inducing morphological changes, macrophage proliferation, NO release, ROS production, and transcriptional activation of key immune–related genes, such as TLR–4, TLR–2, NF–κB, COX2, iNOS, TNF–α, IκB–α, and IFN–γ. These findings underscore the potential of rusenan as a potent biological modifier (Khatua & Acharya 2018). Thus, Rusenan exhibits robust immunomodulatory activity, suggesting its potential as a valuable candidate for further exploration in the development of novel biological modifiers with implications for enhancing immune responses.

Unveiling the Exception: Risks and Clinical Insights

The majority of *Russula* species are generally considered safe, however, *R. subnigricans* stands out as an exception. *Russula subnigricans*, prevalent in East Asia, has been implicated in cases of mushroom poisoning, raising concerns about its potential health hazards. The identification of wild mushrooms presents a formidable challenge due to the inherent complexities associated with diverse species. Inadvertent consumption of wild mushrooms without adept knowledge exposes individuals to substantial health risks, primarily in the form of poisoning. The specific case of *R. subnigricans* is noteworthy in this context. The toxicity exhibited by *R. subnigricans* can be ascribed to the presence of a heat–stable toxin known as russuphelin. This toxin, resistant to elevated cooking temperatures, poses a significant risk to individuals who may unwittingly ingest the mushroom (Takahashi et al. 1992). The clinical manifestations of poisoning by *R. subnigricans* include a spectrum of symptoms, including nausea, vomiting, abdominal pain, diarrhea, dizziness, and, in severe instances, hepatorenal damage. The onset of symptoms exhibits variability, with some cases presenting within hours of ingestion, while others display delayed reactions (Lin et al. 2015, Cho & Han 2016). Several case studies have provided supportive evidence that rhabdomyolysis is linked to the consumption of *R. subnigricans*. The observed clinical outcomes range from gastrointestinal distress to fatal consequences (Lin et al. 2015, Cho & Han 2016, Min et al. 2022, Chun et al. 2023).

Conclusion and future recommendation

Mushrooms contain bioactive compounds with antioxidant properties, including phenolics, polysaccharides, glycosides, phenols, tocopherols, ascorbic acid, organic acids, and various other components. These biomolecules exhibit inhibitory and immunological potential, playing crucial roles in scavenging free radicals and preventing carcinogenesis. This comprehensive review underscores the widespread use of *Russula* mushrooms as both food and supplements, attributed to their rich content of dietary fiber, proteins, minerals, and vitamins. Notably, mushrooms biosynthesize a diverse array of chemically distinct substances, with phenolic biomolecules standing out as naturally occurring substrates for oxidative enzymes, abundantly present in mushrooms. The health benefits of mushrooms, as highlighted in this review, are considerable and suggest potential avenues for enhancing overall quality of life. It is imperative to explore further studies that delve into the antioxidant activities of diverse mushroom species and investigate strategies for formulating active metabolites into food supplements and pharmaceuticals. This approach can contribute to a more profound understanding and utilization of the health–promoting properties inherent in mushrooms.

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Disclosure statement

The authors report there are no competing interests to declare.

Data availability statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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