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Allelopathic Plants : 28. Genus *Panax* L.

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CONTENTS

ABSTRACT

Genus *Panax* L. (Araliaceae) includes very popular medicinal herbs used worldwide. Some species of *Panax* (*P. notoginseng, P. ginseng and P. quinquefolius*) are very allelopathic plants. Researches done in last 30-40 years have (i). determined the allelopathic properties of *Panax* plants, (ii). identified their allelochemicals and (iii). studied the mechanisms in allelopathic interactions. Based on the available literature, we have reviewed of allelopathic *Panax* plant's Morphology and habitats, Phytochemical characteristics, Autotoxicity, Pathogens and Rhizosphere microbiome. Progress in allelopathic research have provided the insights into the sustainable cultivation of *Panax* plants. We have also suggested the future lines of allelopathic research in genus *Panax*.

Keywords: Allelochemical, allelopathic interactions, allelopathic plants, autotoxicity, ginsenoside, microbiome, morphology and habitats, pathogens, phenolic acids, phytochemical characteristics, *P. ginseng*, *P. notoginseng*, *P. quinquefolius*, rhizosphere microbiome.

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1. INTRODUCTION

The genus *Panax* L., (Araliaceae family), was established in 1753 by the famous Swedish botanist Linnaeus based on the distribution pattern of *P. quinquefolius* in North America (51). The genus *Panax* includes very popular and important medicinal plants used worldwide. Their pharmacological activities affect the blood system, cardio- and cerebro-vascular systems, nervous system, metabolism and immune regulation (68). Ginsenosides, the main secondary metabolites of *Panax*, have therapeutic effects on human diseases (7). Interestingly, some ginsenosides act as allelochemicals and affects the performance of *Panax* or other surrounding plants and microorganisms, a phenomenon called allelopathy (132,133). In this paper, the allelopathic effects and underlying allelopathic mechanisms of *Panax* have been reviewed, besides, we have also provided some suggestions for future allelopathic research in this genus.

1.1 *Panax* L.

Globally the genus *Panax* is found in East Asia, North Vietnam, East Siberia and East North America (106). In the book, *Flora of China* (FOC) total of 11 species and their varieties in *Panax* were recorded. It has 7 spp. as under: *P. quinquefolius* L. (Xi yang shen), *P. ginseng* C. A. Mey. (Ren shen), *P. notoginseng* (Burk.) F.H. Chen (San qi), *P. stipuleanatus* C.T. Tsai & K.M. Feng (Pingbian san qi), *P. zingiberensis* C.Y. Wu & K.M. Feng (Jiang-zhuang sanqi), *P. pseudoginseng* Wall. (Jia ren shen), and *P. japonicus* C. A. Meyer (Zhu jie shen). Besides the *P. japonicus* has 4 varieties: *P. japonicus* var. japonicus (Zhu jie shen, yuan bian zhong), *P. japonicus* var. angustifolius (Xia-ye zhu jie shen), *P. japonicus* var. major (Zhu zi shen) and *P. japonicus* var. bipinnatifidus (Ge-da qi) (105). These *Panax* genus species and verities have been listed (Table 1). These *Panax* 3-spp. (*P. ginseng*, *P. notoginseng* and *P. quinquefolius*) are used worldwide due to their high medicinal and economic values, while other species or varieties are used in traditional Chinese medicine (TCM) or folk medicine (68,122).

1.2 Morphology and habitat

Panax plants share some general morphological characteristics (51). They are perennial herbs with stout rootstocks and are hermaphroditic or perhaps andromonoecious. The stems are simple. The plants have 3 or 5 palmate compound leaves and leaflets that are serrated or dentated or pinnately lobed. The inflorescences are solitary umbel, with growth from the terminal end of stems. The pedicels are articulate below bisexual flowers and inarticulate below male flowers. The flowers of *Panax* plants have a short-toothed calyx, 5- imbricate petals and 5-stamens. The fruits of *Panax* are globose drupe and some fruits are slightly compressed or triangular (Table 1). The seeds are laterally compressed and the endosperms are smooth (51,105). The Morphology of plants and roots of 6-*Panax* species are shown in Figure 1. (except *P. pseudoginseng* Wall.) (The pictures of *P. notoginseng* were taken by authors and others were cited from websites http://www.iplant.cn/frps or http://image.baidu.com/). *Panax* had originated in the paleotropical mountain areas during the Tertiary Period (77). Most *Panax* plants are shade-loving, growing mainly in forests on slopes or in valleys at altitudes of ca. 1100-4200 m (34,94,105).

Table 1. Genus *Panax* L. Species Morphology, Economic importance, Morphology and Geographical Distribution

S. N.	Botanical name	Morpholgical parameters					Economic uses	Distribution	References
		Plant height (cm)	Leaves number /plant	Flower colour	Crop duration (years)	Root type			
	Genus *Panax* L species								
1	**P. ginseng* C. A. Mey.	30-60	Leaves 3-6 with leaflets 3-5	Green	Cultivated >6	Fusiform Or Cylindric	Medicine, health products, cosmetics	North China, Japan, Russia, Korean peninsula	105,127
2	*P. japonicus* C. A. Meyer	50-100	Leaves 3-5 with leaflets 5	Yellowish -Green	Cultivated 6	Horizontal, Flagellate Or Moniliform	Medicine	China, Bhutan, North India, Japan, Korea, Myanmar, Nepal, Northeast Thailand, Vietnam	105,130
3	**P. notoginseng* (Burk.) F.H. Chen	20-60	Leaves 3-6 with leaflets 5-7	Green	Cultivated 3	Fusiform	Medicine, health products, cosmetics	Southwest China, North Vietnam	105,122
4	*P. pseudoginseng* Wall.	50	Leaves usually 4 with leaflets 3 or 4	Yellowish -Green	Wild Not Known	Fusiform	Medicine	China, Nepal	105
5	**P. quinquefolius* L.	20–50	Leaves 3-4 with leaflets 5	Green-White	Cultivated 3-6	Spindle-Shaped	Medicine, health products	United states, Canada, China	74,76
6	*P. stipuleanatus* C.T. Tsai et K.M. Feng	45-55	Leaves 3 with 5 or 7	Light Green	Wild Not Known	Fusiform	Medicine	Southwest China, North Vietnam	48,85
7	*P. zingiberensis* C.Y. Wu et K.M. Feng	20-60	Leaves 3–7 with leaflet 3-5	Purple	Cultivated 3-4	Horizontal, resembling the *Zingiber* spp.	Medicine	Southwest China, North Vietnam	103

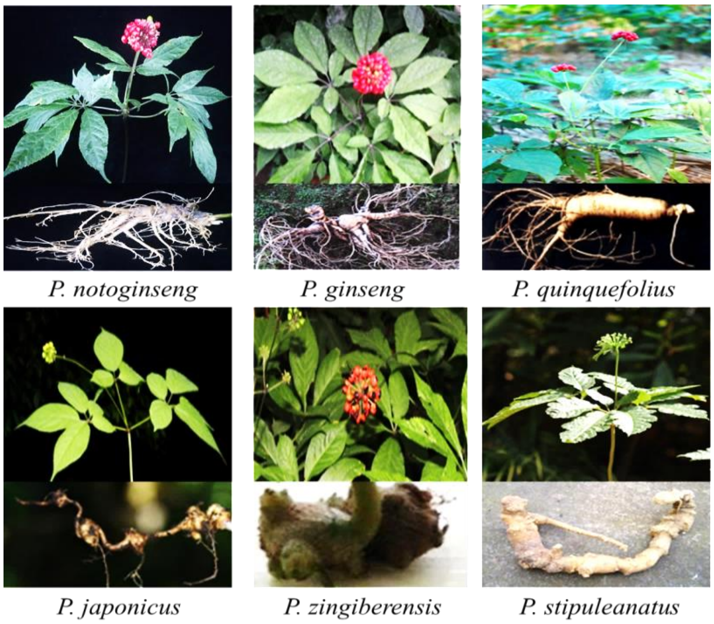

Figure 1. Morphology of plants and roots of each 6-*Panax* species.

Note: Pictures of *P. notoginseng* were taken by authors and others were cited from websites http://www.iplant.cn/frps or http://image.baidu.com/.

1.3 Phytochemistry

The chemical constituents of *Panax* includes **(A). Ginsenosides, (B). Polysaccharides, (C). Volatile Oils, (D). Amino acids and (E). Organic acids** (43,68,71,80,92,107,131) (Table 2).

(A). Ginsenosides: These are triterpenoid glycosides, the main active ingredients associated with the efficacy of *Panax* (63). These ginsenosides exhibit modulatory effects on the central nervous system, beneficial to patients suffering from cardiovascular diseases and have anti-diabetic and anti-tumor properties (121). At least 289 ginsenosides from different *Panax* plants have been identified (121). All ginsenosides of *Panax* based on the skeleton of their aglycones are classified into 3-classes; (i). Dammarane-, (ii). Oleanane- and (iii). Ocotillol-type.

Ginsenosides present in the plant shoot are dammarane- and ocotillol-type and in the root (most commonly used part of *Panax*), divided into two types: (i). Dammarane (found in *P. ginseng*, *P. notoginseng* and *P. quinquefolius*) and (ii). Oleanane (found in *P. zingiberensis*, *P. stipuleanatus*, *P. japonicus* var. angustifolius and *P. japonicus* var. bipinnatifidus) (1,39). Dammarane types, (based on the structural differentiation of the sapogenins) are further classified into two groups as under : (a) protopanaxadiol (PPD) ginsenosides viz., Rb_1, Rb_2, Rb_3, Rh_2, Rg_3, Ra_1, Ra_2, Ra_3, Rc, Rda and (b) protopanaxatriol (PPT) ginsenosides viz., Rg_1, Rg_2, Rh_1, Re, Rf, R_1, R_2, R_3, R_6 (Figure 2) (39,79,111).

Table 2. Allelochemicals in major *Panax* genus species: *P. ginseng, P. notoginseng* and *P. quinquefolium*

Monomeric substances	Species	Sources	References
Ginsenosides			
R_1, Rg_1, Re, Rg_2, Rd	*P. notoginseng*, *P. ginseng*, *P. quinquefolium* L.	Roots, soils and root exudates	53,120, 133
Rb_1	*P. ginseng*, *P. quinquefolium* L.	Rhizosphere soil	132, 133
Rb_2	*P. quinquefolium* L.	Rhizosphere soil	132
Phenolic acids			
p-Coumaric acid, vanillic acid, benzoic acid, *p*-hydroxybenzoic acid, ferulic acid and syringic acid	*P. notoginseng*, *P. quinquefolium* L., *P. ginseng*	Rhizosphere soil, root exudates	30,35,45,102
Salicylic acid	*P. quinquefolium* L., *P. ginseng*	Rhizosphere soil, root exudates	30,45
Phthalic acid	*P. notoginseng*	Rhizosphere soil, root exudates	108
Gallic acid, 3-phenylpropionic acid, Cinnamic acid	*P. ginseng*	Rhizosphere soil, root exudates	45
trans-Cinnamic acid, Vanillin	*P. quinquefolium* L.	Fibrous roots	30
Others			
Stearic acid, Palmitic acid	*P. notoginseng*	Rhizosphere soil, root exudates	108
Butanedioic acid bis (2-methylpropyl) ester, 1,2-benzenedicarboxylic acid bis (2-methylpropyl) ester	*P. ginseng*	Rhizosphere soil, root exudates	32

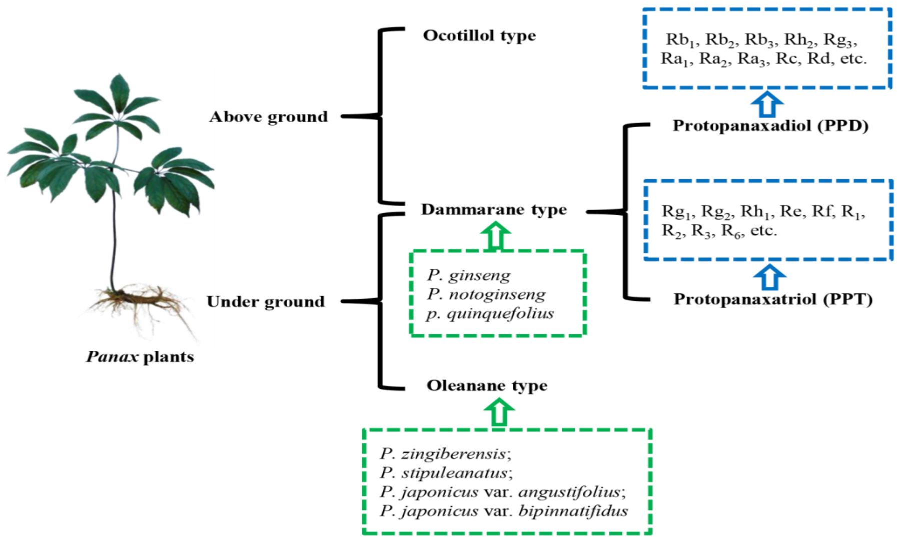

Figure 2. The main types of ginsenosides in *Panax* plants.

(B). Polysaccharides: These are also found in *Panax* and have significant effects on immune regulation and antioxidant activity (89). Studies on the composition and medicinal function of polysaccharides in *Panax* have mainly focused on *P. notoginseng*, *P. ginseng*, *P. quinquefolius and P. japonicus* var. major (11,42,89,144).

(C). Volatile Oils: These oils from *Panax* species are commonly used in health care products or cosmetics (113). Falcarinol is one of the main ingredients in *P. notoginseng* and *P. stipuleanatus* (107).

(D). Amino acids: *Panax* also contains variety of essential amino acids [lysine, phenylalanine and leucine (29)]. These are present in the branched roots or fibrous roots, and are higher than in taproots (29,82,90). Dencichine, a non-protein amino acid in *P. notoginseng*, is primarily responsible for the hemostatic and platelet-increasing properties *in vivo* (67).

(E). Organic acids: These especially phenolic acids secreted by the roots, have been widely reported as allelopathic substances (6,36,131).

2. ALLELOPATHIC RESEARCH

2.1 Allelochemicals

Allelopathy is a common biological phenomenon by which one organism produces biochemicals that influence the growth, survival, development, and reproduction of other organisms. These biochemicals are known as allelochemicals and have beneficial or detrimental effects on target organisms (13). Allelochemicals, which are released through root exudates, leaching, volatiles, or the decomposition of plants, are secondary metabolites (5,26). Medicinal herbs, due to their synthesis and release of large quantities of secondary metabolites, are typically the primary allelopathic plants in the environment (43). Some *Panax* plants, including *P. notoginseng*, *P. ginseng* and *P. quinquefolius*, have been reported as allelopathics (6,26). The root exudates and extracts from the roots or rhizosphere soil of *P. ginseng* and *P. notoginseng* have significant autotoxic effects on the growth of their roots (6,120). Some metabolites (phenolic acids, stearic acid and palmitic acid and esters) are widespread in *Panax* species plants and have been identified as allelochemicals (Table 2) (6,107,115,138). Ginsenosides, the main secondary metabolites of *Panax* plants, have also been identified as allelochemicals (116,120). However, whether ginsenosides are specific to *Panax* remains to be determined. In addition, the sources of allelochemicals in *Panax* genus and their degradation in the soil should be studied in future.

2.2 ALLELOPATHIC EFFECTS

2.2.1. Soil Sickness

The continuous cropping of *Panax* in the same field results in serious root rot disease, which drastically reduces its yield, a phenomenon called soil sickness (12,138) (Figure 3). Obviously, the build-up of detrimental soil biota [fungi (57), bacteria (54), nematodes (54)] is responsible for soil sickness of *Panax*. The fungi *Fusarium solani*, *F. oxysporum*, *Cylindrocarpon destructans* and *Phytophthora cactorum* frequently isolated are very pathogenic (57). Moreover, the soil sickness build-up-process decreases the antimicrobial bacteria (52). On the other hand, allelochemicals also contribute to the soil sickness. Two main types of allelochemicals (ginsenosides and phenolic acids) have been identified as autotoxins of *Panax* as these advesely affects the performance of *Panax* plants and also cause autotoxicity (14,18,30,47,50, 84,96,98,116,120,123,133). It is currently believed that the soil sickness of *Panax* is caused by the synergistic effects of both soil biota and allelochemicals. Phenolic acids and ginsenosides stimulates the growth and pathogenicity of pathogens in rhizosphere soil (61,83,114,118,126). These also modify the rhizosphere microbiome and thereby, adversely affect the health of *Panax* plants (61,118,126).

Figure 3. Effects of soil sickness on plants population and roots growth of *P. notoginseng*

2.2.2. Autotoxicity of *Panax* and its mechanisms

Autotoxicity is harmful allelopathic effect among the individuals plants of same species that severely reduces their yields and quality (15,100). This phenomenon in *Panax* species has been shown as the inhibition of seed germination, seedling growth and root cell death caused by aqueous extracts from the roots, rhizosphere, consecutively cultivated soil, as well as the root exudates (9,96,112,120). Subsequently, two main types of phytochemicals responsible for this autotoxicity identified were: (i). Phenolic acids and (ii). Ginsenosides (30,50, 84,96,116,120,133).

(i). **Phenolic acids :** The Phenolic acids [ferulic acid, benzoic acid, *p*-coumaric acid, trans-cinnamic acid and vanillic acid (Table 2)] inhibited the seed germination and seedling growth of *Panax* in field investigations (30,50,84,96). *p*-Coumaric acid inhibited the growth of radicle and embryo of *P. quinquefolium* (38). This compound also inhibited the growth of aboveground parts by reducing the photosynthetic capacity and the leaves phenylalanine ammonialyase (PAL) activity (38). Benzoic acid induces the accumulation of reactive oxygen species (ROS) to cause oxidative stress in *P. ginseng* (98). Other plants also suffer from the autotoxicity of phenolic acids. Ferulic acid causes the autotoxic damage in *Oryza sativa* L. and *Rehmannia glutinosa* Libosch (14,47). Cinnamic acid inhibits the growth of cucumber through accumulation of reactive oxygen species (ROS) (18,123). Thus, phenolic acids are not specific autotoxins to *Panax* plants. It seems that the over-accumulation of ROS is a general mechanism involved in the autotoxicity caused by these phenolic compounds.

(ii). **Ginsenosides** : These are unique biologically-active compounds produced by *Panax* genus plants. They can be released into the rhizosphere soil by root exudates, leaching and the decomposition of plant residues (61). Ginsenosides R_1, Rg_1, Re, Rb_1, Rb_3, Rg_2 and Rd were identified in the roots and consecutively in cultivated soil (116,120). Rg_1, Re, Rg_2 and Rd were identified in the root exudates of *P. notoginseng* (120). Among them, R_1, Rg_1, Re, Rg_2 and Rd showed significant autotoxicity to *P. notoginseng* in a dose-dependent manner (120). Total ginsenosides (TGS) and monomer Rb_1 had significant autotoxic effects on the seedling growth, root vigour and chlorophyll synthesis of *P. ginseng* (133). Application of 100 mg L^{-1} TGS and Rb_1, damaged the tonoplast, nuclear membrane, other organelles and caused plasmolysis (133). Further study demonstrated that these effects were due to the burst of ROS and increased content of malonaldehyde (MDA) (116,133). Transcriptomic and cellular approaches also confirmed that Rg_1 kills the root cells of *P. notoginseng* by causing the ROS burst and then disrupting the cell membrane and cell wall (116). Interestingly exogenous ascorbate (ASC), an antioxidant involved in the ASC-GSH (glutathione) cycle, gentiobiose, a substance up-regulated the synthesis of GSH and activation of the ASC-GSH cycle and oxalic acid could alleviate the autotoxicity caused by Rg_1 (24,53,86,116). The ASC/DHA (dehydroascorbate) and GSH/GSSG (oxidized GSH) ratio, as well as ASC peroxidase (APX) activity in the roots, were significantly decreased after exposure to Rg_1. Exogenous application of ASC or gentiobiose increased the ASC/DHA and GSH/GSSG ratio and improved the APX activity and even stimulated the activity of dehydroascorbate reductase (DHAR), glutathione reductase (GR) and glutathione S-transferase (GST) (116).

Thus, the genus *Panax* suffers from autotoxicity caused by phenolic acids and ginsenosides. Both types of autotoxins induce a ROS burst to cause cell death (14,18,109,124). The exogenous application of antioxidants could potentially overcome the problem of autotoxicity in agricultural production. Nevertheless, additional studies are needed to elucidate the regulatory mechanism and signaling pathways of the autotoxins associated with antioxidant enzymes and genes. In recent years, the mode-of-action of chemicals has been deeply studied using transcriptomics, proteomics, or metabolomics (32,55,56,116), which could provide a framework for further genetic studies on autotoxicity.

2.2.3. Allelopathic effects of *Panax* on crops

The genus *Panax* plants have allelopathic effects on crops. The laboratory bioassays reported that consecutively cultivated soil, plant parts aqueous extracts and root exudates of *Panax* were inhibitory to seeds germination or seedlings growth of *Raphanus sativus* L., *Brassica chinensis* L., *Lactuca sativa* L., *Triticum aestivum* L., *Zea mays* L. and *Brassica napus* L. (27,84,93,125,132). Researchers further found that ginsenosides and phenolic acids were responsible for these inhibitory effects (84,132). Many crops are rotated with genus *Panax* plants to alleviate the detrimental impacts of continuous cropping. In Japan, *P. ginseng* rotated with *T. aestivum* and *Z. mays* could shorten the period of damage caused by continuous cropping from 30-60 years to 13-19 years (87). In South Korea, *P. ginseng* is rotated with rice in paddy field so that the fields can be again planted by *P. ginseng* (40). In China, *P. notoginseng* rotated with *Z. mays* regulates the structure and functions of the microbial community to avoid replanting failure (136). Thus, the genus *Panax* plants allelopathy to other crops does not significantly hinder the agricultural production.

2.2.4. Allelopathic effects of *Panax* on pathogens

Phenolic acids and ginsenosides are allelopathic to soil-borne pathogens. A series of studies demonstrated that they protects the host plants against pathogen infection (21,37,58,64,65,69,75).

(i). **Phenolic acids :** The infected root tissue of *P. ginseng* had higher contents of phenolic compounds than adjoining healthy tissues (69). Some of these phenolic acids reduces the production of fungal toxins (e.g., trichothecene and 3-acetyl-4-deoxynivalenol) in *Fusarium culmorum* (64,65), or even kill pathogens by inducing programmed cell death (PCD) (75). Both the growth and trichothecene productivity of *F. graminearum* were reduced in moderately resistant *Z. mays* variety rich in chlorogenic acid compared with the susceptible varieties (58). However, some pathogens use the phenolic acids as carbon sources for growth. *Sclerotinia sclerotiorum*, a necrotrophic fungal pathogen that causes diseases in many important crops, degrades the flavonoids by quercetin dioxygenase via catalyzing the cleavage of the flavonol carbon skeleton (10). In *Panax*, phenolic acids (salicylic acid, cinnamic acid and benzoic acid) inhibits the growth of *Cylindrocarpon destructans* but stimulates the activities of hydrolytic enzymes (pectinase and cellulase) in the pathogen (83). Syringic acid and vanillic acid promotes the hyphal growth of *R. solani* (114).

(ii). **Ginsenosides** : These play multiple roles in plant and microbe interactions. Ginsenosides act as chemical defense substance against pathogen infection (21,37). The content of Rb_1 (PPD-type) rapidly increases in the infected roots of *P. quinquefolium* and the conidial germination of *Fusarium* spp. was significantly suppressed by Rb_1 (37). Some PPT-type ginsenosides have antifungal activities and may provide in the defense to *P. ginseng* during the invasion of *Ilyonectria* species (21). The contents of major ginsenosides in *P. ginseng* significantly increased, when the roots were infected by *I. robusta* and *I. leucospermi* (21). In the rhizosphere, ginsenosides could stimulate the growth of soil-borne pathogens. The ginsenosides from *P. quinquefolium* or *P. notoginseng* significantly stimulated the growth of soil-borne pathogens [*Pythium irregulare*, *Phytophthora cactorum*, *I. destructans*, *F. solani* and *F. oxysporum* (60,61,118,126)]. Ginsenosides is hydrolyzed by microbial glycosyl hydrolases to glycosyl, as a nutrient for microbes (91). Further studies showed that 20 (S)-protopanaxadiol ginsenosides (Rb_1, Rb_2, Rc, Rd and to a limited extent G-XVII) could be degraded into minor ginsenoside F_2 by glycosidase secreted by the pathogen *P. irregulare* (126). Yang *et al*. (117) found that *P. cactorum* have high utilization and detoxification ability of ginsenosides (117). Transcriptomic studies showed that when treated with ginsenoside Rg_1, *P. cactorum* significantly up-regulated the detoxification enzyme-related genes and glycoside hydrolase-related genes and thus *P. cactorum* could use Rg_1 as the growth nutrient (117).

Thus the phenolic acids and ginsenosides have the antimicrobial activity in plant tissues but stimulates the pathogens in rhizosphere soil. These may be due to the differences in concentration in the tissue and rhizosphere. Besides, the pathogens may adapt to these allelochemicals. The detailed mechanisms need to be further investigated.

2.2.5. Allelopathic effects of genus *Panax* species to the rhizospheric microbiome

The rhizosphere microbiome of plants regulates the plants nutrition and plants survival (3). Rhizodeposits (e.g., exudates, border cells, mucilage) are the main driving factors shaping the rhizosphere microbiome and affecting the plants health (2,28,66,70). The difference in rhizodeposits composition and content influences the community structure and function of rhizosphere microorganisms (66). Allelochemicals (one type of rhizodeposit) are released into the environment to affect the performance of the same or different plant species (33,78). Some allelochemicals modifies the rhizospheric microbiome to promote the growth and pathogenicity of pathogens (47,101,123,134). Therefore, allelochemicals could affect the interactions between the plant and rhizosphere microbiome. Many phenolic acids with toxicity could modify the rhizosphere microbiome and affect the plants health (95,100,140,141). The plants alters their root exudate composition under biotic and abiotic stress to modify the rhizosphere microbiome, especially by enriching it with the beneficial microbes as an adaptive strategy (4,22,73,110,143).

The rhizospheric microbiome plays an important role in the health of genus *Panax* plants. Wu *et al*. (104) reported that rhizosphere microbiomes differ between healthy and diseased *P. notoginseng* plants (104). The rhizosphere soils of diseased plants were rich in total microbes and Gram-negative bacteria but were poor in actinomycetes and arbuscular mycorrhizal fungi than in healthy plants (97). Dong *et al*. (19) found that fungal diversity significantly decreased in rhizosphere soil that had been consecutively cultured with *P. notoginseng* for three years and the fungal diversity was correlated negatively with the *P. notoginseng* mortality (19). The soil rich in *F. oxysporum* and *Phaeosphaeria rousseliana* causes more plant death, while the richness in *Coniosporium perforans* had lower death rate (19). Luo *et al*. (52) found that the growing of *P. notoginseng* changes the rhizosphere microbiome and increased the rhizospheric Ascomycota, soil-borne pathogens (*F. oxysporum*, *F. solani* and *Monographella. cucumerina*), on the other hand decreased the bacteria (Firmicutes and Acidobacteria, including the genera *Pseudomonas*, *Bacillus*, *Acinetobacter* and *Burkholderia*) (52).

As we know, ginsenosides secreted from *P. notoginseng* and *P. quinquefolius* (61,120) inhibited the growth of *T. hamatum* (61) but stimulated the growth of pathogens [*Phytophthora cactorum*, *F. solani* and *F. oxysporum*] (61,118,126). The change in rhizospheric microbiome may be partly mediated by the secretion of the ginsenosides from the root exudates of *Panax* plants. However, the relationship between the dynamics of the rhizospheric microbiome and root exudates of *Panax* plants needs further studies.

3. REDUCING THE ALLELOCHEMICALS IN SOIL

The allelochemicals excreted from the genus *Panax* plants cause soil sickness in continuous replanting of *Panax* plants. They are not only allelopathic to other plants, but also promote the growth of pathogens and modify the microbial community and function. Therefore, it is critical that allelochemicals in the soil are degraded for the sustainable cultivation of *Panax* plants. Several approaches have been reported to reduce the allelochemicals contents in the soil.

(i). ADSORBENTS: Allelochemicals can be absorbed by materials, such as biochar, bagasse and bamboo charcoal (72,134). The activated charcoal and biochar effectively decreases the concentration of ginsenosides in root exudates to alleviate the autotoxicity in cultivated soil (119,120). Using bagasse as a soil amendment also significantly alleviates the replanting problem of *P. notoginseng* through the adsorption of autotoxins (62).

(ii). REDOX ACTION: Allelochemicals can be eliminated through redox action. Some oxidants (ozone and hydrogen peroxide), alleviates the allelopathy by inactivating the allelochemicals through redox action (97,128). Ozone effectively eliminates the ginsenosides in consecutively cultivated soil and significantly improves the seedling emergence and survival of *P. notoginseng* (128).

(iii). MICROBES: Allelochemicals can be degraded by microbes. Some rhizosphere soil microorganisms can use the autotoxins as carbon sources, thereby reducing their harmful effects on plant growth (8). For example, phenolic acids could be degraded by *Trichoderma harzianum* Tri41 (46). Ginsenosides could be used as carbon sources for the growth of *P. cactorum* (117). The autotoxic ginsenosides may be converted into non-toxic ginsenosides by microbial transformation. For example, Rb_1 could be transformed by the soil fungus *Aspergillus niger* sp. J7 into Rd and ultimately converted into the rare ginsenoside compound K (23).

4. FUTURE RESEARCH

The genus *Panax* plants are very allelopathic to themselves i.e. Autotoxicity. In last 50- years, these allelochemicals have been identified and deciphered the mechanisms in the interactions between the *Panax* plants and other plants or microorganisms. Therefore, the further research may be done in following areas:

4.1 Identification of other allelochemicals: Allelochemicals are released as root exudates, leachates, volatiles, or degradation of biomass. Phenolic acids and ginsenosides are the main allelochemicals in *Panax* plants (6,116,120,138). Besides, numerous phytochemicals (polysaccharides, volatile oils, amino acids and organic acids) are present in *Panax* plants (43,68,71,80,92,107,131). The presence of other potential allelochemicals, as well as their source and allelopathic functions, need to be clarified.

4.2 Allelopathic mechanisms involved in plant-plant or plant-pathogen interactions: The genus *Panax* plants have allelopathic effects on themselves and other plants (30,50,84,96,116,120,132,133). The allelochemicals damages the root cells due to accumulation of ROS in the roots, thus disrupting the cell membrane and cell wall (116). However, the detailed mechanisms are still unknown. Further study on its specific regulatory mechanism can provide insights into the molecular breeding of anti-autotoxic plants. In addition, phenolic acids and ginsenosides play multiple allelopathic roles in plant and microbe interactions. They can inhibit the performance of the same or different plant species, or can promote the growth and pathogenicity of pathogens (47,61,101,134). The synergistic effects between allelochemicals and pathogens on plant health and the underlying mechanisms should be studied on in future.

4.3 Allelochemicals effect on the rhizosphere microbiome: The rhizodeposits (e.g., exudates, border cells and mucilage) plays important roles in shaping the rhizosphere microbial community (28,66,81,88). Allelochemicals are one type of rhizodeposits, that act as carbon sources, signals, and/or antimicrobial substances to shape the rhizospheric microbiota (59,81,88,129). The phenolic acids secreted by *P. ginseng* and *P. quinquefolium* modifies the diversity and functions of the rhizosphere community and affects the occurrence of root rot disease (30,44,95,140,141,142). Notably, ginsenosides can be hydrolyzed by microbial glycosyl hydrolases to release glycosyl as a nutrient for microbes (91,117). Whether ginsenosides or other allelochemicals of *Panax* can modify the rhizosphere microbiome is still unkown. In addition, the ginsenoside Rg_1 has the ability to damage the root cell wall of *P. notoginseng* and releases of cell wall components (116). These cell wall components can be used by microorganisms as carbon sources (16). Goldford *et al*. (25) showed that the source of carbon governs the microbial community (25). Thus, autotoxic ginsenosides that induce root cell wall degradation may have great potential to change the rhizosphere microbiome in *Panax* plants, this aspect also requires further confirmation.

4.4 Biotic and abiotic stresses effects on allelochemicals release and their subsequent effects: The biotic and abiotic stress changes the metabolite composition of plants and thereby alters the composition of root exudates (17,31,41,137). Most *Panax* plants are shade-loving and thus sensitive to biotic and abiotic stresses [pathogen infection, high temperature and strong light] (49,105). It is still unknown that whether biotic or abiotic stresses induce the root metabolites secretion. In addition, whether the biotic or abiotic stresses modifies the allelochemicals and thereby could change the interactions between the plants and associated pathogens or microbiome warrants further exploration.

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