Pyrroloquinoline quinone (PQQ): Role in Plant-Microbe Interactions

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9.1 Introduction

Pyrroloquinoline quinone (PQQ) (Fig. 9.1) is synthesized by bacteria during the stationary phase of their growth. It is heat stable and soluble in water, and was first discovered in methylotrophic bacteria (Salisbury et al. 1979). PQQ, among its various functions, serves as a cofactor and belongs to the family of cofactors of the o-quinone type, which is comprised of other four cofactors well characterized: tryptophan tryptophyl quinone, lysine tyrosyl quinone, cysteine tryptophyl quinone, and topaquinone (Stites et al. 1999).

The enzymes involved in the above types of cofactors have been designated as quinoproteins (Anthony and Gosh 1998; Duine 1999; Matsushita et al. 2002; Miyasaki et al. 2006; Ikemoto et al. 2012). PQQ is the only cofactor in this family that is non-covalently bound to enzymes, such as glucose dehydrogenases, methanol dehydrogenase, sorbitol dehydrogenase, and glycerol dehydrogenase, which are involved in the oxidation of sugars, alcohols, and amines. PQQ is also bound to glutamate decarboxylase and lactate dehydrogenases (Knowles et al. 1987; Duine 1999; Anthony and Gosh 1998; De Biase et al. 1991; Akagawa et al. 2016). PQQ may also activate protein kinase, which is involved in signal transduction (Khairnar et al. 2007; Rajpurohit et al. 2013). Matsumura et al. (2014) reported that, in the basidiomycete *Coprinopsis cinerea*, PQQ may also activate a new type of quinoprotein with a signal peptide for extracellular secretion and a domain for adsorption on cellulose, besides the PQQ-dependent sugar dehydrogenase and cytochrome domains.

PQQ has been found in prokaryotes and eukaryotes, i.e., in both higher and lower organisms (Misra et al. 2012). In food, this molecule is found in quantities ranging

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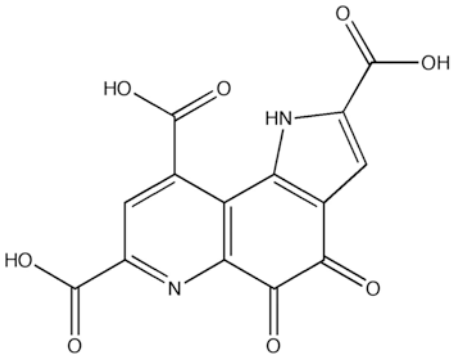

Fig. 9.1 Pyrroloquinoline quinone (PQQ) structure

from 0.7 to 7.0 ng/g (or ml), depending on whether the food is solid or liquid (Noji et al. 2007). Although plants and animals do not produce PQQ themselves, PQQ is present in plant and animal tissues in nanogram-to-gram ranges (Kumazawa et al. 1992, 1995).

The presence of PQQ in food could be related to the production of the cofactor by bacteria present in the food (Stites et al. 1999; Rucker et al. 2009). The existence of PQQ in all these organisms, even if they do not produce it, is relevant, because it may be involved in health, fertility, neonatal development, energy metabolism, and probiotic properties in mammals (Bauerly et al. 2011), in addition to being able to act as a powerful antioxidant in animals and humans (He et al. 2003).

Although PQQ can be present in different organisms and function in them, only some bacteria synthesize it. It has been estimated, by the in silico analysis of approximately 126 bacterial species (mainly gram-negative), that these species contain the genes necessary for the synthesis of this cofactor (Shen et al. 2012; Klinman and Bonnot 2014).

Five genes are required in the synthesis of PQQ, although the number, and their position and nomenclature, vary among genuses and species, and even among strains (Schnider et al. 1995; Choi et al. 2008, Klinman and Bonnot 2014). Some bacterial species (mostly gram-negatives), contain the genes *pqqA*, *pqqB*, *pqqC*, *pqqD*, and *pqqE* organized in an operon; on the other hand, *pqq*F is usually separated from the rest of the genes (Shen et al. 2012; Klinman and Bonnot 2014).

The PQQ synthesis pathway has not been completely elucidated and is not yet fully understood. Bioinformatic studies have elucidated the characteristics of participating proteins, allowing a vision of how PQQ is synthesized. It is now known that the peptide precursor for the synthesis of PQQ (PqqA), is relatively conserved in size, although this may differ between genuses and species, varying between 23 and 39 amino acids (Puehringer et al. 2008).

PqqA contains a region conserving approximately half of its amino acid sequence, which corresponds to Glu-X-X-X-Tir (Stites et al. 1999; Choi et al. 2008; Puehringer et al. 2008). Through mutagenesis studies, it was found that this peptide is essential

for the synthesis of PQQ in most bacteria, although this is not the case for *Methylobacterium extorquens* AM1, because, in *pqq*A mutants, although the production of PQQ continues, the concentration is low in comparison with wild-type strain, and, there was no another copy of the pqqA gene (Toyama and Lidstrom 1998). This finding suggests that, in the mutant strain, there would be a peptide similar in length to that in the wild type, or at least a conserved region of PqqA, and thus there would be slight synthesis in the mutant strain. On the other hand, in *Methylokorus* sp. MP 688, the synthesis of PqqA is increased in the stationary phase under conditions of acidic pH and 50% dissolved oxygen (Ge et al. 2013). PqqB is a necessary protein for the synthesis of this cofactor, which consists of approximately 300 amino acids and is located within the family of metallo-beta-lactamases, as shown by bioinformatic analysis (Puehringer et al. 2008; Shen et al. 2012). In addition, PqqC may catalyze the terminal step in the biosynthesis of PQQ (Magnusson et al. 2004; Puehringer et al. 2008), facilitating the oxidation and cycling of PQQ, as well as accelerating its catalysis in the presence of molecular oxygen (Magnusson et al. 2004). Furthermore, this protein has been proposed as a phylogenetic marker, at least for the genus *Pseudomonas* (Meyer et al. 2011).

PqqD is a chaperone of the family of RiPP chaperone proteins, which consists of approximately 90 amino acid residues (Evans RL III et al. 2016; Puehringer et al. 2008), and can bind the precursor peptide PqqA (perhaps in a hydroxylated state) and provide it to the PqqE enzyme (Evans RL III et al. 2016, Tsai et al. 2009; Wecksler et al. 2010).

Barr et al. (2016) showed that, in the presence of the peptide chaperone PqqD, PqqE is a radical S-adenosylmethionine (SAM) protein that catalyzes the carbon-carbon bond formation between a glutamate and tyrosine side chain within the small peptide substrate PqqA. As a result of linkage of the Cγ of glutamate and Cϵ of tyrosine by PqqE, these two residues are hypothesized to be cleaved from PqqA by PqqF (Wei et al. 2016).

Various conditions can encourage or undermine the production of PQQ. One of these conditions is related to the carbon source available for the growth of bacteria such as *Acinetobacter calcoaceticus*, *Pseudomonas putida*, and *P. stutzeri,* in which the production of PQQ is favored in the presence of ethanol and methanol, but not in the presence of glucose, succinate, and quinate (Van Kleef and Duine 1989). In contrast, *P. aeruginosa pqq* operon was induced upon aerobic growth on ethanol, 1- propanol, 1,2-propanediol, and 1-butanol, however on glycerol, succinate and acetate, transcription was low (Gliese et al. 2010). In some methylotrophic bacteria, the presence of trace elements, such as calcium, zinc, manganese, and copper, can promote the production of PQQ, at low cell density. Otherwise, in the presence of iron, at high cell density, the output of PQQ is deficient (Urakami et al. 1992). Some ions are relevant in the binding of quinoproteins. For example, many studies confirm that Ca^{2+} and Mg^{2+} ions are involved in the binding of PQQ to dehydrogenases (Anthony and Gosh 1998; Asteriani and Duine 1998).

9.2 Functions, Mechanisms, and/or Effects of PQQ in Bacteria and Plants

Some of the mechanisms and attributes by which plant growth-promoting bacteria (PGPB) act, including those that allow them to compete with ? and maintain and promote the growth of plants, are influenced by PQQ or its synthesis genes, either directly or indirectly (Table 9.1).

9.2.1 PQQ as a Plant Growth Promoter

It is now clear that there are several mechanisms by which bacteria stimulate the growth of plants, with PQQ being a molecule that has a direct part in this process. A member of the Rhizobiaceae family, *Rhizobium tropici* CIAT 899, can establish nitrogen-fixing symbiosis with a wide range of legume hosts and synthesize an inactive apo-glucose dehydrogenase (GDH), which requires the presence of PQQ to be activated. Inoculation experiments in *Phaseolus vulgaris* L. beans, when PQQ was added at a concentration of 10 nM, significantly increased shoot and root weight, N and P contents, nodule weight, and acetylene reducing activities compared with plants where PQQ was not added. Further, the synthesis of gluconic acid and 2-keto-gluconic acids, and the solubilization of phosphates, were different in *Rhizobium tropici* CIAT 899 when exogenous PQQ was added, showing that PQQ produced an advantage in the promotion of plant growth (Cho et al. 2003).

Plant growth promotion has been associated with the production of PQQ, as evidenced by a significant increase in the fresh weight of cucumber (*Cucumis sativus*) seedlings when synthetic PQQ was added (5–1000 nM), thereby confirming that PQQ is a plant growth promotion factor. *Pseudomonas fluorescens* B16 is a bacterium that may promote plant growth in the tomato (*Solanum lycopersicum*), among others, and random mutations have identified the possible genes responsible for this phenotype. Phenotype generated by mutation of the *pqq H* gene resulted in a loss of ability to promote growth. In addition, it was demonstrated that pqq H gene acts as a transcriptional regulator that acts on pqq genes, which presented homology with TetR family of transcriptional repressors (Choi et al. 2008). An experimental study has suggested that PQQ acts as an antioxidant in plants, as shown by the treatment of cucumber leaf discs with PQQ and wild-type B16 resulting in the scavenging of reactive oxygen species (ROS) and hydrogen peroxide (Choi et al. 2008). Different species of *Pseudomonas,* isolated from the rhizosphere of peas, were confirmed as being phosphate-solubilizing bacteria, as shown by an increase in the total weight of the plant (Oteino et al. 2015).

Rahnella aquatilis HX2, which was isolated from soybean rhizosphere (Kim et al. 1997) can promote maize growth. The *pqqA* and *pqqB* mutants showed an adverse effect on its growth-promoting activities, such as a decrease in the length, as well as a decrease in the dry and fresh weight of maize plants (Li et al. 2014). In *Pseudomonas aeruginosa* CMG860, *pqq*A-d and *pqq*E mutants obtained with acridine orange, showed a change in their capacity to promote growth in bean plants (a

Table 9.1 Functions, mechanisms or effects of pyrroloquinoline quinone PQQ

Function	Mechanisms and effects	References
PQQ as a plant growth promoter	Higher plant weight, higher fresh weight and dry weight of seedlings, increased nitrogen fixation and phosphorus solubilization	Oteino et al. (2015), Naveed et al. (2015), Li et al. (2014), Ahmed and Shahab (2010), Choi et al. (2008), Cho et al. (2003), and Kim et al. (1997)
	Increased nodulation	
Phosphate solubilization	Phosphorus biofertilizers, secretion of gluconic acid as a phosphate-solubilizing agent	Rodríguez et al. (2000, 2006), Farhat et al. (2013), Patel et al. (2015), Wagh et al. (2014), Stella and Halimi (2015), and Anzuay et al. (2017)
PQQ and biocontrol	Bacterial and fungal biocontrol regulation	Han et al. (2008), Kim et al. (2003), Li et al. (2014), Guo et al. (2009), and Kremmydas et al. (2013)
PQQ and systemic resistance in plants	Induction of systemic resistance in plants	Han et al. (2008)
PQQ and bacterial mutualism	PQQ acts as an exogenous molecule that activates apo-quinoproteins in non-PQQ-synthesizing bacteria	Van Schie et al. (1984), Hommes et al. (1984), Groen et al. (1986), and Shimao et al. (1984)
PQQ and synthesis of antimicrobials	Regulation of antimicrobial synthesis	Schnider et al. (1995), Xu et al. (2014), and Arakawa et al. (2005)
PQQ and oxidative stress	Antioxidant in the cyclic redox system	Khairnar et al. (2003), Misra et al. (2004), Rucker et al. (2009), Paz et al. (1990), Ouchi et al. (2009), and Choi et al. (2008)
	Stimulates catalase and superoxide dismutase activity	
PQQ involved in swarming and chemotaxis	PQQ as a chemoattractant. Biosynthesis of pqq genes is modulated according to swarming motility	Tremblay and Déziel (2010), Van Schie et al. (1985), Matsushita et al. (1997), and De Jonge et al. (1996)
PQQ in signal transduction and UV and γ radiation stress resistance	PQQ as an activator of protein kinases and an antioxidant that prevents damage to proteins and DNA caused by UV and γ radiation	Khairnar et al. (2007) and Rajpurohit et al. (2013)
PQQ as a growth factor	PQQ as a cofactor in different quinoproteins with different metabolic activities	Ameyama et al. (1984), Shimao et al. (1984), and Trček et al. (2006, 2007)

PQQ Pirrolequinolinequinone, *UV* Ultraviolet, *γ* gamma radiation

22–25% reduction), even though they still produced indole acetic acid, a known phytoregulator that promotes plant growth (Ahmed and Shahab 2010).

Regarding P. *fluorescens* QAU67 and P. *putida*, QAU90 have been demonstrated by using in vitro tests that they can synthesize GDH and PQQ when they are inoculated in the roots, and both had played a crucial role for their growth-promoting

effects in lettuce. On the other hand, in vivo test with crops such as rice, bean, and tomato showed a significant increase in the following parameters: plant height, fresh and dry weight (Naveed et al. 2015).

9.2.2 PQQ and Phosphate-Solubilizing Capacity

Phosphorus is the second most crucial nutrient after nitrogen in heterotrophic bacteria (Mills et al. 2008). It is also required by plants for carrying out processes such as photosynthesis, and for transduction and respiration signals, among others (Khan et al. 2010). Phosphorus is mostly present in insoluble complexes, or linked to organic compounds such as phytates, which cannot be assimilated by plants (Sharma et al. 2013). Among the mechanisms by which plants may have access to phosphorus in the soil are those where phosphate-solubilizing microorganisms are involved. These microorganisms, mainly bacteria, can produce organic acids and can synthesize phosphatases to solubilize phosphates (Rodríguez et al. 2006).

Numerous studies have been conducted seeking to implement the solubilization of phosphates in bacteria that are unable to do so for themselves; this has been achieved through the cloning of genes involved in the synthesis of PQQ. The PQQ synthase of *Erwinia herbicola*, which was cloned in *Burkholderia cepacia* S-16 and *Pseudomonas* sp., resulted in a solubilizing phosphate bacterium (Rodríguez et al. 2000). The PQQ biosynthesis genes (*pqqBCDE*) and the *gdh* gene belonging to *Serratia marcescens* were cloned in *Escherichia coli*, and it was observed that, regardless of whether these genes are together or separated, they provide the capacity to solubilize phosphates (Farhat et al. 2013). Of note, there are genetically manipulated growth-promoting bacteria, which, despite having enzymes such as glucose dehydrogenase, are unable to use the enzyme because they do not have the PQQ genes. However, in *Rhizobium leguminosarum,* in which the PQQ genes were cloned from *P. fluorescens* B16, the genes provided the capacity to solubilize phosphate for the bacteria (Patel et al. 2015).

In *Herbaspirillum seropedicae* Z67, the *pqq* genes belonging to *P. fluorescens* and *Acinetobacter calcoaceticus* were cloned, conferring on *H. seropedicae* the capacity to produce PQQ and to solubilize phosphate (Wagh et al. 2014). It has been reported that, owing to their production of PQQ and gluconic acid, various bacteria, such as *Klebsiella* sp., *Enterobacter* sp., and *Pseudomonas* sp., have the capacity to solubilize insoluble phosphates ($Ca_3(PO_4)_2$, $FePO_4$, or $AlPO_4$) (Stella and Halimi 2015). Therefore, these bacteria are considered as potential candidates for use as P-biofertilizers for peanut and maize (Anzuay et al. 2017).

It has been determined that the expression of PQQ synthesis genes is stimulated when bacteria (*P. putida* KT2440) are grown on glucose as the sole carbon source, and with low amounts of soluble phosphate; the levels of expression of the *pqqF* and *pqqB* genes reflect the levels of PQQ synthesized. Multiple studies suggest that one or both of these genes may serve to modulate PQQ levels according to growth conditions (An et al. 2016).

9.2.3 PQQ and Biocontrol

As a continuous and natural process, biocontrol is conceptualized as a balancing force that allows the maintaining of an ecosystem in good condition. Biocontrol is a characteristic of PGPB, and the mechanisms by which these types of bacteria exert biocontrol on pathogens are diverse. One of the indirect mechanisms to achieve this biocontrol seems to be the production of PQQ, and even the synthesis of glucose dehydrogenase is dependent on PQQ.

The *pqq*A mutants of *Enterobacter intermedium*, a biocontrol bacterium that acts on the pathogenic rice fungus, *Magnaporthe grisea*, lose the ability to biocontrol this fungus, in addition to losing the ability to produce gluconic acid, with the loss of capacity to solubilize insoluble phosphates. However, gluconic acid only cannot eliminate this phytopathogenic fungus. It is well known that *E. intermedium* 60-2G produces 3-methylpropanoic acid, an antibiotic with antifungal activity, perhaps PQQ is required for the synthesis of this antifungal agent. This suggests that PQQ is indirectly involved in biocontrol of pathogenic fungus *Magnaporthe grisea* (Han et al. 2008; Kim et al. 2003).

Rahnella aquatilis HX2, as a biocontrol agent of grapevine crown gall, also has the capacity to suppress the crown gall in sunflowers caused by *Agrobacterium viti*. Pqq and gdh mutants of *R. equatilis* caused the loss of biocontrol of *A. vitis*. This phenotype was fully restored when they were genetically complemented (Li et al. 2014; Guo et al. 2009).

In the case of *P. fluorescens,* isolated from the bean rhizosphere, when mutated at random, it lost the ability to exert biocontrol on the fungus *Pythium ultimum*, which causes root rot of beans. The genes involved in this phenotype were identified as *gdh* and there was an open reading frame that appeared to belong to the *pqq* genes (Kremmydas et al. 2013).

9.2.4 PQQ and Systemic Resistance in Plants

The induction of systemic resistance in plants has been demonstrated to be a very efficient mechanism that promotes plant growth by confronting many different pathogens and herbivores, allowing systemic resistance to be classified as an environmentally friendly method to combat these agents (Mhlongo et al. 2018).

It is well known that *Enterobacter intermedium* induces systemic resistance in tobacco plants, but when the *pqq* gene is mutated, *Enterobacter intermedium* is unable to induce this resistance; moreover, under this condition, it does not produce gluconic acid. Of note, gluconic acid itself did not show any induction of systemic resistance to soft-rot disease (Han et al. 2008).

9.2.5 PQQ and Bacterial Mutualism

In a mutualistic relationship, organisms of different species benefit each other; previous studies have shown that, with PQQ, bacteria and plants can have such a

relationship (Goldstein et al. 1999). Also, PQQ can be involved in mutualistic interactions among bacteria.

In this regard, some bacteria cannot synthesize PQQ; it also appears that they produce apo-quinoproteins, which are not functional until PQQ is added exogenously. For example, when PQQ is added to *Acinetobacter lwoffii*, it seems that aldose sugars can be used as an auxiliary energy source, owing to the presence of apoglucose dehydrogenase (Van Schie et al. 1984). Another example involves *E. coli*, which synthesizes a quinoprotein glucose dehydrogenase apoenzyme and supplies an additional route for sugar metabolism, but this is functional only when PQQ is added exogenously or when PQQ biosynthesis genes are introduced into the bacterium (Hommes et al. 1984). *Pseudomonas testosteroni* synthesizes alcohol dehydrogenase (ADH) in its apo-form and metabolizes alcohol only when PQQ is added to the culture medium (Groen et al. 1986); another study showed that *Pseudomonas* metabolized polyvinyl alcohol only when PQQ was added (Shimao et al. 1984).

The question arises of why does a bacterium synthesize an inactive enzyme and depend on exogenously provided PQQ for its activity? A possible reason is that the bacteria live in communities where the presence of PQQ triggers the survival of other bacteria that are deficient in the synthesis of the cofactor. Therefore, a kind of mutualistic bacterial relationship is maintained, causing species to be preserved and bacterial diversity and ecological balance to be maintained.

9.2.6 PQQ and the Synthesis of Antimicrobials

One mechanism by which microorganisms regulate and maintain their populations is by the use of antimicrobials. In many cases, some antimicrobials, contrary to what might be supposed, help to ensure the preservation of bacterial diversity and maintain populations and ecological balance (Kerr et al. 2002; Kirkup and Riley 2004).

In the case of *P. fluorescens* CHA0, it is known that this bacterium produces several secondary metabolites, such as pyoluteorin and 2,4-diacetylphloroglucinol, which are critical antibiotics to control root diseases caused by soil-borne fungal pathogens. It has been determined that a site-directed mutation in the pqqFAB genes in *P. fluorescens* CHA0 to lack glucose dehydrogenase activity. Besides, this bacterium could not utilize ethanol as a carbon source and showed strongly enhanced production of pyoluteorin. Also, a pqqF mutant can grow in ethanol and produce pyoluteorin at levels shown by wild strain when PQQ is added to a final concentration of 16 nM, which indicates that PQQ negatively regulates antibiotic production and their biocontrol activity (Schnider et al. 1995).

Pseudomonas kilonensis JX22 is a bacterium that produces a wide range of antimicrobials and it is used as a biological control for several phytopathogenic fungi, e.g., *Fusarium oxysporum* f. sp. *lycopersici*. A mutation in the *pqqC* gene caused the loss of antifungal activity, which was recovered by complementation with the wild-type *pqqC* gene (Xu et al. 2014).

Streptomyces rochei strain 7434AN4 produces a secondary metabolite of a polycystic nature, called lankacidin, which exhibits significant antibacterial activities

against a wide variety of bacteria, and may have applications in agriculture. In this bacterium, a mutation in the *pqq* genes causes the non-synthesis of lankacidin, but when 2 μg/ml of PQQ is added to the mutant, the synthesis of the antibiotic lankacidin is provoked. Arakawa et al. (2005) have suggested that PQQ plays a crucial role in an oxidation process during lankacidin synthesis.

9.2.7 PQQ against Oxidative Stress

It is known that, under certain circumstances, plants release ROS, which have harmful effects on both the plant itself and microorganisms that coexist with the plant. Beneficial microorganisms stimulate the production of ROS in the plant, and they also stimulate the production of antioxidant agents (Rahman et al. 2018). Besides, the microorganisms possess mechanisms to eliminate ROS (Alquéres et al. 2013), in such a way that both the plant and the microorganisms can coexist.

Various phenotypes are associated with the production of PQQ by PGPB bacteria. These phenotypes can promote the growth of certain plants in different ways, among which are higher activities of catalase and superoxide dismutase (Khairnar et al. 2003). As a result, these phenotypes can protect against the attack of ROS derived from γ-irradiation and can preserve the DNA and proteins (Misra et al. 2004). Redox cycling systems result in repeated chemical reactions in which molecules acting as catalysts are repeatedly oxidized and/or reduced. It has been hypothesized that the PQQ molecule potentially has one of the largest numbers of catalytic cycles (number of repeated reactions), with about 20,000, mainly due to its chemical stability, compared with ascorbic acid, which has only four repeated reactions (Rucker et al. 2009; Paz et al. 1990). It has been suggested that PQQ exists as a reduced form, $PQQH_{(2)}$, throughout the cell and plays a role as an antioxidant, with an antioxidant power greater than those of vitamin C, cysteine, uric acid, and glutathione (Ouchi et al. 2009).

Treatment of cucumber leaf discs with PQQ or *P. fluorescens* B16, a producer of PQQ, resulted in the scavenging of ROS and hydrogen peroxide, suggesting that PQQ acts as an antioxidant in plants (Choi et al. 2008).

9.2.8 PQQ Involved in Swarming and Chemotaxis

Among the first events that occur during the microorganism-plant interaction is that the bacteria respond and move toward the plant. Chemotaxis and motility in the bacteria give them a competitive advantage for roots and rhizoplane colonization (Scharf et al. 2016); the swarming movement has been reported as important for the extension of colonization in plants (Sánchez-Contreras et al. 2002).

In this respect, in *P. aeruginosa* it has been determined that the *pqq* genes are down-regulated in tendril tip cells, and Tremblay and Déziel (2010) propose a model in which tendril tip cells function as “scouts”, whose main purpose is to

spread on uncolonized surfaces while the center population is in a biofilm-like state that allows permanent settlement of the colonized area.

Although *E. coli* is not considered to promote plant growth, several studies have been carried out with this bacterium using it as a genetic background for the expression of *pqq* genes from other bacteria. By using an *E. coli* strain, it was observed that, despite being unable to synthesize PQQ, the *E. coli* strain could activate, in the presence of exogenous PQQ, an apoglucose dehydrogenase, which seems to indicate that *E. coli* can take up PQQ present in the medium (Van Schie et al. 1985; Matsushita et al. 1997). In addition, PQQ in this bacterium can play the role of a chemoattractant, since, when present in concentrations of 10, 50, and 100 μM and with carbon sources such as glucose, fructose, mannose, and gluconate, a "swarming" movement of *E. coli* is caused (De Jonge et al. 1996).

9.2.9 PQQ Involved in Signal Transduction and UV-γ Radiation Stress Resistance

The resistance to UV-γ radiation that microorganisms can have is very important for them to be able to grow and to survive. It has been determined how radiation has a decisive impact both on plants and on the microorganisms that are associated with them (Paul et al. 2012); accordingly, mechanisms that may be involved in such resistance are important.

A quinoprotein called YfgL in *E. coli*, with protein kinase activity, has been reported to be involved in transduction and DNA strand break repair, and to enhance the UV resistance of *E. coli* (Khairnar et al. 2007). Likewise, PQQ activates a Ser/Thr protein kinase in *Deinococcus radiodurans* that improves the organism's resistance to γ radiation, possibly by regulating the differential expression of important genes for bacterial response to oxidative stress and DNA damage (Rajpurohit et al. 2013). PQQ has even been used to increase γ radiation resistance in animals (Xiong et al. 2011).

9.2.10 PQQ as a Growth Factor

Some bacteria, with their versatile metabolisms, can colonize different habitats, adapting their metabolism to replicate in specific host microenvironments. These adaptations are a consequence of the composition of their host niches, and this will cause that allows bacteria remain active and, in some cases, even modify the bacterial soil community structure (Kang et al. 2013).

PQQ has been shown to be an essential factor in stimulating the onset of bacterial growth (Ameyama et al. 1984), by decreasing the adaptive growth lag phase. In *Pseudomonas* sp. VMI5C, it has been shown that PQQ is essential for polyvinyl alcohol degradation (Shimao et al. 1984). The organism *Gluconacetobacter europaeus* can grow at a high concentration of acetic acid, owing to the stability of the PQQ-dependent ADH (Trček et al. 2006, 2007).

9.3 Discussion and Conclusion

PQQ promises to be a key molecule in many aspects of bacterial physiology and microorganism-plant interaction. As has been observed, PQQ affects the growth of several plants, which is sometimes associated with the solubilization of phosphates by the production of gluconic acid through glucose dehydrogenase that is dependent on PQQ as an antioxidant agent, but on other occasions the mechanism by which PQQ affects plant growth is unknown. Phosphate solubilization by bacteria requires PQQ; in other cases *pqq* genes and glucose dehydrogenase are required, enabling these bacteria to act as potential P-biofertilizers in plants. Of interest, it will be of value to investigate how the synthesis of PQQ and the expression of its genes regulate or influence swarming-like motility in bacteria.

PQQ has been shown to be crucial for its biocontrol activity in bacteria and fungi that has an impact on plants of agronomic interest, such as rice, grapes, sunflowers, and beans, but the mechanisms of this biocontrol activity are still to be clarified. Further, there is a report that PQQ induces a systemic response in tobacco, but its mechanism is unknown and needs to be explored in future research (Song et al. 2008).

Several antimicrobials have been reported to be influenced, either negatively or positively, by the presence of PQQ. These antimicrobials have effects on fungi and pathogenic bacteria, and the regulation of these antimicrobial mechanisms needs to be investigated and will be critical to driving the more rational use of these biocontrol agents in agriculture. Some studies have reported the synthesis of apo-quinoproteins in bacteria that cannot synthesize PQQ, and that depends on exogenous PQQ or even, the introduction of PQQ synthesis genes in order to enable it to effectively carry out the metabolism through these enzymatic quinoproteins, different substrates. Perhaps, in natural microenvironments of these bacteria, there are other PQQ-synthesizing bacteria that mitigate the deficiency of this cofactor, in a way that there is a type of bacterial mutualism that allows the non-PQQ synthesizing bacteria to maintain and preserve microbial diversity in these ecosystems in the presence of PQQ. On the other hand, regarding PQQ as a growth factor, it will undoubtedly be relevant to investigate, in different biological systems, the presence of PQQ-synthesizing bacteria and other organisms that cannot synthesize PQQ, but that can elaborate apo-quinoproteins; it will also be necessary to evaluate the ecological impact when PQQ-synthesizing bacteria change their populations.

PQQ has been shown to be a positive regulator that increases the activities of enzymes that combat ROS, such as catalase and superoxide dismutase. PQQ, compared with other antioxidant agents, tends to have the highest number of repeated redox reactions. Therefore, PQQ, by acting as a redox cyclic system, has an impact on enhancing plant growth and conferring protection to bacteria against ROS attack resulting from UV and γ radiation of proteins and DNA. Also, it will be important to determine the signal transduction cascade and gene activation where PQQ acts to combat the effects of this type of radiation.

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