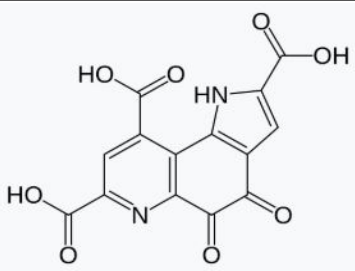
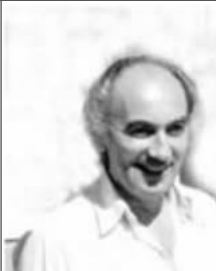


HOME.	PQQ [Pyrroloquinoline Quinone] Discovery; bacterial enzymes; its role in higher organisms; nutritional aspects Return to my main Science page Return to My Research page Return to Bad Science page Pdf for printing	 PQQ	 Jens Hauge and Chris Anthony	First described by Hauge, and by Anthony and Zatman in 1964	 Len Zatman
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<u>Early history of PQQ</u>	<u>Function and structures of quinoprotein enzymes</u> <u>PQQ and higher organisms, especially man</u>
.....	
Early history of PQQ A prosthetic group is the part of an enzyme at the active site that is not the protein such as FAD (a riboflavin derivative) as in succinate dehydrogenase. PQQ was first described in 1964 as the prosthetic group of a soluble bacterial glucose dehydrogenase by Hauge (pdf) and as the prosthetic group of a bacterial methanol dehydrogenase by Anthony & Zatman (pdf). I was Len Zatman's research student. Hauge did no further work on this but it occupied the rest of my career. Very soon after our description a Japanese group (Ameyama and colleagues in Yamaguchi) used our methods to show that the well-known mysterious alcohol dehydrogenase in Acetic acid bacteria has the same novel prosthetic group. For my review of these enzymes Click Here Hans Duine and Hans Frank in Delft then showed that two types of glucose dehydrogenase have this novel prosthetic group and they showed that it has an orthoquinone structure and so suggested that all these enzymes should be called Quinoproteins. Other novel prosthetic groups with ortho quinone prosthetic groups have been described and all are now called quinoproteins. The 1st International Symposium on PQQ and Quinoproteins was held in Delft in 1988 and the 5th in Southampton in 2002. Many of the photographs are from these symposia. The structure of PQQ was published 15 years after its first description by Olga Kennard's group in Cambridge.	   Hans Duine and Hans Frank 'invented' quinoproteins The Yamaguchi group: Matsushita ?Urakami? Ameyama and Adachi. This group have continued working on bacterial PQQ Enzymes. References to this history Full details of all this science are elsewhere on this webs together with links to PDFs: Click here

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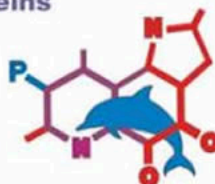
[TOP](#) Participants in the 1988 Symposium in Delft

3rd International Symposium on Vitamin B₆, PQQ, Carbonyl Catalysis and Quinoproteins



University of Southampton, UK

April 14th-19th 2002



Comprising the

**11th International Symposium on Vitamin B₆ and Carbonyl Catalysis
and the 5th International Symposium on PQQ and Quinoproteins**



Programme

The opening session will be late afternoon of Sunday April 14th
The closing session will be the morning of Friday April 19th

To ensure that we cover as wide a range of topics as possible we will have:
Morning sessions: joint symposia; Afternoon sessions: separate symposia

Programme topics will include:

- Vitamin B₆-dependent enzymes (transferases, decarboxylases, other lyases, racemases, mutases, phosphorylase).
- Amine oxidases (TPQ), human semicarbazide-sensitive enzymes, vascular adhesion protein, lysyl oxidase (LTO).
- Quinoprotein dehydrogenases containing PQQ and TTQ and their related electron transport systems.
- Molecular pathology, Physiological and Nutritional aspects, and Molecular evolution of these enzymes and cofactors.
- Biosynthesis of vitamin B₆, PQQ, TTQ, TPQ and LTO. Non-enzymatic models for reactions involving these cofactors.
- Protein engineering and applications of these enzymes and cofactors.

[The 5th PQQ Symposium](#) by then merged with B6 Symposium. This fusion was bought about when it was shown that the prosthetic group of amine oxidases is also an orthoquinone (but not PQQ)

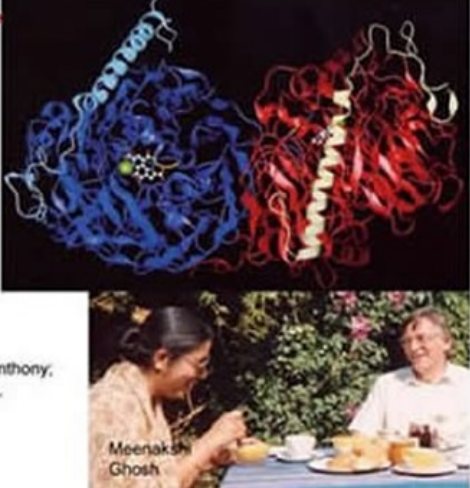
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Basic information on function and structures of quinoprotein enzymes

Methanol dehydrogenase has a beta propeller structure and a small helical subunit. Membrane Glucose dehydrogenase has the propeller structure plus a membrane domain that holds it in the membrane; the soluble glucose dehydrogenase has a rare 6-membered ring structure. The alcohol dehydrogenase has the propeller structure plus a membrane domain and a haem-containing domain.

For full descriptions on this website of the PQQ-containing quinoproteins that are described below [Click Here](#)

The X-ray structure of MDH 1995



The Methanol dehydrogenase of methylotrophic bacteria.

This oxidises methanol to formaldehyde during bacterial growth on methane or methanol. It is a soluble enzyme, located in the periplasm. It has a 'propeller' structure with 8 beta sheets forming the propellers. It has a unique 8-membered ring made by formation of a disulphide bridge between adjacent cysteine residues in the polypeptide chain. There is a calcium ion bonded to PQQ in the active site. This structure was determined by my collaborator, Meenakshi Ghosh.

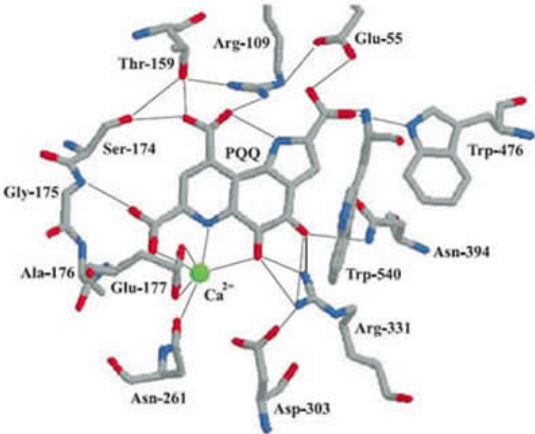


Fig. 2. The equatorial interactions of PQQ and the coordination of Ca²⁺ in the active site of MDH [10]. The figure also shows the proposed active site base (Asp³⁰³) and Arg³³¹ which may also be involved in the mechanism.

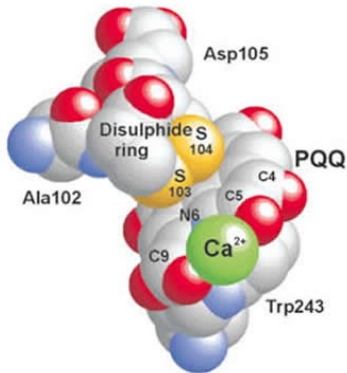
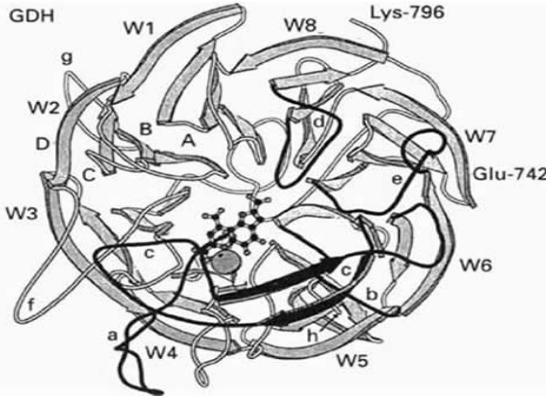
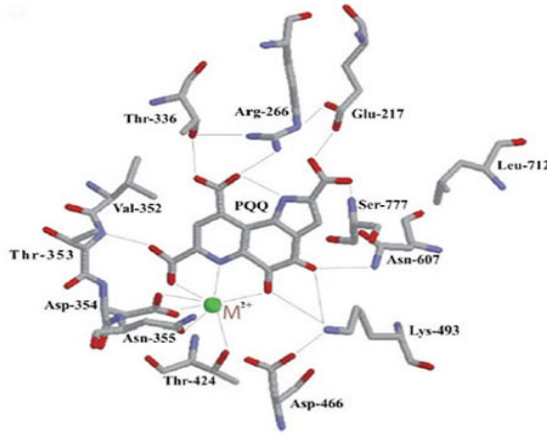
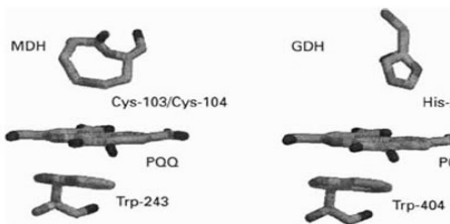
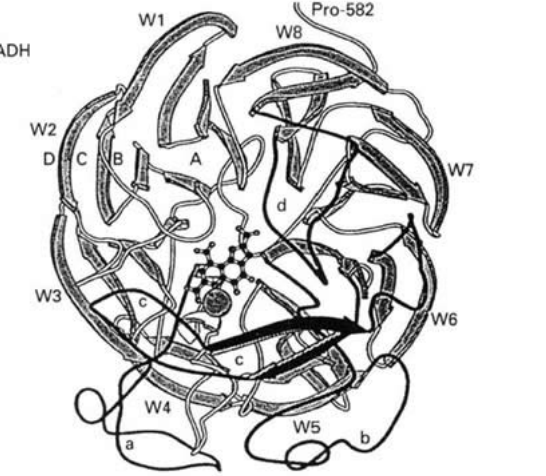
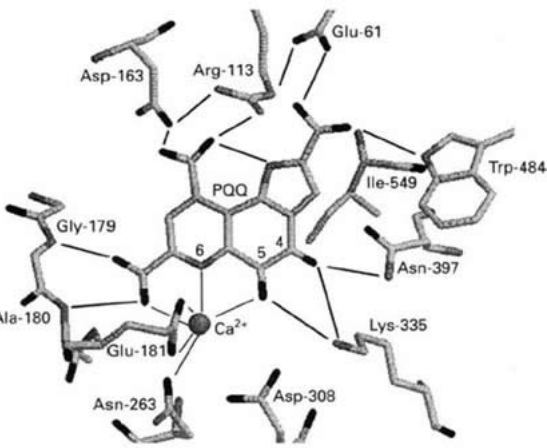


FIGURE 1: Disulfide bridge, PQQ, and Ca²⁺ in the active site MDH.

The membrane Glucose Dehydrogenase of enteric bacteria, acetic acid bacteria and pseudomonads. This quinoprotein is responsible for oxidation of glucose to gluconic acid in enteric bacteria, acetic acid bacteria and pseudomonads. It is anchored in the periplasmic membrane by the C-terminal domain made up of 5 membrane-spanning helices. the reaction is catalysed in the periplasm by the N-terminal domain; the amino acid sequence of this domain is sufficiently similar to that of methanol dehydrogenase (MDH) for its structure to be modelled using the MDH X-ray coordinates.			
This was the work of my student Gyles Cozier	Structure based on the structure of methanol dehydrogenase.	The special disulphide ring of MDH is replaced with histidine	
The glucose dehydrogenase of <i>Acinetobacter calcoaceticus</i>. This soluble enzyme is the enzyme from which. Hauge first isolated PQQ. It is unusual in having only 6 propeller blades.			
The Alcohol Dehydrogenase (ADH) of acetic acid bacteria The ADH of <i>Acetobacter aceti</i> is a membrane enzyme responsible for the first step in oxidation of ethanol to acetic acid. The reaction occurs in the periplasm. It has a haem-containing domain and so is a quinohaemoprotein. The basic superbarrel structure and the active-site region are retained, indicating essentially similar mechanisms of action to methanol dehydrogenase. The amino acid sequence of this domain is sufficiently similar to that of methanol dehydrogenase (MDH) for its structure to be modelled using the MDH X-ray coordinates.			

23/10/2026, 14:51		Untitled Document		Gyles Cozier, who was responsible for all our modelling work
	This was the work of my student Gyles Cozier			
	NOTE: A Coprinospin cinerea (fungus) pyranose dehydrogenase has recently been shown by Takeda et al (pdf) to have PQQ in its crystal structure. It has a 6-membered propeller structure like the solu glucose dehydrogenase from which ens Hauge first isolated PQQ			
TOP				

.....	PQQ and higher organisms, especially man	For Later developments Click here
	Early discussions	
	No plants or animals have PQQ-containing enzymes. If they did so then it is likely that PQQ would be a vitamin; quinoproteins having PQQ would be analogous to flavoproteins having riboflavin (vitamin B2). The 1sr International Symposium on PQQ and Quinoproteins was held in Delft in 1988, organised by Jaap Jongejan and Hans Duine. It attracted more than 100 participants. No X-ray structures were available at this time but there were 37 lectures on structure, mechanisms, assays biosynthesis, etc of PQQ and PQQ enzymes. By contrast the was only one lecture on PQQ as a nutritional requirement for Mice and one on the effect of PQQ on endotoxin shock in rats. Subsequently there has been a huge increase in research aiming to show that PQQ has an essential role in some way mammalian metabolism. This was very confusing at the beginning because some could not be repeated. Over the years there was a huge increase in understanding of microbial PQQ enzymes,, including many new enzymes their X-ray structures and their relevant electron transport pathways and systems for ATP generation. This contrasted with the growing number of reports of the relevance of PQQ to human metabolim which led to no certain understanding. Research funded by big Pharma and Nutrition companies has been welcome but perhaps has led to some of the confusion. There is now a huge literature on this but I think no clear accepted description of the role of PQQ in metabolism. However because of the 'human interest' any search online for information on PQQ provides lots of material on this and often completely ignores a great body of important science of microbial PQQ enzymes. A sort of exciting climax was reached in 2003 when nature announced a new redox cofactor for mice (PQQ). This was claimed to be the first new vitamin for 55 years! As a result Mitsubishi planned to invest millions of dollars in its production. When i heard of this I got Nature to publish the evidence against it and told Mitsubishi who accepted this and invited me to visit and to present the case at a symposium. They have continued with the development and sale of PQQ as a nutritional supplement. For background to this and my lecture at the symposium Click Here TOP	The original announcement by Mitsubishi about proposed development of PC as a vitamin Mitsubishi Announcement: "On August 15, 2008, Mitsubishi Gas Chemical (MGC) announced that it h received official acceptance from the U.S. Food and Drug Administration (FDA) for its notification of coenzyme pyrroloquinoline quinone (PQQ) as a new dietary ingredient. Having received this acceptance, MGC will begin developing the U.S. market for PQQ as an initial step toward the commercialization of PQQ". Mitsubishi statement. NPI Center announcement: Highly-Anticipated PQQ (Pyrroloquinoline Quinone) Finally Commerciali As VitaPQQ(TM) From Maypro Industries: “Hailed as a new vitamin by Nature1, VitaPQQ™ brand PQQ is now available from Maypro for use by vitamin and dietary supplement manufacturers. The launch of VitaPQQ™ is a critical milestone in a decades-long effort to commercialize Pyrroloquinoline Quinone (PQQ), a newly discovered vitamin that offers significant health benefits due to its vitamin-like activity, cognitive function and antioxidant capac: VitaPQQ™ is manufactured utilizing a patented natural fermentation process. “ My PQQ Japan conference lecture

	Later discussions of the role of PQQ in higher organisms
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TOP...	Introduction	Reasons why this work is difficult to evaluate and interpret	Potential Physiological Importance of PQQ	Evaluation of PQQ as a nutritional supplement
	Marketing of PQQ as a nutritional supplement	Dreadful 'interpretation' of work suggesting PQQ has a function related to mitochondria	Recent review in Current Food Science	Healthline: a typical site for nutritional supplements
	PQQ available on Amazon	WEB MD	'Evidence' and criticism from AI search	

TOP

	Introduction Much of the work on the possible role(s) of PQQ in mammalian systems has been driven, or at least affected by the hope of getting evidence for its importance as a nutritional supplement. This has often been funded by companies with a financial interest in this. An important first contribution to this was one of the few contributions on this subject at the 1st International Symposium on PQQ and Quinoproteins in Delft in 1988. This described a positive effect of PQQ on growth of mice that were raised germ-free. This contribution was by Dr R. Rucker who has been perhaps the most important contributor to this subject ever since. These contributions are an attempt to provide information from good sources on the subject and to give some illustrations of misleading and exaggerated claims for PQQ in Mammalian systems.	Reasons why this work is difficult to evaluate and interpret 1. The chemical nature of PQQ. It can exist in 3 redox forms: oxidised quinone, reduced quinol, and half reduced free radical. It is thus a powerful anti-oxidant and it can act as in intermediate in recycling system. These properties can lead to interesting observations which may or may not have physiological significance. 2. Because of its chemical structure it is able to readily bind to a wide range of molecules and can in effect act as a drug rather than a component in a physiological process. 3. Much of the work on PQQ and mammalian systems has been necessarily using cell lines or animal models so there is always the problem of transfer of conclusions or models to whole animals. 4. For final 'proof' tests (sometimes clinical) must be done on human populations (difficult to get permission and expensive)
TOP of Later	Potential Physiological Importance of Pyrroloquinoline Quinone By Robert Rucker et al. Alternative Medicine Review Volume 14, Number 3 2009 Abstract Pyrroloquinoline quinone (PQQ) is a novel biofactor for which a proposition can be made for physiological importance. PQQ was first recognized as an enzyme cofactor in bacteria. It has recently been tentatively identified as a component of interstellar dust. Thus, PQQ may have been present throughout early biological conception and evolution. PQQ is also a potent plant growth factor. Consequently, for animals and humans, there has been constant exposure to PQQ. In animals, PQQ is reported to participate in a range of biological functions with apparent survival benefits (e.g., improved neonatal growth and reproductive performance). There are also benefits from PQQ supplementation related to cognitive, immune, and antioxidant functions, as well as protection from cardiac and neurological ischemic events. Although PQQ is not currently viewed as a vitamin, its involvement in cell signaling pathways, particularly those important to mitochondriogenesis in experimental animal models, may eventually provide a rationale for defining PQQ as vital to life. For humans, such evidence suggests there may be similar parallels or benefits from improving PQQ status. (Altern Med Rev 2009;14(3):268-277) TOP	Evaluation of PQQ as a nutritional supplement on Examine website This website provides a summary plus links to all its sources Summary PQQ is a small molecule once thought to be a vitamin, although its actions in the human body are not related to this hypothesized vitamin-like mechanism. Via its actions as a REDOX agent in cells, it can modify signalling and is thought to support mitochondrial function. PQQ is a small quinone molecule which has the ability to be a REDOX agent, capable of reducing oxidants (an antioxidant effect) and then being recycled by glutathione back into an active form. It appears to be quite stable as it can undergo several thousand cycles before being used up, and it is novel since it associates with protein structures inside the cell (some antioxidants, mostly notably carotenoids like β-carotene and astaxanthin, are located at specific areas of a cell where they exert proportionally more antioxidant effects due to proximity; PQQ seems to do this near proteins like carotenoids do so at the cell membrane). The aforementioned REDOX functions can alter protein function and signalling pathways, and while there is a lot of promising <i>in vitro</i> (outside of a living model) research on what it could do there are only a few promising results of PQQ supplementation, mostly related to either altering some signalling pathways or its benefits to mitochondria (producing more of them and increasing their efficiency). It is a coenzyme in bacteria (so, to bacteria, this would be something like a B-vitamin) but this role does not appear to extend to humans. Since this does not extend to humans, the designation of PQQ as a vitamin compound has fallen through and it is only considered 'vitamin-like' at best.
TOP	TOP of Later	

	The marketing of PQQ as a nutritional supplement PQQ is now marketed widely as a supplement with claims for a wide range of benefits. These claims are based on many nutritional investigations of PQQ and many studies on the effect of PQQ in isolated cells or tissues or whole experimental animals (mice and rats). The website claims of the marketers are often factually incorrect, wildly exaggerated and have many misunderstandings about biochemistry and physiology. For unbiased examination of supplements I strongly recommend the website Examine.com which is an "independent organization that presents un-biased research on supplements and nutrition. We currently have over 25000 references to scientific papers". This is an excellent website that examines claims for nutritional supplements and has a lengthy valuable discussion of PQQ.	
TOP	TOP of Later	

....TOP TOP of Later	Dreadful 'interpretation' of work suggesting PQQ has a function related to mitochondria I am writing this response at some length. The same responses are relevant to many PQQ sellers	
	PQQ and health. Response to an article in Life Extension Magazine Feb 2011 "Generate Fresh Mitochondria with PQQ. Scientists Discover the “Other CoQ10”. By Perry Marcone. Link to the original article The article quotes important work by Rucker and colleagues (see above) . In early studies, he showed that germ-free mice fed chemically-defined diets thrived more if provided with PQQ. He has been at the forefront of this sort of work and his paper relating PQQ to mitochondrial genesis is the one quoted by the article in Life Extension. We should note that this paper studied the effect of PQQ on isolated cell cultures of mouse liver cells. It requires a lot of extrapolation to conclude that PQQ may have an effect on mitochondrial generation in humans and even more to conclude that PQQ as a nutritional supplement will have an effect on ageing. But of course it may achieve this. It should be remembered that even if PQQ does have such effects this is not evidence that it has a ‘normal’ role in human physiology – it is possibly only acting as a ‘drug’. By its chemical nature it reacts powerfully with free radicals and so is an antioxidant. [Also note that there is no evidence that antioxidants in the diet have any benefit at all]. Some specific comments on the article: <i>The paragraphs in italics are taken direct from the article, given in the order in which they appeared.</i> <i>1. The most exciting revelation on PQQ emerged early in 2010, when researchers found it not only protected mitochondria from oxidative damage—it stimulated growth of fresh mitochondria!</i> This refers to the Rucker study which used liver cells in tissue culture. This is important interesting work but it does not show that dietary supplementation with PQQ in animals/humans will lead to mitochondrial production.	<i>3. As the primary engines of almost all bioenergy production, the mitochondria rank among the physiological structures most vulnerable to destruction from oxidative damage. PQQ’s formidable free radical–scavenging capacity furnishes the mitochondria with superior antioxidant protection.</i> Firstly, we should not confuse mitochondrial activity with regeneration [the subject of Rucker’s paper]. Free radicals are inescapable occasional products of reaction with oxygen in the final step in energy production. We have evolved thus far by avoiding damage by these free radicals which are happily mop up by mitochondrial enzymes with that sole purpose. There is no reason to think that “superior antioxidant protection” is needed. <i>4. At the core of this capacity is an extraordinary molecular stability. As a bioactive coenzyme, PQQ actively participates in the energy transfer within the mitochondria that supplies the body with most of its bioenergy (like CoQ10).</i> This is completely untrue. Although it is true that coenzyme Q actively participates in energy transfer within mitochondria,PQQ has not been shown to have any function whatsoever in mitochondria. In bacteria it does have this function. During methanol oxidation for example the first step in energy production is catalysed by a PQQ containing enzyme that is so important that it constitutes 5-10% of the cell’s protein PQQ enzymes have only been described in bacteria. <i>5. Unlike other antioxidant compounds, PQQ’s exceptional stability allows it to carry out thousands of these electron transfers without undergoing molecular breakdown. It has been proven especially effective neutralizing the ubiquitous superoxide and hydroxyl radicals..... A consistent finding in the scientific literature is that nutrients like PQQ provide more wide-ranging benefits than conventional antioxidants . general public relies on.</i> As mentioned above, PQQ is a powerful antioxidant and it is stable and so of course will ‘neutralise’ free radicals. But there is no evidence that this ability of PQQ can be relevant to health. There is good evidence that antioxidants in the diet have no positive health benefit and may have slight negative effect. This is published as a Cochrane Review.

2. Pre-clinical studies reveal that when deprived of dietary PQQ, animals exhibit stunted growth, compromised immunity, impaired reproductive capability, and most importantly, fewer mitochondria in their tissue. Rates of conception, the number of offspring, and survival rates in juvenile animals are also significantly reduced in the absence of PQQ. Introducing PQQ back into the diet reverses these effects, restoring systemic function while simultaneously increasing mitochondrial number and energetic efficiency. Note that to see these effects animals were often reared in extreme unnatural conditions [that is ok as this was the ‘cleanest’ way of showing effects]. Less effect is likely to be seen in animals if given PQQ in normal conditions. This is not surprising because there is a lot of PQQ in many foods, especially if bacteria have been involved in their production; for example vinegar has a lot of PQQ because it is made using bacteria that use a PQQ quinoprotein to oxidise alcohol to the active component of vinegar – acetic acid.	6. According to the most recent research, “PQQ is 30 to 5,000 times more efficient in sustaining redox cycling (mitochondrial energy production) . . . than other common [antioxidant compounds], e.g. ascorbic acid.” This is terrible. Redox cycling is a chemical process that was proposed as a way of measuring PQQ test tube. It not relevant in any way to “mitochondrial energy production”. 7. In a revolutionary advance, an essential coenzyme called pyrroloquinoline quinone or PQQ has been shown to induce mitochondrial biogenesis—the growth of new mitochondria in aging cells! PQQ is not an essential coenzyme in animals [see above]. The studies of PQQ and mitochondrial genes that stimulated this article were on liver cells in lab culture, NOT ageing cells, or whole animals or humans.
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TOP TOP of Later A Recent review in Current Food Science	
Pyrroloquinoline Quinone (PQQ): Its impact on human health and potential benefits: PQQ: Human health impacts and benefits Yan et al. Curr Res Food Sci . 2024 Oct 22;9:100889. doi: 10.1016/j.crfs.2024.100889 Abstract Pyrroloquinoline Quinone (PQQ) is a redox-active quinone molecule with significant implications for human health. Originally identified as a bacterial cofactor, PQQ has since been lauded for its diverse biological and therapeutic activities. 1. It serves as an essential cofactor for oxidative enzymes that are vital for mitochondrial function and ATP synthesis. 2. PQQ exhibits superior antioxidant properties that protect against ROS-mediated oxidative stress, aging, neurodegenerative diseases, certain cancers, diabetes, and metabolic disorders. It also enhances cognitive abilities and reduces insulin sensitivity. PQQ's antioxidant nature helps mitigate oxidative stress, which is implicated in many diseases. It has been shown to target cancer cells selectively, suggesting its potential as a therapeutic agent. Clinical studies have indicated the potential benefits of PQQ supplementation, including improvements in cardiovascular health, cognitive function, weight management, insulin sensitivity, and the prevention of metabolic syndromes. The safety of PQQ has been established, with no reported toxicity or genotoxicity in various studies, and it is considered a safe nutritional supplement. Future research directions should focus on determining the optimal dosages of PQQ for specific health outcomes and assessing its long-term effectiveness and safety. The translation of PQQ research into clinical practice could offer new strategies for managing metabolic disorders, enhancing cognitive health, and potentially extending lifespan. In summary, PQQ is a promising molecule with broad potential health benefits, impacting human health from cellular metabolism to disease prevention and treatment, positioning it as a key player in nutritional science and public health.	Healthline: a typical site for nutritional supplements. Website Pyrroloquinoline quinone (PQQ) is found in dark chocolate and green tea. While initial studies show positive effects on health, more research is needed. That said, there’s minimal risk to trying PQQ supplements. PQQ has recently gained a lot of attention in the health and wellness sphere. PQQ supplements are claimed to increase energy levels, mental focus, and longevity, but you may wonder whether there’s any merit to these claims. This article explains everything you need to know about PQQ supplements, including the evidence behind their possible benefits. The bottom line PQQ is a compound that plays a vital role in human health. It’s found in a variety of foods including dark chocolate and green tea, and PQQ supplements are said to improve brain health, energy levels, and longevity. Yet, current research doesn’t support these benefits. While test-tube and animal studies indicate that PQQ may reduce inflammation and promote mitochondrial health, more research is needed. Although the lack of evidence suggests that there’s no need to supplement with PQQ, the risks of doing so are minimal if you’re interested in trying it.

My comments This has many characteristics of of such reviews stating many things that are guesses or assumptions as if they are established facts. 1. No mitochondrial PQQ-dependent enzymes are known in mammalian systems. UNTRUE 2. Its antioxidant properties might do this but i know of no evidence in humans.			
TOP TOP of Later			
PQQ available on Amazon It is remarkable that these sell when there is no real evidence for any benefit (as with many 'nutritional supplements). A personal note: My first isolation of pure PQQ from methanol dehydrogenase took about 4 months: Growth of large amounts of bacteris; purifiatio n of methanol dehydrogenase; denaturation of my valuable pure enzyme: purification of the PQQ; unknown as PQQ then of course. Final product about 20 tiny red grains of the unknown prosthetic group. I was able to characterise it by its fluorescence.		How it is produced 1. Bacterial Fermentation (Most Common) The vast majority of premium and clinically studied P on the market—such as the widely recognized BioPQQ (sold as MGCPQQ in Europe)—is produc via a natural bacterial fermentation process.The Microorganism: Cultivators utilize specific strain of non-pathogenic, PQQ-producing bacteria, most notably Hyphomicrobium denitrificans. These bacteria naturally synthesize PQQ as a byproduct of their metabolic processes.The Process: The bacteria are grown in large, controlled fermentation vats supplied with precise nutrients. As they metabolize, they secrete PQQ.Purification: Once fermentation is complete, the mixture goes throu rigorous filtration, separation, and purification steps. The final product is usually synthesized as a pyrroloquinoline quinone disodium salt, reaching a minimum purity of 99.0%. It is then dried int reddish-brown, water-soluble powder.	

Results

Check each product page for other buying options.



Ultra High Purity PQQ Capsules
99%+ Highly Purified and Bioavailable
120 Capsules – 20mg Concentrated...

4.5 ★★★★★ (210)
200+ bought in past month

£27⁷⁴ (£0.23/count)
Extra £5.00 off subscription voucher
prime Tomorrow
FREE delivery Tomorrow 07:00 - 13:00

Add to basket



PQQ 20mg Pyrroloquinoline Quinone as PureQQ | Vegan Certified, Non-GMO Gluten Free | by Health Thru...

Capsule

4.6 ★★★★★ (1.9K)
200+ bought in past month

£17⁹⁵ (£0.15/count)
Extra 20% off subscription voucher
prime Tomorrow
FREE delivery Tomorrow, 29 Aug
Or FREE delivery Today 07:00 - 13:00 on £20 of Prime Same-day & Overnight item(s)

Add to basket



PQQ 20mg | High Strength 99% Pure Pyrroloquinoline Quinone | 4-Month Supply | 120 Vegan Capsules | UK...

Capsule

4.9 ★★★★★ (20)
50+ bought in past month

£17¹² (£0.14/count)
prime Tomorrow
FREE delivery Tomorrow, 29 Aug
Or FREE delivery Today 17:00 - 22:00 on £20 of Prime Same-day & Overnight item(s)

Add to basket



PQQ 20mg 120 Capsules Pyrroloquinoline Quinone Supplement – High Purity >99% -...

Capsule

4.2 ★★★★★ (36)
50+ bought in past month

£16⁹⁹ (£0.14/count) RRP: £24.99
Extra 20% off subscription voucher
prime Tomorrow
FREE delivery Tomorrow, 29 Aug

Add to basket



PQQ Supplement 20mg | Pure Pyrroloquinoline Quinone - High Strength | 60 Vegan PQQ Capsules ...

Capsule

4.2 ★★★★★ (21)
£15⁹⁰ (£0.27/count)
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FREE delivery Tomorrow, 29 Aug

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More results



Pure Encapsulations CoQ10 SR with PQQ, 60 Capsules
Antioxidant & Mitochondrial Support,...

4.5 ★★★★★ (28)



PQQ Max 20mg, 120 Capsules – Pyrroloquinoline Quinone - Promotes Mitochondrial Biogenesis, Energy...

Capsule



CoQ10 + PQQ Advanced – Bioavailable Coenzyme Q10 with Ubiquinone & Pyrroloquinoline...

Capsule



Welzo PQQ 20mg – 99%+ Ultra High Purity Pyrroloquinoline Quinone – Bio-Identical Mitochondrial & Cellu...

Capsule



PQQ 20mg | High Strength 99% Pure Pyrroloquinoline Quinone | 60 Vegan Capsules | 2-Month Supply | UK...

Capsule

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TOP. Evidence for health benefits summarised on Google search

 My presentation to The International Interdisciplinary Conference on Vitamins, Coenzymes, and Biofactors 2005 Awaji, Osaka and to Mitsubishi scientists in Niigata For my photos of Japan from this visit Click Here		Summary. The claim of Kasahara and Kato was based on sequence analysis of an enzyme, predicted to be involved in mouse lysine metabolism, using databases and search engines which inappropriately label beta propeller sequences as PQQ-binding sites. The 'sites' wrongly identified by the databases do not represent PQQ-binding sites but represent the Beta -sheets that form the 'blades' of the 'propeller fold' which happens to be a feature of all PQQ-dependent dehydrogenases whose main structure is a superbarrel made up of either six or eight 'propeller blades'. What the evidence actually suggests is that their (predicted) enzyme is an interesting novel protein having eight-bladed beta propeller structure; but there is no evidence that it is a PQQ-dependent dehydrogenase. There is also no evidence that this protein has any relevance to lysine metabolism. This material has been published in the journal Nature (Felton and Anthony, 2005) (Download PDF)
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Role of PQQ as a mammalian enzyme cofactor? *Nature* doi:10.1038/nature03322 Dr

Felton, L. M. & Anthony, C.(2005).

My friend and co-author of our Nature paper
Leigh M. Felton

[Download PDF](#)



There is *no evidence* from structural studies
that PQQ is a mammalian enzyme cofactor



Chris Anthony and Leigh M. Felton

School of Biological Sciences
University of Southampton

Acknowledgements



三菱ガス化学株式会社
MITSUBISHI GAS CHEMICAL COMPANY, INC.



BACKGROUND

A new redox-cofactor vitamin for mammals

Takaoki Kasahara, Tadafumi Kato *Laboratory for Molecular Dynamics of Mental Disorders, Brain Science Institute, RIKEN, Japan*

NATURE | VOL 422 | 24 APRIL 2003 | www.nature.com/nature

“On the basis of our demonstration of its molecular function, we propose that PQQ should be classified as a new B vitamin”



IN THE NEWS

Japanese Discover First New Vitamin in 55 Years

April 24, 2003
By REUTERS

Scientists Add New Member to Vitamin B Family

—Sarah Graham, *Scientific American*, April 24, 2003.

A new page may need to be added to the vitamin B family album. According to a report published today in the journal *Nature*, researchers have determined that the compound known as pyrroloquinoline quinone (PQQ) should be classified as a vitamin in the same class as vitamins B2 and B3. Scientists first isolated PQQ from bacteria in 1979.

The claim that PQQ is a vitamin

This was based on some false assumptions and misinterpretations. However, it appeared that the conclusions were generally accepted; as this could cause problems two refutations have been published: *NATURE*: VOL 433 27 JANUARY 2005:-

Role of PQQ as a mammalian enzyme cofactor?

Leigh M. Felton, Chris Anthony | www.nature.com/nature doi:10.1038/nature03322

“We contend that there is still no compelling evidence for a PQQ-dependent enzyme in the mouse and that the authors’ announcement of a new vitamin was therefore premature”.

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“Our results call into question the identification of PQQ as a new vitamin”

Robert Rucker: Thursday, 16.50 session R13: Physiological and nutritional importance of PQQ

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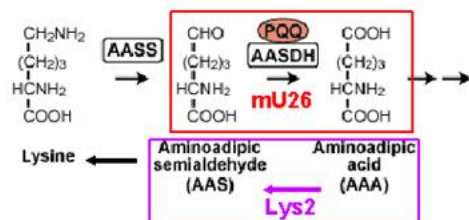
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Lysine metabolism

In yeast, aminoadipate reductase (*Lys2*) catalyses *reduction of aminoadipic acid to the semialdehyde* during lysine *biosynthesis*.

The predicted mouse protein *mU26* is similar (<26% identity) to part of *Lys2* in yeast.

It was proposed that, in the mouse, *mU26* catalyses the *oxidation of aminoadipic semialdehyde to aminoadipic acid*.



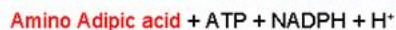
However, the reaction catalysed by *Lys2* is not reversible.

It is *not needed* in mammals because oxidation of the semialdehyde is catalysed by a specific NAD-linked aminoadipic semialdehyde dehydrogenase.

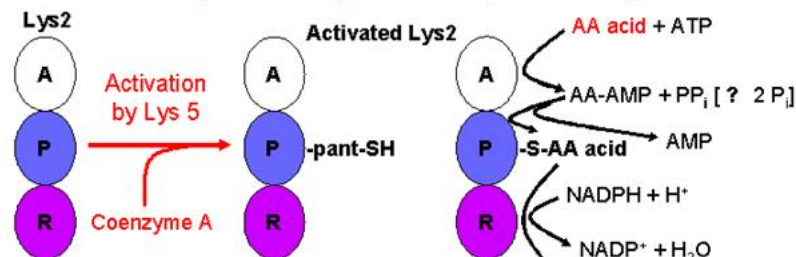
There is no evidence that the predicted enzyme (*mU26*) catalyses oxidation of aminoadipic semialdehyde in the mouse

Reduction of amino adipic acid to the semialdehyde by amino adipate reductase (Lys2) in yeast

Overall reaction after activation of Lys2 by Lys5 + Coenzyme A :



Lys2 ↓



A = Adenylation domain (similar domain in mU26)

P = Phosphopantetheinyl domain (similar domain in mU26)

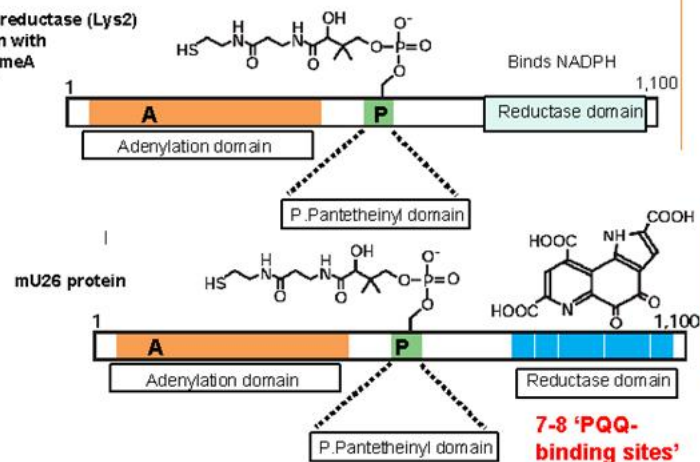
R = Reductase domain (replaced by 'propeller' structure in mU26)

This reaction is not reversible. In mammals the semialdehyde is oxidised to the acid by a specific NAD-linked dehydrogenase

Sequences of Amino adipate Reductase (Lys2) and mU26

The cloned novel mouse gene *mU26* was cloned using the Adenylation (A) and Phosphopantetheinyl (P) domains of yeast Lys2. The reductase domain was not used. *mU26* has the A and P domains and a different C-terminal domain. The sequence search engines 'identified' 7 PQQ-binding sites in this domain.

Amino adipate reductase (Lys2)
After activation with
Lys5 + coenzymeA



The search engines 'identified' PQQ-binding sites in the novel C-terminal 'Reductase' domain in mU26

There is no way to identify PQQ-binding sites

The search engine identified the presence of 7 *repeated sequences* that typically occur in PQQ-containing quinoproteins.

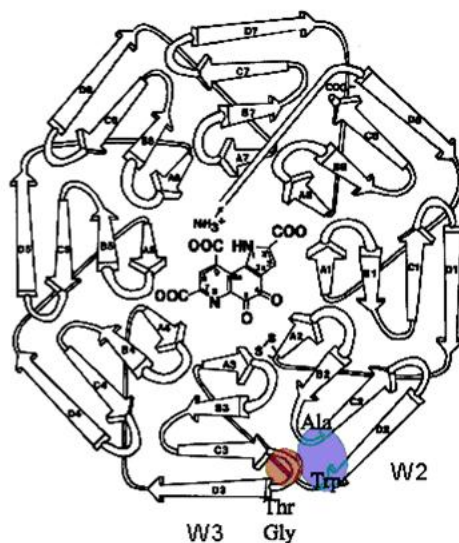
These *sequences* form into the 'propeller blades' of the well-known 'Propeller fold', in which 4-stranded β -sheets (the 'propeller blades') are radially arranged to form a superbarrel structure.

The propeller blades are held together by Tryptophan docking motifs.

The 'propeller blades' – wrongly identified by the search engine as 'PQQ-binding sites' are not directly involved in binding PQQ.

Methanol dehydrogenase is the best-characterised PQQ-containing quinoprotein

Propeller structure of MDH



The propeller blade W2 is bonded to W3 by Trp145 docking between Ala135 and the planar peptide bond between Thr191 and Gly192

The consensus sequence in the tryptophan-docking motifs

Propeller blades W1-W8

Position	1	2	3	4	5	-	6	7	8	9	10	11
Motif	C	C	C				D	D	D	D	D	D
W1	Ala 77	Leu	Gly	Leu	Asp	Asp	Pro	Gly	Thr	Ile	Leu	Trp 88
W2	Ala 135	Leu	Asn	Ala	Glu	-	Thr	Gly	Glu	Thr	Val	Trp 145
W3	Ala 186	Tyr	Asp	Val	Lys	-	Thr191-Gly192	Glu	Glu	Val		Trp 196
W4	Gly 262	Arg	Asp	Ala	Asp	-	Thr	Gly	Glu	Ala	Lys	Phe 292
W5	Thr 337	Leu	Asp	Arg	Thr	-	Asp	Gly	Ala	Glu	Val	Ser 347
W6	Ala 497	Tyr	Asn	Ala	Ile	-	Thr	Gly	Asp	Tyr	Lys	Trp 467
W7	Ala 499	Arg	Asp	Ser	Asp	-	Thr	Gly	Asp	Leu	Leu	Trp 505
W8	Val 577	Phe	Ser	Leu	Asp	-	Glu 59	Leu	Arg	Pro	Ala	Trp 44
MDH Consensus	Ala	X	Asp/Asn	X	X	-	Thr	Gly	Asp/Glu	X	X	Trp
GDH/ADH Consensus	Ala	X	Asp/Asn	X	X	-	Thr	Gly	Lys	X	X	Trp

For example: **Trp145** of strand D in W2 is stacked between **Ala135** in strand C in W2 and **Thr-Gly** at position 6-7 in W3

Taken from T. Kasahara and T. Kato
Nature: doi:10.1038/nature03324

The propeller blades of mU26

The protein mU26 has 8 tryptophan docking motifs.

Sequence analysis also suggests that mU26 has 8 propeller blades

The human homolog is similar

"Cloning and characterization of a novel human homolog of mouse U26, a putative PQQ-dependent AAS dehydrogenase"

Wang et al. 2005, Mol Biol Reports: DOI: 10.1007/s11033-003-2716-4

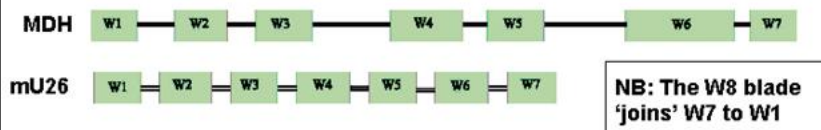
Motif		1	2	3	4	5	6	7	8	9	10	11
W1	MDH	A	L	G	L	D	D	P	G	T	I	L
	mU26	A	V	D	L	S	-	S	G	E	T	R
W2	MDH	A	L	N	A	E	-	T	G	E	T	V
	mU26	A	L	K	S	N	-	S	G	E	K	Y
W3	MDH	A	Y	D	V	K	-	T	G	E	Q	V
	mU26	A	L	D	I	Y	-	E	K	K	C	V
W4	MDH	G	R	D	A	D	-	T	G	E	A	K
	mU26	A	L	N	P	A	-	S	G	S	T	V
W5	MDH	L	D	R	T	-	D	G	A	E	V	
	mU26	L	C	F	T	H	-	S	G	E	Q	V
W6	MDH	A	Y	N	A	I	-	T	G	D	Y	K
	mU26	C	C	S	K	-	E	G	H	L	R	
W7	MDH	A	R	D	S	D	-	T	G	D	L	L
	mU26	L	E	S	R	-	S	G	E	L	R	
W8	MDH	V	F	S	L	D	-	Q	L	R	P	A
	mU26	L	D	L	L	-	C	G	D	E	R	
Consensus												
MDH												
GDH/ADH												
mU26												

Docking motifs in human U26: hU26 A C/L D/N X X - S/T G E/K X X W

Comparison of mU26 propeller blades and the blades in the PQQ-containing methanol dehydrogenase

There is no sequence identity between mU26 and any PQQ enzyme except for the tryptophan docking motifs.

The C-terminal domain of mU26 is similar in *structure* in having 8 'propeller' blades. This structure is remarkable: it is the smallest possible 8-bladed 'propeller' structure, with only the smallest possible blades and the shortest possible loops between them.



	MDH	mU26
Total residues in 'propeller'	543	341
Number of residues in each propeller 'blade'	30 – 69 With internal loops	30 (minimum possible)
Residues in loops between 'blades'	11 – 51 (av. 27)	9 – 18 (av. 13)

Conclusions

Mammals have a gene coding for a protein (mU26 in mouse, hU26 in humans) that codes for a 3-domain protein;

2 domains are similar (<26%) to a yeast gene for biosynthetic amino adipic acid reductase. This is an irreversible enzyme not known in mammals.

Domain A of mU26 is similar to domains in those enzymes that catalyse the ATP-dependent activation of carboxylic acids:-

- a) Activation of fatty acids Fatty acid + ATP ? Fatty acyl-AMP + PP_i
- b) Activation of amino acids Amino acid + ATP ? Aminoacyl-AMP PP_i

Domain P is similar to domains that can be 'activated' by phosphopantetheinyl transferases which add the Phosphopantetheinyl part of Coenzyme A to a conserved serine residue:-

- a) Acyl carrier protein (ACP) domain of fatty acid and polyketide synthases
- b) Peptidyl carrier protein (PCP) domain of microbial non-ribosomal peptide synthases

Domain R is a completely novel small superbarrel whose propeller fold has the minimum number of 'blades' held together by tryptophan docking motifs.

FINAL CONCLUSIONS

There is no evidence that the mU26 protein identified by Kasahara and Kato (or its human equivalent) has any relevance to lysine metabolism.

The C-terminal domain of mU26 has an 8-bladed Propeller fold, with blades held together by tryptophan docking motifs, similar to those in bacterial PQQ-containing dehydrogenases (quinoproteins).

There is no sequence similarity between quinoproteins and mU26, and the propeller 'domain' in mU26 is not likely to have enzymic activity.

The Propeller structure of quinoproteins is not involved in PQQ binding.

**There is no evidence that PQQ is a
cofactor for a eukaryotic enzyme or that it
is a typical B-vitamin**

Thank you for your invitation and your interest

Chris Anthony and Leigh M Felton

Leigh

[TOP](#)