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Research Article

Coenzyme Q10 Supplements which Increase ATP Synthesis within Mitochondria and Protect Against Toxic Sodium Azide

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Abstract

Objectives

Numerous CoQ10 preparations are on the market of which however, very little is known about their bioavailability and most of all there is no information regarding their efficacy on the mitochondrial electron transport chain (ETC), being the prime driver for ATP synthesis.

Methods: Various CoQ10 formulations on the market were analyzed in regard to their ingredients to boost bioavailability but also their efficacy on the synthesis of ATP formation within the mitochondria as outlined in publications. Own experiments in young healthy volunteers were given two CoQ10 supplements over a period of 5 weeks, while ATP concentration was measured in granulocytes before and after, using bioluminescence luciferase probes. In addition, the vitality of mitochondria following inhibition with sodium azide and the recovery rate after wash-out was also determined.

Results: Numerous CoQ10 formulation, in spite of their high bioavailability, however, lack any kind of conclusive data demonstrating an increase in ATP formation, a necessary constituent in the overall function of cells. In addition, the touted higher efficacy of ubiquinol when compared to ubiquinone, is nowhere demonstrated sufficiently. In contrast, ingredients within certain ubiquinol formulations do contain toxic substances for the sake to increase bioavailability, however, having a toxic effect on mitochondria. Two Q10 formulations (Grreenspeed® and Q10 Revolution®) aside from their high bioavailability, at the same time also increase the formation of ATP within the mitochondria and very likely also protect these master organelles from toxic substances of the environment, where sodium azide was used as a toxic inhibitor.

Conclusion: So far two CoQ10 preparations (Q10 Revolution® and Greenspeed®) on the European market demonstrate sufficient bioavailability while at the same time also have a significant effect on ATP synthesis within mitochondria. These Q10 compounds to a certain degree, may even work as protective agents against toxicity induced by the polluted environment.

Keywords: CoQ10; Q10 Formulation; Bioavailability; ATP Synthesis; Greenspeed®, Q10 Revolution®, Mitochondrial Recovery

Introduction

Q10 by the name of ubiquinone is a vitamin-like nutrient that plays an essential role in the energy production of all cells. It is also known as coenzyme Q10 (CoQ10) because its chemical structure is that of a 1,4-benzoquinone, where Q refers to the quinone group while the number 10 refers to the number of isoprenoid sub-units. It is ubiquitously distributed in practically all cells, being the reason why it`s called ubi-quinone, which gives fuel to the mitochondria for a sufficient function [1].

The main function of CoQ10 in the body is the production of cellular energy or adenosine triphosphate (ATP). It is the most critical component in all mitochondria (figure 1) which are present in practically every cell in our body totaling from 600 - 2000 mitochondria per cell [1]. The mitochondria are in fact fuel organelles where the biological energy called ATP (adenosine triphosphate) is produced. In addition, CoQ10 is also a potent antioxidant and it helps protect tissues and cellular components in the body from oxygen radicals (ROS). In addition, CoQ10 has been shown to preserve the myocardial sodium-potassium ATPase activity while stabilizing myocardial calcium-dependent channels and other important functions of CoQ10 such as cell signaling, and gene expression have also been described [1,2].

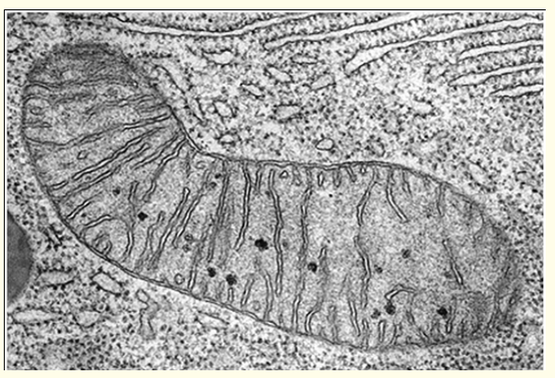

Figure 1: The mitochondrion (top) with its critical components the electron transport chain (ETC, bottom), where the ubiquinone pool (CoQ10) as well as NADH (or Q1) act as fuel leading into the final step, the generation of energy or ATP. Adapted from [3]

CoQ10 is a crucial component within the electron transport chain (aka respiratory chain) in the mitochondria where energy is derived by a process called oxidative phosphorylation from the fuel products of fatty acid and where acetyl-l-carnitine acts like a shuttle for fatty acids, as well as protein and carbohydrate metabolism. These basic fuels are converted into biological energy called adenosine triphosphate (ATP; Figure 1) which finally drives the selective cellular function and all the biosynthetic processes such as hormonal or neurotransmitter synthesis. In this regard CoQ10 is the essential cofactor for all activities of the enzyme systems within the mitochondria affecting complex I, II, III and IV in the electron transport chain [4,5]. Here CoQ10 shifts electrons from complex I (nicotinamide adenine dinucleotide dehydrogenase or NADH) and Complex II (succinate dehydrogenase) to complex III (ubiquinone-cytochrome C reductase) by virtue of its ability to either accept protons, resulting in the formation. of the reduced form of ubiquinone or ubiquinol, or by virtue of oxidation releasing protons into the intermembrane space, which later are used to activate the ATPase at complex V. It is during this process of electron transfer along the electron transport chain that the vital biological energy ATP from ADP is generated (Figure 1).

To days average diet supplies contain only a small amount of CoQ10 and it is estimated that a typical Western diet provides about 5 mg CoQ10 a day [6]. Therefore, supplementation is a necessity for physically active adults, certainly in the elderly population and especially for those who have a chronic disease, since the production of CoQ10 declines with age [7] and in mostly all chronic ailments there is a low concentration of Q10 within the body [8].

Differences in bioavailability of CoQ10 formulations

The most commonly available formulations of CoQ10 are either based on powder, in form of tablets, in form of two-piece capsules, or as soft gel capsules containing an oil suspension. This is because pure CoQ10 is insoluble in water and has only limited solubility in oils and fats. Because of the poor solubility of Q10, powder-based products show poor dissolution in aqueous media, resulting in poor absorption from the gastrointestinal tract with very low bioavailability in humans. Therefore, different lipids had been added in order to increase absorption from the gut and enhance bioavailability, while claims were based on both laboratory tests (dissolution test and cell culture studies using Caco-2 cells) as well as in plasma concentrations studies in human and in animal [9-12].

As outlined in table 1, the major drawback in formulations using CoQ10 capsules, is their very poor dissolution, resulting in a low level of bioavailability. This is because a capsule, even in an oily suspension, cannot readily traverse through the mucous layer of the intestinal tract. Being covered by a thin aqueous film, the mucous layers of the intestinal wall are unable to let any potentially water insoluble agent pass through, not reaching the systemic circulation. Such disadvantage can be circumvented by using either an oily suspension or a mycellation technique but most of all, by a nano dispersion where practically all of CoQ10, because of their minute nanosized particles resulting in anything of 300 nanometers or smaller, are able to pass through the tight junctions of the intestinal cell wall, resulting in a nearly 100% absorption (Table 1).

Product specificity	Dissolution in water (%)
Compressed tablets with fillers	1.0-3.0
Hard shell Caps, a powder-filled formulation	1.0-3.0
Soft gel Caps, a suspension in oil	1.0-3.0
Chewable wafers	1.0-5.0
ChewQ® wafers	75-80
Hydro-Q-Sorb®, a powder with g-cyclodextrin for solubilization	75-100
Q10 Revolution®, a liquid formulation in primrose oil plus NADH	90-100
Greenspeed®, a liquid formulation with natural membrane enhancers	90-100
Liquid Q10, Liquisorb®, aqueous nano dispersion	100

Table 1: Typical dissolution profiles of various coenzyme Q10 products. Adapted and modified from [13].

However, regular use of a Q10-nanodispersion has to be reconsidered with caution. This is because previous in-vitro studies with pulmonary cells which had been exposed to industrial nanoparticles outlined a cytotoxic effect [13]. Because of the change in the physicochemical properties of the original molecule, nanoparticles

practically are able to penetrate though all lipid barriers resulting in a down regulation of cellular growth and an apoptosis (suicide of cells), a reaction that is independent of the concentration of the nano particle being used [14]. One important finding was that the solubility of the nano particle strongly influenced toxicity. As such, low concentrations of nano zinc oxide, triggered a sharp decline in cell metabolism and in the proliferation of cells. At higher concentrations, however, toxicity actually dropped. This may have been due because nano zinc oxide particles clump together with higher concentrations. Also, while uncoated iron nano oxide particles were particularly toxic regardless of their concentration [15], the coated nano iron oxide particles showed no side effect on cellular function. Since all preparations, even the Q10 formulation which are based on a nano technology behave in a similar fashion, the safety of any nano Q10-particles (also those found in Pure Sorb Q40TM from Nisshin Pharma) is more than questionable as they are cytotoxic [16]. This is also because new studies revealed that nanotechnology, lack any kind of safety information [17]. As such, the US. Food and Drug Administration (FDA) currently does not specifically require safety data for foods added with nano particles. It only does require manufacturers to provide superficial tests showing that the food goods they are advertising are safe - be it beer, baby or vitamin products - and are not harmful. Up to this date, there are only a few published industry, government or scientific studies of nanoparticles on health and the environment. This in spite it is known that nano particles to be more chemically reactive and more bioactive. Therefore, safety studies should be done with any nano Q10 formulation which has a bioavailability of up to 100%, and where nano particles act as potential toxic agents to the mitochondria. It is because of such a toxicity, any nano Q10 preparation should not be used unless safety studies have proven otherwise.

In addition, liposomal CoQ10® is a liquid preparation containing CoQ10 in a lipid, that has been shown to be superior in laboratory tests and in human bioavailability studies [10,18]. Thus, liposomal CoQ10 purportedly represents an ideal formulation with enhanced bioavailability for patients requiring oral CoQ10 therapy such as infants, children, elderly, and those with difficulty swallowing. Also, a product that seemingly is suited for individuals who do not wish to or are unable to swallow tablets or capsules is ChewQ®, a chewable CoQ10 tablet formulation using the HydroQsorb® technology to ensure the highest bioavailability possible (aka plasma concentrations) by use of the additive gamma-cyclodextrin. Laboratory tests based on dissolution testing and cell culture studies had shown a 6 times CoQ10 uptake by Caco-2 cells [11].

However, in spite of all these claimed advantages regarding solubilization and absorption through the intestinal tract or the mucous membranes of the buccal cavity, nothing is mentioned about efficacy. This is because solubilization data do not reflect the actual amount of Q10 that will get into the cell, being the amount that is necessary to boost mitochondrial function resulting in a higher output in ATP synthesis.

Ubiquinol better than Ubiquinone?

As mentioned above, ubiquinol is the reduced version of CoQ10 (aka ubiquinone). They're actually the same molecule, but when CoQ10 is reduced it takes up two electrons, which turns it into ubiquinol. In our body, this conversion occurs thousands of times every second inside our mitochondria. This flipping back and forth between these two molecular forms is part of the process that transforms food into energy (Figure 1). Ubiquinone production ramps up from early childhood until our mid- to late 20s. By the time one hits 30, it begins to decline. Young people are able to use CoQ10 supplements quite well, but older people do better with ubiquinol as it's more readily absorbed. In spite the claimed superiority of ubiquinol, the reduced, electron-rich form of CoQ10 that your body produces naturally, and which plays an important role in the electron transport chain of our mitochondria, facilitates the conversion of energy substrates and oxygen into the biological energy (adenosine triphosphate or ATP); its preponderance, however, has not been demonstrated conclusively. In spite being touted as the "better CoQ10 formulation" resulting in higher blood plasma levels, there are no data that show if ubiquinol does indeed result in a higher energy synthesis than ubiquinone. This is because the body, as seen in figure 1, is able to reverse both types of Q10 depending what is needed within that very moment while switching back and forth a number of times within seconds. On the other hand, relative bioavailability of CoQ10 in its reduced form known as ubiquinol, has been shown to be higher than that of CoQ10 in its oxidized form, termed ubiquinone in both animal and human studies [10,18]. In trials with human subjects, the superior bioavailability profile of ubiquinol was demonstrated when it was tested by itself being reflected in a higher than normal plasma levels [10,18]. However, this high plasma level has to be questioned of being of purported advantage as no one so far has demonstrated a high plasma level to result in a better function of cells. Although being claimed by a number of companies who favor ubiquinol instead of using ubiquinone, all tests with ubiquinol were unable to demonstrate a superior ATP synthesis when compared to ubiquinone [19]. Because ubiquinone`s main action is the increase of ATP formation within the mitochondria, ubiquinol`s prime action is that of an antioxidant [20].

In summary, claiming ubiquinol as being superior to ubiquinone is actually only a marketing ploy (!), since it is not the plasma level that automatically will result in a higher production of ATP within the mitochondria. Much more important is how much of this CoQ10 within the plasma will actually pass the cellular membrane in order to be available for the machinery within the mitochondria, the electron transport chain, which will result in an enhanced production of ATP.

It is worth mentioning a product by the name of Ubichinol Q10 from the Visanto company in Poland, that so far was unable to demonstrate an alleged superiority in any study; it also contains toxic adjuncts that are reflected in the E numbers of constituents being used in the formulation. This is because the company, as outlined on their label, uses:

1. Canola oil for dissolution purposes, being a transfat and an inflammation enhancer since a large portion of canola oil used in processed food has been hardened through the hydrogenation process, which introduces levels of trans fatty acids into the final product as high as 40 percent [24,25].
2. E 407 or glycerol ester of fatty acids being used for emulsification purposes. It is a chemical extracted from vegetable oil, another potential transfat and an enhancer of inflammation resulting in the degradation of mitochondria [26].
3. E 901 or soy lecithin bean fat, partially hardened and another transfat affecting mitochondria. What is also troubling is the fact that the soy is a product being from genetically modified organism (GMOs) where the genetic material has been altered using genetic engineering techniques resulting in. allergic reaction, inflammation in the gut [27,28] and it is with good cause that many countries within the European Union and the world (Japan, Australia) because of health problems, abandoned the use of GMO products.
4. E322 or soy lecithin, a chemical derivative from GMO soy, used as an emulsifier; it affects the microbiome, the healthy gut bacteria with an ensuing allergy [29].

5. E1422 is another chemically modified product by the name of acetylated distarch adipate, being a resistant starch against degradation by enzymes in the gut; it may cause abdominal bloating and pain and excessive gas (flatulence) [30,31]. In addition, resistant starches may worsen the symptoms of irritable bowel syndrome (IBS) in some individuals [32].

6. E422 or vegetable glycerol often being used in E-cigarettes another chemically extracted product for tastiness and a liquefier.

7. E 407 or carrageenan, used as a thickener which can increase inflammation leading to a greater likelihood of other diseases [33], such as inflammatory bowel disease, arthritis, tendonitis, or gallbladder inflammation.

8. E150 or sulfite caramel coloring used as an additive, where intestinal problems may occur after ingestion. It´s the same substance that makes the colas brown and gives the beer their amber gold, incorporating a number of advanced glycation end products (AGE) being proinflammatory and proallergic. But most of all, it contains the cancerous byproducts known as 2-MEI and 4-MEI where the state of California added 4-MEI to its list of chemicals known to cause cancer [34].

9. E339 iii or disodium phosphate is used to enhance food characteristics like nutritional value and is also used as an emulsifier in the polish ubiquinol formulation, which can be considered as not being healthy, since it is an independent predictor of cardiovascular events and mortality [35].

Another way to increase solubilization of Q10 is the co-administered with a potent solvent such as polysorbate 20 or 80 or other solvents like poloxamer in order to increase solubilization [36]. While this technique does indeed solve the problem of a reduced bioavailability of CoQ10, polysorbate, however, in cultured human epidermal cells and animal studies have shown toxicity to mitochondria with cellular destruction which is due to a disintegration of cellular membranes, ensuing apoptosis or preprogrammed cell death [16,37,38]. Therefore, the use of polysorbate as a solubilizing agent as found in the VESisorb® technology is simply said not healthy. In spite being a swiss technology, which by itself stands for quality and used in a product by the name of VESisorb® Ubiquinol-QH with an increased absorption from the gut way over 300% in peak blood plasma levels [39], actually surpassing all other formulation, it however has this little side-effect of being toxic to mitochondria.

All the coenzyme Q10 which is built in the liver or the CoQ10 which is taken up from our food is the oxidized ubiquinone, which at any time can be transformed into its reduced form ubiquinol within the body. While it is commonly accepted that the elderly does not have sufficient capabilities to transform ubiquinone into ubiquinol [40], it makes the consumer believe to rather use an ubiquinol preparation; however, this does not solve the problem of a sufficient transmembrane diffusion into the cell where CoQ10 actually is needed. Also, since the body is constantly changing from the oxidized form into the reduced form and vice versa there still will be a deficiency of a sufficient supplementation. In addition, all companies who had done safety and toxicological studies with their CoQ10 formulation, were using ubiquinone and not ubiquinol, blindfolding the user in making them believe that their ubiquinol formulation has undergone similar studies, which however, is not true. Such a transformation from ubiquinone to ubiquinol is done by means of the enzyme thioredoxin reductase containing selenium, and by adding selenium to the CoQ10 preparation, such transformation can be speeded up, a reason why in Q10 Revolution® selenium was added to the formulation.

In addition, ubiquinol is unstable and it is very reactive when getting into contact with oxygen from the air, being converted into ubiquinone. That`s why ubiquinol has to be sold in tight sealed bottles which needs more techniique, and know-how for bottling, getting more expensive than the usual vials with ubiquinone. And while ubiquinol has a creamy white-like appearance you can readily tell once the tight sealing was damaged as now it has changed into ubiquinone having a yellowish to orange color. Such change in color will also happen once alleged tight ubiquinol capsules get into contact with oxygen rapidly changing into the yellowish oxidized form of ubiquinone. In summary:

It is irrelevant which type of CoQ10 you use - while the reduced form is much more expensive in reality it does not result in higher efficacy

Which CoQ10 formulations do increase ATP?

There are only two Q10 formulations which so far have demonstrated to pass through the lipid barriers of cells getting to the mitochondria where they activate the electron transport chain (ETC; Figure 1) with subsequent increase in ATP, by the name of Greenspeed® and Q10 Revolution®. This was nicely underlined in a separate study using Greenspeed®, where the ATP concentration in isolated living granulocytes of human volunteers was measured while at the same time exposing these granulocytes to sodium azide (NaN3), a potential toxin to mitochondria [41] and measure their recovery rate after wash-out. By using a technique based on bioluminescense through the addition of D-luciferine probes, ATP levels were determined before, 2 weeks and 5 weeks after supplementation of the Q10 formulation Greenspeed® (Figure 2). In the presence of magnesium, oxygen and ATP, the protein catalyzed oxidation of the substrate luciferin, which was associated with light emission then was measured and correlated with a standard curve of ATP concentration. Using this strategy, the luciferin targeted the mitochondrial matrix and the outer surface of the plasma membrane, a technique which is described in detail elsewhere [42]. For monitoring of ATP formation and functionality of the mitochondrial matrix and the peri-cellular space in living cells, the overall procedure in the study was broken down into three different steps

1. Measurement of the intracellular in-vitro ATP-profile before, two and five weeks after intake of Greenspeed® formulation in athletes of a mean age of 21 (+/- 5 SD) using a vial of 25 ml/day.

2. In a separate step intracellular ATP formation was blocked by adding the mitochondrial poisonous agent Na-azide to the medium putting a heavy strain on the organelles.

3. Following washout of Na-azide *in-vitro*, regeneration capacity of mitochondria in regard to ATP synthesis was determined, reflecting the viability and the recovery capacity of mitochondria before as well as after the ingestion of Q10 for two and five weeks.

The increase in ATP within granulocytes of volunteers following different times of intake of the Q10 formulation Greenspeed® (fig 2, 3 columns on the left). In addition, granulocytes after having been exposed in-vitro to the mitochondrial toxin sodium azide, reflected a dysfunction of mitochondria, resulted in a reduced formation of ATP. This, however, was partially overcome in relation to the time of the previous intake of Q10 (Fig 2, 3 columns on the right).

It clearly can be seen that the Q10 formulation Greenspeed® results in a significant increase in ATP formation within granulocytes over a time period of five weeks. In addition, when mitochondrial

function was inhibited by Na-azide, this was followed by a reduction in ATP synthesis. However, malfunction could be partially overcome after washout, depending on the previous duration of intake of Q10. Thus, mitochondria become more resistant and viable being able to withstand and recover from such a toxic compound (Figure 2).

Figure 2

These results are in contrast to studies with other preparations of Q10 where in spite the purported rise in CoQ10 plasma concentration, the net effect on ATP synthesis within the cell is not outlined. Such studies for good reasons, were never done, which might have demonstrated nil effect on the mitochondria and its synthesis of ATP. Also, with other Q10 preparations prolonged dosing will be needed. For instance, rats given doses of 200 - 500 mg/kg/day, 1 - 2 months of supplementation was needed to see a significant increase in brain CoQ10 concentrations (i.e.10 - 30%), suggesting that plasma concentrations may not adequately correlate with brain or other cell function.

Additives in CoQ10 formulations boosting ATP synthesis

There are two formulations which because of their additives result in a higher functional output. One of them is Q10 Revolution®, while the other is Greenspeed®. Q10 Revolution® inherits four natural ingredients being vitamin E, evening primrose oil, and being the only one product on the market that contains ubiquinone Q1 or NADH, together with a high dose of 420 mg of ubiquinone Q10, with no artificial additive or solvent such as polysorbate in order to increase solubilization. It is noteworthy that the addition of NADH (or Q1) acts like an ignition key at complex I of mitochondria, further increasing ATP synthesis (Figure 1). Water solubility of Q10 Revolution® is achieved by a unique formulation developed by a company in Switzerland. Contrary to *in-vitro* testing [11] the high bioavailability of Q10 Revolution® was tested in humans. There, patients with myocardial insufficiency and low median of plasma Q10 levels of < 1.4 mg/L in the control period, after intake of the liquid resulted in an increase in plasma levels reaching a mean value > 1,7 mg/l within 1 hour [43].

In addition, the sugar molecule D-ribose is added in Q10 Revolution®, a product from Poland, as well as in Grenspeed®, a product from Switzerland. D-Ribose is a five-carbon sugar, and it's completely safe to consume even for diabetics because it has no impact to blood sugar in the sense of blood glucose activating the hormone insulin. What our bodies does with ribose, is that it gets into the cells where it is converted into the adenosine base, which goes on to have the phosphate ions attached to it to create ADP and ATP (Figure 3). Basically, the importance of D-Ribose as a supplementation, is that even though our bodies produce D-Ribose on its own, this is a very slow process which now is boosted up by adding D-Ribose to the formulation.

Figure 3: The constituents of adenosine diphosphate (ADP) consisting of adenin, ribose and two phosphorous groups, the precursor of adenosine-triphosphate (ATP), being the ultimate fuel for the cell. Incorporating the sugar D-ribose is an essential part in the formation of ATP. Adapted from [3]

D-Ribose very likely is the rate limiting factor in recovery for cardiovascular patients, or patients with myocardial insufficiency and people with chronic fatigue and even in stroke. And since Greenspeed® as well as Q10 Revolution® contain the necessary B-vitamins, which are essential in the formation of the end-product adenosine triphosphate [44], the addition of D-Ribose in their formulation gives the cell an optimal source for survival. This is, because in myocardial infarction and stroke for instance, there is a block in blood flow, causing death to cells because there is not sufficient supply of the oxygen the cell needs. Even though there is death immediately within the core of the infarct, what counts is the periphery of the area of damage, where the low amount of oxygen is enough to meet the demands of peripheral cells. What ends up is that the cells start to go into a lower energy state or a hibernation mode. That doesn't necessarily mean it stops having any need for energy, it still does but just at a reduced level. Once all the oxygen is used up and it still has the energy to manage, resulting in a buildup of ADP without the sufficient energy to transform it into ATP (figure 1). In order to meet the demand of ATP, it will combine two ADPs to create an ATP and an AMP. This ATP can now be used to supply energy, but the residual AMP or Adenosine monophosphate is something that the body cannot use. As a result, there is a gradual decline of ATP, being a reason where D-ribose now jumps in for restorative purposes. The problem arises, once the blood flow is finally restored in the hospital by stent implantation, or by taking a blood thinner. Giving a rush of oxygen to these borderline, previously oxygen deprived cells, ATP-synthase in complex V within the electrical transport chain (ETC) now has the capacity to go at full speed in the formation of ATP. This however

will set up the so-called reperfusion injury as there not sufficient ADP available on-site, resulting in the formation of oxygen radicals which initiates an incredible amount of cell death and damage after blood flow is restored. One of the ways to get around that dilemma is to supply the body with sufficient amounts of adenosine D-ribose (Figure 3), so that cells actually can produce those adenosine molecules, and have enough of those building blocks to ensure that the ATP synthase at complex V continues to run without necessarily creating free radicals. Therefore, D-Ribose is important, probably one of the most important nutritional components for a subgroup of individuals that are suffering from heart attack, stroke, and chronic fatigue. Such claims of the increase in energy after CoQ10 are also underlined by another study with Greenspeed® using the EEG power spectra as a measuring parameter of the efficacy of Q10 within the cortical neuronal cells, overriding the cells important efflux pump [45] with subsequent activation of ATP within neuronal cells. In this comparison study with Q10 Revolution® both demonstrated a significant increase in the activity of brain cells within the EEG [46]. While in the case of Greenspeed® this very likely was due to an inhibition of the membrane efflux pump [45], in Q10 Revolution® this effect very likely was due to another constituent NADH within the formulation [47], being the ignition key within the electronic transport chain at complex I within the ETC (Figure 1) boosting ATP synthesis. So far, no information is available if the two formulations of CoQ10 do result in longer half-life > 6 h being combined with a longer elimination half-life. Since both formulations do seem to be associated with greater protection of mitochondria from toxic substances, however, conclusive data on other toxic substances are presently lacking as in the experiments only Na-azide was used. From the present data with the new Q10 formulations, it however is permissible to speculate, that nuclear apoptosis induced by other environmental toxic substances such as xenobiotics can be reduced. Another interesting outlook which however, needs to be determined in the near future, is the question if both formulations have an effect on sirtuin-related mitochondrial biogenesis. Indeed, this is an interesting question to be tackled, since it has been outlined in a previous paper by Martins that the calorie sensitive sirtuin 1 (Sirt 1) gene is involved in abnormal nutrient metabolism with insulin resistance [50]. It sounds attractive to speculate if this can be resolved by bioactive Q10 formulations attenuating poor xenobitic metabolism which may result in a reduction in obesity and diabetes insulin resistance.

Conclusions

In conclusion, studies are necessary in order to demonstrate the efficacy of any new kind of Q10 preparation on the market, which should conclusively demonstrate its efficacy on ATP synthesis. And since most of todays chronic ailments are related to a malfunction of mitochondrial activity, treatment should be directed towards the cellular level [3]. As such CoQ10 supplementation can not only be helpful, but it actually is an essential part of therapy in an array of different conditions and diseases, including but not limited to traumatic brain injury [48,49], also combatting the negative side effects of drugs. Thus, CoQ10 supplementation has become an important adjunct especially if one takes statins, which exhibit a major impact on mitochondrial function [51], followed by oral antidiabetics like metformin [52], a biguanide or a sulfonylurea medication [53], antihypertensive agents [54,55], hormone replacement therapy [56] and the wide array of psychiatric drugs [54,57]. Therefore, if one takes any of those medications, one will benefit from a CoQ10 supplementation which works on the cellular level, as it can help combat the negative side-effects associated with any of these drugs: Acid blockers or antacids (PPI), allergy medicines, anti-arrhythmic drugs, antibiotics, antidepressants, blood thinners, blood pressure drugs, ACE inhibitors, angiotensin II receptor antagonists, beta-blockers, diuretics, cholesterol lowering agents such as fibrates, any kind of diabetes medication, and even psychiatric drugs including antidepressants like serotonin-reuptake inhibitors (SSRI), sedatives used in anxiety disorders like benzodiazepines, anxiolytics, neuroleptic agents such as butyrophenones used as an antipsychotic, or mood stabilizers being used in bipolar disorders.

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