Research Article

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The impact of micelle size and increased absorption of ubiquinone using a novel delivery system (AquaCelle®)

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Aim: The objective of this study was to determine whether the use of a self-emulsifying drug delivery system AquaCelle®, could improve the absorption of CoQ_{10}. **Materials & methods:** Fifty-seven healthy males and females completed this study with the primary outcome as change in plasma absorption of CoQ_{10} over a 10-h period. **Results:** All AquaCelle groups significantly increased CoQ_{10} concentrations up to three-times that of the standard CoQ_{10} supplement. Ubiquinone with AquaCelle achieved an equivalent absorption to ubiquinol. **Conclusion:** The novel delivery system AquaCelle demonstrates superior absorption for the supply of ubiquinone when compared with a standard ubiquinone extract. These results further indicate that ubiquinone with AquaCelle absorbs as effectively as the typically superior absorbing ubiquinol at the same 100 mg dose.

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Coenzyme Q10 (CoQ_{10}) is an endogenously occurring lipid compound essential to mitochondrial function and bioenergetics. In humans, CoQ_{10} is the most abundant form of coenzyme Q and is present in nearly all tissues [1]. Structurally, CoQ_{10} is similar to vitamin K comprising a benzoquinone ring arrangement with a unique 10-unit isoprenoid side chain [2]. In 2012, over 3 million USA adults had reported using CoQ_{10} as a dietary supplement in the previous 30 days; a 20% increase on the values reported in 2007 [3]. This surge in popularity for CoQ_{10} supplementation over the past decade is largely due to its complementary use in the treatment of various age-related diseases [4–9]. The major limitation with CoQ_{10} supplementation lies with its lipophilicity, resulting in poor oral absorption and difficulty obtaining plasma concentrations required for therapeutic benefit.

To compensate for this poor absorption, numerous delivery systems have been made available, showing enhanced absorption of orally delivered CoQ_{10} when compared with pure crystalline formulas [10]. Much of this research surrounds combined oil–water formulations, which increase the hydrophilicity of crystalline CoQ_{10} [10]. More recently, self-emulsifying formulations have gained much interest. These systems are known to improve absorption of lipophilic agents by increasing drug dissolution in the gut and increasing gastrointestinal epithelial permeability [11]. AquaCelle® is a novel example of this self-emulsifying delivery technique.

CoQ_{10} can exist in both a reduced (ubiquinol) and oxidized (ubiquinone) state. It therefore functions as an antioxidant based on its ability for two electrons to be exchanged in a redox cycle between ubiquinol and ubiquinone [12]. The redox functions of CoQ_{10} extend beyond mitochondria, emphasizing its role in the management of medical conditions linked with oxidative damage [13]. Indeed, supplementation of CoQ_{10} has been shown to be beneficial in people with cardiovascular [4,5], neurological [6,7] and metabolic conditions [8,9]. However, these studies all stress the difficulty in achieving the plasma CoQ_{10} concentrations required for therapeutic benefit due to unfavourable pharmacokinetics.

The oral delivery of CoQ_{10} is extremely challenging. In its most pure crystalline form, CoQ_{10} is water-insoluble and has limited absorption from the gastrointestinal tract. This is speculated to be largely due to its large molecular

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weight and strong lipophilicity [12]. Oral CoQ_{10} formulations in humans report a time to absorption of 5–10 h [14] and a plasma half-life up to 33 h [10,15,16]. However, the half-life may be difficult to assess due to the reported hepatic recirculation [16]. Given therapeutic levels of CoQ_{10} are only seen at two- to three-times [17,18] endogenous levels (0.5–1.7 μM) [19], improved gastrointestinal absorption is required to deliver a positive health effect [16].

Various delivery systems have been developed in recent years to account for this poor absorption, showing that in the presence of a lipid, CoQ_{10} absorption can be significantly improved. Examples of these have utilised oil-based formulations, solubilized formulations and molecular complexes to improve plasma response to an oral CoQ_{10} supplement [20–24]. The responses to these formulations have been varied, indicating further efforts are required to effectively increase CoQ_{10} absorption. AquaCelle is a self micro-emulsifying drug delivery system designed to enhance the absorption of lipids to therapeutic levels. The aim of the present study is to compare the pharmacokinetics of a single dose of CoQ_{10} with multiple CoQ_{10}–AquaCelle formulations to ascertain what, if any, affect micelle sizes and distributions can have on absorption. We hypothesis, that the addition of AquaCelle to CoQ_{10} will increase its absorption above the standard CoQ10 supplement. Furthermore, the smaller micelle particles will further enhance the absorption of CoQ_{10}–AquaCelle.

Materials & methods

Design

A single equivalent dose, randomized, double-blinded study was used to evaluate the pharmacokinetics of five different CoQ_{10} formulations. This study was with ethical approval from Bellberry Limited. Participants were screened for inclusion and exclusion criteria before providing written informed consent prior to commencing the study.

Participants

Healthy male and female volunteers (n = 66) aged 18–30 were recruited to take part in this study. Participants were screened against inclusion and exclusion criteria previously detailed [25]. Briefly, exclusion criteria included but was not limited to; the presence of a clinically significant medical condition (e.g., cardiovascular, neurological, psychiatric, renal disease), supplementation with CoQ_{10} within 3 months of testing, known gastrointestinal or absorption issues. No participant in this trial was taking prescribed medications apart from contraceptives. Screening for known allergies/adverse reactions were performed prior to test product dosing; none were reported.

Study preparations

The study arms were as follows:

- Group 1 (AquaCelle 20) – AquaCelle CoQ_{10} paste: micelle size <20 μm, 100 mg hard capsule (Pharmako Biotechnologies, New South Wales, Australia)
- Group 2 (Standard)† – CoQ_{10} solubilized in MCT 100 mg liquid capsule (standard commercial brand)
- Group 3 (Ubiquinol) – Ubiquinol 100 mg liquid capsule (standard commercial brand)
- Group 4 (AquaCelle 10) – AquaCelle CoQ_{10} liquid: micelle size <10 μm, 100 mg capsule (Pharmako Biotechnologies)
- Group 5 (AquaCelle 15) – AquaCelle CoQ_{10} paste: micelle size <15 μm, 100 mg capsule with polysorbate (Pharmako Biotechnologies)

†The CoQ_{10} in the standard formulation group was also used for each AquaCelle formulation group. All results presented will use Group 2 for superiority comparison.

Apart from Group 3 (ubiquinol), all CoQ_{10} formulations contained the same ubiquinone in a solubilized form. All supplements were provided in identical, nondescript capsules to ensure blinding to the treatment arms was maintained. All preparations used USP grade CoQ_{10}, which was independently tested for identity and assay by Southern Cross University (Therapeutic Goods Administration Licence Number MI-01122004-LI-000264-1). The mean micelle sizes and the percentage of micelles under 10 μm in diameter are reported in Table 1.

Study protocol

Participants were evenly distributed to one of the five treatment groups using random allocation software (sealedenvelope.com). Blinding of participants and investigators was maintained until the completion of all plasma samples analysis.

Table 1. AquaCelle® formulations particle and distribution size analysis.

Group	Dosage type and fill description	CoQ_{10} capsule strength (mg)	Micelle mean size (μm)	Micelle median size (μm)	Percentage population of micelles <10 μm in diameter
AquaCelle 20 Group 5	Soft capsule with paste	100	17.3	16.2	26.4
AquaCelle 15 Group 1	Hard capsule with paste	100	12.8	12.5	38.1
AquaCelle 10 Group 4	Hard capsule with liquid	100	8.4	7.6	59.1

CoQ_{10} pharmacokinetics were quantified from blood samples taken at baseline (t = 0) and 1, 2, 3.5, 5, 7, 9, 10 and 24 h postsupplementation. Blood samples were collected into EDTA containing vacutainers (BD, NJ, USA) and immediately centrifuged at 4°C for 10 min (1500 × *g*). Once spun, the plasma fraction was temporarily stored at -20°C (<48 h) before being stored at -80°C prior to extraction.

Participants abstained from foods high in CoQ_{10} (a list was provided) from 24 h prior to testing until the final blood sample was collected. Participants remained at the research facility during the initial 10 h of sample collection where they were provided with standardized meals that were low in naturally occurring CoQ_{10}. Participants left after the 10-h sample collection, and returned the following morning for a 24-h sample. Adverse reactions to the supplements were monitored throughout the trial.

Sample preparation & analysis

Sample extraction

Plasma concentrations of CoQ_{10} was determined by HPLC using a Shimadzu HPLC system coupled with electrochemical detector (Shimadzu Scientific Instruments, MD, USA). The method used for CoQ_{10} analysis has been previously reported [2,26–28]. Briefly, with minimal light, 200 μl of plasma was added to a microfuge tube and proteins precipitated by adding 200 μl of ethanol. The tubes capped and vortex mixed for 15 s before 200 μl of hexane was added. The tubes were again capped and vortex mixed before being gently rotated for 10 min in the dark. After 10 min, the tubes were centrifuged at 11,000 rpm (11,000 × *g*) for 10 min. A total of 100 μl of the resulting hexane supernatant was transferred to a glass HPLC limited volume insert (200 μl capacity) in an amber HPLC vial, capped (with a teflon liner) and placed on the HPLC autosampler. The intra-assay and interassay coefficient of variance in our laboratory were 4.2 and 8.9%, respectively.

HPLC setup

Samples were analysed using a Shimadzu HPLC coupled with two electrochemical detectors for oxidation of sample. One electrochemical detector had a positive potential, and the other a negative potential. The mobile phase consisted of ethanol/methanol/isopropyl alcohol/lithium perchlorate (0.8 g/l of mobile phase) in water (74/22/3.8/0.2% v/v) run isocratically at 0.8 ml/min. The column used was a Develosil 5 μm RP-Aqueous AR C30, 250 × 4.6 mm with an AQ C18 4 × 3 mm SecurityGuard cartridge (Phenomenex, Sydney, NSW, Australia). A total of 20 μl of sample supernatant was injected with a run time of 22 min.

Particle size analysis was performed using a laser light obscuration instrument, POLA 2000 (Particle & Surface Sciences, NSW, Australia). Samples were prepared at 37°C and allowed to sit for 30 min prior to analyzing.

Statistical analysis

As there is endogenous Q10 in the plasma, the absorption results were calculated as a change from baseline (Baseline corrected) for each participant at each time-point for the measured values. Any data points that resulted in a negative number were given a value of '0'.

Data were analysed using GraphPad Prism 7.0 (GraphPad Software Inc., CA, USA). The peak plasma concentration (C_{max}), maximum increase in plasma concentration (ΔC_{max}), time to reach peak plasma concentration (t_{max}) and baseline adjusted area under the curve between t = 0 and t = 10 (area under curve $[AUC]_{0–10\,h}$) were calculated for each subject. The aforementioned parameters were calculated for mean, standard deviation (SD) and coefficient of variation for descriptive purposes. Normality was checked using the Kolmogorov–Smirnov test. Intergroup differences in CoQ_{10} pharmacokinetics were evaluated using an analysis of variation. All tests were two-tailed and significance was determined at an α-level of <0.05. Results are presented as mean ± SD unless otherwise stated.

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Table 2. Pharmacokinetic coenzyme Q10 parameters after a single 100 mg dose of the five study preparations.

Parameter	Group 1 Aquacelle 15 n = 10	Group 2 Standard n = 10	Group 3 Ubiquinol n = 10	Group 4 Aquacelle 10 n = 9	Group 5 Aquacelle 20 n = 9
Age	23.7 ± 3.1	22.7 ± 2.7	23.0 ± 2.0	23.0 ± 2.5	22.1 ± 3.4
Baseline	0.59 ± 0.4	0.82 ± 0.5	0.64 ± 0.4	1.36‡ ± 0.7	0.87 ± 0.6
C_{max}	1.49†,‡ ± 0.7	1.14† ± 0.6	1.60†,‡ ± 0.8	2.54†,‡ ± 1.0	1.63†,‡ ± 0.9
ΔC_{max}	0.96†,‡ ± 0.6	0.32† ± 0.3	0.95†,‡ ± 0.4	1.17†,‡ ± 0.8	0.75†,‡ ± 0.6
T_{max}	10	9	10	5	5
$AUC_{(0–10\ h)}$	5.62‡	2.21	5.24‡	6.64‡	5.34‡

Age reported in years. Values for baseline, C_{max}, ΔC_{max} are reported in μM. T_{max} is reported in hours.
†Significant compared with baseline value ($p < 0.05$).
‡Significant compared with group 2 – standard CoQ_{10} ($p < 0.05$). Values reported as mean ± standard deviation.
$AUC_{(0–10\ h)}$: Area under the curve between t = 0 and t = 10; ΔC_{max}: Maximum increase in plasma concentration; C_{max}: Peak plasma concentration; T_{max}: Time to reach peak plasma concentration.

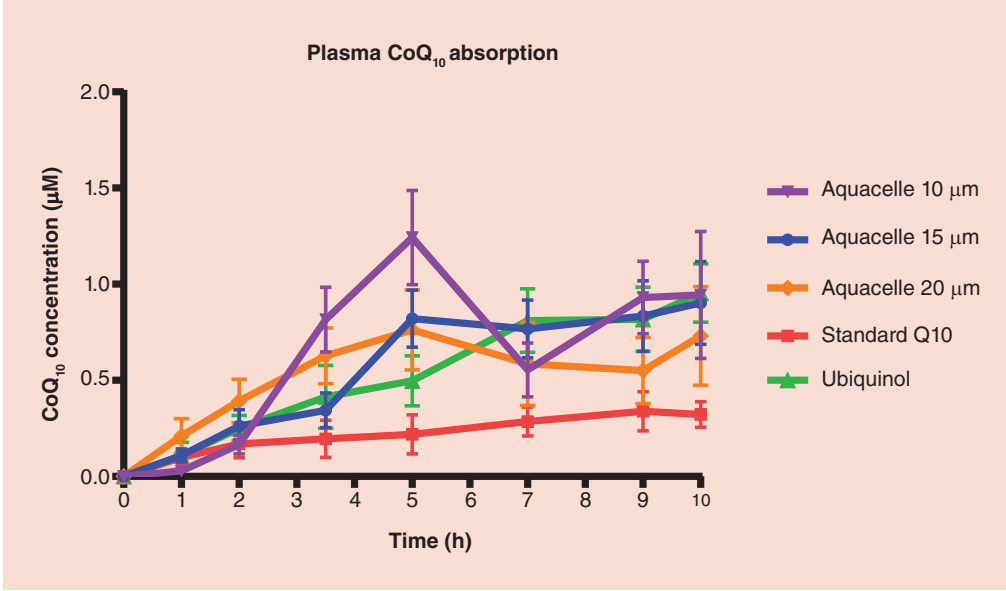

Figure 1. Pharmacokinetics profile of coenzyme Q10: temporal change in plasma CoQ_{10} concentration after a single 100 mg dose of the five study preparations. Concentration reported as μM.

Results

Of the 66 volunteers recruited for this study, 57 participants completed all required components. The average participant age was 23.1 years; all within normal BMI range (20–25), nonsmokers and otherwise healthy. Six participants withdrew during the study due to an inability to provide an adequate blood sample (poor veins, aversion to venepuncture). One participant withdrew due to an unrelated sickness following the 5-h blood sample. Two nonresponders were excluded from the statistical analysis. No adverse events due to the product were reported during the study.

Maximum CoQ_{10} concentration (C_{max}) significantly increased from baseline for all treatment groups (Table 2; $p < 0.05$). Compared with the standard CoQ_{10} preparation (Group 2), $AUC_{(0–10H)}$, C_{max} and ΔC_{max} were significantly higher in Groups 1, 3, 4 and 5 ($p < 0.05$). The AquaCelle CoQ_{10} liquid preparation (Group 4) showed the greatest C_{max} and ΔC_{max} (Table 2). There were no between-group differences for baseline concentrations of CoQ_{10} apart from those seen in Group 4. Pharmacokinetic parameters for CoQ_{10} across all five treatment arms are reported in Table 2.

Figure 1 shows the temporal change in CoQ_{10} concentration between 0 and 10 h. The time of peak concentration ranged from 5 to 10 h. An additional peak in CoQ_{10} concentration was seen at 24 h, however, these data have not been presented, nor included in statistical analysis (more on this in the discussion below).

$AUC_{(0–10\ h)}$ (Figure 2) was significantly greater in all AquaCelle preparations (Groups 1, 4, 5) and Ubiquinol

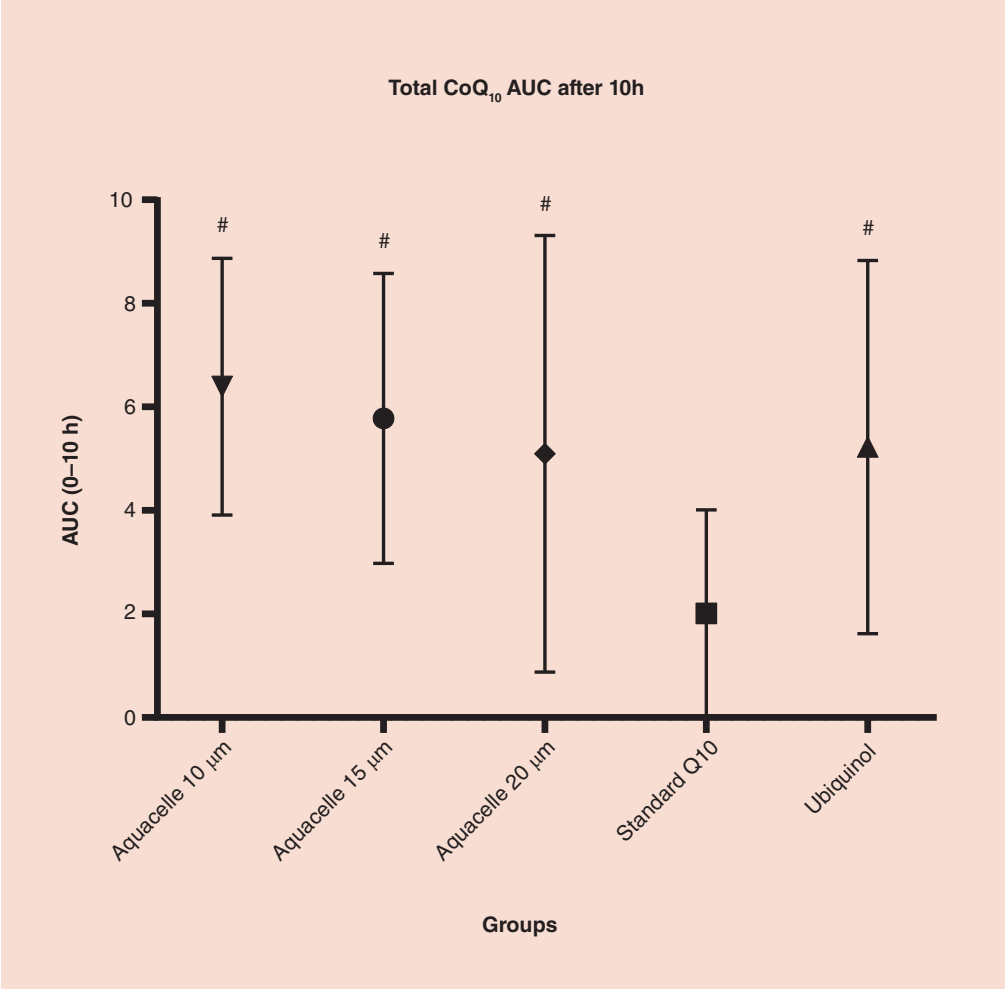

Figure 2. Area under the curve between t = 0 and t = 10 for each study preparation.
AUC: Area under curve.

(Group 3) compared with the solubilized CoQ_{10} preparation (Group 2). Of these, the AquaCelle CoQ_{10} liquid preparation (Group 4) showed the greatest absorption with an $AUC_{(0–10\ h)}$ reported to be threefold greater, when compared with the solubilized CoQ_{10} preparation (Group 2). Group 2 and 5 reported a 2.5- and 2.4-fold higher absorption respectively compared with Group 2.

Particle and distribution analyses showed a relationship between the three AquaCelle formulations and AUC (Table 1 & Figure 2).

Discussion

In the current study, we compared three different AquaCelle CoQ_{10} formulations with two different commercially available CoQ_{10} products. All trial conditions were standardised to control exogenous CoQ_{10} both prior to, and during the study. Apart from AquaCelle CoQ_{10} liquid preparation (Group 4), baseline CoQ_{10} concentrations were consistent and reflect endogenous levels previously reported in humans [11]. The disparity between Group 4 and the remaining groups was largely due to two participants having significantly higher baseline CoQ10 concentrations compared with the rest of participants. Given there were no significant differences in participant age, the disparity seen in Group 4 is unusual and may reflect poor compliance to the preparticipation protocols. Nevertheless, ΔC_{max} can still be used as a comparative measure of absorption in this group.

The AquaCelle formulations delivered ΔC_{max} values threefold (Group 4), 2.5-fold (Group 1) and 2.4-fold (Group 5) greater than the solubilized CoQ_{10} preparation (Group 2). These findings support earlier research which highlights the efficacy of self-emulsifying drug-delivery formulations (like AquaCelle) over solubilized

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formulations such as those used in the solubilized CoQ_{10} preparation [11,14]. According to Artursson *et al.* [29], the rate limiting factor for drug absorption is the single layer of epithelium covering the gastrointestinal lumen. Further, a pre-epithelial aqueous barrier exists which impedes absorption of water insoluble drugs [29]. Considering this, superiority of self-emulsifying agents may be due to; greater surface area for drug delivery provided by the emulsion droplets and formation of mixed micelles; improved diffusion of the emulsion droplets/micelles across the pre-epithelial aqueous layer of the gastrointestinal tract; and increased gastrointestinal epithelial permeability due to the surfactant in self-emulsifying systems [14]. Not surprisingly, all formulations included in this trial delivered greater absorption compared with the standard CoQ_{10} (Group 2) which was without the aid of a delivery system.

The superiority of self-emulsifying drugs to cross the aqueous gastrointestinal tract is further supported by the evidence showing the particle sizes and distribution of particles under 10 microns, appear to be directly related to CoQ10 absorption (Figure 2 – three AquaCelle groups). The formulation comprising predominantly of particles under 10 microns (Group 4 AquaCelle 10) increased 10 h AUC by 18 and 24% above Group 1 (AquaCelle 15) and Group 5 (AquaCelle 20).

In our current study, we found that two of the AquaCelle formulations (Group 1 and 4) were shown to have equivalent absorption (ΔC_{max}) when compared with ubiquinol (Group 3). Given that ubiquinol has previously been shown to have greater absorption than ubiquinone when delivered orally [30], our findings warrant further discussion. Our findings are therefore promising, showing that the AquaCelle delivery system strengthens the absorption of CoQ_{10} (ubiquinone) to a level consistent with ubiquinol; a product that has previously been considered to have pharmacokinetic dominance over ubiquinone [31].

Much of the literature investigating the pharmacokinetics of CoQ_{10} report a biphasic response to an orally delivered dose. An initial peak in plasma concentration is seen between 5 and 10 h postsupplementation, with a secondary peak of similar magnitude arising around the 24-h mark [16,22,24,31]. Our results from the present study support these temporal CoQ_{10} dynamics. The supplementary peak is thought to occur because of both enter-hepatic recycling of CoQ_{10} and a redistribution of the compound from hepatic stores to the circulation [16]. This suggests that the secondary peak is unlikely to result directly from acute CoQ_{10} oral supplementation. Because of this, we have excluded the 24-h data from our report.

The slow absorption of CoQ_{10} from the gastrointestinal tract is possibly due to its high molecular weight and water insolubility. As such, it has been suggested that T_{max} will remain somewhat consistent irrespective of its delivery system [16]. Our findings conflict with this, reporting T_{max} levels of 5 h in Groups 4 and 5 (compared with ~10 h in the remaining groups) despite containing equivalent doses of CoQ_{10}. The polysorbate present in the Group 5 formulation may explain this; increasing the lipophilicity of that CoQ_{10} dose and upregulating its absorption time. The explanation for the 5-h T_{max} reported in Group 4 is less clear. Given that all our T_{max} values were still within the range recorded in other studies [16,22,24,31], the variation we reported could merely result from the physiological differences in gastrointestinal epithelium.

Therapeutic effects of CoQ_{10} have been reported at a plasma level change of approximately 2–4 μM in patients with chronic heart failure [32] and neurodegenerative diseases such as Parkinson's [18]. However, plasma concentrations of CoQ_{10} may need to be higher for some tissues [33] and may not be a direct measure of tissue specific concentrations of CoQ_{10} [34]. The impact this may have on any potential benefit for specific diseases is still uncertain.

Whilst only one formulation group in the present study approached the limits for stated disease benefit, our results are promising, highlighting the safety and efficacy of a novel CoQ_{10} delivery system (AquaCelle) compared with commercially available products. It must however be noted that the aforementioned studies were long-term supplement trials whereas the present study is an acute dose. Further, given that a single 100 mg dose was used in our trial, and up to 1200 mg used in other trials, higher plasma CoQ_{10} concentrations would likely be achieved with continued oral CoQ_{10} supplementation. As the absorption of most supplements, including CoQ_{10}, is not directly proportionate to the dose administered, effective delivery systems may optimise therapeutic concentrations in persons with chronic disease.

This study was designed and conducted in accordance with good clinical practice guidelines. As such, all efforts were made to ensure all participants and samples were treated equally. However, despite best efforts, there are factors that may potentially affect results that were out of our control. First, as this study did not incorporate a crossover design, there is a potential for results to be affected by the absorption differences of individuals in each group. However, even in a crossover design, you could also say that the day-to-day and week-to-week variability of an individual person could also affect the result. This could be, for example, due to a poor night's sleep, a change

in diet or emotional or physiological stress. Therefore, while we acknowledge the potential effect, the design of the study is such that these variables have been adequately accounted for and the effect stated is accurate within reason. This can also be supported by the three AquaCelle groups having a linear trend in relation to the particle size consumed (i.e., AUC increases as particle size decreases).

Another factor that potentially affects the results are the treatment of outliers and nonresponders. We presented above that there were two nonresponders to supplementation and that their data were removed from analysis. We are unsure why they did not respond, but as their CoQ_{10} plasma concentration for each time point predominantly fell outside ±2SD of the mean, we felt it appropriate to exclude these individuals from the analysis to prevent bias of the data. Furthermore, two participants presented with high baseline levels of plasma CoQ_{10}. However, their concentrations were still within physiologically expected values and fell within ±2SDs of the mean. We are not sure why they had elevated baseline levels, however, when we looked at the absorption profile of these two individuals, they followed a similar profile (i.e., similar baseline corrected C_{max} and T_{max}) to the other participants in the groups. Therefore, we felt they may naturally have high CoQ_{10} and that it was appropriate to include these two individuals in the analysis.

A final factor in the consideration of the results is the CoQ_{10} raw material. This study used the same CoQ_{10} raw material in the standard group as the three AquaCelle groups. Therefore, the increased absorption is likely due to the addition of AquaCelle. However, as different raw materials may have different bioavailabilities, it makes comparison of this study to other studies difficult, especially when bioavailability enhancers are used. Specifically, it is unknown if the increased bioavailability observed here with AquaCelle would be seen for different raw material. It may be that different particle sizes (smaller or larger) are formed with different raw materials, and this in kind may affect the absorption.

Conclusion

Whether the findings of this study present a CoQ_{10} formulation that is superior to other formulations is not the aim of this study. The aim of this study was to achieve increased absorption of CoQ_{10} with a novel CoQ_{10} delivery system, AquaCelle. Following a single 100 mg dose of CoQ_{10}, we found three AquaCelle self-emulsifying delivery systems to have significantly higher absorption compared with standard CoQ_{10} in an oil–water dispersion. Further, the AquaCelle formulations were found to deliver equivalent absorption to a commercially available ubiquinol product. These results support previous reports which highlight the importance of delivery systems to aid gastrointestinal absorption of CoQ_{10}.

Future perspective

In recent years, the use of bioavailability enhancers have become increasingly popular and important. They have the ability to increase the bioavailability of compounds that are thought to have efficacy on human health, but unable to be absorbed in adequate quantities to have any effect. Over the next decade, I foresee the use of bioavailabilty enhancers becoming increasingly prevalent to the point that almost all supplements on the market will have some kind of additive, designed to increase bioavaialbilty. This will have the effect of either increasing the amount that is delivered to the system, or allow reduced amounts to be consumed (possibly having a cost saving effect) for the same effect. In addition to this, I see clinical research involving bioavailability enhancers to be increased with many studies revisiting the potential effect of a wide variety of compounds. This may include studies on both healthy and clinical populations for effects on weight loss, exercise performance and/or recovery or disease prevention or treatment for example.

Financial & competing interests disclosure

Pharmako Biotechnologies Pty Ltd sponsored this trial by supplying the test product. AquaCelle® is the registered Trade Mark of Pharmako Biotechnologies Pty Ltd. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The funding organization played no role in the study design; in the collection, analysis and interpretation of data; in writing of the report; or in the decision to submit the report for publication. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

This study was conducted with ethical approval from Bellberry limited (approval number: 2016-04-305-A-6). Further, the authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, written informed consent has been obtained from the participants involved.

Executive summary

- The major limitation with coenzyme Q10 (CoQ_{10}) supplementation lies with its lipophilicity, resulting in poor oral absorption and difficulty obtaining plasma concentrations required for therapeutic benefit.
- Given therapeutic levels of CoQ_{10} are only seen at two- to three-times endogenous levels, improved gastrointestinal absorption is required to deliver a positive health effect.
- AquaCelle® is a novel self microemulsifying drug delivery system tailored to increase the absorption of lipophilic agents to therapeutic levels.
- The aim of the study was to compare the pharmacokinetics of a single dose of CoQ_{10} with multiple CoQ_{10}–AquaCelle micelle delivery complexes to ascertain what, if any, affect micelle sizes and distributions can have on absorption.

Materials & methods

- A single equivalent dose, randomized, double-blinded study to evaluate the pharmacokinetics of five different CoQ_{10} formulations.
- A total of 66 healthy male and female volunteers aged 18–30 years.
- Group 1 (AquaCelle 20) – CoQ_{10} paste: micelle size $<$20 μm, 100 mg; Group 2 (standard) – CoQ_{10} solubilized in MCT 100 mg liquid capsule; Group 3 (Ubiquinol) – Ubiquinol 100 mg liquid capsule; Group 4 (AquaCelle 10) – CoQ_{10} liquid: micelle size $<$10 μm, 100 mg; Group 5 (AquaCelle 15) – CoQ_{10} paste: micelle size $<$15 μm, 100 mg.
- Identical CoQ10 used in both the standard and AquaCelle groups.
- CoQ_{10} pharmacokinetics were determined from blood samples taken at 0, 1, 2, 3.5, 5, 7, 9, 10 and 24 h post supplementation.
- Plasma concentrations of CoQ_{10} was determined by HPLC coupled with electrochemical detector.
- Particle size analysis was performed using a laser light obscuration instrument.

Results

- A total of 57 participants completed all required components.
- Compared with the standard CoQ_{10} preparation (Group 2), area under the curve between t = 0 and t = 10 ($AUC_{[0–10H]}$), peak plasma concentration (C_{max}) and maximum increase in plasma concentration (ΔC_{max}) were significantly higher in Groups 1, 3, 4 and 5 ($p < 0.05$).
- The 10 μm AquaCelle CoQ_{10} preparation (Group 4) showed the greatest C_{max} and ΔC_{max} and a threefold greater AUC when compared with the standard preparation (Group 2).
- Particle size was related to AUC. The smaller the particle size, the greater the AUC.
- AquaCelle CoQ_{10} 10 μm (Group 4) was equivalent to ubiquinol (Group 3).

Discussion

- Baseline CoQ_{10} concentrations were consistent and reflect endogenous levels previously reported in humans.
- Findings support earlier research which highlights the efficacy of self-emulsifying drug-delivery formulations (like AquaCelle) over solubilized formulations such as those used in the solubilized CoQ_{10} preparation.
- The superiority of self-emulsifying drugs to cross the aqueous gastrointestinal tract is supported by the evidence showing the particle sizes appear to be directly related to CoQ10 absorption.
- Our findings show AquaCelle increases the absorption of CoQ_{10} (ubiquinone) to a level consistent with ubiquinol; a product that has previously been considered to have pharmacokinetic dominance over ubiquinone.
- An initial peak in plasma concentration is seen between 5 and 10 h post supplementation, with a secondary peak arising around the 24-h mark. The supplementary peak is thought to occur because of both enter-hepatic recycling of CoQ_{10} and a redistribution of the compound from hepatic stores to the circulation.

Conclusion

- The aim of this study was to achieve increased absorption of CoQ_{10} with a novel CoQ_{10} delivery system, AquaCelle.
- Following a single 100 mg dose of CoQ_{10}, AquaCelle was shown to have significantly higher absorption compared with standard CoQ_{10} in an oil–water dispersion.

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