

## Possible Prophylaxes of Aloe Vera Juice with CoQ<sub>10</sub> to Enhance Muscle Performance

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### ABSTRACT

Coenzyme Q (CoQ<sub>10</sub>) is a major antioxidant principle found in human body which plays a vital role in maintaining several biochemical pathways of body. Deficiency of CoQ<sub>10</sub> in body leads to several potential disorders in oxido-reductive reactions of electron transport chain. Present review offers preliminary insight into using dietary supplements, aloe vera juice with CoQ<sub>10</sub>, to support and optimize quality of life in the people suffering from muscle performance. A questionnaire on aloe vera juice with CoQ<sub>10</sub> supplement was given to adult subjects. The questionnaire included 10 points regarding their mental, circulatory, and muscular functions, and the scoring was recorded from top six conditions in Table 1 and 2. Table 2 summarizes the noteworthy information of aloe vera juice with CoQ<sub>10</sub> supplement. The high molecular weight and lipophilicity of CoQ<sub>10</sub>, making its poor water solubility and leading to low systemic availability, may be reduced by supplementation of aloe vera juice with CoQ<sub>10</sub>. Possible prophylaxes of aloe vera juice with CoQ<sub>10</sub> supplement to enhance muscle performance are fully expected.

**Key words:** Aloe Vera Juice; CoQ<sub>10</sub> Supplement; Heart Failure; High Blood Pressure; Bioavailability; Exercise Ability; Questionnaire

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### INTRODUCTION

Coenzyme Q<sub>10</sub> (CoQ<sub>10</sub>) is a substance that helps convert food into energy, and found in almost every cell in the body, having a powerful antioxidant. Scientists believe free radicals contribute to the aging process, as well as a number of health problems. For a number of years, CoQ<sub>10</sub> was known for its key role in mitochondrial bioenergetics; later studies demonstrated its presence in other subcellular fractions and in blood plasma, and extensively investigated its antioxidant role. These two functions constitute the basis for supporting the clinical use of CoQ<sub>10</sub>. CoQ<sub>10</sub> deficiencies are clinically and genetically heterogeneous. This syndrome has been associated with five major clinical phenotypes: 1. encephalomyopathy, 2. severe infantile multisystemic disease, 3. cerebellar ataxia, 4. isolated myopathy, and 5. nephrotic syndrome<sup>[1]</sup>. CoQ<sub>10</sub> deficiency could result from: (1) impaired CoQ<sub>10</sub> synthesis due to nutritional deficiencies (such as vitamin B6 deficiency, a cofactor essential for CoQ<sub>10</sub> biosynthesis); (2) a genetic or acquired defect in CoQ<sub>10</sub> synthesis or utilization; or (3) increased tissue needs resulting from a particular disease. Since oral administration of CoQ<sub>10</sub> can increase tissue levels of the nutrient, it is possible to correct CoQ<sub>10</sub> deficiency and is particularly essential in the life-treating infantile encephalopathy<sup>[2]</sup>. CoQ<sub>10</sub> may enhance aerobic capacity and muscle performance making it a great supplement for athletes and people suffering fatigue.

Some researchers believe that CoQ<sub>10</sub> supplements, either by themselves or in with other drug therapies, may help prevent or treat the following conditions: 1. heart failure, 2. high blood pressure, 3. high cholesterol, 4. diabetes, 5. improve immune functions in people with AIDS, 6. improve exercise ability in people with angina, 7. help prevent migraines.

Present review article focuses on (1) prevention of heart failure or high blood pressure by aloe vera juice with CoQ<sub>10</sub>; (2) the bio-availability of aloe vera juice with CoQ<sub>10</sub>; (3) improvement of exercise ability by CoQ<sub>10</sub> with dietary supplement, because other subjects, such as prevention of high cholesterol and diabetes immune functions etc., have been discussed in relation to aloe vera on former review articles<sup>[3,4,5]</sup>. In addition to the main theme, a survey of a large number of adults on ingestion of aloe vera juice alone or the juice with CoQ<sub>10</sub> supplement was comparatively conducted by filling out a questionnaire, and the results of questionnaire totaling in a large number of volunteers were summarized in Table 1 and 2. Possible prophylaxes of aloe vera juice with CoQ<sub>10</sub> supplement to enhance muscle performance was indicated based upon the questionnaire responses.

## PREVENTION OF HEART FAILURE OR HIGH BLOOD PRESSURE BY ALOE VERA JUICE WITH COQ<sub>10</sub>

The cardio-excitatory effects of aloe extract on the isolated atria was demonstrated and the chemical and spectral examinations led to the conclusion that compounds I-IV, isolated from Aloe saponaria leaf pulp extract, using solvent partition, nonionic porous resin, and gel permeation chromatographies, are calcium salts of (+)-isocitric, L-(-)-malic, succinic, and of (-)-2-hydroxy- butandiolic acid 4-methyl ester, respectively. Cardiac stimulant activity of calcium (+)-isocitrate isolated and synthesized stereoisomers of calcium isocitrate was demonstrated and a positive inotropic effect showed in isolated guinea pig atria at a concentration of 10<sup>-4</sup> g/ml, only in the form of calcium salts, while no toxic effect such as arrhythmia was observed<sup>[6]</sup>. Oral administration of Aloe vera leaf extract for 21 days in alloxan induced diabetic rabbits produced a significant reduction in fasting blood glucose levels and HbA1c in the study. Also there was significant decrease in serum levels of triglycerides, total cholesterol, low density lipoprotein cholesterol and a concomitant increase in high density lipoprotein cholesterol in Aloe vera treated diabetic rabbit indicates the potential of Aloe vera as anti-diabetic drug. Gupta A. group indicated that the significant decrease in atherogenic index in Aloe vera treated group shows its protection against cardio-vascular diseases<sup>[7]</sup>. Kumar P. group investigated the dose dependent effect of aloe vera gel on repolarization state of myocardium, heart rate, QRS complex and QT interval using electrocardiograph in albino rats. A total of 24 male albino rats were divided into four groups, one control and three experimental. An aqueous solution of Aloe vera was prepared by taking fresh leaf of aloe plant. Animal of all the groups were anesthetized and were treated (i.p.) with aloe vera gel extract in doses of 100, 200 and 300 mg/kg body weight in experimental groups I, II and III, respectively. Electrocardiograms were recorded at 0 (basal), 15 and 30 min after injection of aloe vera/saline. Aloe vera in doses of 200 mg increases QTs from 73.10 ± 3.25 (mv) to 75.04 ± 1.93 (mv) and in 300 mg, QTc increased from 72.10 ± 1.85 to 76.10 ± 1.56 which is statistically significant (*p* < 0.05). Higher doses of aloe vera cause prolongation of QTc interval in albino rat. Therefore, administration of aloe vera in higher doses may be car-

**Table 1** Response of Aloe vera juice to chronic fatigue subjects.

Aloe vera juice	Positive efficacy ratio in single respondents	
Fatigue and languid syndrome	n=119	23.5%
Constipation	n=108	21.3%
Skin irritation	n=88	17.4%
A stiff shoulder and muscle pains	n=77	15.2%
A poor blood circulation	n=70	13.8%
Headache	n=48	9.5%

Questionnaire assessment of volunteer 507 subjects of male: 66, female: 423, unknown, 18; age-ranging from 20th to 70th years old; recovery ratio: 13.8% in single respondent from the total 3681, was carried out during September 1 to November 27, 2014. One hundred ml to 500 ml of International Aloe Science Council (IASC)-certificated aloe vera juice (Forever Living Product, Japan) was orally ingested once a day for three months. Questionnaire evaluation was based on the following scheme: 1. No change, 2. Slightly better, 3. Very much better, 4. Slightly worse, 5. Very much worse. In order to fairly evaluate the juice, only responses to question No.3 were adopted as positive in each health condition. There was no adverse effect through three months trial period.

**Table 2** Response of Aloe vera juice with CoQ<sub>10</sub> ingestion to chronic fatigue subjects.

Aloe vera juice with CoQ <sub>10</sub>	Positive efficacy ratio in plural respondents	
Fatigue and languid syndrome	n=596	46.5%
Constipation	n=525	40.9%
Skin irritation	n=479	37.3%
A stiff shoulder and muscle pains	n=450	35.1%
A poor blood circulation	n=414	32.3%
Headache	n=310	24.2%

Questionnaire assessment of volunteer 1283 subjects of male: 72 female: 1191 unknown: 20; age-range from 20th to 70 th old; recovery ratio: 34.85 %; in plural respondent in the total 3681, was carried out during September 27, 2014 to November 27, 2014. Two hundred ml of IASC-certified aloe vera juice with 80mg of CoQ<sub>10</sub> powder (Forever Living Product, Japan) was orally ingested once a day for three months. Questionnaire evaluation was based on the following scheme.1.No changed, 2.Slightly better, 3. Very much better, 4 Slightly worth, 5.Very much worse. In order to fairly evaluate the juice, only response to question No.3 were adopted as positive in each health condition. There was no adverse effect through three months trial period.

dio-toxic<sup>[8]</sup>. Verma S. group studied the effect of aloe vera gel on contractile and other property of rat myocardium using isolated heart model. A total of 24 male albino rats were divided into four groups, one control and three experimental of six animal each. An aqueous solution of aloe vera was prepared by taking 10 g of gel from the fresh leaf of aloe plant and dissolved in 100 mL of distilled water. The heart were perfused with aqueous solution of aloe in dose of 100mg, 200mg, and 300 mg/L of Krebs's solutions. The results showed that no significant difference in baseline heart rate and force of contraction among control and experimental groups. Aloe vera in dose of 200 mg/L and 300 mg/L of Krebs's-Henseleits solution was intervened showed highly significant change in force of contraction and coronary flow as compared in control. The study showed that aloe vera cause increase in myocardial force of contraction and coronary flow; therefore aloe vera may be cardio protective<sup>[9]</sup>. Jain N. group evaluated markers of oxidative stress in heart tissue along with the protective, antioxidant and anti-diabetic activity of 30% aloe vera gel in diabetic rats. Streptozocin was given as a single intravenous injection and 30% aloe vera gel was given in two doses for 20 days, orally. Blood glucose, glycosylated haemoglobin, blood reduced glutathione, serum lactate dehydrogenase and serum creatine kinase levels were recorded at the end of the study. Different biochemical variables were evaluated in the heart tissue, including thiobarbituric acid reactive substance (TBARS), reduced glutathione, superoxide dismutase and catalase in diabetic and in aloe vera-treated diabetic rats. In streptozocin diabetic rats, the TBARS level

was increased significantly, superoxide dismutase and reduced glutathione significantly decreased, and the catalase level was significantly increased. Aloe vera 30% gel (200 mg/kg) treatment in diabetic rats reduced the increased TBARS and maintained the superoxide dismutase and catalase activity up to the normal level. Aloe vera gel increased reduced glutathione by four times in diabetic rats. In conclusion, aloe vera gel at 200 mg/kg had significant anti-diabetic and cardio-protective activity<sup>[10]</sup>. Drag-reducing polymers (DRP) increase tissue perfusion at constant driving pressure. Macias CA. group evaluated the effects of small-volume resuscitation with a solution containing a DRP in a rat model of hemorrhage. Anesthetized rats were hemorrhaged at a constant rate over 25 min. In protocol A, total blood loss was 2.45 mL/100g, whereas in protocol B, total blood loss was 3.15 mL/100g. Five minutes after hemorrhage, the animals were resuscitated with 7 mL/kg of either normal saline (NS) or NS containing 50 µg/ml of an aloe vera-derived DRP. In protocol B, a third group (CON) was not resuscitated. Whole-body O<sub>2</sub> consumption (V<sub>o2</sub>) and CO<sub>2</sub> production (V<sub>co2</sub>) were measured using indirect calorimetry. In protocol A, 5/10 rats in the NS group and 8/10 rats in the DRP group survived for 4 h ( $p < 0.14$ ). Mean arterial pressure was higher in the DRP-treated group than in the NS-treated group 45 min after resuscitation ( $89 \pm 8$  vs  $68 \pm 5$  mmHg, respectively,  $p < 0.05$ ). In protocol B, survival rats over 2 h in the DRP, NS, and CON groups were 5/15, 1/14, and 0/7, respectively ( $p < 0.05$ ). Compared with NS-treated rats, those resuscitated with DRP achieved a higher peak VO<sub>2</sub> ( $9.0 \pm 1.0$  vs  $6.3 \pm 1.0$  mL/kg/min) and V<sub>co2</sub> ( $9.0 \pm 1.1$  vs  $6.0 \pm 1.0$  mL/kg/min) after resuscitation. Marcias CA. group concluded that resuscitation with a small volume of DRP prolongs survival in rats with lethal hemorrhagic shock<sup>[11]</sup>. Sixteen adult male rats were anaesthetized and mechanically ventilated. An i.v. infusion of either dextran-40 2.5% (control,  $n = 8$ ) or dextran-40 2.5% containing 50 g/mL of an aloe vera-based DRP (DRP,  $n=8$ ) was initiated at 3.5 mL/h. The left anterior descending coronary artery was ligated. Blood pressure, skin-tissue perfusion, and heart rate were monitored and arterial blood samples were analysed. The mortality at 60 min following coronary ligation was 0% in the DRP group vs 50% in the control group ( $p = 0.025$ ). DRP-treated animals maintained higher mean arterial pressure [ $60.9 \pm 5.1$  vs  $47.5 \pm 5.1$  mmHg,  $p = 0.004$ ] and tissue perfusion [ $4.2 \pm 3.4$  vs  $1.2 \pm 0.5$  TPU,  $p = 0.029$ ]. The DRP group tended towards better acid-base status with base excess [ $-5.0 \pm 1.7$  vs  $-8.1 \pm 5.1$  mmol/L,  $p = 0.083$ ] and pH [ $7.42 \pm 0.07$  vs  $7.35 \pm 0.02$ ,  $p = 0.03$ ]. In conclusion, Sakai T. group showed that administration of nanomolar concentrations of aloe vera-based DRP prolonged survival time in animals with acute myocardial ischaemia. DRPs may offer a novel method to treat organ/tissue hypoperfusion<sup>[12]</sup>. Lee BJ. group investigated the effects of CoQ<sub>10</sub> supplementation on inflammatory markers (high-sensitivity C-reactive protein [hs-CAD], interleukin-6 [IL-6], and homocysteine) in patients with coronary artery disease (CAD). Patients with CAD ( $n = 51$ ) were randomly assigned to a placebo group ( $n = 14$ ) or one of two coenzyme Q<sub>10</sub>-supplemented groups (60 mg/d, Q<sub>10</sub>-60 group,  $n = 19$ ; 150 mg/d, Q<sub>10</sub>-150 group,  $n = 18$ ). The intervention was administered for 12 wk. Plasma CoQ<sub>10</sub> concentration, inflammatory markers (hs-CRP, IL-6, and homocysteine), malondialdehyde, and superoxide dismutase activities were measured. Forty subjects with CAD completed the intervention study. The plasma CoQ<sub>10</sub> concentration increased significantly in the Q<sub>10</sub>-60 and Q<sub>10</sub>-150 groups ( $p < 0.01$ ). After 12 wk of intervention, the inflammatory marker IL-6 ( $p = 0.03$ ) was decreased significantly in the Q<sub>10</sub>-150 group. Subjects in the Q<sub>10</sub>-150 group had significantly lower malondialdehyde levels and those in the Q<sub>10</sub>-60 ( $p = 0.05$ ) and Q<sub>10</sub>-150

( $p = 0.06$ ) groups had greater superoxide dismutase activities. Plasma CoQ<sub>10</sub> was inversely correlated with hs-CRP ( $r = -0.20$ ,  $p = 0.07$ ) and IL-6 ( $r = -0.25$ ,  $p = 0.03$ ) at baseline. After supplementation, plasma CoQ<sub>10</sub> was significantly correlated with malondialdehyde ( $r = -0.35$ ,  $p < 0.01$ ) and superoxide dismutase activities ( $r = 0.52$ ,  $p < 0.01$ ). However, there was no correlation between CoQ<sub>10</sub> and homocysteine. In conclusion, CoQ<sub>10</sub> supplementation at a dosage of 150mg appears to decrease the inflammatory marker IL-6 in patients with CAD<sup>[13]</sup>. Low CoQ<sub>10</sub> level have been detected in patients with fibromyalgia (FM). Cordero MD. group assessed the effect of CoQ<sub>10</sub> on symptoms of five patients with FM. Patients were evaluated clinically with visual analogical scale of pain (VAS), and fibromyalgia impact questionnaire (FIQ). Patients with CoQ<sub>10</sub> deficiency showed a statistically significant reduction on symptoms after CoQ<sub>10</sub> treatment during 9 months (300 mg/day). Determination of deficiency and consequent supplementation in FM may result in clinical improvement<sup>[14]</sup>. Tarry-Adkins JL. group demonstrated that rats exposed to a low-protein diet in utero that underwent postnatal catch-up growth (recuperated) have a programmed deficit in cardiac coenzyme Q (CoQ) that was associated with accelerated cardiac aging. The authors investigated whether aortic and white blood cell (WBC) CoQ is programmed by suboptimal early nutrition and whether post-weaning dietary supplementation with CoQ could prevent programmed accelerated aging. Recuperated male rats had reduced aortic CoQ [22d ( $35 \pm 8.4\%$ ;  $p < 0.05$ ); 12m ( $53 \pm 8.8\%$ ;  $p < 0.05$ )], accelerated aortic telomere shortening ( $p < 0.01$ ), increased DNA damage (79 ± 13% increase in neiendonucleasesVIII-like-1), increased oxidative stress (458±67% increase in NADPH-oxidase-4;  $p < 0.001$ ), and decreased mitochondrial complex II-III activity ( $p < 0.05$ ). Post-weaning dietary supplementation with CoQ prevented these detrimental programming effects. Recuperated WBC also had reduced CoQ ( $74 \pm 5.8\%$ ,  $p < 0.05$ ). Notably, WBC CoQ levels correlated with aortic telomere-length ( $p < 0.0001$ ) suggesting its potential as a diagnostic marker of vascular aging. The authors concluded that early intervention with CoQ in at-risk individuals may be a cost-effective and safe way of reducing the global burden of cardiovascular-disease<sup>[15]</sup>. A systematic review of the literature was conducted by using databases including Medline, Embase, the Cochrane central register of control trials, and manual examination of references from selected studies. Studies included were randomized controlled trials of CoQ<sub>10</sub> supplementation that reported the ejection fraction (EF) or New York Heart Association (NYHA) functional class as a primary outcome. Information on participant characteristics, trial design and duration, treatment, dose, control, EF, and NYHA classification were extracted by using a standardized protocol. Fotino AD. group concluded that pooled analysis of available randomized controlled trials suggest that CoQ<sub>10</sub> may improve the EF in patients with congestive heart failure. Additional well-designed studies that include more diverse populations are needed<sup>[16]</sup>. Rathor N. group explored the effect of aqueous extract of Aloe vera gel on behavioural parameters of pain. Pain assessment was performed by the tail-flick and formalin tests. Aloe vera gel extract containing 3.14% aloin was dissolved in distilled water to prepare suspensions of required dose of 100 mg, 200 mg and 400mg/kg. Aloe vera (100 mg/kg, oral) produced an insignificant decrease in the pain response in the tail-flick and formalin tests. Moreover, Aloe vera (200 and 400 mg/kg, p.o.) did not have significant effect on the tail-flick test. However, Aloe vera (200 and 400 mg/kg, p.o.) significantly decreased the second phase of the formalin-induced pain. Thus, these findings suggest that Aloe vera exerts its effect by a peripheral mechanism of action rather than central<sup>[17]</sup>. Garrido-Maraver J. group

reported that CoQ<sub>10</sub> was known for its key role in mitochondrial bioenergetics as electron and proton carrier: rate studies demonstrated its presence in other cellular membranes and in blood plasma, and extensively investigated its antioxidant role. These two functions constitute the basis for supporting the clinical indication of CoQ<sub>10</sub>. Furthermore, recent data indicate that CoQ<sub>10</sub> affects expression of genes involved in human cell signalling, metabolism and transport and some of the effect of CoQ<sub>10</sub> supplementation may be due to this property. CoQ<sub>10</sub> deficiencies are due to autosomal recessive mutations, mitochondrial diseases, age-related oxidative stress and carcinogenesis processes, and also a secondary effect of statin treatment. Many neurodegenerative disorders, diabetes, cancer, fibromyalgia, muscular and cardiovascular diseases have been associated with low CoQ<sub>10</sub> levels. CoQ<sub>10</sub> treatment does not cause serious adverse effects in humans and new informations have been developed that increase CoQ<sub>10</sub> absorption and tissue distribution. Oral CoQ<sub>10</sub> treatment is a frequent mitochondrial energizer and antioxidant strategy in many diseases that may provide a significant symptomatic benefit<sup>[18]</sup>. Five thousand patients of atheromatous heart disease, as angina pectoris, were studied by Agarwal OP, over a period of five years. After adding the 'Husk of isabogol' (*Plantago ovata* seeds) and 'Aloe vera' to the diet, a marked reduction in total serum cholesterol, serum triglycerides, fasting and post prandial blood sugar level in diabetic patients, total lipid and also increase in HDL were noted. Simultaneously the clinical profile of these patients showed reduction in the frequency of anginal attacks and gradually, the drugs like verapamil, nifedipine,  $\beta$ -blockers and nitrates, were tapered. The patients, most benefitted, were diabetic (without adding any anti-diabetic drug). The exact mechanism of the action of the above two substances is not known, but it appears, that probably they act by their high fibre contents. Both these substances need further evaluation. The most interesting aspect of the study was that no untoward side effect was noted and all the five thousand patients are surviving till date<sup>[19]</sup>. The randomized controlled multicenter trial evaluated CoQ<sub>10</sub> as adjunctive treatment in chronic heart failure (HF) was studied by Mortensen SA. group. A total of 420 patients were enrolled. There were no significant changes in short-term endpoints. The primary long-term endpoint was reached by 15% of the patients in the CoQ<sub>10</sub> group vs 26% in the placebo group (hazard ratio: 0.50; 95% confidence interval: 0.32 to 0.80;  $p = 0.003$ ) by intention-to-treat analysis. The following secondary endpoints were significantly lower in the CoQ<sub>10</sub> group compared with the placebo group: cardiovascular mortality (9% vs 16%,  $p = 0.026$ ), all-cause mortality (10% vs 18%,  $p = 0.018$ ), and incidence of hospital stays for HF ( $p = 0.033$ ). In addition, a significant improvement of New York Heart Association class was found in the CoQ<sub>10</sub> group after 2 years ( $p = 0.028$ ). In conclusion, long-term CoQ<sub>10</sub> treatment of patients with chronic HF is safe, improves symptoms, and reduces major adverse cardiovascular events<sup>[20]</sup>. The multicentre randomized placebo-controlled Q-SYMBIO (randomized, placebo-controlled, double-blinded study: CoQ<sub>10</sub>-symbio trial by DiNicolantonio JJ. group) has assessed the impact of supplemental CoQ<sub>10</sub> (100mg three times daily) or placebo and were followed for 2 years. Although short-term functional endpoints were not statistically different in the two groups, CoQ<sub>10</sub> significantly reduced the primary long-term endpoint—a major adverse cardiovascular event—which was observed in 15% of the treated participants compared to 26% of those receiving placebo (HR=0.50, CI 0.32 to 0.80,  $p = 0.003$ ). Particularly in light of the excellent tolerance and affordability of this natural physiological compound, supplemental CoQ<sub>10</sub> has emerged as an attractive option in the management of heart failure, and merits evaluation in additional large studies<sup>[21]</sup>.

## THE BIOAVAILABILITY OF COQ<sub>10</sub> WITH ALOE VERA

Deficiency of CoQ<sub>10</sub> in body leads to several potential disorders like dysfunctions in cellular energetics, neurological degeneration, higher oxidative stress induced damage, breast cancer etc. The high molecular weight and lipophilicity of CoQ<sub>10</sub> makes it poorly water soluble and consequently leads to low systemic availability. Several advancements have been made to enhance the bioavailability of CoQ<sub>10</sub> using various approaches; solid dispersion and ionization, and use of novel drug carriers; liposomes and self-emulsifying system, and cyclodextrin formations.

Ranade AN. group examined to optimize the efficacy of herbal constituents by applying the concept of a novel drug delivery system, and designed to deliver and retain two herbal constituents in the stomach for better action against gastric ulcers. The objective was to develop a bilayer floating tablet of ammonium glycyrrhizin (MG) and Aloe vera gel powder through rational combination of excipients to give the lower possible lag time with maximum drug release in 7 h. Formulation of 2 containing hydroxy propyl methyl cellulose E5, crospovidone and effervescent agents in the ratio 1: 2 gave 98% drug release with desired floating properties. Pharmacodynamic studies in rats showed that the combination of MG and Aloe vera gel gave 99% ulcer inhibition in comparison with 51% ulcer inhibition in the group administered with MG alone. X-ray studies in rabbits proved the gastroretention of the tablet for more than 6 h. This suggests the relevance of novel drug delivery system in delivery of herbal constituents in the treatment of gastric ulcer<sup>[22]</sup>. Pereira GG. group reported the evaluation of the polymer films containing Aloe vera and vitamin E to treat wound caused by burns. Around 30% of vitamin E acetate was released from the polymer films within 12h. The *in vivo* experiments with tape stripping indicated an effective accumulation in the stratum corneum when compared to a commercial cream containing the same quantity of vitamin E acetate. Vitamin E was found in higher quantities in the deep layers of the stratum corneum when the film formulation was applied. The results showed that the bioadhesive films containing vitamin E acetate and Aloe vera could be an innovative therapeutic system for the treatment of burns<sup>[23]</sup>.

The high molecular weight and lipophilicity of CoQ<sub>10</sub> makes it poorly water soluble and consequently leads to low systemic availability. Several advancements have been made to enhance the bioavailability of CoQ<sub>10</sub>, and as one of the solubility enhancement water suspension of CoQ<sub>10</sub> in the form of a complex with  $\beta$ -cyclodextrin was investigated by Zmitek J. group. A randomized three-period crossover clinical trial was performed in which a single dose of CoQ<sub>10</sub> was administered orally to healthy human subjects. The pharmacokinetic parameters of two forms of the novel CoQ<sub>10</sub> material were determined and compared to soft-gel capsules with CoQ<sub>10</sub> in soybean oil that acted as a reference. The mean increase of CoQ<sub>10</sub> plasma concentrations after dosing with CoQ<sub>10</sub> vital forms determined to be over the reference formulation and the area under the curve values, extrapolated to infinity, were also higher with the tested forms; statistically significant 120 and 79% increases over the reference were calculated for the CoQ<sub>10</sub> vital liquid and powder, respectively. In conclusion, the study revealed that the absorption and bioavailability of CoQ<sub>10</sub> in the novel formulations are significantly increased, probably due to the enhanced water solubility<sup>[24]</sup>. Madhavi D. group compared the relative bioavailability of CoQ<sub>10</sub>-dextrin inclusion complex with

2 commercially available formulations: a hard gelatin capsule of crystalline CoQ<sub>10</sub>, MicroActive CoQ<sub>10</sub> complex (5 subjects) and an oil-solubilized CoQ<sub>10</sub> softgel containing a proprietary absorption enhancer (11 subjects). All the subjects in the accumulation phase of the study showed a minimum of doubling in the plasma CoQ<sub>10</sub> levels after 21 days of MicroActive CoQ<sub>10</sub> supplementation, which represents a 100% response rate. The solubilized form showed a response rate of only 44%, again confirming the greater and more uniform bioavailability of MicroActive product. In conclusion, sustained release MicroActive CoQ<sub>10</sub> is more universally bioavailable, thereby improving its ability to deliver both maintenance and the therapeutic doses of CoQ<sub>10</sub><sup>[25]</sup>. Bergamini C. group examined the cellular and mitochondrial ubiquinone content in two cell lines after supplementation with a hydrophilic CoQ<sub>10</sub> formulation (Qter) and native CoQ<sub>10</sub>. The results showed that the water soluble formation is more efficient in increasing ubiquinone levels. The authors had evaluated the bioenergetic effect of ubiquinone treatment, demonstrating that intracellular CoQ<sub>10</sub> content after Qter supplementation positively correlates with an improved mitochondrial functionality (increased oxygen consumption rate, transmembrane potential, ATP synthesis) and resistance to oxidative stress. In conclusion, the improved cellular energy metabolism related to increase CoQ<sub>10</sub> content represents a strong rationale for the clinical use of CoQ<sub>10</sub> and highlights the biological effects of Qter, that make it the eligible CoQ<sub>10</sub> formation for the ubiquinone supplementation<sup>[26]</sup>. Kim EA. group investigated the dispersions of CoQ<sub>10</sub> nanoparticles in aqueous solutions of a maize starch containing high amount of amylose (70g amylose/100g starch). Aqueous dispersion of CoQ<sub>10</sub> nanoparticles could be prepared by using amylo maize starch or its dextrin (average DP 311). CoQ<sub>10</sub> (100mg dry solids) was dispersed in aqueous starch or dextrin solution 8500mg/5ml) at 60-80 °C for 3 days, and then the solids were isolated by centrifugating in the dispersion (25,000 x g, 30 min). The isolated particles consisted of CoQ<sub>10</sub> was confirmed under differential scanning calorimetry, but most of the CoQ<sub>10</sub> in the particles existed as crystalline aggregates. The isolated particles, initially ranged in micrometer, could be re-dispersed in water at nano-sizes by treating with a mild ultrasonication. The aqueous dispersions of CoQ<sub>10</sub> nanoparticles (100mg/100g) exhibited zeta potentials of -33.9 and -51.1 mV, respectively for starch and dextrin dispersions, and remained homogeneous for more than 3 weeks without forming precipitates during an ambient storage<sup>[27]</sup>. Yoon HK. group investigated the stabilization of aqueous dispersion of CoQ<sub>10</sub> nanoparticles using maize starches. Aqueous CoQ<sub>10</sub> dispersions were prepared by blending CoQ<sub>10</sub> (60mg) in aqueous maize starch dispersion (300 mg in 30 ml water) at 60-100 °C for up to 6 h. The CoQ<sub>10</sub> agglomerates were removed by centrifugation (5000 x g, 30 min) and filtration through a glass filter. As the temperature increased, the amount of CoQ<sub>10</sub> which was stably dispersed increased. Normal maize starch was more effective in dispersing the CoQ<sub>10</sub> (57.3%) than waxy (100% amylopectin content) and high-amylose (> 50% amylose content) maize starches (9.3% and 21.9%, respectively). A light scattering analysis revealed that ultra-sonication during cooling was effective in preventing the formulation of CoQ<sub>10</sub> agglomerates. The average particle size of dispersed CoQ<sub>10</sub> was < 150 nm. Differential scanning calorimetry and x-ray diffraction analysis revealed that dispersed CoQ<sub>10</sub> particles had no amylose complex crystals. The CoQ<sub>10</sub> dispersion, however, remained homogeneous without forming precipitates during ambient storage for 2 weeks<sup>[28]</sup>.

## IMPROVEMENT OF EXERCISE ABILITY BY COQ<sub>10</sub>

The changes of oxidative stress and antioxidant markers in plasma after repeated bouts of supramaximal exercise and the effects of CoQ<sub>10</sub> supplementation were determined by Gul I. group. on these changes. The randomized double blind, cross-over study was composed of two 8-week periods of supplementation with either 100mg/day CoQ<sub>10</sub> or placebo. Fifteen healthy and sedentary men participated in the study. Five Wingate tests with 2 min rest between tests were performed. Blood samples were collected at rest, immediately after, 15 and 60 min after the fifth Wingate test for oxidative stress (malondialdehyde, nitric oxide, xanthine oxidase and adenosine deaminase) and anti-oxidant (superoxide dismutase, glutathione peroxidase and uric acid) markers. At baseline exercise session, malondialdehyde increased 15 and 60 min after the exercise compared to the rest and immediately after the exercise. Malondialdehyde at rest, immediately after and 60 min after the exercise decreased with CoQ<sub>10</sub> supplementation when compared to baseline. At baseline exercise session, uric acid increased 15 and 60 min after the exercise when compared to the rest. In conclusion, lipid peroxidation and antioxidant defense increase after repeated short-term supramaximal exercise. CoQ<sub>10</sub> supplementation partially prevents the increase in lipid peroxidation after repeated short-term supramaximal exercise<sup>[29]</sup>. Bloomer RJ. group reported impact of oral ubiquinol on blood oxidative stress and exercise performance. Fifteen exercise-trained individuals (10 men and 5 women; 30-65 years) received reduced CoQ<sub>10</sub> (Kaneka QH ubiquinol; 300mg/day) or a placebo for four weeks in a random order, double blind, cross-over design (3 week washout). After each four-week period, a graded exercise treadmill test and a repeated cycle sprint test were performed (separated by 48 h). Blood samples were collected before and immediately following both exercise tests and analysed for lactate, malondialdehyde, and hydrogen peroxide. Resting blood samples were analysed for CoQ<sub>10</sub> (ubiquinone and ubiquinol) profile before and after each treatment period. Treatment with CoQ<sub>10</sub> resulted in a significant increase in total blood CoQ<sub>10</sub> (138%;  $p = 0.02$ ) and reduced blood CoQ<sub>10</sub> (168%;  $p = 0.02$ ), but did not improve exercise performance (with the exception of selected individuals) or impact oxidative stress. The relationship between the percentage change in total blood CoQ<sub>10</sub> and the cycle sprint total work ( $R^2 = 0.6009$ ) was noted to be moderate to strong. The authors concluded that treatment with CoQ<sub>10</sub> in healthy, exercise-trained subjects increases total and reduced blood CoQ<sub>10</sub>, but this increase does not translate into improved exercise performance of decreased oxidative stress<sup>[30]</sup>. Alf D. group investigated the effect of ubiquinol supplementation on physical performance measured as maximum power outcome in young and healthy elite trained athletes. One hundred young German well trained athletes (53 male, 47 female, age  $19.9 \pm 2.3$  years) received either 300 mg ubiquinol or placebo for 6 weeks. Athletes had to perform a maximum power outcome test and the performance in W/kg of body weight was measured at the 4 mmol lactate threshold on a cycling ergometer before the supplementation treatment (T1), after 3 weeks (T2) and after 6 weeks (T3) of treatment. In these 6 weeks all athletes trained individually in preparation for the Olympic Games in London 2012. The maximum power output was measured in Watt/kilogram body weight (W/kg bw). Both groups, placebo and ubiquinol, significantly increased their physical performance measured as maximum power output over the treatment period from

T1 to T3. The placebo group increased from  $3.64 \pm 0.49$  W/kg bw to  $3.94 \pm 0.47$  W/kg bw which is an increase of  $+0.30 \pm 0.18$  W/kg bw or  $+8.5 (\pm 5.7)$ . The ubiquinol group increased performance levels from  $3.70$  W/kg bw ( $\pm 0.56$ ) to  $4.08$  W/kg bw ( $\pm 0.48$ ) from time point T1 to T3 which is an increase of  $+0.38 \pm 0.22$  W/kg bw or  $+11.0\% (\pm 8.2)$ . The absolute difference in the enhancement of the physical performance between the placebo and the ubiquinol group of  $+0.08$  W/kg bw was significant ( $p < 0.03$ ). In conclusion, this study demonstrates that daily supplementation of 300mg ubiquinol for 6 weeks significantly enhanced physical performance measured as maximum power output by  $+0.08$  W/kg bw ( $+2.5\%$ ) versus placebo in young healthy trained German Olympic athletes. While adherence to a training regimen itself resulted in an improvement in peak power output, as observed by improvement in placebo, the effect of ubiquinol supplementation significantly enhanced peak power production in comparison to placebo<sup>[31]</sup>. Ubiquinol supplementation having a high water dispersion property, plays an important role in bioenergetic process in trained athletes.

## RESPONSE OF ALOE VERA JUICE WITH COQ<sub>10</sub> INGESTION TO CHRONIC FATIGUE SUBJECTS

The questionnaire included 10 points regarding the health conditions and the scoring was recorded from top six conditions in Table 1 and 2. Table 1 and 2 demonstrated the personal experiences on administration of aloe vera juice with and without CoQ<sub>10</sub> supplement under the agreement of the principle of the Helsinki declaration. Specially, the results in Table 2 having an available recovery ratio showed high responses in plural answer. At the end of the study, none of the subjects experienced any side effects or aggravation of health problems from aloe vera juice ingestion with CoQ<sub>10</sub> supplement. Table 1 and 2 demonstrated the noteworthy information for putative prophylaxes of aloe vera juice with CoQ<sub>10</sub> supplement to enhance muscle performance and improve exercise ability.

## CONCLUSION AND FUTURE PERSPECTIVES

People with diabetes and obesity can benefit due to CoQ<sub>10</sub>'s role in energy production. CoQ<sub>10</sub> may enhance aerobic capacity and muscle performance making it great supplement for people suffering chronic fatigue. Yoon HK. group reported that aqueous CoQ<sub>10</sub> dispersion could be prepared simply by physically blending CoQ<sub>10</sub> in starch (high amylose type; V-amylose complex) or its dextrin solution without adding any emulsifier. The dispersion in an aqueous maize starch or dextrin solution could be reproduced a homogeneous dispersion in water with good storage stability. The starch dispersion containing CoQ<sub>10</sub> remained stable during ambient storage for 2 weeks<sup>[28]</sup>. Using maize starch seems to be a simple and convenient way to prepare aqueous dispersion of water-insoluble particles. The transfer processes for gelatinization may be mainly influenced by free amylose for network formation.

Nanoparticles coated with mannan were lyophilizable, and lyophilization was shown to enhance the stability of the nanoparticles. The feasibility of lyophilizing the nanoparticles and their thermal properties and the binding and uptake of the nanoparticles by a macrophages cell line were studied by Cui Z. group. Differential scanning calorimetry provided evidence that the nanoparticles were not a physical mixture of their individual components. The cell binding and uptake studies demonstrated that the nanoparticles coated with mannan, have potential application for cell-specific targeting<sup>[32]</sup>.

CoQ<sub>10</sub> nanoparticles could be lyophilized using low concentrations of disaccharides that served as cryo-protectants during lyophilization. This process was shown to increase the stability of the nanoparticles. The release profile of CoQ<sub>10</sub> from the nanoparticles demonstrated a rapid release followed by a long period of slow release. CoQ<sub>10</sub> nanoparticles with potential application for oral CoQ<sub>10</sub> delivery were engineered readily from microemulsion precursors. Hsu CH. group concluded that CoQ<sub>10</sub> nanoparticles may be considered as a promising carrier for oral delivery<sup>[33]</sup>.

Present review article revealed novel and positive efficacies of aloe vera juice with CoQ<sub>10</sub> supplement in quality of life as shown in Table 1 and 2. The demonstrated efficacies of aloe vera juice ingestion with CoQ<sub>10</sub> supplement in Table 2, may promise greater possibility for promoting and enhancing muscle performance. Acemannan (a main water-soluble polysaccharide of Aloe vera mucilaginous gel consisting of mannose-rich  $\beta$  (1-4) linked-glucomannan back-bone with a Man: Glu ratio of  $\sim 15:1$ ) may contribute, at least in part, to aqueous network formation of CoQ<sub>10</sub> in ingestion of aloe vera juice supplement.

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## CONFLICT OF INTERESTS

The authors declare that they do not have conflict of interests.

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