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Effect of Noni Supplementation on the Serum Creatine Kinase (CK) Levels of Athletes

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Abstract: The ability of NONI juice to improve endurance in athletes was evaluated clinically. A placebo-controlled clinical trial with TAHITIAN NONI® Juice (TNJ) was conducted in 23 highly-trained athletes and RIBENA was given to another set of 23 highly-trained athletes. Ingesting 100 mL of TNJ twice daily increased endurance (time-to-fatigue) and improved antioxidant status. Chemical analyses by multiple laboratories and drug-urine screening of human volunteers revealed that TNJ does not contain any illegal drugs or substances prohibited by the World Anti-doping Agency. The collective results indicated that TNJ improves endurance. The results warrant human clinical trials to assess the dosages and the feasibility of using TNJ by athletes participating in strenuous sports such as football, athletics and basketball. Serum CK is a marker for skeletal and myocardial muscle damage. Muscle damage reduces performance in endurance activities.

Key words: NONI % *Morinda citrifolia* % Antioxidant % Serum Creatine Kinase % Endurance % Performamce % RIBENA

INTRODUCTION

Morinda citrifolia Linn (Rubiaceae) also known as Indian mulberry, is a small evergreen tree. The leaves are 8-10 inches long, oval shaped, dark green and shiny, with deep veins [1]. It is largely used in traditional medicine and has been heavily promoted for a wide range of uses; including arthritis, atherosclerosis, boils, burns, cancer, chronic fatigue syndrome, circulatory weakness, cold sores, congestion, constipation, diabetes, gastric ulcers, gingivitis, heart disease, hypertension and infections [2]. However, detailed studies highlighting the effects of different compounds isolated from the plant on the immune system are lacking [3]. Fruit juice of *M. citrifolia* is a well-known health drink and has various pharmacological properties including antioxidant and anti-inflammatory effects [1, 4].

Prolonged endurance exercise, such as long-distance running, induces marked changes in enzymes of energy metabolism in muscles [5, 6]. The most consistent effect is a large increase in mitochondrial enzymes with concomitant increase in capacity to oxidize carbohydrate and fat [5, 6]. This adaptation, first shown in rats [6], also occurs in human skeletal muscles [6]. Useful and purposeful training is a process in which a person's abilities on a regular basis, gradually and progressively are increased to reach peak performance [7]. Therefore, exercise programmes and make adjustments in power are applied to have the properties to reach peak performance [8].

Endurance training increases maximum oxygen consumption [9], the number of mitochondrial and specific enzymes [7] and the yields stress in the muscle fibers [7, 9]. Palu *et al*. [10] investigated the mechanisms involved in the immunomodulatory effects of *Morinda*

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citrifolia in vitro and *in vivo* in mice. and they suggested that NONI, the juice form of *Morinda citrifolia* modulates the immune system via activating of the CB2 receptors and suppressing of the interleukin (IL-4), but increasing the production of interferon (IFN)-gamma cytokines. It may also exert beneficial immunomodulation effects in conditions involving inadequate immune responses.

In the last two decades, there has been significant accumulation of scientific data regarding athletes' physiology and medicine. Previous investigations have evaluated ideal physiological and anthropometric profile of successful karate and cycling players mostly from Western Europe and America, although there is a lack of descriptive data concerning characteristics of elite karate athletes from Eastern Europe [11, 12]. Aspects such as experience, body composition, endurance, balance between anaerobic and aerobic power, among other factors, are of primary importance in evaluation of elite athletes [12, 13].

Thus, knowing and identifying factors such as energy requirements, mechanical efficiency and oxygen intake, is essential to performance [12, 14]. The results of the study by Serafini *et al*. [15] who suggested that properties of *M. citrifolia* leaf extract should be explored further in order to achieve newer tools for managing painful and inflammation conditions, including those related to oxidant states. In addition, preclinical studies suggested that *M. citrifolia* therapies may have hepatoprotective properties [16-18]. The results published by West *et al*. [19] suggested that *M. citrifolia* leaves are safe for topical use and may be useful in mitigating UVB??-induced injury to the skin.

The present study reported the effect of NONI supplementation on the serum citrate kinase levels of the University of Port Harcourt athletes, Nigeria.

MATERIALS AND METHODS

Population and Sample: A total 23 student-athletes and 7 non-athletes (control group) of the University of Port Harcourt, Nigeria were included in each study group. Samples of blood were collected from the antecubital veins of each athlete and control. The training programmes of the participants during the 30-day period were similar and properly designed. All participants consumed the same meals as provided in the University of Port Harcourt athletes training camp. Food records were monitored during the study. The participants were all treated for malaria prior to the commencement of the study. Otherwise, the use of prescription drugs, vitamins, mineral supplements and other sports nutritional supplements was forbidden during the study. Written informed consent was obtained from participants after detailed explanations of the risks involved in the study. Detailed physical examination was carried out on all the participants to exclude any heart disease.

Endurance Clinical Trial: Forty-six volunteers (23 males and 23 females), who were training for the Nigerian Universities Games were enrolled in the study with the control group (7 males and 7 females). The volunteers and the controls were also divided into 2 groups: a NONI group ages 18-27 years and another group who consumed RIBENA ages 19-28 years. Participants assigned to the NONI group consumed 100 mL of NONI twice daily, 30 min before meals, for 30 days. Those in the RIBENA group consumed RIBENA blackberry juice, following the same dose and consumption schedule as the NONI group. The endurance of all participants was measured by a treadmill run with increasing workload (stepwise every min), until muscle fatigue (time-to-fatigue). The time-to-fatigue was measured pre-study and at day 30. Lactate and other blood measurements were also made at the same intervals using lactate analyzer.

Data Analysis: The data generated were analyzed by multivariate statistical methods. For statistical analysis SPSS software (version 20.0, Chicago, USA) was used, the paired *t* test and independent samples-test were used to compare values of the experimental treatment and control group. A comparison was considered statistically significant if the *P* value was < 0.05.

RESULTS

Table 1 shows the serum creatine kinase (IU/L) levels of participants before and after NONI supplemtation. The study group showed that there was a highly significant difference (P=0.001) between the serum CK values before and after NONI supplementation. The results also showed a significant difference (P=0.001) between the serum CK values (before and after NONI supplementation) of the study group and their controls.

Table 2 shows the serum creatine kinase (IU/L) levels of participants before and after RIBENA supplementation and the control group. The study showed that there was no significant difference (P>0.05) between the serum CK values of athletes before and after RIBENA supplementation. The study also showed no significant difference (P=0.111) between the serum CK values of before and after RIBENA supplementation among the controls.

Table 1: Serum Creatine kinase (IU/L) levels of participants before and after intake of NONI

S/N	SEX	Before NONI Supplementation	After NONI Supplementation
NONI Study Group			
1	M	240±5.4	138±8.1
2	F	215±5.4	111±8.1
3	M	221±5.4	106±8.1
4	M	200±5.4	146±8.1
5	F	225±5.4	152±8.1
6	M	245±5.4	180±8.1
7	M	274±5.4	198±8.1
8	M	219±5.4	109±8.1
9	M	250±5.4	199±8.1
10	F	241±5.4	186±8.1
11	F	190±5.4	212±8.1
12	M	210±5.4	207±8.1
13	F	199±5.4	108±8.1
14	F	198±5.4	192±8.1
15	F	195±5.4	101±8.1
16	M	200±5.4	150±8.1
17	M	190±5.4	101±8.1
18	M	187±5.4	106±8.1
19	F	190±5.4	121±8.1
20	F	186±5.4	178±8.1
21	F	198±5.4	103±8.1
22	F	190±5.4	161±8.1
23	M	163±5.4	141±8.1
Control Group			
24	M	102±4.0	100±3.3
25	F	116±4.0	102±3.3
26	F	109±4.0	101±3.3
27	M	86±4.0	82±3.3
28	M	89±4.0	84±3.3
29	F	98±4.0	92±3.3
30	F	104±4.0	102±3.3

Table 2: Serum Creatine kinase (IU/L) values of participants before and after intake of RIBENA

S/N	SEX	Before RIBENA Supplementation	After RIBENA Supplementation
RIBENA Study Group			
1	M	195±6.6	197±6.5
2	F	185±6.6	201±6.5
3	F	200±6.6	199±6.5
4	M	199±6.6	203±6.5
5	M	190±6.6	188±6.5
6	M	200±6.6	202±6.5
7	M	198±6.6	194±6.5
8	M	190±6.6	186±6.5
9	F	_____	_____
10	F	209±6.6	211±6.5
11	F	218±6.6	224±6.5
12	F	222±6.6	220±6.5
13	M	198±6.6	206±6.5
14	M	195±6.6	213±6.5
15	F	225±6.6	232±6.5
16	M	217±6.6	220±6.5
17	F	216±6.6	212±6.5
18	M	201±6.6	209±6.5
19	F	192±6.6	198±6.5
20	F	138±6.6	126±6.5
21	M	148±6.6	156±6.5
22	F	125±6.6	132±6.5
23	F	113±6.6	128±6.5
Control Group			
24	M	160±7.4	154±5.7
25	F	108±7.4	113±5.7
26	M	137±7.4	144±5.7
27	M	113±7.4	120±5.7
28	F	133±7.4	131±5.7
29	F	116±7.4	124±5.7
30	M	106±7.4	116±5.7

Key: _ = Haemolysis

The study showed no significant difference (P=0.173) in the serum CK values before and after intake of RIBENA among the females in the RIBENA group. There was no significant difference (P=0.341) in the serum CK values before and after RIBENA supplementation among the females in the control group. There was no significant difference (P=0.072) in the serum CK values before and after intake of RIBENA among the males in the RIBENA group. There was no significant difference (P=0.297) in the serum CK values before and after RIBENA supplementation among the males in the control group.

Table 3 shows the serum creatine kinase (IU/L) values of participants group before and after intake of NONI and RIBENA in relation to their sex and age. The study showed that there was a significant difference (P=0.023) between the serum CK values before NONI and RIBENA supplementation among the two study groups. The study also showed a highly significant difference (P=0.001)between the serum CK values of athletes after

Table 3: Comparative analysis of serum creatine kinase (IU/L) values of participants before and after supplementation with NONI and RIBENA in relation to their sex and age.

Study Group	Before Supplemetation	After Supplemetation
NONI		
Males (n=12)	216.6±9.1	148.4±11.4
Females (n=11)	202.5±5.2	147.7±12.2
Total (n=23)	209.8±5.4	148.1±8.1
Control		
Males (n=3)	92.3±4.9	88.7±5.7
Females (n=4)	106.7±3.8	99.3±2.4
Total (n=7)		
RIBENA		
Males (n=11)	193.7±5.1	197.6±5.2
Females (n=12)	185.7±12.4	189.4±12.2
Total (n=23)	189.7±6.6	193.5±6.5
Control		
Males (n=4)	129.0±12.3	133.5±9.2
Females (n=3)	119.0±7.37	122.7±5.2
Total (n=7)		
Total no. of Males	30	30
Total no. of females	30	30
Overall total	60	60

NONI supplementation. There was no significant difference (P>0.05) between the serum CK values of athletes after RIBENA supplementation.

DISCUSSION

The serum levels of skeletal muscle enzymes are a marker of the functional status of muscle tissue and vary widely in both pathological and physiological conditions [20]. An increase in these enzymes may represent an index of cellular necrosis and tissue damage following acute and chronic muscle injuries [20, 21]. Changes in serum levels of muscular enzymes and isoenzymes are also found in normal subjects and in athletes after strenuous exercise [20, 22, 23].

The serum CK level can be raised from the damage of the muscle tissue as a consequence of intense prolonged training. This may be a consequence of both metabolic and mechanical causes [20]. Indeed, metabolically exhausted muscle fibres exhibit a decrease in the membrane resistance following an increase in the internal free calcium ions, which promote the activation of the potassium channel [20, 24-25]. Another mechanism could be the local tissue damage with sarcomeric degeneration from Z-disk fragmentation [20]. CK is an indicator of muscle necrosis, increasing with its extent [20, 26].

In athletes, the study of CK at rest and after exercise could be an important tool for coaches and clinicians [20, 27]. Athletes have higher resting CK when compared with untrained subjects [28], probably because of the greater muscle mass and the daily training performed. However, after exercise, CK serum activity depends on the level of training; although athletes experience greater muscle soreness when compared with untrained subjects, their peak serum activity is lower [20, 29]. In normal serum, total CK is provided mainly by the skeletal muscle. Total CK levels depend on age, gender, race, muscle mass, physical activity and climatic condition. The 2.5 and 97.5 percentile reference limits have recently been revisited [20, 30].

The present study showed a significant difference between serum CK levels and sexes of the subjects. This is in line with previous studies. Young adult males have high serum levels of CK [31], which decline slightly with age during the geriatric period [32]. There are marked sex differences in CK serum levels at rest [33], with lower values in females than in males. After muscular exercise, sex-linked differences are still present [34] and oestrogen may be an important factor in maintaining post-exercise membrane stability, thus limiting CK leakage from the damaged muscle [20, 35, 36].

CK activity is related to body mass and physical activity, with resting levels higher in athletes than in sedentary subjects, given the regular training that athletes undergo [20, 37, 38]. Cold weather induces higher serum CK following a standard exercise bout when compared with the same exercise bout at warmer temperatures [20, 39].

Many factors determine the degree to which serum enzyme activities increase during and after exercise [20]. There is a breakpoint at 300–500 IU/l of CK serum release after exercise and the levels of enzyme are associated with distinctive individual musclar properties [20]. Daily training may result in persistent serum elevation of CK [40], but the significant increases of CK occurring after exercise are usually lower in trained subjects when compared with untrained subjects [29, 41-42].

The decrease in the serum enzyme levels depends on the period of rest after exercise, as short-term physical inactivity may reduce both the lymphatic transport of CK and the release of the enzyme from the muscle fibres [20]. Manual lymph drainage after treadmill exercise is associated with faster decrease in the serum levels of muscle enzymes [43]. Another factor that may reduce muscle damage and serum concentrations of CK following prolonged exercise is supplementation with branched-chain amino acids, often used in sports [20, 44].

CK values show great variability among individuals. Some athletes are low responders to physical training, with chronically low CK serum levels [20]. Some athletes are high responders, with higher values of enzyme In addition, more details about hyperCKemia could come from the evaluation of the kinetics of CK after stress in healthy athletes with high levels of CK due to exercise, comparing the results with the ones obtained from athletes with persistent hyperCKemia at rest. Finally, it would be important to quantify the type of exercise being more suited to athletes with myopathy and the intensity of exercise not dangerous for the progression of the pathology [20].

The purpose of the present study was to evaluate the effect of NONI supplementation and 30-day endurance training on the performance of university athletes. Various combinations of substances have been introduced as sports food, drinks and pills [3, 4, 45]. These supplements mostly commonly contain carbohydrates, vitamins, minerals and trace elements. The use of supplements by competitive athletes has involved the ingestion of preparations which appear on the World Anti-Doping Agency’s list of banned substances [46].

Appropriate penalities have been instituted for the violation of the World Anti-Doping code because the use of such preparation tends to deny equality of opportunity for athletes and also poses a serious threat to the health of users [10, 47, 48]. Though, there has been some interest and concern regarding the composition of herbal and dietary supplements and their possible influence on drug or doping tests [49]. As the use of herbal dietary supplements increases, this issue is of paramount importance. However, with these ergogenic effects in mind, Palu *et al*. [47] in their study showed that TNJ showed no presence of any prohibited substances. An alkaloid screen of the juice was negative. An HPLC based screen was also performed and detected no alkaloids at or above the detection limits of 1 mg/L. Xanthine alkaloids are of particular interest, as NONI belongs to the coffee (Rubiaceae) family [47]. Another assay, specific to caffeine, found none at a detection limit of 50 mg/L [47, 50].

In this study, results showed expected increases in the serum creatine kinase levels of participants following training, signifying exercise-generated muscle damage [20]. Over the test period, NONI reduced the magnitude of exercise-induced elevation in serum creatine kinase levels [20, 46, 51]. The results obtained are consistent with the observations of Coombes and McNaughton [44], Brancaccio *et al*. [20], Palu *et al*. [10, 47, 48] and Tsai *et al*. [46]. Palu *et al*. [47] evaluated TNJ ergogenic effect in mice and indicated that TNJ increases the swimming time of mice (36 to 45%) before becoming fatigued and increases their endurance time (59 to 128%) on a rotarod test, compared to their control. Further, the older mice in the TNJ group performed similarly to the younger ones in the control group, with respect to swimming time and endurance [44, 47].

The findings of this study will help to reduce the use of illegal drugs among athletes. The use of naturally occurring nutritional supplements such as *Morinda citrifolia* is becoming increasingly important to athletes who do not want to violate the World Anti-Doping-Agency code. Consequently, the study of the effect of *Morinda citrifolia* on the enzyme profiles of athletes is necessary to elucidate its mechanism of action.

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