Eur J Appl Physiol (1998) 77: 486–491

ORIGINAL ARTICLE

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Physiological and performance responses to supplementation with thiamin and pantothenic acid derivatives

Accepted: 9 October 1997

Abstract The purpose of this study was to investigate the physiological and performance responses to supplementation with allithiamin and pantethine. On two separate occasions, six highly trained cyclists [maximum O_2 consumption or $\dot{V}O_{2max}$ 61.8 (2.1) ml · kg^{-1} · min^{-1}] performed a 50-km steady-state ride on a cycle ergometer at a workload corresponding to ~60% of $\dot{V}O_{2max}$ followed by a 2000-m time trial. For 7 days prior to each ride, subjects daily ingested either a placebo (PL) or a combination of 1 g of allithiamin and 1.8 g of a 55%/45% pantethine/pantothenic acid compound (AP). Treatments were administered using a randomized, double-blind, counter-balanced design. During the 50-km ride, measures of heart rate, respiratory gas exchange and ratings of perceived exertion were recorded at 5, 15, 25, 35 and 45 km. Blood samples were collected at 10, 20, 30, 40 and 50 km and analyzed for lactate, glucose and free fatty acids. Blood samples for the analysis of lactate were also collected 3 and 5 min after the completion of the 2000-m time trial. There were no significant differences in any of the measured parameters between experimental conditions. Time to complete the 2000-m time trial was also not significantly different between experimental conditions [PL 178.2 (8.4), AP 170.7 (10.2) s; $P = 0.58$]. These results suggest that, despite the reported enhanced absorption properties, supplementation with allithiamin and pantethine does not alter exercise metabolism or exercise performance.

Key words Allithiamine · Allithiamin · Thiamin tetrahydrofurfuryl disulfide · Pantethine · Pantothenate

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Introduction

While the majority of exercise research does not support vitamin supplementation in vitamin-sufficient individuals, there is still widespread practice of vitamin supplementation among both recreational and competitive athletes (Bentivegna 1979; Grandjean et al. 1981). In contrast with most studies of vitamin supplementation, it has been shown that thiamin and pantothenic acid may have ergogenic effects (Knippel et al. 1986; Litoff et al. 1985; McNeill and Mooney 1983; Shock and Sebrell 1944a,b). Both vitamins play key roles in intermediate energy metabolism. Thiamin plays an essential role as a cofactor in numerous reactions of glycolytic metabolism. One particularly important role is its part in the five-enzyme complex pyruvate dehydrogenase (PDH) which catalyzes the movement of pyruvic acid into the tricarboxylic acid cycle as acetyl CoA. Pantothenic acid plays a key role in fatty acid, carbohydrate and amino acid metabolism (Tahiliani and Beinlich 1991), as it is required for the biosynthesis of CoA. While large supplemental doses of these vitamins are theoretically attractive to athletes, both are water soluble and have limited absorption from the intestine (Fenstermacher and Rose 1986; Levy and Hewitt 1971; Thomson and Leevy 1972; Ventura et al. 1969).

The recently available congeners of thiamin (allithiamin) and pantothenic acid (pantethine) have been demonstrated to have greatly increased absorptive and metabolic effects over the traditional forms and appear very attractive to athletes. Oral allithiamin administration results in blood thiamin levels equivalent to that achieved by intravenous administration of thiamin hydrochloride (THCl) and has been demonstrated to rapidly increase thiamin activity in whole blood, red blood cells, cerebrospinal fluid, urine, liver, heart and skeletal muscle (Baker et al. 1974; Fujiwara et al. 1964a–c; Kawasaki et al. 1964; Takenouchi and Aso 1963, 1964). Pantethine ingestion has been shown to raise plasma pantothenate levels 300 times greater than normal

(Wittwer et al. 1985) with increase in the rat liver CoA concentration of 20–30% (Branca et al. 1984). In addition, pantethine administration has been demonstrated to have positive inotropic, negative chronotropic (Minami et al. 1983) and anti-arrhythmic effects on the heart (Hayaski et al. 1985) as well as anti-lipidemic effects (Angelico et al. 1983; Gaddi et al. 1984; Murai et al. 1983; Miccoli et al. 1984).

Considering the key roles of thiamin and pantothenic acid in exercise metabolism and the enhanced absorptive characteristics of allithiamin and pantethine, the purpose of this study was to investigate the physiological and performance effects of a large oral dose of a combination of allithiamin and pantethine prior to steady-state and high-intensity cycling exercise.

Methods

Subjects

Six highly trained, competitive cyclists participated in the study. The procedures of the investigation were explained and all subjects provided written informed consent. All methods and procedures used in this study were approved by the University's ethics committee for the use of human subjects in research.

Anthropometric and physiological characteristics were as follows [mean (SE)]: age 22 (1) year, height 181 (3) cm; body mass 71.4 (2.1) kg, and maximal aerobic power ($\dot{V}O_{2max}$) 61.8 (2.1) $ml \cdot kg^{-1} \cdot min^{-1}$, body fat 7.2 (0.8) percent (Pollock et al. 1990).

Preliminary testing

Each subject completed a preliminary testing session for the determination of $\dot{V}O_{2max}$. The subject performed an incremental exercise test on a Monark cycle ergometer modified for instantaneous application of resistance. The test required the subject to pedal for 3 min at a constant cadence of 80 revolutions $\cdot$ min^{-1} against an initial workload of 80 W. At the end of 3 min the workload was increased by 40 W. This was repeated until the subject could be no longer maintain the pedaling cadence. Total exercise time for the test was approximately 25–30 min. Throughout the test, inspired ventilation volume was measured with an RAM-9200 spirometer (Rayfield Equipment, Waitsfield, Vermont), expired gases were directed into a 3-l mixing chamber and a sample of dry gas was analyzed for the fractional concentrations of oxygen and carbon dioxide using Sensormedic OM-11 and LB-2 analyzers, respectively. Analyzers were calibrated with gases of known concentration prior to, and immediately following, each test. Both the spirometer and gas analyzers were connected to an REP-200 data acquisition system (Rayfield Equipment) interfaced with an Apple lle computer.

Experimental testing

Each subject completed two experimental testing sessions in a randomized, double-blind, counter-balanced fashion. One testing session was performed after a 7-day supplementation with 1 g allithiamin and 1.8 g of a 55% pantethine/45% pantothenic acid compound (AP) (Ecological Formulas, Concord, Calif., USA). The alternate testing session was performed after a 7-day supplementation with a placebo (PL) (white flour). Treatments were presented in gelatin capsules and were indistinguishable from one another. A 21-day washout was performed between the completion of the first testing session and the beginning of supplementation for the second testing session. This washout period was chosen based on a limited number of studies investigating the absorption and excretion of these vitamin derivatives. Two clinical studies of the absorption and excretion of 50 mg allithiamin indicate that a 7-day washout is adequate for a return to baseline thiamin status. Wittwer et al. (1985) reported pantethine to have half-life of ~28 h. During the course of the study, subjects were requested to maintain their "normal" dietary practices. To ensure consistency between the two trials, a dietary recall was performed during the 48 h prior to the first testing session and this diet was replicated during the 48 h prior to the second testing session. None of the subjects reported taking any vitamin or mineral supplements during, or in the months prior to, the study. Subjects were requested to reduce their training volume and intensity in the 2 days prior to each of the cycling trials in a manner they typically used in preparation for a competition. All testing was performed at the same time of day for each subject.

On arrival in the laboratory after an overnight fast, subjects were seated for ~10 min during which time baseline measures of heart rate (HR) (Polar CIC, Port Washington, N.Y., USA) and $\dot{V}O_2$ were recorded. In addition, ~100 µl of capillary blood from an earlobe puncture was collected into heparinized microcapillary tubes. A 25-µl portion of this sample was analyzed for whole-blood lactate concentration ($[La^-]$) (YSI model 2300-STAT, Yellow Springs Instrument, Yellow Springs, Onio, USA). The remaining portion was transferred into a microcentrifuge tube and the plasma was separated from the whole blood by centrifuging the sample tubes in the cold (5°C) at 1000 × g for 15 min. The plasma was frozen (−30°C) for later analysis of glucose (510-A, Sigma, St. Louis, Mo., USA). An additional 200 µl of capillary blood was collected into non-heparinized capillary tubes and immediately transferred into microcentrifuge tubes containing EDTA. Separation of plasma from whole blood was accomplished by centrifuging the sample tubes in the cold (5°C) at 1000 × g for 15 min. The plasma was frozen (−30°C) for later analysis of non-esterified fatty acids (NEFA) (NEFA C, Wako Chemicals, Richmond, Va., USA).

After obtaining baseline measures, subjects performed a 50-km ride on a cycle ergometer at a pedaling cadence of ~80 revolutions $\cdot$ min^{-1} and a resistance corresponding to ~60% of $\dot{V}O_{2max}$ (as determined from the preliminary testing session). At the end of the 50-km ride, the subjects were allowed a 1-min rest period to stretch and then remount the bike. At the end of the rest period, they performed a 2000-m time trial as previously outlined (Webster et al. 1997). Briefly, the subject assumed a static starting position on the cycle with the pedal at approximately 45° above horizontal. The test distance of 2000 m was programmed into a cycle computer (ECHO-J12, Echohowell) and a timer was activated with movement of the flywheel and stopped upon completion of 2000 m. Subjects were allowed visual feedback regarding distance remaining in the trial and verbal encouragement was provided throughout each test to motivate subjects to perform maximally. During the 50-km ride, measures of $\dot{V}O_2$, HR, respiratory gas exchange (RER), and ratings of perceived exertion (RPE) (6–20 point Borg scale) were recorded at 5, 15, 25, 35 and 45 km. Blood samples were collected at 10, 20, 30, 40 and 50 km and analyzed for $[La^-]$, glucose and NEFA. Blood samples for the analysis of $[La^-]$ were also collected 3 and 5 min after the completion of the 2000-m time trial. During the first experimental testing session, subjects were allowed ad libitum water intake. The volume ingested was recorded and this volume was allowed during the subsequent experimental testing session.

Statistical analyses

All data are expressed as mean ± SE. A one-way analysis of variance (ANOVA) with repeated measures was used to determine the statistical significance of any differences in $\dot{V}O_2$, $[La^-]$, glucose, NEFA, RPE, RER, HR, or 2000-m cycling performance time after the ingestion of either a PL or AP. Significance was set at $P < 0.5$.

Results

There was no significant difference in the time required for the subjects to complete the two 50-km rides [PL

Table 1 Serial measures of oxygen uptake ($\dot{V}O_2$), heart-rate, respiratory exchange ratio (*RER*), and rating of perceived exertion (*RPE*) during steady-state cycling after the ingestion of either an allithiamin/pantethine (*AP*) supplement or a placebo (*PL*) for 7 days. There were no statistically significant differences between trials at any measurement point. Data are expressed as mean ± SE ($n = 6$)

Parameter	Measurement point (km)					
	0	5	15	25	35	45
$\dot{V}O_2$ ($l \cdot min^{-1}$)						
PL	0.44 (0.04)	2.83 (0.15)	2.93 (0.18)	3.03 (0.15)	3.03 (0.14)	3.09 (0.13)
AP	0.43 (0.04)	2.79 (0.12)	2.91 (0.13)	2.98 (0.16)	3.00 (0.17)	3.07 (0.15)
Heart rate ($b \cdot min^{-1}$)						
PL	73 (7)	160 (3)	164 (3)	167 (4)	170 (4)	173 (3)
AP	75 (4)	160 (2)	166 (2)	168 (2)	167 (2)	171 (1)
RPE						
PL	0.85 (0.01)	0.96 (0.01)	0.95 (0.02)	0.92 (0.01)	0.91 (0.01)	0.90 (0.01)
AP	0.91 (0.03)	0.94 (0.01)	0.93 (0.02)	0.93 (0.03)	0.91 (0.03)	0.89 (0.03)
RPE						
PL	–	11.8 (0.6)	12.8 (0.6)	13.8 (0.6)	14.0 (0.9)	14.8 (1.1)
AP	–	11.5 (0.6)	12.5 (0.6)	13.7 (0.6)	14.3 (0.9)	15.0 (1.0)

102.2 (0.8); AP 101.7 (0.8) min, $P = 0.64$]. While the initial workload was chosen to corresponded to 60% $\dot{V}O_{2max}$, the first measure of steady-state $\dot{V}O_2$ (5 km) was approximately 64% and 63% of $\dot{V}O_{2max}$ in the PL and AP trials, respectively. As is frequently associated with steady-state exercise, there was an upward drift in $\dot{V}O_2$ reaching a peak of 70% and 69% of $\dot{V}O_{2max}$ in the PL and AP trials, respectively, at the final measurement point (Table 1). At no measurement point were statistically significant differences noted between trials.

HR and RPE (Table 1) exhibited similar responses to that of $\dot{V}O_2$ in that there was a progressive rise across time, with the greatest values recorded at the last measurement point (45 km); however, there were no statistically significant differences in either of these parameters between trials at any measurement point.

In both trials the RER exhibited an initial increase followed by a progressive decline to the final measurement point (Table 1), suggesting a slightly greater reliance on fat toward the end of the steady-state exercise than at the beginning. This notion is supported by serial measures of plasma [glucose] and [NEFA] (Table 2). Over the course of the steady-state exercise bout there was 31% and 29% decrease in plasma [glucose] and a 103% and 89% increase in circulating plasma [free fatty acid] in the PL and AP trials, respectively.

With the onset of steady-state exercise there was the expected increase in [La^-] (Table 2) and this was followed by no further increase despite the fact that the relative work intensity progressively increased as indicated by measures of steady-state $\dot{V}O_2$. As expected, [La^-] was greatest after completion of the 2000-m cycling trial [3-min post-exercise: PL 4.7 (0.4), AP 5.1 (0.7) mM; 5 min post-exercise: PL 5.0 (0.6), AP 5.5 (0.9) mM]. Time to complete the 2000-m cycling trial after completion of the 50-km ride was faster in five of six subjects during the AP trial (range of times: PL 152.8–195.4, AP 150.1–189.3 s). Mean time was slightly faster in the AP trial [PL 178.2 (8.4), AP 170.7 (10.1) s]; however, this difference was not statistically significant ($P = 0.58$). In addition, no order effect was noted between the first and second trails ($P = 0.17$).

Table 2 Serial measures of lactate, glucose and NEFA during steady-state cycling after the ingestion of either an allithiamin/pantethine (*AP*) supplement or a placebo (*PL*) for seven days. There were no statistically significant differences between trials at any measurement point. Data are expressed as mean ± SE ($n = 6$)

Parameter	Measurement point (km)					
	0	10	20	30	40	50
Lactate (mM)						
PL	0.7 (0.1)	1.9 (0.4)	1.6 (0.3)	1.7 (0.4)	1.8 (0.5)	1.7 (0.4)
AP	0.8 (0.1)	1.8 (0.3)	1.7 (0.2)	1.7 (0.3)	1.6 (0.2)	1.5 (0.2)
Glucose (mM)						
PL	5.8 (0.2)	4.3 (0.3)	4.6 (0.2)	4.5 (0.3)	4.2 (0.3)	4.0 (0.3)
AP	5.8 (0.4)	4.4 (0.3)	4.9 (0.3)	4.7 (0.4)	4.4 (0.3)	4.1 (0.3)
NEFA (mM)						
PL	0.31 (0.04)	0.26 (0.08)	–	0.37 (0.08)	–	0.63 (0.08)
AP	0.27 (0.03)	0.19 (0.03)	–	0.29 (0.07)	–	0.51 (0.09)

Discussion

As expected with exercise of the type performed in this study, there were significant time effects in many of the above-measured parameters. More importantly, however, there were no statistically significant differences noted between trials in any of the above-measured parameters at any measurement point.

There are relatively few studies that have investigated either thiamin or pantothenic acid and exercise performance (Knippel et al. 1986; Litoff et al. 1985; McNeill and Mooney1983; Nice et al. 1984; Shock and Sebrell 1944a,b). However, the results of most of these studies suggest a possible ergogenic effect (Knippel et al. 1986; Litoff et al. 1983; McNeill and Mooney 1983; Shock and Sebrell 1944a,b). Knippel et al. (1986) reported decreases in submaximal $\dot{V}O_2$ and blood La^- accumulation and improvements in the La^- threshold in trained cyclists ingesting 900 mg of thiamin $\cdot$ day^{-1} for 3 days. Likewise, McNeill and Mooney (1983) reported improvements in swim time to exhaustion in mice parenterally administered 100 times the minimum daily requirement of thiamin immediately prior to exercise. Litoff et al. (1985) reported decreases in blood La^- and $\dot{V}O_2$ during steady-state cycling at 75% of $\dot{V}O_{2max}$ in trained runners ingesting 2 g $\cdot$ day^{-1} of pantothenic acid for 2 weeks. These findings are supported by the earlier work of Shock and Sebrell (1944a,b) which demonstrated increases in work output by frog muscle perfused with pantothenate.

Allithiamin, a derivative of thiamin, has been effective in the treatment of various thiamin deficiency diseases and it is hypothesized that with allithiamin administration a stimulating effect on PDH may be exerted and/or there will be a generic increases in tricarboxylic acid cycle function (Lonsdale 1991). In the likelihood that either, or both, of these hypotheses are true, this may prove beneficial to individuals undergoing intense physical exercise. Pantethine, a derivative of pantothenic acid, has been demonstrated to be absorbed more readily compared with traditional vitamin forms, as evidenced by plasma pantothenate levels 300 times greater than normal (Wittwer et al. 1985) and an increase in rat liver [CoA] of 20–30% (Branca et al. 1984). In addition, positive inotropic and negative chronotropic effects have been reported (Minami et al. 1983). It has been hypothesized that increased levels of CoA will stimulate the tricarboxylic acid cycle (Maggi et al. 1982) or free fatty acid metabolism (Kameda and Abiko 1980; Morisaki et al. 1983) and promote the mobilization of lipids. Pantethine appears to be rapidly absorbed and distributed throughout body tissues, resulting in significant body storage of pantothenate, and has a half life of ~28 h (Wittwer et al. 1985).

There are no studies reported in the literature that have investigated pantethine ingestion and exercise performance. The relatively few studies investigating allithiamin ingestion and exercise performance report conflicting results (Nishiyama et al. 1972; Doyle et al. 1997; Webster et al. 1997). Nishiyama et al .(1972) reported improvements in leg and grip strength after ingestion of 150 mg of allithiamin $\cdot$ day^{-1}. In contrast, Doyle et al. (1997) demonstrated no changes in isokinetic muscle performance or blood La^- accumulation with the ingestion of 1 g of allithiamin $\cdot$ day^{-1} for 5 days. This is in agreement with a recent study demonstrating no changes in submaximal $\dot{V}O_2$, $\dot{V}O_{2max}$, blood La^- accumulation, La^- threshold, or cycling performance time after the ingestion of 1 g of allithiamin $\cdot$ days^{-1} for 3–4 days (Webster et al. 1997).

Based on the findings of previous studies that have reported a possible ergogenic effect with thiamin or pantothenic acid (Knippel et al. 1986; Litoff et al. 1985; McNeill and Mooney 1983; Shock and Sebrell 1944a,b) and the enhanced absorptive properties of pantethine and allithiamin, the following research hypotheses were developed.

1. If the oral ingestion of the large does of pantethine were to be effective in the present study it would be evident in some, if not all, of the following: increased utilization of fatty acids consequently decreasing the reliance on glycogen, decreased oxygen uptake, HR and RPE during the 50-km steady-state cycling exercise
2. If the large dose of allithiamin were to be effective it would be noted via a decrease in La^- accumulation and an improvement in 2000-m cycling time.

In contrast with these hypotheses, we found thiamin and pantothenic acid derivatives to have no effect on any of the physiological, psychological or performance variables measured in this study.

While the reason for these discrepancies are not readily apparent, certain considerations need to be noted. The first consideration deals with the baseline vitamin status of the individuals. Being that baseline thiamin and pantothenate levels were not measured in the present study one might suggest that prior to one trial the subjects might have been vitamin deficient and that this was corrected with the supplementation. While this is possible it is thought to be unlikely as thiamin and pantothenate are widely distributed in the food groups and deficiencies are relatively rare (Keith 1990). In addition, there was no order effect observed for any of the measured variables.

The second consideration relates to the absorption of the supplements. Once again, because no measures of thiamin or pantothenate were made, this is purely speculative; however, all previous studies indicate an elevated absorption of both allithiamin and pantethine. One study reported whole-blood thiamin activity being elevated by more than 450% 3 h after the ingestion of just 50 mg, a value which is also higher than that obtained with intravenous administration of THCI (Baker and Frank 1976). There have been no absorption studies that have investigated dosages similar to that used in this present study. Oral administration of pantethine, in

dosages similar to that used in the present study, have raised plasma pantethine levels as much as 300 times baseline (Wittwer et al. 1985). Based on the available literature there is no reason to suggest that the supplement was not absorbed.

The third consideration is the possible effect of these compounds on one another. To the author's knowledge there is no reason to suspect an inhibitory action of one of these compounds on the other thereby negating their effect; however, in the large dosages administered, it is likely that these compounds exhibit not only a cofactor effect but also a pharmacological effect. The effect of individual or combined pharmacological doses of vitamins or their congeners has not been addressed in the literature and warrants further investigation.

To our knowledge this is the first reported study to investigate the physiological and performance effects of pharmacological dosages of thiamin and pantothenic acid derivatives during exercise. In contrast with several thiamin and/or pantothenic acid supplementation studies previously reported in the literature, we found the oral administration of these compounds to have no effect on any physiological or performance parameters during steady-state or high-intensity exercise.

Acknowledgements The author would like to express thanks to all the subjects that generously gave of their time and effort and to Matthew Branz for his assistance with data collection. Special appreciation also is expressed to Ecological Formulas/Cardiovascular Research for generously providing the allithiamin and pantethine supplements used in the study. This study was supported in part by a grant from the Illinois Heart Association/Jump Rope for Heart and the Illinois Association for Health, Physical Education, Recreation and Dance.

References

Angelico M, Pinto G, Ciaccheri C, et al. (1983) Improvement in serum lipid profile in hyperlipoproteinaemic patients after treatment with panthethine: a cross-over, double-blind trial versus placebo. Curr Ther Res 33:1091–1096

Baker H, Frank O (1976) Absorption, utilization and clinical effectiveness of allithiamines compared to water-soluble thiamines. J Nutr Sci Vitaminol [Suppl]22:63–68

Baker H, Thomson AD, Frank O, Leevy CM (1974) Absorption and passage of fat- and water-soluble thiamin derivatives into erythrocytes and cerebrospinal fluid in man. Am J Clin Nutr 27:676–680

Bentivegna A (1979) Diet, fitness and athletic performance. Phys Sports Med 7:99–105

Branca D, Scutari G, Siliprandi N (1984) Pantethine and pantothenate effect on the CoA content of rat liver. Int J Vit Nutr Res 54:211–216

Doyle MR, Webster MJ, Erdmann LD (1997) Allithiamine ingestion does not enhance isokinetic parameters of muscle performance. Int J Sport Nutr 7:39–47

Fenstermacher DK, Rose RC (1986) Absorption of pantothenic acid in rat and chick intestine. Am J Physiol 250:G155–G160

Fujiwara M, Sasakawa S, Itokawa Y, Ikeda K (1964a) Urinary excretion of thiamine propyl disulfide-S^{35} after administration. J Vitaminol 10:55–69

Fujiwara M, Sasakawa S, Itokawa Y, Ikeda K (1964b) Affinity of thiamine propyl disulfide-S^{35} to blood. J Vitaminol 10:70–78

Fujiwara M, Sasakawa S, Itokawa Y, Ikeda K (1964c) Affinity of thiamine propyl disulfide-S^{35} to organs. J Vitaminol 10:79–87

Gaddi A, Descovich GC, Noseda G, et al. (1984) Controlled evaluation of pantethine, a natural hypolipidemic compound, in patients with different forms of hyperlipoproteinemia. Atherosclerosis 50:73–83

Grandjean F, Hursh LM, Majure WC, Ahanley DF (1981) Nutrition knowledge and practices for college athletes. Med Sci Sports Exerc 13:82

Hayashi H, Kobayashi A, Terada H, et al. (1985) Effects of pantethine on action potential of canine papillary muscle during hypoxic perfusion. Jpn Heart J 26:289–296

Kameda K, Abiko Y (1980) Stimulation of fatty acid metabolism by pantethine. In: Cavallini D, Gaull GE, Zappia V (eds) Natural sulfer compounds. Plenum, New York, pp 443–452

Kawasaki C, Tomita I, Shinoda S (1964) Penetration of modified thiamine compounds into erythrocytes: I. comparison of thiamine propyl disulfide and thiothiamine. J Vitaminol 10:154–160

Keith RE (1990) Vitamins in sport and exercise. In: Hickson JF, Wolinsky I (eds) Nutrition in exercise and sports. CRC, Boca Raton, Fla., pp 233–253

Knippel M, Mauri L, Belluschi R, Bana G, Galli C, Pusterla GL, Spreafico M, Troina E (1986) Azione della tiamina sulla produzione di acido lattico nei ciclisti. Med Sport 39:11–16

Levy G, Hewitt RR (1971) Evidence in man for different specialized intestinal transport mechanisms for riboflavin and thiamin. Am J Clin Nutr 24:401–404

Litoff D, Scherzer H, Harrison J (1985) Effects of pantothenic acid supplementation on human exercise. Med Sci Sport Exerc [Suppl]17:287

Lonsdale D (1991) Allithiamine and its synthetic derivatives: a review. J Nutr Med 2:305–311

Maggi GC, Donati C, Criscuoli G (1982) Pantethine: a physiological lipomodulating agent in the treatment of hyperlipidemias. Curr Ther Res 32:380

McNeill AW, Mooney TJ (1983) Relationship among carbohydrate loading, elevated thiamine intake and the cardiovascular endurance of conditioned mice. J Sports Med 23:257–262

Miccoli R, Marchett P, Sampietro T, Tognarelli M, Navalesi T (1984) Effects of pantethine on lipids and apolipoproteins in hypercholesterolemic diabetics and nondiabetic patients. Curr Ther Res 36:545–549

Minami M, Yasuda H, Saito H (1983) Positive inotropic and negative chronotropic effect of pantethine on isolated cardiac muscle of guinea-pigs. Experientia 39:1028–1030

Morisaki N, Matsuoda N, Saito T, Jumagai A (1983) Effects of pantethine and its metabolites on fatty acid oxidation in rat liver mitochondria. Tohoku J Exp Med 141:33–39

Murai A, Miyahara T, Tanaka T, Sako Y, Mishimura N, Kameyama M (1983) The effects of pantethine on lipid and lipoprotein abnormalities in survivors of cerebral infarction. Artery 12:234–243

Nice C, Reeves AG, Brinck-Johnsen T, Noll W (1984) The effects of pantothenic acid on human exercise capacity. J Sports Med 24:26–29

Nishiyama I, Tanaka T, Tsumura D (1972) Effect of thaimine tetrahydrofurfuryl disulfide (TTFD) on physical fitness chiefly on muscle strength. Jpn J Phys Fit 21:6–15

Pollock ML, Wilmore JH, Fox SM (1990) Exercise in health and disease, evaluation and prescription for prevention and rehabilitation. Saunders College, Philadelphia

Shock NW, Sebrell WH (1944a) The effect of vitamins of the B complex on the work output of perfused frog muscles. Am J Physiol 142:265–273

Shock NW, Sebrell WH(1944b) The effect of changes in concentration of pantothenate on the work output of perfused frog muscles. Am J Physiol 142:274–278

Tahiliani AG, Beinlich CJ (1991) Pantothenic acid in health and disease. Vitam Horm 46:165–228

Takenouch K, Aso K (1963) Absorption and excretion of thiamine propyl disulfide-S^{35}:I. Mechanism of absorption of thiamine propyl disulfide J Vitaminol 9: 106–120

Takenouch K, Aso K (1964) Absorption and excretion of thiamine propyl disulfide-S^{35}:II. Absorption and excretion of thiamine propyl disulfide-S^{35}(inner). J Vitaminol 10:142–153

Thomson AD, Leevy CM (1972) Observations on the mechanism of thiamine hydrochloride absorption in man. Clin Sci 43:153–163

Ventura UG, Ferrari G, Tagliabue R, Rindi G (1969) A kinetical study of thiamine intestinal transport in vitro. Life Sci (Oxf) 8:699–705

Webster MJ, Scheett TP, Doyle MR, Branz M (1997) The effect of a thiamin derivative on exercise performance. Eur J Appl Physiol 75:520–524

Wittwer CT, Gahl WA, Butler JD, Zatz M, Thoene JG (1985) Metabolism of pantethine in cystinosis. J Clin Invest 76:1665–1672