

Phosphate Supplementation in Exercise and Sport

by

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I. INTRODUCTION

Over the past 20 years, a significant amount of research has been devoted to identifying medically safe nutritional ergogenic aids. One of the most promising nutritional ergogenic substances appears to be phosphorus.¹ Phosphorus is intimately involved in a numerous metabolic pathways. Consequently, researchers have been interested in the potential ergogenic value of phosphorus since the early 1920's. Most of this research has evaluated the role of phosphorus in energy metabolism as well as the effects of either sodium or calcium phosphate supplementation on exercise capacity. Sodium and/or calcium phosphate loading prior to exercise (4-10 g/d for 3- to 6-d) has been reported to affect exercise capacity in a number of ways (see Table 1). Although not all studies have reported ergogenic benefit (particularly with calcium phosphate), most studies indicate that sodium phosphate supplementation is an effective ergogenic aid during certain exercise conditions. The purpose of this chapter is to discuss the theoretical rationale of phosphate supplementation and to overview the literature relative to the effect of phosphate loading on human performance.

[Insert Table 1 about here.]

II. NUTRITIONAL ROLE OF PHOSPHORUS

A. Dietary Sources

Phosphorus is a nonmetallic element found in a variety of foods. Animal meats, dairy products, and eggs provide approximately 60% of the daily intake of phosphorus in industrialized societies because they contain high levels of phospholipids such as phosphatidylcholine (lecithin) which are excellent sources of phosphorus. Grains also contain substantial amounts of phosphorus, but are not considered as good a source as animal products since part of the phosphorus exists as inositol hexaphosphate (phytate) which is not as highly absorbable. Phosphates are commonly added to food in processing. For example, lecithin is a major emulsifying agent and carbonated drinks also contain phosphoric acid. Consequently, phosphorus obtained from food additives typically constitute about 30% of the daily dietary intake.²

The Joint Nutrition Monitoring Evaluation Committee has reported that phosphorus intake in the United States is generally adequate and requires less monitoring than other nutrients.³ The Recommended Dietary Allowance for adults in the United States is 800 mg/d, while the mean daily intake of phosphorus is 1536 and 966 mg/d in males and females, respectively.^{4,5} Generally, about 60 to 70% of dietary phosphorus is absorbed. However, absorption of phosphorus may increase to 90% when blood serum levels are low. Phosphorus toxicity is rare but may occur in individuals ingesting more than 12 g/d of phosphorus.

B. Regulation of Phosphorus

Since phosphorus acts as a threshold substance, serum levels of phosphorus are regulated in part by an overflow mechanism.^{2,6} The normal serum concentration of phosphorus ranges between 0.75 to 1.35 mmol/L with a mean of 1.1 mmol/L. When serum levels are low, additional phosphorus is absorbed from the intestines and/or the proximal tubules of the nephron.^{2,6} When serum levels of phosphorus are high, extra phosphorus is typically excreted by the kidney.⁶ Normal urinary excretion of phosphorus is approximately 175 to 300 mmol/d.^{2,6} Hormonal regulation also affects serum phosphorus levels. For example, the interaction of parathyroid hormone and 1,25-Dihydroxyvitamin D₃, which is intimately involved in maintaining calcium levels, influence serum phosphate levels. Moreover, cortisol and estrogen are also involved in phosphorus regulation.^{2,6}

Approximately 50% of serum phosphorus exists as free phosphate while the remaining phosphorus is bound with sodium, calcium, magnesium and protein. Serum phosphorus levels normally fluctuate by 0.3 to 0.6 mmol/L. The fluctuation generally reflects shifts between intracellular and extracellular concentrations. Since phosphorus is found in a wide variety of foods and serum phosphorus levels are

generally well regulated, hypophosphatemia is rare. However, hypophosphatemia may be observed in alcoholism and with excessive consumption of non-absorbable antacids.² Hypophosphatemia may lead to serious medical consequences, such as hemolytic anemia, congestive heart failure, myopathy, kidney malfunction, respiratory distress, and central nervous system abnormalities.² In the absence of chronic renal disease, hyperphosphatemia is rare^{2,4-6} and exhibits no specific signs or symptoms.^{2,6}

III. THEORETICAL ERGOGENIC VALUE OF PHOSPHATE SUPPLEMENTATION

The average adult contains approximately 11-14 g of phosphorus per kg fat-free body weight. About 85% is stored in the skeletal system, mostly as inorganic orthophosphate complexed with calcium into a crystalline salt, hydroxyapatite. The remaining amount of phosphorus is contained in soft tissues, mainly as organic compounds in conjunction with proteins and amines as well as inorganic phosphate. Although maintenance of bone integrity is important in certain athletic populations susceptible to premature bone mass loss, the theoretical ergogenic value of phosphate supplementation primarily resides in the metabolic role of phosphorus in soft tissues. In this regard, it has been theorized that altering extracellular and intracellular availability of organic phosphorus compounds and/or inorganic phosphate may enhance exercise metabolism leading to improved performance.¹

In support of this contention, serum phosphate levels have been reported to increase in response to intense anaerobic and aerobic exercise.⁷⁻¹⁰ The increase in serum phosphate is related in part to phosphate efflux from the intracellular stores in the muscle to the blood.^{2,10} Furthermore, endurance athletes have been reported to have elevated resting serum phosphate levels or to be hyperphosphatemic (i.e., >1.35 mmol/L).^{8,10-13} The cause of the elevated serum phosphate levels in trained endurance athletes has not been determined. However, Dale and associates¹⁰ have suggested that it may represent a metabolic training effect and/or an inborn metabolic advantage. The following discussion examines the major hypotheses for which phosphate loading has been suggested to affect exercise performance.

A. Enhanced Metabolic Regulation

Phosphate is the major anion of the intracellular fluids⁶ and the proportion of intracellular phosphate available for energy metabolism depends upon the extracellular concentration.¹⁴ Phospholipids, which are the major component of cell membranes,¹⁵ may also serve as donors of phosphate radicals when they are needed for different chemical reactions in the tissues.^{1,5} Phosphate binds reversibly with a number of coenzyme systems and other compounds involved in metabolism.⁵ For example, protein phosphorylation (phosphoprotein) is believed to be a precursor to cellular changes induced by some extracellular signals, particularly as an allosteric regulator of many enzymes.^{3,15} Several vitamins involved in the metabolic regulation of intracellular carbohydrate metabolism are also phosphate dependent, particularly thiamine pyrophosphate (vitamin B₁) during glycolysis and pyridoxal phosphate, a derivative of pyridoxine (vitamin B₆), during glycogenolysis. Additionally, several of the second messengers in the cell are phosphate dependent, such as cyclic adenosine monophosphate (cAMP) and inositol-1,4,5 triphosphate (IP₃), both of which can initiate a cascade of metabolic events in the cell by modifying intracellular calcium metabolism.^{15,16}

Intracellular phosphate is also involved in the regulation of energy metabolism in a variety of ways.^{5,17-19} For example, phosphate is an important component of phosphocreatine (PCr) which is intimately involved in the phosphagen energy system employed during intense exercise as well as oxidative phosphorylation employed during aerobic exercise.¹⁸ Moreover, glucose is phosphorylated upon entry into the muscle cell, while pyridoxal phosphate is needed for glycogenolysis. Enhanced glycogenolysis, glycolysis and oxidative phosphorylation may increase the rate of ATP production and possibly improve cellular metabolism during exercise. There is evidence that phosphate supplementation may stimulate the activity of a variety of enzymes in the erythrocyte, such as phosphofructokinase (PFK) and glyceraldehyde 3-phosphate (G-3-P), involved in glycogen metabolism²⁰⁻²² as well as may increase

hemoglobin levels.⁸ Collectively, increasing the availability of extracellular and intracellular phosphate through phosphate supplementation could theoretically provide an ergogenic effect during intense and endurance exercise by enhancing energy metabolism and/or efficiency.

B. Enhanced ATP and PCr Synthesis

Phosphate is integrally involved in the formation of purines and pyrimidines and thereby DNA and RNA synthesis.¹⁶ In this regard, phosphate contributes to the development of adenine, a component of adenosine as well as provides high energy bonds in adenosine triphosphate (ATP) and PCr. The phosphorylation potential, given as the ratio of [ATP] to [ADP + P_i], is an index for the energy status of the cell and is dependent upon the concentration of P_i. The phosphorylation potential is directly related to the free energy available from ATP.¹⁶ Theoretically, phosphate supplementation may increase the cellular concentrations of ATP and/or PCr as well as provide additional inorganic phosphate for replenishment of ATP and PCr during exercise. Since ATP and PCr are depleted rapidly during high intensity sprint exercise,²³⁻²⁵ rapid restoration of ATP and PCr during and following intense exercise may enhance performance capacity. Additionally, increased availability of phosphate in the electron transport system may promote oxidative phosphorylation.¹⁸ Collectively, phosphate loading may theoretically provide ergogenic benefit during anaerobic and aerobic exercise.

C. Enhanced 2,3-Diphosphoglycerate Synthesis

2,3-diphosphoglycerate (2,3-DPG) is a highly anionic organic phosphate which binds to hemoglobin in the erythrocyte. 2,3-DPG serves to lower the oxygen affinity of oxygen by a factor of 26 thereby facilitating the release of oxygen to the tissues.¹⁶ Several studies have shown increased 2,3-DPG levels in the adaptation to hypoxia at altitude.^{19,26} One of most espoused hypotheses regarding the ergogenic value of phosphate loading suggests that phosphate supplementation may increase erythrocyte 2,3-DPG content thereby facilitating oxygen delivery to the muscle during exercise.²⁷⁻³¹ Although most studies have reported increased 2,3-DPG levels following phosphate supplementation,²⁷⁻³¹ others have reported no effects on 2,3-DPG levels.^{7,8}

D. Enhanced Cardiovascular Responses to Exercise

Phosphate supplementation has also been suggested to affect myocardial function at rest and during exercise. In this regard, hypophosphatemia is associated with depressed myocardial contractility and cardiac output.³⁴ Reversal of hypophosphatemic states has been reported to markedly improved myocardial responses in the canine.^{35,36} In addition, there are several reports indicating that sodium or calcium phosphate supplementation enhances peripheral extraction of oxygen,²⁸ reduces submaximal cardiac output^{29,37-38} and/or stroke volume,⁷ and increases myocardial contractility and ejection fraction³⁹ during intense endurance exercise. Improving cardiovascular efficiency and/or performance would theoretically provide ergogenic benefit to athletes engaged in endurance exercise performance.

E. Enhanced Buffering Capacity

Phosphate loading has also been suggested to enhance acid-base balance during intense exercise. In this regard, phosphate is an active participant in many physiological buffer systems⁶ and is involved in acid-base balance within the plasma and in the cells.² For example, sodium phosphate (Na₂HPO₄) acts as a weak base while sodium dihydrogen phosphate (NaH₂PO₄) is a weak acid. Phosphates may also be combined with other cations, such as potassium. The power of the phosphate buffer system is rather weak in the extracellular fluids. However, the phosphate buffer is very important in the intracellular fluids since its concentration is much greater.^{6,16} This is particularly true with respect to the kidneys. During exercise, the decreased pH usually associated with the production of lactic acid may be mitigated

to some degree by the phosphate buffer system. Since the decline in the force of maximal voluntary muscular contractions has been associated with increases in H_2PO_4^- ,⁴⁰ increases in basic HPO_4^- through phosphate loading could provide ergogenic value in a similar manner as reported with sodium bicarbonate supplementation.⁴¹ Theoretically, a phosphate stimulated enhancement in buffering capacity may improve exercise capacity during high intensity sprint performance or in events in which the athlete competes near the anaerobic threshold. In support of this concept, reports have indicated that phosphate loading decreases lactate levels during submaximal exercise²⁷ as well as increases anaerobic threshold during incremental maximal exercise.^{8,39,42}

F. Enhanced Psychological Responses to Exercise

Phosphate loading has also been suggested to modify psychological processes. Phospholipids like sphingomyelin are important structural components of the brain and nervous tissues. The intracellular functions of phosphates previously noted could influence central nervous system thereby affecting psychological responses to exercise. In support of this hypothesis, Jain and others³³ reported that learning efficiency was significantly better in subjects who were supplemented with phosphate compared to a placebo group. Consequently, phosphate loading may alter psychological responses to exercise potentially allowing the athlete to exercise at higher exercise intensities although perceiving similar psychological stress.

IV. ANALYSIS OF THE ERGOGENIC VALUE OF PHOSPHATE SUPPLEMENTATION

A. Early Research Findings

Studies investigating the ergogenic value of phosphate supplementation date back to the 1920's. Early studies suggested that phosphate salt supplementation could be used to increase physical working capacity and prevent fatigue.^{44,45} Some initial research was also conducted on lecithin or phosphatidyl choline. Lecithin (phosphatidyl choline) has been theorized to possess ergogenic qualities due to either its phosphate or choline content, the latter being involved in the formation of the neurotransmitter acetylcholine.^{41,43} Atzler and Lehmann⁴⁶ reported improvements in both static and dynamic power as well as endurance exercise capacity following lecithin ingestion. In addition, Dennig⁴⁷ reported favorable effects of soya lecithin upon exercise performance. In analysis of this literature, Boje⁴⁸ discredited much of the research on lecithin but noted that many of the studies suggested an ergogenic effect of phosphates concluding that phosphate supplementation could probably increase human work output.

A few additional studies conducted in the 1950s did not support an ergogenic effect of phosphates or lecithin. In a field study, Johnson and Black⁴⁹ reported that champion high school cross-country runners administered one gram of sodium phosphate 2.5 h prior to competing in a 1.5 mi race did not affect run performance times. In addition, Staton⁵⁰ reported that 14-d of soya lecithin supplementation did not significantly affect grip strength. On the other hand, Keller and Kraut⁵¹ reported that athletic performance in a diverse number of events (ranging from a 1,500 meter run to swimming distances of 100 meters to 1,500 meters) were enhanced by the ingestion of sodium phosphate an hour prior to competition. Consequently, early research findings suggested that the ergogenic effects of phosphate supplementation were equivocal.

B. Contemporary Research Findings

1. Basic Research

Much of the contemporary research on phosphates has emanated from medical investigations attempting to identify the regulatory role of phosphate in erythrocytic and cellular metabolism. Anaerobic glycolysis

is the primary metabolic pathway for synthesis of ATP in the mature erythrocyte.^{6,52} Therefore, the rate of glycolysis in the erythrocyte cytoplasm and subsequent synthesis of ATP is essential in order to maintain normal red cell metabolism. Numerous studies in the late 1960s and early 1970s reported that intracellular phosphate is an important regulator of glycolysis in the mature erythrocyte.^{19,21,22,52-60} The increased glycolytic activity has been demonstrated to be due to the influence of phosphate on the regulatory enzymes PFK^{19,62} and G-3-P.^{62,63} Additionally, inorganic phosphate is a required substrate and/or important cofactor in numerous metabolic pathways including: glycolysis; ammoniogenesis; glycogenolysis; deamination of adenine nucleotides; and, the hexosemono-phosphate shunt.^{64,65} Consequently, increasing the availability of extracellular and intracellular phosphate may affect metabolism in a variety of ways.

For example, Brazy and colleagues^{66,67} reported that varying concentrations of intracellular phosphate in the isolated tubules of rabbit renal cortex significantly influenced oxidative capacity. Moreover, addition of succinate, citrate, and malate in the phosphate-free medium preserved the rate of mitochondrial respiration while the addition of these substrates to phosphate treated medium accelerated mitochondrial respiration. The authors suggested that a decline in extracellular phosphate reduces the availability of specific metabolic substrates to the mitochondria, thereby, limiting mitochondrial oxidative capacity. However, increasing extracellular phosphate enhances mitochondrial oxidative capacity. More recent nuclear magnetic resonance (NMR) studies indicate that cellular inorganic phosphate content in canine proximal tubules is regulated by sodium dependent and independent transport mechanisms.⁶⁸ In addition, ATP content was found to be directly proportional to the cellular inorganic phosphate content over a physiological range.⁶⁸

Collectively, basic research studies suggest that intracellular concentrations of inorganic phosphate are affected by extracellular phosphate concentrations and sodium dependent phosphate transport mechanisms. Extracellular and intracellular phosphate concentrations are integrally involved in intracellular metabolism through an influence on glycolytic and tricarboxylic acid intermediates. Furthermore, the metabolic pathways for intracellular metabolism depend on and/or compete for inorganic phosphate regulating the rate of cellular metabolism. While the specific effects of variations of extracellular and intracellular phosphate concentrations on oxidative metabolism in skeletal muscle remain unclear, basic research findings support the hypothesis that alterations in extracellular and intracellular availability of phosphorus may affect oxidative metabolism and thereby exercise performance.

2. Exercise Related Studies

A number of contemporary studies have investigated the effects of sodium and/or calcium phosphate supplementation on exercise capacity. The following discussion examines the primary studies which have evaluated the effects of sodium and/or calcium phosphate supplementation on exercise performance. This discussion is followed by an overall analysis of the literature in an attempt to draw some conclusions regarding the ergogenic value of phosphate supplementation.

a. Studies Reporting an Ergogenic Benefit

Much of the contemporary interest in phosphate supplementation as a potential ergogenic aid emanated from a report by Cade and associates in the early 1980s.²⁷ In this study, ten trained male subjects (VO_2 max 56.2 ml/kg/min) were familiarized with the experimental protocol and performed a preliminary control testing session consisting of submaximal and incremental maximal exercise tests. The control session was followed two weeks later with a series of three randomly assigned supplementation trials (4 g/d of sodium phosphate or a placebo for 3-d) performed one week apart. The supplementation trials were then followed 2 to 3 weeks later by performing a final control session. Results revealed that phosphate loading significantly increased resting serum phosphate (1.17 to 1.22 mmol/L) and red cell 2,3-DPG levels (13.00 to 13.92 mg/g Hgb). In addition, phosphate loading decreased submaximal lactate while increasing maximal oxygen uptake from 6 to 12% depending on the order of administration of

supplementation trials. The greatest increase in maximal oxygen uptake occurred in subjects ingesting sodium phosphate for two consecutive testing trails. These findings provided the first evidence from a well-controlled contemporary study that sodium phosphate supplementation may enhance exercise capacity in well-trained athletes.

Farber and coworkers²⁹ investigated the effects of acute and chronic phosphate loading on oxygen affinity of hemoglobin, red cell 2,3-DPG, P_{50} responses, and cardiovascular responses to exercise in six normal subjects. Subjects were administered either 20 mg/kg/d of dibasic sodium phosphate orally followed by infusion of 1.5 L of 10% fructose with 0.28 mmol/kg/h of phosphate over a 3 h period or the fructose-phosphate infusion without prior dibasic sodium phosphate ingestion. Cardiopulmonary measures were obtained prior to and following performing an incremental cycle ergometry test. Results revealed that the sum of 2,3-DPG and arterial ATP and P_{50} responses were significantly higher after both infusion periods regardless of whether phosphate was ingested prior to the infusion. In addition, while oxygen uptake responses were similar at each workload among test trials, cardiac index was significantly lower as P_{50} levels were increased with phosphate. The authors suggested that phosphate loading stimulated 2,3-DPG synthesis facilitating a shift in the oxyhemoglobin curve as evident by the changes in ATP and 2,3-DPG as well as P_{50} responses.

In a follow-up study, Farber and coworkers²⁸ investigated the effects of phosphate infused hyperphosphatemia on exercise compliance in hypoxemic chronic obstructive pulmonary disease patients (COPD). In this study, nine COPD patients performed a 3-min cycling exercise bout at approximately 60% of the subjects maximal functional capacity while administered 2 to 3 L/min of supplemental oxygen. The subjects were then infused 1.5 L of a 10% fructose and sodium phosphate (2.28 mmol/kg/h) solution over a 3-h period. This protocol was replicated after 24- and 48-h later. Results revealed that although cycling workloads were identical between trials, significant increases in exercise arteriovenous oxygen difference and oxygen extraction expressed as a percent of arterial oxygen flow were found following phosphate infusion. These data suggest that phosphate infusion enhances arteriovenous oxygen difference and peripheral extraction of oxygen in COPD patients. Interestingly, this response could not be attributed to changes in hemoglobin-oxygen affinity as had been previously reported²⁹ since P_{50} data were unchanged following phosphate infusion. The researchers concluded that phosphate administration may be beneficial in hypoxemic states where adequate tissue oxygenation cannot be achieved.

Kreider and associates⁸ investigated the effects of sodium phosphate supplementation on maximal oxygen uptake, ventilatory anaerobic threshold, and 5 mile run performance in elite male runners. In this study, seven elite runners (VO_{2max} 73.9 \pm 6.3 ml/kg/min) participated in a placebo, double blind, crossover experiment. Subjects were randomly assigned to ingest either 4 g/d of sodium phosphate or a glucose placebo for 6-d. On the third day of supplementation, the subjects performed either an incremental maximal exercise test or 5 mile treadmill performance run for time. On the sixth day of supplementation, the subjects then performed the remaining maximal test or performance run. Subjects observed a 14-d washout period and repeated the experiment after ingesting the alternate supplement.

Results demonstrated that resting serum phosphate values in the placebo maximal and performance trials were mildly hyperphosphatemic (1.41 \pm 0.2 & 1.27 \pm 0.3 mmol/L, respectively). Nevertheless, sodium phosphate supplementation significantly increased resting and post-exercise serum phosphate levels by 7 to 12%, respectively. In addition, sodium phosphate supplementation resulted in a 9% increase in maximal oxygen uptake (73.9 \pm 5 to 80.3 \pm 4 ml/kg/min) and an 12% increase in ventilatory anaerobic threshold (58.0 \pm 4 to 64.8 \pm 2 ml/kg/min). During the 5 mile performance run, phosphate loading resulted in an 11.8 sec non-significant ($p=0.14$) decrease in performance time (26.8 \pm 1 to 26.6 \pm 1 min) and a non-significant ($p=0.07$) 2.52-s decrease in average mile split time (5.361 \pm 0.3 to 5.326 \pm 0.2 min). However, mean oxygen uptake during the run was significantly lower in the phosphate supplemented trial suggesting an enhanced physiological efficiency during the performance run which would theoretically be of ergogenic value.

In a similar study, Stewart and colleagues⁶⁹ investigated the effects of sodium phosphate ingestion on maximal oxygen uptake, time to exhaustion, serum 2,3-DPG, and serum phosphate in eight trained male cyclists. The subjects performed one control maximal cycle ergometry test. In a double blind, randomized manner, and crossover manner, subjects were administered a placebo or 3.6 g/d of sodium phosphate for 3-d prior to performing a second maximal exercise test. Subjects then observed a 7-d

washout period and began supplementation with the alternate supplement prior to performing a final maximal exercise test. Results revealed no significant alterations in resting serum phosphate or 2,3-DPG levels. However, post-exercise 2,3-DPG levels were significantly higher in the phosphate trial. Furthermore, maximal oxygen uptake was significantly increased by 11% (control 48.5±9, placebo 47.8±9, phosphate 53.4±6 ml/kg/min) and time to exhaustion was increased by 20% (control 9.9±3, placebo 10.6±3, phosphate 12.3±3 min). In addition, although the subjects performed significantly more work in the phosphate trial, post-maximal exercise lactate values were slightly lower than control and placebo responses (control 12.5±2, placebo 13.0±3, phosphate 12.2±2 mmol⁻¹). These findings indicate that sodium phosphate supplementation may enhance exercise capacity by increasing maximal oxygen uptake possibly by facilitating an increase in 2,3 DPG and/or providing a greater buffering capacity.

Kreider and coworkers³⁹ conducted the most extensive study to date to evaluate the ergogenic value of phosphate loading. In this study, six highly trained male cyclists (VO_2max 69.3±12 ml·kg⁻¹·min⁻¹) participated in a placebo, double blind, crossover study to determine the effects of sodium phosphate loading on metabolic and myocardial adaptations to maximal exercise and 40-km time trial performance. Subjects ingested either 4 g/d of tribasic sodium phosphate or a glucose placebo for 5-d. On the 4th day, subjects performed either an incremental maximal cycling test or a 40-km simulated time trial performed under controlled laboratory conditions using the subjects' racing bicycle attached to a computerized race simulator. Subjects performed the remaining performance test on the subsequent day of the investigation. Subjects observed a 14-d washout period and repeated the testing protocol with the alternate supplement regimen.

Analysis of maximal test results revealed that phosphate loading significantly increased pre-max serum phosphate levels (17%), maximal oxygen uptake (9%), minute ventilation (8%), ventilatory anaerobic threshold (10%), glucose (23%), free fatty acids (23%), echocardiographically-determined mean ejection fraction (4%), and myocardial fractional shortening (8%). During the 40-km time trial, phosphate loading significantly increased mean power output (17%), oxygen uptake (18%), ventilation (15%), heart rate (8%), ejection fraction (13%) and fractional shortening (24%) resulting in an 8% reduction in performance time. Although the etiology of improved myocardial responses to exercise remain to be determined, these findings provide strong evidence that sodium phosphate supplementation provides ergogenic value to highly-trained athletes.

b. Studies Reporting No Ergogenic Benefit

Not all studies evaluating the effects of phosphate loading have reported ergogenic value. For example, Duffy and Conlee⁷⁰ evaluated the effects of acute and chronic ingestion of a commercially available supplement containing sodium and potassium phosphate on leg power and high intensity run performance. In this study, 11 untrained males participated in a placebo, double blind, crossover experiment. Subjects ingested three phosphate containing capsules (each containing 387 mg of sodium phosphate, 27.5 mg tribasic potassium phosphate, and 30 mg vitamin C) or a placebo 60 min prior to performance assessment during the acute phase of ingestion. One week later, subjects began ingesting 9 phosphate containing capsules (3.7 g/d of sodium or potassium phosphate) or a placebo for 6-d. A 1-d washout period was observed and the subjects repeated the 6-d supplementation regimen with the alternate supplement. Results revealed no significant differences in endurance run time to exhaustion following acute or chronic ingestion of the phosphate capsules. Further, no significant differences were observed following acute or chronic phosphate supplementation in 1-min of leg extension power. Consequently, the authors concluded that phosphate supplementation possessed no ergogenic value in high intensity exercise events lasting 1 to 3-min in duration.

In another paper, Bredle and coworkers⁷ investigated the effects of calcium phosphate supplementation on maximal exercise tolerance and endurance capacity in 11 moderately-trained males. In this study, subjects performed a preliminary control maximal treadmill test. Subjects were then randomly and blindly administered capsules containing 5.7 g/d of inorganic phosphate, 7.3 g/d of calcium, and 73 mg/d of vitamin C or a similar placebo containing 5.7 g/d of carbonate in place of the phosphate. Subjects ingested the supplements for 4-d. On the third day of supplementation, subjects

performed a maximal treadmill test. On the fourth day of supplementation, subjects performed an endurance run to exhaustion at a 70% of VO_2max . Results revealed that calcium phosphate ingestion significantly increased serum phosphate levels on the 4th day of loading by 35% while not affecting 2,3-DPG, P_{50} , pH, and plasma bicarbonate levels. Additionally, no significant differences were observed in maximal oxygen uptake or run time to exhaustion. However, there was some evidence ($p < 0.07$) that cardiac output was lower (6%) while stroke volume was significantly higher (5%) at the 10-min mark into the exercise bout following phosphate loading. These findings indicate that calcium phosphate supplementation may increase serum phosphorus levels and influence cardiovascular function during endurance exercise. However, calcium phosphate supplementation does not enhance maximal exercise or endurance exercise performance.

Mannix and associates⁷¹ investigated the effects of a single dose of calcium phosphate on a submaximal exercise performance in 10 untrained males. Subjects performed a preliminary maximal cycle ergometry test. The subjects were then blindly and randomly administered either a single dose of dicalcium phosphate (129 mmol of phosphorus, 5.0 g of calcium, and 50 g of vitamin C) or a flour placebo. In addition, 500 ml of fluid containing 10% glucose was consumed 1-h after ingestion of the dicalcium phosphate supplement and 500 ml of an artificially sweetened fluid was consumed 1-h after ingestion of the placebo. Subjects then rested for 2-h prior to performing a 30-min submaximal exercise bout at 61% of VO_2max . Following the exercise bout, the subjects rested for 15-min and then performed a 10 min exercise bout at 57% of VO_2max followed by a 10-min passive recovery. Subjects observed a 7-d washout period and repeated the testing procedures with the alternate supplement regimen.

Results revealed that the single dose of dicalcium phosphate and glucose significantly increased ($p < 0.05$) pre-exercise serum phosphate levels (13%), 2,3-DPG levels (11%), red cell ATP levels (5%), and P_{50} responses (4%). Serum phosphate, 2,3-DPG levels, and red cell ATP levels remained significantly elevated throughout the exercise session in response to phosphate loading. In addition, plasma pH levels were significantly lower in the phosphate-glucose trial following exercise. However, no significant differences were observed between placebo and phosphate trials in oxygen uptake, cardiac output, stroke volume, heart rate, arteriovenous oxygen difference or in oxygen deficit parameters. Consequently, the researchers concluded that although the dicalcium phosphate-glucose supplement promoted physiologically beneficial alterations, these adaptations did not induce an ergogenic enhancement in cardiovascular responses to exercise.

Kraemer and colleagues⁷² investigated the effects of ingesting a commercially available supplement containing sodium phosphate, potassium bicarbonate, and carnosine on repetitive sprint performance and 2,3 DPG concentrations. In this study, 10 trained and 10 untrained cyclists were administered either a placebo or the multibuffer supplement (4 g/d of sodium phosphate, 0.8 g/d of potassium bicarbonate, 50 mg/d of L-carnosine) for 3.5-d. Subjects then performed four 30-s cycle ergometer maximal effort sprints separated by a 2-min rest recovery. Subjects then observed a 14-d washout period and repeated the experiment following 3.5-d of ingesting the remaining supplement. Results revealed that multibuffer supplementation increased post-exercise 2,3-DPG levels and the ratio of 2,3-DPG/Hb in the trained cyclists. Further, acute recovery of peak power was enhanced in these subjects following phosphate loading. However, no significant differences were observed in acid-base status or repetitive sprint power output. These findings suggest that although this supplement promoted significant increases in 2-3

Finally, Trembley and associates⁷³ investigated the effects of acute calcium phosphate supplementation on submaximal and maximal exercise capacity in untrained and trained subjects. Subjects were divided into trained and untrained groups and participated in a double blind, randomized, and crossover experiment. Subjects ingested either a placebo or 22 g/d of dibasic calcium phosphate 90-min prior to performing a 20-min submaximal cycle ergometry exercise bout at 70% of peak oxygen uptake. Subjects then observed a 30-min rest followed by performing an incremental maximal exercise test to exhaustion. Subjects observed a 7-d washout period and repeated the experiment ingesting the remaining supplement 90-min prior to exercise. Results revealed no significant differences among groups in 2,3-DPG, oxygen uptake, or plasma lactate. The researchers concluded that acute ingestion of calcium phosphate 90-min prior to submaximal and maximal exercise does not provide ergogenic benefit.

C. Analysis of the Ergogenic Value of Phosphate Supplementation

Although a cursory analysis of studies investigating the ergogenic value of phosphate supplementation would suggest equivocal results, critical analysis of these studies indicates that phosphate supplementation may be more or less ergogenic depending on several factors. First, the type and dosage of phosphate appears to impact on the ergogenic value of phosphate supplementation. In this regard, most studies which have reported enhanced physiological adaptations and/or improved exercise capacity following phosphate supplementation have used 3 to 4 g/d of sodium phosphate for 3 to 6-d.^{8,26,28,30,36,39,42,69,72} Studies which have used calcium phosphate^{7,70,71,73} and/or single-dose acute supplementation protocols^{70,71,73} have generally found no ergogenic value and/or limited physiological effects of phosphate loading.

Second, several of the studies which reported no ergogenic benefit employed crossover experimental trials with less than a 14-d washout period.^{70,71,73} Cade and colleagues²⁷ indicated that a minimum of a 14-d washout period was necessary between repeated trials in order to negate any residual effects of phosphate supplementation. Consequently, it is possible that results in studies which employed brief washout periods (i.e., 1- to 7-d) may have been masked by a residual influence of phosphate supplementation.

Third, it appears that sodium phosphate supplementation (3 to 4 g/d for 3 to 4-d) may be more or less ergogenic depending on the type of exercise task evaluated. In this regard, most studies suggest that sodium phosphate supplementation may enhance aerobic capacity^{8,26,39,75} and/or anaerobic threshold.^{8,39} In addition, several studies indicate that phosphate supplementation may enhance cardiovascular responses to exercise.^{8,26,28,30,36,39,42,69,72} However, sodium and/or calcium phosphate supplementation appears to have little ergogenic value during isokinetic and/or high-intensity intermittent exercise.^{70,72} These findings suggest that the potential ergogenic value of sodium phosphate supplementation may be for endurance rather than non-endurance exercise. Finally, although a number of studies have been conducted to evaluate the effects of phosphate supplementation on exercise capacity, the experimental methods and procedures employ vary. Consequently, it is possible that differences in the experimental methods and procedures may account for some of the differences observed.

In analysis of the literature, it is clear that there is a significant body of basic research supporting the potential ergogenic value of phosphate supplementation. Although additional applied research is necessary particularly with athletes, most studies investigating the effects of sodium phosphate supplementation (3 - 4 g/d for 3 to 4-d) on maximal aerobic capacity and/or endurance exercise performance have reported ergogenic benefit.^{8,26,28,30,36,39,42,69,72} The improved exercise capacity has been attributed to enhanced metabolic efficiency, improved myocardial responses to exercise, a phosphate stimulated increase in 2,3-DPG levels, and/or enhanced peripheral extraction of oxygen.^{8,26,28,30,36,39,42,69,72} On the other hand, it appears that acute and/or chronic calcium phosphate supplementation provides little ergogenic value.^{7,70,71,73}

V. SUMMARY

Analysis of well-controlled contemporary research tends to support the hypothesis that short-term supplementation of phosphate (particularly sodium phosphate) may alter various physiological parameters which may affect endurance exercise performance. In this regard, in a variety of conditions and subject populations, phosphate loading has been reported to 1.) elevate extracellular and intracellular phosphate concentrations^{7,8,27-29,31,37-39,69,71,72} promoting a phosphate-stimulated glycolysis;^{14,65-68} 2.) attenuate anaerobic threshold;^{8,27,39,42,69} 3.) increase the availability of phosphate for oxidative phosphorylation and creatine phosphate synthesis;^{18,68} 4.) promote 2,3-DPG synthesis;^{7,27-31,69,71,72} 5.) affect myocardial and cardiovascular responses to exercise;^{7,28-30,37,39} 6.) increase peripheral extraction of oxygen;^{7,28} 7.) increase maximal oxygen uptake;^{8,27,39,69} and, 8.) improve endurance exercise performance and/or efficiency.^{8,37,39}

Although these findings are promising, it should be noted that not all studies report ergogenic benefit of phosphate loading possibly due to differences in the type and amount of phosphate ingested, the

experimental design and procedures employed, and the type of exercise evaluated. Moreover, the specific mechanisms of action remain to be fully understood. Additional research is necessary to evaluate the effects of phosphate loading in various asymptomatic and symptomatic populations under varying exercise conditions. In addition, research should investigate the ergogenic value of phosphate loading for athletes engaged in a variety of athletic events.

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Table 1. Proposed Theoretical Ergogenic Value of Phosphate Supplementation

- Elevates extracellular and intracellular phosphate concentrations.
- Stimulates glycolysis and energy metabolism.
- Increases the availability of phosphate for oxidative phosphorylation and creatine phosphate synthesis.
- Increases 2,3-DPGsynthesis and peripheral extraction of oxygen.
- Enhances myocardial and cardiovascular responses to exercise.
- Serves as a metabolic buffer.
- Increases anaerobic threshold and maximal oxygen uptake.
- Improves endurance exercise performance and/or efficiency.
- May enhance psychological responses to exercise.