THE EFFICACY OF SODIUM PHOSPHATE D6 IN DELAYING THE ONSET OF MUSCLE FATIGUE DURING SHORT DURATION, HIGH INTENSITY EXERCISE

A research report submitted to the Faculty of Health Sciences, Technikon Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Technology.

by

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Johannesburg, 2000

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DECLARATION

I declare that this research report is my own, unaided work. It is being submitted for the Degree of Master of Technology at the Technikon Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination in any other Technikon or University.

(Signature of Candidate)

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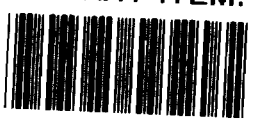

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ABSTRACT

This study aimed to determine the effect of sodium phosphate D6 ingestion in delaying the onset of muscle fatigue during short duration, high intensity exercise. Forty men were separated into a control and experimental group of twenty participants respectively. They were evaluated prior to, during and in recovery from short duration, high intensity exercise. The exercise commenced after each participant ingested one tablet of either a placebo or sodium phosphate D6 every fifteen minutes, commencing 45 minutes after the first lactate reading was determined. Hence, each participant received a maximum of four tablets.

The exercise test consisted of a 30 second cycle on a Monarch exercise bicycle. The resistance was set at 10% of the individual's body weight. Arterial blood was analysed before and after exercise to determine the lactate concentration. Sodium phosphate D6 produced a significantly more alkaline condition in the experimental group compared to the control group.

Therefore, it can be deduced that sodium phosphate D6 has a reduction effect on lactic acid accumulation and thus can be indicated for delaying muscle fatigue onset.

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DEDICATION

To my family and especially to my wife who made everything possible and bearable. Thank you for your support.

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TABLE OF CONTENTS

UNIVERSITY OF JOHANNESBURG

UNIVERSITY OF JOHANNESBURG

Page

UNIVERSITY OF JOHANNESBURG

UNIVERSITY OF JOHANNESBURG

UNIVERSITY OF JOHANNESBURG

LIST OF FIGURES

UNIVERSITY OF JOHANNESBURG

UNIVERSITY OF JOHANNESBURG

CHAPTER ONE – INTRODUCTION

1.1 GENERAL INTRODUCTION

The purpose of the study was to investigate the efficacy of Sodium Phosphate, diluted to a 6 decimal potency, as a buffer in the body. The efficacy was assessed by analysing lactic acid that accumulated during short duration high intensity exercise and hence inducing muscle fatigue onset in skeletal muscle.

1.2 OBJECTIVES

The main objective of the study is to determine the efficacy of sodium phosphate in delaying the onset of muscle fatigue during short duration, high intensity exercise. Previous studies have indicated the benefit of administering sodium bicarbonate in its crude form as a buffer, but side effects were also present.

1.3 LITERATURE REVIEW

1.3.1 Muscle Tissue Overview

Muscle tissue consists chiefly of muscle cells, which are highly specialised for contraction. It produces force as a result of the interaction of its basic contractile elements (Myofilaments). The function of muscle tissue depends on the type of tissue involved i.e. skeletal, smooth or cardiac muscle tissue. In this research project only the effects on skeletal muscle will be considered.

Skeletal muscle can also be referred to as striated, voluntary muscle with extrafusal muscle fibres. The reason for these various terms is that under microscopy, skeletal muscle exhibits a repeating pattern of light and dark bands that are attributed to the protein contractile filaments arrangement within the muscle fibres. The muscle is also under voluntary nervous system control (Vander *et al*. 1994:305).

Scattered throughout the mass of a muscle are tiny stretch receptors referred to as muscle spindles. These spindles provide the central nervous system with information about muscle length. Muscle spindle consist of small bundles of intrafusal fibres to which the endings of several sensory nerves are attached. The extrafusal fibres comprise of the greater part of the mass of the muscle and are responsible for the generation of force (Moffet 1993: 334).

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1.3.1.1 **Functions of Skeletal Muscle**

The primary functions of skeletal muscle are (a) locomotion, where contractions pull tendons and moves the bones of the skeleton. Locomotion ranges from simple extension of the arm to more complex activities such as physical exercise. Tension in skeletal muscles also (b) maintains body posture, an example is when the weight of the body gets balanced above the feet when walking. It assists in the (c) return of venous blood to the heart. (d) Thermogenesis is another important function of the skeletal muscle. Heat is a bypass product of cellular respiration, since a great deal of energy is needed for movement, a great deal of heat is also generated. Biochemical energy produced from food is converted into mechanical and thermal energy therefore also acting as an energy transduance. Skeletal muscle also acts as a protector of internal organs, as the abdominal wall, which consists of skeletal muscle that protects the visceral organs and shields internal tissue from injury. Muscle

tissue is built up largely of proteins, and makes up most of the body's protein resources (Martini 1995: 286).

1.3.1.2 **Characteristics of Skeletal Muscle**

Skeletal muscle has four important characteristics that are important for its primary function, i.e.

1. Irritability
2. Contractility
3. Extensibility
4. Elasticity

Irritability is the ability to receive and respond to a chemical message generated from a neuro-transmitter. The response is characterised by the generation of an electrical current or action potential along the cell membranes.

Contractibility refers to the ability of the skeletal muscle to respond to the chemical message by shortening. This shortening of the muscle produces force. The only tissue capable of producing force is muscle tissue.

Extensibility of the skeletal muscle refers to the lengthening or stretching of the muscle, and elasticity is the return of the muscle to its resting length. All the above characteristics are needed to produce human movement (Plowman and Smith 1996: 424 – 425).

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1.3.2 **Anatomy of Skeletal Muscle**

1.3.2.1 **Macroscopic Structure**

Several kinds of tissue make up skeletal muscle; namely blood vessels, nerve tissue, the muscle cell themselves and various types of connective tissue. The connective tissue also termed fascia, separates and holds the muscle together. Together with the fascia there are three separate layers of connective tissue that surround the skeletal muscle. The epimysium, situated just beneath the fascia surrounds the entire muscle. Dividing the skeletal muscle into a series of compartments or fasciculi is the perimysium, each fasciculi receives branches of blood vessels and nerves. Within the fasciculi the individual muscle fibres are surrounded by a delicate endomysium. These three layers of connective tissue provide the framework that holds the muscle together and they unite to form the tendon that attaches the muscle to the bone (M^{c} Ardle *et al* 1994: 298) (**Figure 1.1**).

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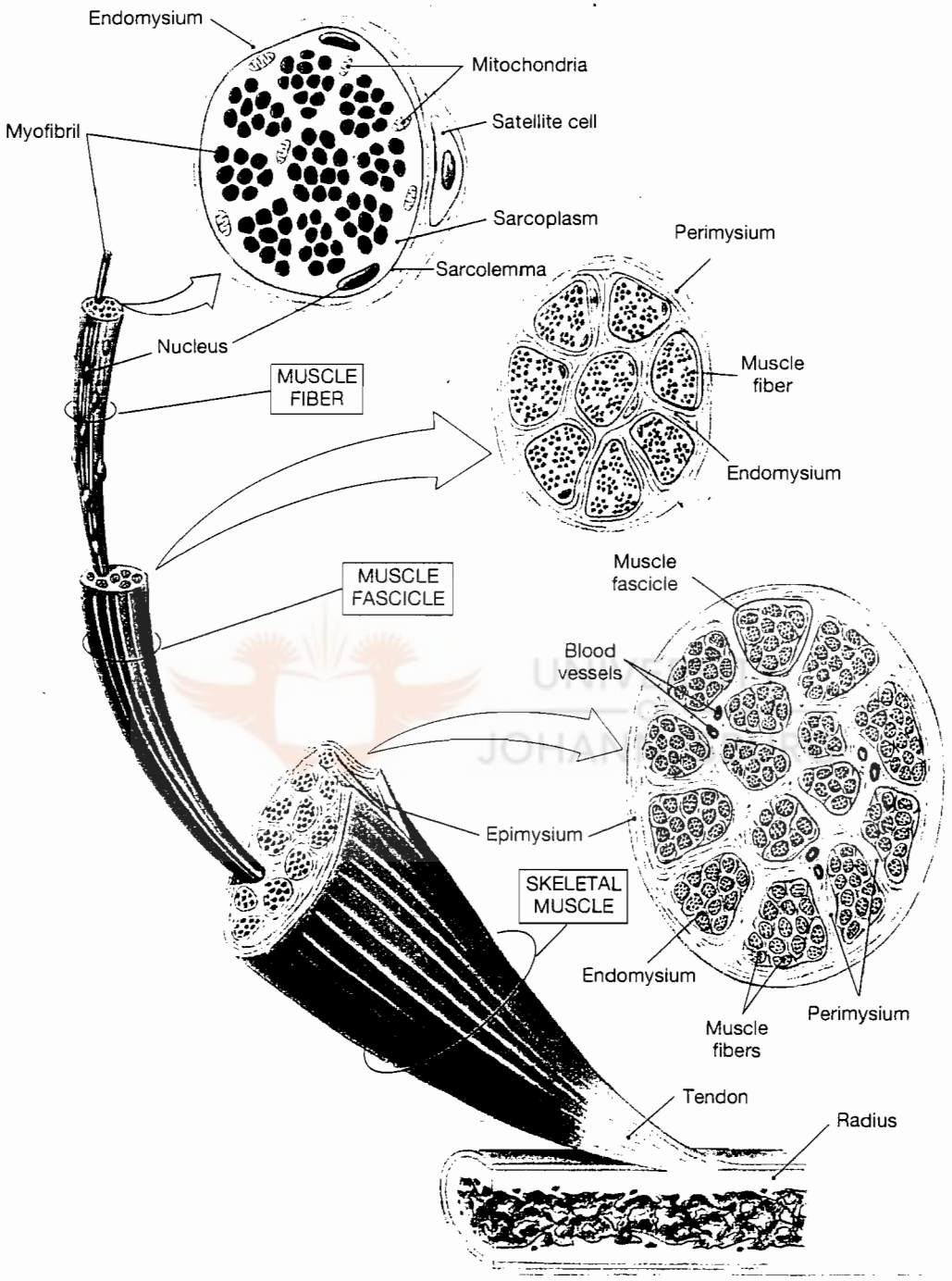

Figure 1.1 Organisation of skeletal muscle (Martini 1995: 287)

1.3.2.2 Microscopic Structure

Skeletal muscle cells are quite different in terms of their shape and size. The factor that distinguishes muscle cells from other cells is that they are multi-nucleate. The reason for being multi-nucleate is as a result of the high metabolic tumour rate. The production of enzymes and structural proteins required for normal contraction needs to be sped up and the genes for production of these products are located in the multiple nuclei (Martini 1995: 288).

Despite their unique shape and size the skeletal muscle cells still contain most of the same organelles present in normal cells, such as mitochondria and lysomes. The cell membrane surrounding the muscle cell is termed the sarcolemma. The sarcolemma is polarised, accounting for the irritability of the muscle. Beneath the sarcolemma is the sarcoplasm, which is similar to the cytoplasm of the normal cells. Within the sarcoplasm are the large amounts of glycogen and oxygen–binding proteins (myoglobin), organelles and myofibrils. The organelles that are of particular interest are the transverse tubules (T-tubule) and the sarcoplasmic reticulums (M^{c} Ardle 1994: 299).

The sarcoplasmic reticulum (SR) is a tubular network that runs parallel with the myofibrils, and is wrapped around it. The major function of the sarcoplasmic reticulum (SR) is to release, take up and store calcium and therefore control muscle contraction. The calcium is stored in cisterns or lateral sacs within the sarcoplasmic reticulum (Berchtold *et al* 2000: 1215-1265)

The transverse tubule organelles, carry the electrical signal from the sarcolemma to the interior of the cell. The t-tubules protrude into the sarcoplasm and run perpendicular to the myofibril. The calcium released

by the SR is facilitated by the spread of the depolarisation through the t-tubules (Vander 1994: 314). As the action potential in a t-tubule passes near the SR, it triggers the opening of some of the calcium channels in the lateral sacs allowing Ca^{2+} to diffuse from the Ca^{2+} rich lumen of the SR to the cytosol. The initial rise in Ca^{2+} produces a rapid opening of the closed Ca^{2+} channels and a positive feedback to rapidly increase cytosol Ca^{2+} (Vander 1994: 314).

Inside the muscle fibre, branches of the transverse tubules encircle cylindrical structures called myofibrils. A myofibril is 1–2 µm in diameter and as long as the entire cell. Each skeletal muscle fibre contains hundred to thousands of myofilaments. Myofilaments are bundles of myofibrils. The myofibrils are also attached to the sarcolemma and can actively shorten the muscle fibres. These are the organelles responsible for skeletal muscle fibre contraction (Martini 1995: 288) (**Figure 1.2**).

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The myofilaments are primarily composed of actin and myosin and can be divided into thick and thin filaments. The thin filament, composed of actin, also contains other regulatory proteins such as troponin and tropomyosin. The thick filaments are made up of the myosin protein.

Myofilaments are organised in repeating functional units called sarcomeres. Sarcomeres are the smallest functional unit of the muscle fibre. Interactions between the thick and thin filaments of the sarcomere are responsible for muscle contraction. Sarcomeres contain thick filaments, thin filaments, proteins that stabilise the thick and thin filaments and proteins that regulate the interaction between thick and thin filaments (**Figure 1.3**).

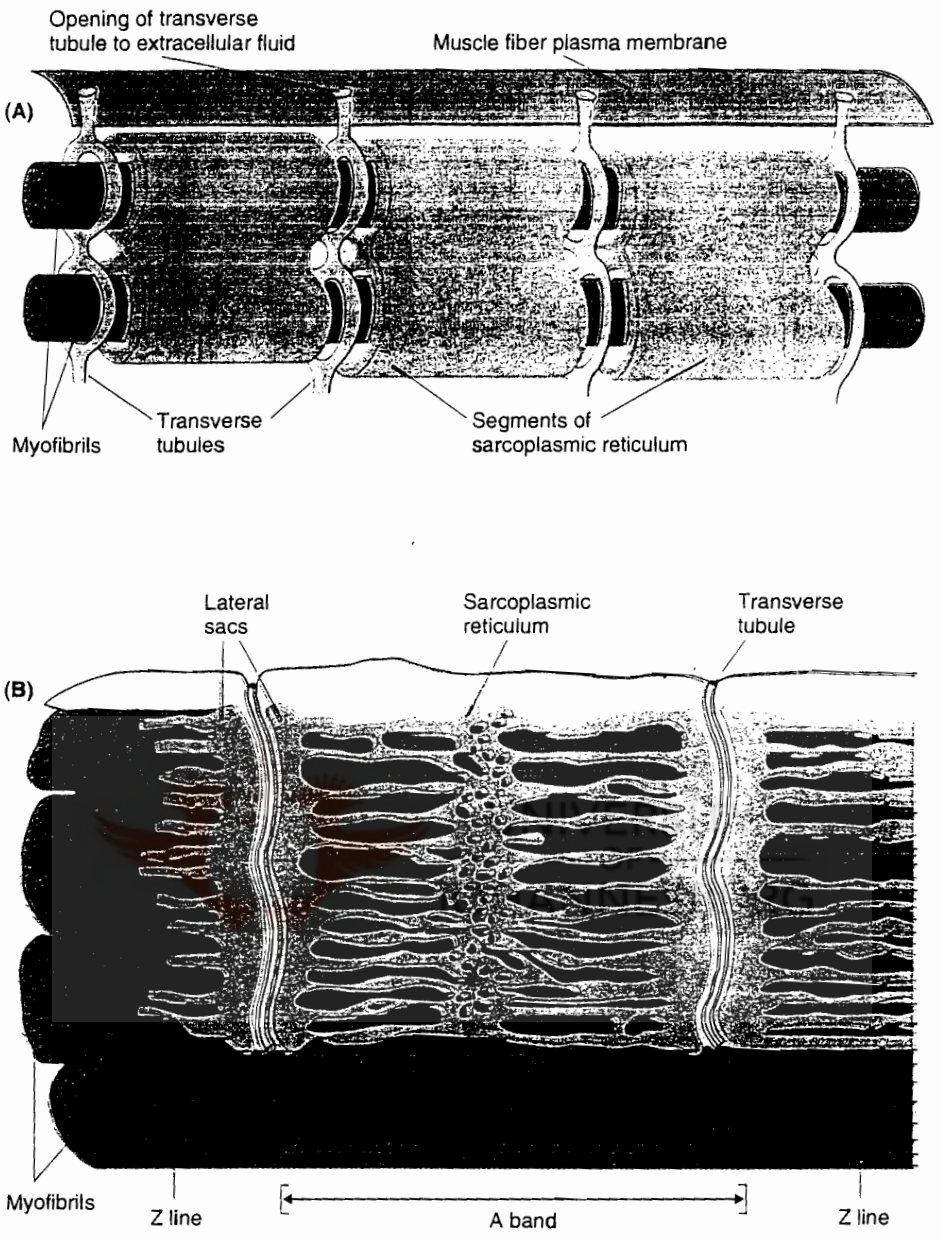

Figure 1.2: (A) Diagrammatical representation of the sarcoplasmic reticulum, transverse tubule and myofibrils

(B) Three dimensional view of the transverse tubules and sarcoplasmic reticulum in a single skeletal muscle fibre (Vander 1994: 315)

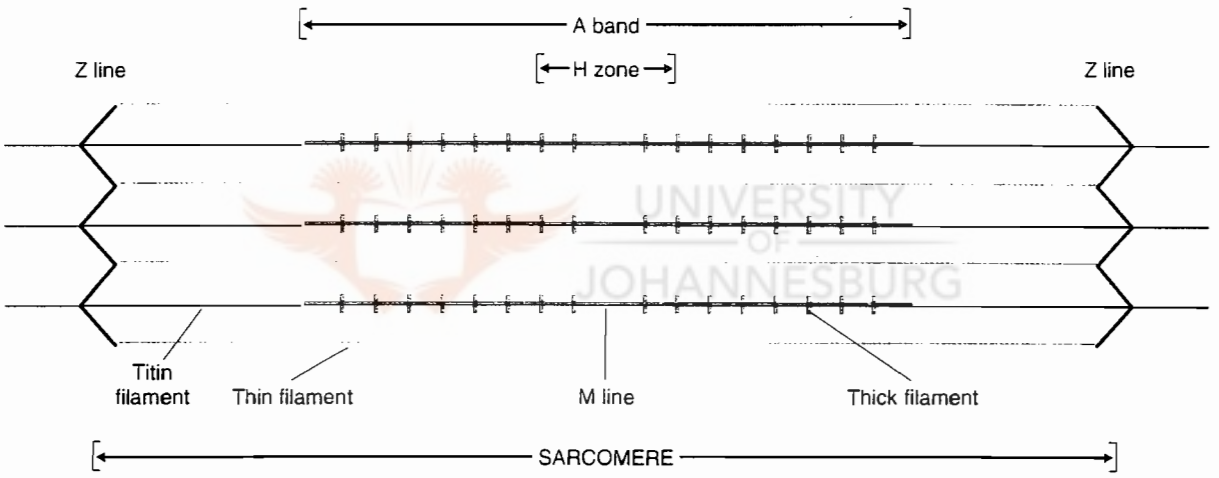

Figure 1.3 **Arrangement of the thick and thin filaments in a single sarcomere (Vander 1994: 308)**

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Difference in the size, density and distribution of thick filaments and thin filaments account for the banded appearance of the sarcomere. The dark areas, which contain the thick filaments and portions of the thin filaments are called A-bands. The lighter areas which only contain thin filaments only are called I-bands.

The A-band includes several subdivisions. The central portion of each thick filament is connected to its neighbours by proteins of the M-line. These proteins help to stabilise the positions of the thick filaments. The M-zone is a lighter region on either side of the M-line, it only contains thick filaments. In the zone of overlap thin filaments are found between the thick filaments. Each thin filament is surrounded by three thick filaments and each thick filament is surrounded by six thin filaments.

The I-band extends from the A-band of one sarcomere to the A-band of the next. The Z-line marks the boundary between adjacent sarcomeres. The Z-line is made up of proteins termed connections that inter-connect thin filaments associated with adjacent sarcomeres (M^{c} Ardle 1994: 300).

- **Thick Filaments**

Each thick filament is composed primarily of myosin molecules. The individual myosin molecule is made up of a rod-like tail and two globular heads. These myosin molecules are orientated in such a way that the tails form the central rod-like structure of the filament. The globular heads project outwards, towards the nearest thin filament, and will form the cross bridges. The head can pivot at its base, and when pivoting, the head swings towards or away from the M-line. Two reactive sites can be found on the myosin head. The first site allows it to bind to the actin protein on the thin filament and the second site binds to ATP. Contraction only takes

place if the myosin head attaches to the actin protein (Sperelakis 1996: 204-205) (**Figure 1.4**).

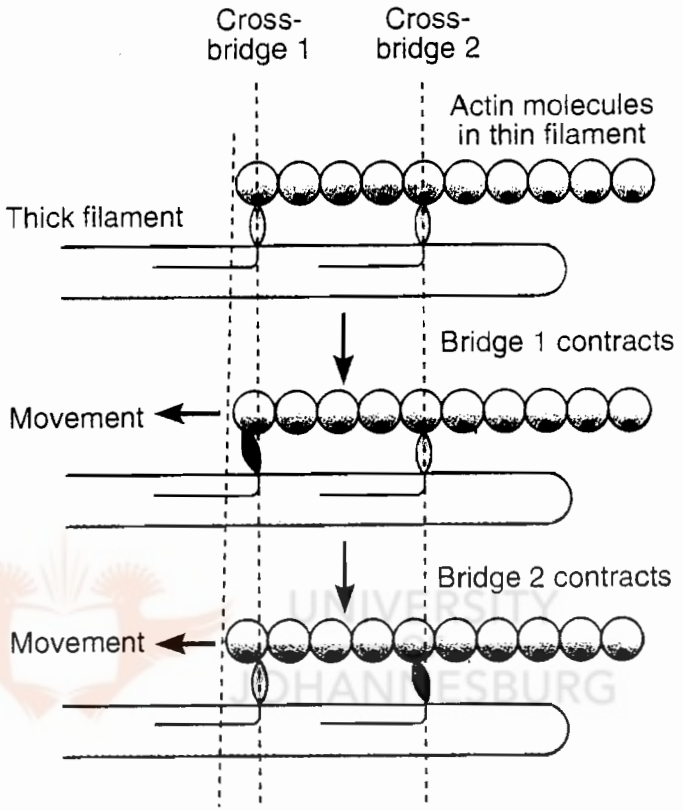

Figure 1.4: Positioning of actin and myosin filaments during the oscillating movement of the cross-bridge (Mc Ardle 1994: 305)

- **Thin Filaments**

Three different proteins i.e. F-actin coiled in a double helical structure, tropomyosin and troponin combine to form a single thin filament. Small globular sub-units called G-actin combine to make up long strands of fibrous actin (F-actin). Tropomyosin and troponin are referred to as regulatory proteins. They regulate the interaction of actin and myosin. Tropomyosin is a long, double stranded helical protein that covers the

active binding sites along the actin filament, thereby blocking interaction between actin and myosin during resting conditions.

Troponin is made up of three globular sub-units, namely troponin C (Tr-C), troponin I (Tr-I) and troponin T (Tr-T). Tr-C has a receptor on to which calcium ion binds, Tr-I prevents actin from binding to myosin, and Tr-T attaches troponin to tropomyosin (**Figure 1.5**).

Contractions can only take place if the calcium ion binds to the Tr-C binding site. The whole troponin complex then undergoes a configurational change. The tropomyosin is removed from the actin sites on the F-actin, and therefore expose the binding sites to myosin (Zhao 2000: 247-254).

As long as the calcium is bound to the Troponin-C, causing actin site exposure, the contraction cycle will continue. If the calcium concentration is not adequate, or waiting for an action potential, the energised cross-bridge of myosin will lay in a resting state until the inhibiting proteins are removed from the actin binding sites (**Figure 1.6**).

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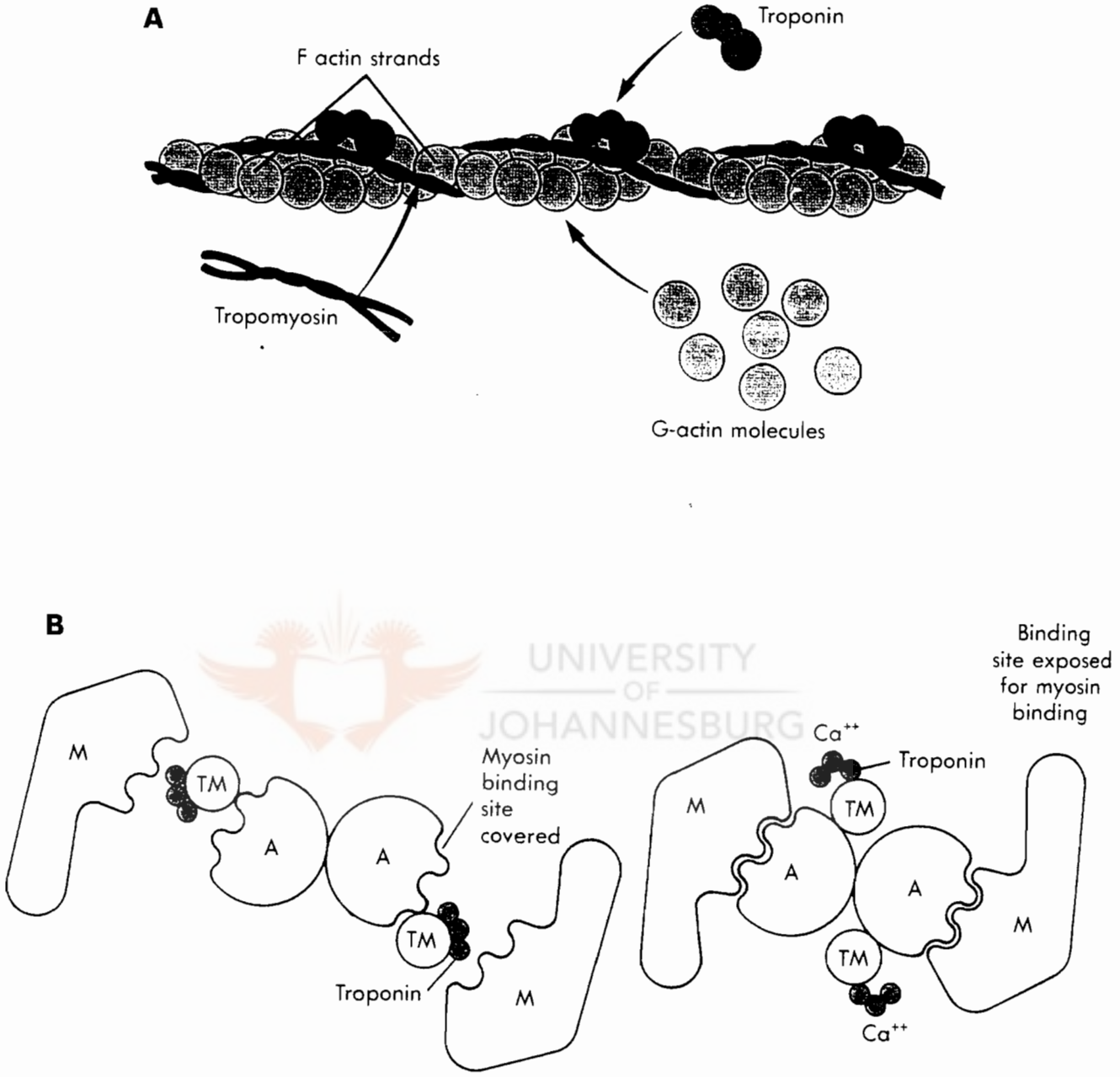

Figure 1.5: (A) Components of thin filaments

(B) Relationship of troponin, tropomyosin (TM) and F-actin
(Moffet 1993: 296)

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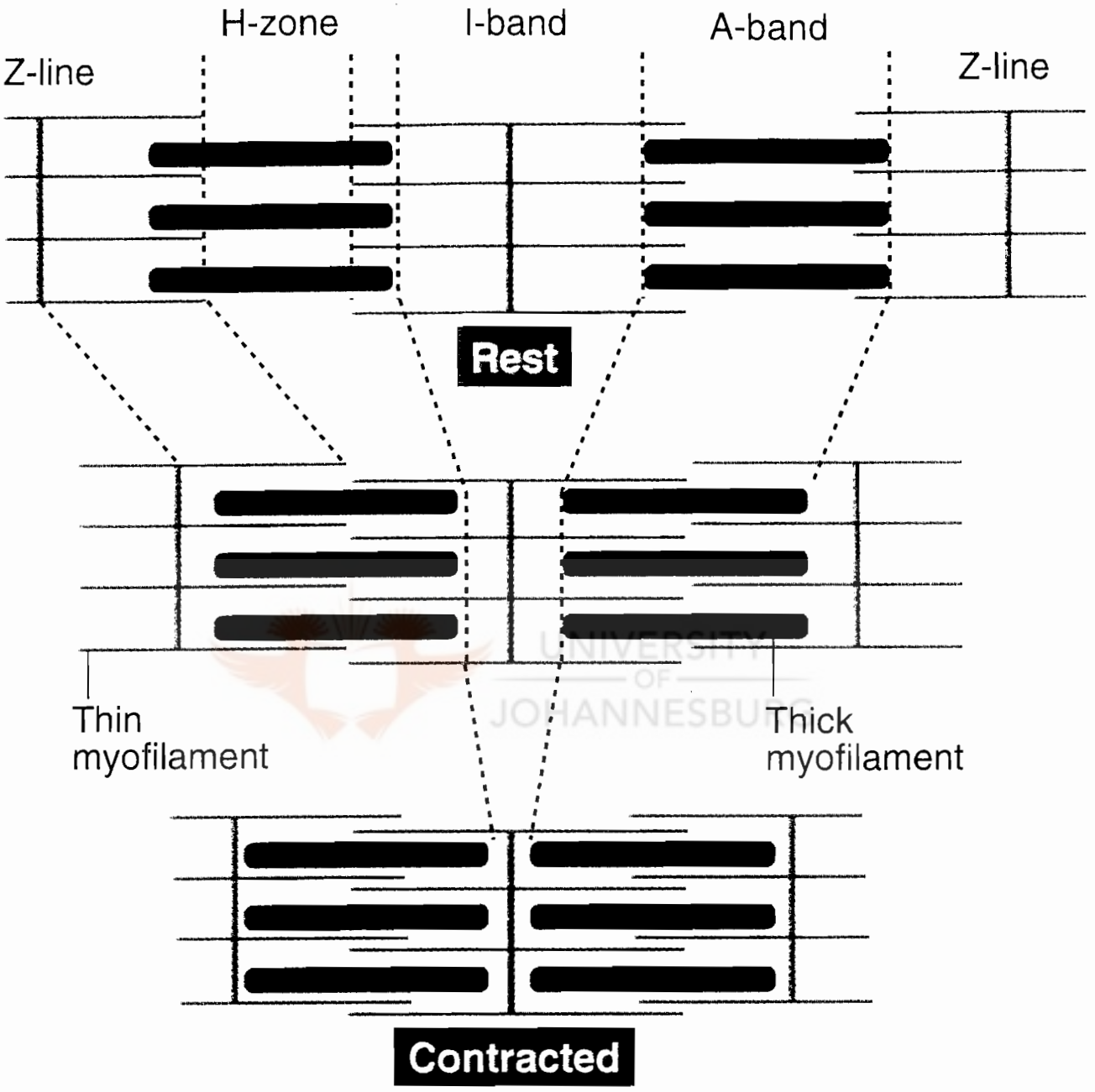

Figure 1.6: Structural rearrangement of actin and myosin filaments at rest and during muscle shortening (McArdle 1994: 304)

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1.3.3 **Muscle Fibre Contraction**

A number of cellular proteins and energy production systems all work together to initiate the complex process of muscle contraction. For the myofilaments to move, action potential needs to be generated in the motor neuron and relayed to the muscle fibre through the neuromuscular junction. The action potential must then reach the interior of the muscle fibre to initiate the movements.

This whole process where movement of the myofilaments are linked to electrical events in the sarcolemma is termed excitation–contraction coupling (Sejersted and Sjorgaard 2000: 1411-1481).

Excitation–contraction coupling, can be categorised into three phases:

a) Spread of depolarisation
b) Calcium binding to troponin
c) Force generation

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The action potential generated from the motor neuron is spread across the sarcolemma to the T-tubule, where calcium is released from the sarcoplasmic reticulum. The released calcium binds to the Tr-C globular protein. This initiates a conformational change in the tropomyosin that removes it from its binding position on the actin.

The next phase is referred to as the cross-bridge cycle. The numerous cross-bridges of the myosin extend out and attach on the actin filament. The myosin cross-bridges are orientated in such a way that they can pull the actin on each side of the sarcomere towards the centre. This pulling results in a decrease in the distance between two Z-lines.

The A-band does not shorten, but moves closer together (Powers and Howley 1990: 151) (**Figure 1.7**).

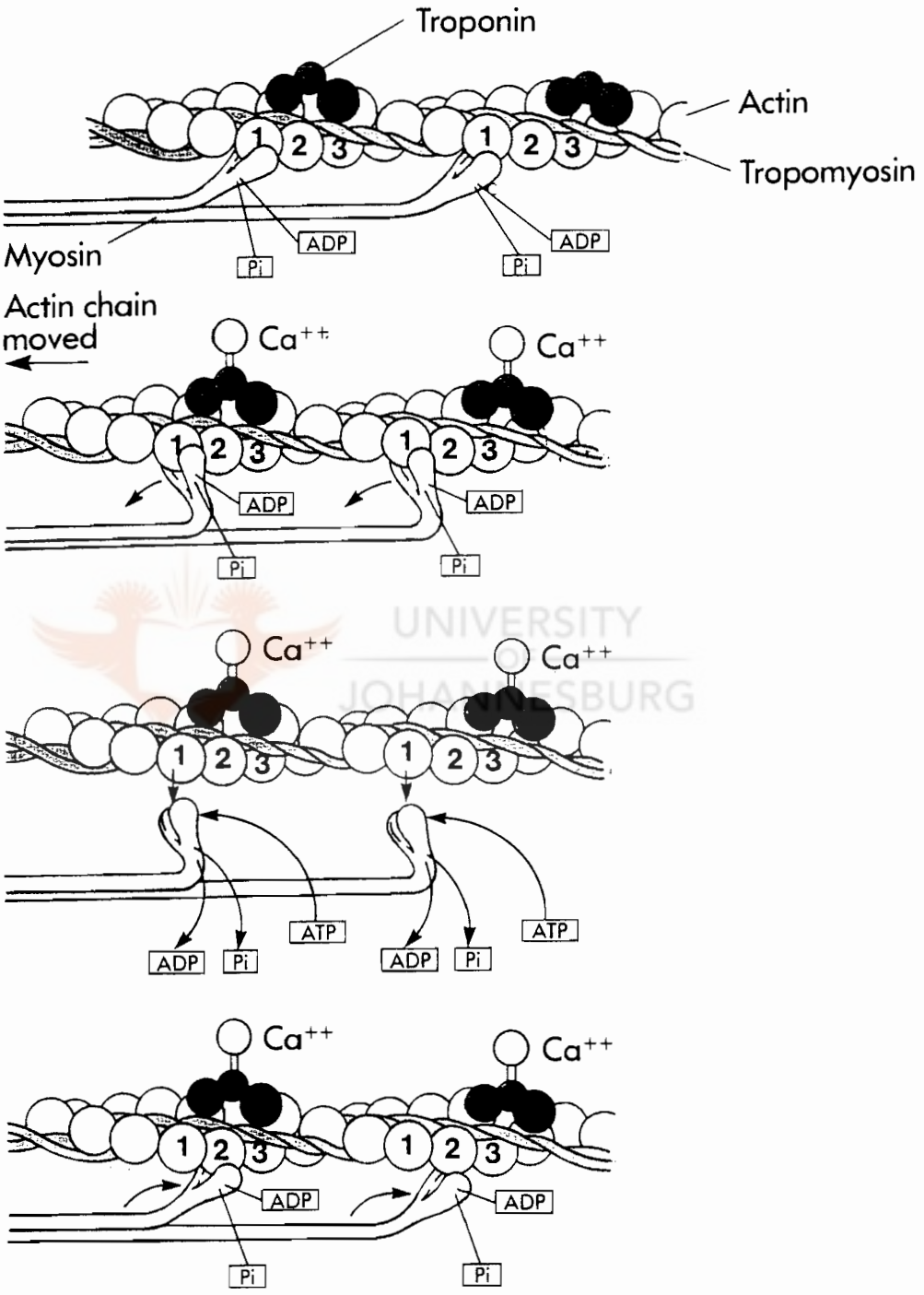

Figure 1.7: Cross-bridge cycle
(Moffet 1993: 298)

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When the action potential stops, the calcium gets pumped back in the sacroplasmic reticulum (SR), by way of a calcium pump located in the SR (Rennie 2000: 3). As the calcium detaches from the troponin-C protein the tropomysin again closes the binding sites on the actin and the cross-bridge interaction stops (Moffet 1993: 296-297).

1.3.3.1 Energy for Contraction

The energy needed to cause muscle contraction comes from Adenosine Triphosphate (ATP). ATP is an energy-carrying molecule which transfers relatively small amount of energy from fuel molecules to the points in the cell that require energy. A typical ATP molecule exists only a few seconds before it is broken down to Adenosine Diphosphate (ADP) and Phosphate (Pi) with the release of energy used to perform a cell function (Vander 1994: 92).

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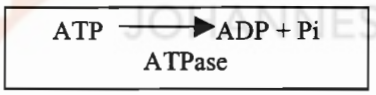

Fig 1.8 Diagrammatic presentation of ATP conversion (Martini 1995: 60)

This process occurs within the myosin head and the cross-bridge is then said to be activated and already bound to the actin filament. The next step is termed the power stroke. This refers to the action where the cross-bridge swivels, pulling the actin molecules over the myosin and thereby shortening the muscle. The energy needed for the power stroke is obtained by the release of ADP and Pi from the myosin head.

The reconverted ATP then binds to the myosin head, resulting in a detachment from the actin. It then gets broken down to ADP and Pi by the ATPase enzyme and it re-energises the cross-bridge head again. The

myosin head will again bind to the actin and another power stroke will follow (**Figure 1.9**).

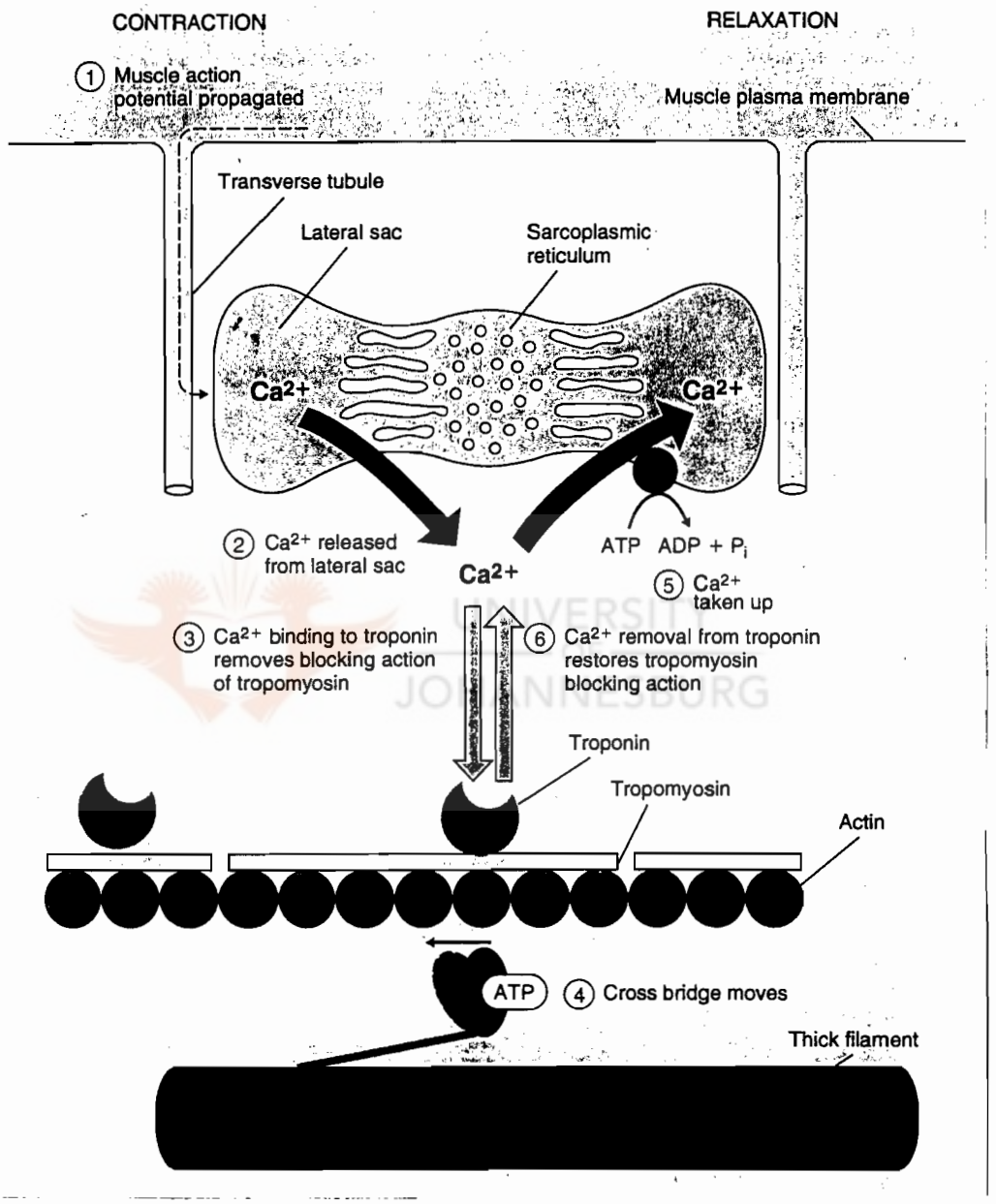

Figure 1.9 Release and uptake of calcium by the sarcoplasmic reticulum during contraction and relaxation of a skeletal muscle fibre
(Vander 1994: 316)

ATP is very important for three reasons, namely:

a) It is needed to activate and reactivate the myosin heads by providing the energy to do so;
b) It is also important to break the myosin head binding on the actin so that the cycle can be repeated; and

c) It is used to energise the calcium pump, to move the calcium back into the SR to maintain resting membrane potential (Plowman and Smith 1996: 436).

Glycolysis produces and utilises ATP. If the initial fuel is glycogen only one ATP is utilised, but two ATP molecules are utilised if the initial fuel is glucose. Three ATP's are gained when glycogen is the initial fuel and two ATP's gained when the initial fuel is glucose. ATP is produced by a process termed substrate level phosphorylation, where transfer of a phosphate (Pi) directly from a phosphorylated substrate to a ADP molecule takes place, without oxidation (Rennie 2000: 3). The products of ATP hydrolysis, ADP and Pi, are converted back into ATP, coupling through reactions that release energy during the catabolism of carbohydrates, fats or proteins (Vander 1994: 93).

1.3.4 **Skeletal Muscle Fibre Type**

There are three types of skeletal muscle fibres in the human body. The fibres are classified according to contractile and metabolic properties.

When referring to contractile properties, the motor neuron that innervates the muscle fibres is termed alpha motor neuron. Alpha motor neurons can be divided into alpha one ($alpha_1$) and alpha two ($alpha_2$) neurons. The $alpha_1$ neurons innervate the fast twitch fibres, and the $alpha_2$ neurons

innervate the slow twitch fibres. The alpha$_2$ neurons are the smaller of the two. The size is very important because smaller neurons have lower excitation thresholds and slow conduction velocities. The larger, fast twitch fibres will therefore need a larger motor unit (alpha$_1$) and also need more contractile proteins, allowing greater force production (Plowman and Smith 1996: 440).

The metabolic properties of the fibres can be divided into glycolytic and oxidative, or a combination of the two. Although all fibres can produce energy via glycolytic and oxidative pathways, one or the other may predominate in the different muscle fibres. The three types can then be classified as slow twitch or slow oxidative fibres, fast oxidative–glycolytic fibres and fast glycolytic fibres. The oxidative fibres have more mitochondria, a high myoglobin content, higher capillary density and higher oxidative enzyme activity (Vander 1994: 327).

The fast twitch fibres' energy is mainly supplied by the glycolytic pathway, therefore it contains less mitochondria. The capillary density is lower as well as the myoglobin content, and the glycolytic enzyme activity predominates. Fast oxidative–glycolytic fibres have a high mitochondrial density, a moderate to medium capillary density and myoglobin content, and have both high glycolytic and oxidative enzyme activity (Moffet 1993: 308-309).

The substrate needed to power the muscle also differs. Slow twitch fibres rely much more on triglycerides as an energy substrate, although it also has glycogen stores. The slow twitch fibres rely far less on these glycogen stores than the fast twitch fibres. The fast twitch fibres rely heavily on glycogen to power the glycolysis cycle for energy (Hargreaves 2000: 225-228).

The capillary density difference in the fibres also shows that the slow twitch fibres will fatigue slower due to its increased oxidative capabilities, and that the fast twitch fibres are less resistant to fatigue. The fast oxidative-glycolytic fibres fits in between the slow and fast twitch fibres with slightly more resistance to muscle fatigue than the fast twitch fibres; but less resistance to fatigue than slow twitch fibres (Plowman and Smith 1996: 441).

Fibre types depend on the activity that the athletes engage in. Endurance athletes have a far higher percentage of slow twitch fibres than athletes who indulge in power activities. Athletes who do power sports such as rugby will have a far greater number of fast twitch fibres in their quadriceps than athletes who participate in endurance running. The size of the muscle can also serve to illustrate this fact. The quadriceps of sprinters who do a short duration high intensity exercise are larger due to the increased muscle fibres and larger fast twitch power fibres, than athletes that compete in the endurance running events that require much more slow twitch endurance fibres (M^{c} Ardle 1994: 308-310).

1.3.5 **Energy Production**

Bioenergetics is the process where the cells convert foods such as fats, proteins and carbohydrates into biologically useable energy. The total of all the biochemical processes or energy transformations underway within the body at a given time is termed metabolism. Anabolism occurs when the energy is used to build up tissues, catabolism is the process where food stuffs are broken down and the energy stored to be available for work.

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Energy needs to be available continuously to power activities of our daily lives. If there is a decrease in energy availability muscle contraction is not possible and work must stop (Noakes 2000: 123-145).

1.3.6 **Carbohydrate Metabolism**

The major product in the carbohydrate metabolism pathway in which it either starts or ends is glucose. It is necessary to understand glucose metabolism because of the important role played by glucose in the body.

The glycolytic or Embden-Meyerhof pathway refers to the process whereby energy is extracted from high energy fuels such as glucose, in the absence of molecular oxygen. The pathway can also be referred to as a fermentation process, a process possessed by all cells of the body. The tissues in the body use glycolysis as a emergency energy-yielding pathway. Oxygen is not necessary for glycolysis, and glycolysis can indirectly be suppressed by oxygen. Various tissue and cells can only utilise glycolysis as a process to produce ATP, e.g. red blood cells, which lack mitochondria and therefore produce lactate instead of CO_2 and H_2O. Thus the fewer the number of mitochondria in the cells or tissues the more reliant it would be on glycolysis for energy (Devlin 1997: 268).

Glucose is stored in the form of glycogen, a chain of glucose molecules chemically linked together, or as adipose tissue. The liver and the muscle cells predominantly store glycogen. Glycogen needs to be broken down to glucose before it can be metabolised further. Carbohydrates composed of carbon, oxygen and hydrogen also needs to be metabolised to a glucose 6-carbon sugar in a hexagonal formation before it can be used (Guyton and Hall 1995: 857).

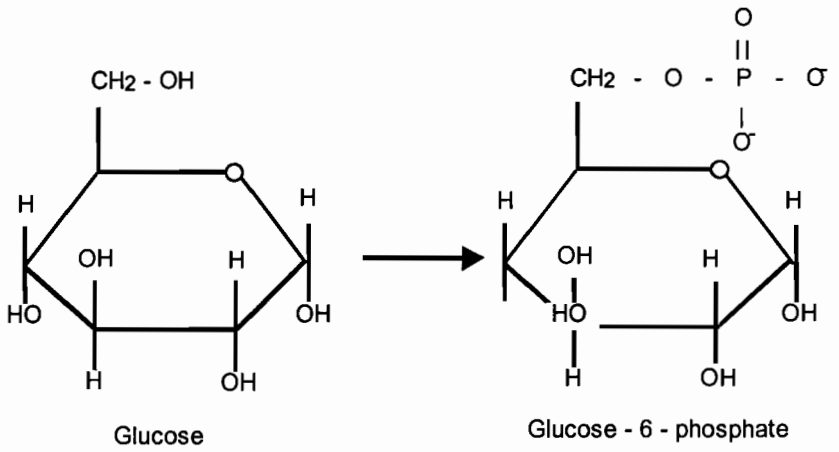

Figure 1.10 Conversion of glucose to a hexagonal -6- carbon Sugar (Vander 1994: 95)

Glycolysis begins with either glucose or glycogen and ends with the production of either pyruvate by aerobic glycolysis or lactate by anaerobic glycolysis (**Figure 1.11**). Each step of the glycolytic metabolic pathway is catalysed by a specific enzyme. Enzymes are proteins that accelerate the speed of the chemical reactions without being changed by the reaction.

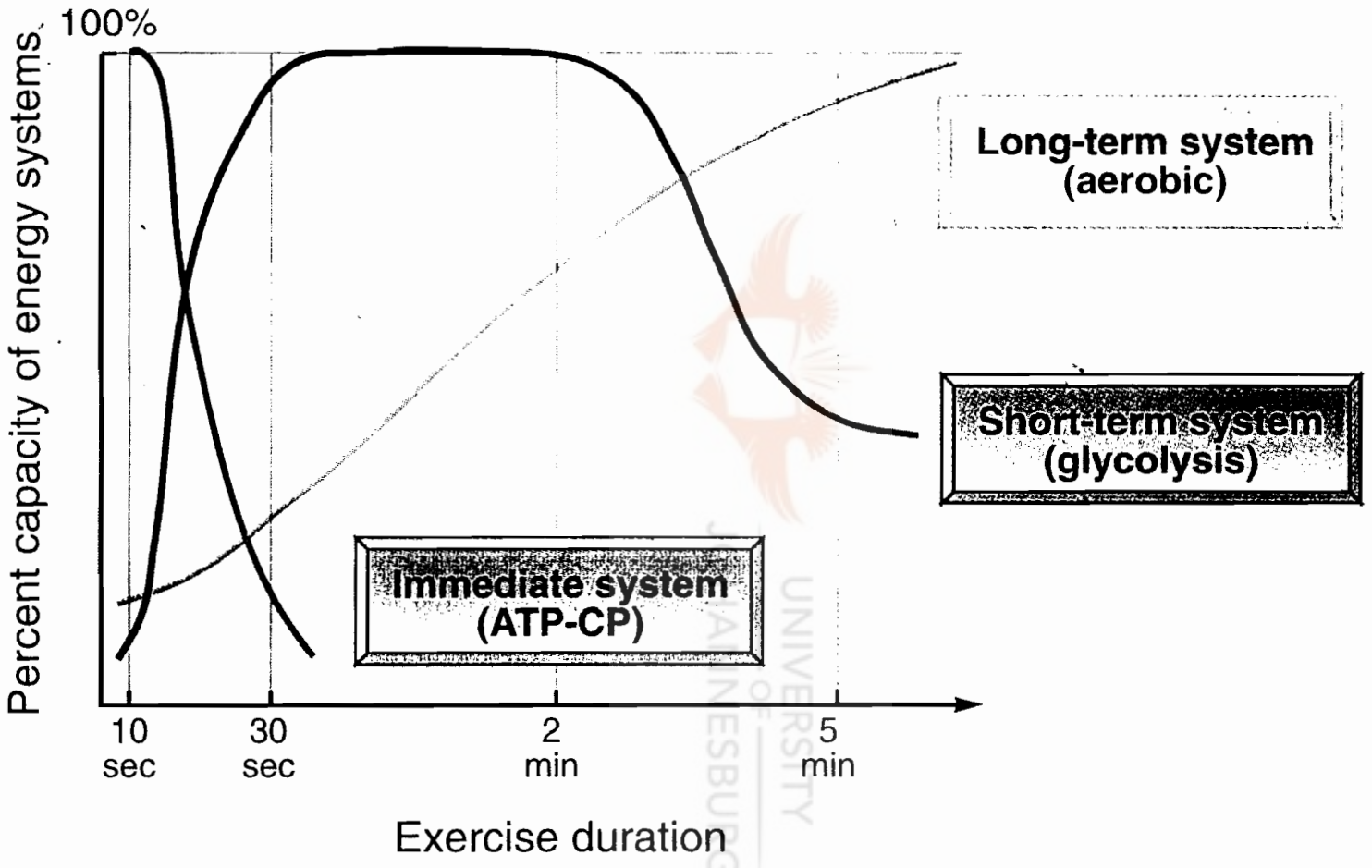

Figure 1.11 **The three energy-transfer systems, and their relative degree of activation during all-out exercise of different duration (McArdle 1994: 345)**

Regulatory or rate limiting enzymes are the most important in controlling the rate of energy production. These enzyme activities are effected by factors such as temperature, pH concentration of the substrate acted on, and the absence or presence of poisons or medications. These enzymes are simply free floating in the cytoplasm when glycolysis takes place (Guyton and Hall: 1996: 861).

Enzymes cannot pass through the cell membrane due to the fact that they are phosphorylated compounds. All of the phosphate intermediates are unable to pass through the cell membrane. These intermediates include ADP and ATP. The cell membrane however, is freely permeable to glucose and lactate (Guyton and Hall 1996:857).

Glucose gets transported into the cell via facilitated diffusion, which is a passive highly selective process that does not require energy expenditure. A protein carrier is utilised and glucose is transported into the cell down the concentration gradient. Glucose is a large lipid-insoluble uncharged molecule. Without the protein carrier it would have difficulty passing into the cell. With facilitated diffusion the glucose molecule first attaches to the binding site on its specific protein carrier. A structural change creates a passageway enabling glucose to cross the membrane into the cell (M^{c} Ardle 1994: 25) (**Figure 1.12**).

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Facilitated diffusion

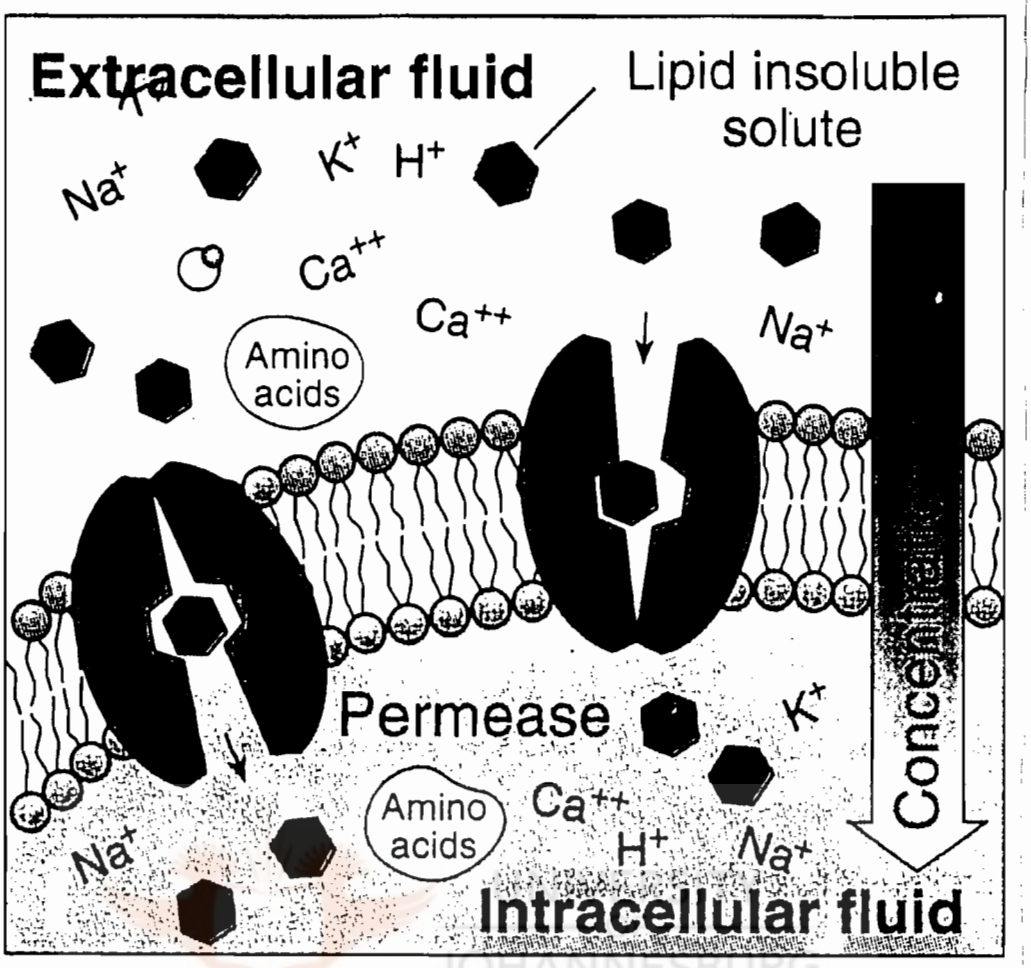

Figure 1.12: Facilitated diffusion
(McArdle 1994: 24)

Within the glycolytic pathway, oxidation and reduction reactions take place. Oxidation can be divided into three types; namely a) a gain of oxygen, b) a loss of hydrogen, or c) a direct loss of electrons. When a substance is oxidised another is simultaneously reduced. The oxidised substance loses energy, where the reduced substance gains energy. Reduction is the process whereby a substance loses an oxygen or gains a hydrogen ion. Oxidation occurs in the form of hydrogen removal in several of the intermediary steps in the pathway. The removed hydrogen ions need to be transported elsewhere, this is done by carriers such as nicotinamide adenine dinucleotide (NAD) and flavin adenine dinucloetide (FAD). The main function of NAD and FAD is to transport hydrogen ions

(reduced) and deliver them at another point (oxidised), without being permanently changed (Guyton and Hall 1996: 860).

In the first step glucose or glycogen undergoes phosphorylation, therefore a phosphate group is attained by the breakdown of ATP or ADP. This process also traps the glucose in the particular cell. In step two the glucose atoms that make up glucose-6-phosphate are then rearranged to form fructose-6-phosphate. In step three another phosphate is added to fructose-6-phosphate by breaking down ATP. This step is catalised by the enzyme phophofructokinase (PFK), one of the most important regulatory enzymes in glycolysis.

The splitting of the 6 carbon chain occurs in step four. The 6 carbon sugar is split into two 3 carbon sugars, which are identical in components, but arranged differently namely dihydroxyacetone phosphate and glyceraldehyde-3-phosphate. In step five the atoms of dihydroxyacetone phosphate are rearranged to glyceraldehyde-3-phospate. In step six, a pair of hydrogen ions are transferred from glyceraldehyde-3-phosphate to NAD^+, by way of a reduction reaction and NAD^+ is converted to NADH + H^+, releasing energy that is used to add another phosphate to the first carbon, becoming 1,3 diphosphoglycerate.

ATP is finally formed in step seven when the phosphate from the first carbon is transferred to ADP, thereby storing energy. Step eight is simply just a rearrangement step where phosphate is moved from the third to the second carbon. Following the removal of a water molecule, the binding between the atom and the remaining phosphate group weakens in step nine. The remaining phosphate is then transferred to ADP to form ATP by way of the enzyme pyruvate kinase in step ten. In the final step the hydrogen atoms carried by NAD^+ as NADH + H^+ is transferred to pyruvic acid (pyruvate), thereby forming lactic acid (lactate) and converting back to

NAD^+. These steps explain the pathway during anaerobic glycolysis where the end product of glycolysis is lactic acid (M^c Ardle 1994: 44-49) (**Figure 1.13**).

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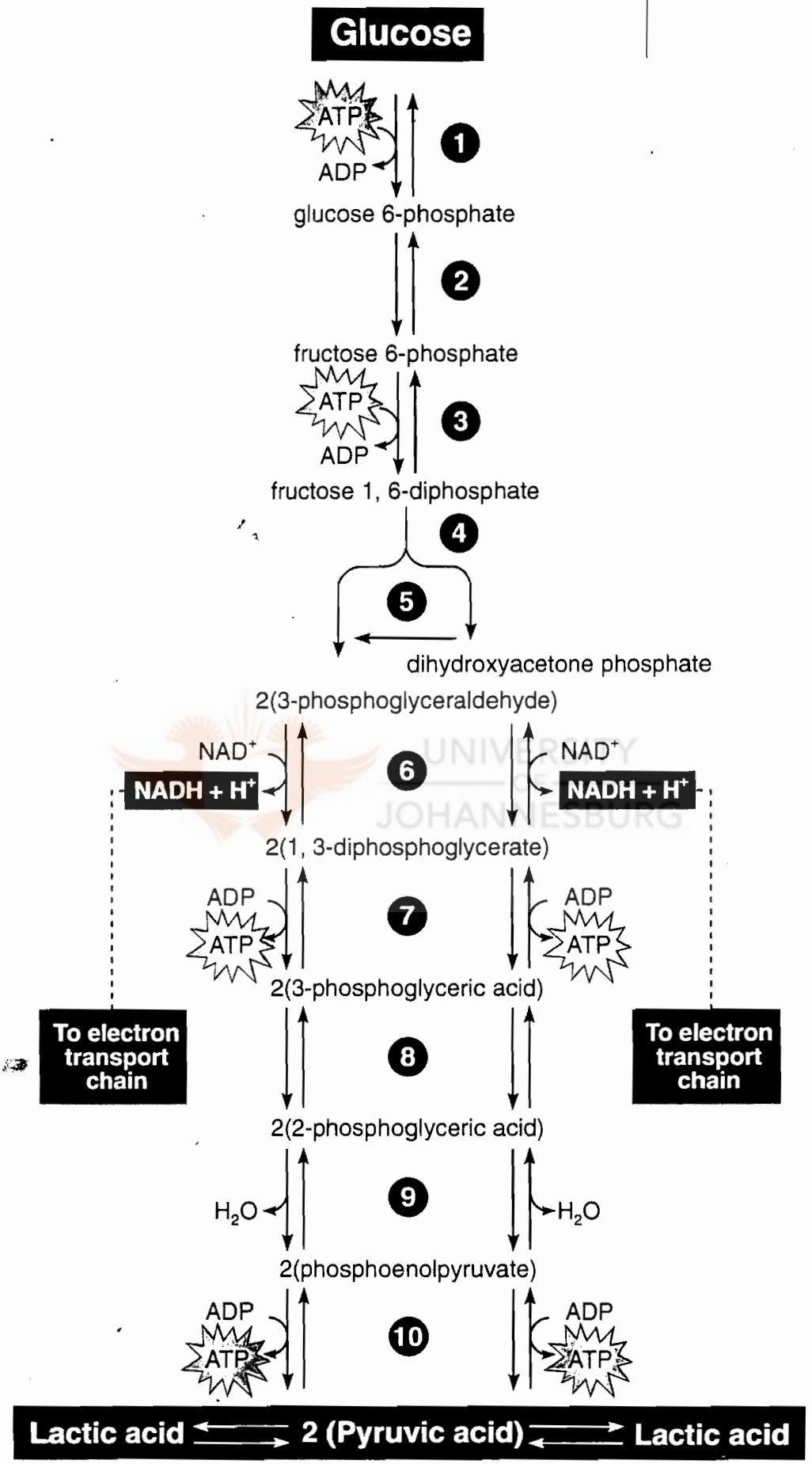

Figure 1.13 Stage 1 Glycolysis reaction (McArdle 1994: 45)

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1.3.6.1 Regulation of Glycolysis – Intracellular

The speed at which the biochemical pathway proceeds depends on the rate-limiting enzyme within the pathway. If there are ample number of enzymes present and ample substrate available, the rate of the chemical reactions will increase.

Rate-limiting enzymes are normally found very early in the metabolic pathway. The reason being that if the enzymes where located later in the pathway the metabolic products would accumulate. The activity of the rate-limiting enzymes is regulated by modulators which can increase or decrease the activity.

ATP is a classical example of a modulator that inhibits the rate-limiting enzymes activity. ADP and phosphate are examples of modulators that stimulate the enzyme activity. Therefore, larger amounts of ATP would decrease the metabolic production of ATP, because it indicates that ATP usage by the cell is low *(***Figure 1.14***)*.

Phosphofructokinase (PFK) is the rate-limiting enzyme in the glycolytic pathway, and the control of PFK is via negative feedback as figure 1.14 illustrates. Stimulators of PFK include ADP, AMP, Pi and an increase in pH levels. Inhibitors include ATP, creatine kinase, citrate and a decrease in pH levels.

The phosphorylase enzyme responsible for the breakdown of glycogen to glucose is another important enzyme. This enzyme is activated by the calcium ion, released from the sarcoplasmic reticulum at the beginning of exercise, when glucose is needed to enter the glycolytic cycle. Epinephirine also indirectly influences phosphorylase enzymes by

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stimulating C-Amp (cyclic-Amp) formation which activates the enzyme (Powers and Howley 1990 : 45-46).

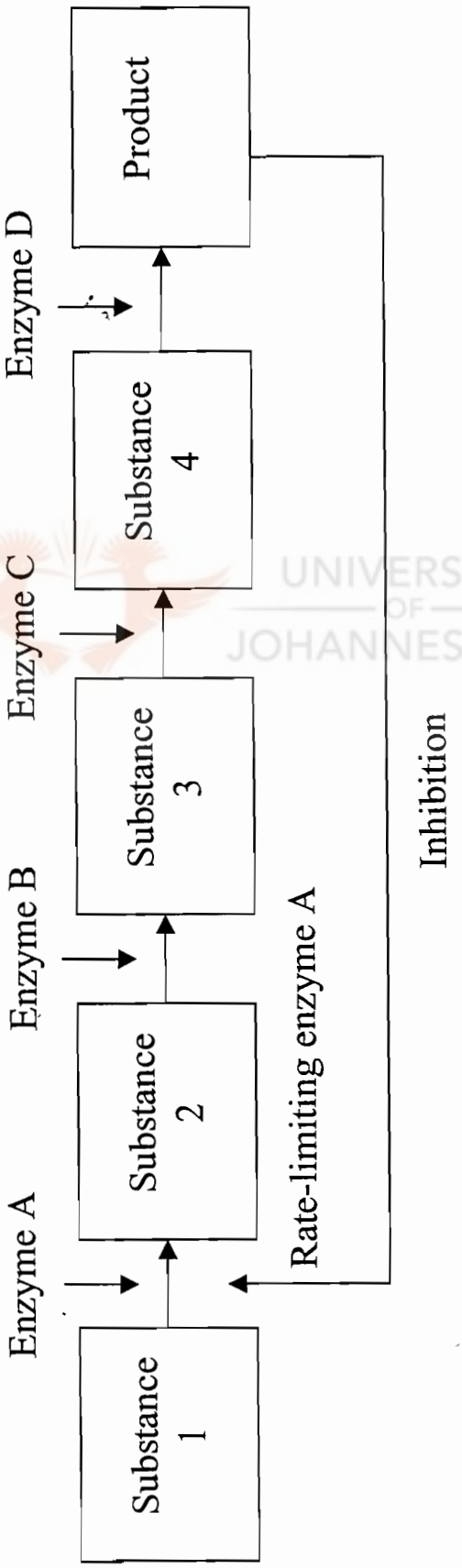

Figure 1.14 **Example of a rate limiting enzyme in a simple metabolic pathway. Here a build-up of the product serves to inhibit the rate-limiting enzyme, which in turn slows down the reaction pathway. (Powers & Howley 1990: 45**

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1.3.7 **Neuro Hormonal Co-ordination**

The catecholamines (epinephrine and nor-epinephrine) and glycogen react to short duration, high intensity exercise within seconds. These hormones assist through an:

a) Increase in mobilisation and utilisation of the free fatty acid stores from extra-muscular (adipose tissue) and intra-muscular stores;

b) Increase in the breakdown of extra-muscular (liver) and intra-muscular stores of glycogen and creation of glucose from non carbohydrate sources (glyconeogenesis) in the liver; and

c) Decrease in the uptake of glucose into the non-working cells (Plowman and Smith 1996: 235).

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During exercise of increasing intensity and duration, the levels of blood glucose and insulin progressively decrease. This is due to an inhibitory effect of catecholamines over insulin. The catecholamine suppression of insulin is proportionate to the intensity of exercise (M^{c} Ardle 1994: 329) (**Figure 1.15**).

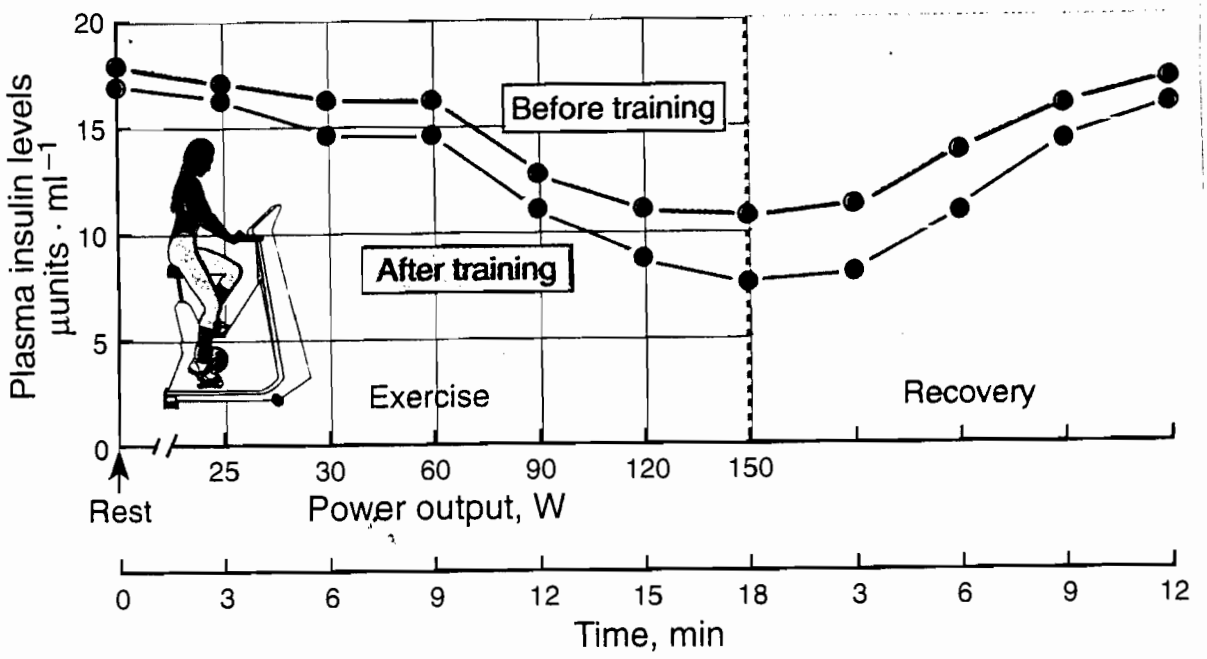

Figure 1.15: Plasma-insulin levels during exercise and in recovery before and after training (McArdle 1994: 329)

Other hormones such as cortisol and growth hormone all play a part in exercise, but the response that they elicit only occurs after several hours. Cortisol secretion can also be influenced by the patient's perception of the exercise event. Thyroxine is another hormone that plays a role during exercise, but its main function is to create an optimal environment for the other hormones to function in. This is done by either influencing the number of receptors on the cell membrane surface or increasing the affinity of the receptors for the hormones.

In conclusion, hormones can be divided into fast acting and slow acting hormonés. Epinephrine, non-epinephrine, insulin and glycogen are the fast acting hormones, and cortisol, thyroxine and growth hormone are slow acting hormones (Powers and Howley 1990: 92 – 100).

1.3.7.1 Lactic Acid Effects on Hormones

During high intensity exercise the plasma levels of glucogen, growth hormone, epinephrine, non-epinephrine and cortisol are elevated, and only insulin is decreased. This arrangement favours the sparing of carbohydrates and the mobilisation of fatty acids to maintain plasma glucose concentration.

However, lactate enters the cell and initiates a fall in the utilisation of free fatty acids for glucose production, leading to a greater utilisation of carbohydrates. If lactate is reduced, it will lead to the athlete utilising more free fatty acids and less carbohydrates as fuel, thereby improving performance (Powers and Howley 1990: 100).

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CHAPTER TWO – LACTATE AND BUFFERS

2.1 LACTIC ACID

Lactic acid *(**Figure 2.1**)* is an example of a weak electrolyte, therefore it does not, when dissolved in water, dissociate totally into positive and negative charged ions.

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Figure 2.1 Lactic Acid Chemical Structure (Vander 1994: 46)

It establishes an equilibrium between un-dissociated and dissociated components. Therefore its ability to carry electrical charge is less than those substances that dissociate totally. The definition of an acid is a substance that donates protons (H^+) and a base is a proton acceptor. An example of a strong acid is sulphuric acid which dissociates totally into hydrogen ions and bicarbonate (OH^-) ions. Lactic acid dissociates only partially and is therefore referred to as a weak acid. The lactic acid reaction establishes an equilibrium between the acid (proton donor), the anion of the acid (negatively charged lactate) and a proton (H^+) (Guyton and Hall 1996: 862).

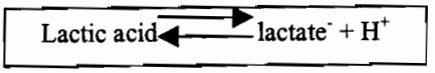

Figure 2.2 Dissociation reaction of lactic acid (Guyton and Hall 1996:862)

Hydrogen ion concentration is expressed in terms of pH, and is calculated as:

$$pH = \log \frac{1}{H^+}$$

Although lactic acid is a weak acid it can still contribute to the pH of the body and influences acidity of the blood plasma, interstitial fluid and cell fluid. The body needs to buffer these hydrogen ions that build up in the body to maintain a pH level of 7.4 in the plasma and in the interstitial fluid and a pH level of 6.9 in the cell fluid.

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Lactic acid, being composed of carbon, hydrogen and oxygen, can also be utilised as a fuel source. Tissues such as skeletal muscle and cardiac muscle change lactic acid through oxidative reactions. The lactic acid is converted back to pyruvate and utilised in the kreb cycle to produce ATP, carbon dioxide and water (M^c Ardle 1994: 73).

To summarise, 55% to 70% of lactic acid produced during heavy exercise gets utilised to produce pyruvic acid for oxidative skeletal muscle fibres and the heart. 20% and less is reconverted back to glycogen in the muscle and liver. 5% to 10% produces carbons for amino acids and other proteins and 2% or less remains as lactic acid (Plowman and Smith 1996: 260).

2.1.1 **Lactate Levels**

The intensity of exercise will determine the lactate levels in the plasma and blood. With the exercise bout being of high intensity and short duration the lactate levels show a rapid increase and a consistent accumulation (M^{c} Ardle 1994: 62-63).

2.1.2 **Acid Regulation**

Regulation of the hydrogen ion concentration is important to maintain enzyme activity and fluid electrolyte balance. The body goes about regulating hydrogen ions in three ways, namely:

a) Hydrogen ion excretion and bicarbonate ion re-absorption by the kidneys;

b) Carbon dioxide excretion by the lungs; and

c) Buffering of hydrogen ions by way of weak acids and bases that form part of the body's natural buffer system.

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The two major sources of daily acid production are a) metabolism of carbohydrates, fat and proteins which leads to the production of fixed organic acids and b) oxidative metabolism that leads to the production of carbon dioxide, which is a volatile acid (Tadlock 1996: 171-172).

During short term exercise the kidneys do not play a significant role in acid-base balance. The principle way that the kidneys regulate the hydrogen ion concentration is by increasing and decreasing the bicarbonate concentration. Thus, if the plasma hydrogen ion concentration increases the amount of bicarbonate concentration is also increased to buffer the excess hydrogen ions. The kidneys are not as

important in short term exercise due to the time factor. It takes several hours for the kidneys to respond to an increase in hydrogen ions and therefore the response is too slow to be effective (Power and Howley 1990: 240).

2.1.2.1 **Acid Regulation during Exercise**

During near-maximal exercise of short duration the pH in the blood and muscles decreases, due to a lactic acid build-up. The amount of lactic acid produced depends on the intensity of exercise, the amount of muscle mass involved and the duration of the exercise.

The initial regulation of lactic acid build-up occurs within the muscle itself. The muscle proteins contribute approximately 60% to the buffering of acids, with the muscle bicarbonate contributing 20–30%. The remaining capacity comes from the intracellular phosphate groups.

Haemoglobin and the blood proteins play only a minor role in buffering the lactic acid build-up in exercise, with the extracellular bicarbonate being the most important buffer in the extracellular compartment. What must also be noted is that as the hydrogen ion concentration increases the blood bicarbonate concentration decreases proportionately. These buffer systems rapidly act to convert strong acids into weak acids (Moffet 1993: 580-583).

2.1.3 **Buffer System**

The definition of a buffer is a solution wherein the hydrogen ion concentration (pH) remains virtually unchanged by dilution or by the addition of an acid or alkali. Buffers are therefore able to bind or release

hydrogen ions in solution and thus minimise fluctuations in hydrogen ions (Guyton and Hall 1996: 385-386).

The buffer is most effective when the pH of the solution equals the dissociation constant (Ka), which describes its tendency to dissociate. The pKa of a buffer is that pH at which equal amounts of buffer exist as the acidic and basic forms (Tadlock 1996: 173). Therefore if the pH = pKa the buffer exists as half in the acidic form and half in the basic form, and will thus be most effective in buffering additions of either an acid or base.

The effect where a strong acid is added to a non-buffered system is noted here. The hydrogen ion concentration increases with each molecule of strong acid resulting in a decrease in pH. In the presence of a buffer the excess hydrogen ions protonate (donates protons) to the conjugate base of the buffers acid. The hydrogen ions are therefore not free in the solution and therefore not contributing to the pH of the solution. Although, there would be a small drop in the pH due to the small amount of hydrogen ions that remain free (Moffet 1993: 588-589).

2.1.4 **Types of Buffers**

2.1.4.1 **Bicarbonate – Carbonic Acid System**

This system is the most important plasma and extracellular buffer. It accounts for 90% of the buffering capacity of the plasma for metabolic acid loads.

2.1.4.2 **Extracellular – Fluid Buffers**

Bicarbonate is the main buffer in the extracellular fluid. Its capacity to buffer is much greater than the plasma, due to its larger volume. The

extracellular fluid is rapidly cleared of proteins and has a low concentration of phosphates, which results in its inability to buffer a carbonic acid load.

2.1.4.3 **Intracellular – Fluid Buffers**

The main buffers in this compartment are proteins and phosphates. The pKa of these buffers are very close to the pH inside the cell. Intracellular buffers account for 50% of the buffering of a metabolic acid load and 95% of a carbonic acid load, due to the inability of extracellular fluid buffers (Tadlock 1996 : 174 – 179).

The buffers that are not important for this dissertation but also need mentioning are red cell buffers (namely haemoglobin), proteins within the plasma and histidine which is an amino acid.

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2.1.5 **Reason for Maintaining Acid-Base Balance**

As lactic acid accumulates in the skeletal muscle due to heavy exercise, it ionises and releases hydrogen ions. Hydrogen ions exert a powerful effect on molecules due to their small shape and positive charge.

Hydrogen ions influence the metabolism by attaching to the molecules and altering their original shape and size. This results in a change of the molecules normal function. The hydrogen ions influence skeletal muscle function by reducing the ability to produce ATP through the inhibition of enzymes responsible for ATP production. Secondly, they compete with the calcium ions for binding sites on the troponin, thereby inhibiting the contraction cycle (Vollestad and Sejersted 1988: 336-837).

Mainwood and Renaud acknowledge that the hydrogen ions do compete with calcium for the troponin binding sites. The binding sites are altered

by the hydrogen ion concentration, thus decreasing the accessibility of the binding site for calcium. At a low pH more calcium is loaded in the sarcoplasmic reticulum and more hydrogen ions are available to bind to receptor sites on the troponin for contraction (Mainwood and Renaud 1984: 412).

Phosphofructokinase, the enzyme that controls the conversion of fructo-6-phosphate to fructose1,6-bi phosphate is very sensitive to lactic acid build-up, and as previously indicated is also the rate-limiting enzyme in the glycolysis cycle (Vander 1994: 90-91).

2.1.6 **Lactic Acid Removal**

The role of lactic acid removal from the system is dependent on five factors. The first factor is the post exercise concentration of lactate, the higher the lactate concentration the higher the rate of removal. Secondly the rate of removal will depend on the subject following a resting or exercise recovery regimen. Evidence suggests that an active recovery stimulates faster lactic acid removal than passive recovery.

Thirdly, if an active recovery is employed, the intensity of the exercise during the recovery phase is of importance. The intensity of the exercise should not exceed an individual's workload maximum, where the lactate removal is optimal and the production is minimal. The fourth factor that influences lactate removal is the type of exercise employed in the recovery phase. Continuous jogging at a self-selected pace was found to be the most beneficial for lactate removal. Finally, for the best results in removal of lactic acid from the system, the activity during the recovery phase should be continuous and not intermittent (Plowman & Smith 1996: 260-261).

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2.1.7 Effects of Sodium Bicarbonate Ingestion on Exercise Performance

The increased reliance on glycolysis during high intensity exercise results in an altered acid base balance. Therefore the excess hydrogen ions produced by lactic acid need to be buffered by available bicarbonate ions. In this process, by decreasing the amount of bicarbonate ions available in the system, the increasing hydrogen ion accumulation will be dealt with. The decrease in the pH value is therefore a large contributing factor to muscle fatigue during high intensity exercise (Guyton and Hall 1996: 387-389).

In addition, if there is an increase in the buffer concentration, the increase may help to delay the onset of fatigue due to decreasing pH. The arterial blood pH level is approximately 7.4 at rest, while the muscle pH level is approximately 6.9. Following high intensity exercise both these values can drop by as much as 0.5 pH units. This drop is directly attributed to the increase in blood lactate concentration (M^{c} Ardle 1994: 408-409).

Studies done by Linderman and Fahey indicated that blood pH was significantly greater and endurance increased in subject that took sodium bicarbonate prior to exercise. Although the intramuscular pH was the same irrespective of taking placebo or sodium bicarbonate. The study showed that extracellular pH effects a muscle's capability to generate force and recover from fatigue.

In conclusion, if added bicarbonate ions are ingested it causes an enhanced movement of hydrogen ions from inside the cell towards the extracellular environment. It takes place by way of facilitated diffusion by a membrane bound transporter. The membrane bound transporter is stereospecific for lactate in its L(+) form. It displays saturation

characteristics and is dependant on pH and temperature. The main effect of bicarbonate is therefore to enhance the pH gradient between the intra and extracellular environment, thereby favouring a lactate efflux. Enhanced transport of hydrogen ions may delay the onset of intracellular acidosis that causes inhibition of contractile properties of the muscle cell. (Linderman and Fahey 1991: 71-76).

Costill *et al* demonstrated that despite the alkalinization of the extracellular compartment, no effect was noted on the intramuscular pH. This phenomenon can be explained by looking at the cell membrane and its impermeability to bicarbonate ions. Thus, only the extracellular compartment benefits from increased buffer ingestion (Costill *et al* 1984: 230-231).

According to Webster *et al* for bicarbonate loading to have the most beneficial effect four factors need to be adhered to, namely: the subjects need to be trained; the exercise bout must result in exhaustion within one to seven minutes; a treatment dose of 300 mg of sodium bicarbonate per kilogram needs to be ingested; and treatment with bicarbonate should start 90 to 120 minutes before the exercise event. Short duration, high intensity exercise is therefore utilised to maximally enhance lactic acid release and thus the pH value (Webster et al 1993: 963-964).

Recovery period pH was also shown to be higher in the group that received the buffer, over the placebo group. The type of exercise was also said to play a significant role in the pH levels (M^{c} Ardle 1994: 350-351).

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2.1.7.1 **Effective Dose**

Webster *et al* (1993: 963-964) as well as Verbitsky *et al* (1997: 337) propose that the most effective dose of bicarbonate ingestion should be 300 mg per kilogram.

2.1.7.2 **Adverse Effects of Bicarbonate Loading**

Large doses of bicarbonate loading can produce effects such as diarrhoea and vomiting and in extreme cases can be fatal. Therefore the Olympic Committee has ruled that bicarbonate ingestion is illegal during competitions (Powers and Howley 1990: 240).

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CHAPTER THREE – BIOCHEMICAL REMEDIES AND SODIUM PHOSPHATE

3.1 BIOCHEMICAL REMEDIES

3.1.1 Theory of Biochemical Remedies

To maintain a healthy physiological balance, the structure and vitality of the organs of the body rely heavily on the correct quantities and proportions of organic constituents.

Organic constituents comprise of elements of carbon, hydrogen and oxygen. Inorganic compounds do not contain carbon and hydrogen in their primary structure, whereas carbon and hydrogen always form the basis of organic compounds (Martini 1995: 40-41).

The inorganic components (or biochemical tissue salt) are absolutely essential to the structure and function of organs. According to Schussler's theory, imbalances are caused by any disturbance in the molecular motion of the inorganic components in living tissue (Boericke and Dewey 1914: 15).

The imbalance can be rectified by the administration of the same inorganic compound (or biochemical tissue salt) in small quantities. The main inorganic materials found in muscle cells are magnesium phosphate, potassium phosphate, sodium, iron and sodium chloride, where sodium phosphate is the inorganic compound mainly found in the blood plasma (Boericke and Dewey 1914 : 16-17).

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3.1.2 **Function of Biochemical Remedies**

Chapman summarised the function of the mineral salts into three points, namely:

a) These salts give rigidity and relative permanence to the skeletal tissue of which they are constituents.

b) These minerals form essential parts of the organic compounds that make up the soft tissue.

c) The salts are held in solution in the body fluids, from where they supply the material to the digestive juices and other secretions (Chapman 1973: 3).

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3.1.3 **Cellular Pathology**

Chapman states that the human body is made up of a collection of single cells, and that the physiology of the whole organism is merely the sum of the physiological activities of the separate cell. It therefore stands to reason that in order to understand the life processes of the whole body, the individual cell must be analyzed.

Research has shown that under different mineral salts in the surrounding fluid, different reactions take place in the cell. The cell will reject minerals that it does not need and absorb those that are in demand. The demand is dependant on the mineral salt concentration inside and outside the cell wall (Chapman 1973: 5).

It is therefore self-evident that mineral salts are essential for life processes and that a deficiency of the salt would inhibit or hinder metabolism. The sensible thing therefore is to restore the balance of the concentrations of mineral salts (Chapman 1973: 5-6).

Metabolism, as defined by the Oxford Concise medical dictionary, is the sum of all the chemical and physical changes that take place within the body to enable its continued growth and functioning. Metabolism involves the breakdown of complex organic constituents of the body with the liberation of energy, which is required for other processes, and the building up of complex substances (Martin 1994: 406).

These chemical and physical changes which take place are all influenced by the mineral salts, and the continued occurrence of metabolism is dependant on the presence of normal concentrations of these inorganic elements (Chapman 197: 7).

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Chapman stated the five principles of tissue salt biochemistry:

i) If the cell metabolism is normal, disease does not occur.

ii) As far as the body is concerned, nutritional substances are either organic or inorganic in nature.

iii) Metabolism of the cell is normal if the cell's nutrition is sufficient.

iv) When there is a deficiency in the inorganic mineral constituent of the cell tissue, the ability of the body to utilise nutritional material is impaired.

v) By normalising the cellular metabolism through supplying the required material, adequate cell nutrition will be restored (Chapman 1973: 10).

3.1.4 **Link between Biochemical Remedies and Homoeopathy**

There are two differences between biochemical remedies and homoeopathy. The first mentions that the use of biochemic remedies is determined by physiological chemistry alone, where homoeopathic remedies are ascertained by proving on healthy volunteers. Secondly, biochemic remedies act by way of homogenous substances, while homoeopathy attains its curative ends by way of heterogenous substances (Chapman 1973: 10).

Although both statements are correct, these biochemic remedies are active ingredients in many homoeopathic remedies. In the Homoeopathic Materia Medica these biochemic remedies are found to be complementary to the homoeopathic remedies, therefore the biochemic remedies play an individual as well as a complementary role, and the link between homoeopathy and the biochemic remedies is very strong, albeit not perfect (Chapman 1973: 10).

3.1.5 **Preparation of Biochemical Remedies**

The biochemic remedies are prepared by trituration according to the decimal scale. Trituration involves the grinding of the material with a specific amount of lactose sugar, in a pestle and mortar, for a total of three hours. This method of grinding is used to make the substance soluble in alcohol (Vitkoulkas 1980: 161).

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One part of the pure chemical is triturated with nine parts of lactose sugar for at least two hours, this gives the first decimal trituration. One part of the first decimal is then triturated with nine parts of lactose sugar to make the second trituration. This process is then repeated, each time one part of the previous trituration is used to make the following trituration, up to a sixth decimal potency (10^{-6}) (Devlin 1997 : 26).

The reason for the five subdivisions of the crude substance is to facilitate assimilation and proper diffusion into the cell and tissues of the body and corresponding prompt therapeutic action (Chapman 1973 : 11).

3.1.6 **Frequency of Dose**

One milligram of a substance is estimated to contain 16 trillion molecules. Thus to determine the dose of a biochemic remedy the amount of morbid product involved is an important factor. Accordingly in acute cases a dose every hour two is indicated, where in severe, painful affections, a dose every ten to fifteen minutes is advised (Devlin 1997 : 28).

3.2 **SODIUM PHOSPHATE**

3.2.1 **Chemical Properties**

a) Formula : $Na_2 HPO_4$, $12H_2O$

b) Specific gravity: 1,55

c) Taste: cooling saline taste

d) Solubility : soluble in 2 parts of hot water or/and six part of cold water. Insoluble in alcohol. Solutions are slightly alkaline

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e) Prepared: neutralising orthophosphoric acid with carbonate of sodium. Also made from bone-ash.

f) Crystallisation: crystallise in large, transparent monoclinic prisms containing twelve molecules of water of crystallisation.

3.2.2 **Physiological – Chemical Data**

Sodium phosphate is found in the blood, muscles, nerves and brain cells as well as in the intercellular fluids. It is the remedy for conditions arising from lactic acid build-up. The biochemical salt exerts its action by absorption of carbonic acid, taking up two molecules for every molecule of the biochemic remedy. The absorbed carbonic acid is then transported to the lungs where it is exchanged for oxygen. The biochemic remedy largely promotes the decomposition of lactic acid in the blood, thus purifying the fluid organ from lactic acid (Devlin 1997: 123).

The liver is the prime laboratory in the animal body, one of its main functions is the production of glycogen from starch and carbohydrate foods. The glycogen is then carried away to be stored in the muscular tissue. In the muscle as previously noted, it provides lactic acid that is transformed by sodium phosphate in the blood to carbonic acid and water (Devlin 1997: 124).

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3.2.3 Adverse Effects and Treatment of Acute Sodium Phosphate Ingestion

Sodium phosphate in its crude form may cause hyperphosphataemia. This in turn can lead to development of hypocalcaemia and ectopic calcification may occur due to precipitation of calcium phosphate.

Adverse effects of sodium phosphate if introduced intravenously in its crude form includes:

a) Hypocalcaemic tetany

b) Hypotension

c) Tachycaradia

d) Fever

e) Oedema

f) Acute renal failure

Treatment of the adverse effects involves withdrawal of phosphate and general supportive measures. Correction of the serum electrolyte concentrations especially calcium is essential (Reynolds 1989: 1035).

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3.3 IMPORTANCE OF *IN-VIVO* EXPERIMENTS

The *in-vivo* experimentation is very important to clarify the relationship between the substance administered and the effect on the physiological make up of the person.

What has already been established is that after oral introduction of a homoeopathic substance the first effect develops in the entire organism before it develops in the sub-cellular organelles.

Although the effect that the remedy has on the person cannot be recognised with precision, it is important that this effect be resolved, to answer questions involving homoeopathy (Ernst & Hahn 1998: 176-179).

3.4 ERGOMETRY

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The function of a bicycle ergometer is to measure the 'work' output of an individual. Bicycling has proved to be a very suitable work form, since at a given load it demands about the same energy output, whether the subject is young or old, trained or out of condition. The bicycle ergometer has been widely used in physiological laboratories ever since. This instrument provides an exact measurement of the performed external work, and thus a graded and measurable load can be applied to the subject (Fernandez-Garcia 2000: 1002-1006).

Changes in circulation, respiration and metabolism can be studied during and after work. During the last ten years, ergometry has been applied within sport, physiology, hygiene, industry and medicine. Consequently the bicycle ergometer has become an important aid in the evaluation of the physical work capacity and physical condition.

The muscle capacity for variation in metabolism surpasses that of any other tissue, and calculations indicate that the muscular metabolic rate can increase by a factor of 100 from the resting condition. In this situation major demands are placed upon the service organs particularly upon the respiratory and circulatory apparatus. The available energy is obtained via the combustion of fat and carbohydrates in the muscles (Astrand 1950: 7-16).

In research directed at the regulation of respiration and circulation, the investigation must be extended to work tests, including both submaximal and maximal work (M^{c} Ardle 1994: 274).

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CHAPTER FOUR – METHODS AND MATERIAL

4.1 MATERIALS

4.1.1 Accutrend® Lactate Meter

The Accutrend® lactate meter is used to determine the lactate concentration quickly and easily in the blood. The meter uses light impulses to measure the colour produced on the lactate test strip during the reaction, and compares this with the baseline value. The higher the lactate concentration, the greater the colour change. The measurements range from 0,8 – 22 mmol per litre of blood.

Before measurement starts the meter has to be set on the blood mode, not the plasma mode as only blood is used and not plasma. The meter also needs to be calibrated. This serves to adjust the meter to the specific characteristics of the pack of test strips being used, and thus ensures accurate results.

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4.1.2 Lactate Measurement

The Accutrend® lactate meter was used to determine lactate concentrations in more than one person. In order to rule out the risk of infections such as AIDS and hepatitis, the blood was applied to the strip outside the meter. Capillary blood was used, therefore a new lancet for each person was required. If the meter was contaminated with blood or if contamination was suspected, the meter was disinfected with 70% alcohol. Used lancets and test strips was collected in a rigid container with a lid and disposed of accordingly.

4.1.3 **Lactate Test Strips**

BM-lactate test strips are used for quantitative determination of lactate in the range 0,8–22 mmol per litre in the blood, by using the Accutrend® reflectance photometer. Blood seeps through the yellow protective mesh into a glass fibre fleece where the erythrocytes are retained. Only the plasma reaches the detection film. Lactate is determined by reflectance photometry via a colorimetric lactate oxidose mediator reaction. Only capillary blood may be used. As previously mentioned for each new pack of test strips the Accutrend® meter needs to be calibrated. The meter will not accept a lactate test strip for which it has not been calibrated.

When using individually sealed test strips the foil must be undamaged. The lactate test may be affected by a haematocrit value exceeding 55%, and an intravenous infusion of ascorbic acid. The pack must be stored at temperatures below 2°C or above 30°C.

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4.1.4 **Softclix®II Lancing Device and Lancets**

Softclix®II is an easy to use lancing device for obtaining blood from the tip of the finger, virtually without pain. Depth of penetration should be selected so that only the amount of blood necessary for testing is obtained. For this purpose the lancet device can be set to different penetration depths ranging from 0,5mm to 5,5mm. These values are indicated on the cap by the numbers 1 to 5.

Recommended penetration settings:

0,5 – 1,5 for soft skin
2 – 3,5 for normal skin
4 – 5,5 for thicker skin

4.2 METHODS

4.2.1 Blood Collection Method and Measurement

After the lactate meter had been switched on, a BM lactate strip was inserted into the slot at the bottom edge of the meter, in the direction of the arrows. The flap of the meter was opened as soon as the meter had read the code on the strip.

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The finger was pierced with the Softclix lancing devise and a drop of blood collected on the mesh of the BM lactate strip, without touching the pad directly with the fingertip.

The flap of the meter was closed and the results were displayed after a 60 second period. If the value measured was below 0,8mmol/litre the meter displayed low (LO). If the measure value was at or above 22 mmol/litre the meter displayed high (HI).

4.2.2 Medication Administration

The readings, medication administration and testing was done by the biokineticist at the centre. The experimental and placebo groups were randomly selected.

Before the medication was introduced the first lactate measurement was conducted (reading one). The biochemic remedy, sodium phosphate, purchased from Natura was administered in tablet form. The participants where instructed to select a plastic vial containing four tablets. Each of the plastic containers where labelled A or B. The vials that contained the active ingredients were labelled Sample A, and the placebo vials were labelled Sample B. The placebo tablets were also purchased from Natura manufacturers. They looked and tasted exactly the same as the active ingredient tablets.

The participants were instructed to place the tablets under their tongues to absorb the sodium phosphate D6 quicker into the bloodstream. As soon as the first lactic acid measurement was completed, the first tablet was introduced. Following the first tablet dosage the second, third and fourth tablet was administered at 15 minute intervals. As soon as the last tablet was taken and dissolved, the Wingate Anaerobic Test commenced.

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4.2.3 **Wingate Anaerobic Test**

Before the first lactate reading, the participants were asked to provide their weight and length. These figures were used to determine the weight in kilograms resistance at which they would cycle. Approximately 7,5% of the body weight was used to determine the weight of resistance. The length was important for the setting of the bicycle seat so that maximum quadricep force could be determined. The Monarch 834E Medicycle was linked to a computer that determined the variables.

The participants were instructed to cycle as fast as they could for 30 seconds. As soon as the participants reached their maximum speed, the weight was dropped and the 30 second time period commenced.

Following the 30 second time period the participants where instructed to rest for a period of one and a half minutes before the second lactate reading was taken (reading two).

4.2.3.1 Information Associated with Wingate Test

Together with the lactate measurement other factors where also monitored by the Wingate test. Refer to **APPENDIX A** (lactic acid evaluation form).

4.3 PARTICIPANTS

Only male participants were used in this study. The age of the participants was limited to between 18 and 23 years of age, the reason being that their physical activity was expected to be at its peak and that most of the participants would not have any other metabolic diseases or health problems.

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Rugby players were mostly used as this sports activity closely resembles high intensity, short duration anaerobic exercise. Before the tests were started the participants were required to fill in two forms. The first was the Health Status Questionnaire (**APPENDIX B**) and the second the Physical Activity Readiness Questionnaire (**APPENDIX C**). These questionnaires were used to assess the physical status of the participants to try and eliminate any other factors that could influence the lactic acid testing.

4.3.1 **Sampling**

Participant samples were taken from different Rugby Clubs in the Johannesburg and West Rand area. They were addressed in a group as to the aim of the study and the methodology to be applied to get the results. Volunteers where then requested from the groups. The participants were recruited at their training facilities and permission was requested and received by the different Club Managers (**APPENDIX I**).

4.4 APPLICATIONS OF LACTATE MONITORING

A lactate level determination in capillary blood is used to assess the physical performance limits of people during strenuous physical exertion and to monitor the intensity of training by determining lactate build-up during training.

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4.5 STATISTICAL ANALYSIS

A t-test was performed on the sample group. The computer programme used to analyse the data was termed the SPSS for MS Windows. The probability level was set at $p < 0,05$.

CHAPTER FIVE

5.1 RESULTS

Two groups where analysed. The control group or Group B received the placebo tablets. The experimental group or Group A received the active substance (Sodium Phosphate D6). Two readings of each group where taken. Reading one determined lactic acid levels in the bloodstream before ingestion of sodium phosphate D6 or placebo. Reading two determined lactic acid levels in the bloodstream after administration of sodium phosphate D6 (or placebo) and high intensity short duration exercise. These readings were measured in both the control and experimental group.

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The difference between reading one and reading two for each participant of each group was calculated. The mean for these value differences between reading one and reading two were evaluated and plotted on a histogram along with the means of reading one and reading two for each group.

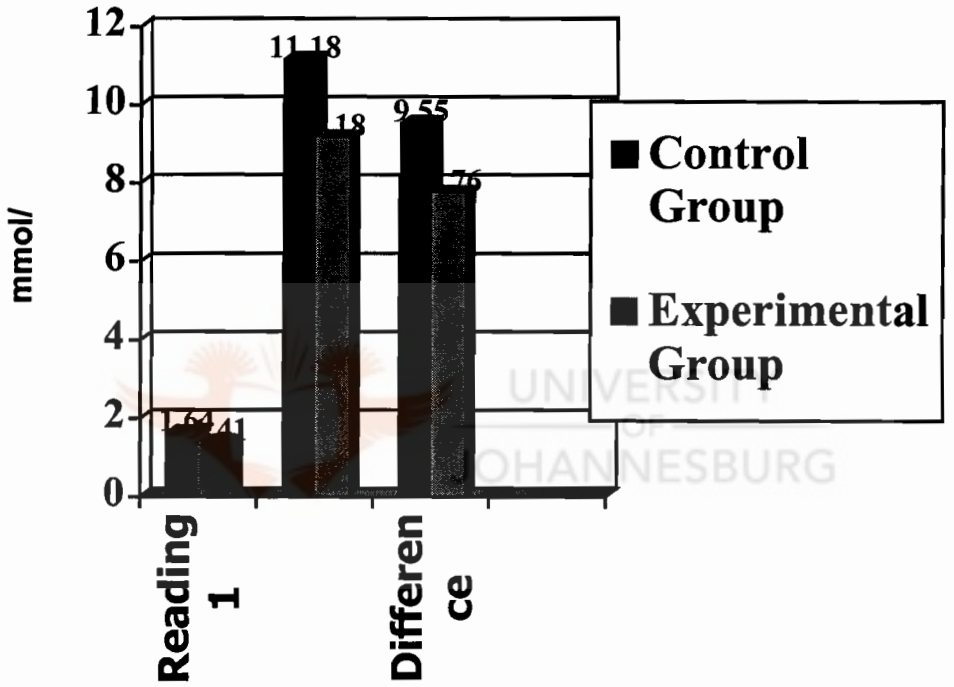

Fig 5.1 Illustrates histogram of group A versus group B in terms of their readings before and after exercise and the difference between reading one and reading two.

5.1.1 Descriptive Results

The average age of the participants was 20 years and all of the participants had a height of between 155cm and 195cm. The mean for their average power was 603,76 watts (w), and their weight ranged between 52 and 117 kg.

The mean for reading one was 1,522 mmol/L with the mean for reading two 10,13 mmol/L. The difference value between reading one and reading two had an average of 8,6 mmol/L. (For a more complete descriptive analysis, refer to **APPENDIX D** and **APPENDIX E**).

5.1.2 Analytical Results

5.1.2.1 Difference value between Reading 1 and Reading 2

Statistical evaluations were made on the means of the difference value between reading 1 and reading 2 of the respective groups. The evaluation revealed that the difference value for the control group was significantly higher compared to the experimental group ($t = 4,97$ and $p = 0,032$). Therefore a statistical significant difference exists between the means of the different groups (mean difference = 1,79).

5.1.2.2 Difference between Reading 2 of Different Groups

Comparing reading 2 of the control versus experimental group also reflects a significant statistical difference ($t = 4,19$ and $p = 0,048$). The mean difference between the two groups was 2,00.

5.1.2.3 Variables

Both the control and experimental groups were statistically evaluated in terms of their age, weight, height and average power. The mean values did not reflect any statistical significant difference between them. (Refer to **APPENDIX F, APPENDIX G** and **APPENDIX H** for a complete analytical summary).

5.1.2.4 Multiple Regression

A stepwise multiple regression evaluation was also performed to assess if any of the variables would have influenced the outcome of the results. According to the evaluation, the influence of the variables on reading one had a R-square value of 1,00 and reading two had a R-square value of 0,944.

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CHAPTER SIX

6.1 DISCUSSION

The central issue of this study was to investigate the influence of acute ingestion of a biochemical remedy sodium phosphate, on the lactic acid levels during high intensity, short duration exercise, and if it could be used to reduce onset of muscle fatigue.

Published works on the effect of sodium bicarbonate on anaerobic performance show variable results (Webster *et al* 1993*:* 963 – 964 and Wijnen *et al* 1994: 130–132). Reasons for the variable results are that (1) the intensity of the resistance exercise was not high enough; (2) the size of the samples were too small; (3) confusion over the length of the exercise test for complete exhaustion; and (4) some individuals were more responsive than others to sodium bicarbonate ingestion (Webster *et al* 1993: 964).

The methodology adopted was to use the Wingate anaerobic test to provoke an isometric contraction of the quadriceps femoris skeletal muscle. The rationale behind this methodology was as follows:

a) Because not all participants were of equal fitness levels, the Wingate test is designed to give an accurate reflection of the participants anaerobic capabilities irrespective of fitness levels.

b) Although, in the cycling exercise, several muscle groups are being activated, involving both peripheral and central mechanisms, it has been reported that in high intensity bicycle exercise the dominant

subjective sensation limiting further exercise was fatigue of the quadriceps muscle.

The Wingate test was also used to maximally increase intensity and therefore fatigue in each participant. The size of the sample was also increased from 36 to 40 to gain better readings and better interpretation of the results.

The ergogenic properties of sodium phosphate D6 has never in the past been the focus of investigations, contrary to sodium bicarbonate which has (Verbitsky *et al* 1997: 336). Previous studies done on sodium bicarbonate ingestion have proved that it does enhance the buffer capacity of the body (Mc Ardle 1994: 408-411).

Dealing with Homoeopathy and its dilution factor it was not anticipated that sodium phosphate D6 would have any physiological effects or contribute to the buffer capacity of the body and hence delay exhaustion and improve performance. The results obtained from the research have however proven that sodium phosphate in a 10^{-6} dilution does reduce lactic acid build-up. Therefore it could be argued that it would buffer a pH decrease resulting from high intensity, short duration exercise.

The direct evidence of this statement is reflected in the difference in the lactic acid readings between the control and experimental group. The results obtained from the first reading showed no significant difference between the control and experimental group ($p = 0.161$). When referring to the histogram, group A had a mean value for reading one of 1.41 mmol/L, whereas group B had a mean value of 1.64 mmol/L. A statistical significant difference can be seen when the mean values of reading two is reflected on the histogram ($p = 0.048$). Group A had a mean value for reading two of 9.18 mmol/L with group B a higher mean value of 11.18

mmol/L. To further assess any difference between the central and experimental group, a value was used that reflected the difference between reading one and reading two in both the control and experimental groups.

On the histogram the value that reflects the difference between reading one and reading two of the control and experimental groups revealed a significant statistical difference ($p = 0.032$). The mean value for group A was 7.76 mmol/L, group B had a mean value of 9.55 mmol/L.

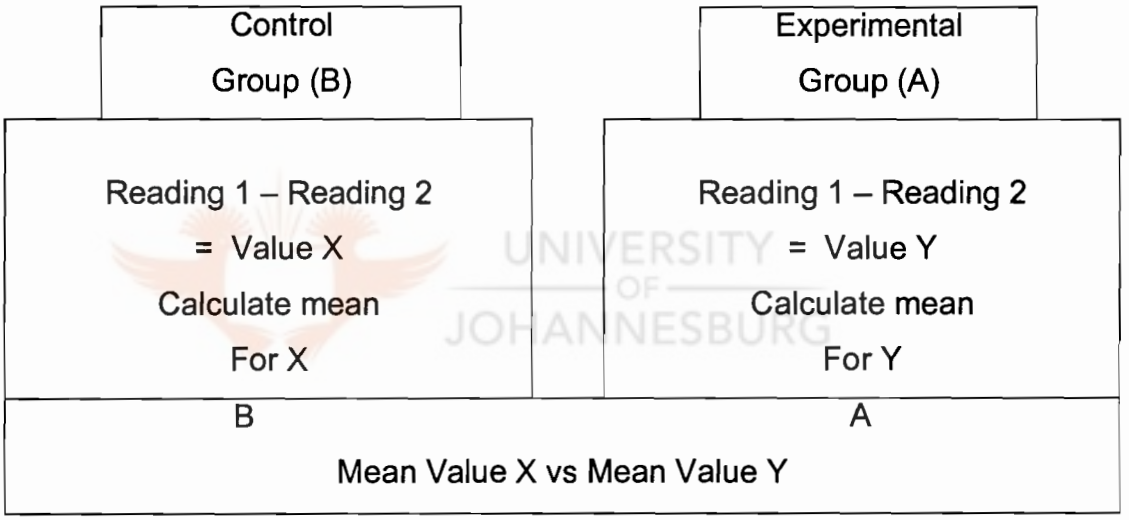

Fig 6.1 Calculation of the value reflecting the difference between reading one and reading two of control and experimental groups

Other variables needed to be scrutinised before a positive conclusion could be drawn. A multiple regression analysis was used to assess the influence of all the variables on reading one and reading two. The evidence obtained from these analyses was that the variables did not influence the readings and were therefore not considered as significant in the outcome of the test.

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Thus, in contrast to earlier investigations that attempted to assess the influence of sodium bicarbonate ingestion, sodium phosphate D6 was used to increase buffer capacity. Sodium phosphate D6 had sufficient time to facilitate the efflux of lactic acid from the muscle, thereby lessening the drop in extramuscular and possibly intramuscular pH. This study supported the concept that the accumulation of lactic acid in muscle is responsible, at least in part, for fatigue and exhaustion in short duration, high intensity exercise.

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CHAPTER SEVEN

7.1 CONCLUSION

On the basis of the results obtained, it may be concluded that acute ingestion of sodium phosphate D6 is an effective means for increasing the buffer capacity of the body and thus reduce muscle fatigue and prolong exercise duration.

So far little conclusive information on biochemical remedies and their pharmacological effects is available. Review of the literature reveals a gap in our knowledge not just of the biochemical remedies, but also the metabolic processes associated with fatigue.

It has been pointed out that the calcium ion might also be an important factor in the onset of muscle fatigue, which if substantiated, will link fatigue processes and muscle pain.

Whatever the mechanism of the sodium phosphate D6 turns out to be, the fact that a mechanism exists seems to be of considerable importance in the regulation of muscle performance and buffer effects.

Acidosis alone does not appear to account for all of the contractile suppression seen during fatigue. However, it does play a significant role both directly and indirectly on muscle contraction. Thus it must also be kept in mind that acidosis is a natural process in the body that is part of a protective feedback mechanism which prevents overload that may result from mismatching of muscle perfusion with its work load.

7.2 RECOMMENDATIONS

Further studies could look at

(i) Sodium phosphate as a mineraloid;

(ii) Participants could be evaluated in terms of a set weight eg. only 80-90kg;

(iii) Other tissue salts can replace sodium phosphate to evaluate their effects on lactic acid;

(iv) Females can do the test to assess if gender would influence the results;

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(v) The effect of sodium phosphate on calcium concentrations can also be assessed, due to the fact that calcium is such an important factor for muscle contraction;

(vi) Participants can be screened in terms of their average power to eliminate this variable;

(vii) Participants can be required to do the test twice, once with a placebo the second time with the active substance; and

(viii) Other investigations can be implemented to assess lactic acid build-up in the system (urine dipsticks).

APPENDIX A

LACTIC ACID EVALUATION FORM

Name & Surname: .....

Weight: ..... kg

Height: ..... cm

Date of birth: ...../...../.....

Peak Power: ..... w

Peak Power/kg: ..... w/kg (11,8)

Minimum Power: ..... w

Minimum Power/kg: ..... w/kg

Average Power: ..... w

Average Power/kg: ..... w/kg

Power drop: ..... w/s

Power drop/kg: ..... w/s/kg

Fatigue index: ..... %

Time	5	10	15	20	25	30
RPM						
Power						

RPM at start: .....

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Health Status Questionnaire

Subject No……..

Instructions:

Complete each question accurately. All information provided is confidential.

Part 1. Information about the individual

1. …… ……
Name **Date**

2. …… ……
Mailing address **Home phone**

…… ……
Business phone

3. …… ……
Personal physician **Phone**

4. ……
Address

5. …… ……
Person to contact in emergency **Phone**

6. **Date of birth :** ……
Month **Day** **Year**

7. **Number of hours worked per week:**
Less than 20 …… 20-40 ……. 41-60 …… Over 60

8. **More than 25% of time spent on job (circle all that apply)**
Sitting at desk Lifting or carrying loads Standing Walking Driving

Part 2. Medical history

9. **Circle any who died of heart attack before age 50:**

Father Mother Bother Sister Grandparent

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10. Date of

Last medical physical exam: .....
Year

Last physical fitness test: .....
Year

11. Circle operations you have had:

Back	Heart	Kidney	Eyes	Joint	Neck
Ears	Hernia	Lung	Other		

12. Please circle any of the following for which you have been diagnosed or treated by a physician or health professional:

Alcoholism	Diabetes	Kidney problem
Anaemia, sickle cell	Emphysema	Mental illness
Asthma	Eye problems	Neck strain
Back strain	Gout	Phlebitis
Bleeding trait	Hearing loss	Rheumatoid arthritis
Bronchitis, chronic	Heart problem	Stroke
Cancer	High blood pressure	Thyroid problem
Cirrhosis, liver	Hypoglycaemia	Ulcer
Concussion	Hyperlipidemia	Other .....
Congenital defect	Infectious mononucleosis	

13. Circle all medicine taken in last 6 months:

Blood thinner	Epilepsy medication	Nitroglycerin
Diabetic	Heart rhythm medication	Other .....
Digitalis	High blood pressure medication	
Diuretic	Insulin	

14. Any of these health symptoms that occurs frequently is the basis for medical attention. Circle the number indicating how often you have each of the following:

5 = Very often
4 = Fairly often
3 = Sometimes
2 = Infrequently
1 = Practically never

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a.	**Cough up blood** 1 2 3 4 5	g.	**Swollen joints** 1 2 3 4 5
b.	**Abdominal pain** 1 2 3 4 5	h.	**Feel faint** 1 2 3 4 5
c.	**Low-back pain** 1 2 3 4 5	i.	**Dizziness** 1 2 3 4 5
d.	**Leg pain** 1 2 3 4 5	j.	**Breathless with slight exertion** 1 2 3 4 5
e.	**Arm or shoulder pain** 1 2 3 4 5	k.	**Palpitation of fast heart beat** 1 2 3 4 5
f.	**Chest pain** 1 2 3 4 5	l.	**Unusual fatigue with normal activity** 1 2 3 4 5

Part 3: Health-related behaviour

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15. Do you now smoke? Yes ..... No .....

16. If you are a smoker, indicate number smoked per day:

Cigarettes: 40 or more ... 20-39 .... 10-19 .... 1-9 ....
Cigarettes or pipes only: 5 more or any inhaled .....
Less than 5, none inhaled .....

17. Do you exercise regularly? Yes ..... No .....

18. How many days per week do you accumulate 30 minutes of moderate activity?

0 1 2 3 4 5 6 7 days per week

19. How many days per week do you normally spend at least 20 minutes in vigorous exercise?

0 1 2 3 4 5 6 7 days per week

20. Can you walk 6,4 km briskly without fatigue? Yes ..... No .....

21. **Can you jog 4,8km continuously at a moderate pace without fatigue?**
Yes …….. No …….

22. **Weight now: …… One year ago: …….. Age 18: ……..**

Part 4: Health-related attitudes

23. These are traits that have been associated with coronary-prone behaviour. Circle the number that corresponds to how you feel:

6 = Strongly agree
5 = Moderately agree
4 = Slightly agree
3 = Slightly disagree
2 = Moderately disagree
1 = Strongly disagree

I am an impatient, time-conscious, hard-driving individual

1 2 3 4 5 6

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24. List everything not already included in the questionnaire that might cause you problems in a fitness test or fitness program:

……..

……..

……..

Physical Activity Readiness Questionnaire

Name of participant _____

Date _____

PAR Q & YOU

PAR-Q is designed to help you help yourself. Many health benefits are associated with regular exercise, and the completion of PAR-Q is a sensible first step to take if you are planning to increase the amount of physical activity in your life.

For most people physical activity should not pose any problem or hazard. PAR-Q has been designed to identify the small number of adults for whom physical activity might be inappropriate or those who should have medical advice concerning the type of activity most suitable for them.

Common sense is your best guide in answering these few questions. Please read them carefully and check (√) the ☐ YES or ☐ NO opposite the question if it applies to you.

YES	NO	
☐	☐	1. Has your doctor ever said you have heart trouble?
☐	☐	2. Do you frequently have pains in your heart and chest?
☐	☐	3. Do you often feel faint or have spells of severe dizziness?
☐	☐	4. Has a doctor ever said your blood pressure was too high?
☐	☐	5. Has your doctor ever told you that you have a bone or joint problem such as arthritis that has been aggravated by exercise or might be made worse with exercise?
☐	☐	6. Is there a good physical reason not mentioned here why you should not follow an activity program even if you wanted to?
☐	☐	7. Are you over age 65 and not accustomed to vigorous exercise?

If You Answered

YES to one or more questions

If you have not recently done so, consult with your personal physician by telephone or in person BEFORE increasing your physical activity and/or taking a fitness appraisal. Tell your physician what questions you answered YES to on PAR-Q or present your PAR-Q copy.

programs

After medical evaluation, seek advice from your physician as to your suitability for

- unrestricted physical activity starting off easily and progressing gradually;
- restricted or supervised activity to meet your specific needs at least on an initial basis. Check in your community for special programs or services.

NO to all questions

If you answered PAR-Q accurately, you have reasonable assurance of your present suitability for

- A GRADUATED EXERCISE PROGRAM—a gradual increase in proper exercise promotes good fitness development while minimizing or eliminating discomfort.
- A FITNESS APPRAISAL—Canadian Standardized Test of Fitness (CSTF).

postpone

If you have a temporary minor illness, such as a common cold.

Developed by the British Columbia Ministry of Health. Conceptualized and compared by the Multidisciplinary Advisory Board on Exercise (MABE). Translation, reproduction and use in its entirety is encouraged. Modifications by written permission only. Not to be used for commercial advertising in order to solicit business from the public.

Reference PAR-Q Validation Report British Columbia Ministry of Health 1978.
Produced by the British Columbia Ministry of Health and The Department of National Health and Welfare.

DESCRIPTIVE RESULTS SUMMARY

	Age (years)	Length (cm)	Average Power (w)	Weight (kg)	Readings before Exercise (mmol/L)	Readings after Exercise & Medication (mmol/L)	Difference between Readings (mmol/L
1. Mean	20,725	180,725	603,767	79,55	1,522	10,130	8,608
2. Median	20,00	182,00	568,865	75,50	1,200	10,050	8,800
3. Mode	19,00	176,00	354,25	65,00	0,800	12,30	8,200
4. Range	6,00	40,00	616,87	65,00	4,50	15,60	15,90

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DESCRIPTIVE RESULTS SUMMARY - CONTINUED

	Age (years)	Length (cm)	Average Power (w)	Weight (kg)	Readings before Exercise (mmol/L)	Readings after Exercise & Medication (mmol/L)	Difference between Readings (mmol/L)
5. Minimum	18,00	155,00	354,25	52,00	0,800	2,60	1,40
6. Maximum	24,00	195,00	971,12	117,00	5,300	18,20	17,30
7. Standard deviation	1,739	8,342	152,725	15,247	0,896	3,793	3,790

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ANALYTIC RESULTS SUMMARY

Mean Values	Age (years)	Length (cm)	Average Power (w)	Weight (kg)	Reading 1	Reading 2	Difference between Readings
1. Control Group	20,263	179,42	581,314	76	1,636	11,184	9,547

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ANALYTIC RESULTS SUMMARY - CONTINUED

Mean Values	Age (years)	Length (cm)	Average Power (w)	Weight (kg)	Reading 1	Reading 2	Difference between Readings
2. Experimental Group	21,142	181,904	624,082	82,761	1,419	9,176	7,757

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ANALYTIC RESULTS SUMMARY - CONTINUED

Mean Values	Age (years)	Length (cm)	Average Power (w)	Weight (kg)	Reading 1	Reading 2	Difference between Readings
3. Mean Differences	-0,879	-2,483	-42,768	-6,761	0,217	2,008	1,790

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SUBJECT INFORMATION AND CONSENT FORM

Efficacy of Sodium Phosphate D6 as a buffer in delaying the onset of muscle fatigue during short duration, high intensity exercise.

The purpose of this study is to determine the buffer capacity capabilities of Sodium Phosphate D6, by assessing if the onset of muscle fatigue will be delayed, under anaerobic conditions.

You will be placed into two groups of eighteen participants each, one is an experimental group and the other a control group. The experimental group will receive the treatment, while the control group will receive a placebo. Neither the subjects nor the Researcher will know who will receive treatment.

All subjects will be requested to do an anaerobic bicycle ergometer test that will last for 30 seconds. You will be requested to take the Homoeopathic medicine at fifteen minutes interval, commencing one hour before the event.

Two blood samples will be taken from each subject by way of a finger-lancing device, and the blood collected on a lactate strip that will be inserted into a lactate meter for reading. The first test will be done before administration of the remedy and the second reading two minutes after completion of the event.

The potential benefits for those who receive the study medicine, is that the treatment may reduce the onset of muscle fatigue by acting as a adjunct buffer to the normal buffer systems prevalent in the body and therefore increase exercise duration.

Participation in the study is voluntary and you are free to refuse to participate or to withdraw your consent and to discontinue participation at any time. A signed copy of this consent form will be made available to you.

I have fully explained the procedures, identifying these, which are investigational, and have explained their purpose. I have asked whether any questions have arisen regarding the procedures and have answered these questions to the best of my ability.

Date: ..... Researcher: .....

I have been fully informed as to the procedures to be followed, including those which are investigational and have been given a description of the attendant discomforts, and benefits to be expected and the appropriate alternate procedures. In signing this consent form I agree to this method of treatment and I understand that I am free to withdraw my consent and discontinue my participation in this study at any time. I also understand that if I have any questions at any time, they will be answered.

Date: ..... Patient: .....

or Guardian/Next of Kin: .....

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UNIVERSITY OF JOHANNESBURG

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