Review Article

MUSCLE PHYSIOLOGY AND ADAPTOGENS

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ABBREVIATIONS
ACh — Acetylcholine
ADP — Adenosine diphosphate
ATP — Adenosine triphosphate
CP — Creatine phosphate
Pi — Inorganic phosphate
RNA — Ribonucleic acid
TCM — Traditional Chinese Medicine

Introduction

Trainers of athletes (human or non-human) and human athletes themselves are always looking for ways to enhance performance, the ability to do exercise well; increase stamina via improving circulation and boosting energy and health; and increase endurance (duration of exercise before exhaustion). To understand what will improve these parameters of athletics, one must first fully understand the physiology of muscle in order to improve the exercise.

Adaptogens are a classification of herbs that are known and documented to improve muscle physiology. This group of herbs helps bodies cope with stress, physical or otherwise. The ways in which adaptogens aid muscles have been well-researched.

Muscle Physiology

There are three 3 types of muscle in the mammalian body: smooth, cardiac, and skeletal. Muscle is responsible for all movement in the body, internally and externally. Skeletal muscle comprises more than half our body weight. It controls every conscious action, and some unconscious as well. Muscles have functions besides movement, including maintaining posture, stabilizing joints and generating heat.

Muscle fiber and muscle cell are synonymous terms: a muscle cell is multinucleate and runs the length of the muscle itself. The many nuclei are needed to make proteins locally for muscle function. Muscle fibers are bundled into fascicles surrounded by connective tissue called perimysium. A "muscle" is a bundle of fascicles surrounded by an epimysium. The perimysium and epimysium fuse into a tendon that attaches the muscle to a bone, usually across a joint. One end of a muscle is the origin and the other is the insertion — muscle contraction is always toward the origin.

A muscle cell is broken down into sarcomeres. Sarcomeres are the contractile unit and are comprised of myofilaments. These myofilaments have 2 main proteins, actin and myosin. These proteins are the backbone of the sliding filament theory, which was discovered in 1954, and is still undisputed. The sliding filament theory states that actin has myosin binding sites. When the muscle is relaxed, these binding sites are covered by another protein called tropomyosin. When the muscle is stimulated to contract, these binding sites uncover and myosin binds to the actin. Calcium, which is stored in the sarcoplasmic reticulum (an organelle similar to the endoplasmic reticulum, but specific to muscle cells), triggers the protein troponin to shift the tropomyosin off the binding sites on the actin. Calcium is pivotal to muscle contraction; it is the only ion that causes shortening, and it controls the strength and duration of the contraction.

When myosin and actin bind, these are called cross-bridges. Myosin has 2 regions, sub-fragments 1 and 2 (S1 and S2). The S1 region of myosin is flexible, containing multiple hinges, to "walk" along actin, and the S2 region also is flexible. In the myosin-actin cycling process, myosin reaches forward, binds to actin, contracts, releases actin, and then repeats. The binding of the myosin to the actin is called a cross-bridge; this bridge extends from the thick myosin filaments to the thin actin filaments. The contraction of myosin's S1 region is called the power stroke, and this power stroke requires energy via the hydrolysis of adenosine triphosphate (ATP) (1).

Muscles are stimulated to contract by neural impulses via the neuromuscular junction. A motor neuron stimulates a skeletal muscle, but it is not a 1:1 relationship. A motor unit consists of the motor neuron plus all the muscle cells it stimulates. This varies in number. Acetylcholine (ACh) is the neurotransmitter that is released by the motor neuron and travels across the synaptic cleft to stimulate the muscle. Once the ACh is released, the action potential causes an "all or nothing" response: the muscle will twitch. The degree of force of the muscle's response is graded by the amount of ACh released. Therefore, the control of muscle contraction is with the neural stimulation, not the muscular response.

There are 4 types of graded responses: twitch, a single brief contraction; summing of contractions in which the stimulation recurs in an additive way before the muscle is relaxed; unfused/incomplete tetanus with incomplete relaxation in between contractions; and fused/complete tetanus with no relaxation between contractions resulting in a smooth sustained contraction.

Adenosine triphosphate (ATP) is the energy used for muscle contractions. The hydrolysis of ATP to create energy is used in 2 parts of the myosin-actin cycle. The myosin S1 head uses the energy released from the cleavage of ATP into adenosine diphosphate (ADP) and phosphate to bind to the actin. Then the release of the phosphate energizes the contraction of the myosin S1 (1). ATP is synthesized in mitochondria with more mitochondria enabling production of more ATP, longer duration of muscle contraction, and more endurance. Many studies point to the idea that adaptogens increase the number of mitochondria in the muscle cells.

There are 4 sources of ATP, depending on the length of muscle use. Free ATP in the muscle cell lasts about 3 seconds. The phosphocreatine pathway, which is anaerobic, lasts 10–20 seconds. Creatine is stored in the muscle cell as phosphocreatine, and ATP is stored in the cell as ADP; creatine kinase enzyme transfers the phosphate from phosphocreatine to ADP, forming ATP. The glycolysis pathway is also anaerobic, but it lasts 90–120 seconds. In glycolysis, glucose in the cytoplasm of the cell is broken down into 2 pyruvates and 2 ATPs, with the byproducts of lactic acid and hydrogen. The last pathway is aerobic which theoretically lasts indefinitely. This occurs in mitochondria, and the nutrients come from carbohydrates primarily and fats secondarily. Glucose is again broken down into pyruvate but in the presence of oxygen, which releases 32 ATPs but much more slowly.

When muscle is fatigued, it will no longer contract. Muscle fatigue is a sequela of any 1 of 3 situations: tissue oxygen deprivation, glycogen or phosphocreatine depletion, or an increased level of lactic acid in the blood and/or muscle (2).

There are 3 types of muscle fibers: slow oxidative, intermediate, and fast glycolytic. These can be understood as they manifest in different horse breeds. Slow oxidative fibers (also called Type I fibers) are loaded with myoglobin (muscle cells' equivalent of hemoglobin), which makes them red and bloody. They use primarily an aerobic pathway, and therefore contain many mitochondria, which is the organelle responsible for aerobic energy formation. They are weak but fatigue resistant, and used for endurance. Since they are more repeatedly stimulated than fast fibers, these cells contain higher levels of intracellular calcium. This is the primary fiber type in an Arabian horse. Intermediate fibers are in between, as is seen in Thoroughbreds; they race intermediate distances. The fast glycolytic fibers (also called Type II fibers) are pale and do not contain myoglobin. They use anaerobic pathways and are quick to fatigue but very strong. This is the primary fiber type in a Quarter Horse. All muscles are heterogeneous — they contain a mix of fibers. Formation of slow fibers is neurally driven, but the formation of fast fibers is thyroid hormone dependent.

Muscle is dynamic as it continuously adapts in a variety of ways, from the fiber type to the number of sarcomeres. Fiber type changes are precipitated by the frequency of the activity, while muscle size (number of sarcomeres and muscle fibers) is precipitated by the weight endured during the exercise (3). Exercise increases muscle size, strength, and/or endurance. Endurance increases the number of mitochondria per cell such that the more mitochondria, the more ATP produced. Size and flexibility come from an increased number of sarcomeres, and stretching causes the production of new sarcomeres. The ways in which different exercises cause changes in the muscles and the different energy source pathways are the rationale for different athletes eating and training differently. Sprinters need more sarcomeres to move all at once, while endurance athletes need more mitochondria to make more ATP through the aerobic pathway. Sprinters can eat diets high in protein to make sarcomeres while endurance athletes need carbohydrates to have an energy source for aerobic glycolysis (4).

Adaptogens

In 1969, Russian doctor Israel Brekhman coined the term "adaptogen" and described it as follows:

> "(a) An adaptogen should be innocuous and cause minimal disorders in the physiologic functions of an organism; (b) The action of an adaptogen should be nonspecific, i.e., it should increase resistance to adverse influences of a wide range of factors of physical, chemical, and biological nature; (c) An adaptogen may possess normalizing action irrespective of the direction of the foregoing pathologic changes" (5).

Panossian and Wikman further refined Brekhman's definition to state that adaptogens must not only reduce damage from stress but should also be stress-protective; they must be stimulatory, and cause increased work capacity and mental performance, especially during stress and fatigue; and adaptogens must be normalizing — they cannot hinder normal body functions, but instead should enhance healthy functioning (6).

Stress is an important adaptogenic concept as basically adaptogens increase the body's resistance to stress. Stress has been defined as a "convenient, but imprecise term" that refers to either an external threat or to the internal response to the threat (7).

Another important herbal concept is "amphoterism," which is the normalizing effect of an herb. Herbs that are amphoteric bring a condition that is either high or low back to normal. This is very important to keep in mind when dealing with adaptogens and athletes, as many studies do not show much effect on fit athletes. These athletes are already "normalized" to the exercise intensity; the role of the adaptogen is to make an unfit athlete perform like a fit athlete.

Adaptogens have long been used by athletes and have become more well-known around the world due to the successes of Russian and Chinese Olympic athletes. A literature search as well as contact with some oversight committees revealed no evidence of adaptogens being banned by any oversight committee, including those of racetracks and the Olympics. For athletes, they improve performance by increasing time to fatigue as well as recovery from fatigue. However, the exact mechanism(s) of action by which they achieve these effects is unknown to date. There are many postulations but no proven theories.

Adaptogenic Herbs

Panax ginseng

Panax ginseng is in the family Araliaceae and is native to China and Korea. Ironically, in China, the favored ginseng species is *Panax quinquefolius*, which is native to the United States. In China it is called "t'u-tsing" which loosely translates to vital energy of the soil (8). Ginseng is said to owe its adaptogenic properties to the life-force it borrows from the earth (8). The part used is the root, and it is at its most medicinal when it is 7–8 years old. The length of time it takes to grow a quality root and the fact that it is hard to grow makes ginseng very expensive as well as often adulterated. It is on the United Plant Savers "at risk" list.

Ginseng is considered to have only one active constituent, ginsenosides, which are saponins. The lack of alkaloids in the plant is the main reason it is considered safe to use long-term. It is hard to pin down traditional uses for ginseng as it was used as a general "panacea" to treat everything — this goes back to the concept of adaptogen: they work systemically on the body as a whole, so they treat and/or prevent almost everything. In fact, *Panax*, the genus, is derived from the Greek *Panakos* (a panacea), which is a reference to the miraculous virtue the Chinese believed this herb has and the fact that they consider ginseng a wonderful remedy for most diseases (9). Traditional Chinese Medicine (TCM) has used ginseng for over 7000 years.

There are a myriad of studies using ginseng to aid athletes, both human and non-human. These studies propose multiple mechanisms of action and results. Effects of ginseng researched include: increased free fatty acid utilization in lieu of glucose for energy demands, increased capillary density and oxidative capacity, improved mitochondrial metabolism, inhibition of corticosterone increase, mediation of the hypothalamic-pituitary-adrenal axis and enhanced nitric oxide synthesis (10–14). Numerous studies have been performed on ginseng, many consisting of 4 experimental groups: placebo, exercise only, ginseng only, and exercise with ginseng. There was no additive effect of exercise and ginseng, and exercise and ginseng categories had similar results. Additionally, in studies of fit animals/humans, ginseng showed no effect. Due to these findings, many researchers felt that they "failed" to prove that ginseng has an effect on exercise endurance; however, an alternative interpretations is that ginseng works well to increase stamina and endurance in the unfit user, not in people or animals already in shape. The ultimate conclusion of these studies is that ginseng may help the unfit athlete perform like a fit athlete, but appears to give no added advantage to the fit athlete.

Eleutherococcus senticosus

Eleuthero, which is also in the Araliaceae family, was often called "Siberian ginseng" due to its similarity of function to *Panax spp*. However, it is a completely different genus and now is usually simply called "eleuthero." Like ginseng, the main active constituents are saponins, in this case called eleutherosides. Again, it contains no alkaloids. Eleuthero root has been used in TCM as long as ginseng. It too was used as a tonic; however, it was primarily used for arthritis, rheumatism, and low back pain.

The whole underlying concept of adaptogens is that they work to help improve stamina, however, no physical body can work beyond its capacity. Some of the research postulations about how eleuthero works include: increased oxygen consumption, a shift to aerobic energy sources, inhibition of corticosterone increase, and increased number of mitochondria per myocyte (15–17). The actual mechanism of action for eleuthero has yet to be elucidated, but it has clearly been proven that it is a very effective adaptogen.

Rhodiola rosea

Rhodiola is in the family Crassulaceae, with the root being used as the medicinal part. Not only is this herb in a different family from the previous adaptogens, but it also has a different primary chemical constituent. Instead of a saponin, rhodiola uses glycosides called salidrosides, and antioxidants such as p-tyrosol for its medicinal effect. These are the main 2 active constituents in all *Rhodiola spp*. However, *Rhodiola rosea* is the only species that contains rosin, rosavin, and rosarin, which are active constituents that make it different from all other plants in the *Rhodiola genus*.

Rhodiola has been used for thousands of years by the cultures that were familiar with it. One article listed numerous and varied traditional uses from around the world. In the Republic of Georgia, mountain villagers give a bouquet of rhodiola roots to wedding couples to enhance fertility and produce healthy children. Rhodiola was considered the most effective treatment for colds and flus during Asian winters. In Mongolia, doctors prescribed it for tuberculosis and cancer. Chinese expeditions were ordered by emperors to acquire the "golden root" from Siberia for medicinal use while Siberians themselves transported rhodiola to the Caucasian mountains in secret to trade with the Georgians for wine, fruit, garlic, and honey. Vikings used rhodiola to enhance their strength and endurance. Lastly, Linnaeus documented rhodiola as an astringent useful for treating hernias, leucorrhea, hysteria and headache (18).

There are many studies and postulations about rhodiola's adaptogenic mechanisms. These include increased protein and RNA (ribonucleic acid) levels, increased ATP and CP (creatine phosphate) levels, increased fat metabolism, increased synthesis and resynthesis of ATP, stimulation of energy repair after exercise, increased glucose uptake, increased oxygenation, and increased antioxidant mechanisms (18–23).

Two studies were the most realistic in terms of how humans actually exercise. Noreen, et al. (24) studied 18 "recreationally active" college women who did a 10 minute warm up followed by a 6-mile stationary bike ride. One group was administered *R. rosea* at 3mg/kg PO 1 hour prior to exercise and the other received a placebo. Results showed 1) heart rate after warm up decreased in a statistically significant manner, 2) time to completion decreased, 3) average power increased, 4) absolute workload increased, 5) rate of perceived exertion decreased in a statistically significant manner, and 6) fatigue post exercise decreased. These last 2 results were hypothesized to be due to an increased production of endogenous opioids or increased opioid receptor sensitivity which would make the perceived exertion seem less and therefore the fatigue seem less.

De Bock, et al. (25) studied 24 healthy, active male and female students who were tested on endurance exercise capacity to exhaustion on a stationary bike and on muscle strength via weighted knee extensions. There were 2 tests: acute dosing (100 mg R. rosea standardized to 3% rosavin and 1% salidroside PO 1 hour prior to exertion) (group A); and chronic dosing (100 mg BID for 4 weeks) (group B). Both tests were run against a placebo. The results were broken down into the categories of endurance and muscle strength and then the subcategories acute and chronic. Category 1 was endurance, with group A being acute; time to exhaustion was increased by an average of 24 seconds or 3%, with increased oxygen uptake and carbon dioxide output. No change was reported in the endurance group B. The second category was muscle strength, and there was no change reported for either subgroup A or B. De Bock, et al. hypothesized that these results were due to endorphin release, and strength is not affected by endogenous opioids (endorphins) as explained by Noreen, et al. (24). From these studies, Rhodiola rosea appears to be an acute use herb. If used chronically, it loses its exercise enhancing effect, and is best used only on the day of competition.

Cordyceps sinensis

Cordyceps, also known as "caterpillar fungi," is in the Clavicipitaceae family. The part used is the dried fungus fruiting body on the dead caterpillar larvae. The fungus and the caterpillar are symbiotic, and the fungus does not produce a fruiting body until or unless the caterpillar larva dies. At that point, the fungus produces a fruiting body in order to survive. Cordyceps contains all 8 essential amino acids, sugars, vitamins, and minerals. The main active constituents are cordycepin (3'-deoxyadenosine, a derivative of nucleoside adenosine) and cordycepic acid (a.k.a. D-mannitol). These 2 chemicals as well as polysaccharides are thought to be the medicinal constituents. The whole fungus has been used in TCM for centuries for stamina, sexually as well as athletically. All the polysaccharides are present in water extracts which are used for most studies on exercise performance. Alcohol extracts contain different constituents which cause corydceps' cholesterol-lowering, cardiovascular, and immune system effects (26). Cordyceps was discovered around the world after there was international publicity about the performance of the Chinese Women's Field and Track team at the Chinese National games in 1993. In this competition, the women broke 9 world records by substantial margins, and the team's coach attributed their success to the use of cordyceps (27). Cordyceps only natively grows on the Tibetan plateau, so at this point it is rare and endangered in the wild. However, it is now being grown commercially for medicinal use. It should be bought only from a commercial grower. There is only one that advertises that it mimics the growing conditions of the Tibetan plateau and has cordyceps with an equivalent chemical make-up.

Cordyceps both enhances endurance and performance and it also alleviates fatigue (28). The use of cordyceps is thought to be due to its effects of increased oxygen utilization, increased ATP production, and the stabilization of blood sugar metabolism (27). Many studies show an increase in the ATP:inorganic phosphate (Pi) ratio in skeletal muscle and liver cells after cordyceps ingestion. The ratio of ATP:Pi denotes increased intracellular energy. The results are either due to enhanced triphosphate synthesis or reduced ATP consumption. The levels show statistically significant improvement after 1 week, and the levels return to baseline after 1week without supplementation. The increase lasts the duration of the cordyceps administration. Another study found that use of a standardized extract of cordyceps during prolonged submaximal exercise minimized lactate acidosis, caused better functioning of cellular mitochondria, and improved insulin sensitivity and basal glucose metabolism which may contribute to higher levels of steady state of ATP in the muscle cells (26).

Dosages and Safety

Panax ginseng:

Dried herb dosage: human: 5 g TID; veterinary: 50 mg TID (28). Safety: There are no reports of toxicity with ginseng overdose (29). May interact with warfarin or monoamine oxidase inhibitors (30).

Eleutherococcus senticosus:

Dried herb dosage: human: 5 g TID; veterinary: 50 mg/kg TID (28). Safety: Eleutherococcus senticosus is very safe (17). May cause insomnia if given in the evening.

Rhodiola rosea:

Dried herb dosage: human: 1.5 g SID (31). No veterinary dosage confirmed (recommended dosage [extrapolated from human]: 0.25 mg/kg TID). Safety: The Natural Medicines Comprehensive Database states Rhodiola rosea is "possibly safe," and there are no reports of adverse reactions (32). Caution with use with bipolar disorders.

Cordyceps sinesis:

Dried herb dosage: human: 3 g TID (33). No veterinary dosage confirmed (recommended dosage [extrapolated from human]: 0.45 mg/kg TID. Safety: Very safe for long-term usage (26–28).

Adaptogens have been shown by multiple human Olympic teams to support and enhance exercise performance, increase stamina, and prolong endurance. The ones discussed in this article are just a few of the many that have been researched and proven to affect muscle activity. Additionally, it is important to realize that muscles are just one part of the body, and the whole body has to be functioning optimally to obtain the best results. Nutrition is of course the backbone of good health and functionality, but adaptogens' ability to support and normalize the whole system are a helpful and safe addition to any athlete's diet.

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Additional Resources

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