MEDICINAL PLANTS IN PHYSICAL EXERCISE: A REVIEW

Review Paper

Nikole Costa Dias[1]; Natália Pandolfi Marinho[1]; Sandra Maria Barbalho[1,2,3]; Adriano Cressoni Araújo[1,2]; Claudia Rucco Penteado Detregiachi[2]; Mauro Audi[2]; Eduardo Federighi Baisi Chagas[2]; Rogério Leone Buchaim[4]; Daniela Vieira Buchaim[2,5]; Elen Landgraf Guiguer[1,2,3]

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[1]Department of Biochemistry and Pharmacology, School of Medicine, University of Marília (UNIMAR), Avenida Higino Muzzi Filho, 1001, Marília –Brazil / Brazil; [2]Postgraduate Program in Structural and Functional Interactions in Rehabilitation - UNIMAR - Marília – SP, Brazil; [3]Department of Biochemistry and Nutrition, Faculty of Food Technology of Marília, Marília, São Paulo – Brazil; [4]University of São Paulo (FOB–USP), Alameda Doutor Octavio Pinheiro Brisolla, Bauru, Brazil; [5]Medical School, University Center of Adamantina (UniFAI), Adamantina, Brazil.

ABSTRACT

Background: The use of medicinal plants may have an effective action on the performance of athletes.

Aims: This review aimed to evaluate the effects of the use of medicinal plants and some phytocompounds on physical performance.

Methodology: MEDLINE/PUBMED and EMBASE were consulted following the PRISMA guidelines.

Results: *Panax ginseng* increases the anti-fatigue effect, decreases the stress promoted by the physical exercise, and improves muscular function through gene expression enhancement. *Arnica montana* has a crucial anti-inflammatory action showing relief of muscular pain a. *Zingiber officinale* has an anti-inflammatory and analgesic role on muscular pain, and it can be used to speed up the recovery of muscular strength after intense activity. *Ephedra sinica* is related to thermogenic and sympathomimetic effects, being able to increase the energetic state. *Capsaicin* increases the energetic expenditure due to fat oxidation, promotes the anti-fatigue effect, and enhances the athlete's resistance. *Caffeine* has ergogenic importance related to its antioxidant capacity, and it improves mental alertness condition.

Conclusion: The nutritional supplementation with products derived from medicinal plants may be an efficient alternative to improve the athlete's performance, being a natural substitute for synthetic supplements, which usually are forbidden in competitions.

Key-words: physical exercises, *Panax ginseng, Zingiber officinale*, *Arnica montana*, *Ephedra sinica*, caffeine, capsaicin.

1. INTRODUCTION

Nutrition and the use of dietary supplements have an effective contribution to the performance of athletes. The use of some types of supplements may be positive, on improving heavy training, relief of muscular pain, recovery of exercise lesion, changes of the physical structure, and mood improvement. Nevertheless, according to World Anti-Doping Agency (WADA) there are several substances, which are considered illegal, and that infringes the antidoping rule, such as peptide hormones, growth factors and related substances; beta-2 agonists; hormone and metabolic modulators; diuretics and masking agents [1-3].

An alternative to improve the performance of athletes is the use of herbal supplements. Such supplements may be applied to stimulate muscular growth, increase fat metabolization, give resistance and strength performance and decrease oxidative stress, increasing muscular healing and energy maintenance during the more intense exercises [4,5]. The combination of plant extracts, such as *Antrodia camphorata* and *Panax ginseng*, can also bring benefits once they are efficient to promote the anti-fatigue effect and help eliminate metabolites related to this condition. Fatigue is one of the most common reactions in athletes, leading to symptoms like exhaustion, tiredness, and lack of energy. In the long term, it can cause premature aging, cancer, and other chronic degenerative diseases [6,7]. Physical activity itself may favor free radicals and oxygen reactive species that cause damage and reduce performance. The use of herbal supplementation is related to minor side effects than synthetic drugs [8,9].

Bioactive compounds can be found in leaves, barks, fruits, roots, seeds, stalks, or flowers. In addition to being used as a therapeutic adjuvant for several pathologies, they can promote biochemical and physiological alterations that can improve individuals who practice physical activities. Athletes commonly use *Panax ginseng, Arnica montana, Zinziber officinale, Ephedra sinica, and compounds like caffeine and capsaicin* once related to physical performance improvement (Figure 1) [10-15]. For these reasons, this revision aimed to evaluate the effects of these plants and compounds on physical performance.

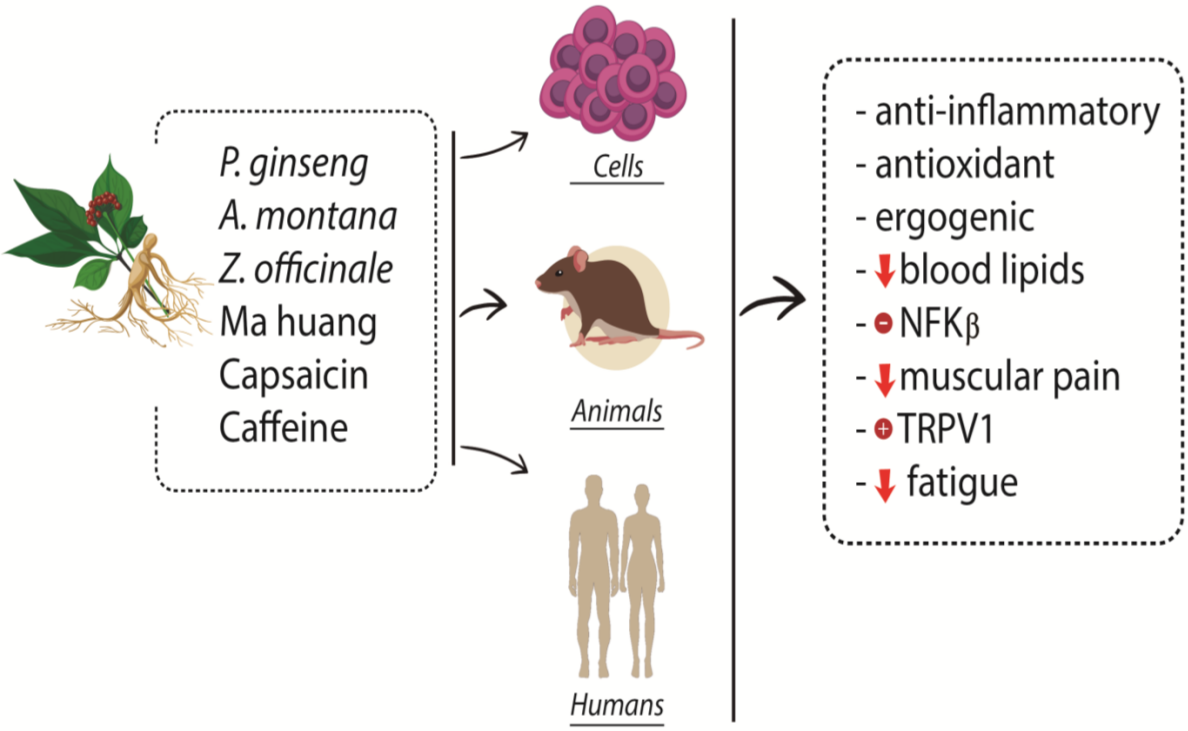

Figure 1. Some general effects of *Panax ginseng, Arnica montana, Zinziber officinale,* Ma huang (*Ephedra sinica*), capsaicin, and caffeine. NFKβ: Nuclear Factor Kβ; TRPV1: Transient receptor potential vanilloid 1 subfamily V member 1.

2. METHODS

2.1 Data Sources

The search was performed in MEDLINE-PubMed and EMBASE databases following the PRISMA guidelines (Preferred Reporting Items for a Systematic Review and Meta-Analysis, Moher et al., 2009). This review was conducted to answer the following question: Can plants bring benefits to physical exercises?

Research

Our review included randomized clinical trials, cohort studies, cross-sectional studies, case-control, experimental, and *in vitro* studies. The combination of terms and key-words used for this search was *Panax ginseng* or *Arnica montana* or *Zingiber officinale* or *Ma huang* or Capsaicin or Caffeine and physical exercises.

With the list of references obtained with the above descriptors' combination, we selected articles to construct the flow diagram (Figure 2). Other studies on physical exercises and medicinal plants were used to build the discussion.

2.2 Eligible criteria and study selection

Our review included both studies that discuss the use of medicinal plants, caffeine and capsaicin, and the effects on physical exercises. We have included English articles from the last ten years that showed correspondence with the descriptors used for searching.

2.3 Extraction of data

The extraction of the data was performed by two authors who used the pre-defined descriptors. Data were extracted from eligible articles that included the date, author, study design, information related to medicinal plants, and physical exercises. Only original and full articles were selected for the construction of Tables 1 and 2.

Inclusion criteria were articles that used randomized clinical trials, cohort studies, cross-sectional studies, case-control, *in vitro*, and *in-vitro* and experimental studies. The exclusion criteria were non-English articles, case reports, poster presentations, and letters to the editor.

3. RESULTS & DISCUSSION

Eight articles about *Panax ginseng* (Table 1) were selected, one clinical trial (randomized, double-blind, and placebo-controlled), two *in vitro* studies, and five experimental studies. Clinical trials included 117 participants of both genders and individuals 20 years old or over. The searching for *Arnica montana* resulted in four articles (Table 1); two were clinical trials (randomized, double-blind, and placebo-controlled study) and 2 *in vitro* studies. In the clinical trials, 40 men and women 20 years old and over were included. For the ginger (Table 1), the selection resulted in 1 experimental study and six clinical trials (randomized, double-blind, and placebo-controlled studies) with 214 men and women aged between 20 and 75 years old. For *Ma huang* (Table 1), two articles on experimental models (studies with rats and mice) were selected.

Concerning capsaicin, five articles were selected (Table 2): one clinical trial (randomized, double-blin, and crossover), one *in vitro* study, and three experimental models. The clinical trials included ten men aged between 18 and 26 years old. The search on caffeine resulted in four clinical trials that included 66 men aged between 21 and 29 (Table 2). Figure 2 shows the selection of the articles.

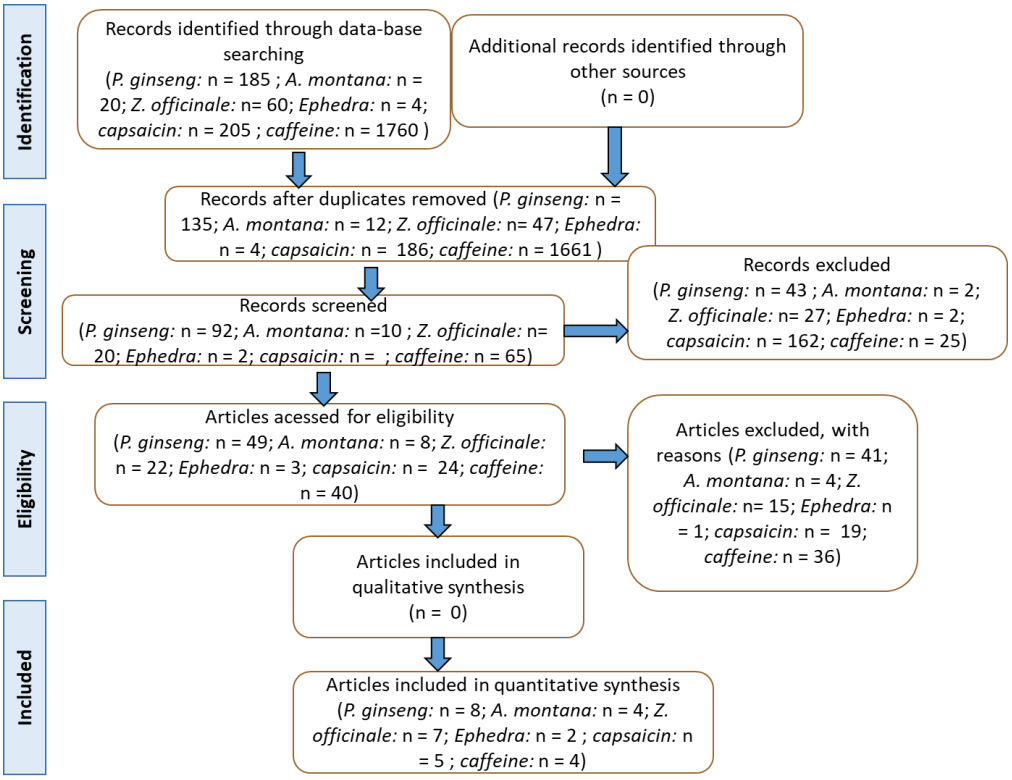

Figure 2. Flow diagram according to PRISMA guidelines (Moher et al., 2009)

As mentioned above, there are many plants related to benefits for the execution of physical exercises. Some of them act preferably on reducing fatigue, and others are related to energetic expenditure. Although some are natives of different countries, the acquisition of these plants or their extracts or fractionated compounds may be worldwide traded, or they can be on-line purchased.

3.1 Panax ginseng

Panax ginseng is a medicinal plant from the Araliaceae family, is commonly used in several countries around the world, and it has a 2000-year-old history in Chinese traditional medicine. The main compound of this root is the *ginsenoside Ro*, a bioactive compound with a great ergogenic potential, which is related to physical performance,

fatigue, and the enhancement of the biochemical profile. Its benefits range from improvement in cognition, metabolic and immune functions, anxiety, and inflammation to carcinogenesis. Table 1 shows the effects of ginseng in different studies [6,16-21].

Furthermore, the ginseng species have vitamins (A, B, C, and E), minerals (potassium, magnesium, phosphorus, and iron), proteins, fibers, saponins, and ginsenosides. Ginseng has antioxidant properties that inhibit the hydroxyl radical and lipid peroxidation, increasing the metabolic efficiency in mitochondria over physical exercise. The ergogenic effect of this root is commonly related to athletes' physical condition, and its chronic use can bring improvement to cardiopulmonary function and reduce the blood lactate concentrations. In people moderately trained, it is possible to observe resistance to fatigue by stimulating cortisol release and the beneficial effects on the central nervous system. Besides, ginseng also produces anti-fatigue activity and reduces lactate dehydrogenase and CPK levels, biomarkers of stress and fatigue. Likewise, experimental evidence showed that the ginseng extract has therapeutic effects with several cardiovascular activities, such as regulating blood circulation, reducing the myocardium size, and improving the lipid profile [4,8,17,22].

This plant exerts anti-adipogenic activity through the modulation of different signaling pathways. There is evidence of the beneficial effects of *P. ginseng* on neurodegenerative diseases, which are attributed to the antioxidant and immunomodulatory activities of its ginsenoside compounds. Ginsenoside Rg1 is one of the main active compounds, and it is efficient in inhibiting the inflammatory process and oxidative stress. Studies have shown that this compound increases muscle fiber size and also muscle strength. Furthermore, it showed an improvement of oxidative muscular metabolism [23-27].

The ginsenoside produces an increase of cortisol, signalizing the organism's answer capacity to a stress agent. In the case of athletes who have regular physical activity, ginsenosides can promote the answer to stress in the sense of preserving homeostasis and reducing possible damages [28-30]. Moreover, it has immunomodulatory action, leads to the proliferation of lymphocytes, boosts cytokines' production, enhances the phagocytic activity of macrophages and neutrophils, and causes the rise of natural-killer cells (NK). The serum levels of IgG and IgA antibodies are also raised through ginseng administrations [31-34]. Ginsenosides also inhibit

cytokines' production and increase the expression of the cyclo-oxygenase 2 gene (COX 2) and the release of histamine. For this reason, it decreases typical symptoms of the inflammatory answers, such as pain, redness, heat, swelling, and loss of function [32,35]. Ginseng has antioxidant action once it has free radicals scavenging capacity and exhibits a protective effect against lipid peroxidation [36].

3.2 Arnica montana

Arnica montana is a rhizomatous perennial herb of the Compositae family, originating from Siberia and Central Europe, and it is one of the most used medicinal plants in popular medicine. It is mainly used as an ointment, cream, and pill. Dried flowers, roots, or rhizomes of *Arnica montana* are usually used as an anti-inflammatory product. Its active compounds are sesquiterpene lactones, such as helenalin and 11-alpha, 13-di-hydro-helenalin, acetic and isobutyric acids, methacrylic acid, flavonoids, thymol, arnicin, coumarins, and carotenoids. Helenalin inhibits the transcription factor Nuclear Factor Kβ (NFkβ) and acts like corticosteroids, inhibiting the enzyme phospholipase A. Furthermore, *arnica* possesses flavonoids that can change the functional properties of mast cells, basophils, smooth muscle, and platelets. Such alterations occur due to the interference in a great number of enzymatic systems, mainly in Phospholipase A2, COX, LOX, and Phospholipase C, and has a fundamental role in the reduction of pro-inflammatory mediators. These roles are beneficial for physical activity because they reduce injuries and improve performance [37-39].

This plant helps relieve muscular pains that are usually related to high-intensity physical exercise and pain that represent the athlete as an obstacle to a good performance. As arnica has anti-inflammatory action, it can work as an efficient agent to treat bruises, pains, sprains, trauma, and arthritis. In the short term, it can be used to reduce pain and increase muscular strength. Some studies suggest that its use reduces muscular pain and cell damage after the marathon of professional athletes. Late muscular pain is also common in people that remained a considerable time without exercising, and this condition may cause more frequent muscular damages and intensify the muscular pain. In these cases, arnica can also have beneficial effects [4,14].

Moreover, arnica is used for tissue healing and the treatment of skin lesions or inflammation processes in tendons and articulations [37,40,41]. The compounds that are

responsible for its pungent features are gingerol, shogaol, and gingerone. Table 1 shows the results of some studies with *A. montana* and its effects on physical exercise.

3.3 Zingiber officinale

Zingiber officinale, popularly known as ginger, is an herb from the Zingiberaceae family and is originally found in South Asia Rainforest. It is a common spice in many regions, and it has been used as a medicinal plant for decades. Studies show that ginger has anti-inflammatory, antioxidants, anti-carcinogenic and antiangiogenic effects and can help reduce the lipid profile due to bioactive compounds such as gingerols, shogaols, paradols, and zingerone. Zingerone is one of the main compounds from the ginger root, and it is a non-toxic, antioxidant, antimicrobial, anti-inflammatory, and antithrombotic compound [4,42-45].

Ginger is also related to inhibiting the release of pro-inflammatory cytokines, and it suppresses inflammation inhibiting the activation of NFkB, which leads to inhibiting the genetic expression of pro-inflammatory cytokines, COX, chemokines, as well as osteoclastogenesis. Pro-inflammatory cytokines have a role in the exacerbation of muscular pain induced by athletes' daily physical exercises, and supplementation with ginger may be efficient in accelerating muscular strength recovery after intense exercises. Besides that, studies indicate that the main elements of ginger reduced MCP-1 (monocytes chemotactic protein) and ICAM-1 (intercellular adhesion molecule-1) in different cells through the activation inhibition of the NFκB, as an answer to inflammatory stimuli [13,46-48].

Its bioactive compounds may work as agonists of TRPV1 (transient receptor potential vanilloid 1), which acts on the peripheral and central nociceptive signaling, inhibiting prostaglandin release leukotrienes, modulating the activated biochemical pathways in the process of chronic inflammation. For these reasons, ginger may be more efficient in reducing the pain caused by physical exercise and the inflammatory process by activating this receptor [49-52]. Table 1 shows the effects of ginger on physical exercises in several studies.

3.4 Ephedra sinica (Ma Huang)

Ma Huang is a medicinal herb commonly used in Chinese medicine for over 5000 years, and it is derived from the dry herbal stalk of *Ephedra sinica* Stapf. It is traditionally used to treat asthma, bronchitis, and tremblings, and it also has anti-obesity effects. The herb has as the main compound the alkaloid ephedrine. In pharmacological terms, it is a sympathomimetic agent, stimulating and thermogenic, which is acting on the rise of energetic expenditure and body weight loss. Its action mechanism is on the sympathetic neuronal release of norepinephrine and epinephrine, activating α-1, α-2, and β-1 receptors, consequently exciting the cardiovascular system. However, the indiscriminate use of such substances may cause side effects like tachycardia, high arterial pressure, and agitation [53,54].

The thermogenic effect of ephedrine is related to stimulating the sympathetic nerve due to the activation of the β3 adrenergic receptors, having as aim the fat degradation and helping with glucose metabolism, in such a way that it decreases the glucose levels during fast, as well as the insulin levels in obese individuals. Ephedrine also inhibits the monoamine oxidase; thus, it prevents norepinephrine degradation, increasing this neurotransmitter's effects. These effects can bring benefits to the athletes [54,55].

Besides the alkaloids of ephedrine, there are other substances like polysaccharides, organic acids, flavonoids, and tannins, which have antioxidant effects. Besides decreasing oxidative stress, these compounds can also reduce the arterial pressure and blood glucose, affecting fat metabolism [54,56].

However, according to the World Anti-Doping Agency (WADA), the consumption of alkaloids derived from ephedrine was forbidden in urinary concentrations higher than 150 μg/mL for pseudoephedrine. Due to its actions in stimulating the central nervous system, the excessive use of this substance can induce sleeplessness, nervousness, trembling, and anxiety, and, in continuous doses, can induce psychotic episodes, such as paranoia, hallucinations, and other mental disorders [57,58]. Table 1 shows different studies about Ma Huang and its different effects on physical exercise.

3.5 *Capsaicin*

Capsaicin (CAP, trans-8-methyl-N-vanillyl-6-nonenamide) is an active compound of the red pepper, chili, and to a lesser extent, of ginger, which are plants of the gender *Capsicum*. This compound is originally from the Americas, and studies show that it can boost analgesic, antioxidant, anti-inflammatory, anti-cancer, and anti-obesity effects. It also promotes the raising of energetic expenditure and reduction of plasmatic cholesterol effects. Physical exercise, together with the supplementation with capsaicin, promotes a significant raising of the cyclical AMP and protein kinase A (PKA) levels, pointing to the raising of lipolysis. Besides, capsaicin activates the oxidative phosphorylation and the oxidation of the fatty acids in the striated skeletal muscle [59-61].

Another benefit of capsaicin is on raising the energetic metabolism through the activation of TRPV1 by the mitochondrial function. This activation stimulates the mitochondrial function, enhances the biogenesis, improves the energy metabolism and physical exercise resistance, and positively regulates the PGC-1α (peroxisome proliferator-activated receptor-γ coactivator-1α) in the skeletal muscles. Besides that, the activation of TRPV1 associated with constant physical exercises promotes cell adaptation, like muscular hypertrophy and ATP production in the muscle [62,63].

The activation of TRPV1 in the skeletal muscle by capsaicin also increases the sarcoplasmic reticulum's calcium release. The exhausting exercise reduces the calcium-releasing rate in the vesicles of the sarcoplasmic reticulum, contributing to reducing the strength generation of the myofibrils. Therefore, the increase of calcium by the capsaicin results in greater interaction between the filaments of actin and myosin, causing, by example, greater strength and resistance for the athletes [64,65]. Table 2 shows the effects of capsaicin related to physical exercise in several studies.

3.6 *Caffeine*

Caffeine is an alkaloid of xanthine found with an ergogenic effect. Physical exercise supplementation with caffeine can benefit aerobic performance and physical resistance once it increases the serum levels of catecholamines and immune response. Besides that, it can help in the performance in different levels of intensity of exercises and improve mood and the mental alertness state. Furthermore, the ergogenic effect of caffeine can be associated with its antioxidant properties [4,66].

This alkaloid has many mechanisms of action, including the increase of sodium and potassium pump activity and the rise of the release of calcium of the sarcoplasmic reticulum through the decoupling of the ATPase activity in the skeletal muscle. Furthermore, it shows a greater answer to catecholamines and the ability to be a competitive antagonist to the adenosine receptor in the central nervous system, contributing to reducing the feeling of pain and fatigue. Due to these mechanisms, caffeine can increase lipolysis, decreased kalemia during the physical exercise; increase of muscular contraction strength, and decreased muscle glycogen expenditure. Caffeine can also act directly on the central nervous system as a way to stimulate the release of the adrenocorticotropic hormone (ACTH) and beta-endorphin, which are hormones that change the feeling of pain and fatigue related to physical exercise. Studies show that caffeine intake has an ergogenic effect and is usually used to increase the athletes' performance. The supplementation with caffeine before doing supine increases de bar velocity in the eccentric phase of the movement and decreases the time of repetitions. Another experiment also showed that caffeine is effective for judokas' performance and capacity [4,66-68]

By the end of 2003, the World Anti-Doping Agency (WADA) removed caffeine from the forbidden products list, and its use was released for Sporting competitors. However, in higher doses, the athletes are subjected to anxiety and sleeplessness before and after competitions. Furthermore, caffeine has, as other xanthines, inotropic, tachycardiac, and bronchodilator effects and stimulates gastric secretion. Caffeine can also cause tolerance, and its suspension can cause headaches, irritability, and lethargy [69]. Table 2 shows the effects of caffeine on physical exercises.

3.7 *Summary of the main effects of Panax ginseng, Arnica montana, Zingiber officinale, Ephedra sinica, capsaicin, and caffeine*

Panax ginseng shows effectiveness on physical performance due to the anti-fatigue effect, reduction of the stress promoted by the exercise, and improved muscular function due to the enhancement of the gene expression. Besides, ginseng has anti-adipogenic activity and increases aerobic capacity [16-18].

Arnica montana has a critical anti-inflammatory action, showing relief of muscular pain in athletes. Furthermore, it has an activity related to tissue healing and repair [4,14,37].

Zingiber officinale has an anti-inflammatory and analgesic role and can accelerate muscular strength recovery after intense activity. It is also related to lipid profile improvement [46-48].

Ephedra sinica is related to thermogenic and sympathomimetic effects and can increase the energetic state and body weight loss [54,55].

Capsaicin increases the energetic expenditure due to fat oxidation, promotes the anti-fatigue effect, improves the athlete's resistance, and increases the liver's glycogen content [64,65].

Finally, *caffeine* has ergogenic importance related to its antioxidant capacity and improves the mental alertness condition [4,66-68].

4. CONCLUSION

The supplementation with medicinal plants or derivatives can be an efficient alternative to improve the performance of the athlete, being a natural substitute to synthetic supplements that are usually forbidden during competitions. These substances can decrease fatigue, lead to relief of muscular pain, and accelerates the lesion's recovery. It is important to stress that more clinical studies should be performed to establish the doses to be used, the best delivery method, and the types of exercises that can obtain beneficial effects with medicinal plants and their compounds.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

Table 1. Studies showing the effects of *Panax ginseng, Arnica montana, Zinziber officinales*, and Ma huang on *in vitro* studies, experimental models, and humans.

Reference	Model	Intervention	Outcomes	Conclusion
Panax ginseng				
Shin et al., 2019	Sprague-Dawley mice	1) Mice were divided into 2 groups: a group treated with cultivated wild ginseng (cWG) (n=6) and a group treated with saline solution (n=6). The mice took forced swimming tests for 5 days, and BUN, LAC, LDH, and glycogen were measured. 2) Mice were divided into 3 groups: vehicle group (n=5), group treated with 0,1 mg/Kg of panaxydiol (n=5), and group treated with 0,25 mg/Kg of panaxydiol. The forced swimming test was also taken,	The group treated with cWG had forced swimming time significantly higher than the control group. CWG did not affect glycogen levels. The groups treated with panaxydiol also had a significant rise in the forced swimming time if compared with the control group. There was a significant decrease in the serum levels of LDH in the groups treated with panaxydiol, but there weren´t any effects on the levels of BUN, LAC, and glycogen in the liver and muscle.	The distilled extract of cWG and its active compound panaxydiol produce anti-fatigue activity, reducing the LDH activity.

		and the biochemical profile was evaluated.		
Bang et al., 2019	Wistar Male Mice	The animals were divided into 6 experimental groups (n=8) and treated with the extract of *Rhodiola rosea* (RR) or of *Panax ginseng* (PG) 5 x/w/30 days, and they had swimming activity.	No significant differences were seen on the anthropometric and biochemical parameters. However, the animals treated with PG and RR had their levels of CPK and LDH reduced after physical stress.	These plants can be used to minimize the stress promoted by the practice of physical exercises.
Jeong et al., 2019	C57BL / 6J Male rats.	The rats were divided into a control group and group treated with 0,4 mg/mL of water added of Rg1. To evaluate the muscular strength, grip strength tests were taken. The hindquarter muscles were dissected, and histological and molecular evaluations were taken.	Treatment with Rg1 showed high levels of myosin heavy chain, suggesting that Rg1 promoted the gene expression not only in the oxidative muscle fibers but also in the glycolytic muscle fibers. There was also an increase in myofiber size, raised muscular strength, and improvement of the expression of genes involved in oxidative muscle metabolism. Besides that, the muscles treated with Rg1 showed increased levels of anabolic signaling of S6 kinase.	The treatment with Rg1 improved muscular functions through the enhancement of muscular gene expression and oxidative muscle metabolism.

Liang Liu et al., 2018	*In vitro* (cell culture), cardiomyocytes H9c2 submitted to treatment with H/R and treated with AP1 (200 µg/mL) were used.	The cardioprotective effect in cardiomyocytes H9c2 submitted to hypoxia and re-oxygenation was evaluated. Cell viability, apoptosis, and mitochondrial breathing were examined.	AP1 restored the mitochondrial function maintaining the mitochondrial membrane potential, blocking the cytochrome C release, raising the ATP production and the consumption rate of oxygen of the cardiomyocytes. It also induced the expression of GR and ER.	AP1 had a protective effect on the myocardial lesion through the maintenance of the myocardial function, inhibiting the myocardium apoptosis and raising the expressions of GR and ER.
Yang et al., 2017	*In vitro* (cell culture), a mixture of ginsenosides of the protopanaxadiol type in adipocytes 3T3-L1 was taken.	Use of a mixture of ginsenosides Rg5: Rk1 of the protopanaxadiol type with a concentration of 1-100µg.mL^{-1} in 3T3-L1 adipocytes.	The treatment with ginsenoside Rg5: Rk1 showed an inhibition of the accumulation of lipid droplets and a decrease in the content of TG. Besides that, the expression of STAT3, PPARγ, CEBPα, and ap2 decreased in a dependent way of the dose. In the same way, the treatment with Rg5: Rk1 reduced the expression of	The treatment with Rg5: Rk1 shows anti-adipogenic activity through negative regulation of the signaling via STAT3/PPARγ/CEBPa in the cell line of

			the proteins PPARγ and CEBPα.	adipocytes3-L1.
Lee et al., 2017	Randomized, double-blind, placebo-controlled clinical trial, with a sample of 117 male and female sedentary and healthful individuals, over 20 years old.	The individuals were divided into 3 groups: Group supplemented with 100 mg/d of ginsenosides, with 500 mg/d, and placebo group. All of them were submitted to aerobic treatment for 12 weeks with supervision.	The ginsenosides groups showed an increase in the maximum volume of oxygen and muscular strength during the physical treatment. There were no changes over time in the levels of anaerobic threshold and lactic acid. There were no differences in the VO_2 max among the treated groups and the placebo group and in the muscular strength during the physical treatment among the groups.	The supplementation with a high dose of ginsenoside increased the aerobic capacity through physical exercise.
Hsiao et al., 2017	6-month-old ICR Mice were supplemented with AG.	Mice were divided into 4 groups; control group, group supplemented with AG-1X (0,984 g/Kg/day of AG); AG-3X group (2,952 g/Kg/day of AG); and AG-6X group (5,904 g/Kg/day of AG). They were submitted to exhaustive	In the resistance-swimming test and in the strength tests, the AG-1X, AG-3X, and AG-6X groups showed anti-fatigue effect and increased strength, respectively, dose-dependent. After swimming, the serum levels of lactate, ammonia, BUN, and creatine kinase of the groups supplemented with ginsenosides were	The supplementation with AG resulted in a potential pharmacological anti-fatigue effect.

		swimming test, grip strength tests, frontal, and it was analyzed the content of glycogen in the muscles and liver.	smaller if compared with the control group.	
Ma et al., 2017	ICR mice	Mice were divided into 3 groups: control group, CMG-1X group (0, 5 mg/kg/day of CMG) and CMG-5X group (25 mg/kg/day of CMG). Extract of CMG in different doses was given for 4 weeks, and the mice were submitted to swimming tests.	Extract of CMG raised the muscular weight, the relative muscular weight, the grip strength tests, and the swimming time significantly. There were decreases in the serum levels of lactate, ammonia, creatine-kinase and blood urea, nitrogen, and levels of glucose after exercise.	The supplementation with CMG showed decreases in the serum levels of creatine and triacylglycerol, as well as a rise in total proteins and glucose.
Arnica montana				
Marzotto et al., 2016	Cultured and differentiated monocyte-macrophage human THP-1 with phorbol-myristate acetate and IL-4, then exposed for 24h to *A.*	Cultivated cells, differentiated by phorbol-myristate acetate and IL-4 exposed to *A. montana* for 24 hours.	Protein trial confirmed a statistically significant rise in fibronectin production.	The action of arnica is related to tissue healing and repair.

	montana.			
Pumpa et al., 2014	Randomized, double-blind, placebo-controlled clinical trial with 20 men (25,3 years old medium age).	They were divided into active group and placebo group and received gel product with arnica, which was applied on the skin, on the quadriceps, and gastrocnemius muscles, and later reapplied in the same regions every 4 hours.	The use of arnica reduces pain, which was evaluated through the muscle sensibility 72 hours after exercise. Topic arnica did not affect the injury or muscular inflammation markers neither the blood markers (interleukin-1 beta, interleukin-6, tumor necrosis tumoral-α, C-reactive protein, myoglobin, and creatine kinase).	The gel with arnica showed to release the pain 3 days after eccentric exercise.
Craciunescu et al., 2012	NCTC cell line similar to mice fibroblasts.	Ethanolic extracts of *Arnica montana* and *A. Absinthium* were evaluated on their chemical composition, antioxidant activity and protective effect against stress-induced through H2O2 in NCTC cells.	*A. absinto* showed a higher antioxidant capacity than the extract of *A. montana*. Besides having *a* higher capacity to absorb oxygen radicals and eliminate free radicals of 2,2-diphenyl-1-picrylhydrazyl, both vegetal extracts protected the fibroblastic cells against the oxidative damage induced by hydrogen peroxide.	The extract showed antioxidant activity and cytoprotective effect against the oxidative damage in cells that are similar to fibroblasts.
Plezbert; Burke, 2005	Randomized, double-blind trial with 20 individuals without	Individuals were submitted to exercises with the elbow flexors. The arnica extract and the	The rise of muscular enzymes was similar in the days after the protocol of eccentric exercise. The post-exercise time profiles	This study's results did not substantiate the clinical efficacy of

	specification of gender and age.	placebo were administered in a random way. Evaluations of late muscular pain and muscular functions were done, and blood samples were collected before the exercise and 24, 48, and 96 hours after exercise, which was used to measure the muscle enzymes.	reduce in maximum voluntary contraction torque and muscle shortening ability. There were also increases in muscle swelling, and spontaneous muscle shortening was similar for each treatment intervention.	arnica in high power for the moderation of late muscular pain and accompanying symptoms of muscular dysfunction.
Zingiber officinale				
Nayebifar et al., 2016	Random experimental and controlled trial, with 30 women individuals (between 20 and 30 years old).	Individuals were randomly divided into 3 groups (n = 10), HIIT + ginger, HIIT + placebo, and ginger. The protocol of exercise was obtained through a run of 40m (to evaluate the anaerobic function) /3x a week/10 weeks. Individuals from the ginger and HIIT + ginger groups received 3000 mg of pills of ginger daily.	There were significantly different alterations in the VO2max (before and after test) among the groups. VO2max was increased in the "HIIT + ginger", and "HIIT + placebo" groups in comparison to the "ginger" group. Significant differences in the alterations of MCP-1, ICAM-1, and IL-10 among the groups were not observed. Wilcoxon signed-rank tests showed a significant rise in VO2max and a significant decrease in the	10-week-long intense exercise, singly or together with the use of ginger, improved MCP-1, and the use of oxygen, but without any significant effect in the soluble ICAM-1 and soluble IL-10.

			concentration of MCP-1 in "HIIT + ginger" and "HIIT + placebo", respectively, after 10 weeks of intervention.	
Khosravni et al., 2015	Randomized trial with the control group, using a sample of 32 male mice.	Mice were randomly divided into 4 groups: 1) aerobic exercise, 2) ginger extract, 3) aerobic exercise combined with ginger extract, and 4) control group. Individuals from the 3 first groups received ginger extract (250 mg/kg). The program of exercises was of 3 sessions a week on 3 different days for 4 weeks.	The TG concentration in the control group was significantly more significant, and the smallest values were in the group treated with ginger and exercise. The concentrations of CT and LDL-c were significantly reduced in all groups if compared to the control group. The combination of aerobic exercises and the use of ginger led to a significant rise in the levels of HDL-c.	The study suggests that the combination of aerobic exercise and the use of ginger extract may be an efficient method to reduce the lipid profile.
Karimi et al., 2015	Randomized placebo-controlled trial; n = 40 obese women with breast cancer (47-50 y).	Individuals were divided into 4 groups: placebo, physical training in water, ginger supplementation, and physical training + ginger supplementation. Supplementation was made with	Supplementation with ginger and exercise decreased hs-CRP, IL-10, insulin, glucose, insulin resistance, LDL-c, TG; But there was a rise in the HDL-c and HDL-c/ LDL-c.	The use of ginger associated with exercise has an important role in improving inflammatory and

		4 capsules/7 days a week/ 6 weeks.		metabolic answers.
Matsumura et al., 2015	Randomized, double-blind, placebo-controlled trial. The sample had 10 men and 10 women (29-37 years old, approximately).	10 men and 10 women without training; 10 individuals were designed to the ginger group (4g/d) and 10 to the placebo group. Individuals were instructed to have similar activity and diet over the study (12 days).	5 days of supplementation with ginger can accelerate the strength recovery after a protocol of eccentric exercise with high intensity. Ginger accelerated the muscular strength's initial improvement, but it did not influence the strength 72 and 96 h after the exercise session.	Supplementation with ginger may be used to accelerate the muscular strength recovery after intense exercises, but it does not influence the muscular strength indicators.
Amorndoljai et al., 2015	60 patients (50 to 75 years old), without distinction of gender.	All the individuals received ginger extract in NLC, which was applied to the said place of pain 3 times a day for 12 weeks.	The nanoparticles of ginger extract improved the global evaluation of the patient, the knee joint pain, the daily activities symptoms, the sports activities, and the life quality after 12 weeks of treatment.	The nanoparticles of ginger extract relieve the pain and improve the life quality of the patients.
Hoseinzadeh et al., 2015	Randomized, double-blind, placebo-controlled trial with 36 women with ages	Patients were randomly divided into 3 groups: intake of 60 mg of ginger extract in GIBE, GIAE, and PL. The blood samples were	A significant decrease in pain in GIBE was observed if compared to GIAE after 24 hours and 48 hours of EE, and GIAE compared to PL. Ginger showed an	The study suggests that 60 mg of ginger extract can have anti-inflammatory and

	between 21 and 24.	collected before the exercise, 1 hour, 24 hours, and 48 hours after the exercise to test CK and IL-6.	inhibiting effect on IL-6 in GIBE compared to GIAE and PL.	analgesic effects on late muscular pain.
Zehsaz et al., 2014	Randomized, double-blind, placebo-controlled trial with 28 men between 21 and 23 years old.	The individuals were divided into a control group and an experimental group. After completing the first period of six weeks of the physical training protocol, the ginger group (experimental) and the placebo group received capsules of 500 mg of ginger powder and placebo 3 times a day for 6 weeks.	The extended training for 6 weeks for male runners can significantly increase the plasma levels of several pro-inflammatory cytokines. In the ginger group, there was a significant difference in the medium concentrations of IL-1β by the end of the 6^{th} and 12^{th} weeks, and the rates at the end of the 12^{th} week were 18,95% smaller than those at the end of the 6^{th} week.	The use of ginger for 6 weeks can reverse the rise of pro-inflammatory cytokines, minimizing inflammatory conditions in post-exercise periods and reducing fatigue.
***Ephedra sinica* (Ma Huang)**				
Zheng et al., 2015	Sprague-Dawley Mice.	They were treated with *Ma huang* and *Ma huang-gui zhi* (Ma Huang and gui zhi, which is also called Cinnamomi *ramulus*), is adjusted based on the content of	In an open field test, the mice that received *Ma huang* showed higher locomotor activity than the mice treated with a placebo. The exam of the anxiety parameters showed that *Ma huang*	*Gui Zhi* showed a neuroprotective effect against the hyperactivity induced through *Ma huang*.

		ephedrine. It was a realized open field test.	decreased the central activity.	The study shows the advantage of the two plants being used together.
Hwang et al., 2014	Sprague-Dawley male mice.	Mice were divided into *Ma Huang* group (1,0 g *Ma huang*/2 mL of PBS) and control group (2 mL of PBS), and, later, they were submitted to treadmill test, rotarod, and open field test.	The locomotion capacity with *Ma huang* was smaller if compared to the control group's mice, but the length stays when a shock was delivered showed to be longer than in the mice fed with PBS, showing that the treatment leads to a higher capacity to handle external stimulus.	The group that was treated showed a higher capacity to handle external stimulus and a sense of direction.

cWG: cultivated wild ginseng; BUN: blood urea nitrogen; LAC: lactate acid; LDH: lactate dehydrogenase; TG: triglyceride; CPK: creatin kinase; STAT3: activator of transcription 3; PPARγ: peroxisome proliferator-activated receptor gamma; CEBP: CCAATT enhancer binding proteins; VO_2 max: maximum volume of oxygen; H/R: hypoxia/reoxygenation; AP1: Acid polysaccharide fraction of ginseng; GR: Glucocorticoids receptor; ER: Estrogen receptor; AG: formulation of Antrodia camphorata and Panax ginseng; CMG: Changbai Mountain Ginseng; H2O2: hydrogen peroxide; NLC: nanostructure of the lipid carrier; PL: placebo group; CK: creatin kinase; GIBE: 1 hour before having step exercises for 20 minutes; GIAE: ginger intake immediately after exercise; EE: eccentric exercise; IL: interleukin; PBS: Phosphate buffered saline solution; CNS-OT: Central nervous system oxygen toxicity; ICAM-1:intercellular adhesion molecule-1; MCP-1: 1 monocytes chemo tactic protein; HIIT:

High intensity interval training; CT: total cholesterol; TG: triglyceride; LDL: Low density lipoproteins; IL-10: interleukina 10; hs-CRP: Changes in the inflammatory markers; IL-6: Interleukina 6; IL-1β: *interleukina 1* beta

Table 2. Effects of capsaicin and caffeine on *in vitro* studies, experimental models, and humans.

Reference	**Model**	**Intervention**	**Outcomes**	**Conclusion**
Capsaicin				
Rossi et al., 2018	Randomized, double-blind trial with 10 trained men (age = 22,7 ±4,0 years).	Anthropometric measures and body composition were evaluated. Each individual took a placebo or *capsaicin* (12 mg) and, following, he performed 4 sets of squats until the transitory muscular failure. Blood lactate was analyzed.	The total weight lifted and the total number of repetitions were higher for the individuals who used capsaicin if compared to a placebo. The blood lactate significantly increased after each set of exercises and the effort rate was significantly smaller for the group that used capsaicin.	The acute use of capsaicin improves the resistance training performance for young trained men.
Somoza et	Adipocytes 3T3-	Capsaicin and nonivamide (1	Accumulation of lipids was reduced with both tested	Concentrations of

al., 2018	L1 and HepG2.	nM and 10 μM) were used in 3T3-L1 completely different adipocytes and in metabolically active HepG2.	substances. The producers' routes of energy were decreased after the incubation with both the capsaicinoids at the concentration of 100 μM, as it was indicated by the reduced use of mitochondrial oxygen and reduction of the glucose uptake and oily acid. In HepG2 cells, the use of oxygen and the energy loading potential decreased.	capsaicin and nonivamide between 0,1 and 100 μM modulate the mechanisms of the energetic cellular metabolism into a similar extension.
Xia-Guo et al., 2017	Female mice.	Animals were divided into 4 groups: b and d received capsaicin; a and c were treated with placebo. Afterward, the groups c and d were submitted to HLS, while the groups a and b were submitted to the total load of the hindquarters.	The trabecular bone volume was reduced by 40% and 50% in the groups b and c, respectively, and it was also significantly reduced in group d. In comparison to the group a, the maximum strength in group b decreased by 20,3%, while it did not significantly change in group c.	The effect of capsaicin is similar to HLS, but this last does not have the same effect of capsaicin on reducing the bone density and the mechanical properties.
Yi-Ju et al.,	8-week-old ICR	Animals were divided into 4	Grip strength tests and exhausting swimming time of	Capsaicin improved

2016	female rats.	groups: control, CAP-1X group (205 mg/kg), CAP-2X group (410 mg/kg) and CAP-5X group (1025 mg /kg). The anti-fatigue activity and the exercise performance were evaluated using grip strength tests, exhausting swimming time and serum lactate levels, ammonia, glucose, BUN, and CK, after swimming exercise of 15 minutes.	the CAP-5X group were higher than the other groups. The supplementation with CAP reduced the serum lactate, ammonia, levels of BUN and CK, and it increased the glucose concentration after the 15-minute-long swimming test. Besides that, CAP also increased liver glycogen content.	the grip strength tests and resistance performance. The parameters related to fatigue induced through exercise improved in a dose-dependent way.
Ohyama et al., 2014	C57BL/6J male rats.	Animals were divided into 4 groups: high-fat diet (HFD, Control); HFD with 0,3% of CSNs; HFD with voluntary wheel exercise, and HFD with 0,3% of CSNs and voluntary wheel exercise (Exercise +	The supplementation with CSN and exercise reduced the body weight gain and fat accumulation and increased the body energy expenditure in comparison to the exercise alone. It also improved the metabolic profile; it prevented the hepatic steatosis and decreased the size of the adipose cells in the white adipose tissue. It increased the lipolysis, the	CSNs promote the raise of the energetic expenditure through the activation of the fat oxidation in the skeletal muscle.

		CSN).	oxidative phosphorylation activation, and the oxidation of oily acids in the skeletal muscle.	
Caffeine				
Krzysztof et al., 2019	Randomized, double-blind, placebo-controlled trial with 22 male judokas, aged 21,7± 3,7 years old.	The athletes received supplementation of 3, 6 or 9 mg/kg of body weight of caffeine or placebo 60 minutes before the tests session. During each session, all the athletes had a warm-up (Special Judo Fitness Test) and an activity of combat. The heart rate and effort rate were monitored.	The supplementation with 6 and 9 mg/kg of caffeine improved the performance of SJFT, while with 9 mg/kg the combat activity was raised. Doses of 3 mg/kg of caffeine did not show any positive ergogenic effect.	The supplementation with caffeine is effective in the performance and exercise capacity at judo.
Wilk et al., 2019	Randomized placebo-controlled trial. The study had 20 male individuals	Individuals were divided into 2 groups: caffeine (5mg/Kg b.m) and placebo. After warming-up, individuals took a set of supine exercises with a load of	There was a significant difference in the time under tension for the group supplemented with caffeine if compared to the placebo group. There was also an increase in velocity at the eccentric phase of the movement. There was no significant difference in	Caffeine before the exercise does not affect the power and the velocity at the concentric phase of

	aged 25,7 ± 2,2 years old.	70% for 1RM (102,3 ± 8,5 kg) until the momentary failure. The eccentric and concentric phases were taken at maximum velocity.	the power and velocity at the concentric phase of the movement.	the movement, but it increases the velocity of movement of the bar at the eccentric phase.
Moore et al., 2018	Control repeated study, double-blind, placebo-controlled with 11 male athletes, aged 25 ± 4 years old.	Individuals had a session that occurred after a regular night's sleep, and the other two sessions that occurred after 24 hours of sleep privation. Later, a group received supplementation of 6 $mg.kg^{-1}$ of caffeine and the other received a placebo. During each session, vertical high jump, straight-up racing for 20m and 5-meter-long race	Significant differences were not identified when comparing no-sleep-depriving interventions and sleep-depriving interventions on any of the outcome measures evaluated. Furthermore, there were no significant differences observed on any of the measures when comparing the caffeine and the placebo data during the sleep privation.	During 24 hours of acute sleep privation, there was no significant impact of caffeine on the anaerobic performance and the anaerobic performance during the sleep privation state.

		were realized.		
Casazza et al., 2018	Randomized, double-blind, crossover, placebo-controlled trial with 13 male runners.	Male runners (n=13) who ran 1 mile after the intake of 90 mg/kg of coffee, 90 mg/kg of decaffeinated coffee, or placebo.	The 1-mile run times were 1,3% faster after the intake of coffee if compared to the decaffeinated coffee, and 1,9% faster if compared to placebo.	Caffeine is ergogenic support commonly used to increase performance, mainly of athletes.

CNS-OT: Central nervous system oxygen toxicity; CAP: capsaicin; CSNs: capsinoids; HLS: hind limb suspension; HFD: high-fat diet; BUN: blood urea nitrogen; CK: creatine kinase.

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