Review

Phytochemical Contain, Biological Properties and Toxicities of Herbals Used for Doping

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Phytochemical Contain, Biological Properties and Toxicities of Herbals Used for Doping

Modeste Traore [1,*], Samson Guenne [1,*], Ghislain Kobende [2], Arthur A. A. Dabone [1], Mamounata Diao [2], Hemayoro Sama [2], Juste Y. Bonzi [3], Gérard Coulibaly [3], Adama Hilou [1] and Martin Kiendrebeogo [1,*]

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Abstract: Substances derived from herbals are much in demand in doping practices because of their interesting biological properties for physical exercise and sport. This review aimed to investigate anti-fatigue herbals, their properties, analysis methods and toxicity. Data indicate that phytomolecules have beneficial effects on the physiological and biochemical parameters of the body undergoing exercise. They reduce fatigue and promote recovery by improving antioxidant enzyme activities, immune responses, blood pressure, body composition and by reducing the accumulation of toxic metabolites and systemic inflammation. Thus, the use of herbal could provide relief to people who exert intense physical activities such as farmers and athletes; for this, these peoples must do careful, the use of doping herbal must be done in accordance with all the previsions which take into account the need for the use of herbal supplement, the doses. In addition, these benefits attributed to herbals should not conceal the drawbacks of using them in sport. Some phytomolecules are toxic when used in large quantities, and others, in this case alkaloids, should be avoided by athletes.

Keywords: doping herbal; phytomolecule; antioxidant; antifatigue; phytotoxicity physical exercise

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1. Introduction

Today's daily life places human beings in an environment where they face many challenges to overcome if they want to demonstrate their existence. The major challenges are adapting quickly to new situations that are imposed on him and the requirement for results, proof of performance. Performance in competitive societies is the essential criterion in all spheres of activity. It is more remarkable in the fields of physical and sports activities[1]. Generally, regular physical and sports activity is a health factor both in terms of preventing the main chronic diseases, maintaining or even improving health capital and managing most chronic diseases[2,3]. The medical prescription of a physical and sports activity is an important element of public health in primary and secondary prevention of many diseases [4]. Thus it is recommended 2 hours and 30 minutes (150 minutes) of moderate intensity aerobic activity every week and muscle-strengthening activities on 2 or more days a week that work all major muscle groups [5].

However, physical activity practiced chronically or in competitive sport can develop deficiencies in physiological functions and myocardial damage [6]. It is considered as a powerful stimulus influencing the overall physiology of the human body and lead to biochemical changes in various tissues and impact gene expression [7](Świątowy et al., 2021). Exercise itself can be a form of stress

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and cause fatigue or various types of damage to the body [8]. Also, psychological stress, mental tension and lack of sleep in their daily life could lead to fatigue (J. Chen et al., 2023).

Fatigue is defined as physical and/or mental weariness resulting from exertion, and an inability to continue exercise at the same intensity. Accumulated fatigue can affect an individual's performance [9](Teng & Wu, 2017). Fatigue also is a common symptom both in sickness and in health and is also a common symptom in the community, with up to half of the general population complaining of fatigue [10,11](L. Hu et al., 2015; Jinchun & Jie, 2011).

The factors which induce fatigue are the consumption and depletion of energy sources, production and accumulation of metabolic products in the body, production of imbalance between the body's oxidation and anti-oxidation system which will put the body in a state of oxidative stress and bring injury to the body by attacking large molecules and cell organs[7,12]. The exercise leads to muscular fatigue development and can increase the risk of athlete's injuries[13] (Morana & Perrey, 2009). The competition in sports is getting tougher, and the drives to achieve better result has led the athletes to indiscriminately use dietary supplements, including herbal ones [14]. Thus, it is common to observe doping behavior in the context of these physical and sporting activities. Indeed, for a very long time, man has sought to improve his sporting and intellectual performance by resorting to doping behaviors. Doping practices are defined as the use of artificial means to improve physical or intellectual performance [1]. Doping practices are based on the tools and methods of modern medicine and above all alternative medicine, which one is based on phytotherapy. Various synthetic or natural substances called performance enhancing drugs (of animal or vegetable origin) are used and these drugs are grouped into several broad categories: improving concentration and alertness; enhancing strength, power and explosiveness; improving the oxygen-carrying capacity of blood, augmenting recovery, recuperation, and reconstitution of the athlete and ameliorating inflammation and pain [5]. Herbals can improve physiological capacities by decreasing exercise-induced physical fatigue and improve [15–17]. That can explain the increase of use of herbal medicinal products and supplements during last decades[18]. The exercise performance can be improved by various compounds found in tropical fruits such as banana, cherry, grape, pomegranate, and watermelon. Overall, tropical fruits can aid sports performance by improving physical strength, increasing the recovery in injury, attenuate muscle soreness, and reducing fatigue [14].

The objective of this review aimed to investigate anti-fatigue plants in the world through a description of the plants, their compounds or molecules, the analysis of the methods used to study their anti-fatigue properties, the techniques and methods of evaluation of sport performance and the toxicity of anti-fatigue plants.

2. Methods

To collect scientific papers, databases as "ScienceDirect", "PubMed" and "Google Scholar" were queried. Key words "Plants used in doping", "Anti-fatigue activity", "Antioxidant plants", "immunity system and sports activity", "sports performance and sport", "sport activity and intellectual capacity", "sport and neuropsychiatric disorders, "antifatigue compounds from plants", "plants and bioenergy", "herbal toxicity". This review, covered the period from 1985 to 2023 and analyzed 199 documents.

3. Anti-fatigue herbals

The various social pressures encountered in work and non-work situations give rise to physical fatigue, which can impair work efficiency and quality of life [19]. Fatigue is also a common symptom of many serious illnesses [20,21]. Exercise-induced fatigue is a multi-origin physical and mental phenomenon [22]. According to Luo et al., the mechanisms involved in fatigue could be due to by reduction or polymorphism of neurotransmitters in the central nervous system, by alteration of the autonomic system in the peripheral nervous system, by accumulation of metabolites, reduction in the free energy of ATP degradation, limited availability of oxygen or substrate, by mitochondrial dysfunction, reduced glycogen storage and blood sugar levels at the metabolic level or by increased levels of pro-inflammatory cytokines in the immune system[20]. It is therefore necessary and important to develop effective and safe drugs or treatment regimens to combat fatigue and facing failure of main pharmacological therapies for fatigue with their serious side-effects, natural drugs with anti-fatigue effects offer new alternatives[23]

An increasing number of studies have shown that active components of natural foods can safely and effectively prevent and relieve fatigue, indicative of the potential of these components as anti-fatigue agents. Meanwhile, antioxidants from some natural herbals were found to possess a remarkable anti-fatigue effect [20].

Herbs have been used as medicine throughout history [24] and can be used for medicine, cooking, cosmetics and as a perfume or dye [25]. In the traditional sports, herbs are used to increase physical resistance and performance[26,27]. In their ethnobotanical surveys carried out in Burkina Faso, researchers have identified a multitude of plants species used in the optimization of exercise and these plants are known to prevent muscle and skeletal disorders, aches and pains, fatigue and mental disorders[28,29]. Athletes are among those who use herbs for their own benefit, to help them improve performance, speed recovery, maintain health and fitness during intense training periods, increase muscle mass and reduce their body fat[25]. More and more researchers devoted themselves to studying natural active ingredients in organism as the anti-fatigue drugs and scientific scrutiny with controlled clinical trials has only recently been used to study such effects [10,26].

3.1. Rhodiola rosea L. (Crassulaceae)

This herb is in traditional medicine to stimulate the nervous system, treat stress-induced fatigue and depression, improve physical performance and work productivity [30] and is considered as an adaptogen plant [31]. There are a large number of scientific publications on the clinical efficacy in terms of cognitive function and mental performance, including various symptoms of life stress, fatigue and physical performance in athletes of various preparations of this plant [30,32]. It has been demonstrated that chronic supplementation of extract provide anti-fatigue potential, improve body resistance to physical strenuous efforts by decreasing the fatigue biochemical marker levels and increasing the time to fatigue through the increase in tissue oxygenation level, liver glycogen content [31,33]. However Jówko *et al*. indicated that chronic ingestion does not affect physical performance, but may improve the results of certain psychomotor tests in young, healthy, physically active males[34]. A study examined the protective effects of fermented extract against fatigue and exercise stress and has demonstrated that fermented extract effectively protects against fatigue caused by strenuous exercise by increase swimming time, hepatic superoxide dismutase content, and serum lactate dehydrogenase in mice [32]. The effects of short-term has been examined by Williams *et al*. who indicated that supplementation may enhance explosive resistance training performance but may also impair upper body strength-endurance on blood lactate, catecholamines, and performance during repeated bench press exercise[35]. The effects of an acute dose on endurance exercise performance in eighteen female students engaged in recreational activities showed a decrease in submaximal exercise heart rate and an improvement in exercise performance, endurance exercise by reducing perceived exertion [36]. By investigating the effect of acute doses and 4 weeks, De Bock *et al*. showed that both doses can improve endurance capacity in young volunteer athletes[37]. A randomized, double-blind, placebo-controlled, parallel-group clinical study with an additional no-treatment group was performed by Shevtsov *et al*. on the one hand to measure the effect of a single dose of standardized extract on the capacity for mental work in a context of fatigue and stress and on the other hand to find the difference between two doses [38](a standard average dose in accordance with well-established medical use as a psychostimulant, the other dose being higher). This study showed a pronounced anti-fatigue effect with a dose dependent relationship in favor of the lower dose in psychometric tests but without any dose relationship in physiological tests . Another study on supplementation (Rhodiola rosea and caffeine) provided practical evidence that this combination could serve as a potential supplement for individuals, especially resistance exercise trained subjects, to enhance physical performance effectively and safely security[39].

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3.2. *Camellia sinensis (L.) Kuntze (Theaceae)*

The tea plant Camellia sinensis is a member of the theaceae family. Green tea is provided from fresh leaves at high temperatures, thereby inactivating the oxidizing enzymes and leaving the polyphenol content intact [40]. This herbal has showed an anti-fatigue effect on forced swimming on mice and these effects were dose-dependent; when dosage was high, it normally would improve the effects much better [10,40]. Machado *et al*. has demonstrated that tea extract preserves neuromuscular activation and muscle damage markers in athletes subjected to cumulative fatigue and suggested that a supplementation may have potential to serve as a strategy to improve performance and recovery in conditions of cumulative exercise[41]. Jówko *et al.* has demonstrated that supplementation prevents oxidative stress induced by repeated cycle sprint tests in sprinters, but this does not seem to hinder training adaptation in antioxidant enzyme system. On the other hand, neither prevention of exercise-induced muscle damage, nor an improvement in sprint performance is noted after green tea extract administration[34].

3.3. *Panax ginseng C.A. MEYER (Araliaceae)*

Panax ginseng C. A. Meyer (ginseng), a Chinese medicinal plant of the genus Panax, boasts a rich historical record of usage that dates back to the paleolithic period, is becoming increasingly popular as a remedy for fatigue and asthenia[42–45]. This plant, a worldwide renowned adaptogen, is believed to reduce stress and augment endurance performance [46]. Panax ginseng treatment (100 mg/kg) protected muscles from eccentric exercise injuries and was effective in preserving mitochondrial membrane integrity and reduced carbonyl contents in the muscles [47]. An investigation concluded that acute supplementation of 200 mg, one hour prior to the exercise exerted significant effect on the physiological parameters measured during the endurance running by ameliorating exercise induced oxidative stress and there by augmenting exercise performance[46]. An high-dose ginsenoside complex supplementation on exercise performance in healthy adults during a 12-week supervised exercise program showed that high doses of ginseng supplementation could improve aerobic capacity during physical training [42]. The evaluation of the potential beneficial effects of the mix formulation (*Antrodia camphorata* and *Panax ginseng*) on fatigue and ergogenic functions following physiological challenge demonstrated a reduction of serum lactate, ammonia, BUN and CK activity after the swimming test, as well as increase in glucose [48]. Oh *et al*. has investigated the anti-fatigue activities of its compound in mice, using the weight loaded swimming and the rota-rod tests[49]. Their authors found that certain ginseng compound significantly increased the weight loaded swimming time, inhibited the weight loaded swimming-induced increase in corticosterone, lactate, lactate dehydrogenase, and creatinine levels as well as the reduction in glucose level [12,49]. Therefore, ginseng supplementation did not exert an ergogenic property on aerobic fitness enhancement in well-fit individuals [50]. Many other medicinal plants have been studied about their anti-fatigue properties. Luo et al. indicated that combined oyster peptide and ginseng extracts can be used as an effective anti-exercise-fatigue and sexual improvement supplement by decreasing the accumulation of metabolites like LA and BUN, declining the oxidative damage and the consumption of liver glycogen[12]. Also, the combination showed a synergistic effect on the improvement of mating ability after exercise fatigue in male ICR mice. The Table 1 gives an overview of some herbals whose effects following physical exercise have been studied.

Table 1. Anti-fatigue herbals studied.

Species names	Famillies	Properties	Parts used	References
Acanthopanax senticosus	Araliaceae	anti-fatigue	Root	[51]
Acanthopanax senticosus	Araliaceae	anti-fatigue	stem bark	[52]
Anisomeles indica	Lamiaceae	Anti-fatigue	Whole plants	[53]
Antrodia camphorata	Fomitopsidaceae	Physical fatigue	Fruiting body	[48,54]

Astragali Radix and Angelicae Sinensis Radix		Antifatigue	root	[55]
Bambusa tuldoides Munro	Gramineae	Anti-fatigue		[56]
Cannabis sativa L	Cannabaceae	Anti-fatigue	leaves	[57]
Castanea mollissima Blume	Fagaceae	anti-fatigue	flowers	[58]
Cistanche deserticola Y.C. Ma	Orobanchaceae	Antifatigue	stems	[59]
Camellia sinensis (L.) O. Kuntze var.	Theacaea	Antifatigue		[34,40,41]
Cordyceps militaris	Cordycipitaceae	anti-fatigue		[60]
Eriobotrya japonica (Thunb.) Lindl.	Rosaceae	Physical capacity	leave	[61]
Fagopyrum tataricum	Polygonaceae	Antifatigue	grain	[62]
Fagopyrum esculentum Moench	Polygonaceae	Antifatigue	grain	[55]
Glossogyne tenuifolia		Anti-Fatigue		[63]
Moringa oleifera Lam.	Moringaceae	antifatigue	leave	[64]
Morus alba L. (Mulberry)	Moraceae	anti-fatigue	leave	[65]
Panax ginseng CA Meyer	Araliaceae	anti-fatigue		[42,45,46,48]
Panax quinquefolium	Araliaceae	anti-fatigue		[66]
Passiflora edulis Sim	Passifloraceae	Anti-fatigue	fruit epicarp	[67]
Paullinia cupana linn	Sapindaceae	Anti-fatigue		[68]
Physalis pubescens L	Solanaceae	anti-fatigue	Fruit	[69]
Polygonum cuspidatum	Polygonaceae	Physical capacity	root , rhizome	[70]
Portulaca oleracea L.	Portulacaceae	Anti-fatigue	leave	[17]
Punica granatum L.	Punicaceae	physical performance	fruit	[71]
Radix notoginseng	Araliaceae	anti-fatigue	Root	[72]
Rhodiola rosea	Crassulaceae	Antifatigue	root	[30,32,34,35,39,73,74]
Rhododendron adamsii Rehder	Ericaceae	physical performance	Leave	[75]
Rubus coreanus Miquel	Rosaceae	Antifatigue	Fruit	[76]
Senna siamea	Polygonaceae	Antifatigue	leaves	[77]
Siraitia grosvenorii	Cucurbitaceae	anti-fatigue.	Fruits	[78]
Taraxacum officinale	Asteraceae	physical fatigue		[11]
Toona sinensis Roemor	Meliaceae	antifatigue	leavef	[79]
Trigonella foenum-graecum L.	Fabaceae	anti-fatigue	Dry seeds	[80]
Withania somnifera	Solanaceae	physical performance	root	[81]
Zea mays L.	Poaceae	anti-fatigue	Corn silk	[82]
Citrullus lanatus cv	Cucurbitaceae	Sore Muscle Relief in Athletes	watermelon juice	[83]

4. Secondary metabolites with anti-fatigue properties

The antifatigue properties of herbals are associated with secondary metabolites that they contain. Authors which have evaluated anti-fatigue potential of herbal, has sought to know and identified the different groups of phytochemicals metabolites (polyphenols, terpenoids, saponins and alkaloids, saponins glycosides, polyacetylenes, phytosterols) which could lead to improvement of athletic performance and reducing fatigue [9,84].

4.1. Phenolics compounds

Phenolics compounds are characterized structurally by two or more hydroxyl groups attached to one or more benzene rings (Figure 1) and provide the taste and color characteristics of fruits and vegetables. They are radical scavengers and metal chelators. Polyphenols represent a natural and benign component of the human diet, possess anti-inflammatory properties and have been shown to enhance brain health and cardiovascular function via nitric oxide-mediated mechanisms [85,86].

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Several studies have shown that the anti-fatigue potential of plants is attributable to their phenolic compounds, as taking polyphenol supplements reduces inflammation and oxidative damage induced by intensive exercise. [85,87]. It would appear that acute supplementation with 300 mg of polyphenols 1 to 2 hours before exercise improves exercise capacity and that 1000 mg of polyphenols per day for 3 days or more before and after exercise improves recovery from muscle damage via antioxidant, vascular and anti-inflammatory mechanisms [85]. Liudong *et al*. has indicated that green tea polyphenol has prolonged the swimming time of mice with less fatigue[40]. The same effect was observed with phenylethanoid-rich extract of *Cistanche deserticola* Y.C. Ma, by decreasing muscle damage, delaying the accumulation of lactic acid and by improving the energy storage [59]. Flavonoids compounds had also showed anti-fatigue activity [58,88,89]. Anti-fatigue activity of flavonoids of *Castanea mollissima, Fagopyrum esculentum* and *Puerariae radix* has been studied and authors has showed incrising energy reserves, oxidative stress inhibition and improvement of the metabolic control of exercise [58,88,89]. Assessment of biochemical parameters of blood related to fatigue, has demonstrated that acute or chronic resveratrol (Figure 1), a natural flavonoid polyphenol, may support the attenuation of soreness and inflammation, improve mitochondrial function in skeletal muscle and the antioxidant defense after extensive exercise and is beneficial for suppressing the aging-related decline in physical performance and for performance recovery [32,87,90–92]. Indicating that (-)-epigallocatechin-3-gallate (EGCG) (Figure 1) is the most abundant polyphenol in green tea that exhibits a variety of bioactivities, Teng & Wu demonstrated that EGCG significantly prolonged exhaustive swimming time and decreased the levels of BLA, SUN, SCK and MDA, which were accompanied by corresponding increases in liver and muscle glycogen contents, and SOD, CAT, and GPx activities[9]. Polyphenols supplementation may enhance exercise performance and recovery from intensive exercise with the mechanisms most likely to be related to antioxidant and vascular effects. However, this research is at an early stage and more work is required to optimize dosing strategies and to determine the specific modes, intensities and durations of exercise for which ergogenic effects may be achieved [85].

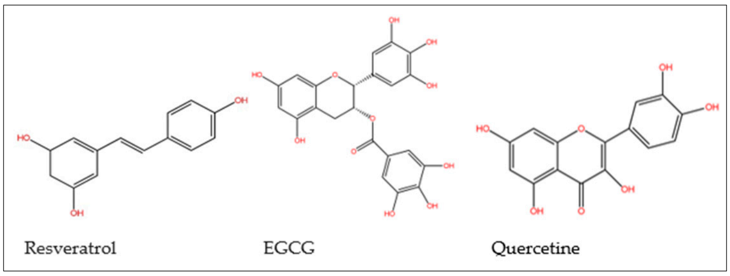

Figure 1. Strucutures of phenolic compounds.

4.2. Terpenoids

Terpenoids are a class of natural products derived from mevalonic acid (MVA) which are composed of a plurality of isoprene (C5) structural units. They are a set of important in plants with diverse structures. Terpenoids have many potential applications, such as insect resistance, immunoregulation, antioxidation, antiaging, and neuroprotection [93]. Terpenoids have all been shown to improve relevant aspects of cognitive function and alertness [86]. It was suggested that the terpenoids are the active components contributing to the antioxidant effect such as inhibition of lipid peroxidation and prevention of the formation of proximities through scavenging nitric oxide and superoxide anion, and help to regulate the body testosterone level especially when the level was abnormally high by inhibiting the production of 5α-reductase which was an important enzyme to activate testosterone[94]. Evaluation of the anti-fatigue activity of a pentacyclic triterpenoid extract from the bark of Bambusa tuldoides Munro in mice showed a great potential for their anti-fatigue activity [56]. Huang et al. identified ergostane-type triterpenoids, dehydrosulphurenic acid (Figure 2), 15α-acetyldehydrosulphurenic acid, lanostane-type triterpenoids in extracts of A. camphorata which has showed antifatigue activity by decreasing plasma lactate and ammonia levels and increasing blood glucose concentration and liver and muscle glycogen deposition, thereby elevating exercise performance in mice[54]. Major anthocyanins such as cyanidin-3-O-glucoside, cyanidin-3-O-rutinoside and peonidin-3-O-glucoside identified in purified anthocyanin of purple passion fruit epicarp has prolonged the weight-loaded forced swimming time, decreased lactate dehydrogenase, blood lactate and blood urea nitrogen levels, and increased the liver glycogen content[67]. Ginsenoside from panax ginseng supplementation has increased improvement of aerobic capacity [42]. Findings has suggested that 20(S)-ginsenoside Rg3, protopanaxadiol-type and protopanaxatriol-type ginsenosides had antifatigue effects, by activation of energy metabolism, elimination of metabolites accumulated, and protection from exercise induced oxidative stress[49,95] . The ginsenosides are considered as the main constituents of ginseng having different pharmacological activities such as anti-fatigue, anti-cancer, anti-aging, anti-oxidant, anti-hyperglycemic, anti-obesity [84].

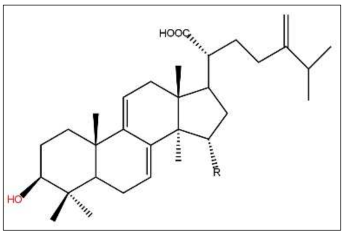

Figure 2. Structure of Dehydrosulphurenic acid.

4.3. Alkaloid

Alkaloids are a huge class of natural occurring organic molecules, which contain nitrogen atom or atoms in their structures. They are present not only in human daily life, in food and drinks but also as stimulant drugs, medicines, narcotics, insecticides and in many physiological activities. They showed strong biological effects on animal and human organisms even in very small doses [96]. Hsu et al. found that capsaicin (Figure 3) supplementation could improve grip strength and endurance performance[97]. Caffeine (Figure 3) has enough scientific evidence indicating an ergogenic effect [98]. Low doses of caffeine are also ergogenic in some exercise and sport situations, do not alter the peripheral wholebody responses to exercise; improve vigilance, alertness, and mood and cognitive processes during and after exercise[99]. In trained men, caffeine at 3–5 mg/kg may improve high-intensity sprint performance when ingested 30 minutes before exercise [100]. Nicotine seems to have ergogenic potential to Athletes and appear to benefit from activation of the sympathoadrenal system with increased catecholamine release and subsequent increases in muscle blood flow and lipolysis [98].

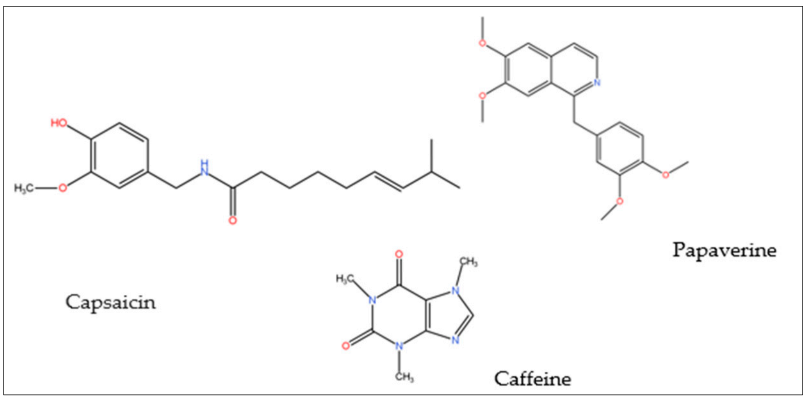

Figure 3. Structure of some alkaloids.

5. Primary metabolites with sports endurance property

Energy sources are essentially based on the three categories of primary metabolites that constitute the nutrients that meet the needs of basic physiological functions. Nevertheless, the anti-fatigue effects of primary metabolites have been evaluated among protein and polysaccharides extracted from plants and amino acids.

5.1. Protein

The effect on physical and athletic performance of proteins has been studied. Wang et al. have reported that natural bioactive peptides alleviate exercise-induced fatigue via a variety of complex biological reactions and molecular mechanisms that include involvement and regulation of energy metabolism, inhibition of inflammatory responses, reduction of reactive oxygen species and regulation of neurotransmitters[101]. The proteins used include aspartate, asparagine, cystine and glutamine mixture, L-Citrulline, taurine, NO3−rich supplements, dietary nucleotides [5,15,22,102–104]. American ginseng proteins showed anti-fatigue activity in mice, measured by physiological indices of fatigue according Qi et al.[66]. The results of aspartate and asparagine supplementation on the determinants of fatigue in Wistar rats exercised to exhaustion showed that their supplementation can increase the contribution of oxidative metabolism to energy production and delay fatigue during exercise performed above the anaerobic threshold[102]. Findings also suggested that NO3-rich supplements could be a suitable strategy to improve performance in sports modalities in which power and acceleration largely determine performance [15]. Data suggested that taurine supplementation modulates various cellular remodeling parameters after overuse-induced muscle damage, and that these positive effects may be related to its antioxidant capacity [103]. Known as a nitric oxide precursor and to enhance high-intensity exercise performance, beetroot juice supplementation has an ergogenic effect, NO3−rich supplements could be a suitable strategy to improve performance in sports modalities [15]. A study on the anti-fatigue effects of dietary nucleotides (NTs) on mice has suggested that NTs exert anti-fatigue effects, which may be attributed to the inhibition of oxidative stress and the improvement of mitochondrial function in skeletal muscles. NTs could be used as a novel natural agent for relieving exercise fatigue [104]. Ma et al. revealed that cystine and glutamine mixture supplementation attenuate fatigue during endurance exercise in healthy young men by enhancing fatty acid utilization[22]. High protein intake and exercise are two factors that preserve and enhance muscle and protein intake in the range of at least 1.2 to1.5 g/kg/day is recommended [5].

5.2. Polysaccharides

The polysaccharide extracts have been credited with multiple benefits such as improved muscle glycogen and athletic performance, increased endurance times, resistance to fatigue, decreased oxidative stress after intense exercise, detoxification of the body, immunomodulatory, hepatoprotective, antitumor, anti-aging, antioxidant and hypoglycemic activities [105,106]. Polysaccharides extracted from Portulaca oleracea L. prolonged the riding times and exhaustive swimming times of mice, decreasing blood lactic acid and serum urea nitrogen levels, as well as increasing the liver and muscle glycogen contents [17]. Results of Liu et al. provided theoretical support for the application of polysaccharides extracted from Hericium erinaceus (HEP) in the field of sports nutrition with significant anti-fatigue activity[106]. Jo et al. indicatited that consumption of carbohydrate-rich meals before exercise resulted in less disruption of circulating numbers of leukocytes, neutrophils, and T-cell subsets, and less elevation of plasma IL-6 concentrations immediately after exercise and during the 2 h recovery period. Moon et al. revealed that large (48-g) and small (24-g) of daily isonitrogenous doses of rice and whey protein in combination with an eight-week resistance training program led to similar changes in body composition and performance outcomes such as improvements in strength and fat-free mass [107] The tables 2 and 3 summarizes products derived from plants whom enhance physical performance potential was studied.

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Table 2. Results of studies of some Phyto molecules identified.

Class	Molecule	Subjects	Exercises Tests	Doses et duration of administration	Results	References
steroidal glycoside	Ginsenoside	sedentary Individuals	Aerobic exercises and muscle strengthening.	100mg/j and 500mg/j 12 weeks	↑VO2max ↑muscle strength	[42]
	Ginsenoside-Rg1	Rats	Exhaustive swimming	0.1 mg/kg bodyweight per day for 10-week.	↑antioxidant defense system in skeletal muscle ↓membrane lipid peroxidation	[108]
	20(S)-Protopanaxadiol 20(S)-Protopanaxatriol	Mice	Weight-loaded wimming and rota-rod tests	5 and 10 mg/kg	↑riding time in the rota-rod test, inhibiting corticosterone, lactate, and creatinine levels.	[49]
	20(S)-Ginsenoside Rg3	Mice	Forced swimming tests	10, 20 and 40 mg/kg once a day lasting for 28 days	↑exhaustive exercise time, ↓decreased blood lactic acid, serum urea nitrogen levels, ↑GLU, SOD, glutathione peroxidase and catalase in liver and muscle, ↓MDA levels	[95]
Alkaloid	Capsaicin	Male ICR mice	Forelimb grip strength, exhaustive swimming	4 weeks at 0, 205, 410, and 1025 mg/kg/day	↓serum lactate, ammonia, BUN and CK levels ↑glucose concentration	[109]
	Caffeine C + ephedrine E	Athletes	Cycling exercise	C (5 mg / kg), E (1 mg / kg), C+E	↑exercise time to exhaustion and central nervous system stimulation.	[110]
Flavonoid	Eleutheroside	Mice	load-weighted swimming test, sleep deprivation test	500 mg/kg and 200 mg/kg	Relief of physical and mental fatigue	[51]
	Resvératrol	Mice	forelimb grip strength, exhaustive swimming	25 mg/kg mice/day for 28 consecutive days	Improved muscle strength and endurance	[111]
	Resveratrol	Male ICR mice	forelimb grip strength, exhaustive swimming time	0, 25, 50, and 125 mg/kg/day 21 days	↑exhaustive swimming time and grip strength, CK activity and glucose levels ↓serum lactate, ammonia levels	[92]
	(-)-Epigallocatechin-3-gallate	mice	forced swimming exercise	50, 100, and 200 mg/ kg by oral gavage for 28 days.	↑exhaustive swimming time, glycogen contents, antioxydant activities. ↓levels of blood lactic acid, serum urea nitrogen, serum CK and MDA	[9]

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	Glabridin	Male mice	swimming exhaustive exercise	5, 10, 20 mg/kg) for 28 consecutive days	inhibited fatigue, delayed the elevation of blood lactic acid and increase storage of liver and muscle glycogen	[57]
Vitamin	vitamin C supplementation	healthy endurance trained males	single bout of endurance exercise (2.5 h cycling exercise in man)	2 weeks of supplementation with vitamin C, 1,000 mg /day	↑antioxidant defence, modulating the leukocytosis and neutrophilia responses	[56]
Amino acid	Aspartate and Asparagine	Wistar rats	exercised to exhaustion by swimming	350 mM ASP + 400 mM ASG day–1 for 7 days	↑exercise time ↓blood lactate concentration	[102]
Amino acid	γ-aminobutyric acid	Mice	loaded-swimming test	0.15, 0.3, 0.9 g/kg GABA/animal weight,	↑ swimming time	[112]
Amino acid	L-Citrulline	Athletes	maximum effort test in a cycloergometer		reduce the recovery heart rate and muscle soreness after 24 h.	[83]

Table 2. Results of studies of some Phyto constituents identified.

Substance	Subjects	Exercises Tests	Doses	Results	ref
Panax quinquefolium proteins	mice	Forced swimming test	125, 250 and 500 mg/kg of body weight for 28 days	↑swimming ability, ↑GLU levels ↓accumulation of BLA and SUN,	[66]
Ginseng polysaccharides	mice	Forced swim test	15 days	↑anti-fatigue activity	[45]
Polysaccharides from *Portulaca oleracea* L.	mice,	Rotarod test, Forced swimming test	75 /150and 300 mg/kg bw duringg 30 days	↑GLU contents, ↓blood lactic acid and serum urea nitrogen level	[17]
Taraxacum officinale extract	male	Forced swimming test	10, 30 and 100mg/kg b.w for a period of 42 days.	↑swimming capacity, ↓lactate and triglyceride concentrations	[11]
Extract of *Rubus coreanus* fruit	Mice	Forced swimming test	(500 mg/kg/day for 4 weeks	↑forced swimming capacity of mice ,↓plasma ammonia accumulation	[76]
Extract of *Toona sinensis* Roemor	Mice	Swimming test	40, 80 and 160 mg/kg) for 21 days	↑swimming time of the mice, ↓lactic acid,↑liver and muscle GLU, ↓oxidative stress.	[79]
Extract of saponins of Radix notoginseng	Mice	Swimming test	20, 40 and 80 mg/kg body weight/day for 28 days	↑exhaustive swimming time , ↓lactate in the blood, ↑tissue glycogen contents	[72]
Extract of *Siraitia grosvenorii* Fruits	Mice	Swimming test	100, 200 and 400 mg/Kg bw/day for 28 days.	↑swimming time,liver muscle glycogen , ↓BLA, SUN	[78]
Extract of Acanthopanax senticosus.	Mice	forced swimming test	100, 200 and 400 mg/kg	↑tissue glycogen contents ↓ BLA, SUN contents	[52]
Triterpenoid-Rich Extract from *Antrodia camphorata*	Mice	Swimming test.	0, 50, and 200 mg/kg/day	↑exhaustive swimming time, tissue GLU contents and activity of enzymes, ↓BLA, BUN	[54]
Pentacyclic triterpenoid from	Mice	weight-loaded swimming test and climbing test	0.04; 0.08 and 0.25 g/kg body weight	↑swim time, blood glucose, muscular and hepatic GLU	[56]

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Bambusa tuldoides Munro				levels, ↓plasma lactate and ammonia levels and CK activity	
Antrodia camphorata and *Panax ginseng* extract	Mice	swimming test forelimb grip	orally administered for 4 weeks at 0.984, 2.952 and 5.904 g/kg/day.	↓lactate, ammonia, BUN and CK activity, ↑exhaustive swimming time and forelimb grip strength	[48]
Beetroot Juice	young men	Wingate and jump tests	70 mL of BJ (containing 6.4 mmol of NO3−)	Ergogenic effect in a 30-s all-out Wingate test increasing Wpeak,	[15]
watermelon juice	seven athletes	maximum effort test in a cycloergometer	500 mL of natural watermelon juice (1.17 g of L-citrulline)	helped to reduce the recovery heart rate and muscle soreness after 24 h.	[83]
Tartary buckwheat (Fagopyrum tataricum)	Mice	Exhaustive Swimming Time of Mice	60, 120 and 240 mg/kg body weight every day for 28 days	↑exhaustive swimming time, tissue GLU contents and the activities of antioxidant enzymes, ↓BLA, BUN	[62]
Astragali Radix and *Angelicae Sinensis Radix*	Mice	weight-loaded and forced swimming	21.64 ;10.82 and 5.41 g/kg bw daily for 15 days	↓levels of BLA and BUN ↑ SOD.	[113]
Tea seed oil (*Camellia oleifera* Abel)	Mice	weight-Loaded Forced Swimming	0.5 ,1.0, 2.0 g/kg/day At 0 week, 2 weeks and 4 weeks	anti-fatigue effects; improve the effects much better on BUN and hepatic GLU	[10]
Eriobotrya japonica extract	Mice	Exhaustive Swimming	1 g kg-1 per day for 14 days	Enhancing utilization of fatty acid, facilitating lipid catabolism, and ↑ antioxidant capability.	[61]
Irpex lacteus extract	Mice.	swim test, rotating rod and running test.	0.04, 0.2 and 1.0g/kg Seven-day	increased the level of super oxide dismutase reduced the level of malondialdehyde in the liver	[114]
Extract of *Trigonella foenum-graecum* L.	rat	weight loaded forced swim test	10 mg/kg of bw/per day) for a period of two weeks.	Ameliorating various impairments associated with physical fatigue.	[80]
Extract of Anisomeles indica (L.) Kuntze	mice	swimming test	125, 250; 500 mg/kg/day for 28 days	↑swimming time, hepatic GLU muscle glycogen levels, ↓triglyceride, ammonia levels	[53]
Extract of Cistanche deserticola	Mice	forced swimming test	0.25, 0.50, 1.00 g/kg administered orally to mice for 3 weeks.	↑swimming capacity of mice, ↓muscle damage, ↓lactic acid, ↑energy storage	[59]
Extract of Allium sativum L.	rats	Endurance exercise	2.86 g/kg 30 min before every exercise for 4 weeks	↓ levels of NO metabolites, ↑SDH and SOD activities,	[8]
γ-aminobutyric acid from Morus alba L. leaves	Mice	-swimming test	0.15, 0.3, 0.9 g/kg GABA/animal weight,	Increase swimming time	[112]
vitamin and mineral supplement + guarana	young adults (	Cognitive Demand Battery	200 mg/day, and 400 mg/day	Improved cognitive performance and mental fatigue	[115]
creatine + guarana	athletes	test of six maximal sprints	creatine (1000 mg) + guarana (1500 mg)	Beneficial effect on muscle power and decisional cognitive performance	[116]

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6. Methodology used for anti-fatigue phyto molecules identification

Bioactive compounds present in herbal material exist as multicomponent mixtures. Characterization, analysis, separation and identification of bioactive phytoconstituents that may be at the origin of the anti-fatigue potential of herbal involves approaches which the application of common phytochemical screening assays, chromatographic and spectrometrique techniques [23,117,118]. The development of applied untargeted metabolomic assays presents a new direction for the discovery of metabolite indicators for sport and exercise science[119]. The analytical techniques used in metabolomics are nuclear magnetic resonance spectroscopy (NMR) and mass spectrometry (MS) combined with chromatography [120]. Sportomics, application of metabolomics in sport to study the metabolic effects of physical exercise is carried out through the analysis of metabolites present in a biological fluid, such as saliva, blood, feces and urine. sportomics analyzes could be used to know muscle damage or fatigue, prevent and manage injuries, define the best diet and training programs to obtain the best performance from athletes, promote the choice of suitable physical [121]. The Table 4 presents some of the technique used according to the families of groups of compounds.

Table 4. Methodology used for anti-fatigue phyto molecules identification.

flavonoid	Identification technical	Compounds identified	Plant species	Ref.
Phenolic	HPLC -RP	Resveratrol	Passiflora edulis	[122]
Phenolic	HPLC - MS/MS	salidroside, rhodiolosides, luteolin, catechin, quercetin,quercitrin, sacranoside	Rhodiola rosea	[123]
Phenolic	HPLC - MS	castanolB	*Castanea mollissima*	[124]
Phenols	UHPLC	Chlorogenic acid, gentisic acid, rutin, p-coumaric acid; m-coumaric acid, protocatechuic acid; p-hydroxybenzoic	P. ginseng	[125]
Flavonoid	H-NMR, 13C-NMR, HMBC, HMQC and ESI-Q-TOF MS	Kaempferol	*Castanea mollissina* Blume	[126]
Flavonoids	HUVEC/CMC-LC-MS	puerarin, daidzin, pueroside D and 3'-hydroxypuerarin	*Puerariae Radix*	[127]
Flavonoids	HPLC, ESI-MS and NMR	epigallocatechin, epicatechin, EGCG and epicatechin gallate	*C. sinensis* fruits	[128]
Flavonoids	PLC-MS/MS analysis	myricetin-3-O-glucoside, quercetin-3-O-rutinoside, kaempferol	*Castanea mollissima* flower	
anthocyanins	HPLC/UPLC-MS/MS analysis	cyanidin-3-O-glucoside ; cyanidin-3-O-rutinoside, peonidin 3-O-glucoside	*Passiflora edulis* Sims fruits	[67]
Terpenoids	UPLC-Q-TOF-MS	Kankanoside E , Daucosterol, Diosgenin	*Cistanche deserticola* YC Ma	[129]
Terpenoids	LC electrospray mass spectrometric	Ginsenosides	*Panax ginseng*	[130]
TERPENOID	HR-FAB-MS, 1D, 2D-NMR and CD MS	kauranoid diterpene glycoside mollioside	nuts of *Castanea mollissima* Blume	[131]
terpenoids	HPLC analysis.	lupeol, stigmasterol, β-sitosterol, and squalene	seeds of *Panax ginseng*	[132]
terpenoids	NMR and MS analyses	antcins B, C, H, I, K (ergostane-type triterpenoids) and dehydrosulphurenic acid, 15α-acetyldehydrosulphurenic acid (lanostane-type triterpenoids).	fruiting of *Antrodia camphorata*	[54]
terpenoids	GC–MS analysis.	Farnesyl acetone, nootkatone and jasmatone leaf	Anisomeles indica Kuntze essential oil	[133]

allkaloid	RP-HPLC	caffeine and theophylline	seeds of Paulinia cupana Kunth	[134]
allkaloid	DART -TOF-MS	capsaicin	Capsicum annuum	
allkaloid	RP-HPLC	capsaicin	Capsicum annuum	[135]
Alkaloid	LC-MS analysis	Sparteine, papaverine, Caffeine, naloxone	Bambusa. tuldoides	[136]
alkaloid	HPLC-ESI-MS- NMR	caffeine	Camellia sinensis fruits	[128]
alkaloid	HPLC-DAD	Theophiline; Caffeine	Camellia sinensis leaves	[137]

7. Antioxidant, immune system and sports activities

7.1. Exercise and the antioxidant system

Studies provide data on the effects of physical exercise on antioxidant systems, sometimes with contradictory results [138]. The antioxidant system groups together all the body's antioxidant defense tools, which are made up of antioxidant enzymes (superoxide dismutase, catalase and glutathione peroxidase, etc.) and non-enzymatic antioxidants (coenzyme Q10, glutathione, uric acid, lipoic acid, bilirubin, etc.). These antioxidants are molecules that reduce the rate of oxidation of a substrate and the oxidative damage induced by exercise [139]. Physical exercise is a factor that enhances the antioxidant response and promotes the activation of anabolic pathways and mitochondrial biogenesis in skeletal muscle[140]. It leads to an increase of glutathione content in skeletal muscle and in the activity of enzymes in the glutathione redox cycle [141] and to a specific adaptation of antioxidant systems in muscle tissue and fibers [142] . Although exercise leads to increased production of free radicals, Viña et al. report that there is growing evidence that reactive oxygen species (ROS) are not just toxic [143]. ROS generated during muscular activity may play a central role in the adaptive responses of muscles to exercise-induced oxidative stress [144]. They lead to an increase in antioxidant enzymes, their activity and thus increased resistance to oxidative challenges to such an extent that exercise itself could be considered an antioxidant [140,145]. These exercise-induced free radicals are involved in cell signalling and in the regulation of gene expression and activate redox-sensitive signal transduction [140,145]. Important signalling pathways that can be activated in response to ROS stimulation include NFκB, Nrf2 and MAPK [140,145]. Exercise induces activation of MAP kinases that activate the NF-κB pathway and, consequently, the expression of important enzymes associated with defence against ROS such as superoxide dismutase[146]. The exercise-induced production of ROS may also be an important signal to activate proliferator-activated receptor-γ coactivator-1α, a key player in the adaption of muscle cells to exercise peroxisome [147]. Moderate-intensity exercise increases the expression of SOD enzymes [148], the activity of xanthine oxidase and NADPH oxidase which are critical modulators of redox homeostasis [143,149,150]. Powers et al. indicates that ROS production could be a double-edged sword in those moderate levels of ROS production during exercise promote positive physiological adaptation in active skeletal muscle and high levels lead to damage to macromolecular structures[151].

7.2. Exercise and immune system

Immunity is a host defense function that aims to prevent abnormal cells such as tumor cells and foreign microorganisms from invading the body, and involves actions from several types of immune cells (T cells, macrophages, natural killer (NK) cells, neutrophils and bioactive substances (cytokines) that control these immune cells [152]. The effects of exercise have an impact on multiple aspects of the immune response, modulatory effects on immunocyte dynamics and possibly on immune function including T-cell phenotype and proliferation, antibody response to vaccination and cytokine production. These effects are mediated by diverse factors including exercise-induced release of proinflammatory cytokines, classical stress hormones, and hemodynamic effects leading to cell redistribution [153,154]. Physical training has controversial effects on the immune system, depending

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on the protocols adopted [148]. The impact of exercise on tissue homeostasis elicits an adaptive response that depends on the type, duration and intensity of the stimulus outcome [155,156]. The intensity, more than the duration of exercise, is responsible for the degree of increment in the number of NK cells. intense exercise of long duration declines the concentration of NK cells and NK cytolytic activity [153]. Prolonged exercise can alter T-cell, NK-cell and neutrophil function, alter lymphocyte proliferation, alter the balance of cytokines and blunt immune functions[153,156]. On the other hand, regular moderate exercise boosts neutrophil functions, including chemotaxis, phagocytosis, and oxidative burst activity, improves and strengthens immune function by reducing the production of ROS and thus attenuate the cytotoxic activity of immune cells [5,148,152,153,155,157]. Physical exercise decreases pro-inflammatory signals and promotes the activation of anabolic pathways and mitochondrial biogenesis in skeletal muscle [140]. Regular PE increases the percentage of regulatory macrophages in muscle and that IL-10 is an essential mediator in the analgesia produced by regular physical activity [158]. PE leads to the release of myokines. These molecules exert auto-, para- and/or endocrine effects and include cytokines, interleukins such as IL-6 and other peptides that are produced, expressed and released by muscle fibers and play a role in protecting against inflammation-associated diseases [145]. Skeletal muscle contraction produces IL-6, which is able to direct natural killer cells to the tumour site during exercise and therefore appears to be involved in mediating exercise-induced anti-cancer effects [159].). Physical exercise exerts beneficial impacts on the gut microbiota and a protective role in neuroimmunomodulator effects in part via changes in the gut microbiome [160].

8. Method and technique for evaluating sport performance

The evaluation of sports performance takes into account several contexts associated with the purposes of this evaluation. These contexts are variable and evaluated the performances either following a training program or following a supplementation to see the effects of a product or the effects of an exercise program associated with a supplementation and a better information on fatigue, physical capacity and performance characteristics takes into account measurements of body composition, metabolic and muscular capacity and exercise endurance [20,32,33,39,40,64,119]. From a practical point of view, the studies measured variables at two levels. On the one hand, the measurement of variables related to physical capacities and, on the other, the evaluation of physiological parameters. These measurements are taken before, during or after the administration of physical stress tests. The different tests above and the parameters to be assessed depend on the animal model used for the experiment (human model and animal model). In view of the anatomical and physiological similarities between humans and animals, new therapies are generally evaluated in animal models before being tested in humans [101].

8.1. Measurement of variables related to physical capacities

8.1.1. Non-human Animal model

- Forced swim

Forced swim test or exhaustive swimming test involves using mice or rats allow to know the swimming endurance capacity, the most widely used comprehensive swim test to show an animal's ability to withstand exercise-induced fatigue. It was commonly accepted that swimming was an experimental exercise model [70]. Swimming time or time to exhaustion is measured at the time of exhaustion when the nose of the mouse was sinking below the water's [101,102,118]. The forced swim test can also be discontinued after some time (normally 20-30 min), which could reflect changes in biochemical indices in mice/rats after exercise under similar conditions. intensity and same duration[161].

- Rotarod test

The rotarod test is designed to screen the neurologic effects of drugs, to analyze motor behavior, to measure fatigue levels and physical performance and also becomes a useful method to evaluate

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motor function and was carried out to test drugs that interfere with motor coordination. The general procedures of rotarod test as follows: (i) Before the test, all mice are trained for a few days to adapt to the rotarod instrument (ii) On the test day, the mice are placed on the rotating lane of the rotarod instrument and the test starts. The time of the mice staying on the stick is recorded to evaluate the fatigue state. The difference in fall time observed between the negative control group and the group treated with the extract is an indication of muscle relaxant activity [101,118].

- Treadmill test

This test assesses cardiac capacity. Generally, the animal undergoing running training is placed on the track and the exercise begins. When the mice are unable to keep up with the speed of the treadmill, this indicates the onset of fatigue. The running mileage is recorded [101,118].

- Tail suspension test

The tail suspension test is another widely used method for assessing anti-fatigue activity in mice/rats. It is a rapid behavioral test that assesses the psychotropic effects of drug substances such as antidepressants and sedatives. The test involves suspending the mouse by the tail for a short period of time, and the animal's behavior during the session (which typically lasts 6 minutes) is recorded using a video recording device; the time of immobility during the session is determined by analyzing the video files [101,107].

- Forelimb Grip Strength Test

This test is used to assess maximum strength and neuromuscular function in mice and rats [39,162].

- Open field test

The open field is an unconditioned anxiety test to record general motor activity, locomotion and locomotion speed in mice[162,163].

- Hole-board test

This test has been described for assessing specific components of mouse behaviour, such as curiosity or exploration and sedative effects (Garige et al., 2016)

8.1.2. Human Animal model test

The multiple and are a function of the parameters or physical qualities to be assessed (strength, flexibility, agility, balance, muscular strength and endurance, coordination, speed). Muscular strength can be assessed by the Grip Strength Test, the Sargent Test, the Trunk Strength Test (sit-ups) and the Wingate Test. To assess endurance and cardiorespiratory capacity, the 6-minute walk test, the Cooper test or the bicycle ergometer test can be used [39,107].

8.2. Evaluation of biochemical parameters

The most integrative approach of oxidative stress multi-marker panels in response to physical activity instead of selecting one preferential biomarker to quantify physical activity-induced oxidative stress [164]. Theses mesearements are made from preparation taken from saliva, blood, urine samples, organ tissue samples or the breath [162,163,165]. Thus, in several studies have determinate biochimistries parameters of physical performance or antifatigue effects by measuring of muscles damages by determination creatine kinase, oxidative stress biomarkers (lipid hydroperoxides, total antioxidant capacity and superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), malondialdehyde (MDA), serum blood urea nitrogen (BUN), lactate dehydrogenase (LDH), and lactic acid (LA), thiobarbituric acid–reacting substances (TBARS), Lactic acid (LD), blood urea nitrogen (BUN), liver glycogen (LG), malonaldehyde (MDA), glutathione peroxidase (GSH-Px), superoxide dismutase (SOD) and catalase (CAT) [32,34,163,165], by estimated total protein[1], skeletal muscle glycogen content, hepatic glycogen in the liver, malonylCoA content, oxygen consumption and respiratory exchange [32,90].

9. Toxicity of doping molecules and herbal

Doping molecules originate from synthetic products or plants. If natural doping products derived from plants are considered safe alternatives to synthetic doping products and seem to offer advantages with fewer inconveniences for physical activity and sport, it should be noted that whatever the source of the products can present toxic effects [86,166]. There is no guarantee that herbal supplements are safe for anyone and this has not helped clear up the confusion surrounding the use of herbs in sports in particular [18]. The results have shown that the extract rich in polysaccharides of corn silk a LD50 value in mice much more than 20g/ kg [167]. Lynch et al. indicated that there is a rare case of death associated with ingredients based on plants or food supplements and the cases of death encountered are linked to inappropriate use[168]. The presence of the toxicants shows that these leaves should be properly processed before consuming them (Smith, 2009). Thus, studies have evaluated the toxicity of certain antifatigue plant showed that leaves and stems of Rubus coreanus induced no toxicological changes in rats at a single dose of 2500 mg/kg/day and no adverse effects at or at repeated oral doses of 625, 1250 and 2500 mg/kg/day [169]. Moringa oleifera could have severe toxic and abortifacient effects when taken in large amounts; although signs of acute toxicity were observed with lethal dose of more than 3,873 mg kg−1 with no adverse effect observed at concentrations lower than 3,000 mg kg−1. The authors indicate that Moringa oleifera leaf extract has no toxic effects when administered in concentrated doses over a short period[170–172]. Hydro-alcoholic extract of Portulaca oleracea at the dose level of 500 mg/kg can be used for further pharmacological activity and at the dose level of 400mg/kg have significant hepato protection [173]. The toxicity of compounds (phenolics, terpenoids and alkaloids) of certain anti-fatigue plants was also evaluated.The flavonoid fraction of the leaves of the Anisomelles Indica Kuntze seems to be safe for oral administration and has been shown that it is non-toxic following acute exhibitions with mice under experience conditions where the maximum tolerated dose is assessed at more than 5000 mg / kg B.W [63,174]. Sergi, considered that EGCG is toxic in childhood because of the potential adverse effect on immature or fast-developing liver cells [175]. It was indicated that higher bolus doses of EGCG are hepatotoxic to mice associated to oxidative stress including increased hepatic lipid peroxidation, plasma 8-isoprostane, hepatic metallothionein and γ-histone 2AX protein expression [176]. Dietary EGCG supplementation exhibits antihypertensive and nutrigenomics effects through activation of intrarenal Ace and Agtr2 and suppression of Ren mediators, while a high dose of EGCG induced liver damage in spontaneously hypertensive rats. the no-observed-adverse-effect level of EGCG was established at 250 mg/kg b.w.[177]. Isbrucker et al. concluded that EGCG is non-genotoxic, even when administered to animals at doses which are significantly higher than those intended for humans[178]. The mean oral lethal dose (LD50) of 20(S)-ginsenoside Rg3 is above 1600 mg/kg and 800 mg/kg in animal in acute toxicity and the no-observed-adverse-effect level was 180 mg/kg (C. Li et al., 2020), more than 1,600 mg/kg/day subchronic toxicity (Shin et al., 2014). [179] draw attention to both the harmful and protective effects of certain toxic terpenoids identified plants (cicutoxin, atractyloside, daphnetoxin, digoxin and gibberellic acid). Authors suggest that molecule branching, the presence of heteroatoms and electronegativity play a dominant role in terpenoid toxicity, citing potentially toxic terpenoids such as β-citronellol, (E,E)-farnesol, (S)-citronellal, (Z))-nerolidol geranic acid, linalool, citral, geranic acid and (±)-α-terpinyl acetate found in plants [180]. Most alkaloids are inappropriate in a sports context due to their toxicity and legal status [86]. Numerous reports acid nephrotoxic alkaloids derived from plants are often implicated in kidney damage[166], cardiovascular dysfunction[181], abdominal pain, genotoxicity, neurotoxicity, tumorigenicity, acute toxicity, nausea, chronic toxicity [96]. For Meredith et al., a nontrivial proportion of caffeine users develops clinically meaningful features of caffeine dependence, including a persistent desire or unsuccessful efforts to cut down or control caffeine use, continued use despite harm, and a characteristic withdrawal syndrome[182].

10. Conclusions

The aim of this review was to study the plants used in physical activity and sport, their anti-fatigue potential, an analysis of the methods used to study their anti-fatigue and phytochemical properties, their toxicity and the techniques and methods used to assess physical performance. It is clear that the value of plants in physical exercise and sport has been the subject of numerous scientific studies for a very long time, although the approaches used have evolved considerably. Medicinal plants represent a potential reservoir of subjects for applied research into physical activity and sport, due to the impact of the consumption of these plants by the sporting world on health and on the physiological and biochemical parameters of physical and mental performance. The data indicate that herbals can improve glycogen storage, antioxidant enzyme activities and the regulation of immune responses, and reduce the accumulation of toxic metabolites. Phyto molecules improve plasma lipid concentrations, blood pressure, body composition, antioxidant capacity, systemic inflammation and glycogen storage, and control blood sugar levels. The data indicate that moderate exercise is considered as a booster of the antioxidant and immune systems like antioxidant herbal; Therefore, an alternative therapy strategy based on a combination of adapted physical exercise ant herbal could be promising for treating diseases. The data also provides evidence that plants help to promote recovery after physical effort and reduce fatigue. Thus, the use of herbal could provide relief to people who exert intense physical activities such as farmers and athletes; for this, these peoples must do careful, the use of doping herbal must be done in accordance with all the previsions which take into account the need for the use of herbal supplement, the doses. In addition, these benefits attributed to herbals should not conceal the drawbacks of using them in sport. From a toxicological point of view, certain phyto molecules derived from these plants are toxic when used in large quantities. The use of certain plants with high levels of alkaloids should be avoided by sportsmen and women, as the majority of alkaloids are prohibited substances. The plants whose anti-fatigue properties have been studied are mainly derived from traditional medicine in Asian countries where this alternative medicine is highly developed. Few similar studies have been carried out on plants from regions of sub-Saharan Africa, where the majority of the population uses medicinal plants. This increases the vulnerability of these populations to the dangers of the use of doping plants for their health, and in the practice of sport, to doping. These observations demonstrate the need for research into medicinal plants used for doping purposes south of the Sahara.

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