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REVIEW ARTICLE

Nutrological aspects of polyphenols and gut microbiota in sports performance: a systematic review

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Abstract

Introduction: In the context of nutrology and sports performance, the focus for intake in athletes and physically active individuals has been directed to the main class of polyphenols. Interest in a personalized approach is increasing in sports to maximize each individual's athletic ability in endurance and strength sports. Polyphenols represent a heterogeneous class of compounds with marked antioxidant and anti-inflammatory properties. The impact of the gut microbiota on the bioavailability and activity of polyphenols is highlighted. **Objective:** It was to carry out a systematic review to highlight the main relationships between polyphenols, gut microbiota, and sports performance. **Methods:** The systematic review rules of the PRISMA Platform were followed. The research was carried out from May to July 2023 in Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument. **Results and Conclusion:** A total of 115 articles were found, and 81 articles were evaluated in full and 76 were included and developed in this systematic review study. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 6 studies with a high risk of bias and 10 studies that did not meet GRADE. As a result and conclusion, it was shown that the metabolic mechanisms favored by polyphenols improve sports performance, improve cardiometabolic functions, reduce recovery times and post-exercise pain, maintain a low degree of oxidative stress, and avoid unregulated inflammatory processes. Thus, polyphenols are able, through their interaction with the gut microbiota, to favor the proliferation of bacterial genera of great importance for metabolic and cognitive functions, such as Akkermansia, Lactobacilli, and Bifidobacteria. Gut microbiota metabolizes polyphenols in the colon to produce small bioactive molecules that exert epigenetic mechanisms on biochemical pathways modulating gene expression. Polyphenols have multiple biological effects, and future exercise studies should be appropriately and specifically designed to determine the physiological interactions between exercise and the selected supplement, rather than just considering performance.

Keywords: Nutrology. Polyphenols. Gut microbiota. Sports performance.

Introduction

In the context of nutrition and sports performance, the focus for intake in athletes and physically active individuals has been directed towards the main class of polyphenols. Anthocyanins provide health benefits in part through anti-inflammatory and antioxidant effects. High-intensity and duration exercises provide cellular oxidative stress and inflammation. The anti-inflammatory and antioxidant effects of anthocyanins justify examining ergogenic potential in athletes **[1,2]**.

In this sense, interest in a personalized approach is increasing in sports to maximize each individual's athletic capacity in endurance and strength sports **[3,4]**. Research has increasingly focused on the genetic aspects that characterize elite athletes **[5]**, as well as their precise nutrition, and recently great interest has been directed to plants and their phytocomplexes, which provide precious molecules of interest for sports performance **[4]**.

Among the various phytochemicals, polyphenols represent a heterogeneous class of compounds with marked antioxidant and anti-inflammatory properties **[6]**. Polyphenols can act as key signal molecules when introduced into an organism. This can be achieved through a multitude of mechanisms, both direct in receptor proteins and indirect through modulation of transcription of factors or enzymes critical in survival and bioenergetic signal pathways **[7-10]**. In this aspect, one of the biggest challenges is to understand the mechanisms of the interrelationship between polyphenols and the human body, also considering the fundamental role played by the gut microbiota in their absorption and bioavailability **[10]**.

In this aspect, the impact of the gut microbiota on the bioavailability and activity of polyphenols stands out. The use of polyphenols in sports performance also presents a holistic approach, considering all relevant biological layers, so that the effects of polyphenols in sports present both epigenetic and genetic aspects **[11]**.

In this sense, dietary recommendations for individuals who exercise should emphasize the consumption of a well-balanced diet and/or natural foods rich in antioxidants, such as cocoa and chocolate, rather than taking antioxidant supplements. This strategy has been increasingly proposed as a potential tool suitable for preventing or reducing oxidative stress and related inflammation during intensive physical training. In particular, in addition to being energy-dense foods, cocoa and cocoa products, including chocolate, are a rich source of antioxidant polyphenols that have been shown to have health-promoting effects through their antioxidant, anti-inflammatory, and metabolic properties **[12]**. Added to this, flavonoids such as quercetin, catechins, and other polyphenols such as resveratrol have been highlighted for improving athletic performance **[13]**.

Given this, the present work aimed to carry out a systematic review to highlight the main relationships between polyphenols, gut microbiota, and sports performance.

Methods

Study Design

The systematic review rules of the PRISMA Platform Available at: www.prismastatement.org/ were followed. Accessed on: 06/10/2023.

Search Strategy and Search Sources

The literary search process was carried out from May to July 2023 and was developed based on Web of Science, Scopus, PubMed, Science Direct, Scielo, and Google Scholar, covering scientific articles from various eras to the present. The descriptors (MeSH Terms) were used: *"Nutrology. Polyphenols. Gut microbiota. Sports performance"*, and using the Boolean "and" between the MeSH terms and "or" between historical discoveries.

Study Quality and Risk of Bias

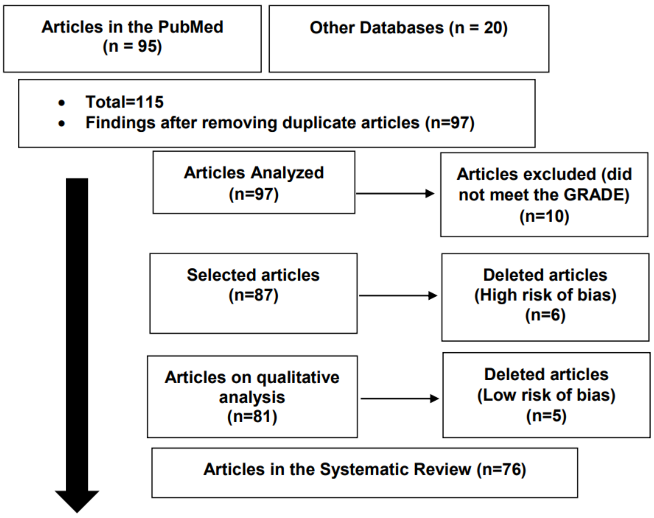
Quality was classified as high, moderate, low, or very low in terms of risk of bias, clarity of comparisons, precision, and consistency of analyses. The most evident emphasis was on systematic review articles or meta-analyses of randomized clinical trials, followed by randomized clinical trials. The low quality of evidence was attributed to case reports, editorials, and brief communications, according to the GRADE instrument. The risk of bias was analyzed according to the Cochrane instrument by analyzing the Funnel Plot graph (Sample size versus Effect size), using the Cohen test (d).

Results and Discussion

Summary of Findings

A total of 115 articles were found that were subjected to eligibility analysis and, subsequently, 76 of the 81 final studies were selected to compose the results of this systematic review. The studies listed were of medium to high quality (Figure 1), considering in the first instance the level of scientific evidence of studies such as meta-analysis, consensus, randomized clinical, prospective, and observational. The biases did not compromise the scientific basis of the studies. According to the GRADE instrument, most studies showed homogeneity in their results, with X^2=90.5%>50%. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 6 studies with a high risk of bias and 10 studies that did not meet GRADE.

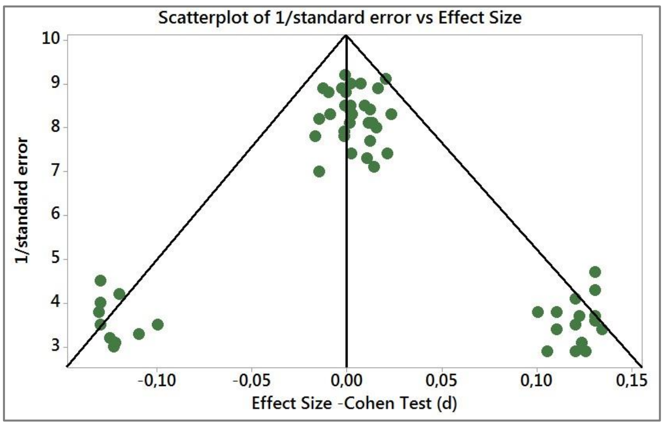
Figure 1. Flowchart showing the article selection process.



Source: Own authorship.

Figure 2 presents the results of the risk of bias of the studies using the Funnel Plot, showing the calculation of the Effect Size (Magnitude of the difference) using the Cohen Test (d). Precision (sample size) was determined indirectly by the inverse of the standard error (1/Standard Error). This graph had a symmetrical behavior, not suggesting a significant risk of bias, both between studies with a small sample size (lower precision) that are shown at the bottom of the graph and in studies with a large sample size that are presented at the top.

Figure 2. The symmetric funnel plot suggests no risk of bias among the small sample size studies that are shown at the bottom of the plot. High confidence and high recommendation studies are shown above the graph (n=76 studies).



Source: Own authorship

Nutrigenomics, Gut Microbiota and Sports Performance

In the human gut microbiota, about 90% of bacteria live in the gastrointestinal tract **[14-19]**. Individual responses to nutrients and non-nutritive molecules can be largely affected by three important biological layers. The gut microbiome can alter the bioavailability of nutrients and other substances, the genome can influence the kinetics and dynamics of molecules, while the epigenome can modulate or amplify the properties of the genome. The use of omics and bioinformatics techniques allows the construction of individual multilayer networks and, thus, the identification of personalized strategies that have recently been considered in all medical areas, including sports medicine **[11]**.

In this sense, the composition of each athlete's microbiome influences sports performance both directly by acting on energy metabolism and indirectly through modulating the availability of nutrients or non-nutritive molecules that, ultimately, affect the individual epigenome and genome. Among non-nutritive molecules, polyphenols can enhance physical performance through different epigenetic mechanisms **[1]**.

In this way, polyphenols interact with the gut microbiota, undergoing extensive metabolism to produce bioactive molecules, which act on transcription factors involved in mitochondrial biogenesis, antioxidant systems, glucose and lipid homeostasis, and DNA repair **[2]**. Thus, omics disciplines, including epigenomics (the study of the complete set of epigenetic modifications in a cell's genetic material, known as the epigenome), aim at the complete characterization and quantification of pools of biological molecules that affect the structure, function, and dynamics of a cell body. In nutrition, omics technologies are useful for customizing dietary strategies for each individual, providing personalized dietary approaches **[20,21]**.

In this aspect, the standardized nutritional approach, preferably related to guidelines for healthy nutrition, such as those established by the World Health Organization (WHO), must be reviewed and updated, considering the influence that genetic, environmental, and microbiota factors have on each individual, to optimize nutritional and nutraceutical choices and promote the health of individuals according to their characteristics **[22]**.

At the genetic level, two nutritional fields analyze the intricate relationships between nutrients, genes, and biological systems: nutrigenetics and nutrigenomics. Nutrigenetics aims to understand how our genetic background can modulate the absorption, distribution, metabolism, and elimination of nutrients, affecting the response to diet. Nutrigenomics focuses on individual sensitivity to nutrients in terms of influence on gene and protein expression and subsequently metabolite production, thereby providing actionable information on the effects of diets and enabling effective tailoring of dietary intervention strategies to prevent disease-related diseases diet **[23,24]**.

One of the most useful applications of nutritional genomics is certainly in sports performance. Genetic factors are responsible for approximately 50% to 80% of the inter-individual variation in body mass, and this has an essential impact on the muscle growth response **[25]**. Furthermore, endocrine functions, muscle fiber composition, psychological aspects, and nutrition may have differences associated with the genotype and influence athletic performance **[26]**.

A meta-analysis study showed that foods rich in polyphenols and nitrate provide trivial benefits for resistance exercise performance, although these effects may be food-dependent. Highly trained endurance athletes do not appear to benefit from consuming nitrate-rich foods but may benefit from consuming polyphenols. More research into dietary sources, dosage, and duration of supplementation to optimize the ergogenic response to polyphenol consumption is needed **[27]**.

Polyphenols and Sports Performance

Polyphenols represent a considerable heterogeneous class of compounds with common phenolic structural units present in nature in a wide variety of foods, such as fruits, vegetables, cereals, tea, and chocolate, among others **[28]**. The various polyphenol groups are distributed according to the number of phenolic rings in flavonoids, over 10,000 natural compounds, which can be further subclassified into many flavones, flavonols (*Capparis spinosa*), flavones or flavan-3-oils or catechins (*Theobroma cacao*, *Camellia sinensis*), anthocyanins or anthocyanidins (*Vaccinium myrtillus*), isoflavones and chalcons (*Glycine max*); and non-flavonoid polyphenols, such as tannins, diferuloylmethanes (*Turmeric Longa*), coumarins, benzophenones, secoiridoids, stilbenes (*Polygonum cuspidatum*), phenolic acids, etc. **[6,29,30]**.

In general, several health properties have been attributed to polyphenols, including antioxidants, anti-inflammatory, antibacterial, antiviral, antipruritic, antiparasitic, and cytotoxic **[7,9,31-34]**. In athletic performance, several studies have investigated the antioxidant and antiinflammatory potential of various polyphenols **[35,36]**. In this sense, individuals who carry specific genetic mutations (e.g., N-acetyltransferase (NAT) 1/2, SOD1/2, glutathione peroxidase (GPX) 1, paraoxonase (PON) 1, X-ray repair cross-complementation family (XRCC) 1) may have lower efficiency to modulate oxidative stress and inflammation during exercise and therefore require a significant increase in antioxidants with epigenetic mechanisms such as polyphenols **[37-41]**. One of the most innovative areas for understanding the health-related mechanisms of polyphenols in sports performance is the study of bidirectional interactions with the gut microbiota **[10,28]**.

Furthermore, in plants, polyphenols are generally found in their glycosylated form, although esterified or polymerized forms may also be present. Once ingested, polyphenols are recognized by the human body as xenobiotics, therefore their absorption rate is notably lower than that of nutrients introduced with the diet and varies greatly depending on the degree of polymerization or the complexity of their chemical structure. Only 5-10% of polyphenols are absorbed in the small intestine, while the remaining 90-95% reach the colon, where they undergo fermentation processes by the gut microbiota and subsequently generate metabolites with different physiological implications. After oral ingestion of 10 to 500 mg of polyphenols, the maximum plasma concentration generally does not exceed 1 μM, mainly due to poor absorption and metabolism by tissues and gastro gut microbiota **[42]**.

Also, polyphenols are also substrates for ATP-binding transporters, which are mainly efflux transporters and eliminate their substrates outside the cell. These proteins can influence the oral availability and tissue distribution of polyphenols, limiting their beneficial effects **[43,44]**. Genetic mutations affecting these transporters, such as those affecting hepatic and intestinal cytochromes, must be taken into consideration to determine the dosage of polyphenols based on the subject's genotypic characteristics (poor, intermediate, or extensive metabolizers) **[45-47]**.

Once in the large intestine, polyphenols can modulate the proliferation of specific bacteria and act as prebiotics for some other microorganisms **[48,49]**. A meta-analysis showed that polyphenol supplementation increases the abundance of Lactobacillus and Bifidobacterium and reduces the abundance of some pathogenic Clostridium in the human gut microbiota **[50,51]**.

Polyphenol supplementation should be provided before or after physical exercise and not immediately after, mainly because post-exercise inflammatory processes are essential for muscle hypertrophy and the learning of muscular actions (Table 1). With the advent of omics technologies, it has become possible to analyze the individual genome, epigenome, and other classes of biologically relevant molecules, as well as the genetic composition of the gut microbiota (microbiome). The biological data contained in the genetic/epigenetic fingerprint and the composition of the individual microbiota together provide valuable information to understand a subject's sensitivity and response to external/internal stimuli and dietary xenobiotics. This, in turn, can enable personalized interventions across all medical fields, including sports medicine, where personalized nutritional and nutraceutical regimens can be undertaken to maximize athletic performance.

Table 1. Average daily dose and general human benefits of polyphenol supplementation on sports performance.

Polyphenols	Average Daily Dose	Impacts on Sports Performance	References
Curcumin	80–200 mg	✓ Reduces muscle fatigue, loss of muscle mass, muscle pain and post-exercise recovery; ✓ Improves redox homeostasis and insulin sensitivity	**[47,52,53]**
Resveratrol	100–500 mg	✓ Improves muscle strength and tolerance to fatigue and muscle regeneration after disuse; ✓ Increases the mitochondrial capacity of skeletal muscle; ✓ Exerts ergogenic and anti-obesity properties; increases beta-oxidation of fatty acids and glucose metabolism; ✓ Improves glucose control and insulin sensitivity in diabetic or pre-diabetic individuals, without altering glycemic measurements in non-diabetic individuals ✓ Induces vasodilation, improves endothelial function, and reduces blood pressure; ✓ Increases cerebral blood flow;	**[54-57]**
Cocoa Flavanols	200–500 mg	✓ Improves vascular function; ✓ Reduces exercise-induced oxidative stress; ✓ Alters the use of fat and carbohydrates during exercise without affecting athletic performance;	**[58,59]**
Quercetin	200–1000 mg	✓ Increases athletic performance and energy expenditure; ✓ Increases physical and mental performance; ✓ Improves neuromuscular performance during and after resistance training sessions; ✓ Attenuates the severity of muscle weakness caused by eccentric-induced myofibrillar rupture and sarcolemmal action potential ✓ Propagation deficiency; ✓ Reduces post-stroke muscle pain, localized pain, oxidative stress, cramps, and post-exercise recovery time;	**[60-63]**
Green tea	250–1000 mg	✓ Reduces muscle damage and oxidative stress with positive effects on the neuromuscular parameters of muscle fatigue;	**[64-66]**
Blueberry	75–150 g	✓ Improves recovery after exercise; ✓ Improves vascular functions and vasodilation;	**[67,68]**
Pycnogenol®	100–800 mg	✓ Improves physical performance and protects against post-exercise oxidative stress; improves training and performance in both normal individuals and semi-professional athletes with high performance in difficult and high-stress sports, such as triathlon.	**[69]**
Montmorency cherry juice	30 mL	✓ Increases muscle recovery and reduces postexercise pain, especially in strength sports.	**[70,71]**
Ecklonia cava polyphenols	40 mg	✓ Increases glucose oxidation; ✓ Reduces lactate production during intense exercise;	**[72]**

In recent years, the consumption of chocolate and, in particular, dark chocolate has been "rehabilitated" due to its high content of antioxidant cocoa polyphenols. Although it is recognized that regular exercise improves energy metabolism and muscle performance, excessive or unusual exercise can induce cellular damage and impair muscle function, triggering oxidative stress and tissue inflammation. The interpretation of available results on the antioxidant and anti-inflammatory activities of cocoa polyphenols remains questionable, probably due to the variety of physiological networks involved. Further experimental studies are mandatory to clarify the role of cocoa polyphenol supplementation in exercise-mediated inflammation **[12]**.

One study investigated the effects of polyphenol supplementation on the composition of the gut microbiota in humans. The study followed a randomized, double-blind, placebo-controlled (PLA) model, involving 37 overweight and obese men and women (18 men/19 women, 37.8 ± 1.6 years, body mass index: 29.6 ± 0.5 kg/m^2) who received epigallocatechin-3-gallate and resveratrol (EGCG + RES, 282 and 80 mg/day, respectively) or PLA for 12 weeks. Fecal Bacteroidetes abundance was higher in men than in women, while other bacterial taxa assessed were comparable. EGCG+RES supplementation significantly decreased Bacteroidetes and tended to reduce *Faecalibacterium prausnitzii* in men (p=0.05 and p=0.10, respectively), but not in women (p=0.15 and p=0.77, respectively). Other bacterial genera and species were not affected by EGCG + RES supplementation **[73]**.

Thus, dietary polyphenols exert several beneficial effects on sports performance, demonstrated in vivo and human studies. The health-related mechanisms of polyphenols mainly concern the modulation of mitochondrial biogenesis and the stimulation of stress-related enzymes or transcription factors, as well as a nutritional deficiency, which regulates gene expression of essential antioxidant proteins (SOD, Catalase, Glutathione system, etc.) **[74]**. They have also been shown to modulate inflammatory processes and the immune system response (Th1/Th2 balance). Furthermore, some polyphenols favor vascular regulation and endothelial function in humans, increasing endothelial nitric oxide synthesis **[75]**.

Finally, dark-colored fruits have an abundant presence of the polyphenol anthocyanin, which has been proven to bring health benefits. Studies with black currant berries have provided remarkable observations with application to athletes and physically active individuals. Changes in exerciseinduced substrate oxidation, high-intensity repeated running and cycling time trial exercise performance, and cardiovascular function at rest and during exercise were observed with New Zealand blackcurrant ingestion. The dynamic plasma bioavailability of blackcurrant anthocyanins and anthocyanin-derived metabolites must have altered cellular function to provide significant in vivo physiological effects. This perspective will be reflected in research studies to obtain the in vivo effects applied by ingesting anthocyanin-rich supplementation, the question of individual responses, and the strong emerging potential of anthocyanins for sports and exercise nutrition **[76]**.

Conclusion

It was concluded that the metabolic mechanisms favored by polyphenols improve sports performance, improve cardiometabolic functions, reduce recovery times and post-exercise pain, maintain a low degree of oxidative stress, and avoid unregulated inflammatory processes. Therefore, polyphenols are able, through their interaction with the gut microbiota, to favor the proliferation of bacterial genera of great importance for metabolic and cognitive functions, such as Akkermansia, Lactobacilli, and Bifidobacteria. The microbiota metabolizes polyphenols in the colon to produce small bioactive molecules that exert epigenetic mechanisms on biochemical pathways modulating gene expression. Polyphenols have multiple biological effects, and future exercise studies should be designed appropriately and specifically to determine the physiological interactions between exercise and the selected supplement, rather than considering performance alone.

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Informed consent

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No additional data are available.

Conflict of interest

The authors declare no conflict of interest.

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