EFFECTS OF CAFFEINE CONSUMPTION ON SPORTS PERFORMANCE (SCOPING REVIEW)

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EFFECTS OF CAFFEINE CONSUMPTION ON SPORTS PERFORMANCE

(SCOPING REVIEW)

By

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CERTIFICATE

This is to certify that the thesis entitled “EFFECTS OF CAFFEINE CONSUMPTION ON SPORTS PERFORMANCE: SCOPING REVIEW” is the bona fide record of research work done by of research work done by Ms “MANJJHARI RAJAMOHAN” during the period from “March” 2021 to July 2021 under my supervision. I have read this dissertation and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a thesis to be submitted in partial fulfilment for the degree of Bachelor of Health Science (Honours) (Exercise and Sports Science).

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DECLARATION

I hereby declare that this dissertation is the result of my investigations, except where otherwise stated and duly acknowledged. I also declare that it has not been previously or concurrently submitted as a whole for any other degrees at Universiti Sains Malaysia or other institutions. I grant Universiti Sains Malaysia the right to use the dissertation for teaching, research and promotional purposes.

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Date: 11 July 2021

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LIST OF ABBREVIATIONS

CHO	Carbohydrate
PPA	Phenylpropanolamine
RM	Repetition Maximum
P	Placebo
ARG	Arginine
CAFF	Caffeine
BCAA	Branched chain amino acids
ATP	Adenosine triphosphate

KESAN PENGAMBILAN KAFEIN TERHADAP PRESTASI SUKAN: TINJAUAN SKOP

ABSTRAK

Kafein adalah salah satu bahan ergogenik yang biasa digunakan dalam bidang sukan, dan keberkesanannya disokong oleh bukti-bukti kukuh yang menunjukkan pengambilan kafein meningkatkan prestasi aktiviti aerobik dan anaerobik. Kelaziman penggunaan kafein oleh atlet telah diperiksa sejak penguguran kafein daripada senarai Badan Anti-Doping Sedunia yang dilarang pada tahun 2004. Pengambilan kafein harian secara keseluruhan untuk kebanyakan atlet, termasuk dos sebelum dan semasa-latihan, tidak boleh melebihi 3 $mg.kg^{-1}$ berat badan kerana ini akan meningkatkan dos kafein yang diminum sebelum-pertandingan untuk menghasilkan apa-apa kesan ergogenik. Oleh itu, tinjauan ini bertujuan untuk menentukan kesan pengambilan kafein terhadap jenis prestasi sukan dan dos kafein yang diminum, dan masa penggunaannya dalam kalangan atlet dan individu yang aktif secara fizikal. Kajian berkaitan dicari secara elektronik melalui pangkalan data berikut: Scopus, PubMed, EbscoHost dan ScienceDirect. Analisis dilakukan sesuai dengan kriteria Item Pelaporan Pilihan untuk Ulasan Sistematik dan Analisis Meta (PRISMA). Dari 14 kajian yang dimasukkan, semua kajian dilakukan pada manusia. Skop kajian dari artikel yang diambil itu terutama mengenai kesan penggunaan kafein terhadap prestasi sukan. Jumlah bilangan peserta untuk semua 14 artikel adalah 217 peserta lelaki. Rekabentuk kajian dalam semua artikel yang dikaji terdiri daripada kajian terkawal plasebo secara rawak dan reka bentuk silang ‘double-blind’. Dari segi protokol senaman untuk mengukur hasil prestasi, dua belas kajian telah melaporkan ujian masa sementara dua kajian melaporkan masa senaman sehingga kelesuan.

Lapan kajian melaporkan protokol intervensi kafein sebelum sesi senaman, lima kajian melaporkan protokol intervensi kafein semasa sesi senaman dan satu kajian melaporkan protokol intervensi kafein sebelum dan semasa sesi senaman. Sebagai rumusan tinjaun ini, artikel-artikel yang relevan mendapati bahawa suplemen kafein pada dos 6 mg/kg berat badan 60 min sebelum senaman terbukti dapat meningkatkan prestasi aerobik dan juga mempunyai kesan ergogenik pada prestasi anaerobik dengan meningkat purata kuasa, kuasa puncak, dan masa yang diperlukan untuk mencapai kuasa puncak dalam kalangan atlet-atlet elit dan atlet-atlet terlatih rekreasi.

EFFECTS OF CAFFEINE CONSUMPTION ON SPORTS PERFORMANCE: A SCOPING REVIEW

ABSTRACT

Caffeine is one of the most common ergogenic compounds used in sports, and its efficacy is supported by a strong body of evidence that demonstrated improvement in both anaerobic and aerobic performance. The prevalence of caffeine use in athletes has been examined since the withdrawal of caffeine from the banned list of the World Anti-Doping Agency in 2004. The overall daily caffeine intake for most athletes, including pre-and intra-training doses, should not exceed 3 mg/kg body weight, as this will greatly increase the minimum pre-competition caffeine dose to elicit any ergogenic effect. Therefore, this review aims to determine the effect of caffeine consumption on sports performance, types and dosage of caffeine consumed and the timing of its consumption among athletes and physically active individuals. Related studies were searched electronically using the following databases: Scopus, PubMed, EbscoHost and ScienceDirect. The analysis was done in compliance with the criteria of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). From the 14 included studies, all the studies were conducted on humans. The scope of study from those retrieved articles was primarily on the effects of caffeine consumption on sports performance. The total number of participants for all the 14 articles are 217 male participants. The study design in these reviewed articles include randomised placebo-controlled trial and double-blind cross-over design. In terms of exercise protocol to measure performance outcome in the articles reviewed, twelve studies reported on time trial performance while another two studies reported exercise time to exhaustion. Eight studies reported on caffeine intervention protocol before the exercise session, five studies reported caffeine intervention protocol during

the session while one study reported on caffeine intervention protocol before and during the session. As a summary of this review, the relevant articles found that caffeine supplementation at the dosage of 6 mg/kg body weight at 60-min prior to exercise has shown to improve anaerobic performance, enhances reaction speed and also had an ergogenic effect on anaerobic performance by improving average power, peak power and the time needed to reach peak power in elite and trained-recreational athletes.

CHAPTER 1

INTRODUCTION

1.1 Background of Study

The US Food and Drug Administration categorises caffeine as a stable food (Huang et al., 2019). Caffeine is one of the most common ergogenic compounds used in sports, and its efficacy is supported by a strong body of evidence to improve anaerobic and aerobic activities (Maughan et al., 2018). In a variety of other items, caffeine exists in energy drinks, bars, sports gel, alcoholic beverages and diet aids. The prevalence of caffeine use in athletes has been examined since the withdrawal of caffeine from the banned list of the World Anti-Doping Agency in 2004 (Del Coso et al., 2011).

The ergogenic effect of caffeine on athletic performance is primarily attributed to the activation of the central nervous system (i.e., adenosine receptor blockade and release of neurotransmitters such as dopamine, catecholamine and acetylcholine) (McLellan et al., 2016). In contrast, a high amount of caffeine infusion (up to 4.3 mg/kg) is able to stop up to 50% of adenosine receptors in the human brain (Elmenhorst et al., 2012). Caffeine may impact dopamine function by blocking tonic adenosine input to A2a-adenosine receptors (Ferré et al., 2007). Caffeine would be predicted to impair the function of most neuronal circuits in the brain indirectly via blocking adenosine receptors. Caffeine's effects on adenosine receptors A1 and A2A (Ferre et al., 2008) have increased interest in its use as a preventative or therapeutic strategy for parkinsonian symptoms (Prediger, 2010). Furthermore, the motivational significance of DA-adenosine receptor interactions has emerged in recent years with reference to processes like behavioural activation and effort-related decision-making that are disrupted in depression or other diseases (Salamone and Correa, 2009).

Oral intake of caffeine has been shown to have a beneficial impact in running time to exhaustion trials and the continuous exercise of up to 2 hours (Doherty & Smith, 2005). For adults, harmful levels of more than 10 g a day are considerably higher than the average dose of less than 500 mg per day (Heckman et al., 2010). Depending on what' bean' (seed) is used, how it is roasted (darker roasts have less caffeine) and how it is processed, a cup of coffee has 80-175 mg of caffeine. Most urine samples (67.3%) had urinary caffeine concentrations below 5 $\mu g \cdot mL^{1}$). Only 0.6% of urine samples exceeded the former threshold for caffeine doping (12 $\mu g \cdot mL^{-1}$). Triathlon (3.3 ± 2.2 $\mu g \cdot mL^{-1}$, cycling (2.6 ± 2.0 $\mu g \cdot mL^{-1}$), and rowing (1.9 ± 1.4 $\mu g \cdot mL^{-1}$) were the sports with the highest levels of urine caffeine concentration.

While caffeine has the potential to improve physical efficiency, there are several unresolved variables such as time of day and training status that may affect the magnitude of caffeine's impact. Usually, existing regulations prescribed the consumption of caffeine about 60 minutes before exercise (Goldstein et al., 2010). For instance, consuming low-dose caffeine, ranging from 3 to 6 mg/kg body $weight^{-1}$, approximately 60 minutes before the latter stages of a time trial (TT) may appear to be more efficient than before (> 80 min) or later (> 40 min) (Southward et al., 2018), but this has yet to be tested under similar test conditions.

Caffeine improved peak power output, pace, and isokinetic strength in sprint and power events that depend primarily on the phosphagen system. (Anselme et al., 1992). Caffeine did not boost performance in activities that strongly rely on the glycolytic mechanism (15 seconds to 3 minutes) and it may have been detrimental to performance during prolonged bouts of exercise (Greer et al., 1998). ATP resynthesis from anaerobic glycolysis reduced during repeated bouts of exercise, and phosphocreatine and oxidative metabolism became incredibly prominent sources of ATP (Trump et al., 1996). Improved muscular force production as a result of increased intracellular calcium concentration and improved sodium and potassium ATPase pump activity was proposed as the mechanisms for relatively short sprint and power efficiency (Herrmann-Frank et al., 1999). In relatively brief events, reduced reaction time may be another consideration (Schneiker et al., 2006).

Caffeine, on the other hand, has been shown to have no effect or to be a negative factor in the power and sprint output in repeated bouts of maximal exercise that last 15 seconds to 3 minutes and thus depend heavily on anaerobic glycolysis, likely due to an increase in plasma ammonia levels and thus rely heavily on anaerobic glycolysis (Jackman et al., 1996).

Experiments investigating the ergogenic impact of caffeine are more applicable to athletes using a time-trial protocol (Ganio et al., 2009). Research further shows that when participants perform an exhaustion test vs. a time trial, a higher coefficient of variance is observed (Esfarjani & Laursen, 2007). The variability of 5-km and 1500-m time trial tests were significantly less than for similar time to exhaustion (Laursen et al., 2007). Therefore, this review aims to determine the effect of caffeine consumption on sports performance types and dosage of caffeine consumed and the timing of its consumption among athletes and physically active individuals.

1.2 Problem Statement

Many studies have demonstrated that caffeine used as an ergogenic aid has improved endurance performance in several sports. Caffeine intake was also shown to improve muscular strength and power. However, there are number of issues in these studies that need to be addressed to provide more conclusive evidence on the ergogenic effect of caffeine. Therefore, the aim of this review is to analyse and compare the effects of different types, dosage and timing of caffeine consumed on aerobic and anaerobic performance among athletes or physically active individuals.

1.3 Objectives of the Review

1.3.1 Main objective:

The main aim of the review is to identify the effect of caffeine consumption on different types of sports performances among athletes and physically active individuals.

1.3.2 Specific Objectives:

a) To identify the effects of caffeine consumption on aerobic performance.
b) To identify the effects of caffeine consumption on anaerobic performance.
c) To identify the dosage and timing of caffeine consumption on aerobic sports performance.
d) To identify the dosage and timing of caffeine consumption on anaerobic sports performance.

1.4 Research Questions of the Review

a) What are the effects of caffeine consumption on aerobic performance?

b) What are the effects of caffeine consumption on anaerobic performance?

c) What are the dosage and timing of caffeine consumption to enhance sports performance?

1.5 Significance of the Review

The information obtained from this review is important for athletes and physically active individuals to determine the dosage of caffeine intake to enhance sports performance either during training or competition. In addition, the results obtained from this review can be used by the athletes or physically active individuals to determine the most appropriate timing of caffeine consumption that will improve physical performance in both aerobic and anaerobic activities.

CHAPTER 2

LITERATURE REVIEW

2.1 Overview of Caffeine

Polyphenols, alkaloids, fibers, and dark-coloured compounds produced during the roasting process, namely melanoidins, all contain high concentrations of bioactive compounds that may have a beneficial effect on human health (Ludwig et al., 2014). Polyphenols are compounds that are produced because of the plants' secondary metabolism and are used for a variety of functions which biological activity has been observed in humans and their home plant (Williamson, 2017). Chlorogenic acids are the most common polyphenolic compounds in coffee (CGAs). These important compounds are known for their strong antioxidant properties, which can help to improve human health (Tajik et al., 2017).

Chlorogenic acid is the most abundant antioxidant in coffee; however, roasting degrades it, resulting in the formation of alternative antioxidant organic compounds (Kamiyama et al., 2015). Caffeine has other antioxidant contents such as cafestol and kahweol, two diterpenes that stimulate enzymes involved in carcinogen detoxification and intracellular antioxidant protection (Cavin et al., 2002) and assisting in the anti-carcinogenic effect. The mechanism behind the beneficial associations between coffee intake and liver fibrosis, cirrhosis, and liver cancer is likely to be due to these antioxidant and anti-inflammatory effects (Salomone et al., 2017).

Barnung et al. (2018) and Kuang et al. (2018) investigated the influence of coffee consumption on gene expression and the lipidome, respectively. The findings of a population-based whole-blood gene expression study of coffee intake (Barnung et al., 2018) pointed to metabolic, immune, and inflammation pathways. Kuang et al. (2018) used samples from a randomized trial of coffee consumption to demonstrate that coffee consumption resulted in lower levels of lysophosphatidylcholines. Van Dijk et al., (2018) analysed the impact of caffeine on myocardial blood flow, concluding that recent caffeine consumption has an important and clinically applicable influence on cardiac perfusion measurements during adenosine and dipyridamole-induced hyperaemia. Original observational studies on the relationship between habitual coffee consumption and liver fibrosis (Yeow et al., 2009), depression (Navarro et al., 2018), hearing (Lee et al., 2018) and cognition indices (Haller et al., 2018) have all broadened the scope of study in these fields.

Coffee and caffeine have also been related to oestrogen metabolism in premenopausal women (Sisti et al., 2015) and increased sex hormone binding globulin (SHBG) concentrations in postmenopausal women in observational studies (Sisti et al., 2015). Lower unbound testosterone but not unbound oestradiol concentrations were correlated with increased globulin concentrations (Kotsopoulos et al.). Low levels of oestradiol and high levels of sex hormone-binding globulin have been linked to a higher risk of fracture (Goderie-Plomp et al., 2004).

Caffeine consumption has a long history as a performance-enhancing technique for sports, but it has gained popularity to support training goals (Graham, 2001). Caffeine is widely used by athletes to overcome exhaustion associated with routine training (Duncan and Oxford, 2011) as well as sleep disturbance caused by early morning training sessions (Cook et al., 2011) and jet lag (Arendt, 2009). Caffeine's analgesic properties can also mask soreness after intense exercise or competition (Hurley et al., 2013), offering another avenue for performance improvement. As a result, while caffeine use in athletes and non-athletes is usually treated separately, there is a lot of overlap between the two. This is shown by research into the optimum caffeine dose for performance enhancement; traditionally doses of 6 to 9 mg/kg body weight and sometimes as high as 13 mg/kg body weight (Pasman et al., 1995) were used, but such doses are difficult to achieve without targeted supplementation.

As compared to other forms of drinks such as water and energy-containing beverages, caffeine-containing beverages did not increase 24-hour urine volume in stable, free-living men (Mustapha et al., 2014). Higher doses of caffeine (above 180 mg per day) have been shown to improve urinary production, resulting in a diuretic effect in a short period of time (Vianna et al., 2008).

2.2 Prevalence of Caffeine Use in Athletes

Caffeine is a common ergogenic aid used in sports to improve athletic performance and endurance (Lara et al., 2019). Caffeine has been reported to be used as an ergogenic aid by 74 percent of elite athletes before or during the competition (Del Coso et al., 2011). During exercise performance, lower doses can be just as effective as higher doses and restarting caffeine consumption at a low level before a performance can have the same ergogenic effects as acute ingestion after a period of abstinence._Caffeine should be taken in small doses over 3 to 4 days to avoid tolerance and right before heavy training to maintain workout intensity. Caffeine can also increase cognitive aspects of success such as focus when an athlete hasn't slept well (Doherty & Smith, 2005)

The majority of research on the impact of caffeine on muscle function has used participants that were either caffeine-naive or had a low-to-moderate daily caffeine intake of 58 to 250 mg/day (Grgic and Mikulic, 2017). According to research, 75–90% of athletes ingest caffeine before or during training sessions and competitions (Desbrow and Leveritt, 2006), implying that studies on the efficacy of acute caffeine consumption are particularly relevant in habitual caffeine users. The overall daily caffeine intake for most athletes, including pre-and intra-training doses, should not exceed 3 mg/kg, as this will greatly increase the minimum pre-competition caffeine dose. Caffeine intake later in a training session sometimes necessitates a lower dose (Cox et al., 2002), which can help avoid habituation.

Coffee consumption may be unappealing to athletes, particularly in the morning, due to the time commitment required to drink strong and hot beverages (Richardson and Clarke, 2016). Muscle and cognitive performance fluctuate during the day, with higher levels throughout the afternoon and lower levels throughout the morning (Facer-Childs et al., 2018). Athletes can also be required to practice very early in the morning due to a tight match schedule, resulting in lower muscle strength and impacting long-term training adaptations.

To counteract this, higher caffeine benefits in the morning can be considered. According to Mora-Rodrguez et al. (2015), 6 mg/kg/bm of anhydrous caffeine counteracted the morning decrease in muscle performance but had no impact on neuromuscular performance and increased the incidence of negative side effects recorded in the evening. Lower doses and coffee type, on the other hand, had no impact on muscle and cognitive output in the early morning. Caffeine's positive effects on cognitive performance such as increased arousal, response speed and vigilance have also been well reported in sports environments (Hogervorst et al., 2008).

2.3 Effects of Caffeine on Sports Performance

Caffeine has been shown to primarily benefit 20-50 percent of longer-term endurance exercise (Spriet, 1995) and resting metabolic rate (Graham & Spriet, 1995). Ingestion of 3-6 mg of caffeine per kg of body weight has an ergogenic effect comparable to higher doses (Graham et al., 1998). The consumption of 5 mg of caffeine per kg of body weight improved endurance running performance but did not have a major impact on other heat-acclimatized recreational runners' cardiorespiratory parameters in hot and humid conditions (Ping et al., 2010). After ingestion of either 5 mg. kg body weight^{-1} of caffeine or a placebo, 15 well-trained and 15 recreational athletes completed two randomised 5-km time trials. For both well-trained and recreational runners, caffeine intake was likely to generate a small but major increase in 5-km running performance (O'Rourke et al., 2008).

Ingestion of caffeine also increases efficiency during single short-term high-intensity exercise attempts (Grgic & Mikulic, 2017) and repetitive sprints (Paton et al., 2001). However, there have been few reports of caffeine's impact on shorter duration (10-30 min) of high-intensity exercise. There was no substantial difference between supplementation with caffeine and placebo in time to complete the total sprint test (Jordan et al., 2012). On the other hand, Bridge and Jones (2006) stated that caffeine improved performance by about 1.3% in an 8-km run. During endurance performance, caffeine is geared towards providing ergogenic benefits.

The impact of caffeine on athletic performance may mainly be due to improved muscle contraction (i.e. improved calcium output from the sarcoplasmic reticulum to the sarcoplasm after the opportunity for muscle activity, and increased motor unit recruitment) (Williams, 1991). Caffeine supplementation enhanced anaerobic performance in Olympic-level boxers without affecting lower limb electromyography (EMG) function and fatigue levels (San Juan et al., 2019). The effect of caffeine on anaerobic efficiency (strength-power) was more equivocal, with some studies suggesting benefits (McNaughton et al., 2008), while others show no substantial difference in the performance of resistance exercise (Astorino et al., 2008). Muscle performance is defined by the characteristics of a complex network of mental and physical elements, investigating caffeine's effect on cognitive performance will help us better understand its ergogenic properties.

Previous research on the effects of caffeine on runners has shown that when compared to a placebo, caffeine improves running efficiency (Wiles et al., 1992). When running at 85% potential oxygen absorption before exhaustion, 4.5 mg/kg body weight caffeine increased exercise distance by 2–3 km (Graham et al., 1998). In middle-distance events, 1500-m (Wiles et al., 1992) and one-mile (Clarke et al., 2018) running results increase by 1.3–1.9 percent after ingestion of 150–200 mg and 3 mg/kg body weight, respectively. Another research showed that amateur athletes performed equally in the 800-meter run after receiving either a placebo or 5.5 mg/kg body weight of caffeine (Marques et al., 2018). As a result, there is contradictory evidence about the use of caffeine as an ergogenic aid to increase athletes' middle-distance race results.

Caffeine ingestion increases resting cardiac autonomic function and accelerates autonomic recovery in recreationally active young men following post-exercise after a period of anaerobic exercise. However, no variations were found between doses of caffeine and cardiac autonomic reactivity (Sarshin et al., 2020). Caffeine's impact on efficiency and anaerobic capacity depends on the individual. While few studies have focused on sports modalities that encourage a predominantly anaerobic metabolism than one that is primarily oxidative-dependent, caffeine may now appear to have an ergogenic impact on anaerobic efforts as well (Grgic, 2018).

2.4 Caffeine dosage and side effects

Caffeine levels in foods differ greatly depending on how they are prepared, eg. a cup of coffee, tea, or cola (i.e., soft drink) contains around 60 to 150 mg, 40 to 60 mg, and 40 to 50 mg of caffeine, respectively (Lieberman, 2003). Caffeine has drawn the interest of many competitive and non-competitive athletes as a legitimate ergogenic help, even though it has no nutritional benefit. Coffee is a complex mixture of potentially beneficial compounds known as "nutraceuticals." Indeed, coffee contains approximately 1500 different substances, with about half of them being soluble (Benvenga et al., 2008). Phenolic polymers (pulp) account for 8% of the water-soluble constituents, polysaccharides for 6%, chlorogenic acids for 4%, minerals for 3%, caffeine for 1%, organic acids for 0.5%, sugars for 0.3%, lipids for 0.2% and aroma for 0.1%. Coffee's water-soluble components hinder thyroxine absorption in the intestine, most likely due to physical sequestration of the hormone (Benvenga et al., 2008).

Many research using moderate to high doses of caffeine (5-9 mg/kg body weight) found ergogenic effects in endurance-type activities, as well as pronounced effects on physiological responses to exercise, including increased heart rate, a doubling of blood catecholamine levels, higher blood lactate levels, and even increased blood free fatty acid (FFA) and glycerol levels in some subjects.(Desbrow et al., 2012).

Depending on the dosage, acute caffeine ingestion affects some symptoms. At doses greater than 9 and 13 mg/ kg body weight, caffeine can cause dizziness, headaches, jitteriness, nervousness, insomnia, and gastrointestinal discomfort in nonusers and users, respectively (Evans and Griffiths, 1992). At high doses, these signs and symptoms can be related to reduced performance in some athletes (Roti et al., 2006). While evidence indicates that caffeine has no additional ergogenic effects above doses of 9 mg/kg (Graham and Spriet, 1995), athletes who regularly consume moderate-to-high doses of caffeine (4–5 mg/kg body weight) can reach a point where additional caffeine consumption does not restore caffeine's maximum ergogenic potential. Although such habitual intakes can seem severe, in some research studies (Fisher et al., 1986), subjects' daily intakes exceed this amount. Furthermore, higher caffeine doses can increase the risk of reported side effects including tremors, insomnia, and a faster heart rate (Astorino et al., 2008).

With long-term use, excessive anhydrous caffeine consumption can cause gastrointestinal issues, tachycardia, sinus, tingling sensations, and negative health effects (Astorino and Roberson, 2010), and dose-response studies have recently increased (Pallarés et al., 2013). The optimal dose needed to have ergogenic effects can vary based on sex (Sabblah et al., 2015), muscle group size (Pallarés et al., 2013) and habitual caffeine intake (Wilk et al., 2019). The results for the same dosage can be influenced by apparent variations in body size, lean body mass and hormonal functioning between sexes (Mielgo-Ayuso et al., 2019).

The chemical structure of phenylpropanolamine is similar to that of ephedrine and amphetamines, and it can raise blood pressure. When consumed in large doses, caffeine has been shown to increase blood pressure (Robertson et al., 1978). While ingestion of 25 mg of *phenylpropanolamine* did not raise blood pressure in normal volunteers (Silverman et al., 1980), ingestion of 85 mg of phenylpropanolamine caused a substantial increase in both systolic and diastolic blood pressure in all normal volunteers (Horowitz et al., 1979).

Some people experienced a harmful spike in blood pressure when ingesting 85 mg of phenylpropanolamine (Tarnopolsky, 2008). Subarachnoid or intracerebral haemorrhage could result (Tetsuka & Ogawa, 2019) from an acute increase in systemic mean arterial pressure, which can cause the failure of cerebral blood flow autoregulation and "breakthrough" of the blood-brain barrier (Lataro et al., 2015). Humans have encountered these side effects since taking "look-alike" pills and diet pills. Acute tubular necrosis was identified in a previously healthy 25-year-old man after an overdose of diet pills containing phenylpropanolamine caffeine in one of these studies (Dunphy et al., 2019).

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Likely, hypertensive people are often "at-risk" when they take PPA/caffeine. While humans rarely take more than the recommended doses of PPA/caffeine, "individual" variability indicates that reactions to lower concentrations and doses could occur. (Skinner et al., 2010) found that a significant percentage of our hypertensive population is unaware of their condition and because hypertension is more prevalent in overweight people who take diet pills (Mishra et al., 2006) the "at-risk" community is large. As a result, it is natural to inquire about "over-the-counter" diet pills or "look-alike" pills in young patients who present with cerebral haemorrhage prior to the incident.

In conclusion, there is evidence that caffeine ingestion of 3-6 mg per kg of body weight has an ergogenic impact comparable to greater dosages, which is beneficial to sports performance, particularly endurance exercises. Furthermore, moderate dosages of caffeine have been shown to have a positive influence on athletic performance. However, this ergogenic effect is not found in habitual caffeine users and adverse side effects are influenced by a variety of interpersonal factors including age, the use of other drugs or treatments that may interact with caffeine effects, circadian aspects, or the time of consumption. Caffeine tolerances (where a higher dose is required to achieve the same physiological impact as previously consumed lower doses) and genetic predispositions are both factors in some cases (Kendler et al., 2008).

CHAPTER 3

METHODOLOGY

3.1 Data Sources

Related studies were obtained electronically using the following databases: Scopus, PubMed, EbscoHost and ScienceDirect. The selected studies were hand-searched using the same eligibility criteria as mentioned below. Furthermore, to obtain additional details, cross-referencing of similar previous studies was carried out. Articles peer-reviewed in English were used in the period from 2016 up to 2020. There were no attempts to approach the authors for more information.

3.2 Study Selection

The analysis was done in compliance with the criteria of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Figure 1). The keywords used during the search were #Caffeine and (#sports performance or #exercise to exhaustion). Articles were screened for employing caffeine as intervention and exercise to exhaustion or sports performance as outcome measures or stimulus. This review only included controlled trials and laboratory tests on humans. The interventions comprised of caffeine with placebo control, caffeine with other dietary supplements, and caffeine in combination with exercise performance. Time trial and exercise to exhaustion are described as aerobic performance, anaerobic performance (eg: cycling protocol) or specific performance tests for sports.

The initial search from the databases identified 407 potential articles while another 2 were found through cross-referencing. After removing duplicates, 399 articles were assessed based on titles and abstracts against the selection criteria. A total of 385 articles were excluded because they did not investigate caffeine and sports performance. For the inclusion criteria, articles from 2016 up to 2020 were included. After a detailed analysis of full-text articles, only 14 articles were included (Figure. 1).

3.3 Data Extraction

The titles and abstracts of retrieved articles were reviewed using the criteria specified to determine whether full texts were available for further study. Each full-text report was systematically reviewed according to the study: (1) objectives, (2) study characteristics (design of the study, participants and sample size), (3) intervention content (types of intervention, duration of intervention or mode of exercise measured, (4) targeted outcomes and (5) main exercise performance finding.

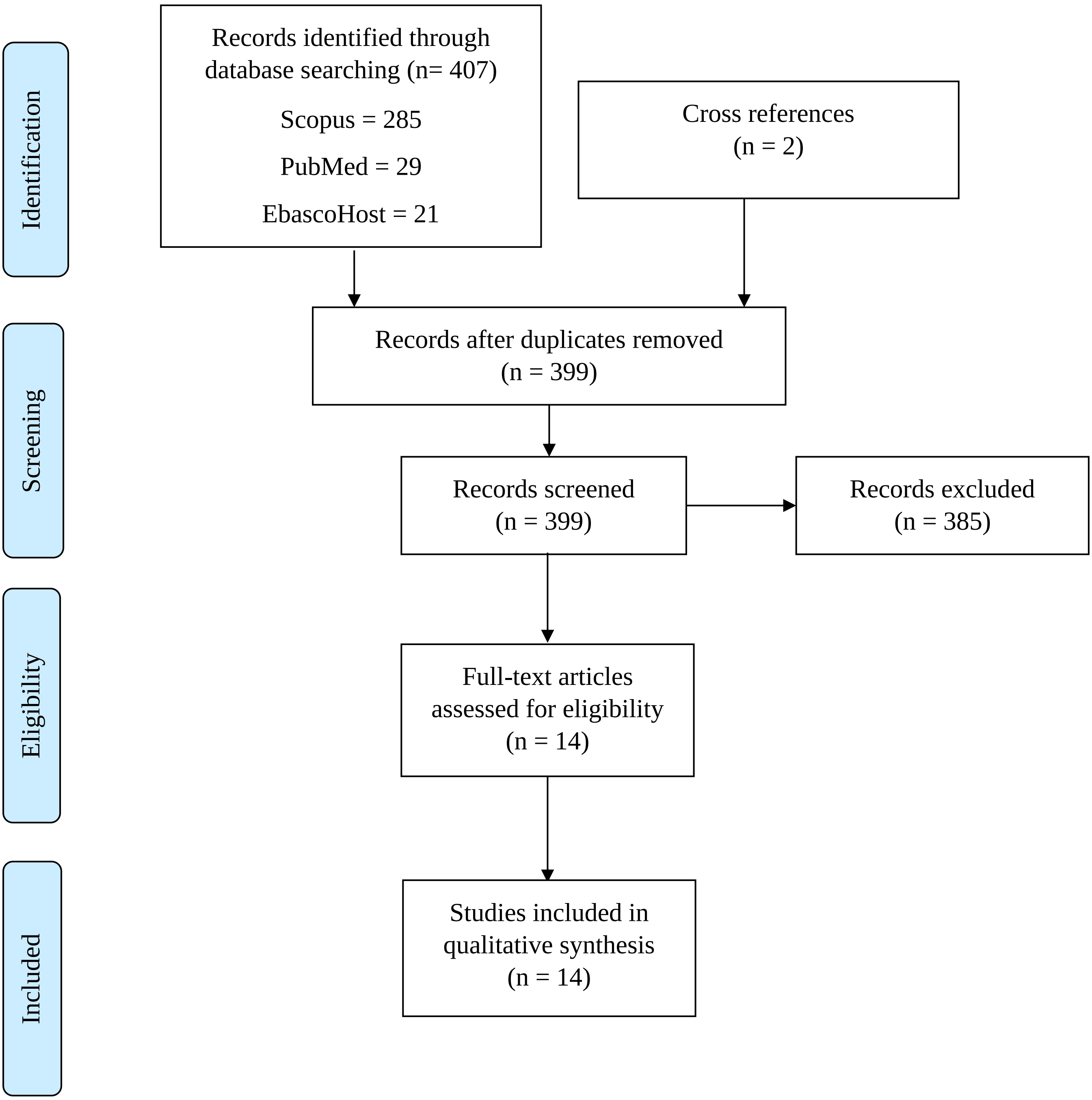

Figure1: PRISMA flow diagram for the study selection.

CHAPTER 4

RESULTS

4.1 Search Results

The initial search from the databases identified 407 potential articles while another 2 were found through cross-referencing. After removing duplicates, 399 articles were assessed based on the titles and abstracts against the selection criteria. A total of 385 articles were excluded because they did not investigate caffeine and sports performance. Following further screening for inclusion and exclusion criteria, only 14 articles were included in the review. Data extracted from each article are presented in Table 1.

4.2 Article Characteristics

All 14 articles were published between 2016 and 2020. The number of articles published was as follow: 2020 (n=6), 2019 (n=2), 2018 (n=1), 2017 (n=1), 2016 (n=2), 2008 (n=1) and 2006 (n=1). The total sample and gender of participants for all the 14 articles were 217 male participants. Among the articles, six articles studied on healthy and active participants, two articles investigated on soccer players, two articles investigated on runners, one article investigated on endurance trained cyclists, one article investigated on resistance trained, one article investigated on sub-elite hurling athletes and one article investigated on mountain bikers.

In term of caffeine supplementation, eleven articles used caffeine capsule, two articles investigated caffeine supplement (creatine and arginine-nitrate in powder form). One article studied on caffeine tablet.

4.3 Exercise Performance and Intervention Protocols

All the studies used different methods of exercise for assessment. To measure aerobic and anaerobic performance, eight articles used cycling protocol and another six articles adopted the running protocol. Twelve articles measured time trial performance while two articles measured time to exhaustion performance. The analysis revealed that eleven articles investigated caffeine supplementation prior to exercise, two articles studied on caffeine supplementation during exercise, and one article investigated on both prior and during exercise.

4.4 Synthesis of Result

4.4.1 Caffeine Intake on Aerobic Performance

Based on the articles reviewed, three studies reported improvement in aerobic performance after caffeine supplementation. In a 4-km time trial performance, the participants improved their cycling performance after the ingestion of caffeine (Viana et al., 2020). Another article reported that caffeine consumption improved performance the 5-km running time trial performance significantly ($p = 0.01$) compared to control trial. In that 5-km time trial, the magnitude of performance improvement was similar for both groups, ranging from 1.0% (CI 0.4—1.6%) for the well-trained runners to 1.1% (CI 0.2—2%) for the recreational runners

(O'Rourke et al., 2008). In an experiment replicating the physiological demands of a soccer game, caffeine was effective to enhance aerobic performance among soccer players. However, there was no difference in time to exhaustion between groups and no treatment-by-group interaction ($p = 0.05$) recorded by the study done by (Apostolidis et al., 2020).

4.4.2 Caffeine Intake on Anaerobic Performance

Based on the articles reviewed, eight studies reported an improvement in anaerobic performance. A significant difference in repeated sprint ability was detected between caffeine supplement and control trials ($p = 0.002$) (Keane et al., 2020). When peak power was examined, an article found that cycling anaerobic performance showed a significant influence of supplementation (Grgic et al., 2020). Caffeine supplementation resulted in greater W_{peak} values than placebo (11.22 ± 0.65 vs 10.7 ± 0.84 W) but trained-recreational athletes had a higher W_{peak} (11.31 ± 0.73 W) compared to elite athletes (10.52 ± 0.62 W) in the caffeine trial (Jodra et al., 2020). For the study on Olympic athletes, it was found that caffeine consumption had a substantial and large effect on W_{peak} in Olympic-level boxers ($p= 0.01$) (San Juan et al., 2019). This article reported that there were no differences in running performance among the types of beverages (caffeine, arginine and branched chain amino acids) ($p=0.071$) and time trial ($p= 0.86$) (Ermolao et al., 2017). In recreationally trained athletes, acute intake of a commercially available pre-workout nutritional supplement can significantly improve both anaerobic peak power and mean power. In comparison with the Wingate Anaerobic Power Test, (Martinez et al., 2016) showed significant within-subjects impact for anaerobic peak power ($p = 0.001$) and anaerobic mean power ($p = 0.007$). This article reported on improvement of acute caffeine consumption following a supramaximal effort at 115% of iVO2max during supramaximal cycling performance (Miyagi et al., 2018).

4.4.3 Caffeine Dosage and Timing

Consumption of 3 $mg.kg^{-1}$ of body mass of caffeine an hour prior to exercise was able to improve the 8-km time trial performance (Bridge and Jones, 2006). Similar dosage was applied by (Lara et al., 2019) but no significant difference was observed between caffeine and placebo treatment'. Acute ingestion of a similar moderate dosage of caffeine (3 mg/kg body weight) relatively has small performance-enhancing effect on anaerobic performance (Grgic et al., 2020). Meanwhile, there were 6 studies investigating a dosage of 6 $mg.kg^{-1}$ body weight of caffeine on exercise performance (Viana et al., 2020 ; Apostolidis et al., 2020 ; Jodra et al., 2020) ; San Juan et al., 2019 ; Miyagi et al., 2018 ; Boyett et al., 2016). In another study, (Sarshin et al., 2020), used $3mg/kg^{-1}$ body mass and $6mg/kg^{-1}$ body mass of caffeine and they have shown no significant difference in cycling performance between these two caffeine dosages. One study used $5mg.kg^{-1}$ body mass (O'Rourke et al., 2008) and 2 other studies gave a fixed dosage not based on body weight, i.e. 200 and 300 mg caffeine (Keane et al., 2020 and Ermolao et al., 2017), respectively.

Table 1: Data extracted from each article included for review (N=14)

Articles	Study Participants	Study Design	Test Protocol	Caffeine Intervention	Caffeine Dosage	Key Exercise Performance Finding
Viana et al., 2020.	Endurance-trained cyclists.	Randomised placebo-controlled trial.	4-km time trial.	Before	6 mg/kg^{-1} of body mass).	Ingestion of caffeine resulted in increase of aerobic performance.
Apostolidis et al., 2020.	Soccer players.	Double-blind. cross-over.	3 intervals between four periods of running	Before	6mg/kg^{-1} of per body mass.	There is a significant effect of caffeine on time to exhaustion compared to placebo.
Keane et al., 2020.	Sub-elite hurling players.	Randomised, double-blinded.	Repeated sprint time trial	Before	200mg of caffeine capsule.	No significant difference observed from CHO+CAFF and placebo trials.
Grgic et al., 2020.	Resistance trained athletes	Randomised, double-blind and cross-over design.	2 main trials of cycling	Before	3 mg/kg^{-1} of body mass	Caffeine ingestion may have a relatively small performance-enhancing effect on anaerobic performance.
Jodra et al., 2020.	Elite athletes	Randomised, double-blind and placebo controlled.	2 trial sessions of cycling	Before	6mg/kg^{-1} per body weight	Acute effect of caffeine supplementation on anaerobic performance. Athletes showed higher peak

						value after consumption of caffeine compared to placebo.
Sarshin et al., 2020.	Active athletes	Randomised, double-blind, placebo controlled.	3 sessions per week for 20 days of cycling.	Before and during	$3mg/kg^{-1}$ – $6mg/kg^{-1}$ of body mass.	No significant difference in caffeine dosages of placebo and controlled group.
San Juan et al., 2019.	Healthy National Olympic boxing team athletes	Randomised, double-blind, placebo-controlled design.	2 test sessions of cycling.	Before	$6\ mg/kg^{-1}$ of body mass	Caffeine supplementation improved peak power and enhanced more on anaerobic exercise performance.
Lara et al., 2019.	Healthy active participants	Randomised double-blind, placebo-controlled, and cross-over.	8 trials of exercises of cycling	Before	$3mg/kg^{-1}$ per body mass/day	No significant difference between caffeine and placebo treatment.
Miyagi et al., 2018.	Mountain bikers	Randomised, double-blind, placebo-controlled design	3 trial sessions of cycling	Before	$6\ mg/kg^{-1}$ per body weight.	Improvement of acute caffeine consumption on anaerobic performance.