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Caffeine in Sport: Performance Enhancer or Hidden Player in Cancer Biology?

A Narrative Review

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Abstract

Caffeine is one of the most widely used ergogenic aids in sport, known for its performance-enhancing effects on endurance, strength, and cognitive function. Beyond these well-established roles, emerging evidence suggests that caffeine may also influence biological pathways associated with carcinogenesis. This narrative review provides a sports-oriented perspective on caffeine as a bioactive compound with potential implications extending beyond performance. Current evidence indicates that caffeine modulates mechanisms such as DNA damage response, apoptosis, oxidative stress, and immune regulation. While experimental findings suggest possible anticancer effects, human evidence remains inconsistent and largely observational. Given the widespread and repeated use of caffeine in athletic populations, understanding its broader biological impact is essential. Although caffeine cannot be considered an anticancer agent, its dual role in performance enhancement and health-related pathways highlights the need for integrative research bridging sports science and oncology.

Background. Caffeine is one of the most commonly consumed psychoactive substances worldwide and a well-established ergogenic aid in sport. It is widely used by athletes to improve physical performance, delay fatigue, and enhance cognitive function during training and competition. In sports practice, caffeine supplementation typically ranges from 3 to 6 mg/kg body mass, with some individuals using even higher doses through concentrated pre-workout

formulations. Beyond its role in exercise performance, caffeine has been increasingly recognized as a biologically active compound capable of influencing multiple physiological systems. Recent research suggests that caffeine may modulate pathways involved in DNA damage response, apoptosis, oxidative stress, and immune function—processes that are also central to carcinogenesis. Given the frequency and intensity of caffeine use in physically active populations, its potential long-term biological effects have become an important topic not only in sports science but also in broader health research.

Aim. The aim of this narrative review was to critically evaluate current evidence on caffeine as a compound linking sports performance and health, with particular emphasis on its potential role in cancer-related biological mechanisms. The review integrates findings from molecular, experimental, and human studies while considering exposure patterns relevant to athletes and physically active individuals.

Materials and methods. This study was conducted as a narrative review. A structured literature search was performed using PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar to identify relevant studies published between 2000 and February 2026. The search strategy included keywords related to caffeine, sport, exercise, supplementation, cancer, carcinogenesis, and molecular mechanisms. Studies were selected based on predefined inclusion and exclusion criteria, focusing on research investigating caffeine exposure in relation to biological processes relevant to both performance and cancer development. A total of 27 peer-reviewed publications were included in the final qualitative synthesis, comprising molecular studies, in vitro and animal experiments, observational human studies, and review articles. Due to heterogeneity in study design and outcomes, a qualitative approach was applied without formal meta-analysis.

Results. Current evidence indicates that caffeine exerts multidirectional biological effects. In sports-related research, caffeine consistently improves endurance, strength, and cognitive performance. At the same time, molecular and experimental studies demonstrate that caffeine modulates key pathways involved in carcinogenesis, including DNA damage response signaling, apoptosis, oxidative stress, and immune regulation. Experimental findings suggest antiproliferative and potential chemosensitizing effects of caffeine in various cancer models. However, these effects are often observed at concentrations exceeding those typically achieved in humans. Human studies provide inconsistent results, with some evidence suggesting protective associations between caffeine-containing beverages and selected cancers, while others show no significant relationship.

Conclusions. Caffeine should be considered not only as a performance-enhancing substance but also as a biologically active compound with potential implications for long-term health.

Although current evidence does not support its use as an anticancer agent, its widespread and repeated use in athletic populations highlights the importance of understanding its broader physiological effects. Future research should focus on physiologically relevant dosing models and interdisciplinary approaches integrating sports science, nutrition, and clinical research to determine whether caffeine exposure may influence cancer-related outcomes.
Keywords: caffeine; sport performance; athletes; exercise supplementation; carcinogenesis; apoptosis; sports nutrition; oxidative stress; health effects; narrative review

Content

1. Introduction

Caffeine is one of the most widely used ergogenic aids in sport and is consistently recognized for its ability to enhance endurance, strength, and cognitive performance. It is commonly consumed by athletes in both recreational and elite settings, often in the form of coffee, energy drinks, or concentrated supplements. Typical supplementation protocols range from 3 to 6 mg/kg body mass, with some individuals using higher doses during training cycles and competition. Due to its widespread and repeated use, caffeine has become one of the most extensively studied substances in sports nutrition. While its acute effects on performance are well established, increasing attention has been directed toward its broader physiological impact, particularly in the context of long-term health in physically active populations. Caffeine (1,3,7-trimethylxanthine) is a biologically active compound that interacts with multiple cellular pathways, including those involved in metabolism, oxidative stress, inflammation, and cellular signalling. Recent research suggests that these mechanisms may extend beyond performance-related adaptations and may also influence processes associated with disease development. In particular, emerging evidence indicates that caffeine may modulate pathways involved in carcinogenesis, including DNA damage response, apoptotic signalling, oxidative stress regulation, and immune function. These observations have generated growing scientific interest in understanding whether a commonly used ergogenic aid may also have broader biological implications. Importantly, caffeine exposure in athletes may differ substantially from that observed in the general population. Repeated supplementation, higher dosing strategies, and chronic use during training and competition may result in sustained systemic exposure, potentially influencing physiological processes beyond short-term performance outcomes. Despite increasing research interest, current evidence remains fragmented, with inconsistencies between molecular findings, experimental models, and human studies. Moreover, the relevance of these findings for physically active populations has not been clearly established. Therefore, the aim of this narrative review is to critically evaluate current evidence on caffeine as a compound linking sports performance and health, with particular emphasis on its potential role in cancer-related biological processes. By integrating findings from molecular, experimental, and human studies, this review seeks to provide a comprehensive and sport-oriented perspective on the broader physiological effects of caffeine.

2. Research materials and methods

2.1 Study design and literature search strategy

This study was conducted as a narrative review aimed at synthesizing and critically evaluating current scientific evidence regarding the potential anticancer effects of caffeine, including molecular mechanisms, experimental findings, epidemiological data, and implications for physically active populations and athletes. The study selection process was performed by the research team. A comprehensive literature search was performed using the following electronic databases: PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar. The search covered studies published from January 2000 to February 2026, with particular emphasis placed on literature from the last 5–7 years to ensure up-to-date evidence. The literature search was performed using predefined keywords, such as: *caffeine, cancer, carcinogenesis, apoptosis, tumor cells, exercise, sport, caffeine supplementation, athletes*. Boolean operators AND and OR were applied to combine search terms. When multiple reports described the same dataset, the most comprehensive or recent publication was selected. In addition, reference lists of selected publications were manually screened to identify further relevant studies not captured during the initial database search. The initial search yielded a larger pool of potentially relevant publications. After screening titles, abstracts, and full texts according to predefined eligibility criteria, 27 peer-reviewed studies were included in the final qualitative synthesis.

2.2 Inclusion criteria and exclusion criteria

Studies were included if they met the following criteria:

1. Published in peer-reviewed scientific journals.
2. Written in English.
3. Investigated caffeine exposure as a primary or independent variable.
4. Addressed outcomes related to cancer biology, carcinogenesis, tumor progression, or anticancer mechanisms.
5. Included molecular, experimental, observational, or review study designs.
6. Provided sufficient methodological information to assess scientific relevance.

The following publications were excluded:

- conference abstracts without full text,

- opinion papers and non-scientific reports,
- duplicate publications,
- studies investigating coffee components other than caffeine without isolating caffeine-related effects,
- articles lacking adequate methodological transparency.

2.3 Methodological considerations

Due to heterogeneity in study designs, outcome measures, caffeine dosing protocols, and population characteristics, a meta-analysis was not performed. Instead, emphasis was placed on critical appraisal of methodological quality, reproducibility, and biological plausibility of reported findings. Moreover, findings were grouped and interpreted according to three major categories:

- molecular and metabolic mechanisms
- experimental evidence (in vitro and animal studies)
- human and epidemiological evidence.

This approach allowed identification of consistent patterns, mechanistic insights, and existing knowledge gaps in current research on caffeine and cancer-related processes.

3. Research results

3.1 Metabolic and molecular mechanisms

Caffeine is a methylxanthine alkaloid characterized by rapid gastrointestinal absorption and high systemic bioavailability, with peak plasma concentrations typically reached within 30–60 minutes after oral administration. Supplemental intake commonly used in athletic populations (3–6 mg/kg body mass) produces substantially higher systemic exposure than dietary intake alone (Guest et al., 2021), which is relevant when comparing physiological conditions with experimental oncology models.

At the molecular level, caffeine influences multiple signaling pathways implicated in carcinogenesis. One of the most consistently reported mechanisms is inhibition of the ATR–Chk1–mediated DNA damage response, leading to disruption of checkpoint control and enhanced apoptosis in damaged cells (Tsabar et al., 2015; Heffernan et al., 2009). Additional

studies demonstrate modulation of p53-dependent signaling and caspase activation in breast cancer models (Amira et al., 2025).

Caffeine has also been shown to affect PI3K/Akt/mTOR and related proliferative pathways (Song et al., 2025), as well as to increase reactive oxygen species (ROS) levels in tumor cells, promoting oxidative stress–mediated apoptosis (Amin et al., 2024). Emerging findings further suggest potential immunomodulatory effects, including enhancement of antitumor T-cell activity (Liu et al., 2025). Collectively, these mechanisms support a biologically plausible anticancer role, although effects appear strongly dose-dependent and model-specific.

3.2 Experimental evidence

In vitro studies consistently report that caffeine reduces cancer cell viability and proliferation while promoting apoptotic signaling across several tumor models, including breast, colorectal, prostate, and skin cancer cell lines (Amira et al., 2025; Amin et al., 2024). Synergistic effects have also been observed when caffeine is combined with chemotherapeutic agents such as paclitaxel, suggesting potential chemosensitizing properties (Gencoglu et al., 2026).

Preclinical animal studies provide partial support for these observations, demonstrating suppression of tumor growth, reduced angiogenesis, and increased apoptosis following caffeine administration (Liu et al., 2025). However, available preclinical evidence remains limited and heterogeneous with respect to dosing protocols, tumor types, and experimental design, which complicates direct comparison between studies and limits translational interpretation.

3.3 Human evidence

Observational studies examining caffeine or coffee consumption in relation to cancer risk yield heterogeneous findings. Several analyses report inverse associations for selected malignancies, including liver and colorectal cancers (Choi et al., 2026; Nguyen et al., 2025), whereas others show neutral or inconsistent results after adjustment for confounding variables such as smoking, diet, alcohol intake, and lifestyle factors (Jin et al., 2024).

Clinical evidence directly evaluating caffeine as an anticancer intervention remains scarce, and most human data derive from observational research rather than controlled trials. Moreover, it is often difficult to isolate caffeine-specific effects from those of other bioactive compounds present in coffee or tea (Qu et al., 2024). Consequently, current human evidence does not allow definitive conclusions regarding a causal anticancer effect of caffeine.

3.4 Summary of included studies

The characteristics and main findings of the studies included in this review are summarized in Table 1.

Table 1. Characteristics and main findings of studies included in the review.

Ref. No.	First Author (Year)	Study Type	Cancer Type / Population	Caffeine Exposure	Main Finding
1	Amira (2025)	In vitro	Triple-negative breast cancer	µM concentrations	Increased apoptosis and reduced telomerase activity
2	Abbasi (2024)	Umbrella review	Glioma risk	Dietary intake	No consistent association between coffee intake and glioma risk
3	Heffernan (2009)	Cellular model	UV-induced DNA damage	mM concentrations	ATR–Chk1 pathway inhibition promotes apoptosis
4	Fałczyńska (2026)	Review	Athletes	3–6 mg/kg	Ergogenic effects and increased systemic caffeine exposure
5	Qu (2024)	Epidemiological	Colon cancer	Dietary intake	Mixed associations between caffeine intake and colon cancer prevalence
6	Yu (2025)	Systematic review	Elite athletes	Supplemental	Dietary supplements including caffeine improve performance outcomes
7	Choi (2026)	Meta-analysis	Hepatocellular carcinoma	Coffee consumption	Inverse association between coffee intake and liver cancer risk
8	Tsabar (2015)	Molecular	DNA repair mechanisms	mM concentrations	Caffeine impairs DNA repair via reduced nuclease activity
9	Guest (2021)	Position stand	Athletes	3–6 mg/kg	Established effective and safe ergogenic dosing range
10	Jin (2024)	Meta-analysis	Lung cancer	Coffee intake	No consistent association with lung cancer risk
11	Rembiałkowska (2025)	Molecular review	Various cancers	Experimental	Caffeine modulates multiple oncogenic signaling pathways
12	Aborziza (2024)	In vitro	Various cancer cell lines	Extract/caffeine	Antiproliferative and chemopreventive properties observed
13	Song (2025)	Prospective cohort	Prostate cancer	Coffee intake	Association with PI3K signaling pathway activity
14	Liu (2025)	Cellular and animal	Colorectal cancer	Physiological exposure	Enhanced antitumor T-cell activity
15	Chen (2025)	Systematic review	Athletes	Supplemental	Improved exercise performance with caffeine intake
16	Matsumura (2026)	Systematic review	Exercise physiology	Supplemental	Identified methodological gaps in caffeine supplementation research
17	Amin (2024)	In vitro and animal	Breast cancer	Coffee extract	Antitumor effects observed in experimental models
18	Dahran (2025)	In vitro	Breast cancer	Nano-formulation	Enhanced cytotoxicity via oxidative stress and apoptosis
19	Song (2024)	Molecular review	Various cancers	Experimental	Multifunctional biological effects of caffeine

20	Dai (2025)	Narrative review	Digestive system cancers	Coffee intake	Mixed evidence regarding protective effects
21	Antonio (2024)	Review	Athletes	Supplemental	Clarification of safety and dosage misconceptions
22	Gencoglu (2026)	In vitro	Breast cancer	Combination therapy	Synergistic effects with paclitaxel
23	Nguyen (2025)	Observational	Head and neck cancer	Coffee and tea intake	Possible inverse association with cancer risk
24	Janiszewski (2025)	Human study	Athletes	Supplemental	Improved endurance and strength performance
25	Isemura (2025)	Molecular	Various cancers	Polyphenols/caffeine	Regulation of microRNA linked to anticancer activity
26	Tej (2019)	Experimental	Tumor immune response	Experimental	Enhanced cytotoxic T-cell activity through PD-1 modulation
27	Wang (2022)	Systematic review and meta-analysis	Endurance athletes	Supplemental	Caffeine improves endurance performance and time to exhaustion

Abbreviations: ROS – reactive oxygen species; TNBC – triple-negative breast cancer.

3.5 Implications for athletes and physically active populations

The findings of this review have direct relevance for athletes and physically active populations, in whom caffeine is widely used as a performance-enhancing substance. Regular supplementation practices, often involving repeated dosing during training and competition, may lead to higher and more sustained systemic exposure compared to the general population. Although current evidence does not support a direct anticancer effect of caffeine, its interaction with biological pathways such as oxidative stress regulation, immune function, and DNA repair suggests that it may influence long-term physiological processes beyond performance outcomes. From a practical perspective, caffeine should be considered not only in terms of its ergogenic benefits but also as a biologically active compound. Future sports nutrition strategies should integrate both performance optimization and long-term health considerations, particularly in populations exposed to chronic supplementation.

4. Discussion

From a sports science perspective, caffeine is widely recognized as one of the most effective ergogenic aids; however, the present review extends this perspective by synthesizing current evidence regarding its potential anticancer properties across molecular, experimental, and human research levels. The collected data indicate that caffeine interacts with multiple

biological pathways implicated in carcinogenesis, including DNA damage response systems, apoptotic signaling, oxidative stress regulation, and immune modulation (Heffernan et al., 2009; Amira et al., 2025; Liu et al., 2025). Such multimodal activity suggests that caffeine may act as a biologically active compound capable of influencing tumor development and progression rather than functioning solely as a central nervous system stimulant.

Experimental findings provide the strongest support for an anticancer role of caffeine. In vitro studies consistently demonstrate reduced cancer cell viability, increased apoptosis, and modulation of signaling pathways involved in proliferation and survival (Amira et al., 2025; Amin et al., 2024). Similarly, several animal studies suggest that caffeine administration may suppress tumor growth and enhance sensitivity to chemotherapy or radiotherapy. However, interpretation of these results requires caution, as many experimental protocols employ concentrations exceeding physiologically achievable levels in humans, which limits direct translational applicability. From a sports perspective, this limitation is particularly relevant, as even commonly used supplementation protocols (3–6 mg/kg body mass) may not fully replicate experimental conditions observed in laboratory settings.

Another aspect that deserves attention is the potential interaction between caffeine and the tumor microenvironment. Tumor progression is influenced not only by malignant cells themselves but also by surrounding stromal cells, immune components, and signaling molecules within the local microenvironment. Future experimental models should therefore consider these complex interactions when evaluating the potential anticancer effects of caffeine. Importantly, physical activity itself is known to modulate immune function and inflammatory processes, which may further interact with caffeine-related biological effects in athletes.

Human evidence remains less conclusive. Epidemiological studies report heterogeneous associations between caffeine or coffee intake and cancer risk, with some analyses suggesting protective relationships for selected malignancies, particularly liver and colorectal cancers, while others show neutral findings after adjustment for confounding variables. Differences in lifestyle factors, genetic polymorphisms affecting caffeine metabolism, and variation in beverage composition complicate interpretation of observational data. Future studies should also consider the potential interaction between caffeine metabolism and genetic polymorphisms affecting CYP1A2 activity. Moreover, it is difficult to distinguish caffeine-specific effects from those of other bioactive compounds present in coffee or tea, such as polyphenols and diterpenes. From a sports science perspective, an additional limitation is the lack of athlete-specific data, as most available studies are based on general population cohorts.

An additional consideration is the dose-dependent nature of caffeine's biological activity. Physiological exposure from dietary intake differs markedly from concentrations frequently used in experimental research, which may exaggerate observed cellular effects. This discrepancy highlights a common limitation in translational oncology research, where mechanistic findings do not always correspond to clinically achievable pharmacokinetic conditions. Nonetheless, studies conducted in athletic populations indicate that supplemental caffeine intake can produce substantially higher systemic exposure than habitual dietary consumption, suggesting that certain physiological contexts may approach experimentally relevant ranges.

From a sports perspective, caffeine is widely used not only as an acute ergogenic aid but also as a regularly consumed supplement during training cycles and competitive seasons (Guest et al., 2021). In many athletic settings, supplementation protocols involve repeated intake several times per week, which may result in chronic systemic exposure distinct from occasional dietary consumption.

Importantly, potential biological effects of caffeine may differ between acute and chronic exposure patterns. While acute administration is typically associated with transient pharmacodynamic responses, long-term supplementation could theoretically influence adaptive cellular mechanisms, including oxidative stress balance, inflammatory signaling, and DNA repair regulation. However, current evidence remains insufficient to determine whether chronic caffeine exposure modifies cancer-related risk profiles in physically active populations.

The potential clinical relevance of caffeine as an adjunct compound in oncology remains an open question. Evidence indicating enhanced sensitivity of tumor cells to chemotherapeutic agents or radiation suggests possible therapeutic utility; however, these findings are preliminary and require validation in controlled clinical trials. At present, caffeine should not be considered an anticancer treatment but rather a biologically active compound with mechanistic properties that warrant further investigation. From a sports science perspective, this reinforces the importance of interpreting caffeine supplementation not only in terms of performance outcomes but also in the context of long-term physiological effects.

This review also highlights several limitations within the current body of literature. Available studies vary widely in methodological design, dosing protocols, outcome measures, and model systems, which restricts comparability and prevents quantitative synthesis. The predominance of in vitro research further limits generalizability, while human data are largely observational and therefore unable to establish causality. In addition, publication bias toward positive findings cannot be excluded, particularly in experimental studies.

Despite these limitations, the convergence of mechanistic and preclinical evidence suggests that caffeine possesses biologically plausible anticancer activity. Future research should prioritize standardized dosing protocols, translationally relevant exposure models, and well-designed clinical trials capable of clarifying whether the molecular effects observed experimentally translate into measurable clinical benefit. Distinguishing caffeine-specific effects from those of whole coffee remains a critical methodological challenge. Greater attention should also be given to interindividual variability in caffeine metabolism, as genetic and physiological factors may influence biological responses and potentially modify cancer-related outcomes. In particular, polymorphisms affecting CYP1A2 activity may significantly alter systemic caffeine exposure and downstream biological effects, which could partly explain inconsistencies observed across epidemiological studies.

In summary, current evidence indicates that caffeine demonstrates multiple mechanistic properties consistent with anticancer activity, yet clinical confirmation remains insufficient. Importantly, from a sports and health perspective, these findings highlight the need for interdisciplinary research integrating exercise physiology, nutrition, and clinical science to better understand the long-term implications of caffeine use in athletes.

5. Conclusions

The present review demonstrates that caffeine exhibits multiple biological properties that may be relevant to cancer biology. Evidence from molecular and preclinical studies indicates that caffeine modulates key pathways involved in carcinogenesis, including DNA damage response signaling, apoptotic regulation, oxidative stress mechanisms, and selected proliferative cascades. These findings provide a biologically plausible framework supporting further investigation of caffeine as a potential modulator of tumor-related processes. Experimental data consistently show reduced cancer cell viability and enhanced apoptotic signaling in various tumor models, as well as possible chemosensitizing and radiosensitizing effects under specific conditions. However, interpretation of these findings must remain cautious, as many reported effects are dose-dependent and frequently observed at concentrations exceeding typical dietary exposure levels. Epidemiological studies suggest possible protective associations between caffeine-containing beverages and certain malignancies, particularly liver and colorectal cancers, yet results remain heterogeneous and strongly influenced by confounding factors. Importantly, current human evidence does not establish a causal anticancer effect of caffeine, and controlled interventional trials are lacking. From a sports and public health perspective, caffeine represents one of the most commonly consumed and supplemented psychoactive

compounds worldwide. Given that athletes and physically active individuals may achieve higher systemic exposure through supplementation protocols, understanding the broader biological effects of caffeine, including potential long-term implications, is of increasing relevance. Nevertheless, existing evidence does not justify the use of caffeine as a preventive or therapeutic oncological agent. In conclusion, caffeine demonstrates mechanistic properties consistent with anticancer activity, yet clinical confirmation remains insufficient. Future research should prioritize physiologically relevant caffeine concentrations, standardized experimental protocols, and rigorously designed clinical trials to determine whether promising molecular and preclinical findings translate into measurable benefits in humans. Additionally, from a sports science perspective, caffeine should be regarded as a compound requiring not only performance-based evaluation but also long-term health-oriented assessment in athletic populations.

5. Disclosure

Author's contribution

Conceptualization: [JB], [AC]
Methodology: [JBa], [MP], [MK]
Check: [KK], [KP], [MC]
Investigation: [JB], [DS], [JZ]
Data curation: [JBa], [AC], [MC], [MK]
Writing - rough preparation: [MP], [DS], [KK]
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The authors declare no conflict of interest.

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