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Natural product supplementation and high-performance in athletes: The potential of the dipeptide balenine

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Abstract
Fatigue affects athletes and is also a critical topic of study in sports science and medicine research. Fatigue affects performance and the recovery process is highly dependent on both the physical and mental state of the athlete. Over-training due to pressure to perform in combination with fatigue compounds the situation and results in burn-out or even worse a lack of motivation depression and even suicide. Stress and anxiety affect the recovery process ultimately performance. Research on performance enhancement has attracted attention over a long time. And understandably so as winning in sports is prized and a source of national pride for both as an individual (athlete) and society. Technology techniques and the role of nutrition (supplementation) cannot be underestimated when it comes to an athlete's performance state i.e. to be able to perform to the highest level during a competition. This particular research focuses on the importance of nutrition in context of human-high performance and looks at a new nutritional component the dipeptide balenine (from whale meat extract) as a potential nutraceutical or ergogenic aid in sports i.e. athlete performance.

Keywords: Anxiety burn-out fatigue over-training recovery stress

Introduction
The Hot Topic
Natural Product Supplementation and Athlete Performance
While 'performance' may appear as an abstract concept for the general population for athletes it is a defining element of their identity and success (Figure 1). It can be considered as one of the most important determinations of the ability and sometimes the only motivation (goal) for which he/she keeps going and undertaking day-and-night practices. In 2001 Haff Whitley and Potteiger stated that a determiner of an athlete's success is how powerfully he/she performs the outputs (Haff *et al*. 2001) [9]. Also a huge part of that performance can be dependent on the nutrition as that specific nutrition can help mitigate the biochemical imbalances caused by the stresses rooting from athletic exercises (Brotherhood 1984) [4]. To improve the performance and lower the problems associated with injuries and overtraining athletes need to sustain a balance between training dietary nutrients and other supplementations (Burke 2019) [5]. Kaufman and the colleagues (2022) reported that nutrient supplementation is highly prevalent among trained athletes as some studies show the usage ranging from 40% to 100% though few athletes have a trusted source of information for their supplement decisions (Kaufman *et al*. 2022) [14]. And just recently in September 2025 a comprehensive 'SYSTEMATIC REVIEW' article was published and interestingly was part of the research topic "The Role of Nutritional Interventions in Optimizing Exercise Outcomes and Recovery" (Yu and Ding 2025) [30]. This not only highlighted the growing importance of topic (performance) among athletes and sport scientists but also critically analysing the role of supplements and their use by athletes for recovery from fatigue injury prevention and general health (Alfieri *et al*. 2023) [1]. The most recent 2025 study comprising 46 literatures revealed a predominance of male participants highlight a clear underrepresentation of the female athletes in such studies (Yu and Ding 2025)

[30]. The key point as expected was that the use of supplements was not conclusive and showed variable results but amino acids and probiotics were promising amongst the various studies conducted in fatigue prevention and exercise tolerance (Yu and Ding 2025) [30]. These researchers once again emphasized follow-up and extensive research and addressing various challenges including on research in women athletes and minor sports (Alfieri *et al*. 2023; Yu and Ding 2025) [1, 30]. This bring us back to our area of interest natural food/product supplementation and key amino acids. The reason that there is a wide range of natural product supplements at the market containing amino acids plant extracts and vitamins to improve the performance and recovery of athletes might be the fact that they often carry lower risks compared to synthetic alternatives; however to guarantee the safety factors such as purity dose interactions and related ones must be carefully evaluated. Here we look specifically at the dipeptide balenine containing histidine (Jędrejko *et al*. 2025; Wada *et al*. 2016; Ishihara *et al*. 2021; Shigemura *et al*. 2022 2024) [12, 13, 25, 26, 31].

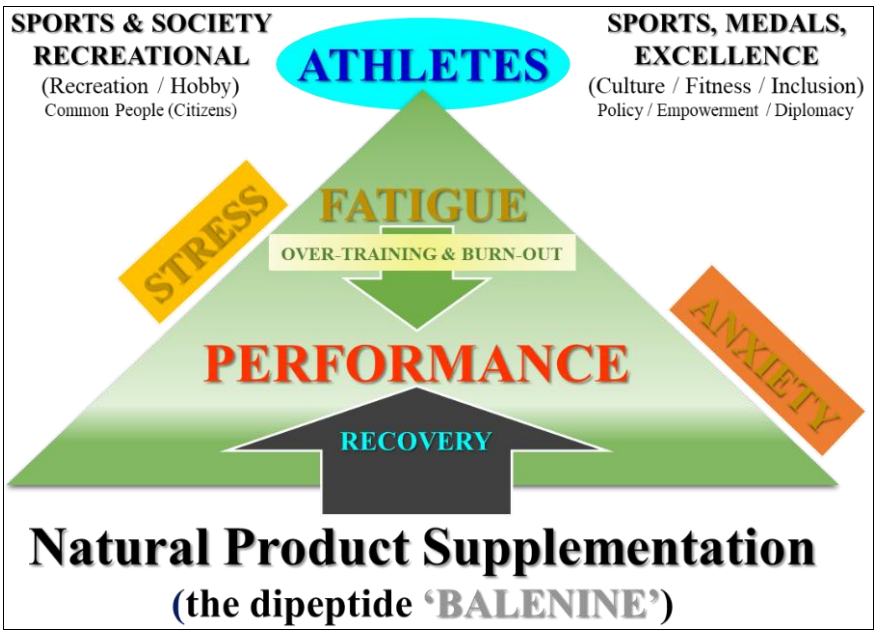

Fig 1: Role of Biological Supplementation (Marine Products) in Sports (Athlete Performance). A conceptual diagram of athlete performance in context of fatigue and potential role of a bioactive dipeptide balenine.

Histidine and the Imidazole Dipeptide Balenine

Histidine is an amino acid playing a crucial role in protein synthesis and can be found naturally in animal products with high protein content such as beef fish and chicken (Jędrejko *et al*. 2025) [13]. The dipeptide balenine is a compound containing histidine and has a value in nutrient supplements as a functional food ingredient with potential health benefits (Wada *et al*. 2016; Ishihara *et al*. 2021; Shigemura *et al*. 2022 2024) [12, 25, 26, 31]. Moreover balenine has shown promising results on mice on the alternation of the brain characteristics in order to enhance the memory and learning ability (Wada *et al*. 2016) [31]. In addition balenine has a higher stability *in vivo* compared to some other supplement-related dipeptides which makes it a better suit for ergogenic supplements (Shibato *et al*. 2024) [24]. Similarly the group of de Jager (2023) has studied the histidine-containing bioactives carnosine anserine and balenine (de Jager *et al*. 2023a 2023b) [8, 9]. Although one research indicates inability of acute synthetic balenine supplementation to elicit performance improvement (similar as carnosine and anserine) in recreational cyclists (de Jager *et al*. 2023a) [8] their second research mentions opportunities for balenine as nutraceutical or ergogenic aid (de Jager *et al*. 2023b) [9].

With the above literature and considering the wide-ranging beneficial effects of balenine the question being considered by the group of Shioda Takenoya and colleagues was how it affects the nutritional requirements of athletes (Wada *et al*. 2016; Shibato *et al*. 2024; https://www.shioda.co.jp/) [24, 31]. A recently published narrative review on histidine-containing compounds including balenine has discussed their effects on exercise capacity in both animals and humans (Jędrejko *et al*. 2025) [13]. Although there is not much research on balenine in relation to exercise performance in athletes available studies reviewed by Jędrejko and colleagues show promising results in enhancing muscle regeneration and counteracting the effects of oxidative stress (Jędrejko *et al*. 2025) [13]. Balenine is supposed to have a buffering characteristic at the early stages of exercise meaning it can delay the fatigue (Jędrejko *et al*. 2025) [13]. In long intense exercise a performance-impairing compound "lactic acid" is produced in the working skeletal muscles reducing the pH which leads to fatigue (Cairns and Lindinger 2025) [6]. This suggests that balenine can have potential benefits for mental fatigue focus and recovery. Nevertheless new research will be critical in clarifying the potential of balenine in athletic performance especially through natural food supplementation (e.g. whale meat extract; Wada *et al*. 2016; Shibato *et al*. 2024; https://www.shioda.co.jp/) [24, 31]. This article will therefore consider the effect of natural (food-derived) balenine on the fatigue level and enhanced performance of athletes (student-athletes elite athletes including female athletes) as a next step and is presented at the end of the article. Before that it is useful to define the key components of the concepts. Though well know and of common knowledge it is imperative that these are defined and presented in line with topic at hand with reference literatures.

Key Terminolgies and Concepts

The keyword definitions are sourced from the Merriam-Webster dictionary and scientific literatures are referenced including "*direct quotes*" by authoritative researchers (scientific relevance).

Fatigue

A state or attitude of indifference or apathy brought on by overexposure (reference https://www.merriam-webster.com) and it reduces the performance both physically and mentally (Bestwick-Stevenson *et al*. 2022) [3]. Accordingly fatigue has been defined as "a subjective state that goes beyond feeling tired and sleepy cannot be predicted by effort exerted and interferes with carrying out duties and responsibilities" (Strahler *et al*. 2016) [28]. In several populations stress especially for a long term can strongly be linked to the development of fatigue (Kurokawa *et al*. 2011; In: Strahler *et al*. 2016) [17 28].

Burn-out

Exhaustion of physical or emotional strength or motivation as a result of prolonged stress or frustration (https://www.merriam-webster.com/). It is defined as *"a* psychological syndrome consisting of three symptoms termed emotional and physical exhaustion reduced sense of accomplishment and sport devaluation" (Raedeke 1997; Raedeke and Smith 2001; In: Olsson et.al. 2024) [20-22]. It happens when the person feels depleted of physical and emotional resources as well as low productivity in sports contexts (Raedeke 1997; Raedeke and Smith 2001; In: Olsson et.al. 2024) [20-22].

Over-training

It is to train to excess or beyond advantage (https://www.merriam-webster.com/). "Overtraining is an imbalance between training and recovery" (Kuipers and Keizer 1988) [16]. In athletes when fatigue is coupled with some physical and psychological symptoms it is called as the 'staleness' or 'overtraining syndrome' (Kuipers and Keizer 1988) [16]. For clarity staleness is defined by Kuipers and Keizer (1988) as "a dysfunction of the neuroendocrine system localised at hypothalamic level" and might "occur when physical and emotional stress exceeds the individual coping capacity" (Kuipers and Keizer 1988) [16]. However it can clinically be divided into the sympathetic and parasympathetic determined by the dominance of either system and both can be explained as expressions of the body's stress response (Kuipers and Keizer 1988) [16].

Stress

It is a physical chemical or emotional factor that causes bodily or mental tension and may be a factor in disease causation (https://www.merriam-webster.com/). Ntoumanis and Biddle in 1998 referring to the sports arena have mentioned that "athletes face numerous stressful situations which are generated from different sources" (Ntoumanis and Biddle 1998) [19]. There are many situations that are considered threatening or challenging for athletes such as competing with others in a competition underperformance etc. both the methods they use to manage these challenges and their evaluation of how well these methods work significantly affect their emotional status in sport (Ntoumanis and Biddle 1998) [19].

Anxiety

A mentally distressing concern or interest (https://www.merriam-webster.com/). "Anxiety states are emotional reactions that consist of a unique combination of feelings of tension apprehension and nervousness; unpleasant thoughts (worries) and physiological changes" (Spielberger 1990) [27]. In elite athletes anxiety might arise from both general population factors and sport-specific ones as indicated by a systematic review and meta-analysis study of 88 articles (Rice *et al*. 2019) [23].

Recovery

It has been defined as the process of combating a disorder (such as alcoholism) or a real or perceived problem (https://www.merriam-webster.com/). Kellmann and co-workers have published research where they tried to provide a consensus statement on recovery and performance in sport (Kellmann *et al*. 2018) [15]. According to Kellmann *et al*. (2018): "Recovery is regarded as a multifaceted (e.g. physiological psychological) restorative process relative to time. In case an individual's recovery status (i.e. his or her biopsychosocial balance) is disturbed by external or internal factors fatigue as a condition of augmented tiredness due to physical and mental effort develops" (Halson 2014; In: Kellmann *et al*. 2018) [11, 15]. Although performance and physiological indicators are important an athlete's own perception of readiness is a crucial element of recovery process and monitoring the balance between recovery and fatigue is the important initial step in performance enhancement (Kellmann *et al*. 2018) [15].

Conclusion and Future Prospects

With the above conceptual diagram key terms and defining the focus of the study namely how a natural product (balenine a component found in specific types of meat such as whale meat etc.) supplementation can influence an athlete's high performance the authors propose (a tentative research plan) an experiment to confirm the hypothesis (Figure 2). Briefly the research plan follows the recent protocols being developed by Shioda *et al*. (Wada *et al*. 2016; Shibato *et al*. 2024; https://www.shioda.co.jp/) [24, 31] and a double-blind randomized trial will include 16 Japanese women athletes (preferably a team sport). Participants will be randomized into groups that received balenine containing capsules and the control group received cornstarch capsules. Balenine group will take 80 mg balenine three times a day. The groups will take each capsule for 4 to 12 weeks. Morphological and physical fitness measurements physiological analysis and emotional profile testing (POMS) were performed before intake 4 weeks after intake 8 weeks after intake and 12 weeks after intake. The male athletes will be recruited for sex differences. The uniqueness of such a study is the fact that balenine exists naturally in specific types of meat that people can consume even in daily life. If the results are positive as we hypothesize there is promising evidence that athletes could benefit without incurring additional expenses for off-the-shelf supplements which are often unaffordable. Moreover there have been some concerns associated with the safety of commercial supplements (LaMotte 2025) [18] or unhealthy additives such as excess sugar etc. This can raise an important question: should we just reconsider our lifestyle and eating habits obtaining functional foods directly from natural food sources rather than relying on processed supplements? The idea of food and supplement as one can bring health through nutritious and safe dietary sources to athletes. Balenine can be considered one such functional food obtained from whale meat extract (Wada *et al*. 2016; Shibato *et al*. 2024; https://www.shioda.co.jp/) [24, 31]. among other animal sources or through incorporating whale meat (or its extract) in the regular diet.

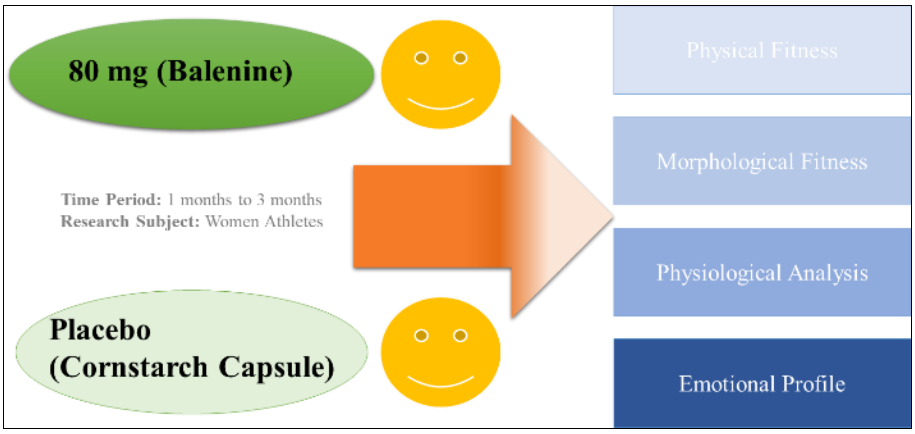

Fig 2: A Proposed Experiment for Investigating the Effect of Balenine of Athlete Performance. A case of women's athletes.

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