Drugs on the edge of performance enhancement

Abstract The official laboratories responsible for detecting cases of sports doping must know very precisely the list of prohibited products (PEDs, performance-enhancing drugs, performance enhancing products) as defined and updated each year by the World Anti-Doping Agency (WADA) in order to be able to develop specific and targeted methods. These efficient modern methods are used to detect minute quantities of drugs on the list, at picogram levels and sometimes even lower. Nowadays it is very likely that any banned substance on the list will be detected. This becomes more complicated when we consider the "WADA Prohibited List" to include related substances in many chemical categories, making the list undefined and nearly infinite in scope. The plurality of wording and "catch-all" notes in many categories such as "including, but not limited to", or "and other substances having a similar chemical structure or similar biological effect(s)", can expand the scope to include any substances related to those on the list. If an unlisted substance has a similar chemical structure to a banned substance on the list, it may be identified during targeted testing and declared to be a doping agent. This has happened twice so far: for example, for 1,3-dimethylamylamine (DMAA), detected and banned due to its similarity to tuaminoheptane, similarly for N,α-diethylphenylethylamine (N,α-DEPEA), due to similarity to methamphetamine. DMAA and N,α-DEPEA are popular illegal pre-workout supplement ingredients. However, if a substance has a similar biological effect that may provide similar performance enhancement to related substances on the WADA Prohibited List, it may escape detection by targeted testing. This therefore requires that such substances be identified first so targeted methods can be created, or detected using non-targeted methods. Several categories of substances on the WADA Prohibited List include only a few medications. Related substances that fit in these categories are likely to be abused as alternative doping agents that are not yet targeted in testing. Among these categories, nootropics and anti-ischemic and antihypoxant drugs that act as metabolic modulators are likely to improve performance and evade current targeted testing. These drugs are on the edge of performance enhancement today.

Keywords **Nootropics, anti-ischemic, antihypoxants, performance enhancement, cognitive health.**

Résumé **Des produits, voire des drogues, pour augmenter les performances**

Les laboratoires officiels chargés de détecter les cas de dopage sportif doivent connaître très précisément la liste des substances interdites (médicaments améliorant la performance, produits améliorant la performance) telle que définie et mise à jour chaque année par l'Agence mondiale antidopage (AMA) afin de pouvoir développer des méthodes spécifiques et ciblées. Ces méthodes modernes et efficaces sont utilisées pour détecter des quantités infimes de drogues figurant sur cette liste, à l'échelle du picogramme et parfois même à des niveaux inférieurs. De nos jours, il est très probable que toute substance interdite figurant sur la liste soit détectée. Cela devient plus compliqué lorsque l'on considère que la liste des interdictions de l'AMA inclut des substances apparentées dans de nombreuses catégories chimiques, ce qui rend la liste infinie. La pluralité de formulations et de notes « fourre-tout » dans de nombreuses catégories telles que « y compris, mais sans s'y limiter », ou « et d'autres substances ayant une structure chimique similaire ou un (ou des) effet(s) biologique(s) similaire(s) », peut élargir le champ d'application pour inclure toutes les substances liées à celles figurant sur la liste. Si une substance non répertoriée a une structure chimique similaire à une substance interdite figurant sur la liste, elle peut être identifiée lors de tests ciblés et déclarée comme agent dopant. Cela s'est produit deux fois jusqu'à présent : par exemple, pour la 1,3-diméthylamylamine (DMAA), détectée et interdite en raison de sa similitude avec le tuaminoheptane, de même pour la N,α-diéthylphénylethylamine (N,α-DEPEA), en raison de sa similitude avec la méthamphétamine. La DMAA et la N,α-DEPEA sont des ingrédients de suppléments pré-entraînement illégaux et populaires. Toutefois, si une substance a un effet biologique similaire susceptible d'améliorer les performances de manière similaire à celle des substances apparentées figurant sur la Liste des interdictions de l'AMA, elle peut échapper à la détection par des tests ciblés. Cela nécessite donc que ces substances soient d'abord identifiées afin que des méthodes ciblées puissent être créées ou détectées à l'aide de méthodes non ciblées. Plusieurs catégories de substances figurant sur la Liste des interdictions de l'AMA ne comprennent que quelques médicaments. Les substances apparentées entrant dans ces catégories sont susceptibles d'être utilisées de manière abusive comme agents dopants alternatifs qui ne sont pas encore ciblés par les tests. Parmi ces catégories, les nootropes et les médicaments anti-ischémiques et antihypoxants, qui agissent comme modulateurs métaboliques, sont susceptibles d'améliorer les performances et d'échapper aux tests ciblés actuels. Ces médicaments sont aujourd'hui à la pointe de l'amélioration des performances.

Mots-clés **Nootropes, anti-ischémiques, antihypoxants, amélioration des performances, santé cognitive.**

Nootropics

In 1998 fonturacetam, also known as carphedon or phenylpiracetam, became the first nootropic banned in Olympic sport by the International Olympic Committee (IOC). Developed in 1983 in Russia to improve the performance of cosmonauts in harsh environments, phenylpiracetam is a prescription drug registered in Russia under trade name Phenotropil. In the last 25 years no other nootropics have been added to the WADA Prohibited List. Nootropics are loosely

categorized as brain health or cognitive enhancement agents but they can have a variety of impacts including antihypoxant or actoprotective effects. Brain health supplements have grown into an $8 billion industry as of 2022. Unauthorized ingredients or unapproved pharmaceuticals in the US or EU, including phenylpiracetam, have been sold around the world as nootropic dietary supplements or in an apparently unregulated category of products sold under the guise they are "*Not for human consumption*" or are "*For research use only*". These are products often packaged like dietary supplements or food supplements but not labelled as such theoretically putting them out of reach of regulators. They also come without use guidelines or instructions so any potential consumers become guinea pigs and must do their own research to determine appropriate use. Combining nootropics with antihypoxants could significantly enhance the final pharmacological effects especially in terms of reduction of fatigue, improvement of brain and muscle oxygenation, better concentration or focus or other parameters important to sport performance. It is important to realize that while some of the substances discussed here may have acceptable safety profiles on their own at doses designed for use as single ingredient medicines, safety profiles have not necessarily been explored at higher doses or in combination with other ingredients and this should be considered from a public health perspective. Furthermore, while nootropics may provide clinical benefits to individuals in a disease state they may provide enhancement instead to healthy individuals [1].

Many nootropics such as phenibut, racetams and picamilon are derivatives of γ-aminobutyric acid (GABA). Other compounds such as pyritinol or pirisudanol are derivatives of vitamin B6. Explored here is a brief review of some of the available literature on how nootropics impact exercise capacity, physical condition, muscle strength or other skills important in specific sports (such as visual function, precision, decision making, motivation for competition). Of note, fonturacetam and omberacetam, more commonly known as noopept, were developed to enhance performance and workload capacity of cosmonauts in conditions of stress, anxiety, extreme temperatures, or reduced oxygen. These protective effects sometimes result in these compounds being described as synthetic adaptogens or actoprotectors, which are synthetic agents that do not increase oxygen consumption but do increase physical work capacity. Whereas, nootropics are designed to primarily enhance mental capacity but may also have impacts on physical capacity [1].

In the majority of sports mental acuity, attention, focus, and movement precision combined with relevant strength plays a key role. Supporting cognitive performance may correlate with enhanced cerebral processes that can benefit focus, memory, motivation, attention, recognition or even physical resiliency. These factors can significantly impact overall performance. As an example, one competition that requires intense concentration, attention and focus is chess. The International Olympic Committee (IOC) recognized chess as sport discipline in 1999. Chess players competing in a major tournament, such as the World Cup of Chess, can burn up to 6000 calories per day as a result of extreme mental effort, decision making, strategy planning, forecasting, and the stress and emotions associated with the game [2]. Mental performance is not just vital in chess, but in all sports, and a small advantage in the mind just might be the advantage the body needs to perform at its best. Here is a look at some of the most prominent nootropics and potential impacts on sport performance.

Piracetam, phenypiracetam and other racetams

Piracetam (2-oxo-1-pyrrolidinoacetamide) is a pyrrolidone derivative of GABA and part of a larger class of drugs called racetams that share a pyrrolidone nucleus. Piracetam improves blood supply and oxygenation of the brain. Fonturacetam, also known as carphedon or 4-phenylpiracetam, is a derivative of piracetam used as stimulant and actoprotector agent. Previously 100 mg dose was shown to support exercise performance [1,3]. The phenyl substituent in R3 position increases lipophilicity of the molecule and enhances penetration of the blood–brain barrier (BBB) and final nootropic effect [4]. A large amount of an unknown substance later identified as fonturacetam was found in the urine of a skater in 1997 [1]. Carphedon was also detected in 16 samples during doping control of athletes at the Athletics World Championships in Athens in 1997 [5]. In 1998 fonturacetam (under the name carphedon) became the first nootropic prohibited in elite sport in the IOC Medical code prohibited classes of substances and prohibited methods and it remains on the WADA Prohibited List as a stimulant, a category where the catchall language is relevant. There are a number of other racetams considered to be nootropics that demonstrate similar biological effects as piracetam or phenylpiracetam including aniracetam, oxiracetam, pramiracetam and omberacetam (noopept) [1]. In the Netherlands the "Risky Ingredient List" from 2017 prepared by the Doping Authority included carphedon and other related racetams such as piracetam, aniracetam and noopept.

In addition to piracetam, other racetams are registered drugs in selected countries. Aniracetam in 750 mg or 1500 mg dose is registered in Italy (*Ampamet*), Greece (*Memodrin*, *Referan*) and by Pfizer in Argentina (*Pergamid*). Pramiracetam in 600 mg dose (*Amacetam*, *Ectapram*, *Pramistar*, *Neupramir* and *Remen*) is registered in Italy. Oxiracetam is registered in Italy and Portugal under trade names such as *Neuractiv*, *Neuromet*, *Senex*. Nefiracetam (*Translon*) is only registered in Japan. Fasoracetam and coluracetam are still not registered are remain investigational drugs. These racetams are available around the world on various internet sites. The figure demonstrates some structure-activity relationships among racetams (*figure 1*) [4].

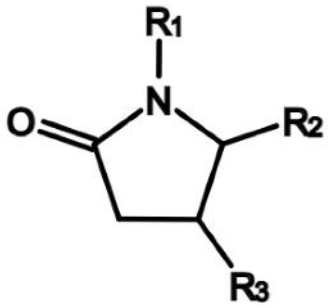
Omberacetam (Noopept)

Omberacetam also known as noopept (N-phenylacetyl-L-prolylglycine ethyl ester) is an example of a racetam with a more complex chemical structure. It has become one of the most popular nootropics today, registering as #29 on Amazon best sellers in analytical reagents October 13, 2023 and on the label of 28 supplement products on the US National Institute of Health (NIH) Dietary Supplement Label Database. A study conducted on young healthy subjects demonstrated that noopept contributes to fast adaptation to difficult environmental conditions and in hot climate it also improved physical capacity [6]. Another study suggested noopept is 200-50000 times more potent than piracetam as a nootropic agent based on comparison of effective dose for both compounds [7].

Phenibut

Phenibut (4-amino-3-phenylbutyric acid, phenyl-GABA) is a synthetic derivative of γ-aminobutyric acid (GABA). GABA is metabolized to succinic semialdehyde by the enzyme GABA transaminase (GABAT) then succinic semialdehyde dehydrogenase (SSADH) transforms succinic semialdehyde to

A)



B)

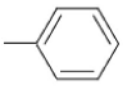
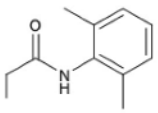
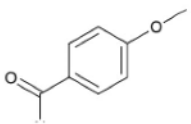
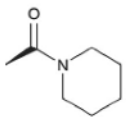
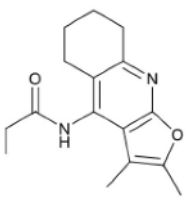
Compound	R1	R2	R3	Half-life (hours)	Single or daily dose (registered or used in clinical trials)	Pharmacological profile	
Piracetam		–H	–H	4-5	400-1200	Unclear receptors and neurotransmitters affinity	Strong nootropic Lower anticonvulsant component
Phenylpiracetam		–H		3-5	100-200	Cholinergic; affinity to nicotinic acetylcholine (nACh) receptors	Strong nootropic Lower anticonvulsant component
Oxiracetam		–H	–OH	3-6	25-40 mg/kg/d	Positive allosteric modulator of AMPA receptors (ampakine effect)	Strong nootropic
Nefiracetam		–H	–H	3-5	600-900	Cholinergic receptors NMDA receptors	Strong nootropic and anticonvulsant
Aniracetam		–H	–H	0.5-1	750-1500	Cholinergic Positive allosteric modulator of AMPA receptors (ampakine effect)	Nootropic
Fasoracetam	–H		–H	4-6.5	100 mg	Metabotropic glutamate receptor (mGluR) GABA-B receptors	Nootropic
Coluracetam		–H	–H	1-2	1-10 mg/kg/d	Cholinergic NMDA receptors	Nootropic

Figure 1 - A) General structure of racetams and substituents ; B) Structure-activity relationships for selected racetams.

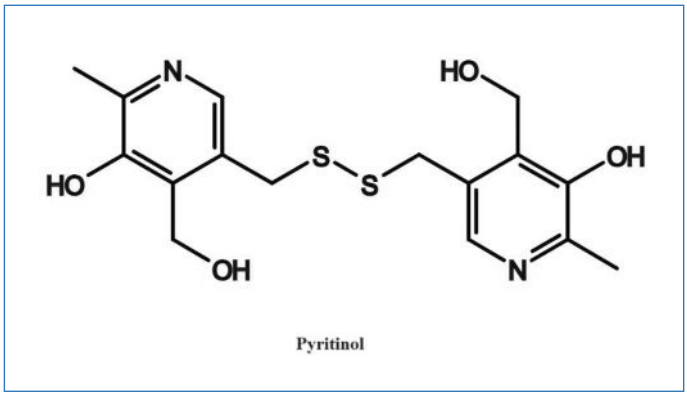


Figure 2 - Chemical structure of pyritinol.

succinic acid. Succinic acid is a key component in the Krebs energy cycle and thus human metabolism. Phenibut is registered as a psychotropic drug under various trade names including *Anvifen*, *Bifren*, *Citrocard*, and *Noofen* in several countries including Russia, Latvia and Ukraine. It has not been approved as a drug by the US FDA or in the European Union (EU). Most of the research on phenibut has been conducted in Russia [1]. Experiments with rats showed that phenibut combined with succinic acid improved exercise performance. Human performance studies on phenibut have mostly been done with other nootropic or actoprotective substances. One study demonstrated that acute intake of phenibut with bemitil, a primary member of the actoprotector category, enhanced thermal resistance in humans during physical load [8]. Another study also showed thermal resistance with a combination of phenibut, piracetam, and obsidian [9].

Picamilon

Picamilon (pikatropin) is a N-nicotinoyl-GABA derivative that is a prescription Russian drug indicated for various neurological conditions typically available in 50 mg tablets. Picamilon has also been sold as a dietary supplement in western countries including the US and EU. It is often found as a powder in multi-ingredient pre-workout or nootropic supplements or capsules with up to six times the prescription dose up to 300 mg. The US FDA has clarified picamilon is an illegal dietary supplement ingredient but it is still found in 133 supplements on the market in the NIH Dietary Supplement Label Database. After oral administration, picamilon rapidly crosses the blood–brain barrier then is hydrolysed into nicotinic acid and GABA. The final result is improving blood flow and circulation and increasing the supply of oxygen and nutrients to the brain [1].

Pyritinol

Pyritinol is a synthetic derivative of vitamin B6 created in the early 1960s. The chemical structure of pyritinol include two molecules of vitamin B6 conjugated by a disulfide bridge (*figure 2*). This drug improves glucose metabolism and blood circulation in ischemic areas of the brain and increases oxygen supply. Pyritinol under trade name such as *Encephabol* (Merck) or *Enerbol* (Polfa) is indicated for treatment of cerebral atherosclerosis, impaired memory in the course of dementia, psychosomatic exhaustion. Pyritinol is available in the form of tablets (100 mg and 200 mg) and as a liquid/suspension in dose 80 mg/5 mL. Pyritinol demonstrates high bioavailability approximate 85% and is rapidly absorbed after oral administration with half-life estimated on the range 2.5 hours. A study with a small number of healthy volunteers (n = 12) investigated the effect of three days administration of pyritinol at 600 mg daily or 1200 mg daily on psychomotor functions. Performance improved significantly in selected psychomotor parameters such as in Critical Flicker Fusion Test (CFFT) and Choice Reaction Time (CRT) [10].

Pirisudanol

Pirisudanol also known as pyrisuccideanol (trade names *Mentium*, *Mentis*, *Nadex*, *Stivane*), presents an interesting chemical structure as a succinate double ester of pyridoxine (vitamin B6) and dimethylaminoethanol (DMAE), another nootropic. In a group of 10 adult volunteers the effects of amphetamine, a stimulant on the WADA Prohibited List, and pirisudanol were compared on motor reactions (H-reflex test) and psychometric attention tests. Results showed pirisudanol increased motor reactions and attention in performed tests to optimal level while amphetamine decreased performance in both aforementioned tests [11].

Xanthinol nicotinate

Xanthinol nicotinate is a derivative of theophylline and nicotinic acid (vitamin B3). Xanthinol nicotinate is a vasodilator that improves cerebral and peripheral blood circulation and supports tissue oxygenation and nutrition of brain and limbs. Mechanism of pharmacological activity is by blocking the adenosine receptors (AR) and enzyme phosphodiesterase (PDE) which increases the concentration of adenosine monophosphate (AMP) in the cells and increases oxidative phosphorylation and adenosine triphosphate (ATP) synthesis. There is also an antiplatelet effect through activation of fibrinolysis. Xanthinol nicotinate is available in the form of tablets (150-500 mg) or injections (150 mg/mL) under trade names *Complamin* (in Germany) or *Sadamin* (in Poland). Xanthinol nicotinate as *Complamin* was discussed during the "IOC World Conference on Doping in Sport" in Lausanne 1999, as one of the examples of borderline substances but no further action was taken.

Naftidrofuryl

Naftidrofuryl (*figure 3*) is a complex derivative of diethylaminoethanol (DEAE) available under many alternative trade names such as *Artocoron*, *Dusodril*, *Praxilene*, *Gevatran*, *Iridus*, *Sodipryl* or *Vascuprax*. It had been used in pharmacotherapy for treatment of cerebral disorders caused by vascular insufficiency. Naftidrofuryl enhances tissue oxidative metabolism by activation of succinic dehydrogenase (SDH), a Krebs cycle enzyme involved in energy production and metabolism.

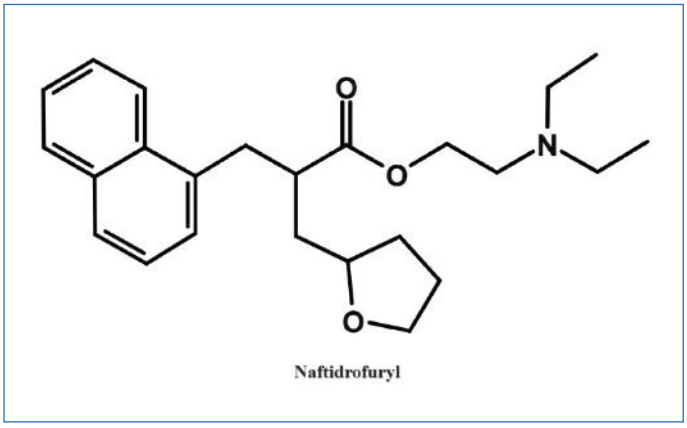


Figure 3 - Chemical structure of naftidrofuryl.

One study investigated the influence of acute oral administration of 300 mg/day naftidrofuryl on five healthy male volunteers 20-40 min before exercise on a bicycle ergometer. Naftidrofuryl contributed to a reduction in the lactate/pyruvate ratio in the volunteers during exercise. This finding suggests naftidrofuryl increases the efficiency of aerobic metabolism in oxygen-deprived tissues during physical load [12]. It should be noted that naftidrofuryl is banned in equine sport by the Fédération équestre internationale (FEI) but it is not banned by WADA in human sport. In the investigation of a doping case involving Dutch cyclists it was reported that a retired cyclist turned race director for a prominent cycling team had naftidrofuryl in his urine sample. It is unclear if it enhances performance but naftidrofuryl appears to have been used to at least aid performance.

Anti-ischemic and antihypoxant drugs

While steroids and stimulants are some of the best known PEDs, more obscure categories like metabolic modulators have been in the spotlight more recently. The anti-ischemic antihypoxant heart medications meldonium (*Mildronate*) and trimetazidine (*Vastarel*) have both become high profile infamous doping agents. The 2022 Winter Olympic Games were jolted when it was reported Russian skater Kamila Valieva returned a positive drug test the previous December for trimetazidine an anti-ischemic antihypoxant antianginal heart medication. She also admitted to using hypoxen (polyhydroxyphenylene thiosulfonate sodium), another antihypoxant drug not yet banned in sport that is advertised to support physical activity. Previously meldonium, another anti-ischemic drug, was added to the Prohibited List in 2016 and became the number one reported substance by WADA that year with 515 adverse analytical findings. It is clear anti-ischemic antihypoxant substances are being sought after and used yet meldonium and trimetazidine are the only two on the WADA Prohibited List in category S4.4 "metabolic modulators". It stands to reason athletes looking to dope would look for related substances. When meldonium was added to the WADA Prohibited List Russian sport officials said they already had alternatives that worked better than meldonium. Succinic acid derivatives such as *Mexidol* and *Cytoflavin* demonstrate antihypoxic, anti-ischemic, reoxygenation effects similar to meldonium and trimetazidine and are used in similar clinical circumstances including for treatment of ischemic stroke or mitochondrial dysfunction. These antihypoxant, anti-ischemic drugs developed in Eastern Europe are not yet prohibited and may be used as ergogenic aids today [13,14].

Mexidol

Mexidol (emoxypine succinate or 2-ethyl-6-methyl-3-hydroxypyridine succinate) is a synthetic 3-hydroxypyridine derivative of vitamin B6 that is registered as a medicine in Russia and Ukraine. It was developed at the Institute of Pharmacology, Russian Academy of Medical Sciences, in the early 1980s and has been in clinical use since 2003 as a treatment for ischemia. It can be found online on sites that cater to Russian medicines as a suggested alternative to meldonium. Emoxypine succinate is available under various trade names including *Mexidol*, *Mexiprim*, *Mexibel*, *Mexidant*, *Mexifin*, *Neurox* in Russia, and *Armadin Long*, *Limontar*, *Nicomex* and *Elfunat* in Ukraine. A review of the available administration studies done on healthy subjects suggests there is a potential for performance enhancement. One example with *Mexidol* used at a high dose (200 mg/kg/day) demonstrated an increase in strength among young male athletes aged 19-22 with improvement in deadlift and bench press performance [15]. A study done with a lower dose of 1800 mg/day of *Armadin Long* showed improved performance in strength tests like military press or the jerk used in Olympic style Weightlifting as well as a decrease in time to perform workouts and in lactate acid concentration [16].

Other anti-ischemic antihypoxant 3-hydroxypyridine derivatives are being developed and explored. The effects of emoxypine L-aspartate were found to be equal to or greater than those of bemitil and bromantane, which are considered to be the primary representatives of the actoprotector category [17]. Bemitil is not on the WADA Prohibited List but it has been included in the WADA monitoring program. Bromantane is on the WADA Prohibited List as a stimulant.

Actoprotectors are not often considered in western pharmacology. Actoprotectors are described as synthetic adaptogens that increase work capacity without increasing oxygen consumption or heat production. Adaptogens are generally considered to be natural or synthetic substances that help the body manage biological stress. Actoprotectors and psychostimulants, like amphetamine that are prohibited by WADA as stimulants, improve physical resiliency but actoprotectors do so in non-exhaustive fashion without producing heat and with distinct pharmacological action. Actoprotectors can have antihypoxic activity but they differ in that they also directly stimulate protein synthesis and working capacity. The performance enhancing potential and biological effects of antihypoxant anti-ischemic substances like *Mexidol* may be compared not only to metabolic modulators like trimetazidine or meldonium but also potentially to psychostimulants that are banned in sport [13].

Cytoflavin

Cytoflavin is a registered drug in Russia available in formulation as tablets or injections. *Cytoflavin* is a multi-component drug including meglumine sodium succinate, nicotinamide (vitamin B3), inosine (riboxin) and riboflavin (vitamin B2). A study among 60 volleyball players aged 18-35 demonstrated that intake of 4 tablets of *Cytoflavin* per day (providing 1200 mg meglumine sodium succinate, 200 mg inosine, 100 mg nicotinamide, 20 mg riboflavin) contributed to improvements in memory and attention on the Visual Analog Scale (VAS) test. Additionally there was an increased level of subjective satisfaction with physical and mental performance [18]. In another publication administration of *Cytoflavin* to 60 ice hockey players registered a slight improvement in time to exhaustion (TTE) and also an increase in maximal oxygen consumption (VO_2 Max) on a treadmill ergometer [19].

The edge of perfomance enhancement

The nootropic and anti-ischemic antihypoxant substances reviewed here appear to have similar biological effects as substances on the WADA Prohibited List and are likely to be sought after as alternative doping agents. While research studies may be limited in scope and scale, they do seem to support the use of these substances as potential ergogenic aids albeit in non-traditional ways like cognitive enhancement or improved oxygenation. Message boards show that these

substances are being used to enhance sports performance. Many have been developed as drugs and are available as such in Eastern Europe while in Western countries they are often made available as illegal dietary supplement ingredients or chemicals clearly meant for human consumption but sold for research purposes only. Substances like the pharmaceutical nootropics or anti-ischemic antihypoxant agents explored here deserve further attention and debate in the effort to maintain clean sport. They are also worthy of discussion from the larger public safety and health perspective as these substances are sold for the purposes of brain health, enhancing cognition, stress reduction, managing anxiety, and more. As such they are attractive not only as potential doping agents for athletes looking for a chemical advantage but also to general consumers looking to boost their daily lives and performance. While some of these substances may demonstrate reasonable safety profiles at lower doses studied and intended for medical use they may not have been tested and may not be safe at higher doses or when used in combinations with potentially synergistic ingredients as seen in some dietary supplements. As we watch the glory of the 2024 Paris Olympics unfold some may wonder what substances athletes might be using to achieve peak performance. The ones highlighted here remain legal to use as ergogenic aids but appear to be teetering on the edge of performance enhancement.

[1] K. Jędrejko *et al.*, Unauthorized ingredients in "nootropic" dietary supplements: a review of the history, pharmacology, prevalence, international regulations, and potential as doping agents, *Drug Test. Anal.*, **2023**, *15(8)*, p. 803-839.
[2] S. Golf, Doping for chess performance, *J. Sports Med. Doping Stud.*, **2015**, *5*, p. 160.
[3] V.A. Semenov, S.L. Bolotov, V.F. Sizoi, New stimulant of russia-carphedon. recent advances in doping analysis, *Sport und Buch Strauß*, **1999**, p. 337-348.
[4] A.G. Malykh, M.R. Sadaie, Piracetam and piracetam-like drugs, *Drugs*, **2010**, *70*, p. 287-312.
[5] C.G. Georgakopoulos *et al.*, Doping control analysis: the 6th World Championships of Athletics, Athens, Greece, *TrAC Trends in Analytical Chemistry*, **1999**, *18*, p. 1-13.
[6] P.D.Shabanov, V.P. Ganapol'skiĭ, P.V. Aleksandrov, Meteoadaptogenic properties of peptide drugs in healthy volunteers, *Eksp. Klin. Farm.*, **2007**, *70*, p. 41-47.
[7] R.U. Ostrovskaia *et al.*, The original novel nootropic and neuroprotective agent noopept, *Eksp. Klin. Farm.*, **2002**, *65*, p. 66-72.
[8] V.I. Makarov *et al.*, The enhancement of human thermal resistance by the single use of bemitil and fenibut, *Eksp. Klin. Farm.*, **1997**, *60*, p. 68-71.
[9] V.S. Baculin, V.I. Makarov, Thermoprotective efficiency of piracetam, phenibut and obsidan during submaxmal physical loads in conditions of reduced heat loss, *J. Volg. St.e Medic. Un.*, **2011**, *8*, p.23-26.
[10] I. Hindmarch, D.M. Coleston, J.S. Kerr, Psychopharmacological effects of pyritinol in normal volunteers, *Neuropsychobiology*, **1990**, *24*, p. 159-164.
[11] N.Bathien, J.C.Willer, A. Hugelin, Effect of psychotropic drugs on physiological variations and psychometric scores during attention, *Encephale*, **1976**, *2*, p. 55-60.
[12] S.W.J. Shaw, R.H. Johnson, The effect of naftidrofuryl on the metabolic response to exercise in man, *Acta. Neuro.l Scand.*, **1975**, *52*, p. 231-237.
[13] S. Oliynyk, S. Oh, The pharmacology of actoprotectors: practical application for improvement of mental and physical performance, *Biomol. Ther.*, **2012**, *20*, p. 446.
[14] V.E. Novikov, O.S. Levchenkova, E.N. Ivantsova, V.V. Vorobieva, Mitochondrial dysfunctions and antihypoxants, *Обзоры*, **2019**, *17*, p. 30-41.
[15] Н.А. Фудин, А.А. Хадарцев, А.А. Несмеянов, Возможности Активации Митохондриальной Активности у Спортсменов Мексидолом, *Вестник новых медицинских*, **2015**, *9*, p. 12.
[16] V.L. Voitenko, L.M. Gunina, V.G. Oleshko, E.V. Nosach, Assessing action mechanisms of pharmacological agent based on succinic acid derivative under physical loads of submaximal intensity, *World Med. Biol.*, **2018**, *14*, p. 28-32.
[17] V.V. Yasnetsov *et al.*, Studying some pharmacological effects of new 3-hydroxypyridine derivative, *Eksp. Klin. Farm.*, **2016**, *79*, p. 3-8.
[18] P.N. Chainikov *et al.*, Clinical effectiveness of cytoflavin in the correction of cognitive functions for mental and physical working capacity in male floor volleyball players, *Eksp. Klin. Farm.*, **2018**, *81*, 25-29.
[19] V. Zaborova *et al.*, Metabolic and body composition changes in ice hockey players using an ergogenic drug (cytoflavin), *Biology*, **2023**, *12*, p. 214.

Oliver CATLIN[1]*, president, and **Karol JĘDREJKO**[2], researcher.

[1]Anti-Doping Sciences Institute & Banned Substances Control Group (BSCG), Los Angeles, États-Unis.
[2]Jagiellonian University Medical College, Faculty of Pharmacy, Department of pharmaceutical botany, Krakovie, Pologne.

* ocatlin@bscg.org