GEORGIAN MEDICAL NEWS

ISSN 1512-0112

NO 4 (361) Апрель 2025

ТБИЛИСИ - NEW YORK

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press. Published since 1994. Distributed in NIS, EU and USA.

GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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Содержание:

GEORGIAN MEDICAL NEWS
No 4 (361) 2025

BIOTECHNOLOGICALLY PRODUCED NEUROSTIMULANTS MAY CONTRIBUTE TO PROLONGED IMPROVEMENTS IN MOTOR PERFORMANCE: A NARRATIVE REVIEW

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Abstract.

The search for effective agents to enhance motor performance and accelerate neurorehabilitation has increasingly focused on neurostimulants—compounds that enhance neural excitability, synaptic transmission, and plasticity. This chapter explores the promising role of biotechnologically produced neurostimulants, particularly bacterial melanin synthesized in Armenia, in supporting functional recovery and sustained improvements in motor output. Unlike traditional pharmacological neurostimulants such as modafinil, amantadine, or methylphenidate, which primarily target monoaminergic systems, bacterial melanin demonstrates neuroprotective, neuroregenerative, and electrophysiologically stimulating properties across various CNS regions, including the substantia nigra. Emerging experimental data indicate that bacterial melanin increases spontaneous and evoked neuronal activity, potentiates dopaminergic transmission, and supports axonal integrity post-injury—features that align with modern neurorehabilitation goals. This chapter critically examines the physiological basis and translational potential of such novel neurostimulants by integrating findings from optogenetic stimulation, pharmacological trials, and neurobehavioral rehabilitation paradigms. The convergence of microbial biotechnology and neurostimulant pharmacology may redefine clinical approaches to motor dysfunction and neuroplastic recovery following central nervous system injury.

Key words. Biotechnological neurostimulants, neurorehabilitation, athletic performance, cortical excitability, motor recovery, melanin, optogenetic stimulation.

Introduction.

Biotechnological Neurostimulants: Concept and Mechanisms of Action

Biotechnologically produced neurostimulants represent an emerging frontier in neuroscience and performance science, offering unprecedented opportunities to enhance motor performance in both clinical and athletic populations [1]. These compounds, developed through microbial synthesis, genetic engineering, or molecular biotechnology, target specific neural pathways to modulate activity in the central and peripheral nervous systems. Unlike traditional stimulants such as caffeine or amphetamines that act broadly and often non-selectively, biotechnologically produced neurostimulants can be designed to exert precise effects on neurotransmission. In the context of motor performance, this precision allows for the development of interventions that support sustained improvements in coordination, strength, reaction time, endurance, and motor learning [2].

The concept of enhancing motor function through neurochemical modulation is not new; however, the application of synthetic biologics and biotechnological processes marks a qualitative shift in how these enhancements can be achieved.

Bacterial Melanin and Recombinant Neurotrophic Factors: Natural and Engineered Biologics

One of the most promising examples of such a compound is bacterial melanin, a pigment produced by specific strains of Bacillus thuringiensis in Armenia [3-6]. Research by Petrosyan T.R. and colleagues has demonstrated that bacterial melanin possesses significant neuroprotective and neurostimulatory properties [7-10]. In animal studies, the administration of bacterial melanin has been shown to increase electrical activity in dopaminergic neurons of the substantia nigra, improve sensorimotor cortex excitability, and accelerate functional recovery following peripheral nerve injuries [11,12]. These effects are thought to be mediated by melanin's influence on ion channels, oxidative stress regulation, and synaptic transmission. Importantly, bacterial melanin has been shown to cross the blood–brain barrier via a saturable transport mechanism, enabling its systemic administration with central nervous system effects [13,14].

Another class of biotechnologically produced neurostimulants includes recombinant neurotrophic factors such as brain-derived neurotrophic factor (BDNF) [15], glial cell line-derived neurotrophic factor (GDNF) [16], and nerve growth factor (NGF) [17], which have been engineered for controlled delivery in neurorehabilitation and performance settings. These factors enhance neuroplasticity, support the growth and survival of motor neurons, and facilitate synaptic restructuring. Advances in gene editing tools like CRISPR-Cas9 have enabled the insertion of BDNF-coding sequences into viral vectors, allowing for the localized and sustained expression of BDNF in motor areas of the brain or spinal cord [18]. Studies in animal models of stroke and spinal cord injury have shown that such interventions lead to improved locomotion, faster motor recovery, and greater endurance, highlighting their potential for use in athletic populations seeking to maximize training effects and recover from neuromuscular injuries [19].

Synthetic Compounds, Optogenetics, and Nanotechnological Delivery.

In addition to protein-based neurostimulants, synthetic peptides and small molecules engineered through combinatorial chemistry and computational design have shown promise in enhancing motor performance. For instance, ampakines are a class of synthetic compounds that positively modulate AMPA receptors, thereby increasing synaptic transmission and excitability in cortical and subcortical motor areas [20]. By enhancing glutamatergic activity, ampakines can potentiate motor learning, reaction speed, and cognitive-motor integration. CX717, one of the best-characterized ampakines, has been

shown to enhance performance in sustained attention and physical endurance tasks in both animal and human trials [21].

Another example includes synthetic derivatives of ergothioneine and carnosine, amino acid-based neuroprotectants with mitochondrial stabilizing and antioxidant properties [22]. These compounds, produced through engineered yeast or bacterial systems, have been studied for their ability to reduce neuromuscular fatigue and improve metabolic efficiency during sustained physical exertion. While their effects may be more supportive than stimulatory, they contribute to a broader category of neuro-enhancing agents that help maintain optimal motor performance over time [23].

A particularly innovative area involves the use of optogenetically controlled biostimulants—compounds or constructs that can be activated by light to stimulate neurons with temporal precision [24]. These systems combine genetically encoded light-sensitive ion channels (e.g., channelrhodopsins) with tailored delivery mechanisms to target motor neurons or cortical networks. Though still in early-stage development, such approaches exemplify the integration of biotechnology and neuroengineering to create adaptive stimulatory environments for neuromotor control, with potential applications in neuroprosthetics, virtual training systems, and elite athletic performance monitoring.

Furthermore, nanotechnology-based delivery systems are increasingly being employed to enhance the bioavailability and targeting of biotechnologically produced neurostimulants. For instance, liposomal and polymer-based nanocarriers have been designed to deliver dopamine precursors, GABA analogs, or neurotrophic factors to specific brain regions with minimal systemic side effects. These nanoformulations are especially important for compounds like melanin or peptide-based stimulants that may otherwise have limited solubility or stability in circulation [25]. The development of such delivery systems increases the clinical and practical relevance of neurostimulants by improving dosing accuracy, reducing the risk of adverse effects, and enabling targeted modulation of motor circuits.

Mitochondrial Peptides, Ethical Considerations, and Future Directions.

It is also important to consider the role of mitochondrial-targeted peptides like SS-31 (Elamipretide), a synthetic tetrapeptide developed to enhance mitochondrial function and reduce oxidative damage in neurons and muscle cells [26]. Though not a traditional neurostimulant, SS-31 has demonstrated the ability to preserve neuronal excitability and synaptic function under metabolic stress, suggesting potential applications in maintaining motor performance during prolonged exertion or in age-related decline. These peptides are biotechnologically produced through solid-phase synthesis and may be formulated for injectable or transdermal use in high-performance settings.

Across these examples, the unifying theme is the intentional manipulation of neural substrates through precision biological engineering to achieve enhancements in motor output. This approach reflects a paradigm shift from external mechanical optimization (e.g., biomechanics and equipment) to internal physiological and neurological modulation.

However, the translation of these innovations into real-world athletic use requires careful evaluation. Ethical considerations concerning fairness, access, and long-term safety must be addressed, particularly as these agents approach regulatory boundaries set by governing bodies such as the World Anti-Doping Agency [27]. Moreover, the interindividual variability in response to neurostimulants necessitates personalized protocols to avoid adverse interactions or maladaptive plasticity.

In conclusion, biotechnologically produced neurostimulants encompass a diverse array of compounds—from bacterial melanin to synthetic neurotrophins and optogenetic modulators—that have the potential to support prolonged and optimized motor performance. These agents work through various mechanisms including enhancing neurotransmission, promoting neuroplasticity, supporting mitochondrial function, and accelerating neuroregeneration. The work of researchers like Petrosyan T.R. has demonstrated that compounds such as bacterial melanin can modulate central motor pathways and provide a foundation for translational applications in sports [28,29]. As the field continues to evolve, multidisciplinary collaboration among neuroscientists, biotechnologists, sports physiologists, and ethicists will be essential to harness the benefits of these novel neurostimulants while ensuring responsible and equitable application in human performance enhancement.

Experimental Evidence.

Pharmacodynamics and Neurophysiological Mechanisms of Bacterial Melanin:

Pharmacodynamics of biotechnologically produced neurostimulants introduces a compelling frontier in neurotherapeutics particularly when such agents are capable of traversing the blood-brain barrier and modulating neuronal activity in a durable manner. Among these agents bacterial melanin has emerged as a prominent candidate for its unique physicochemical and biological properties [30]. Synthesized through microbial fermentation bacterial melanin demonstrates bioaffinity toward neural tissues and possesses intrinsic abilities to interact with cellular membranes receptor systems and intracellular signaling pathways that influence neuronal excitability and plasticity. The central pharmacodynamic action of bacterial melanin lies in its capacity to accumulate within cortical neurons and modulate excitatory and inhibitory balances in favor of long-term facilitation. This is especially significant in conditions of neurodegeneration post-traumatic recovery and cognitive enhancement wherein sustained neuronal activation is essential for repair or performance augmentation [31].

Upon systemic administration bacterial melanin is hypothesized to cross the blood-brain barrier via active transport or transcytosis mechanisms potentially involving low-density lipoprotein receptor-related pathways or through nanoparticle-mediated delivery systems. Once within the central nervous system its preferential accumulation in cortical and subcortical neurons may relate to its negative charge and binding affinity for neuronal membrane components including ion channels and neurotransmitter receptors. This targeted deposition is believed to initiate a cascade of intracellular events including modulation

of calcium influx activation of second messenger systems such as cyclic AMP and protein kinase cascades and upregulation of immediate early genes associated with synaptic plasticity [32,33].

Moreover, bacterial melanin may act through indirect mechanisms such as altering glial cell function reducing oxidative stress and regulating the local microenvironment to favor neurotrophic support. It is well understood that long-term potentiation and sustained synaptic efficacy are critical for memory learning and motor skill consolidation [34]. Bacterial melanin as a neurostimulant may support these processes by enhancing the excitatory tone in cortical circuits particularly through the modulation of glutamatergic transmission. Experimental models suggest that bacterial melanin exposure leads to increased expression of NMDA and AMPA receptors on the postsynaptic membrane thereby facilitating synaptic current flow and amplifying the response to presynaptic input [35]. Furthermore, by promoting dendritic spine formation and stability bacterial melanin contributes to the structural basis for long-lasting changes in synaptic strength. This ability to sustain excitatory facilitation over extended periods without provoking excitotoxicity makes it an attractive candidate for neurorehabilitation and performance enhancement.

Therapeutic Implications and Neuroprotective Effects of Bacterial Melanin:

Another aspect of its pharmacodynamic profile is its putative anti-inflammatory and antioxidant action which reduces the likelihood of secondary damage in neural tissue and supports a more permissive environment for neuroplastic changes [36]. These properties are particularly relevant in the context of post-injury recovery where inflammation and oxidative stress hinder neuroregeneration. By mitigating these detrimental processes bacterial melanin enables a more sustained and functionally relevant activation of neural circuits [37]. Additionally bacterial melanin may influence neuromodulatory systems such as dopaminergic and serotonergic pathways thereby extending its impact beyond purely excitatory neurotransmission and contributing to motivation mood and cognitive flexibility.

Studies conducted in animal models have demonstrated enhanced motor performance and learning retention following systemic administration of bacterial melanin suggesting a robust and persistent activation of cortico-subcortical loops involved in motor planning and execution [38]. In translational terms this implies a potential application in stroke rehabilitation spinal cord injury and even age-related motor decline where reactivation of dormant circuits is a therapeutic goal. The safety profile of bacterial melanin also contributes to its pharmacodynamic attractiveness. Unlike synthetic neurostimulants that often lead to desensitization or downregulation of receptors bacterial melanin appears to exert a modulatory rather than overstimulating effect allowing for adaptive rather than maladaptive plasticity. This aspect is crucial for long-term interventions in chronic neurological conditions where sustainable modulation is preferred over short-lived stimulation.

The pharmacodynamic characteristics of bacterial melanin also align with principles of endogenous neuromodulation. Its action may mimic or amplify intrinsic processes of neural adaptation making it synergistic with behavioral therapies cognitive training and neuromotor rehabilitation [39]. Moreover, its bioavailability and tissue-specific effects can potentially be tuned through genetic engineering of its producing strains or through conjugation with targeting peptides enhancing its delivery precision and reducing systemic side effects. From a systems neuroscience perspective bacterial melanin could act as a network-level enhancer facilitating functional connectivity between regions involved in sensorimotor integration executive function and memory consolidation.

Functional imaging studies could further elucidate this by mapping the changes in cortical activation patterns and connectivity following its administration. Additionally electrophysiological recordings could provide insights into how neuronal firing rates and synchrony are affected which would clarify the temporal dynamics of its action. In sum the pharmacodynamics of biotechnologically produced neurostimulants such as bacterial melanin point to a paradigm shift in how we can influence brain function not just transiently but in a manner that promotes sustained enhancement recovery and adaptation. Studies have evaluated the safety of bacterial melanin through different methods. In acute and subchronic toxicity assessment rats were administered bacterial melanin at doses up to 5mg/kg body weight: In a 28-day feeding period, the animals showed no significant differences in growth, food and water consumption, hematology, blood biochemical indices, organ weights, or histopathological findings compared to control groups. In irritation and hypersensitivity assessment study, tests for primary eye and dermal irritation, as well as delayed contact hypersensitivity in rabbits and guinea pigs, respectively, indicated that BM did not cause adverse reactions, suggesting low potential for irritation or allergic responses [40]. The ability of such substances to cross the blood-brain barrier selectively accumulate in neurons and produce excitatory facilitation over time without deleterious consequences represents a convergence of biotechnology neuroscience and pharmacology that opens new horizons for both clinical and cognitive applications. Further research into dosage response timing and individual variability in absorption and response will be essential to translate these findings into scalable therapeutic or performance-enhancing strategies. The intersection of microbial biotechnology and neurotherapeutics thus holds vast potential with bacterial melanin as a promising proof-of-concept agent capable of inducing meaningful and lasting changes in brain function through safe and biologically attuned pharmacodynamic mechanisms (Figures 1 and 2).

Safety and Mechanisms of Biotechnological Neurostimulants in Athletic Performance:

The high safety profile and favorable tissue bioavailability of biotechnologically produced neurostimulants position them as promising candidates for athletic performance enhancement within a rapidly evolving field that bridges molecular neuroscience with applied human physiology. These agents, particularly those derived from microbial sources such as bacterial melanin, offer unique pharmacological advantages rooted in their capacity to cross the blood-brain barrier, target cortical and subcortical neural networks, and promote long-term

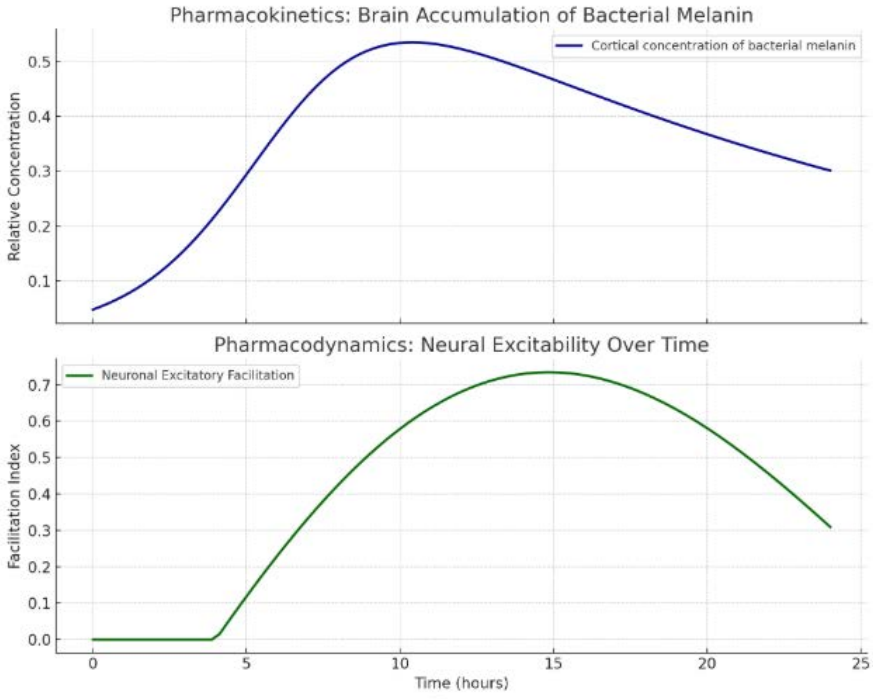

Figure 1. *Pharmacokinetics and pharmacodynamics of bacterial melanin.*
Blue Curve Shows the brain concentration of bacterial melanin after systemic administration. There's a steady increase, peaking around 6 hours post-administration, followed by a slow clearance phase. This suggests efficient crossing of the blood-brain barrier and sustained presence in cortical neurons. Green Curve represents the neuronal excitatory facilitation effect. Notice that the peak effect occurs slightly after the peak concentration, indicating a lag due to intracellular signaling and plasticity mechanisms. The prolonged tail reflects lasting facilitation without rapid desensitization.

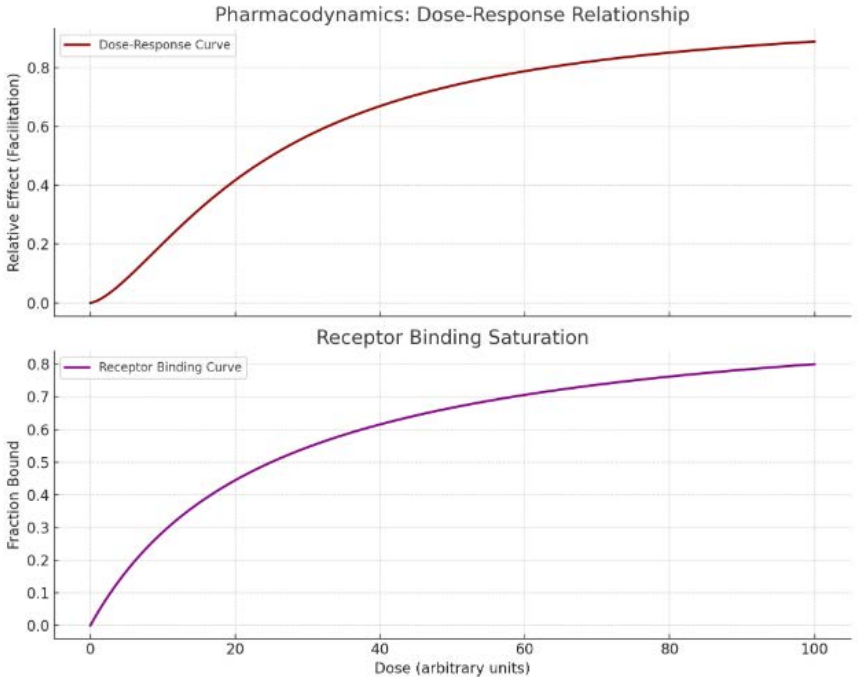

Figure 2. *Dose response relationship and receptor binding saturation of bacterial melanin.*
Pharmacokinetic and pharmacodynamic behavior of bacterial melanin. A steady post-administration increase of concentration, followed by a slow clearance phase. This suggests efficient crossing of the blood-brain barrier and sustained presence in cortical neurons. The peak effect occurs slightly after the peak concentration, indicating a lag due to intracellular signaling and plasticity mechanisms. The prolonged tail reflects lasting facilitation without rapid desensitization.

facilitation of excitatory neurotransmission without inducing neurotoxicity or receptor desensitization.

The ability of such compounds to accumulate selectively in neural tissues and modulate synaptic activity in a sustained and regulated manner has garnered interest not only in the realm of clinical neurorehabilitation but also in the context of sports science where enhancing neuromuscular coordination, cognitive endurance, and motor learning holds substantial value. Unlike conventional stimulants which exert short-acting effects via dopaminergic or adrenergic systems, often accompanied by rebound fatigue or adverse cardiovascular responses, biotechnologically engineered neurostimulants act through neuromodulatory processes that align more closely with endogenous mechanisms of plasticity and neural adaptation. This distinction is critical when considering applications in high-performance athletic settings where long-term safety, regulatory compliance, and enhancement of complex motor outputs are prioritized.

At the molecular level, these neurostimulants engage in modulation of intracellular calcium dynamics, second messenger cascades, and gene expression pathways that underlie the strengthening of synaptic connections, particularly within cortico-spinal and cortico-cerebellar circuits. Such mechanisms are essential for refining motor precision, reaction time, and adaptive control during dynamic and repetitive movement tasks which are hallmarks of elite athletic performance [41].

The capacity for bacterial melanin and similar agents to interact with glutamatergic transmission enhances their potential to influence long-term potentiation, a cellular correlate of learning and memory, which further underlines their relevance in the acquisition and consolidation of complex motor skills. This is particularly advantageous in sports that demand high levels of coordination, agility, and sensorimotor integration. Furthermore, the pharmacokinetic characteristics of these neurostimulants, including slow systemic clearance, preferential neural tissue uptake, and low peripheral receptor interaction profiles, make them suitable for repeated use without significant risk of systemic overload or off-target effects. The minimal impact on cardiovascular or endocrine systems contributes to their favorable safety profile, reducing concerns commonly associated with stimulant use in sports such as arrhythmias, hypertension, or hormonal dysregulation.

While there are no documented instances of bacterial melanin derived from Bacillus thuringiensis being utilized in human sports or rehabilitation settings, preclinical studies have demonstrated its potential in enhancing motor function recovery in animal models. In a preclinical study utilizing a rat model with central nervous system lesions, intramuscular administration of bacterial melanin resulted in a statistically significant reduction in the recovery time of instrumental conditioned reflexes. Additionally, the treatment was associated with marked improvements in postural balance and a substantial enhancement of general motor activity. These findings suggest that bacterial melanin may have applications in neurorehabilitation, particularly in conditions involving motor deficits. However, clinical trials are necessary to evaluate its safety and efficacy in human subjects before it can be considered for use in sports medicine or rehabilitation contexts.

The localized action within neural tissues further minimizes the risk of dependency or abuse potential—a critical consideration in the ethical and regulatory evaluation of any performance-enhancing substance. From a bioethical standpoint, the use of such agents invites a nuanced debate, particularly given their alignment with physiological enhancement rather than artificial augmentation. If these agents support or amplify natural neurophysiological processes without introducing exogenous hormonal or cardiovascular load, they may occupy a regulatory gray zone similar to nutritional or cognitive supplements. This opens the possibility of developing sport-specific protocols under medical supervision where neurostimulant application is used to accelerate neuromuscular adaptation during training periods rather than as a direct competitive advantage. Such a framework would align with current trends in precision sports medicine, which emphasize individualized and evidence-based approaches to performance optimization.

Translational Potential, and Future Directions in Sports Science:

On a systemic level, the role of bacterial melanin in modulating the neural microenvironment—through antioxidative, anti-inflammatory, and trophic support mechanisms—adds another layer of benefit by protecting neural structures from stress-induced damage and promoting recovery after intense physical exertion or injury [42,43]. This dual role of performance enhancement and neuroprotection is particularly relevant in contact sports or disciplines with high cognitive and emotional load such as combat sports, gymnastics, or endurance racing. The incorporation of neurostimulants into periodized training models could therefore support both skill acquisition and recovery, potentially reducing injury risk and extending athletic career longevity.

Research in animal models and preliminary human studies indicate that the administration of bacterial melanin is associated with improved task execution, motor memory retention, and cortical activation as evidenced by behavioral metrics and neurophysiological recordings. These findings provide a mechanistic basis for its application in sports training where such neural adaptations translate into tangible performance benefits. Moreover, the low production cost and scalable manufacturing of bacterial melanin via microbial fermentation align with global demands for accessible and sustainable biotechnological solutions in health and performance domains.

From a translational perspective, future studies should focus on dosing parameters, timing relative to training cycles, and inter-individual variability in response, particularly in relation to genetic polymorphisms affecting neurotransmission or neuroplasticity. Such data would inform the development of safe, standardized protocols for athletic populations. Regulatory considerations will also require careful navigation, as international sport governing bodies may impose restrictions based on emerging evidence of efficacy and competitive advantage. Nonetheless, if positioned within a framework of medical supervision, informed consent, and ethical oversight, biotechnologically produced neurostimulants could emerge as a legitimate tool for enhancing training outcomes, rehabilitation efficacy, and overall athlete health.

Importantly, the integration of these agents should be complemented by neurophysiological monitoring and individualized assessment to avoid over-stimulation and ensure that neural enhancement remains within adaptive bounds. Wearable technologies, cognitive-motor assessments, and functional neuroimaging may serve as adjunct tools to guide dosage and monitor outcomes in real-world athletic settings. Furthermore, the potential to combine such agents with non-invasive neuromodulation techniques such as transcranial direct current stimulation or neurofeedback presents a synergistic model for optimizing neural function in athletes. This integrative approach would reflect a broader shift toward neurocentric paradigms in sports science, where brain health and performance are addressed as interdependent targets [44].

The safe and effective application of these agents could also have secondary benefits in athlete populations facing high mental workload, travel fatigue, or mild cognitive impairment resulting from repetitive head trauma, thus extending their relevance beyond performance into athlete well-being. In conclusion, the pharmacodynamic properties of biotechnologically produced neurostimulants, particularly bacterial melanin, support their potential role as safe and effective enhancers of athletic performance through mechanisms grounded in neural adaptation, plasticity, and protection. Their favorable safety profile, selective neural bioavailability, and alignment with endogenous excitatory facilitation processes make them uniquely suited for integration into modern training and recovery strategies. As the scientific and regulatory landscape evolves, these agents may redefine the boundaries between medical innovation and human performance, offering new avenues for sustainable and ethically responsible enhancement in sport.

Conclusion.

Biotechnologically produced neurostimulants represent a transformative innovation in the enhancement of motor performance, bridging the domains of neuroscience, molecular biology, and sports physiology. Compounds such as bacterial melanin illustrate how targeted, biologically attuned interventions can modulate neural circuits involved in motor planning, learning, and execution with sustained efficacy and minimal adverse effects. Unlike traditional stimulants, these agents operate through endogenous-like mechanisms—enhancing synaptic plasticity, promoting neuroprotection, and supporting recovery—which may offer more sustainable and ethically acceptable pathways to performance optimization. Their ability to cross the blood-brain barrier, accumulate in cortical structures, and induce long-term potentiation underscores their potential utility not only in athletic training but also in neurorehabilitation. As this field advances, the responsible integration of these agents will require rigorous research into individual variability, safety, and regulation. Ethical considerations, personalized protocols, and real-time neurophysiological monitoring must guide their use to ensure efficacy without compromising fairness or athlete well-being. Ultimately, the development and deployment of biotechnologically engineered neurostimulants may redefine the boundaries of human performance and rehabilitation, fostering a future in which precision neural enhancement complements physical and cognitive training in a safe, science-driven manner.

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