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THE IMPORTANCE OF NOOTROPIC DRUGS IN MEDICAL PRACTICE AND THE RELEVANCE OF THEIR IMPROVEMENT

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Abstract. Nootropics, also known as “smart drugs” are a diverse group of medicinal substances whose action improves human thinking, learning, and memory, especially in cases where these functions are impaired. This review provides an up-to-date overview of the potential effectiveness and importance of nootropics. Based on their nature and their effects, this heterogeneous group of drugs has been divided into four subgroups: classical nootropic compounds, substances increasing brain metabolism, cholinergic, and plants and their extracts with nootropic effects. Many healthy people increasingly utilize "smart drugs" to try to improve their mental function, even though nootropics are intended to address cognitive issues associated with medical disorders. The clinical concerns around common nootropics and other drugs used for this purpose are reviewed in this paper. It is difficult to determine how effective these medications are as supplements or therapies because research on them varies widely, particularly for age-related brain diseases. The applications, indications, experimental treatments, dosage, potential side effects, and contraindications are covered for each of the numerous primary representatives of each class of nootropics. A brief explanation of each plant representative, including its occurrence, history, and chemical makeup of the therapeutic part, is also included for the nootropic plant extracts. Finally, detailed guidelines for the usage of nootropics by healthy and sick people are outlined. Methylphenidate, modafinil, amphetamines, and psychedelics are the most popular smart drugs, which are frequently taken under pressure or stress at work or school. The effectiveness of these medications in enhancing cognitive and decision-making abilities is still unknown, though. There are health dangers associated with using them, particularly if you don't have a prescription. Additionally, there is a dearth of up-to-date, comprehensive information regarding the prevalence of these substances and their effects. Improved training for physicians, pharmacists, and other healthcare professionals may assist identify issues early and increase patient safety.

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Keywords. Learning, antioxidant action, brain damage, piracetam, Panax ginseng, nootropics, memory, *Paullinia cupana*, and ayurvedic.

Introduction. Everyone has at some point wished to increase their intelligence, learn more in less time, think and act more quickly, and improve their memory. Currently, there are substances on the market that offer different combinations of the aforementioned advantages. The term "nootropics" refers to this class of drugs. These drugs are of interest to healthy people due to their capacity to boost intellect and enhance memory, even if they work better in situations where cognitive abilities are clearly compromised. The great majority of these chemicals are naturally occurring, do not require a prescription, and are typically readily available as herbal extracts or food supplements. They are not widely available in synthetic form, and obtaining certain medicines does require a legitimate prescription. Patients with cognitive deficits often tolerate nootropics well; adverse effects are rare and typically mild. Since most nootropics don't work right away after a single dose, long-term use is required to get the intended effects [1-6]. However, it is still unknown how they will affect healthy people in the long run. Clinicians use "nootropics" to treat cognitive impairments in patients with Alzheimer's disease, schizophrenia, stroke, attention deficit hyperactivity disorder, or aging. On the other hand, using a variety of medications or chemicals to enhance brain function in healthy people is referred to as using "smart drugs." Cognitive enhancers, pharmacological neuroenhancement (PNE), "study" medications, and "brain doping" chemicals are some examples of synonyms. The ability to analyze information and apply knowledge is referred to as cognition. Memory, attention, executive functions, perception, language, and psychomotor functions are all involved (see Bayne et al. for a comprehensive overview). Here, nootropics seemed to be a diverse class of medications that influence the metabolism of neurons in the central nervous system. They might enhance cognitive performance, particularly when there is damage or degeneration, but for noticeable results, they might need to be used for a long time. Memory, consciousness, and learning impairments may be associated with their clinical implications. Additionally, nootropic medications, which are usually well tolerated and have infrequent, modest adverse effects, may promote degenerative disorders. Specifically, memory is the capacity to recall events or information that has been taught; attention is the ability to focus on one thing while ignoring distractions; and creativity is the capacity to produce unique goods or concepts. Salience, which describes how noticeable or emotionally meaningful something may be, is another crucial component [7-12]. On the other hand, the majority of smart medications are self-administered by intelligent, otherwise healthy people who are usually involved in high-level jobs or academics. It's interesting to note that whereas "depressant" CE drug users might be more motivated by managing stress, "stimulant" clever drug users are thought to have antisocial traits and be unconcerned with regulations. However, given that the majority of smart medicines are strong DAergic stimulants, one could contend that the associated alteration of central noradrenaline, glutamate, and dopamine levels may result in neurological, psychological, and cardiovascular problems. Additionally, the use of smart medicines has been linked to addictive behavior and paradoxical short- and long-term cognitive impairment. The potential significance of nootropics, as well as their types, applications, dosages, and adverse effects, are summarized in this review of the literature. Our investigation took into account pertinent animal studies in addition to original research articles, meta-analyses, and systematic reviews. Instead than restricting our research to particular findings, we concentrated on offering a current summary of easily accessible medicines, mostly over-the-counter, that are also utilized by healthy individuals like students as medications or food supplements. We made an effort to list every "smart drug" that is currently in demand. Stimulants, vitamins, and other medications having a mostly non-nootropic activity were excluded, as were illegal substances. Since there aren't many research on young people in good health, we attempted to explain how these drugs affected people with cognitive

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impairments as well [13-20]. Finally, we provided a summary of their possible efficacy along with usage suggestions. Healthy people may have some positive effects from long-term high dosages of cognitive enhancers, but there is frequently a higher chance of negative consequences. Since their baseline performance is already close to ideal, those without cognitive impairment or deficit have little opportunity for cognitive enhancement. As a result, instead of experiencing a "supernormal" boost, these people are more likely to have adverse effects, such as anxiety, mood swings, sleep disruptions, reward-system dysfunctions and addictive behaviors, and other psychopathological symptoms. Therefore, in healthy groups, the risk-benefit ratio may be negative, especially when long-term or unsupervised usage is involved [21-28].

The main purpose of the submitted manuscript is to provide a brief analysis of the significance of nootropic drugs in medical practice and the relevance of their improvement based on the results of authoritative scientific works.

Nootropics. Nootropics are generally believed to enhance brain function without attaching to receptors or directly releasing neurotransmitters. In fact, they should help improve the brain's supply of both glucose and oxygen; offer anti-hypoxic actions and prevent neurotoxicity; stimulate the synthesis of proteins and nucleic acids in neurons; and support the metabolism of phospholipids in neurohormonal membranes. Additionally, they could increase erythrocyte flexibility, improve blood flow, and aid in the removal of oxygen-free radicals (see Malík and Tlustoš for a comprehensive analysis). For optimal brain metabolism, all nootropics may need to cross the blood–brain barrier (BBB); although they are thought to be metabolically active, their benefits take time to manifest. Numerous nootropics, both artificial and natural, have been discovered. Because of their various composition, natural nootropics—which are typically derived from plant parts like flowers, leaves, and roots—offer a variety of synergistic effects. However, there are problems with preservation, authenticity, and falsification, and certain natural substances need significant dosages to be effective. On the other hand, synthetic nootropics may offer pharmaceutical purity and specificity of action; they can be chemically altered to improve benefits; and they work at lower doses, however there may be greater risks of toxicity [17-27].

Action Mechanism. Numerous theories have been put up to explain how the nootropics work. ***Change in Energy Metabolism:*** Research has concentrated on altering neural metabolism because neurotransmitter-based strategies have not been very successful. According to this perspective, piracetam consumption has been linked to elevated adenylate kinase activity, enhanced glucose utilization in low oxygen environments, increased 32P absorption in neuronal and glial cells, and accelerated EEG recovery. In contrast, piracetam did not result in an increase in the use of glucose levels. ***Cholinergic Impact.*** Nootropic-based research eventually turned its attention to the role of acetylcholine (ACh) in Alzheimer's disease (SDAT) as this neurotransmitter's function became more clear. In fact, it has been demonstrated that piracetam increases choline absorption and cholinergic receptor density in the frontal cortex, whereas oxiracetam stops ACh levels from falling in the cortex and hippocampus after electroconvulsive therapy procedures in animals [3-13]. Overall, research results were inconsistent, and there is still conflicting and untrustworthy evidence regarding cholinergic processes in nootropics. ***Excitatory amino acids are involved.*** Long-term potentiation (LTP) in glutamate transmission is the subject of recent studies. By regulating the α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor, LTP may contribute to improving receptor-mediated activity. According to this theory, oxiracetam may increase glutamate release in hippocampal slices while somewhat mitigating the behavioral effects of NMDA receptor antagonists. However, it's unclear if aniracetam and LTP have the same effects [15-21].

Classification of Nootropics. Nootropics can be broadly classified as synthetic chemicals, compounds of natural origin, and vasodilatory drugs that increase brain metabolism (see Napoletano et al. for comprehensive studies).Traditional synthetic nootropics. These substances include a variety of synthetic substances that have been investigated for their potential to improve cognition (for a summary, see Malík and Tlustoš; Mondadori). Many of these

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substances work on cholinergic pathways or cerebral metabolism. For example, meclofenoxate and deanol (DMAE) are choline precursors that support acetylcholine production and may enhance memory and learning; recommended daily dosages range from 500 to 2000 mg. Nicergoline, an ergot derivative, is usually taken at a dose of 30–60 mg per day and is believed to enhance mood, alertness, and cognitive function [6-13]. The well-known nootropic piracetam increases neuronal excitability by modulating calcium and potassium ion channel activity; acute dosages range from 4 to 8 g/day, while maintenance doses are between 2 and 4 g/day. Although greater doses (>600 mg/day) are frequently used in clinical settings, pyritinol, a derivative of vitamin B6, is given at least 300 mg/day and may improve choline acetyltransferase activity. ***Enhancers of Brain Metabolism.*** Certain substances have hemorheological, vasodilatory, and nootropic effects that overlap. For instance, vinpocetine, which is started at 2–5 mg/day and increased to 10–30 mg, is believed to improve brain oxygenation. At doses of 300–600 mg daily, naftidrofuryl improves blood rheology and peripheral circulation [18-23].

Natural; Nootropic Plants and Their Extracts. The group includes a variety of chemicals (see Malík and Tlustoš and Graziano et al. for comprehensive reviews). A number of plant extracts have been linked to improved cognitive function. Phosphatidylcholine, a crucial component of lecithin, a chemical found in different plant and animal sources lecithin functions as a choline reservoir. With preventative use of about 3.6 g/day and therapeutic doses exceeding 10–15 g/day, older persons may need far greater doses for therapeutic efficacy. With a suggested dosage of up to 6 mg/day, dihydroergotoxine, a compound of ergot alkaloids, has demonstrated promise in controlling cognitive decline and shielding neuronal tissue from hypoxic damage. Ginseng (*Panax ginseng*) has been demonstrated to improve memory in patients; usual dosages are 0.5–2 g/day of dried root or 200 mg/day of standardized extract (containing 1.5–7% ginsenosides). The majority of research has been on P. ginseng ginsenosides, which may be the cause of the effects on the neurological system. Phytosterols, sesquiterpenes, flavonoids, polyacetylenes, alkaloids, and phenolic compounds are other potentially bioactive components [4-14]. Ginseng may stabilize excitable cells and modulate neuronal activity by influencing the monoamine neurotransmitter system, increasing the expression of neurotrophic factors like BDNF, and interacting with different ion channels (Ca2+, K+, Na+) and ligand-gated ion channels (GABAA, 5-HT3, nicotinic acetylcholine, and NMDA receptors). Patients with neurodegenerative diseases or cerebral insufficiency may benefit from ginkgo biloba's antioxidant and vasodilatory qualities. Standardized extract doses (EGb 761®) typically range from 120 to 300 mg/day. Increased cerebral blood flow, antioxidant and anti-inflammatory properties, and antiplatelet actions linked to flavone and terpene lactones are among the mechanisms of action. While flavonoids and terpenoids can shield brain cells from oxidative damage, improved circulation can improve oxygen and nutrition supply to brain cells, thereby reducing the consequences of ischemia and enhancing cognitive function. Consuming flavonol derivatives has been linked in preclinical research to increases in dopaminergic and cholinergic neurotransmission in the prefrontal cortex. Although it is contraindicated in cardiovascular diseases, guarana (Paullinia cupana), which is high in caffeine (~12% in extract) and hence largely acts through its stimulant qualities, is associated with improved memory and physical performance. Lastly, as an adaptogen, maca, often known as "Peruvian ginseng," has been researched for its ability to improve cognitive and motor function; daily doses are usually between 1.5 and 3 g [16-25].

Natural vs. synthetic nootropics: benefits and drawbacks. Natural origin medications derived from various plant parts (flower, leaf, root, etc.) have the undeniable advantage of having a wider range of potentially advantageous pharmacological effects. This is because a herbal medication contains a variety of compounds that can have additive or synergistic effects. Additionally, natural nootropics are typically less toxic, which lowers the risk of overdose injury. Nevertheless, some substances have the ability to lessen the pharmacological activity of other substances. Plant extracts are frequently utilized since higher doses of such a herbal medication

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are required to provide the intended effect. Additionally, there are issues with storage, potential falsification, and authenticity verification. The pharmaceutical purity, specificity of action, and potential for increased effect through chemical structural alteration are the benefits of synthetic substances. Because they are typically active at smaller levels, there is a higher chance of overdosing [17-26].

Discussion. While "nootropics" are designed to cure a variety of cognitive deficits associated with medical disorders, the generally healthy "smart drugs" user consumes a variety of medications or chemicals to boost mental function. This study sought to give a summary of the clinical pharmacological problems associated with both the most widely used nootropics and the wide variety of medications being employed as potential cognitive enhancers/smart pharmaceuticals, given the growing levels of related concerns. Research technique varied significantly when it came to the cognitive decline linked to neurological degenerative illnesses. This article provides an updated narrative summary of the pharmacological, clinical pharmacology, and toxicological concerns associated with the range of compounds that are either prescribed or self-administered/misused to achieve notable levels of cognitive improvement. Given that half of the current studies cited here were published between 2020 and 2025, one could claim that interest in these compounds has recently surged [3-10]. Therefore, before recommending their widespread use, the overall efficacy of these medications as supplements or adjuvant therapy in diverse illnesses of the central nervous system needs to be further proven. Methylphenidate, modafinil, amphetamine-based compounds, and psychedelics were the most widely used smart drugs, self-administered to manage high perceived stress and pressure from work and school. However, there is now a significant degree of ambiguity regarding the efficacy of smart medicines in enhancing executive functions. The lack of current and contextualized epidemiological data makes it difficult to address the health risks linked to the use of cognitive enhancers. Specifically, the use of stimulant smart medicines by otherwise healthy people without a prescription seems to raise a number of clinical issues. Monitoring and early intervention efforts can be strengthened by providing prescribers, pharmacists, and other healthcare workers with improved training. Overall, there seems to be a wide variety of potential nootropics, cognitive enhancers, smart medications, and study pharmaceuticals. Napoletano et al. used a mixed-methods, web-based, netnographic investigation to better identify and characterize the variety of these compounds [12-19]. Plants/herbs/products (29%), prescription drugs (17%), image and performance enhancing drugs (IPEDs) (15%), psychostimulants (15%), miscellaneous (8%), phenethylamines (6%), GABAergic drugs (5%), cannabimimetics (4%), tryptamine derivatives (0.5%), and piperazine derivatives (0.5%) were among the ten categories into which they listed. Healthy people may get some desired advantages from long-term high dosages of cognitive enhancers, but there is frequently a higher chance of negative consequences. Since their baseline performance is already close to ideal, those without cognitive impairment or deficit have limited possibility for cognitive enhancement. As a result, instead of experiencing a "supernormal" boost, these people are more likely to have adverse consequences, such as anxiety, mood swings, sleep disruptions, reward-system dysfunctions/addiction behaviors, and other psychopathological symptoms. Therefore, in healthy populations, the risk-benefit ratio may be negative, especially with long-term or non-medically supervised use [22-28].

Conclusions. The dearth of current and contextualized epidemiological data makes it difficult to address the health risks linked to the use of smart drugs, nootropics, and cognitive enhancers. Given the lack of solid clinical evidence on these compounds' efficacy in healthy users, there seem to be a variety of clinical problems with their non-prescription use by otherwise healthy individuals. From this perspective, future research will need to take into account a wide variety of participant groups (e.g., in terms of age, gender, health status, and occupation/discipline), with an emphasis on young, healthy users.

Neuroimaging should be used more frequently to confirm any potential cognitive consequences linked to these medications' effects. There was a notable degree of heterogeneity

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in research technique, even when it came to the cognitive loss linked to degenerative illnesses like Alzheimer's dementia. Therefore, before their widespread use can be advised, the overall efficacy of these medications as a supplement or adjuvant therapy in various disorders of the central nervous system must be established through high-quality multicenter randomized controlled clinical trials with a sufficient sample size and optimized study design. Designer medicines, which are synthetically altered compounds made to imitate the effects of regulated substances while evading legal limits, are also an increasing source of worry.

These substances are frequently designed with minute chemical changes that could drastically change pharmacological characteristics and toxicity profiles, putting users at grave risk. The creation of NPS may be accelerated by the emergence of AI-driven molecular design tools, which would complicate identification and regulation. Lastly, the creation of a corpus of information about the trends and effects of smart drug usage will be necessary to guide future health policy measures. Monitoring and early intervention efforts can be strengthened by providing prescribers, pharmacists, and other healthcare workers with improved training. Managing the various issues presented by smart drug usage still requires a multidisciplinary strategy that incorporates medical, psychological, and social support.

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