

Dihexa-Methylene-Blue-Tesofensine-Oral

PEPTIDES

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DIHEXA Dihexa , aka N-hexanoic-Tyr-Ile-(6) aminohexanoic amideor PNB-0408, is a relatively new drug for the treatment of a wide array of conditions that affect cognitive function, including Alzheimer's and Parkinson's. Furthermore, it improves stroke recovery, accelerates recovery from spinal cord injury and nerve damage, and protects against hearing loss. Unlike other drugs for AD, this potent nootropic not only impedes the progression of the disease but actually repairs the damage in the synapse between neurons. By binding to hepatocyte growth factor (HGF), Dihexa increases HGF's activity while lowering harmful chemical reactions in the body. This in turn doubles the capacity of the available growth factors to promote signaling cascades necessary for cell development and regeneration. **BENEFITS** Aids in the treatment of Alzheimer's and Parkinson's diseases Improves cognitive function, particularly in such areas as memory retention and learning ability Improves stroke recovery Accelerates recovery from spinal cord injury and nerve damage Protects against hearing loss Aids in treating memory and motor dysfunctions by enhancing synaptic connectivity through the formation of new functional synapses Builds new brain cell connections Prevents learning and memory dysfunction after sustained cerebral ischemia (periods of decreased blood flow to the brain) by protecting injury to brain neurons Increases the production of acetylcholine and/or dopamine Activates HGF, which induces long-term neuroprotection and stroke recovery Prevents stroke by increasing blood flow to the brain Slows the progression of spinal cord injury caused by amyotrophic lateral sclerosis (ALS) Helps to heal damage to the sciatic nerve **POSSIBLE SIDE EFFECTS** Anxiety Change of taste Insomnia Irritability Mood swings Nausea Headache Mental Overstimulation Light sensitivity Racing thoughts Increased focus bordering agitation Emotional intensity **INTERACTIONS** Other strong neurotrophic agents: e.g. Cerebrolysin, Semax/NA-Semax, Selank, NSI-189, BDNF-inducing stacks, Lion's Mane (high doses). Potential reactions may include anxiety, insomnia, neuroexcitation. Dopaminergic Agents: Possible amplification of stimulants (amphetamine, methylphenidate), bromantane, and MAO inhibitors. Potential reactions may include agitation, insomnia, and sympathetic activation. Growth-Factor/Regenerative Peptides: Theoretical additive proliferation signaling with IGF-1 LR3, GH secretagogues (CJC/Ipamorelin), and TB- 500, and BPC-157. Anti-Cancer Therapies: Potential antagonism with c-MET inhibitors and chemotherapy relying on growth suppression. **USE WITH CAUTION/UNDER CLOSE MEDICAL SUPERVISION** Bipolar or severe anxiety disorders Epilepsy or seizure history Brain tumors Retinal vascular disease Autoimmune CNS disease **CONTRAINDICATIONS** History of metastatic cancer Precancerous lesions under monitoring

Pregnancy or breastfeeding (no safety data) Pediatric use METHYLENE BLUE Methylene blue, also known as methylthioninium chloride, is a synthetic dye that has been widely used for various purposes, including as a stain in histology and microbiology and in a variety of industrial and medical applications. The World Health Organization has placed it on their List of Essential Medicines, which means that they consider it to be a vital medication for a basic health system. BENEFITS Facilitates electron transfer in the mitochondrial respiratory chain, which bypasses certain complex deficiencies to reduce oxidative stress. This ultimately improves mitochondrial function, promoting cellular energy production and potentially offering therapeutic benefits for neurodegenerative conditions. Acts as an antioxidant, meaning it can neutralize harmful free radicals³ that can damage cells and contribute to aging and disease. By eradicating these free radicals, cells are protective from damage and oxidative stress. Modulates nitric oxide levels, which has positive implications for cardiovascular health and blood flow regulation. Offers neuroprotective effects by preserving nerve cells' viability and function, potentially reducing the risk of neurodegenerative disorders. Enhances cognitive function by increasing blood flow to the brain and improving memory and attention. Methylene Blue's antimicrobial properties disrupt bacterial or microbial functions, making it an effective adjunct to traditional antimicrobial therapies. Its lipophilic nature facilitates efficient blood-barrier penetration, with high brain concentration observed after dosing. Counteracts premature cellular senescence and aging Reduces markers of aging in cellular tissues Reduces amyloid-binding alcohol dehydrogenase (ABAD), which damage brain cells while increasing levels of estradiol Helps mitigate symptoms of hepatic encephalopathy (loss of brain function due to impaired removal of toxins from the blood due to liver damage) Works with macroautophagy⁴ (a fundamental cellular process that involves the degradation and recycling of cellular components) to safeguard brain cells from dying when they lack essential nutrients Is an antidote for cyanide or carbon monoxide poisoning Helps to treat urinary tract infections Reduces the death rate from those with low blood pressure after heart surgery (postoperative vasoplegia or vasoplegic syndrome) Septic shock management Drastically reduces harm and fatalities in children suffering from fluid and catecholamine therapy-resistant shock Increases mean arterial pressure, which decreases the patient's need for other medications, reduced length of hospital stay, and improved heart function and oxygenation in patients with septic shock. Can treat psychotic and mood disorders, enhance memory in fear-extinction training, and shows promise in short and long-term treatment of bipolar disorder; offers antidepressant and anxiolytic effects in bipolar treatment without inducing manic episodes. Enhances skin fibroblast proliferation and delayed cellular senescence. Application of Methylene Blue improves skin viability, wound healing, hydration, dermis thickness, and altered gene expression of extracellular matrix proteins. Shows superior UVA and UVB absorption and protection against DNA damage For sufferers of chronic refractory idiopathic pruritus ani (IPA), a condition characterized by persistent itching and discomfort in the anal area. Patients who didn't respond to standard treatments were given intradermal injections of 1% methylene blue solution up to the dentate line, which is the boundary between the upper anal canal and the lower rectum and their symptoms resolved within 4 weeks without serious side effects and with over a Effective in treating conditions such as malaria, urinary tract infections, shock, and methemoglobinemia, stands as the singular known substance capable of restraining the excessive generation of reactive species and cytokines, suggesting its potential to treat COVID-19 and SARS CoV2 infections. Particularly effective antiviral for the management of flavivirus infections, particularly Zika virus. Methylene Blue is an anticancer agent

and aids promotes apoptosis (cell death) in tumors. For patients suffering from oral mucositis, a complication of cancer therapy which causes severe pain impacting oral function, nutrition, and quality of life, potentially leading to treatment nonadherence and dose-limiting toxicity, rinsing with Methylene Blue allowed patients to achieve a significant reduction in pain within the first three treatments. Helps to treat methemoglobinemia. POSSIBLE SIDE EFFECTS Mild nausea Blue/green urine Blue/green tongue/saliva Headache (usually at higher doses) Insomnia Restlessness Sweating Dizziness Anxiety/jitteriness Tachycardia Elevated blood pressure Tremor Hyperreflexia Agitation Hemolytic anemia: Methylene Blue increases oxidative stress in red blood cells lacking NADPH protection Serotonin Syndrome: Inhibits monoamine oxidase (specifically MAO-A). When combined with other drugs that increase serotonin (e.g. SSRIs, SNRIs, MAOIs, and tricyclic antidepressants) this can precipitate serotonin syndrome. Symptoms of Serotonin Syndrome include hyperthermia, agitation, increased reflexes, tremors, muscle rigidity, confusion or delirium, tachycardia, seizures, and blood pressure fluctuations. Hemolytic Anemia: can induce hemolytic anemia, particularly in individuals with glucose-6-phosphate dehydrogenase (G6PD) deficiency, a condition that makes red blood cells more susceptible to oxidative stress. Methemoglobinemia: Although it is used to treat this condition, overuse or inappropriate dosing can exacerbate the condition in certain situations, especially when the patient has other blood disorders. dosing leads to inadequate oxygenation. Cardiovascular issues: Tachycardia (fast heart rate) and hypertension (high blood pressure) can occur, especially when high doses are used or in patients with pre-existing heart conditions. Neurotoxicity: Seizures, confusion, or psychosis may occur at very high doses, particularly when administered intravenously or as part of an experimental or off-label use for neuroprotection or cognitive enhancement. INTERACTIONS Serotonergic drugs: SSRIs, SNRIs, tricyclic antidepressants, and MAOIs can lead to serotonin syndrome when combined with methylene blue. Antidepressants: Because it inhibits MAO-A, combining it with MAO inhibitors (e.g. Phenelzine, Tranylcypromine) can increase the risk of hypertensive crises and serotonin syndrome. Anticoagulants/Antiplatelet Drugs: Methylene blue may affect platelet aggregation and blood clotting. Caution is needed when taking anticoagulants like warfarin or heparin, as Methylene Blue may increase the risk of bleeding, although this effect is more commonly noted with intravenous administration. Sympathomimetic Drugs: Combining methylene blue with sympathomimetic drugs (ue with sympathomimetic drugs (e.g., epinephrine, dopamine, amphetamine, or pseudoephedrine) can increase the risk of hypertension and tachycardia due to its stimulating effects on the adrenergic system. Cytochrome P450 Enzyme Inhibitors or Inducers: Methylene blue is metabolized by the liver enzyme CYP1A2, so drugs that either inhibit (e.g., ciprofloxacin) or induce (e.g., carbamazepine) this enzyme could affect its metabolism, leading to altered drug levels and effects. Other MAO Inhibitors: Combining methylene blue with other MAO inhibitors, even those in non-antidepressant categories (e.g., selegiline), can increase the risk of hypertensive crises and serotonin syndrome. Dantrolene: There are potential interactions between methylene blue and dantrolene, a drug used for malignant hyperthermia. Methylene blue can reduce the effectiveness of dantrolene in treating this rare but serious condition. Caffeine: Caffeine and methylene blue may have synergistic effects on nervous system stimulation, increasing the likelihood of nervousness, insomnia, or tachycardia. CONTRAINDICATIONS Do not use Methylene Blue if you are pregnant or breastfeeding. G6PD Deficiency: due to a risk of hemolytic anemia, a genetic disorder impairing red blood cells' ability to protect themselves from oxidative stress. Active or recent use of

SSRI's, SNRI's, tricyclic antidepressants, or MAO inhibitors- concurrent use can result in serotonin syndrome. Severe liver or kidney disease/dysfunction: increased risk of toxicity due to the inability of these organs to metabolize and eliminate the TESOSENSINE. Offers a range of potential benefits, including promoting weight loss, improving cognitive health, enhancing mood, regulating blood sugar, boosting energy, addressing sexual dysfunction, treating eating disorders, managing ADHD, improving sleep quality and aiding in the fight against alcohol addiction. Tesofensine (NS2330) is a serotonin–noradrenaline–dopamine reuptake inhibitor or also known as a triple reuptake inhibitor, which means that it inhibits the reabsorption of the neurotransmitters (brain chemicals) serotonin, norepinephrine, and dopamine. This process increases the levels of these neurotransmitters. The therapeutic benefits of tesofensine are attributed to this effect because each of these neurotransmitters exerts an important function at different locations in the brain. Initially researched as an adjunct to other Alzheimer's treatments, but caught on as a weight loss drug once its weight loss effects were realized. Tesofensine has been shown to have a good safety profile and has been well tolerated through an increased number of adverse events (e.g. increased heart rate and blood pressure). Blood pressure tends to be increased by 1-3mmHg and up to 8bpm. Results in an average 10% average weight loss within 24 weeks.

BENEFITS

- Promotes weight loss
- Improves cognitive function
- Mood stabilizer
- Improves blood sugar levels
- Treats sexual dysfunction
- Treats eating disorders
- Treats ADHD
- Improves sleep quality
- Combats alcohol addiction
- Enhances erections
- Improves insulin sensitivity
- Increases resting energy expenditure
- Reduces fat oxidation
- Reduces fat tissue
- Improves sex drive
- Improves memory
- Increases thermogenesis

May be used to treat brain disorders like Alzheimer's and Parkinson's. Increases levels of brain-derived neurotrophic factor (BDNF), thereby triggering an antidepressant effect.

POSSIBLE SIDE EFFECTS

- Constipation
- Diarrhea
- Dry mouth
- Headache
- Changes in blood pressure (increased)
- Elevated heart rate
- Insomnia
- Nausea
- Decreased appetite
- Anxiety or irritability
- Dizziness

INTERACTIONS

Serotonin Syndrome is a serious reaction caused by medications that build up high levels of serotonin in the body. Too much serotonin causes signs and symptoms that can range from mild (shivering and diarrhea) to severe (muscle rigidity, fever, seizures, and death). It is most commonly caused by combining medications that contain serotonin, such as a migraine medication and an antidepressant. Some illicit drugs and dietary supplements are similarly associated with serotonin syndrome.

Symptoms of Serotonin Syndrome

- Agitation or restlessness
- Insomnia
- Confusion
- Rapid heart rate and high blood pressure
- Dilated pupils
- Loss of muscle coordination or twitching muscles
- High blood pressure
- Heavy sweating
- Diarrhea
- Headache
- Shivering
- Goosebumps

Signs of Severe Serotonin Syndrome

- High fever
- Tremor
- Seizures
- Irregular heartbeat
- Unconsciousness

Drugs and Supplements that Could Cause Serotonin Syndrome

Serotonin and Norepinephrine Reuptake Inhibitors: antidepressants such as desvenlafaxine (Pristiq), levomilnacipran (Fetzima), milnacipran (Savella), duloxetine (Cymbalta, Drizalma Sprinkle) and venlafaxine (Effexor XR)

Selective Serotonin Reuptake Inhibitors (SSRIs): antidepressants such as citalopram (Celexa), fluoxetine (Prozac), fluvoxamine (Luvox), escitalopram (Lexapro), paroxetine (Paxil, Pexeva, Brisdelle) and sertraline (Zoloft)

Bupropion (Zyban, Wellbutrin SR, Wellbutrin XL), an antidepressant and tobacco-addiction medication

Tricyclic antidepressants, such as amitriptyline and nortriptyline (Pamelor)

Monoamine oxidase inhibitors (MAOIs), antidepressants such as isocarboxazid (Marplan) and phenelzine (Nardil)

Anti-migraine medications, such as carbamazepine (Tegretol, Carbatrol, others), valproic acid and triptans, which include almotriptan, naratriptan (Amerge) and sumatriptan

(Imitrex, Tosymra, others) Pain medications, such as opioid pain medications including codeine, fentanyl (Duragesic, Abstral, others), hydrocodone (Hysingla ER), meperidine (Demerol), oxycodone (Oxycontin, Roxicodone, others) and tramadol (Ultram, ConZip) Lithium (Lithobid), a mood stabilizer Illicit drugs, including LSD, ecstasy, cocaine and amphetamines Herbal supplements, including St. John's wort, ginseng and nutmeg Over-the-counter cough and cold medications containing dextromethorphan (Delsym) Anti-nausea medications such as granisetron (Sancuso, Sustol), metoclopramide (Reglan), droperidol (Inapsine) and ondansetron (Zofran) Linezolid (Zyvox), an antibiotic Ritonavir (Norvir), an anti-retroviral medication used to treat human immunodeficiency virus (HIV). High Risk: Do Not Use MAO Onhibitors: e.g. Phenelzine, Tranylcypromine, Selegiline (high dose), Isocarboxazid, Linezolid due to risk of Severe Phychiatric instability: Active psychosis, bipolar mania, severe anxiety disorders, uncontrolled mania Do not use if pregnant or breastfeeding Use of Sympathomimetic Stimulants such as Amphetamines, Phentermine, Methylphenidate, Ephedrine, high caffeine content: May result in tachycardia, hypertension, arrhythmia, and anxiety and panic GLP Medications: Do not combine GLP medications with each other. Moderate Risk: Use with Extreme Caution/Under Close Medical Supervision GLP-1/GIP/Glucagon Receptors : excessive appetite suppression, nausea amplification, dehydration, resting tachycardia. Growth Hormone Secretagogues (e.g. Ipamorelin, Sermorelin, Tesamorelin, and CJC-1295): Monitor your fasting glucose, sleep quality, and beware of cortisol activation IGF-1 LR3: Beware of glucose instability, appetite dysregulation, and headaches Stimulatory/Neuroactive Peptides (e.g. Dihexa, Semax, Selank, and Cerebrolysin) : Additive dopaminergic activity leading to anxiety and/or overfocus Thyroid Active Compounds: Additive metabolic stimulation may cause palpitations, heat intolerance, and excessive weight loss USE WITH CAUTION/UNDER CLOSE MEDICAL SUPERVISION Controlled hypertension Tachycardia >90bpm baseline Insomnia disorders ADHD medications Anxiety disorders Migraine disorders Poorly controlled diabetes CONTRAINDICATIONS Pregnant or breastfeeding MAOI use within the previous 14 days Uncontrolled hypertension Significant cardiovascular disease Recent stroke or myocardial infarction Sever arrhythmias Hyperthyroidism (untreated) History of serotonin syndrome Severe anxiety disorder Active psychosis or bipolar mania DOSING Dihexa 5mg/Methylene Blue 50mg/Tesofensine 500mcg Take 1 per day Take in the morning Best taken with a light meal that contains a small amount of protein/fat; avoid heavy carbs

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