The Integrative Mental Health Series: Formulated with James Greenblatt, MD

Dr. James Greenblatt has dedicated his professional career to Integrative Psychiatry. He has worked with thousands of children, adolescents and adults, employing both medical and complementary therapies. Dr. Greenblatt is dually board certified in child and adult psychiatry. He received his medical degree and completed his adult psychiatry residency at George Washington University in Washington, D.C. He completed a fellowship in child and adolescent psychiatry at Johns Hopkins Medical School. In addition to being the Founder and Medical Director of Comprehensive Psychiatric Resources, Inc. in Waltham, MA, Dr. Greenblatt is a clinical faculty member at Tufts Medical School, Department of Psychiatry.

Dr. Greenblatt has been involved with product development in the nutraceutical industry since 1995. He is the author of two books on integrative mental health: The Breakthrough Depression Solution, and Answers to Anorexia. Dr. Greenblatt lectures extensively to health professionals on Integrative Medicine for Mental Health.
Integrative Mental Health

The mind is an exquisitely complex system of cognitive and emotional faculties that orchestrate thought, reasoning, behavior and emotion. The mind and brain speak a language in which neurons function cooperatively in elaborate ensembles. To precisely coordinate every mental and emotional process, neurons must communicate using biochemical messengers known as neurotransmitters. Therefore, effective synthesis and activity of these critical molecules is essential for mental health.

Mental and emotional health depend on the availability of nutrient building blocks and cofactors for the biosynthesis of neurotransmitters. In addition to these essential precursors, non-essential dietary components, such as antioxidants and phytochemicals, support neurotransmitter dynamics in a generalized manner by modulating enzymes and maintaining healthy reuptake systems. The Integrative Mental Health product line, formulated based on decades of research and clinical experience, delivers strategic combinations of three evidence-based nutritional approaches.*

1. **Amino acids** that serve as precursors to key neurotransmitters*

2. **Cofactors** that are critical for neurotransmitter biosynthesis and receptor function*

3. **Enzyme and reuptake support** maintains the stability and function of neurotransmitters*

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**DopaPlus**

Supports dopamine production*

**Amino acids**: L-tyrosine, L-DOPA

**Cofactors**: Metafolin® L-5-MTHF, zinc

**Enzyme modulators**: Rhodiola, green tea

**Clinical Applications**:
- Cognitive function for daily mental tasks*
- Mental sharpness and alertness*

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**SeroPlus**

Supports serotonin production*

**Amino acids**: 5-HTP

**Cofactors**: Magnesium, P5P, Metafolin® L-5-MTHF, vitamin C

**Maintains healthy reuptake**: Taurine, inositol

**Clinical Applications**:
- Relaxation and calming*
- Moderates occasional stress*
- Supports healthy eating behavior*

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**NeuroPure**

Combined dopamine and serotonin support*

**Amino acids**: dl-Phenylalanine, 5-HTP

**Cofactors**: Metafolin® L-5-MTHF, zinc, P5P

**Enzyme modulators**: Curcumin, quercetin

**Clinical Applications**:
- Enhanced emotional balance, mood stability*
- Overall neurotransmitter support*

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*These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.
Amino acids

Neurotransmitters that are highly relevant to mental and emotional wellness include dopamine and serotonin, which are synthesized from specific amino acids*:

- **L-phenylalanine, L-tyrosine, L-DOPA → Dopamine**
- **L-tryptophan, 5-hydroxytryptophan (5-HTP) → Serotonin**

Cofactors

Conversion of amino acids to an active neurotransmitter requires the availability of nutrient cofactors, which are commonly depleted in individuals as a result of medications, dietary deficiencies and environmental exposures. Maintaining nutritional adequacy of the following cofactors enhances the capacity of biosynthetic pathways to maintain neurotransmitter levels in the brain*:

- **Folate (L-5-MTHF)** plays a particularly critical role in maintaining general mental health and emotional wellness. Contrary to folic acid, L-5-MTHF readily crosses the blood brain barrier to elevate folate concentrations in the central nervous system. Metafolin® is a clinically researched L-5-MTHF that is the sole form of folate in the Integrative Mental Health product line. Metafolin® serves as the active coenzyme in critical steps of serotonin and dopamine synthesis.*

- **Vitamin B₆** is required by enzymes that synthesize dopamine and serotonin. To be an active coenzyme, it must be converted to pyridoxal 5’-phosphate (P5P).*

- **Zinc and magnesium** are critical for serotonin and dopamine homeostasis in the central nervous system. Clinical research shows that adequacy of these minerals maintains healthy serotonin and dopamine levels. Zinc and magnesium also moderate the activity of glutamate receptors to support both emotional wellness and long-term neuroprotection.*
Maintaining healthy reuptake support*

Essential nutrients constitute indispensable structural and functional building blocks of dopamine and serotonin. However, the activity of these compounds is compromised by two factors: (1) degradation by enzymes in the synapse, and (2) removal from the synapse by reuptake. Reuptake of neurotransmitters refers to their transport back into the neuron that released them. This reduces their residence time in the synapse, limiting their ability to activate receptors. Accordingly, prolonging synaptic presence increases the activity and benefits of neurotransmitters.*

Studies show that the following nutrients can support neurotransmitter stability by targeting enzymes in the brain:*

- **Curcumin**
- **Quercetin**
- **Green tea flavonoids**
- **Grape seed proanthocyanidins**

The following nutrients can also maintain healthy reuptake to support healthy receptor activation:*  

- **Taurine (serotonin reuptake)**
- **Rhodiola rosea extract (dopamine reuptake)**
- **Green tea extract (dopamine reuptake)**

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DopaPlus

Dopamine plays indispensable and diverse roles in cognition, learning, mood and behavior. Importantly, this critical neurotransmitter controls the flow of information to maintain mental sharpness, alertness, memory and cognitive performance. The biosynthesis of dopamine requires the precursor L-tyrosine and the cofactors 5-MTHF and activated vitamin B$_6$ (pyridoxal 5’-phosphate, or P5P) (Figure 1).*

Dopamine may be degraded by two enzymes, monoamine oxidase (MAO) and catechol O-methyltransferase (COMT). Recent research indicates that various polyphenols, including curcumin and quercetin, maintain healthy MAO activity. In addition, unique polyphenols found in green tea, known as catechins, directly bind and modulate COMT to maintain dopamine levels. An additional benefit of these compounds is protection of neurons from oxidative stress, which is not only implicated in long-term neuroprotection, but in maintaining a positive mood and the ability to relax.*

*Figure 1. Dopamine neurotransmission. L-tyrosine is converted to L-DOPA by tyrosine hydroxylase (TH), which requires active folate (5-MTHF). Conversion of L-DOPA to dopamine is mediated by aromatic amino acid decarboxylase (AADC), which requires active vitamin B$_6$ (pyridoxal 5’-phosphate, or P5P). In the communication between neurons, dopamine is released into the synapse, or the space between the two neurons, and subsequently binds to dopamine receptors on the receiving (postsynaptic) neuron. Dopamine receptors translate the message to support cognitive function, mental sharpness and alertness. Dopamine remaining in the synapse is susceptible to reuptake or degradation by two enzymes, monoamine oxidase (MAO) and catechol O-methyltransferase (COMT).*

Each product is designed to be used individually, along with the co-support of magnesium and essential fatty acids. These products are not intended to replace SSRI, MAOI or other psychiatric medications and should only be used under the supervision of a healthcare practitioner.
**DopaPlus:** Supports dopamine production and maintains healthy reuptake to enhance daily mental function and sharpness*

- Provides the dopamine precursors L-tyrosine and L-DOPA from *Mucuna pruriens* *
  - In a randomized, controlled, double-blind, crossover trial, *Mucuna pruriens* supplementation promoted peak L-DOPA plasma concentrations *

- Includes the synergistic cofactors vitamin B₆, Metafolin® L-5-MTHF, and zinc to support dopamine production *

- Enhances the stability of dopamine and maintains healthy dopamine reuptake with rhodiola and green tea polyphenols *

- Encourages cognitive function and mental sharpness by supporting healthy theta brain wave activity with grape seed proanthocyanidins *

- Protects neuronal health and function with green tea and grape seed polyphenols *

- Supports optimal serum levels of zinc and folate to promote positive mood *

*Metafolin® is a registered trademark of Merck KGaA, Darmstadt, Germany. 

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**three vegetarian capsules contain**

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<tr>
<th>Ingredient</th>
<th>Quantity</th>
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<tbody>
<tr>
<td>Folate (as Metafolin®, L-5-MTHF)</td>
<td>500 mcg</td>
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<tr>
<td>Zinc (as zinc picolinate)</td>
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<td>L-tyrosine (free-form)</td>
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<tr>
<td>Velvet bean (mucuna pruriens) extract (seed) (standardized to contain 15% L-DOPA)</td>
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<td>Rhodiola (rhodiola rosea) extract (root) (standardized to contain 3% total rosavins and min. 1% salidrosides)</td>
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<td>Grape (vitis vinifera) extract (seed) (standardized to contain 92% polyphenols)</td>
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<td>Green tea (camellia sinensis) extract (leaf) (standardized to contain 90% total tea catechins and 70% EGCG)</td>
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<td>Pyridoxal 5’-phosphate (activated B₆)</td>
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Other ingredients: vegetarian capsule (cellulose, water) 

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**3-6 capsules daily, in divided doses, between meals.**

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SeroPlus

Serotonin supports critical behavioral and physiological functions, including the regulation of mood, emotions and appetite. The biosynthesis of serotonin begins with L-tryptophan, which is converted to serotonin through a pathway requiring 5-MTHF and P5P (Figure 2). Like dopamine, serotonin is susceptible to degradation by MAO.*

Figure 2. Serotonin neurotransmission. L-tryptophan is converted to 5-HTP by the enzyme tryptophan hydroxylase (TPH), which requires 5-MTHF. Subsequent conversion to serotonin is mediated by aromatic amino acid decarboxylase (AADC), which requires P5P and zinc. Magnesium is required for supporting the overall integrity of this pathway. When released into the synapse, serotonin is subject to reuptake or degradation by MAO. The remaining serotonin binds to serotonin receptors on the postsynaptic neuron, which use inositol-mediated signal transduction to translate the message into signals that support relaxation, moderation of occasional stress and healthy eating behavior.*

Each product is designed to be used individually, along with the co-support of magnesium and essential fatty acids. These products are not intended to replace SSRI, MAOI or other psychiatric medications and should only be used under the supervision of a healthcare practitioner.
**SeroPlus:** Supports serotonin production to promote positive mood, moderate occasional stress, and maintain healthy eating behavior*

- Provides the serotonin precursor 5-HTP
- Enhances healthy sensitization of serotonin receptors and nervous system function with inositol*
- Supports healthy serotonin activity and maintains healthy reuptake with taurine*
- Enhances 5-HTP availability with niacinamide and zinc*
- Includes the synergistic cofactors magnesium, vitamin C and vitamin B₆ and Metafolin® L-5-MTHF to support serotonin production and positive mood*

Metafolin® is a registered trademark of Merck KGaA, Darmstadt, Germany.

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two vegetarian capsules contain

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<td>niacin (as niacinamide)</td>
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<tr>
<td>folate (as Metafolin®, L-5-MTHF)</td>
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<td>magnesium (as di-magnesium malate)</td>
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<tr>
<td>pyridoxal 5’-phosphate (activated B₆)</td>
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Other ingredients: vegetarian capsule (cellulose, water)

2-4 capsules daily, in divided doses, between meals.
NeuroPure: Comprehensive support*

Serotonin and dopamine levels are determined by a dynamic balance of biosynthesis and degradation. While supplying amino acids and cofactors supports biosynthesis, stabilizing serotonin and dopamine by targeting the enzymes accountable for degradation presents an advanced approach to supporting healthy neurotransmission.*

**Maintaining serotonin levels by targeting indoleamine 2,3-dioxygenase (IDO)**

The serotonin precursor, tryptophan, is obtained from dietary protein. Once in the brain, it is subject to degradation by the enzyme indoleamine 2,3-dioxygenase (IDO). Depletion of active tryptophan by IDO produces metabolites that activate excitatory pathways involving glutamate receptors, which negatively influence both mood and emotional health. Protection from excessive glutamate receptor activation is a well-researched avenue toward serotonin support and emotional well-being. Since IDO is activated by oxidative stress, maintaining antioxidant protection with curcumin and quercetin helps to maintain healthy tryptophan levels for serotonin production.*

**Maintaining general neurotransmitter pools by targeting monoamine oxidase (MAO)**

MAO is an enzyme present in neurons that is responsible for oxidative degradation of dopamine and serotonin. Phenylethylamine (PEA), a metabolite of the amino acid phenylalanine that enhances the release of dopamine and serotonin, is also degraded by MAO. Recent studies show that curcumin, quercetin and grape seed proanthocyanidins directly modulate this enzyme to maintain the stability of these neurotransmitters.*

**NeuroPure: Offers key nutrients to support overall neurotransmitter function, neuronal health and emotional balance**

- Promotes the production of both serotonin and dopamine*
- Includes the serotonin and dopamine neurotransmitter precursors 5-HTP and dl-phenylalanine*
- Contains the synergistic cofactors vitamin B₆, Metafolin® L-5-MTHF and zinc to support neurotransmitter production*
- Enhances phenylethylamine (PEA) activity to boost mood and alertness*
- Supports healthy serotonin receptor and modulates healthy monoamine oxidase enzyme function with curcumin*
- Maintains healthy cytokine balance with curcumin and quercetin to support neurotransmitter synthesis and emotional balance*
- Supports optimal serum levels of zinc and folate to promote positive mood*

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Phytosome More Bioavailable is a trademark of Indena S.p.A.

Metafolin® is a registered trademark of Merck KGaA, Darmstadt, Germany.
**Integrative Mental Health: Mechanistic Overview**

**Figure 3.** DopaPlus supports dopamine synthesis while maintaining healthy reuptake and degradation via MAO and COMT. SeroPlus supports serotonin synthesis, maintains healthy reuptake and supports postsynaptic receptor function. NeuroPure delivers generalized support for emotional wellness through targeting IDO, glutamate receptor activation, serotonin synthesis, COMT and MAO.*

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