WHITEPAPER 2022

THE SCIENCE BEHIND UPDATE



ABSTRACT

We are excited to introduce you to Update™, a new caffeine-free, sugar-free energy drink. Update™ leverages a new ingredient called paraxanthine, which is a metabolite of caffeine that provides everything you love about caffeine and energy drinks without the side effects you're used to (no crash, no jitters, no digestive consequences etc.).

This whitepaper is our attempt to open source our learnings and present the science behind Update™.

As a company, we believe in transparency and make every effort to build in public, bringing awareness to what we are doing in real time. This whitepaper is just one aspect of that and we will continue to learn, iterate and share our findings as they come up.

If there is anything you think we are missing or could improve upon, please let us know.



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CAFFEINE

For most people, it's hard to imagine a day that starts without a cup of coffee. In fact, 85% of Americans consume caffeine daily¹, making It the most consumed psychoactive substance in the world. We crave caffeine because it stimulates our central nervous system and shortly after consuming it, we get a jolt of energy and a boost of alertness and attention. Despite the widespread use of caffeine, not all consumers are created equal. Due to variability in genetics, many don't get the full benefits from caffeine, instead suffering several side effects².

So what exactly is caffeine?

Caffeine is a methylxanthine, a compound with physiological effects that is commonly known for its stimulatory qualities. The substance is often synthesized and also occurs naturally in plants and fruits, and it is typically consumed in beverages like coffee, tea, soda, and energy drinks. The caffeine molecule is typically absorbed into the blood within 45 minutes of consumption, where it is mostly broken down in the liver by P450 enzymes. It has a 5–7 hour half-life³ with variability related to several genetic and environmental factors.

How does caffeine work?

Humans need a constant supply of energy. We get this by metabolizing an energy molecule called adenosine triphosphate (ATP)⁴. In the process of breaking down this molecule, adenosine is released – the body's key sleep-inducing molecule. Adenosine helps regulate the daily sleep-wake cycle. It binds to neurons in the brain, causing them to slow down their signals. As a result, we get tired. The molecule also inhibits the dopamine pathways responsible for promoting good moods and pleasure sensations⁵.

The caffeine molecule has a similar structure to adenosine, so when you consume caffeine, it binds to the receptors in its place. This prevents adenosine from binding to neurons, and stops us from slowing down⁶, so we feel less tired and more stimulated. While caffeine does temporarily block the adenosine neuromodulator, it does not stop the brain from producing adenosine. As caffeine wears off, adenosine floods the brain, and this why we "crash"⁷.

Caffeine sensitivity varies amongst individuals

Humans metabolize caffeine at different rates⁸. The key determinant is a genetic factor known as the CYP1A2 gene, which produces the enzyme that breaks down caffeine in our bodies. We have two copies of the CYP1A2 gene, one inherited from each parent. The gene has two forms (alleles), a fast version and a slow version. If you have two fast versions, you are considered a fast metabolizer. You're the person who can have a coffee and go "straight to bed". If you have two slow versions, you are considered a slow

https://pubmed.ncbi.nlm.nih.gov/24189158/

² https://pharmrev.aspetjournals.org/content/70/2/384#sec-8

³ https://link.springer.com/chapter/10.1007/978-3-642-13443-2_3

⁴ https://www.ncbi.nlm.nih.gov/books/NBK553175/

⁵ https://pubmed.ncbi.nlm.nih.gov/15767841/

⁶ https://thebrain.mcgill.ca/flash/i/i_03/i_03_m/i_03_m_par/i_03_m_par_cafeine.html

⁷ https://www.caffeineinformer.com/caffeine-hangover-caffeine-crash

[%]https://assets-global.website-files.com/61278f4a0fe77893a00f1f11/613ded271ac7a9355c1b3516_Caffeine_Metabolism_ Report-DESIGNED-290518.pdf

metabolizer. You probably feel jittery and can't fall asleep if you have too much coffee or drink it too late in the day⁹.

About 59% of the population are slow metabolizers, getting fewer benefits from caffeine and increased negative side effects¹⁰.

Surprisingly, neither group experiences the optimal effects from caffeine. For the former, it is a short-lived experience while the latter are plagued with negative side effects. Some of the population fall into the moderate metabolizer group, and they typically have the best experience with caffeine.

Drawbacks of caffeine

If you don't fall into the fast metabolizer group, you are likely well acquainted with the side effects that caffeine has to offer¹¹.

- **Dependency and tolerance buildup** Over time, your brain produces more adenosine to counteract that which is inhibited by caffeine consumption. To maintain that alert and wakeful feeling, we need to consume even more caffeine to block the greater number of adenosine molecules¹². This contributes to a snowball effect of increasing caffeine consumption.
- **Withdrawal** If you start consuming less caffeine, or stop altogether, withdrawal symptoms such as headaches and irritability may occur¹³.
- **Deteriorating sleep** Blocking adenosine indirectly inhibits the release of dopamine and serotonin¹⁴. Consequently, caffeine can disrupt your sleep quality and reduce your ability to reach REM (deep) sleep¹⁵.
- **Increased anxiety, jitters and stress** Caffeine consumption increases epinephrine and cortisol, which increase stress and anxiety¹⁶.
- **Stomach aches, urination problems, and digestive issues** Caffeine consumption increases the rate of gastric emptying. It is also a diuretic, which causes dehydration¹⁷.
- **Crash** As mentioned, caffeine's inhibitive effect on adenosine production creates a buildup of the molecule, which culminates in an eventual crash once it wears off.

What's next for caffeine?

More recently, consumers have been seeking healthier and cleaner sources of caffeine. As a result, substances like yerba maté, matcha, guayusa leaf, guarana, kola nut and green tea extract have been growing in popularity¹⁸ among health-conscious consumers. While these sources may be healthier, they still don't address the inherent downside of caffeine. As caffeine is still the root of energy in these ingredients, its negative physiological effects remain.

 $^{{\}it https://assets-global.website-files.com/61278f4a0fe77893a00f1f11/613ded271ac7a9355c1b3516_Caffeine_Metabolism_Report-DESIGNED-290518.pdf}$

https://selfdecode.com/blog/article/caffeine-heart-disease-cyp1a2-55/

¹¹ https://www.fda.gov/consumers/consumer-updates/spilling-beans-how-much-caffeine-too-much

https://pubmed.ncbi.nlm.nih.gov/6298543/

https://pubmed.ncbi.nlm.nih.gov/3772801/

https://www.ncbi.nlm.nih.gov/books/NBK223808/

https://www.sciencedirect.com/science/article/abs/pii/S1087079216000150

https://pubmed.ncbi.nlm.nih.gov/2195579/

https://pubmed.ncbi.nlm.nih.gov/19774754/

https://wholefoodsmagazine.com/front-page/raise-a-glass-to-healthy-energy/

Caffeine's metabolites

While caffeine is often touted for its energy-boosting properties, what is often overlooked are its metabolites - the resulting molecules caffeine breaks down. Metabolites might actually be responsible for most of the benefits and drawbacks of caffeine.

When we consume caffeine and it's metabolized in the liver, it breaks down primarily into three molecules 19:

- 1. Paraxanthine
- 2. Theobromine
- 3. Theophylline

Paraxanthine is the major metabolite in humans, with about 80% of caffeine intake becoming this molecule after it is broken down by the body. It belongs to the same methylxanthine family as caffeine, though it is the least familiar of the three and the least common. Paraxanthine is most likely to have greater universal appeal, given it doesn't exhibit the negative side effects of caffeine, theobromine, and theophylline²⁰.

Theophylline is used in therapy for respiratory diseases like asthma, or chronic obstructive pulmonary disease. Its side effects include nausea, diarrhea, increased heart rate, and arrhythmia. Due to the severity of its side effects, theophylline is becoming less desirable as a solution for the afflictions it is used to treat²¹.

Theobromine is usually found in cacao, tea leaves, and coffee beans. While it has similar properties to caffeine, it is also less effective. Llke theophylline, this substance also contributes to side effects of caffeine intake, which include headaches, sweating, trembling, jitters, and digestive issues²².

¹⁹ https://www.ncbi.nlm.nih.gov/books/NBK223808/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6273298/

²¹ https://www.clinicalkey.com/#!/content/book/3-s2.0-B9780323655873000647

 $[\]label{lem:condition} $22 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3672386/\#: $$\sim: text=While%20 the obromine%20 did%20 not%20 significantly, of%20 individual%20 differences%20 in%20 sensitivity.$

PARAXANTHINE

Paraxanthine, or 1,7-dimethylxanthine, is a natural dietary component, and the main metabolite of caffeine in humans²³. The substance, like caffeine can be synthesized for use and also occurs naturally in various plant species like grapefruit, cocoa, and tea²⁴. When caffeine is broken down in the liver, \sim 80% of it converts to paraxanthine²⁵.

Like caffeine, paraxanthine is a central nervous stimulant with similar anti-adenosine actions, though research has consistently reported that paraxanthine exhibits slightly higher binding potency for adenosine A1 and A2A receptors. Essentially, this means paraxanthine promotes wakefulness and enhance alertness more effectively than caffeine 26 .

Paraxanthine has also displayed lower toxicity and lesser anxiety driven effects than caffeine.²⁷ This could be explained by the pharmacological properties of other caffeine metabolites. For instance, theophylline, has a narrow therapeutic window with several negative side effects, as detailed above. Similarly, theobromine has a lower potency as a central nervous system stimulant than caffeine, but stimulates the heart more dramatically.

Benefits of Paraxanthine

The following are the benefits of paraxanthine:

- The wake-promoting effect of caffeine is the most desirable to consumers, and paraxanthine has proven to be a more effective agent for promoting wakefulness due to its greater affinity for A1/A2 adenosine receptors in the brain.
- Paraxanthine does not induce sleep rebound, hypothermia, or anxiety, while caffeine does.
- Unlike caffeine, paraxanthine provides neuroprotective benefits by warding against dopaminergic cell death. This suggests that paraxanthine is a better wake-promoting supplement for normal consumption, as well as those suffering from neurological conditions.²⁹
- Paraxanthine benefits sustained attention, reaction time, and short-term memory³⁰.
- It helps with reasoning and response time to cognitive challenges, as well as help sustain attention.³¹
- There were no additional benefits when caffeine was added to paraxanthine supplementation.³²
- Human studies with paraxanthine have not reported withdrawal effects previously noted with caffeine.³³
- Paraxanthine may play a role in increased lipolysis (burning fat).³⁴

 $^{^{23}} https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3562388/\#: \sim: text = Caffeine \% 20 is \% 20 metabolized \% 20 to \% 20 several, of \% 20 caffeine \% 20 Caffeine \% 20 to \% 20 and \% 20 the obrowine.$

²⁴ https://www.sciencedirect.com/science/article/abs/pii/S0031942299001193?via%3Dihub

https://link.springer.com/article/10.1007%2FBF00987675

https://www.sciencedirect.com/science/article/abs/pii/S0176161704705970?via%3Dihub

 $^{^{25}} https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3562388/\#: \sim : text = Caffeine \% 20 is \% 20 metabolized \% 20 to \% 20 several, of \% 20 caffeine \% 20 Caffeine \% 20 to \% 20 to \% 20 to \% 20 metabolized \% 20 metab$

²⁶ https://www.sciencedirect.com/topics/neuroscience/paraxanthine

 $^{^{27}\ \}text{https://www.sciencedirect.com/science/article/abs/pii/0278691588900737?via\%3Dihub}$

²⁸ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2894435/

²⁹ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2894435/

³⁰ https://www.mdpi.com/2072-6643/13/11/3980

³¹ https://www.mdpi.com/2072-6643/13/11/3980

³² https://www.mdpi.com/2072-6643/14/4/893

³³ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4389645/

 $^{^{34}}$ https://www.jstage.jst.go.jp/article/jnsv1973/47/2/47_2_139/_pdf/-char/en

Why has it taken this long for people to become aware of paraxanthine?

For a product that's so effective without much downside, it's reasonable to wonder why no one had cracked its code before, just as we did. There is some interest on social media and inquiries about its availability, but not as much as you might expect after reading about its benefits. The following are the primary factors we believe are adversely affecting its popularity:

- Complexity Our scientific team, Ingenious Ingredients has been working to isolate paraxanthine (enfinity®) for over 8 years. Unlocking its potential is no easy feat.
- Perception Given that ~80% of caffeine breaks down into paraxanthine, some have perceived that
 isolating and synthesizing paraxanthine was unnecessary. They may not be considering the
 additional negative effects of theobromine and theophylline, however.
- Manufacturing methods Producing paraxanthine was previously a monetary challenge, because
 the compound only occurs in large amounts in the human body as a result of caffeine metabolism.
 Only trace amounts are produced in plants. Synthetic methods to produce it were complex,
 inefficient, and expensive, evidenced by the current cost of paraxanthine exceeding \$1,950 per kg
 from the few non-ING2 suppliers).
- GRAS certification Before our exclusive partners and paraxanthine suppliers ING2 self affirmed GRAS, no other group had completed the necessary clinical studies to do so, making paraxanthine unusable in food items until now.
- Intellectual property Our scientific partners have filed numerous patents for the use of paraxanthine.

How is it paraxanthine made?

Ingenious Ingredients, Update's exclusive scientific partners have developed a proprietary method to manufacture paraxanthine and they have branded the end product as enfinity®. This method involves a series of scientific reactions incorporating specific ingredients with one another.

Paraxanthine clinical studies

Many clinical studies discuss paraxanthine. To make sure we're not relying on the information of others, our scientific partners, Ingenious Ingredients, have recently conducted their own research on paraxanthine (enfinity®). The results are displayed below:

CLINICAL STUDY #1

200MG PARAXANTHINE VS. PLACEBO

Design: Double-blind, placebo-controlled, crossover, trial

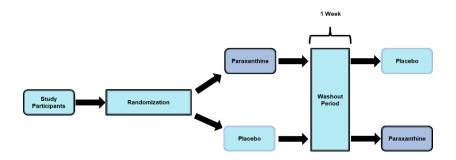
Intervention: 200mg paraxanthine or placebo, 1 week washout

Subjects: 13 healthy male (n=10) and female (n=3) subjects (age: 24±5 years, height: 170.0±11.8 cm,

weight 72.9±19.3 kg)

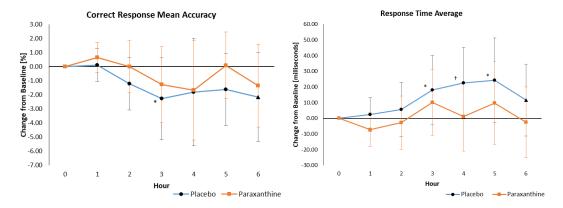
Measures at baseline: 1, 2, 3, 4, 5, and 6 hours after supplementation:

- Attention and impulsivity control (Go/No Go Test)
- Ability to remain heedfully vigilant (Vigilance Task Test)
- Short-term/working memory (Sternberg Test)
- Cognitive flexibility (Berg-Washington Card Sorting Task Test)



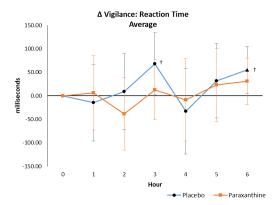
Results for attention and inhibitory control:

- Paraxanthine supplementation resulted in faster response times (shows less metal fatigue)
- Paraxanthine maintained percentage of correct answers, while placebo showed a significant decrease in correct answers
- Paraxanthine increased the capacity for sustained attention and response control



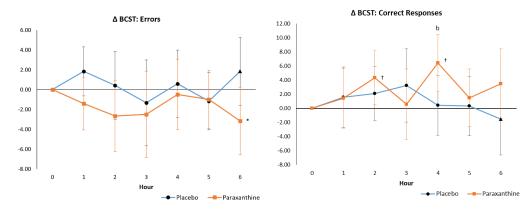
Results for sustained attention:

- Paraxanthine resulted in sustained attention (maintained reaction times, prevention of mental fatigue), measuring a person's ability to remain heedfully vigilant
- In contrast, placebo showed significantly reduced reactions times (overall hours 3 and 6)



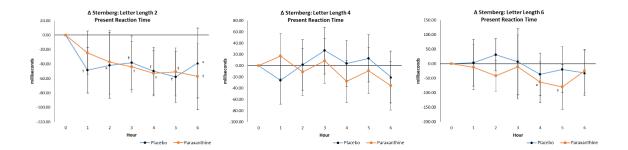
Results for cognitive flexibility:

- Paraxanthine significantly increased the number of correct answers, while reducing the number of errors
- Paraxanthine increased cognitive flexibility or set-shifting between old/new rule changes



Results for working memory:

- Paraxanthine decreased mean response times by 3.9% (faster) compared to baseline, whereas the placebo group was 2.7% faster
- Paraxanthine significantly increased short-term/working memory in one measure (letter length 6, present reaction time after 4 and 5 hours, see figure below on the right)
- As the list length increases, probe judgments become less accurate and slower, indicating increases in short-term memory and working memory demands



Read the full study <u>here</u>.

CLINICAL STUDY #2

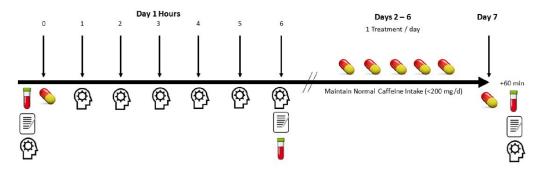
200MG PARAXANTHINE VS. 100MG PARAXANTHINE VS. 50MG PARAXANTHINE VS. PLACEBO

Design: Double-blind, placebo-controlled, crossover, trial

Intervention: 200 mg paraxanthine or 100 mg paraxanthine or 50 mg paraxanthine or placebo, 1 week washout

Measures at baseline: 1, 2, 3, 4, 5, and 6 hours after supplementation, and 1 hour after 1 week repeated supplementation:

- Attention and impulsivity control
- Ability to remain heedfully vigilant
- Short-term/working memory
- Cognitive flexibility



Key findings:

- Paraxanthine improves
 - Short-term memory
 - Reasoning
 - o Response time to cognitive challenge
 - Attention
- No habituation effect (no diminished effects of repeated supplementation)
- Paraxanthine in as little as 50mg shows cognitive benefits, however, higher doses studied seem to have greater benefits

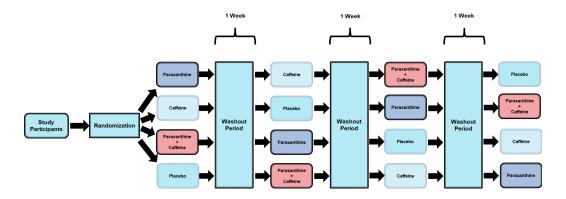
Read the full study here.

CLINICAL STUDY #3

200MG PARAXANTHINE VS. 200MG CAFFEINE VS. 200MG PARAXANTHINE + 200MG CAFFEINE VS. PLACEBO

Design: Double-blind, placebo-controlled, crossover, trial

Intervention: 200mg paraxanthine or 200mg caffeine or 200mg paraxanthine + 200mg caffeine placebo, 1 week washout



Subjects: 12 healthy trained male runners (age: 26 ± 5 years, weight: 68.5 ± 9.2 kg, BMI: 22.2 ± 2.7 kg/m2, 16.2 ± 5 % fat, 52.4 ± 10 ml/kg/min VO_{2peak})

Testing:

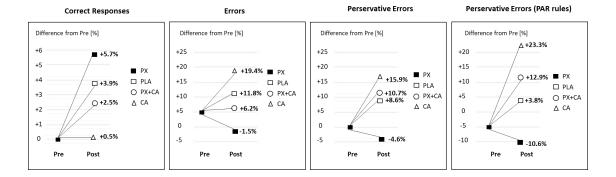
- Baseline cognition tests (PRE)
- Ingest supplement, 60 min rest
- Pre-race cognition test (PRE-EX, effect of supplementation)
- 10-km run on a treadmill (48.4±6.7 min)
- Post-race cognition test (POST-EX, effect of supplementation and exercise)

Measures:

- Ability to remain heedfully vigilant (Vigilance Task Test)
- Cognitive flexibility (Berg-Washington Card Sorting Task Test)

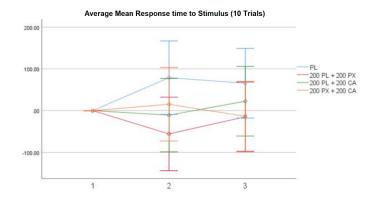
Results for cognitive flexibility:

- Paraxanthine increases processing speed and reduces errors, while caffeine actually increases the amount of errors (aka, overstimulated, rushing through a task and thereby making more mistakes. Paraxanthine didn't show an increase in errors)
- Paraxanthine increased correct responses and reduced errors, caffeine increased errors
- POST-EX all groups, but paraxanthine increased total errors (fatigue). Paraxanthine significantly improved errors over caffeine (p=0.04, paraxanthine -10.6%, caffeine +23.3%)
- Paraxanthine tended to have faster response times POST-EX in comparison to PL (p=0.096).



Results for sustained attention:

- Paraxanthine showed faster response times POST-EX in comparison to PL (p=0.047), and caffeine (p=0.047)
- Paraxanthine showed faster response times PRE-EX (post supplementation) in comparison to PL (p=0.035)



Read the full study <u>here</u>.

Additional areas of study currently underway include:

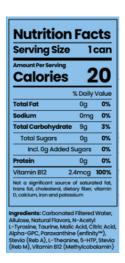
- E-Sports
- Weight management (lipolysis, thermogenesis)
- Cognition
- Sports nutrition (swagger, performance)

A deeper look inside the Update formula

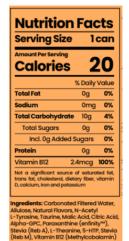
We have spent over two years working with leading scientists, researchers, and physicians to develop the Update formula. It was important to us that every ingredient and dose was supported by science and peer-reviewed research. Consequently, our formula is complex and expensive to produce. We use only the effective doses for our ingredients, we don't just feather dust them in. While we engineered Update around its most groundbreaking ingredient, paraxanthine, we also refined it with several powerful nootropics to enhance the overall formula to give consumers more sustainable energy throughout the day.

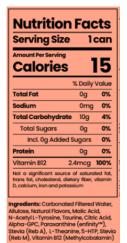
Summary of our nootropic stack:

- **Paraxanthine** Our main ingredient is a highly wake-promoting compound considered more effective and less toxic than caffeine. It boosts energy, confidence, and attention, as well as cognitive and executive function.
- N-Acetyl L-Tyrosine An amino acid precursor to dopamine for enhanced focus and epinephrine
 for enhanced alertness. It's also a precursor to the thyroid hormones that throttle our bodies'
 metabolic rates and energy levels. Tyrosine is a conditionally essential amino acid required by the
 body in times of anxiety to relieve stress. The acetylation of aminos changes their action and
 allows them to more readily pass the blood brain barrier.
- Alpha GPC A compound that rapidly crosses the blood-brain barrier as a precursor to acetylcholine for memory formation and enhances muscular power output, sharpens agility, and delays fatigue.
- **L-Theanine** An amino acid found in green tea, which works with paraxanthine to promote relaxed alertness, attention, and task-switching.
- **Taurine** In the brain, it is neuroprotective, and can modulate the levels of other neurotransmitters like GABA for calming effects, and act as a neurotransmitter itself.
- **5-HTP** A precursor to serotonin for mood elevation. Tryptophan (5-HTP) is an essential amino acid that must be provided to the body from external sources since we don't produce it naturally.
- Vitamin B12 (Methylcobalamin) A form(vitamer) of Vitamin B12, which is active in the cytoplasm
 and required for many cellular functions, especially in the nervous system, bone marrow, and in
 DNA synthesis.









N-ACETYL L-TYROSINE

N-Acetyl L-Tyrosine is the acetylated, more stable, highly soluble, and bioavailable form of L-tyrosine. Tyrosine is an amino acid your body uses to make protein and is a building block for the synthesis of many neurotransmitters such as epinephrine, norepinephrine and dopamine³⁵.

Your body converts L-Tyrosine into L-DOPA which is a precursor to the neurotransmitter dopamine and eventually neurotransmitters epinephrine and norepinephrine³⁶. As your dopamine levels increase, you're better able to concentrate, organize your thoughts, and stay productive.

Tyrosine supplementation has been shown to maintain and improve cognitive performance under stressful environments³⁷. Increasing Tyrosine levels has been found to counteract decreases in working memory and information processing that are induced by demanding situational conditions³⁸. This may be explained by tyrosine's ability to restore and maintain epinephrine, norepinephrine and dopamine levels amidst natural environmental factors that otherwise would see a decline in such neurotransmitters³⁹.

Key benefits of N-Acetyl L-Tyrosine

- Levels out and may increase catecholamine neurotransmitters: epinephrine, norepinephrine and dopamine⁴⁰
- Can improve cognitive performance under stressful situations⁴¹
- Supports working memory and one's ability to process information⁴²
- Promotes deep thinking⁴³
- Enhances cognitive flexibility (i.e. reduced switching cost between tasks)⁴⁴

N-Acetyl L-Tyrosine used by Update™ is certified:

- GRAS
- Kosher
- Gluten Free
- Non-GMO
- Vegan

 $^{^{35}} https://www.differencebetween.com/difference-between-1-tyrosine-and-vs-tyrosine/\#:\sim:text=1\%2Dtyrosine\%20is\%20the\%20most,neurotransmitters\%2C\%20melamine\%2C\%20and\%20hormones.$

https://www.sciencedirect.com/science/article/abs/pii/S0091305715000945?via%3Dihub

³⁷ https://www.sciencedirect.com/science/article/abs/pii/0361923094902003?via%3Dihub

³⁸ https://www.sciencedirect.com/science/article/abs/pii/S0091305715000945?via%3Dihub

³⁹ https://pubmed.ncbi.nlm.nih.gov/25797188/

⁴⁰https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4325185/#:~:text=Thus%2C%20supplemental%20tyrosine%20can%20increase,of%20stress%20(Leh nert%20et%20al.

 $^{^{41}} https://pubmed.ncbi.nlm.nih.gov/8293316/\#: \sim : text=While \%20 performing \%20a\%20 number \%20of, as \%20 highly \%20 sensitive \%20 to \%20 stress.$

⁴² https://www.sciencedirect.com/science/article/abs/pii/S0091305799000945

⁴³ https://link.springer.com/article/10.1007/s00426-014-0610-4

⁴⁴ https://www.sciencedirect.com/science/article/abs/pii/S0028393215000299?via%3Dihub

ALPHA-GPC

Alpha-glycerophosphocholine (Alpha-GPC) is a choline-containing phospholipid and is a highly bioavailable source of choline for the brain⁴⁵. Alpha-GPC is metabolized into choline which is a precursor to the neurotransmitter, acetylcholine. Alpha-GPC boosts choline and the release of acetylcholine and these are both important drivers for many cognitive functions: working memory, attention, reasoning, spatial memory and the growth of new synapses (neuroplasticity)⁴⁶.

Alpha-GPC also plays a role in muscle movement. There is a positive correlation relationship between choline levels and growth hormone secretion. Therefore, by augmenting choline you may enhance muscle performance⁴⁷.

Key benefits of Alpha-GPC

- Choline and acetylcholine improve synaptic plasticity and enhance the processing and memory formation of stimuli⁴⁸
- Improves information processing and cognitive function⁴⁹
- Maintain muscle performance after exhaustive exercise⁵⁰
- May enhance muscle performance⁵¹

Alpha-GPC used by Update[™] is certified:

- GRAS
- Kosher
- Gluten Free
- Non-GMO
- Vegan

45 https://examine.com/supplements/alpha-gpc/

⁴⁶ https://www.sciencedirect.com/science/article/pii/0896627395900942?via%3Dihub

⁴⁷ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4650143/

⁴⁸ https://www.frontiersin.org/articles/10.3389/fnbeh.2012.00024/full#h4

⁴⁹ https://www.frontiersin.org/articles/10.3389/fnbeh.2012.00024/full#h3

⁵⁰ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4650143/

⁵¹ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4650143/

L-THEANINE

L-Theanine is an amino acid found most commonly in green tea. L-Theanine enhances alpha brain waves which are associated and correlate with an alert and relaxed state of mind, reducing stress, the perception of stress and promoting cognitive function.

L-Theanine is considered a nootropic and modulates brain waves. It boosts neurotransmitters GABA, serotonin and dopamine levels in the brain and increases Brain-Derived Neurotrophic Factor (BDNF) and Nerve Growth Factor (NGF) thus improving thinking speed, memory, and mood.

L-Theanine may also protect the brain from overstimulation caused by an increase in the glutamate neurotransmitter.

Key benefits of L-Theanine

- Promotes an alert state of relaxation without drowsiness, as indicated by an increase in Alpha brain waves, and a decrease in Beta brain waves⁵²
- Relaxed alertness⁵³
- Improving thinking speed, memory, and mood⁵⁴
- Enhance mental relaxation and concentration⁵⁵
- Reduces acute psychological and physiological stress feelings⁵⁶
- Support cognitive function⁵⁷

L-Theanine used by Update[™] is certified:

- GRAS
- Kosher
- Gluten Free
- Non-GMO
- Vegan

⁵² https://www.liebertpub.com/doi/abs/10.1089/10762800151125092

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6836118/

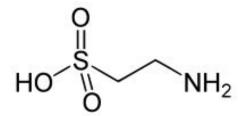
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8080935/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8080935/

⁵⁶ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6836118/

⁵⁷ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8080935/

TAURINE



Taurine is a sulfur-containing amino acid, one of the most abundant in the human body found in almost all human tissue and in the central nervous system⁵⁸. Taurine is considered a "conditional" amino acid because some of this amino acid is synthesized naturally in your body. The synthesis of taurine in the body is relatively slow compared to what one physiologically needs, and therefore supplementing it can be beneficial.

In the brain, taurine is neuroprotective. It can modulate the levels of other neurotransmitters and be calming since it aids the neurotransmitter GABA⁵⁹. Hence, during prolonged exercise, taurine can aid in endurance by reducing the stress hormones.

Key benefits of Taurine

- It can keep our nervous system relaxed⁶⁰
- It's cytoprotective and contributes to overall brain and muscle health⁶¹
- It's an antioxidant supporting healthy vision⁶²

Taurine used by Update™ is certified:

- GRAS
- Kosher
- Gluten Free
- Non-GMO
- Vegan

⁵⁸https://pubmed.ncbi.nlm.nih.gov/30892104/#:~:text=It%20is%20known%20that%20taurine,GABAA%20and%20GABAB.

⁵⁹ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5933890/

⁶⁹https://pubmed.ncbi.nlm.nih.gov/30892104/#:~:text=It%20is%20known%20that%20taurine,GABAA%20and%20GABAB

⁶¹ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5933890/

⁶² https://pubmed.ncbi.nlm.nih.gov/14752617/

5-HTP

5-HTP is a chemical that the body makes from an essential amino acid, tryptophan (An essential amino acid means your body does not make it and it needs it from the diet to live/thrive). Once converted from tryptophan into 5-HTP, the body converts 5-HTP to the neurotransmitter serotonin, a chemical that serves many functions related to mood, sleep, appetite, and pain sensation⁶³. An increase in serotonin levels may elevate overall mood.

Most of your body's serotonin is made in the intestines however, it cannot cross the blood brain barrier. Therefore, the serotonin your brain needs must be made in the brain and this is where 5-HTP comes in. 5-HTP crosses the blood-brain barrier more readily than tryptophan. And gets synthesized into serotonin at a faster rate than from tryptophan⁶⁴.

Key benefits of 5-HTP

- A precursor to the synthesis of serotonin⁶⁵
- Supports boosted mood⁶⁶

5-HTP used by Update™ is certified:

- GRAS
- Kosher
- Gluten Free
- Non-GMO
- Vegan

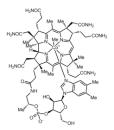
⁶³ https://www.opss.org/article/5-htp-depression-and-other-conditions

⁶⁴ https://pubmed.ncbi.nlm.nih.gov/9727088/

 $^{^{65}} https://pubmed.ncbi.nlm.nih.gov/9727088/\#: \sim: text = 5\% 2DHTP\% 20 is \%20 well \%20 absorbed, (CNS)\%20 synthesis \%20 of \%20 serotonin.$

⁶⁶ https://pubmed.ncbi.nlm.nih.gov/16023217/

VITAMIN B12 (METHYLCOBALAMIN)



Vitamin B12 is a nutrient required for many cellular functions especially in the nervous system, bone marrow, and in DNA synthesis.

Vitamin B12 is a cobalt-containing compound and as such also known as Cobalamin. Vitamin B12 can be converted to either of the two cobalamin coenzymes that are active in human metabolism: methylcobalamin and 5-deoxyadenosylcobalamin⁶⁷.

And while Vitamin B12 is available in many forms (methylcobalamin, adenosylcobalamin, hydroxycobalamin and cyanocobalamin) methylcobalamin is the metabolically active form of vitamin B12 and more highly bioavailable and does not contain cyanide like cyanocobalamin⁶⁸.

Key benefits of Vitamin B12

- Required for the development and function of the central nervous system.⁶⁹
- A cofactor in the synthesis of neurotransmitters dopamine, GABA, norepinephrine, and serotonin thus affecting alertness, cognition, memory, and mood.⁷⁰

Vitamin B12 used by Update™ is certified:

- GRAS
- Kosher
- Gluten Free
- Non-GMO
- Vegan

⁶⁷ https://www.ncbi.nlm.nih.gov/books/NBK114302/

⁶⁸ https://ods.od.nih.gov/factsheets/VitaminB12-HealthProfessional/

⁶⁹ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6930825/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3262614/

OUR FLAVOR ENHANCEMENT SYSTEM

Working with a leading flavor house, we used the latest technologies on front to back sweetening to keep everything high impact on taste and low impact on calories. Our specific blend of natural sweeteners: allulose and stevia glycosides proved to be the optimal mix to pair with our functional stack. Unlike many energy drinks that use synthetic sweeteners, it was important that our sweeteners were not only natural, but also clean tasting and low in calories.

Allulose

Allulose is a natural sweetener with a similar taste and textural profile to sugar, except it has 1/10th the amount of calories and it is 70% as sweet. Allulose is not metabolized in the human body, but absorbed and excreted through the kidneys. It contributes very little to calories, so it doesn't elicit a physiological response like other sweeteners that provoke spikes and crashes. Allulose does not increase blood sugar levels.

Steviol glycosides

Stevia rebaudiana Bertoni (Stevia) is a plant found in South America. Eight different Stevia sweeteners are formed by extracting and purifying steviol glycosides from the dried leaves of the Stevia plant. We selected the non-caloric sweeteners Rebaudioside A (Reb A) and Rebaudioside M (Reb M) to enhance Update's taste profile. Both extracts sweeten different ends of the palette, providing a full, natural taste profile. Our work shows they have great synergy in the right ratios.

Sourcing ingredients

Each of our ingredients is based on benefits measured by peer-reviewed scientific research and dosed at scientifically deemed effective levels. This increases the cost of the formula, but we accept this as part of creating something truly revolutionary.

We also try and adhere to naturalist, ethical, and religious concerns, so all our ingredients are:

- GRAS
- Kosher
- Vegan
- Gluten Free
- Non-GMO

THE TEAM BEHIND UPDATE

Update is led by a group of best friends and supported by an experienced group of scientific advisors who each contributed to the creation of our formula.

Daniel Solomons

Co-founder

Michael Hess

Co-founder

Justin Hauser

Co-founder

David Hess

Co-founder

Scientific Advisory Team

Shawn Wells

Shawn is known as the "Ingredientologist", the scientist of ingredients. Having over 20 years in the industry, patents on over 15 novel ingredients (R-BHB, dihydroberberine, theacrine, and many more) that are in thousands of products and having formulated over 700 products, he's cemented his reputation in the industry as a go-to mind with all things supplements.

Dr Ralf Jäger

Dr. Jäger is a world-class inventor of functional foods and dietary supplements, as well as an award-winning speaker in these subject areas. He has developed many new products that currently lead the market in the supplement industry, as well as having designed and conducted clinical studies on prominent ingredients and respected products.

Dr Martin Purpura

Dr. Purpura is a highly regarded expert in new product development in the nutritional and health category, and guides companies from concept to commercialization. An earned his doctorate in organic chemistry from the University of Bonn, Germany.

Kylin Liao

Kylin Liao is the founder and CEO of NNB Nutrition. He graduated with a Masters in Chemistry and has more than 10 years of experience in the dietary supplement industry. He has built a 9-figure business with over 100 employees in more than 10 countries.

Dr Ted Achacoso

Dr. Ted Achacoso attained a college degree in biology at the age of 18 and a doctor of medicine at the age of 22. He is the founding pioneer of the clinical practice of Health Optimization Medicine and Practice (HOMe/HOPe), which is the detection and correction of imbalances at the level of the metabolome.

David Tomen

David started nootropicsexpert.com to showcase his work to find new, safe ways to boost mental performance. His research is a source for the world of nootropics, the latest neuroscience research, and tips for boosting your brainpower. He is also the author of Secrets of the Optimized Brain and Head First.

APPENDIX

WHAT ARE NOOTROPICS?

no·o·trop·ic /nō-ə-'trō-pik/ comes from the *Greek* words "noos" meaning "mind or intellect" and "tropos" meaning "turn". Figuratively, it means 'to bend or shape the mind'. The term nootropic was coined by Romanian chemist Dr. Corneliu Giurgea in 1972, to designate compounds that have the following create the following effects:

- Enhance learning acquisition and increase resistance to impairing agents—i.e. enhancing memory and ability to learn.
- Facilitate inter-hemispheric transfer of information. Specifically, to assist brain function under disruptive conditions.
- Enhance brain resistance to physical and chemical injuries, or to protect the brain from toxins.
- Increase cortico-subcortical control--i.e. increasing natural cognitive processes.
- Lack of side effects; specifically, being non-toxic to humans.

The term nootropic usually characterizes a substance--be it an artificial or natural compound--which enhances cognition, memory, alertness, concentration, focus, and facilitates learning.

Nootropics come in two categories: health optimization nootropics and performance optimization nootropics. A health optimization nootropic optimizes the health of the brain, its neural networks, its neurons, and the basic cell from which glial cells and neurons are specialized. A performance optimizing nootropic optimizes the fitness of the brain to perform tasks like memorizing, learning, and focusing without necessarily being healthy for the brain.

How do nootropics work?

Nootropics work by modulating neuronal metabolism, cerebral oxygenation, neurotransmitter availability, increasing neurotrophic factors, and by affecting other cellular processes. In turn, they influence alertness, wakefulness, memory, focus, concentration, and mood.

- They work through multiple pathways
- They tend to cross the blood-brain barrier entering the brain with a higher bioavailability

The exact mechanism of action will depend on the compound.

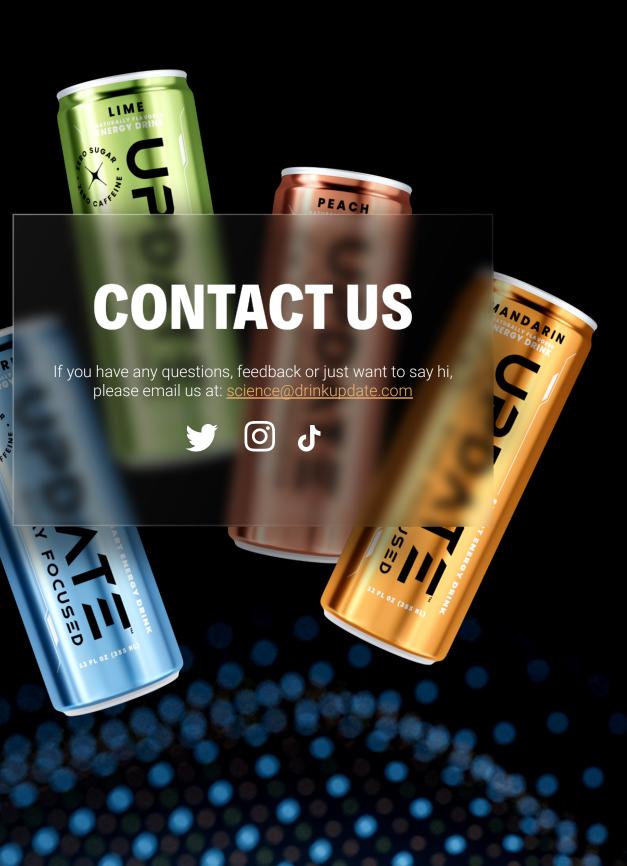
Appendix – Neurotransmitters 101

Neurotransmitters are chemical messengers within the body. They are molecules used by the nervous system to transmit messages between neurons, or from the neurons to muscles. A neurotransmitter influences a neuron in one of three ways:

- 1. Excitatory promotes the generation of electrical signaling in the receiving neuron.
- 2. Inhibitory suppresses and prevents electrical signaling in the receiving neuron.
- 3. Modulatory regulates many neurons at once, usually enhancing the excitatory or inhibitory neurotransmitters

Most neurotransmitters fall into the categories of small amine molecules, amino acids, or neuropeptides. In this document, we will focus on the most common neurotransmitters:

NEUROTRANSMITTER	PRIMARY ASSOCIATION	ROLE THEY PLAY
Acetylcholine	Learning	Necessary for thought, memory and learning and associated with attention. Also needed for muscle activity.
Adrenaline	Flight or flight	Released in stressful situations, increasing blood pressure and heart rate, raising awareness.
Dopamine	Pleasure	Feelings of reward, reinforcement and motivation - pleasure and addiction. Required for memory.
GABA	Calming	Helps balance mood by modulating alpha and beta brainwaves and prevents anxiety driven signals.
Glutamate	Memory	Responsible for sending signals between the neurons and important for learning and memory.
Endorphins	Euphoria	Overall wellbeing and excitement.
Noradrenaline	Concentration	Increases heart rate and blood flow, stimulating concentration, attention and arousal.
Serotonin	Mood	Helps sleep cycle, memory, mood and digestive regulation - wellbeing and happiness



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