FAT BURNER- Scientific Research

Higenamine:

Higenamine is a molecule derived from a variety of fruits and plants that appears to have anti-asthmatic properties via dilating the bronchial tubes (a mechanism known as Beta(2)adrenergic agonism). This mechanism is also the same one underlying the fat burning potential of Ephedrine, and as such Higenamine is currently used as a potent fat burner.

Currently it appears to be similarly potent to some established beta(2)adrenergic agonists in preliminary studies (in regards to anti-asthmatic effects).

Beyond that mechanism, it may also exert anti-inflammatory effects and injections may be useful in a clinical setting against sepsis.

Also Known As

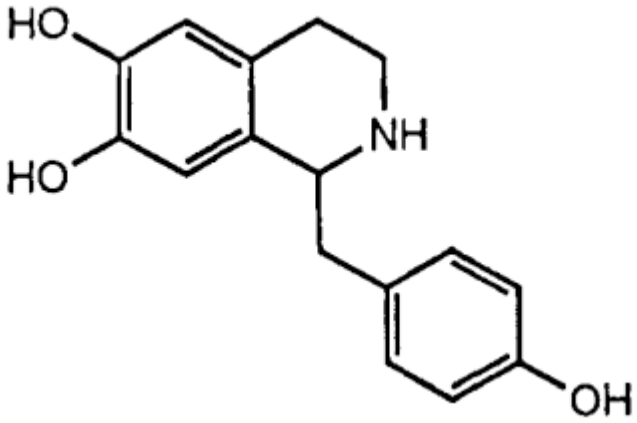
Norcoclaurine, 1-[(4-hydroxyphenyl)methyl]-1, 2, 3, 4-tetrahydroisoquinoline-6, 7-diol

How to Take

Recommended dosage, active amounts, other details
Higenamine tends to be dosed in similar levels as Synephrine or Ephedrine, meaning a dose of 20-30mg taken 2-3 times daily. There is currently no evidence to support this as an optimal dose.

Structure and Properties

Higenamine, also known as norcoclaurine, is known as a benzyltetrahydroisoquinoline.[1]



It is found in ethanol extracts of the plant rather than water extracts alongside the related compound Nantenine.[2] When the extract was divided into 12 sub fragments to isolate the plant compounds, the fragment that contained higenamine (at 49%) was as potent as the plant itself on tracheal relaxation.[2] Despite the ethanol extract above, the structure is highly polar. Higenamine is unstable in basic solution,[11] and has a molecular weight of 271.31g/mol.

Minimal pharmacokinetic data at this moment in time, but Higenamine appears to exert a very rapid absorption phase with a very rapid half-life as well. There appears to be a degree of inter-individual difference in how much Higenamine gets into the blood, which may be mediated by Glucuronidation enzymes (possible synergism with Piperidine fromBlack Pepper if this is the case)

Receptor Interactions

The EC^{50} value of Higenamine in trachea cells is 47.6+/-1.8ng/mL when looking at a fragment of 49% higenamine extracted from *Nandina*.[2] although a molar value of 86.0+/-3.3nM was found when looking at Higenamine in isolation; giving Higenamine itself an EC_{50} of 23.33ng/mL.[2] Synthetic Higenamine appears to have slightly higher EC^{50} than does that derived from *Nandina*.[2]

The IC^{50} value on RAW 264.7 cells (an experimental mouse line of leukocyte immune cells) was 53uM after a 10mg/kg bodyweight I.P injection.[7]

3**Neurology**
Acetylcholine

A concentration of 10uM Higenamine in motor neurons isolated form mice (*in vitro* study) appear to enhance acetylcholine release, and are blocked by propanolol (thus mediated via Beta(2)adrenergic agonism, a known mechanism of Higenamine).[15] Concentrations of 30-100uM Higenamine diminished the ability of motor neurons to release acetylcholine when stimulated, suggesting peak efficacy in the 10-30uM range.[15] Spontaneous release of acetylcholine (without nerve stimulation) was slightly increased.

Possesses possible benefits to muscular output (via increasing acetylcholine release from motor neurons), but no *in vivo* evidence to assess potency nor optimal dose; mechanism is via beta(2)adrenergic activation

Dopamine

At a concentration of 20mM, Higenamine has been shown *in vitro* to deplete dopamine concentrations in PC12 neuronal cells by 55.2% with an IC_{50} of 18.2mM;[16] this was thought to be through inhibition of tyrosine hydroxylase, which converts L-DOPA into dopamine.[17]

May inhibit tyrosine hydroxylase and suppress dopamine, but no *in vivo* evidence exists

Ischemia

In a rat model of MCAO injury (middle cerebral artery occlusion), 10mg/kg Higenamine (not disclosed whether oral or intracerebral) significantly reduce the infarct size suggesting neuroprotective effects under periods of ischemia.[18]

In vitro, it appears Higenamine increases cell viability in a concentration dependent manner up to 10uM where it stabilizes (higher concentrations not being more effective) which may have been secondary to Higenamine inducing expression of HO-1 (Heme-Oxygenase 1; an anti-oxidant protein which downregulates the proinflammatory HMGB1) at concentrations of 10uM or higher in normoxia and only requiring 1uM in periods of hypoxia.[18] In C6 cells (glial cells), Higenamine induced phosphorylation of PI3K/Akt in a concentration dependent manner which was causative of this increase in HO-1 vicariously through activation of Nrf2.[18]

Induction of HO-1 also appears to be the mechanism underlying protection against myocardial ischemia-reperfusion from Higenamine.[19]

Higenamine appears to be protective under instances of Ischemia (lack of oxygen), with the exact mechanisms known but not yet compared to an active control (to assess potency of these protective effects)

4Cardiovascular Health

Platelets

In serum isolated from rats and humans, Higenamine appears to have antiplatelet aggregating propeties with an IC_{50} value of 140uM in response to Arachidonic Acid (AA) induced clotting, noted to be half as effective as Aspirin (used as an active control), but against U46619-induced aggregation Higenamine (73uM IC_{50}) was more effective than Aspirin on rat platelets[20] and show efficacy on collagen and ephinephrine-induced aggregation as well.[21] Higenamine may directly compete at TA receptors (Arachidonic acid metabolizes to Thromboxane A2 and acts on these receptors to induce platelet aggregation[22]) since it seems fairly weak at actually suppressing Arachidonic Acid metabolism into Thromboxane A(2) with an IC_{50} 2990uM.[20] Anti-thrombotic effects have been observed in mouse acute thrombosis model and rat AV shunt models after oral ingestion of 50-100mg/kg bodyweight[23] and after oral administration of 10-50mg/kg Higenamine in a rat model of disseiminated intravascular coagulation;[24] the S-Enantiomer may be more potent than the R-enantiomer of Higenamine,[25] but the previous studies used a racemic mixture of the two.

Higenamine *per se* appears to have anti-thrombotic potential, which seems to be related to competing with Thromboxane A(2) at the receptor level. These have been noted at oral intakes of 50-100mg in rats (8-16mg in humans)

Cardiac tissue

Higenamine can increase the rate and force of contraction of the heart with EC_{50} values of 38nM and 97nM respectively, with the maximal response (3uM) being comparable to isoproterenol (100nM) although on the EC_{50} basis it was 20-fold less potent.[26] This positive chronotropic response to Higenamine was via activation of the adrenergic B1 receptors, and submaximal concentrations of Higenamine (2.5nM) that *per se* do not influence contractile rate can augment Aconitate-induced contractile rate secondary to B1 agonism.[26]

A positive ionotropic effect of Higenamine also exists with an EC_{50} of 97nM (95% CI of 81.5-115.2nM), again being approximately 20-fold less potent than isoproterenol.[26]

Has the same mechanisms as other beta adrenergic agonists to increase heart rate; the oral dose required for this is not currently known

5Interactions with Fat Metabolism

Mechanisms

Higenamine is known as a Beta-adrenergic receptor agonist, a mechanism shared by Ephedrine andSynephrine for their ability to reduce Fat Mass. These effects appears to be wide-reaching affecting intestinal tissue,[27] bronchiol tissue (where it

acts as a vasodilator),[8] cardiac tissue (atria[26][28] and ventricles[6]). It appears to act on both the Beta(1) and Beta(2) subunit, with the Beta(3) subunit unexplored.

In regards to the alpha-adrenergic receptors, Higenamine appears to be a weak A(1) antagonist and a weak A(2) agonist.[29][8]

Possesses the same mechanisms as other stimulant fat burners to induce fat loss, but currently no evidnce exists to suggest potency of these effects *in vivo*

6**Inflammation and Immunology**
Mechanisms

Higenamine is able to inhibit LPS-induced nitrite accumulation in macrophages, with an IC_{50} value of 53.4+/-2.6μM; this measurement for the racemic mixture was mostly due to S-Higenamine with an IC_{50} of 26.2+/-7.6μM (R-Higenamine with a value of 6, 86.3+/-5.4μM).[30] Reductions in the inflammatory response in isolated macrophages have been replicated elsewhere with similar potency to *tetrandrin* at the same concentration (0.01mM).[31]

A subsequent injection of 10mg/kg of the S-enantiomer reduced serum nitric oxide (induced by exposure to endotoxin) from 88+/-7μM to 28+/-5μM (68% decrease), with some efficacy from the racemic mixture and a higher dose of 20mg/kg being required for the weaker R-enantiomer.[30]These effects may be downstream of Higenamine reducing induction of iNOS (IC_{50} 53+/-2.6μM) via NF-kB inhibition,[7] and decreases in serum nitric oxide (elevated during shock) replicated[7] and possibly secondary to NF-kB inhibition.[7]

Appears to possess anti-inflammatory mechanisms and may be useful in clinical settings for septic shock

Interactions with Organ Systems
Lungs and Asthma

Higenamine was found secondary to the fruits of *Nandina domestica*, which are a tradional asthmatic medication, to act on beta(2)adrenergic recpetors; the same receptor class that Ephedrineand Synephrine act upon.[2] The anti-asthmatic effects of Higenamine are wholly mediated via this receptor,[2][8] and activation of the beta(2)adrenergic receptor is anti-asthmatic in nature due to inducing bronchiol dilation (widening of breathing tubes). It should be noted that usage of *Nandina domestica* for anti-asthmatic effects may be more effective than Higenamine in isolation due to nantenine, another bioactive that has anti-asthmatic effects.[3]

When guinea pigs are exposed to histamine who were pretreated with test drugs, Higenamine was able to delay bronchiol convulsion by 1.7-fold relative to control (slightly underperforming salbuterol as active control, which exerted a 2.3-fold delay over control).[8] The benefit was dose dependent, and a higher concentration of Higenamine was more effective.

Nandina domestica has a long history of being helpful for asthmatics, and Higenamine is thought to contribute benficially. No actual interventions in living creatures exist aside from one Hamster study, suggesting similar potency to Salbuterol

Safety and Toxicity

A study cited in this paper[11] but otherwise inaccessible, from the journal *Zhongguo Lin Chuang Yao Li Xue Za Zhi* (Y.R Du et al.) suggests that the highest safe/recommended dose in humans is 24mcg/kg bodyweight as higenamine hydrochloride. Rabbit studies appear to use 50mg/kg acutely with no harm acutely (correlates to 11mg/kg[32]).

DMBA- Scientific Research

What is DMBA?

On a chemical level DMBA is very similar to AMP-citrate; an ingredient that is highly favoured by many members of the bodybuilding community.

It is also often compared to the equally controversial ingredient DMAA, but it is generally accepted that DMBA has the greater potency and can provide better results, both as a fat fighting compound and as a bodybuilding aid.

1. Go steady on the intensity of your workout until you know how you go with DMBA. It is a powerful, heart accelerating stimulant, after all. Don't do a Max Heart-Rate treadmill run after taking it!

DMBA Fat Burning Benefits

DMBA assists weight loss by initiating thermogenic fat burning. This is a process by which calories are converted to heat. Science informs us that everything in the universe is energy in one form or another and heat is the lowest form of energy.

The calories provided by food are a form of chemical energy. When the body is provided with too many calories those calories are converted to body fat (a different form of chemical energy).

When DMBA is introduced to the body it initiates a chemical reaction that produces a slight rise in the body's core temperature which then, via a complicated set of processes, causes the body to begin losing an increased amount of calories as heat.

Then, as the body is robbed of its main energy supply, it is forced to turn to its back up energy provider, body fat.

DMBA Bodybuilding Benefits

DMBA is a potent stimulant that can be very useful for providing extra energy so, not surprisingly, it is often favoured by

bodybuilders who are looking for a pre-workout supplement to provide them with the extra edge they need to train harder and get better results.

It is also worth noting DMBA has a greater bioavailability than many similar ingredients and is, therefore, usually faster acting.

The fact that DMBA can also provide fat burning provides an added bonus that bodybuilders are sure to appreciate because hard, toned, muscles cannot be shown off to their best advantage if they are covered in layers of fat.

DMBA vs AMP-Citrate

The fact that DMBA and AMP-citrate are so similar can often make the process of choosing the right supplement more difficult than would normally be the case.

On a chemical level the only difference is DMBA is bound to a molecule of hydrochloride, while AMP-citrate is bound to a molecule of citrate.

So which is the best? As is often the case scientific opinions can differ, but it is generally accepted that DMBA is the more powerful of the two.

Possible Side Effects

Just like any other ingredient, DMBA may cause some users to experience side effects and the severity and range of side effects will vary on an individual basis.

Many people may experience little or no side effects at all, but possible side effects include headaches, insomnia, and increased heart rate.

Again, such side effects are typical of many other ingredients.

Typical Usage

Dosage is also somewhat of an issue because there are no official recommendations regarding this, but Criminal Supplements suggests a dosage of 200mg per day taken one hour before training.

This is less than a typical dosage of AMP-citrate, but bearing in mind the fact that DMBA has a greater potency the dosage could be seen to be about right.

When taken as a bodybuilding supplement at least one of the doses is usually taken before training is commenced.

CAN CAFFEINE HELP YOU LOSE WEIGHT?

You've probably noticed that caffeine is a staple ingredient in many popular diet pills as well as homemade fat-burning stacks. And you've probably also heard experts suggest that you drink coffee or other caffeinated beverages to help you lose weight. All of this begs the question, can caffeine really help you lose weight?

The answer is yes. And it primarily helps you lose weight in two ways:

BY BOOSTING YOUR METABOLISM

Ingesting caffeine jumpstarts the process of lipolysis, which is when your body releases free fatty acids into the bloodstream. This occurs when your body is breaking down your fat stores to convert it into energy. In other words, caffeine boosts your metabolism slightly and helps you burn fat.[2]

BY GIVING YOU AN ENERGY BOOST

If there's one thing that everyone knows about coffee and similar beverages and pills, it's that caffeine is a stimulant. It increases alertness and wards off drowsiness temporarily, which means that you can perform certain tasks for longer.

However, this isn't just limited to mental tasks. This includes physical tasks as well, such as running or lifting weights. This means a little shot of caffeine can give you the energy you need to give 100% during your workout. And giving 100% in the gym means you'll get the results you want more quickly.

So now that we've established that caffeine can indeed help you with your weight loss efforts,that brings us to the next question.

HOW MUCH CAFFEINE DO YOU NEED?

This is a bit tricky to answer, since different people react to caffeine in different ways. I'm sure you know what I'm talking about - some people drink one cup of coffee and they get all hopped up for hours. Others can drink cup after cup all day long with seemingly very little effect.

> TIP
>
> If you're someone who drinks a lot of caffeine and thus you have a high tolerance for it, you may want to consider first breaking your addiction and letting your body get used to no caffeine for a while. That way, when you eventually do ingest a small amount of caffeine you'll actually benefit from the effects.

If you don't regularly ingest a lot of caffeine, then a couple hundred milligrams will likely produce noticeable effects. You may want to start with 100 milligrams to see how it goes, then up your intake to 200 milligrams. You can then increase the dose by 50 milligrams if you're still not feeling any effects.