**N-Methyltyramine (4-Hydroxy-N-methylphenethylamine)**

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![Chemical Structure of N-Methyltyramine](image)

**Background**

N-Methyltyramine is the methylated version of L-Tyramine (through the addition of a methyl group at the N terminal), a naturally occurring monoamine compound that acts as a catecholamine releasing agent. N-Methyltyramine can be found in nature from plants such as barley and Citrus aurantium, the latter being commonly used for Synephrine content (N-Methyltyramine is converted to Synephrine by Dopamine β-hydroxylase). Unlike Synephrine, N-Methyltyramine has not been observed to display any lipolytic activity, due to the lack of a beta-hydroxyl or a beta-ketone. It’s mechanisms of action imply that it acts as a peripheral sympathomimetic compound. NMT is similar to Synephrine and Hordenine, with the addition of a hydroxyl group at β distinguishing Synephrine from NMT, and substitution of a dimethyl group at the N terminal resulting in Hordenine.

In general, when dealing with sympathomimetic compounds, a primary or secondary aliphatic amine separated by 2 carbons from a substituted benzene ring is minimally required for high agonist activity. Along with possessing this characteristic common to adrenergic agents, the presence of a hydroxyl group in the benzene ring at the 4th position shows that N-Methyltyramine has excellent alpha and beta activity adrenergic receptor activity.

**Pharmacokinetics**

- 39% bioavailability through p.o use.
- 90% of orally ingested NMT is absorbed in the small intestine, particularly in the lower jejunum and the ileum.
- NMT is metabolized in the liver, but not in the small-intestinal mucosa.
- Hepatic intrinsic clearance value is 2 liters an hour.
- The plasma concentration time curve and bioavailability of NMT after oral ingestion were well predicted by the GI transit absorption model with the hepatic first-pass metabolism process.

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**Actions**

N-Methyltyramine is known to possess $\beta_2$ adrenergic receptor activity, to increase plasma and myocardial cGMP and cAMP levels, has been observed to increase renal and cerebral vascular resistance, and lacks a beta-hydroxyl or a beta-ketone group, implying it is an indirect acting amine that releases cytoplasmic norepinephrine from sympathetic nerve endings, similar to tyramine. Vasoconstriction during exercise due to the use of NMT is not likely because during exercise, the $\alpha_1$-adrenergic receptors activated by the norepinephrine released by NMT can be selectively blocked by sympathetic nervous activity, allowing the $\beta_2$-adrenergic receptors to dominate. While it may appear to have $\beta_1$-adrenergic activity, there is no observed action on amylase activity after administration of N-Methyltyramine.

N-Methyltyramine most importantly has the properties of an $\alpha_2$-adrenoceptor antagonist, albeit a weak one. $\alpha_2$ blockers significantly increase adrenergic, dopaminergic and serotonergic neurotransmitters, increase insulin secretion and decrease blood sugar levels. The usage of N-Methyltyramine also leads to an increase in blood pressure, relaxation of the ileum, an increase in force of the right atrium due to norepinephrine release, and an increase in rate of contraction in right atrium due to norepinephrine release.

N-Methyltyramine has also been found to be a constituent of beer. When tested, N-Methyltyramine was found to stimulate pancreatic secretion via the cholinergic gastro-pancreatic reflex, meaning the stimulation of pancreatic secretion observed after drinking is likely due to N-Methyltyramine. Although gastrin production may of concern to those looking to use N-Methyltyramine, it is likely only to be an issue for those who are predisposed to illnesses such as hypercalcaemia, and the dosage required of NMT for this likely exceeds doses that will be utilized for p.o use. As always, consumers should check with their physician before the use of any supplement, so if there is any concern, please check with your physician before using NMT.

**Summary**

N-Methyltyramine is the methylated version of L-Tyramine, a naturally occurring monoamine compound that acts as a catecholamine releasing agent. It is known to:

- Significantly increase adrenergic, dopaminergic and serotonergic neurotransmitters by acting as an indirect sympathomimetic amine.
- Increases insulin secretion and decreases blood sugar levels.
- Increase plasma and myocardial cGMP and cAMP levels.