

## Product Data Sheet

Product Name: Nicotianamine

Cat. No.: GC18766

### Chemical Properties

Cas. No. 34441-14-0

Chemical Name  $\alpha$ S-[[[(3S)-3-amino-3-carboxypropyl]amino]-2S-carboxy-1-azetidinebutanoic acid

SMILES OC([C@@H](NCC[C@H](N)C(O)=O)CCN1[C@H](C(O)=O)CC1)=O

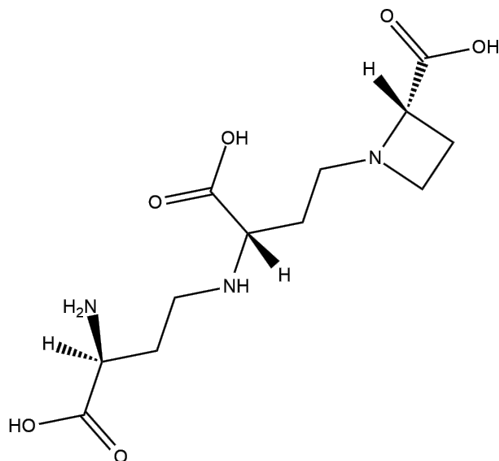
Formula  $C_{12}H_{21}N_3O_6$  M.Wt 303.3

Solubility Slightly soluble in Methanol & Water Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



### Protocol

#### Cell experiment [1]:

Cell lines Caco-2 cells (human epithelial colorectal adenocarcinoma cell line)

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Caco-2 cell monolayers were cultured in high-glucose Dulbecco's modified Eagle's medium (DMEM) supplemented with 10% fetal bovine serum and 1% penicillin/streptomycin at 37°C in a 5% CO<sub>2</sub> atmosphere. Cells were incubated with in vitro digested milled rice samples containing varying Nicotianamine (10µM) concentrations for measurement of iron bioavailability.

Reaction Conditions      10µM; 30min

Applications      Nicotianamine significantly enhanced iron bioavailability in Caco-2 cells.

### Animal experiment [2]:

Animal models      ICR mice

Mice were fed synthetic AIN-93M diet for 1 week to eliminate dietary NA effects, fasted for 16 hours, then orally administered NA-Fe(II) complex [Nicotianamine (33mM) /Fe (3.3mM) molar ratio=10:1] or free Fe(II) via intragastric gavage (200µL). Blood, spleen, liver, kidney, and small intestine tissues were collected at 0.5, 2, and 5 hours post-administration for isotope analysis.

Dosage form      33mM; oral gavage

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### Applications

Nicotianamine -Fe(II) complex administration resulted in significantly higher Fe accumulation in kidney and spleen tissues compared to free Fe(II) at 5 hours post-administration. Nicotianamine-Fe(II) also induced a slight increase in hemoglobin concentration, while free Fe(II) caused a decrease due to fasting effects.

### References:

- [1] Zheng L, Cheng Z, Ai C, et al. Nicotianamine, a novel enhancer of rice iron bioavailability to humans. PLoS One. 2010 Apr 16;5(4):e10190.
- [2] Murata Y, Yoshida M, Sakamoto N, et al. Iron uptake mediated by the plant-derived chelator nicotianamine in the small intestine. J Biol Chem. 2021 Jan-Jun;296:100195.

### Background

Nicotianamine is a secondary metabolite synthesized by plants that plays a central role in maintaining metal ion homeostasis<sup>[1]</sup>. Nicotianamine can form stable chelates with various metal ions, for example, iron, zinc, copper, and manganese, thereby promoting their transport and distribution within plants<sup>[2]</sup>. Nicotianamine is essential for metal nutrition and metal homeostasis in flowering plants, and its deficiency leads to growth abnormalities and imbalances in metal ion distribution<sup>[3]</sup>. Additionally, Nicotianamine exhibits inhibitory activity against angiotensin-converting enzyme (ACE), with IC<sub>50</sub> values of 76nM (against rhACE2) and 59nM (against rhACE)<sup>[4]</sup>.

In vitro, treatment of Caco-2 cells with Nicotianamine (10μM) together with an iron-containing solution significantly increased cellular ferritin synthesis levels, enhancing iron bioavailability<sup>[5]</sup>. When supplemented (100 μM) into airway mucosal secretions (AMS) and used to pretreat *Pseudomonas aeruginosa* (PAO1) and ΔPA4834 mutant strain for 16 hours, Nicotianamine maintained the growth capacity of both PAO1 and the ΔPA4834 mutant in AMS and significantly improved bacterial iron acquisition efficiency<sup>[6]</sup>.

In vivo, oral administration of a Nicotianamine (33mM) and ferrous iron (3.3mM) chelate via gastric gavage to 8-week-old ICR mice significantly promoted iron absorption in the proximal jejunum and

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increased iron content in the kidneys and spleen within 5 hours<sup>[7]</sup>. In ovo injection of Nicotianamine (1.6mM) into 17-day-old chicken embryos significantly elevated serum iron concentration in the chickens and suppressed the expression of iron homeostasis genes such as DcytB and DMT1 in the duodenum<sup>[8]</sup>.

### References:

- [1] Bouazaoui M, Mari S, Czernic P, et al. Synthesis and biological activity of nicotianamine and analogues. *Adv Exp Med Biol.* 2009;611:555-7.
- [2] Trampczynska A, Küpper H, Meyer-Klaucke W, et al. Nicotianamine forms complexes with Zn(II) in vivo. *Metallomics.* 2010 Jan;2(1):57-66.
- [3] Clemens S, Deinlein U, Ahmadi H, et al. Nicotianamine is a major player in plant Zn homeostasis. *Biometals.* 2013 Aug;26(4):623-32.
- [4] Takahashi S, Yoshiya T, Yoshizawa-Kumagaye K, et al. Nicotianamine is a novel angiotensin-converting enzyme 2 inhibitor in soybean. *Biomed Res.* 2015;36(3):219-24.
- [5] Zheng L, Cheng Z, Ai C, et al. Nicotianamine, a novel enhancer of rice iron bioavailability to humans. *PLoS One.* 2010 Apr 16;5(4):e10190.
- [6] Gi M, Lee KM, Kim SC, et al. A novel siderophore system is essential for the growth of *Pseudomonas aeruginosa* in airway mucus. *Sci Rep.* 2015 Oct 8;5:14644.
- [7] Murata Y, Yoshida M, Sakamoto N, et al. Iron uptake mediated by the plant-derived chelator nicotianamine in the small intestine. *J Biol Chem.* 2021 Jan-Jun;296:100195.
- [8] Beasley JT, Johnson AAT, Kolba N, et al. Nicotianamine-chelated iron positively affects iron status, intestinal morphology and microbial populations in vivo (*Gallus gallus*). *Sci Rep.* 2020 Feb 10;10(1):2297.

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