# Product Data Sheet

Product Name: Nicotianamine
Cat. No.: GC18766

## Chemical Properties

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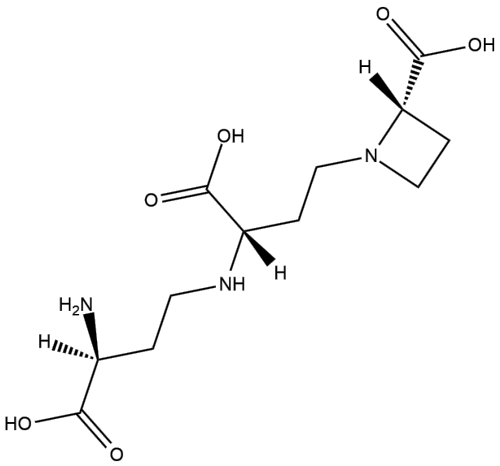
| Cas. No. | 34441-14-0 | | |
| Chemical Name | αS-[[(3S)-3-amino-3-carboxypropyl]amino]-2S-carboxy-1-azetidinebutanoic acid | | |
| SMILES | OC([C@@H](NCC[C@H](N)C(O)=O)CCN1[C@H](C(O)=O)CC1)=O | | |
| Formula | $C_{12}H_{21}N_3O_6$ | M.Wt | 303.3 |
| Solubility | Slightly soluble in Methanol & Water | 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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| Preparation Method | 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% $CO_2$ 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]:**

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| Animal models | ICR mice |
| Preparation Method | 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 |

***Caution: Product has not been fully validated for medical applications. For research use only.***
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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[1]. Nicotianamine can form stable chelates with various metal ions, for example, iron, zinc, copper, and manganese, thereby promoting their transport and distribution within plants[2]. 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[3]. Additionally, Nicotianamine exhibits inhibitory activity against angiotensin-converting enzyme (ACE), with $IC_{50}$ values of 76nM (against rhACE2) and 59nM (against rhACE)[4].

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[5]. 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[6].

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

increased iron content in the kidneys and spleen within 5 hours[7]. 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[8].

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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