Milnacipran

**Chemical name:** 2-(Aminomethyl)-N,N-diethyl-1-phenylcyclopropanecarboxamide  
**CAS number:** 92623-85-3  
**Molecular formula:** C_{15}H_{22}N_{2}O  
**Molecular mass (g mol⁻¹):** 246.3  
**InChI:** 1S/C15H22N2O/c1-3-17(4-2)14(18)15(10-13(15)11-16)12-8-6-5-7-9-12/h5-9,13H,3-4,10-11,16H2,1-2H3  
**InChIKey:** GJJFMKBJSRMPLA-UHFFFAOYSA-N

### Biological activity

Milnacipran (brand name: Savella) is a serotonin–norepinephrine reuptake inhibitor used to treat major depressive disorder and fibromyalgia.

### In vivo metabolism

Metabolism and excretion of [¹⁴C]-milnacipran hydrochloride (1) were studied in six healthy male subjects after a single oral 100-mg dose. Metabolites in plasma, urine, and feces were analyzed by liquid scintillation counting, liquid chromatography–tandem mass spectrometry, and liquid chromatography high-resolution mass spectrometry methods. After oral administration, approximately 93% of the total radioactivity was excreted in the urine. Unchanged 1 (55% of the dose) was the most abundant material found in urine. Primary metabolic reactions included N-dealkylation and N-formylation followed by glucuronide formation.
2 Milnacipran

Scheme 1 Metabolic pathway of milnacipran (1) in humans.

Major metabolites identified were milnacipran carbamoyl $O$-glucuronide (2) and $N$-desethyl milnacipran (3), accounted for 19 and 8% of the total radioactivity, respectively.\(^1\) Metabolic pathway of milnacipran in humans is shown in Scheme 1.

\[ \text{Scheme 1} \]

Xin Zhou

*Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, People’s Republic of China*

Reference

Abstract:
Milnacipran is a serotonin-norepinephrine reuptake inhibitor used to treat major depressive disorder and fibromyalgia. Metabolism and excretion of [¹⁴C]-milnacipran were studied in healthy male subjects after a single oral 100-mg dose. Approximately 93% of the total radioactivity was excreted in the urine. Unchanged milnacipran (55% of the dose) was the most abundant material found in urine. Primary metabolic reactions included N-dealkylation and N-formylation followed by glucuronide formation. Major metabolites were milnacipran carbamoyl O-glucuronide and N-desethyl milnacipran, accounted 19% and 8% of the total radioactivity, respectively.

Keywords:
milnacipran; Savella; 92623-85-3; drug; human metabolism; in vivo metabolism