

## SBML Model Report

# Model name: “Grange2001 - PK interaction of L-dopa and benserazide”



May 6, 2016

## 1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following two authors: Lukas Endler<sup>1</sup> and Vijayalakshmi Chelliah<sup>2</sup> at October 27<sup>th</sup> 2009 at 2:45 p. m. and last time modified at October tenth 2014 at 11:18 a. m. Table 1 shows an overview of the quantities of all components of this model.

Table 1: Number of components in this model, which are described in the following sections.

Element	Quantity	Element	Quantity
compartment types	0	compartments	7
species types	0	species	9
events	0	constraints	0
reactions	14	function definitions	0
global parameters	31	unit definitions	5
rules	9	initial assignments	4

## Model Notes

Grange2001 - PK interaction of L-dopa and benserazide

A pharmacokinetics of L-dopa in rats after administration of L-dopa alone (BIOMD0000000321) or L-dopa combined with a peripheral AADC (amino-acid-decarboxylase) inhibitor (this model: BIOMD0000000320) has been studied using noncompartmental analysis.

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This model is described in the article: [A pharmacokinetic model to predict the PK interaction of L-dopa and benserazide in rats](#). Grange S, Holford NH, Guentert TW Pharmaceutical Research [2001, 18(8):1174-1184]

Abstract:

**PURPOSE:** To study the PK interaction of L-dopa/benserazide in rats. **METHODS:** Male rats received a single oral dose of 80 mg/kg L-dopa or 20 mg/kg benserazide or 80/20 mg/kg L-dopa/benserazide. Based on plasma concentrations the kinetics of L-dopa, 3-O-methyldopa (3-OMD), benserazide, and its metabolite Ro 04-5127 were characterized by noncompartmental analysis and a compartmental model where total L-dopa clearance was the sum of the clearances mediated by amino-acid-decarboxylase (AADC), catechol-O-methyltransferase and other enzymes. In the model Ro 04-5127 inhibited competitively the L-dopa clearance by AADC.

**RESULTS:** The coadministration of L-dopa/benserazide resulted in a major increase in systemic exposure to L-dopa and 3-OMD and a decrease in L-dopa clearance. The compartmental model allowed an adequate description of the observed L-dopa and 3-OMD concentrations in the absence and presence of benserazide. It had an advantage over noncompartmental analysis because it could describe the temporal change of inhibition and recovery of AADC.

**CONCLUSIONS:** Our study is the first investigation where the kinetics of benserazide and Ro 04-5127 have been described by a compartmental model. The L-dopa/benserazide model allowed a mechanism-based view of the L-dopa/benserazide interaction and supports the hypothesis that Ro 04-5127 is the primary active metabolite of benserazide.

The volumes and variables in this model are taken for a rat with 0.25 kg. The initial dose for L-Dopa (`L_Dopa_per_kg_rat`) and Benserazide (`Benserazide_per_kg_rat`) are to be given in umole per kg. 80 mg/kg L-Dopa correspond to 404 umol/kg, 20 mg/kg benserazide to 78 umol/kg. To change the model to a different mass of rat the compartment volumes, and the parameters `rat_body_mass` and `Q` have to be changed accordingly.

The model has three species (`A_dopa`, `A_B`, `A_M`) whose initial concentrations are calculated from a *listOfInitialAssignments*. While running for the first time the time-course (24hrs) for this model in COPASI (up to version 4.6, Build 33), the resulting graph displays only straight lines for all the species. Any subsequent runs should provide proper plots (i.e. without making any change to the model, just by clicking the „run„ button again).

The above issue is caused by some initial assignments which are not calculated when COPASI imports the file. This issue should not be present in newer releases of COPASI.

This model is hosted on [BioModels Database](#) and identified by: [MODEL0910130001](#).

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## 2 Unit Definitions

This is an overview of eight unit definitions of which three are predefined by SBML and not mentioned in the model.

## 2.1 Unit substance

**Name** micromole

**Definition** nmol

## 2.2 Unit umol\_per\_kg

**Name** micromole\_per\_kg

**Definition** nmol · kg<sup>-1</sup>

## 2.3 Unit per\_h

**Name** per\_h

**Definition** (3600 s)<sup>-1</sup>

## 2.4 Unit l\_per\_h

**Name** l\_per\_h

**Definition** l · (3600 s)<sup>-1</sup>

## 2.5 Unit time

**Name** hours

**Definition** 3600 s

## 2.6 Unit volume

**Notes** Litre is the predefined SBML unit for volume.

**Definition** l

## 2.7 Unit area

**Notes** Square metre is the predefined SBML unit for area since SBML Level 2 Version 1.

**Definition** m<sup>2</sup>

## 2.8 Unit length

**Notes** Metre is the predefined SBML unit for length since SBML Level 2 Version 1.

**Definition** m

## 3 Compartments

This model contains seven compartments.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
gut		0000290	3	1	litre	<input checked="" type="checkbox"/>	
Vdopa	V_L_Dopa	0000290	3	0.496	l	<input checked="" type="checkbox"/>	
V_3_OMD		0000290	3	0.128	l	<input checked="" type="checkbox"/>	
V1_B		0000290	3	0.202	l	<input checked="" type="checkbox"/>	
V2_B		0000290	3	0.127	l	<input checked="" type="checkbox"/>	
V1_M		0000290	3	0.0691	l	<input checked="" type="checkbox"/>	
V2_M		0000290	3	3.2	l	<input checked="" type="checkbox"/>	

### 3.1 Compartment `gut`

This is a three dimensional compartment with a constant size of one litre.

**SBO:0000290** physical compartment

### 3.2 Compartment `Vdopa`

This is a three dimensional compartment with a constant size of 0.496 litre.

**Name** `V_L_Dopa`

**SBO:0000290** physical compartment

### 3.3 Compartment `V_3_OMD`

This is a three dimensional compartment with a constant size of 0.128 litre.

**SBO:0000290** physical compartment

### 3.4 Compartment `V1_B`

This is a three dimensional compartment with a constant size of 0.202 litre.

**SBO:0000290** physical compartment

### 3.5 Compartment `V2_B`

This is a three dimensional compartment with a constant size of 0.127 litre.

**SBO:0000290** physical compartment

### 3.6 Compartment V1\_M

This is a three dimensional compartment with a constant size of 0.0691 litre.

**SBO:0000290** physical compartment

### 3.7 Compartment V2\_M

This is a three dimensional compartment with a constant size of 3.2 litre.

**SBO:0000290** physical compartment

## 4 Species

This model contains nine species. Section 9 provides further details and the derived rates of change of each species.

Table 3: Properties of each species.

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
A_dopa		gut	nmol	$\square$	$\square$
A_B		gut	nmol	$\square$	$\square$
A_M		gut	nmol	$\square$	$\square$
C_dopa		Vdopa	$\text{nmol} \cdot \text{l}^{-1}$	$\square$	$\square$
C_OMD	C_3-OMD	V_3_OMD	$\text{nmol} \cdot \text{l}^{-1}$	$\square$	$\square$
C1_M		V1_M	$\text{nmol} \cdot \text{l}^{-1}$	$\square$	$\square$
C2_M		V2_M	$\text{nmol} \cdot \text{l}^{-1}$	$\square$	$\square$
C1_B		V1_B	$\text{nmol} \cdot \text{l}^{-1}$	$\square$	$\square$
C2_B		V2_B	$\text{nmol} \cdot \text{l}^{-1}$	$\square$	$\square$

## 5 Parameters

This model contains 31 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
F_c		0000381	0.000	dimensionless	<input type="checkbox"/>
F_H		0000381	0.000	dimensionless	<input type="checkbox"/>
F_G		0000381	1.000	dimensionless	<input checked="" type="checkbox"/>
CL_H		0000035	0.000	$1 \cdot (3600 \text{ s})^{-1}$	<input type="checkbox"/>
Q		0000002	0.828		<input checked="" type="checkbox"/>
f_H		0000381	0.130	dimensionless	<input checked="" type="checkbox"/>
CL_dopa		0000035	0.000	$1 \cdot (3600 \text{ s})^{-1}$	<input type="checkbox"/>
f_rest		0000381	0.000	dimensionless	<input type="checkbox"/>
f_AADC		0000381	0.690	dimensionless	<input checked="" type="checkbox"/>
f_COMT		0000381	0.100	dimensionless	<input checked="" type="checkbox"/>
CL_AADC		0000035	0.000	$1 \cdot (3600 \text{ s})^{-1}$	<input type="checkbox"/>
CL_rest		0000035	0.000	$1 \cdot (3600 \text{ s})^{-1}$	<input type="checkbox"/>
CL_COMT		0000035	0.000	$1 \cdot (3600 \text{ s})^{-1}$	<input type="checkbox"/>
CL_AADC0		0000035	0.000	$1 \cdot (3600 \text{ s})^{-1}$	<input type="checkbox"/>
ki		0000288	0.002		<input checked="" type="checkbox"/>
CL_dopa0		0000035	0.823	$1 \cdot (3600 \text{ s})^{-1}$	<input checked="" type="checkbox"/>
ka_c		0000035	1.290		<input checked="" type="checkbox"/>
ka_M	ka_m	0000035	2.470		<input checked="" type="checkbox"/>
ka_B	ka_b	0000035	0.940		<input checked="" type="checkbox"/>
F_B		0000381	0.022	dimensionless	<input checked="" type="checkbox"/>
CL_OMD	CL_3_OMD	0000035	0.009	$1 \cdot (3600 \text{ s})^{-1}$	<input checked="" type="checkbox"/>
CL_B		0000035	1.670	$1 \cdot (3600 \text{ s})^{-1}$	<input checked="" type="checkbox"/>
fm		0000381	0.150	dimensionless	<input checked="" type="checkbox"/>
CL_M		0000035	4.290	$1 \cdot (3600 \text{ s})^{-1}$	<input checked="" type="checkbox"/>
CL_dB		0000035	0.072	$1 \cdot (3600 \text{ s})^{-1}$	<input checked="" type="checkbox"/>
CL_dM		0000035	1.060	$1 \cdot (3600 \text{ s})^{-1}$	<input checked="" type="checkbox"/>
L_Dopa_per- _kg_rat		0000197	404.000	$\text{nmol} \cdot \text{kg}^{-1}$	<input checked="" type="checkbox"/>
Benserazide- _per_kg_rat		0000197	78.000	$\text{nmol} \cdot \text{kg}^{-1}$	<input checked="" type="checkbox"/>
rat_body- _mass		0000002	0.250	kg	<input checked="" type="checkbox"/>
A_bens_tot		0000196	0.000	nmol	<input checked="" type="checkbox"/>
B_M_frac	Bens_Ro04-5127- _fraction_gut	0000381	0.070		<input checked="" type="checkbox"/>

## 6 Initialassignments

This is an overview of four initialassignments.

### 6.1 Initialassignment `A_dopa`

**Derived unit**  $\text{nmol} \cdot \text{kg}^{-1} \cdot \text{kg}$

**Math** `L_Dopa_per_kg_rat · rat_body_mass`

### 6.2 Initialassignment `A_B`

**Derived unit** contains undeclared units

**Math** `A_bens_tot · (1 - B_M_frac)`

### 6.3 Initialassignment `A_M`

**Derived unit** contains undeclared units

**Math** `A_bens_tot · B_M_frac`

### 6.4 Initialassignment `A_bens_tot`

**Derived unit**  $\text{nmol} \cdot \text{kg}^{-1} \cdot \text{kg}$

**Math** `Benserazide_per_kg_rat · rat_body_mass`

## 7 Rules

This is an overview of nine rules.

### 7.1 Rule `F_c`

Rule `F_c` is an assignment rule for parameter `F_c`:

$$F_c = F_H \cdot F_G \quad (1)$$

**Derived unit** dimensionless

### 7.2 Rule `F_H`

Rule `F_H` is an assignment rule for parameter `F_H`:

$$F_H = 1 - \frac{CL_H}{Q} \quad (2)$$



### 7.3 Rule CL\_H

Rule CL\_H is an assignment rule for parameter CL\_H:

$$CL_H = f_H \cdot CL_{dopa} \quad (3)$$

**Derived unit**  $1 \cdot (3600 \text{ s})^{-1}$

### 7.4 Rule CL\_dopa

Rule CL\_dopa is an assignment rule for parameter CL\_dopa:

$$CL_{dopa} = CL_{AADC} + CL_{rest} + CL_{COMT} \quad (4)$$

**Derived unit**  $1 \cdot (3600 \text{ s})^{-1}$

### 7.5 Rule f\_rest

Rule f\_rest is an assignment rule for parameter f\_rest:

$$f_{rest} = 1 - (f_{AADC} + f_{COMT}) \quad (5)$$

### 7.6 Rule CL\_AADC

Rule CL\_AADC is an assignment rule for parameter CL\_AADC:

$$CL_{AADC} = \frac{CL_{AADC0}}{1 + \frac{[C]_M}{k_i}} \quad (6)$$

### 7.7 Rule CL\_rest

Rule CL\_rest is an assignment rule for parameter CL\_rest:

$$CL_{rest} = CL_{dopa0} \cdot f_{rest} \quad (7)$$

**Derived unit**  $1 \cdot (3600 \text{ s})^{-1}$

### 7.8 Rule CL\_COMT

Rule CL\_COMT is an assignment rule for parameter CL\_COMT:

$$CL_{COMT} = CL_{dopa0} \cdot f_{COMT} \quad (8)$$

**Derived unit**  $1 \cdot (3600 \text{ s})^{-1}$

### 7.9 Rule CL\_AADC0

Rule CL\_AADC0 is an assignment rule for parameter CL\_AADC0:

$$CL_{AADC0} = CL_{dopa0} \cdot f_{AADC} \quad (9)$$

**Derived unit**  $1 \cdot (3600 \text{ s})^{-1}$

## 8 Reactions

This model contains 14 reactions. All reactions are listed in the following table and are subsequently described in detail. If a reaction is affected by a modifier, the identifier of this species is written above the reaction arrow.

Table 5: Overview of all reactions

Nº	Id	Name	Reaction Equation	SBO
1	l_dopa- _absorption	L-Dopa absorption from gut	$A\_dopa \longrightarrow C\_dopa$	0000185
2	l_dopa_blood- _hepa_clearance	hepatic and blood L-Dopa clearance	$A\_dopa \longrightarrow \emptyset$	0000179
3	ro_04_5127- _absorption	ro 04-5127 absorption from gut	$A\_M \longrightarrow C1\_M$	0000185
4	benserazide- _absorption	benserazide absorption from gut	$A\_B \longrightarrow C1\_B$	0000185
5	benserazide- _gut_clearance	benserazide clearance from gut	$A\_B \longrightarrow \emptyset$	0000179
6	AADC_clearance	L-Dopa clearance via AADC	$C\_dopa \longrightarrow \emptyset$	0000399
7	COMT_clearance	L-Dopa clearance via COMT	$C\_dopa \longrightarrow C\_OMD$	0000214
8	rest_clearance	rest clearance of L-Dopa	$C\_dopa \longrightarrow \emptyset$	0000179
9	_3_OMD- _clearance	3-OMD clearance	$C\_OMD \longrightarrow \emptyset$	0000179
10	bens_clearance	benserazide clearance	$C1\_B \longrightarrow \emptyset$	0000179
11	bens_metabolism	benserazide metabolism to ro 04-5127	$C1\_B \longrightarrow C1\_M$	0000211
12	ro_clearance	ro 04-5127 clearance	$C1\_M \longrightarrow \emptyset$	0000179
13	bens- _distribution	benserazide distribution	$C1\_B \rightleftharpoons C2\_B$	0000185
14	ro_distribution	ro 04-5127 distribution	$C1\_M \rightleftharpoons C2\_M$	0000185

### 8.1 Reaction `l_dopa_absorption`

This is an irreversible reaction of one reactant forming one product.

**Name** L-Dopa absorption from gut

**SBO:0000185** transport reaction

#### Reaction equation



#### Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
A_dopa		

#### Product

Table 7: Properties of each product.

Id	Name	SBO
C_dopa		

#### Kinetic Law

**SBO:0000049** mass action rate law for first order irreversible reactions, continuous scheme

**Derived unit** contains undeclared units

$$v_1 = k_{a,c} \cdot A\_dopa \cdot F_c \quad (11)$$

### 8.2 Reaction `l_dopa_blood_hepa_clearance`

This is an irreversible reaction of one reactant forming no product.

**Name** hepatic and blood L-Dopa clearance

**SBO:0000179** degradation

#### Reaction equation



## Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
A_dopa		

## Kinetic Law

**SBO:0000049** mass action rate law for first order irreversible reactions, continuous scheme

**Derived unit** contains undeclared units

$$v_2 = k_{a.c} \cdot A_{dopa} \cdot (1 - F_c) \quad (13)$$

## 8.3 Reaction [ro\\_04\\_5127\\_absorption](#)

This is an irreversible reaction of one reactant forming one product.

**Name** ro 04-5127 absorption from gut

**SBO:0000185** transport reaction

## Reaction equation



## Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
A_M		

## Product

Table 10: Properties of each product.

Id	Name	SBO
C1_M		

### Kinetic Law

**SBO:0000049** mass action rate law for first order irreversible reactions, continuous scheme

**Derived unit** contains undeclared units

$$v_3 = k_{a\_M} \cdot A\_M \quad (15)$$

### 8.4 Reaction `benserazide_absorption`

This is an irreversible reaction of one reactant forming one product.

**Name** benserazide absorption from gut

**SBO:0000185** transport reaction

### Reaction equation



### Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
A_B		

### Product

Table 12: Properties of each product.

Id	Name	SBO
C1_B		

### Kinetic Law

**SBO:0000049** mass action rate law for first order irreversible reactions, continuous scheme

**Derived unit** contains undeclared units

$$v_4 = k_{a\_B} \cdot A\_B \cdot F\_B \quad (17)$$

### 8.5 Reaction `benserazide_gut_clearance`

This is an irreversible reaction of one reactant forming no product.

**Name** benserazide clearance from gut

**SBO:0000179** degradation

### Reaction equation



### Reactant

Table 13: Properties of each reactant.

Id	Name	SBO
A_B		

### Kinetic Law

**SBO:0000049** mass action rate law for first order irreversible reactions, continuous scheme

**Derived unit** contains undeclared units

$$v_5 = k_{a\_B} \cdot A\_B \cdot (1 - F\_B) \quad (19)$$

## 8.6 Reaction AADC\_clearance

This is an irreversible reaction of one reactant forming no product.

**Name** L-Dopa clearance via AADC

**SBO:0000399** decarboxylation

### Reaction equation



### Reactant

Table 14: Properties of each reactant.

Id	Name	SBO
C_dopa		

### Kinetic Law

**SBO:0000049** mass action rate law for first order irreversible reactions, continuous scheme

**Derived unit**  $(3600 \text{ s})^{-1} \cdot \text{nmol}$

$$v_6 = \text{CL\_AADC} \cdot [\text{C\_dopa}] \quad (21)$$

### 8.7 Reaction COMT\_clearance

This is an irreversible reaction of one reactant forming one product.

**Name** L-Dopa clearance via COMT

**SBO:0000214** methylation

### Reaction equation



### Reactant

Table 15: Properties of each reactant.

Id	Name	SBO
C_dopa		

### Product

Table 16: Properties of each product.

Id	Name	SBO
C_OMD	C_3-OMD	

### Kinetic Law

**SBO:0000049** mass action rate law for first order irreversible reactions, continuous scheme

**Derived unit**  $(3600 \text{ s})^{-1} \cdot \text{nmol}$

$$v_7 = \text{CL\_COMT} \cdot [\text{C\_dopa}] \quad (23)$$

### 8.8 Reaction rest\_clearance

This is an irreversible reaction of one reactant forming no product.

**Name** rest clearance of L-Dopa

**SBO:0000179** degradation

### Reaction equation



### Reactant

Table 17: Properties of each reactant.

Id	Name	SBO
C_dopa		

### Kinetic Law

**SBO:0000049** mass action rate law for first order irreversible reactions, continuous scheme

**Derived unit**  $(3600 \text{ s})^{-1} \cdot \text{nmol}$

$$v_8 = CL\_rest \cdot [C\_dopa] \quad (25)$$

## 8.9 Reaction [\\_3\\_OMD\\_clearance](#)

This is an irreversible reaction of one reactant forming no product.

**Name** 3-OMD clearance

**SBO:0000179** degradation

### Reaction equation



### Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
C_OMD	C_3-OMD	



### Kinetic Law

**SBO:0000049** mass action rate law for first order irreversible reactions, continuous scheme

**Derived unit**  $(3600 \text{ s})^{-1} \cdot \text{nmol}$

$$v_9 = \text{CL\_OMD} \cdot [\text{C\_OMD}] \quad (27)$$

### 8.10 Reaction `bens_clearance`

This is an irreversible reaction of one reactant forming no product.

**Name** benserazide clearance

**SBO:0000179** degradation

### Reaction equation



### Reactant

Table 19: Properties of each reactant.

Id	Name	SBO
C1_B		

### Kinetic Law

**SBO:0000049** mass action rate law for first order irreversible reactions, continuous scheme

**Derived unit**  $(3600 \text{ s})^{-1} \cdot \text{nmol}$

$$v_{10} = \text{CL\_B} \cdot [\text{C1\_B}] \quad (29)$$

### 8.11 Reaction `bens_metabolism`

This is an irreversible reaction of one reactant forming one product.

**Name** benserazide metabolism to ro 04-5127

**SBO:0000211** removal of a chemical group

### Reaction equation



## Reactant

Table 20: Properties of each reactant.

Id	Name	SBO
C1_B		

## Product

Table 21: Properties of each product.

Id	Name	SBO
C1_M		

## Kinetic Law

**SBO:000049** mass action rate law for first order irreversible reactions, continuous scheme

**Derived unit** contains undeclared units

$$v_{11} = \frac{fm}{1 - fm} \cdot CL\_B \cdot [C1\_B] \quad (31)$$

## 8.12 Reaction `ro_clearance`

This is an irreversible reaction of one reactant forming no product.

**Name** ro 04-5127 clearance

**SBO:0000179** degradation

## Reaction equation



## Reactant

Table 22: Properties of each reactant.

Id	Name	SBO
C1_M		

### Kinetic Law

**SBO:0000049** mass action rate law for first order irreversible reactions, continuous scheme

**Derived unit**  $(3600 \text{ s})^{-1} \cdot \text{nmol}$

$$v_{12} = \text{CL}_M \cdot [\text{C1}_M] \quad (33)$$

### 8.13 Reaction `bens_distribution`

This is a reversible reaction of one reactant forming one product.

**Name** benserazide distribution

**SBO:0000185** transport reaction

### Reaction equation



### Reactant

Table 23: Properties of each reactant.

Id	Name	SBO
C1_B		

### Product

Table 24: Properties of each product.

Id	Name	SBO
C2_B		

### Kinetic Law

**SBO:0000080** mass action rate law for first order forward, first order reverse, reversible reactions, continuous scheme

**Derived unit**  $(3600 \text{ s})^{-1} \cdot \text{nmol}$

$$v_{13} = \text{CL}_{dB} \cdot ([\text{C1}_B] - [\text{C2}_B]) \quad (35)$$

## 8.14 Reaction `ro_distribution`

This is a reversible reaction of one reactant forming one product.

**Name** `ro_04-5127_distribution`

**SBO:0000185** transport reaction

### Reaction equation



### Reactant

Table 25: Properties of each reactant.

Id	Name	SBO
C1_M		

### Product

Table 26: Properties of each product.

Id	Name	SBO
C2_M		

### Kinetic Law

**SBO:0000080** mass action rate law for first order forward, first order reverse, reversible reactions, continuous scheme

**Derived unit**  $(3600 \text{ s})^{-1} \cdot \text{nmol}$

$$v_{14} = CL\_dM \cdot ([C1\_M] - [C2\_M]) \quad (37)$$

## 9 Derived Rate Equations

When interpreted as an ordinary differential equation framework, this model implies the following set of equations for the rates of change of each species.

Identifiers for kinetic laws highlighted in gray cannot be verified to evaluate to units of SBML substance per time. As a result, some SBML interpreters may not be able to verify the consistency of the units on quantities in the model. Please check if

- parameters without an unit definition are involved or

- volume correction is necessary because the `hasOnlySubstanceUnits` flag may be set to `false` and `spacialDimensions > 0` for certain species.

### 9.1 Species `A_dopa`

**SBO:0000247** simple chemical

**Initial assignment** `A_dopa`

This species takes part in two reactions (as a reactant in `l_dopa_absorption`, `l_dopa_blood-hepa_clearance`).

$$\frac{d}{dt}A\_dopa = -v_1 - v_2 \quad (38)$$

### 9.2 Species `A_B`

**SBO:0000247** simple chemical

**Initial assignment** `A_B`

This species takes part in two reactions (as a reactant in `benserazide_absorption`, `benserazide-gut_clearance`).

$$\frac{d}{dt}A\_B = -v_4 - v_5 \quad (39)$$

### 9.3 Species `A_M`

**SBO:0000247** simple chemical

**Initial assignment** `A_M`

This species takes part in one reaction (as a reactant in `ro_04_5127_absorption`).

$$\frac{d}{dt}A\_M = -v_3 \quad (40)$$

### 9.4 Species `C_dopa`

**SBO:0000247** simple chemical

**Initial concentration**  $0 \text{ nmol} \cdot \text{l}^{-1}$

This species takes part in four reactions (as a reactant in `AADC_clearance`, `COMT_clearance`, `rest_clearance` and as a product in `l_dopa_absorption`).

$$\frac{d}{dt}C\_dopa = v_1 - v_6 - v_7 - v_8 \quad (41)$$

## 9.5 Species C\_OMD

**Name** C\_3-OMD

**SBO:0000247** simple chemical

**Initial concentration** 0 nmol · l<sup>-1</sup>

This species takes part in two reactions (as a reactant in [\\_3\\_OMD\\_clearance](#) and as a product in [COMT\\_clearance](#)).

$$\frac{d}{dt}C\_OMD = v_7 - v_9 \quad (42)$$

## 9.6 Species C1\_M

**SBO:0000247** simple chemical

**Notes** Ro 04-5127, an inhibitor of amino-acid carboxylase (AADC), in the central compartment

**Initial concentration** 0 nmol · l<sup>-1</sup>

This species takes part in four reactions (as a reactant in [ro\\_clearance](#), [ro\\_distribution](#) and as a product in [ro\\_04\\_5127\\_absorption](#), [bens\\_metabolism](#)).

$$\frac{d}{dt}C1\_M = v_3 + v_{11} - v_{12} - v_{14} \quad (43)$$

## 9.7 Species C2\_M

**SBO:0000247** simple chemical

**Notes** Ro 04-5127 in the peripheral compartment

**Initial concentration** 0 nmol · l<sup>-1</sup>

This species takes part in one reaction (as a product in [ro\\_distribution](#)).

$$\frac{d}{dt}C2\_M = v_{14} \quad (44)$$

## 9.8 Species C1\_B

**SBO:0000247** simple chemical

**Notes** Benserazide in the central compartment

**Initial concentration** 0 nmol · l<sup>-1</sup>

This species takes part in four reactions (as a reactant in [bens\\_clearance](#), [bens\\_metabolism](#), [bens\\_distribution](#) and as a product in [benserazide\\_absorption](#)).

$$\frac{d}{dt}C1\_B = v_4 - v_{10} - v_{11} - v_{13} \quad (45)$$

## 9.9 Species C2\_B

**SBO:0000247** simple chemical

**Notes** Benserazide in the peripheral compartment

**Initial concentration** 0 nmol · l<sup>-1</sup>

This species takes part in one reaction (as a product in [bens\\_distribution](#)).

$$\frac{d}{dt}C2\_B = v_{13} \quad (46)$$

## A Glossary of Systems Biology Ontology Terms

**SBO:0000002 quantitative systems description parameter:** A numerical value that defines certain characteristics of systems or system functions. It may be part of a calculation, but its value is not determined by the form of the equation itself, and may be arbitrarily assigned

**SBO:0000035 forward unimolecular rate constant, continuous case:** Numerical parameter that quantifies the forward velocity of a chemical reaction involving only one reactant. This parameter encompasses all the contributions to the velocity except the quantity of the reactant. It is to be used in a reaction modelled using a continuous framework

**SBO:0000049 mass action rate law for first order irreversible reactions, continuous scheme:** Reaction scheme where the products are created from the reactants and the change of a product quantity is proportional to the product of reactant activities. The reaction scheme does not include any reverse process that creates the reactants from the products. The change of a product quantity is proportional to the quantity of one reactant. It is to be used in a reaction modelled using a continuous framework.

**SBO:0000080 mass action rate law for first order forward, first order reverse, reversible reactions, continuous scheme:** Reaction scheme where the products are created from the reactants and the change of a product quantity is proportional to the product of reactant activities. The reaction scheme does include a reverse process that creates the reactants from the products. The rate of the forward process is proportional to the quantity of one reactant. The rate of the reverse process is proportional to the quantity of one product. It is to be used in a reaction modelled using a continuous framework.

**SBO:0000179 degradation:** Complete disappearance of a physical entity

**SBO:0000185 transport reaction:** Movement of a physical entity without modification of the structure of the entity

**SBO:0000196 concentration of an entity pool:** The amount of an entity per unit of volume.

- SBO:0000197 specific concentration of an entity:** Concentration of an object divided by the value of another parameter having the dimension of a concentration
- SBO:0000211 removal of a chemical group:** Covalent reaction that results in the removal of a chemical group from a molecule
- SBO:0000214 methylation:** Addition of a methyl group (-CH<sub>3</sub>) to a chemical entity
- SBO:0000247 simple chemical:** Simple, non-repetitive chemical entity
- SBO:0000288 IC50:** Also called half maximal inhibitory concentration, it represents the concentration of an inhibitor substance that is required to suppress 50% of an effect.
- SBO:0000290 physical compartment:** Specific location of space, that can be bounded or not. A physical compartment can have 1, 2 or 3 dimensions
- SBO:0000381 biochemical proportionality coefficient:** A multiplicative factor for quantities, expressions or functions
- SBO:0000399 decarboxylation:** A process in which a carboxyl group (COOH) is removed from a molecule as carbon dioxide

SBML<sup>2</sup>LaTeX was developed by Andreas Dräger<sup>a</sup>, Hannes Planatscher<sup>a</sup>, Dieudonné M Wouamba<sup>a</sup>, Adrian Schröder<sup>a</sup>, Michael Hucka<sup>b</sup>, Lukas Endler<sup>c</sup>, Martin Golebiewski<sup>d</sup> and Andreas Zell<sup>a</sup>. Please see <http://www.ra.cs.uni-tuebingen.de/software/SBML2LaTeX> for more information.

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