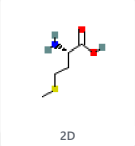
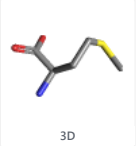
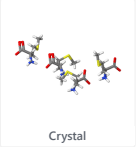
Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

PubChem

COMPOUND SUMMARY

Methionine

PubChem CID	6137
Structure	 2D  3D  Crystal Find Similar Structures
Chemical Safety	Laboratory Chemical Safety Summary (LCSS) Datasheet
Molecular Formula	$C_5H_{11}NO_2S$
Synonyms	L-methionine 63-68-3 methionine h-Met-oh (S)-2-Amino-4-(methylthio)butanoic acid More...
Molecular Weight	149.21
Dates	Modify 2022-12-03 Create 2004-09-16

Methionine is one of nine essential amino acids in humans (provided by food), Methionine is required for growth and tissue repair. A sulphur-containing amino acid, methionine improves the tone and pliability of skin, hair, and strengthens nails. Involved in many detoxifying processes, sulphur provided by methionine protects cells from pollutants, slows cell aging, and is essential for absorption and bio-availability of selenium and zinc. Methionine chelates heavy metals, such as lead and mercury, aiding their excretion. It also acts as a lipotropic agent and prevents excess fat buildup in the liver. (NCI04)

- NCI Thesaurus (NCIt)

L-methionine is the L-enantiomer of methionine. It has a role as a nutraceutical, a micronutrient, an antidote to paracetamol poisoning, a human metabolite and a mouse metabolite. It is an aspartate family amino acid, a proteinogenic amino acid, a methionine and a L-alpha-amino acid. It is a conjugate base of a L-methioninium. It is a conjugate acid of a L-methioninate. It is an enantiomer of a D-methionine. It is a tautomer of a L-methionine zwitterion.

- ChEBI

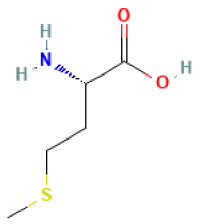
Methionine is a metabolite found in the aging mouse brain.

- West Coast Metabolomics Center-UC Davis

1 Structures

1.1 2D Structure

Chemical Structure Depiction



PubChem

1.2 3D Conformer

PubChem

1.3 Crystal Structures

CCDC Number	276855
Crystal Structure Data	DOI:10.5517/cc992tg
Crystal Structure Depiction	

The Cambridge Structural Database

2 Biologic Description

SVG Image	
IUPAC Condensed	H-Met-OH
Sequence	M
PLN	H-M-OH
HELM	PEPTIDE1{M}$$$$
IUPAC	L-methionine

PubChem

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

3 Names and Identifiers

3.1 Computed Descriptors

3.1.1 IUPAC Name

(2*S*)-2-amino-4-methylsulfanylbutanoic acid

Computed by Lexichem TK 2.7.0 (PubChem release 2021.05.07)

PubChem

3.1.2 InChI

InChI=1S/C5H11NO2S/c1-9-3-2-4(6)5(7)8/h4H,2-3,6H2,1H3,(H,7,8)/t4-/m0/s1

Computed by InChI 1.0.6 (PubChem release 2021.05.07)

PubChem

3.1.3 InChIKey

FFEARJCKVFRZRR-BYPYZUCNSA-N

Computed by InChI 1.0.6 (PubChem release 2021.05.07)

PubChem

3.1.4 Canonical SMILES

CSCCC(C(=O)O)N

Computed by OEChem 2.3.0 (PubChem release 2021.05.07)

PubChem

3.1.5 Isomeric SMILES

CSCC[C@@H](C(=O)O)N

Computed by OEChem 2.3.0 (PubChem release 2021.05.07)

PubChem

3.2 Molecular Formula

C5H11NO2S

CAMEO Chemicals; Wikipedia; PubChem

3.3 Other Identifiers

3.3.1 CAS

63-68-3

CAMEO Chemicals; CAS Common Chemistry; ChemIDplus; DrugBank; DTP/NCI; EPA Chemicals under the TSCA; EPA DSSTox; European Chemicals Agency (ECHA); FDA Global Substance Registration System (GSRS); Hazardous

3.3.2 Deprecated CAS

24425-78-3, 7005-18-7, 1437749-32-0, 1437749-60-4, 1437749-65-9, 1437749-75-1, 1437749-80-8, 1437769-00-0, 1437870-94-4, 1437870-95-5, 1437870-97-7, 1437870-98-8, 1437871-20-9, 1463481-01-7, 1463481-06-2, 1463481-15-3, 1463481-19-7, 1463481-23-3, 1463481-27-7, 1463481-31-3, 1463481-37-9, 1463481-41-5, 1463481-46-0, 1463481-51-7, 1463481-58-4, 1463481-73-3, 1463481-80-2, 1463481-89-1, 1463610-75-4, 1463610-76-5, 1466415-57-5

ChemIDplus

1437749-32-0, 1437749-60-4, 1437749-65-9, 1437749-75-1, 1437749-80-8, 1437769-00-0, 1437870-94-4, 1437870-95-5, 1437870-97-7, 1437870-98-8, 1437871-20-9, 1463481-06-2, 1463481-15-3, 1463481-19-7, 1463481-23-3, 1463481-27-7, 1463481-31-3, 1463481-37-9, 1463481-41-5, 1463481-46-0, 1463481-51-7, 1463481-58-4, 1463481-73-3, 1463481-80-2, 1463481-89-1, 1463610-75-4, 1463610-76-5, 1466415-57-5, 24425-78-3, 7005-18-7

EPA DSSTox

3.3.3 European Community (EC) Number

200-562-9

European Chemicals Agency (ECHA)

3.3.4 NSC Number

760117

DTP/NCI

3.3.5 UNII

AE28F7PNPL

FDA Global Substance Registration System (GSRS)

3.3.6 DSSTox Substance ID

DTXSID5040548

EPA DSSTox

3.3.7 Wikipedia

Methionine

Wikipedia

3.3.8 Wikidata

Q22124685

Wikidata

3.3.9 NCI Thesaurus Code

C29600

NCI Thesaurus (NCIt)

3.3.10 RXCUI

6837

NLM RxNorm Terminology

3.4 Synonyms

3.4.1 MeSH Entry Terms

L-Isomer Methionine
L-Methionine
Liquimeth
Methionine
Methionine, L Isomer
Methionine, L-Isomer
Pedameth

Medical Subject Headings (MeSH)

3.4.2 Depositor-Supplied Synonyms

L-methionine	(L)-Methionine	L-Homocysteine, S-methyl-	L-Met	CHEMBL42336
63-68-3	Methionine (VAN)	L(-)-Amino-gamma-methylthiobutyric acid	Butanoic acid, 2-amino-4-(methylthio)-, (S)-	CHEBI:16643
methionine	Acimethin	L-alpha-Amino-gamma-methylthiobutyric acid	(S)-2-amino-4-(methylthio)butyric acid	Poly-L-methionir
h-Met-oh	Metionina [DCIT]	L-gamma-Methylthio-alpha-aminobutyric acid	Toxin WAR (Bacillus thuringiensis strain PS205C)	L-2-Amino-4met
(S)-2-Amino-4-(methylthio)butanoic acid	L-Methionin	met	(2S)-2-Amino-4-methylsulfanylbutanoic acid	NSC-22946
Cymethion	(2S)-2-amino-4-(methylsulfanyl)butanoic acid	CCRIS 5528	L-a-Amino-g-methylthiobutyric acid	58576-49-1
L-(-)-Methionine	(S)-methionine	CCRIS 5536	carbon-11 methionine	Polymethionine
S-Methionine	L-alpha-Amino-gamma-methylmercaptobutyric acid	METHIONINE, L-	S-Methyl-L-homocysteine	Methionine [USA
Liquimeth	h-Met-h	HSDB 4317	(S)-(+)-Methionine	C-11 Methionine
L-Methioninum	Methioninum [INN-Latin]	2-Amino-4-methylthiobutanoic acid (S)-	MFCD00063097	I-2-Amino-4-(me
Methilanin	metionina	2-Amino-4-(methylthio)butyric acid, (S)-	AE28F7PNPL	EINECS 200-562-
Neo-methidin	Methioninum	(2S)-2-amino-4-methylsulfanyl-butanoic acid	gamma-Methylthio-alpha-aminobutyric acid	UNII-AE28F7PNF

PubChem

4 Chemical and Physical Properties

4.1 Computed Properties

Property Name	Property Value	Reference
Molecular Weight	149.21	Computed by PubChem 2.1 (PubChem release 2021.05.07)
XLogP3	-1.9	Computed by XLogP3 3.0 (PubChem release 2021.05.07)
Hydrogen Bond Donor Count	2	Computed by Cactvs 3.4.8.18 (PubChem release 2021.05.07)
Hydrogen Bond Acceptor Count	4	Computed by Cactvs 3.4.8.18 (PubChem release 2021.05.07)
Rotatable Bond Count	4	Computed by Cactvs 3.4.8.18 (PubChem release 2021.05.07)
Exact Mass	149.05104977	Computed by PubChem 2.1 (PubChem release 2021.05.07)
Monoisotopic Mass	149.05104977	Computed by PubChem 2.1 (PubChem release 2021.05.07)
Topological Polar Surface Area	88.6 $Å^2$	Computed by Cactvs 3.4.8.18 (PubChem release 2021.05.07)
Heavy Atom Count	9	Computed by PubChem
Formal Charge	0	Computed by PubChem
Complexity	97	Computed by Cactvs 3.4.8.18 (PubChem release 2021.05.07)
Isotope Atom Count	0	Computed by PubChem
Defined Atom Stereocenter Count	1	Computed by PubChem
Undefined Atom Stereocenter Count	0	Computed by PubChem
Defined Bond Stereocenter Count	0	Computed by PubChem
Undefined Bond Stereocenter Count	0	Computed by PubChem
Covalently-Bonded Unit Count	1	Computed by PubChem
Compound Is Canonicalized	Yes	Computed by PubChem (release 2021.05.07)

PubChem

4.2 Experimental Properties

4.2.1 Physical Description

Minute hexagonal plates from dilute alcohol. (NTP, 1992)

National Toxicology Program, Institute of Environmental Health Sciences, National Institutes of Health (NTP). 1992. National Toxicology Program Chemical Repository Database. Research Triangle Park, North Carolina.

CAMEO Chemicals

Solid; [Merck Index] Colorless or white solid with a faint odor; [HSDB] White powder; [Sigma-Aldrich MSDS]

Haz-Map, Information on Hazardous Chemicals and Occupational Diseases

Solid

Human Metabolome Database (HMDB)

4.2.2 Color/Form

Minute hexagonal plates from dilute alcohol

O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 2006., p. 1032

Hazardous Substances Data Bank (HSDB)

Colorless or white, lustrous plates or as white, crystalline powder

FCC; Food Chemicals Codex. Committee on Food Chemicals Codex, Food and Nutrition Board, Institute of Medicine. 5th. Washington, DC: National Academy Press p. 286 (2003)

Hazardous Substances Data Bank (HSDB)

4.2.3 Odor

Faint

Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 12th ed. New York, NY: Van Nostrand Rheinhold Co., 1993, p. 752

Hazardous Substances Data Bank (HSDB)

4.2.4 Taste

Sulfurous

Gerhartz, W. (exec ed.). Ullmann's Encyclopedia of Industrial Chemistry. 5th ed.Vol A1: Deerfield Beach, FL: VCH Publishers, 1985 to Present., p. VA2: 79 (1985)

Hazardous Substances Data Bank (HSDB)

4.2.5 Boiling Point

sublimes at 367 °F (NTP, 1992)

National Toxicology Program, Institute of Environmental Health Sciences, National Institutes of Health (NTP). 1992. National Toxicology Program Chemical Repository Database. Research Triangle Park, North Carolina.

- CAMEO Chemicals

181 °C (decomposes)

Lide, D.R. CRC Handbook of Chemistry and Physics 88TH Edition 2007-2008. CRC Press, Taylor & Francis, Boca Raton, FL 2007, p. 3-328

- Hazardous Substances Data Bank (HSDB)

4.2.6 Melting Point

536 to 540 °F decomposes 541.4-543.2 °F (NTP, 1992)

National Toxicology Program, Institute of Environmental Health Sciences, National Institutes of Health (NTP). 1992. National Toxicology Program Chemical Repository Database. Research Triangle Park, North Carolina.

- CAMEO Chemicals

283 dec °C

PhysProp

- DrugBank

280-282 °C (decomposes, sealed capillary)

O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 2006., p. 1032

- Hazardous Substances Data Bank (HSDB)

284 °C

- Human Metabolome Database (HMDB)

4.2.7 Solubility

Soluble (NTP, 1992)

National Toxicology Program, Institute of Environmental Health Sciences, National Institutes of Health (NTP). 1992. National Toxicology Program Chemical Repository Database. Research Triangle Park, North Carolina.

- CAMEO Chemicals

56600 mg/L (at 25 °C)

YALKOWSKY,SH & DANNENFELSER,RM (1992)

- DrugBank

Soluble in water but the crystals are somewhat water-repellant at first

O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 2006., p. 1032

- Hazardous Substances Data Bank (HSDB)

Soluble in warm dilute alcohol; insoluble in absolute alcohol, ether, petroleum ether, benzene, acetone

O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 2006., p. 1032

- Hazardous Substances Data Bank (HSDB)

Slightly soluble in acetic acid

Lide, D.R. CRC Handbook of Chemistry and Physics 88TH Edition 2007-2008. CRC Press, Taylor & Francis, Boca Raton, FL 2007, p. 3-328

- Hazardous Substances Data Bank (HSDB)

In water, 56.6 g/L at 25 °C

Yalkowsky, S.H., He, Yan., Handbook of Aqueous Solubility Data: An Extensive Compilation of Aqueous Solubility Data for Organic Compounds Extracted from the AQUASOL dATAbASE. CRC Press LLC, Boca Raton, FL. 2003., p. 175

- Hazardous Substances Data Bank (HSDB)

56.6 mg/mL

YALKOWSKY,SH & DANNENFELSER,RM (1992)

- Human Metabolome Database (HMDB)

4.2.8 Density

1.178 at 68 °F (NTP, 1992)

National Toxicology Program, Institute of Environmental Health Sciences, National Institutes of Health (NTP). 1992. National Toxicology Program Chemical Repository Database. Research Triangle Park, North Carolina.

- CAMEO Chemicals

4.2.9 Vapor Pressure

0.00000052 [mmHg]

- Haz-Map, Information on Hazardous Chemicals and Occupational Diseases

8.14X10-8 mm Hg at 25 °C (est)

US EPA; Estimation Program Interface (EPI) Suite. Ver. 4.0. Jan, 2009. Available from, as of Feb 19, 2010: https://www.epa.gov/oppt/exposure/pubs/episuitedl.htm

Hazardous Substances Data Bank (HSDB)

4.2.10 LogP

-1.87

HANSCH,C ET AL. (1995)

DrugBank

log Kow = -1.87

Hansch, C., Leo, A., D. Hoekman. Exploring QSAR - Hydrophobic, Electronic, and Steric Constants. Washington, DC: American Chemical Society., 1995., p. 15

Hazardous Substances Data Bank (HSDB)

-1.87

HANSCH,C ET AL. (1995)

Human Metabolome Database (HMDB)

4.2.11 LogS

-0.42

ADME Research, USCD

DrugBank

4.2.12 Henry's Law Constant

Henry's Law constant = 2.11X10-11 atm-cu m/mol at 25 °C (est)

US EPA; Estimation Program Interface (EPI) Suite. Ver. 4.0. Jan, 2009. Available from, as of Feb 19, 2010: https://www.epa.gov/oppt/exposure/pubs/episuitedl.htm

Hazardous Substances Data Bank (HSDB)

4.2.13 Optical Rotation

Specific optical rotation: +8.12 deg at 25 °C/D (c = 0.8); -21.19 deg at 25 °C/D (c = 0.8 in 0.2N HCl) /Methione, D-form/

O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 2006., p. 1032

Hazardous Substances Data Bank (HSDB)

Specific optical rotation: 22.5 deg at 25 °C/D (1 N HCl)

Lide, D.R., G.W.A. Milne (eds.). Handbook of Data on Organic Compounds. Volume I. 3rd ed. CRC Press, Inc. Boca Raton ,FL. 1994., p. V4: 3432

Hazardous Substances Data Bank (HSDB)

Specific optical rotation: -8.2 deg at 25 °C/D (c = 0.8); +23.40 at 20 °C/D (c = 5.0 in 3.0N HCl)

O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 2006., p. 1032

Hazardous Substances Data Bank (HSDB)

4.2.14 Decomposition

When heated to decomposition it emits very toxic fumes of /nitric oxide/ and /sulfur oxide/.

Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 2334

Hazardous Substances Data Bank (HSDB)

4.2.15 pH

pH (1% aqueous solution) = 5.6-6.1

Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 12th ed. New York, NY: Van Nostrand Rheinhold Co., 1993, p. 752

Hazardous Substances Data Bank (HSDB)

4.2.16 Ionization Efficiency

Ionization mode	Negative
logIE	-0.62
pH	10.5
Instrument	Agilent XCT
Ion source	Electrospray ionization
Additive	ammonia (10nM)
Organic modifier	MeCN (80%)
Reference	DOI:10.1021/acs.analchem.7b00595

Kruve Lab, Ionization & Mass Spectrometry, Stockholm University

Ionization mode	Positive
logIE	2.7
pH	2.7
Instrument	Agilent XCT
Ion source	Electrospray ionization
Additive	formic acid (5.3nM)
Organic modifier	MeCN (80%)
Reference	DOI:10.1021/acs.analchem.7b00101

Kruve Lab, Ionization & Mass Spectrometry, Stockholm University

4.2.17 Dissociation Constants

pKa

2.28 (at 25 °C)

ULLMANN VA2:63 (1985)

DrugBank

pKa = 2.28; pK2 = 9.21

Drauz K et al; Ullmann's Encyclopedia of Industrial Chemistry. 7th ed. (2008). NY, NY: John Wiley & Sons; Amino Acids. Online Posting Date: Apr 15, 2007.

Hazardous Substances Data Bank (HSDB)

4.2.18 Collision Cross Section

133.65 Å² $[M+H]^+$ [CCS Type: DT, Method: stepped-field]

https://pubs.rsc.org/en/content/articlelanding/2017/sc/c7sc03464d

CCSbase

152.05 Å² $[M-H]^-$ [CCS Type: DT, Method: stepped-field]

https://pubs.rsc.org/en/content/articlelanding/2017/sc/c7sc03464d

CCSbase

127 Å² $[M+H]^+$ [CCS Type: TW, Method: calibrated with polyalanine]

https://pubs.acs.org/doi/abs/10.1021/ac500405x

CCSbase

133.1 Å² $[M+H]^+$ [CCS Type: DT, Method: single field calibrated with ESI Low Concentration Tuning Mix (Agilent)]

https://pubs.acs.org/doi/abs/10.1021/acs.analchem.8b04322

CCSbase

132 Å² $[M-H]^-$ [CCS Type: DT, Method: single field calibrated with ESI Low Concentration Tuning Mix (Agilent)]

https://pubs.acs.org/doi/abs/10.1021/acs.analchem.8b04322

CCSbase

134.08 Å² $[M+H]^+$ [CCS Type: DT, Method: stepped-field]

https://pubs.acs.org/doi/abs/10.1021/acs.analchem.7b01729

CCSbase

132.9 Å² $[M+H]^+$

133.6 Å² $[M+H]^+$

140.5 Å² $[M-H]^-$

S50 | CCSCOMPEND | The Unified Collision Cross Section (CCS) Compendium | DOI:10.5281/zenodo.2658162

NORMAN Suspect List Exchange

4.2.19 Other Experimental Properties

Platelets from alcohol. mp 281 °C (decomposes), density 1.340; pKa1 = 2.28, pKa2 = 9.21; pH of 1% aqueous solution 5.6-6.1; Rf value 0.77. Solubility in water (g/L) at 0 °C: 18.18; at 25 °C: 33.81; at 50 °C: 60/.70; at 75 °C: 15.2 °C. Soluble in dilute acids, alkalies. Very slightly soluble in 95% alcohol. Insoluble in ether. /Methionine, DL-form/

O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 2006., p. 1032

Hazardous Substances Data Bank (HSDB)

UV: 1-65 (Organic Electronic Spectral Data, Phillips et al, John Wiley & Sons, New York) /Methionine (DL)/

Lide, D.R., G.W.A. Milne (eds.). Handbook of Data on Organic Compounds. Volume I. 3rd ed. CRC Press, Inc. Boca Raton ,FL. 1994., p. V4: 3431

Hazardous Substances Data Bank (HSDB)

Hydroxyl radical reaction rate constant = 5.13X10-11 cu cm/molec-sec at 25 °C (est)

US EPA; Estimation Program Interface (EPI) Suite. Ver. 4.0. Jan, 2009. Available from, as of Feb 19, 2010: https://www.epa.gov/oppt/exposure/pubs/episuitedl.htm

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

- Hazardous Substances Data Bank (HSDB)

4.2.20 Chemical Classes

Biological Agents -> Amino Acids and Derivatives

- Haz-Map, Information on Hazardous Chemicals and Occupational Diseases

5 Spectral Information

5.1 1D NMR Spectra

1D NMR Spectra	NMRShiftDB Link

NMRShiftDB

5.1.1 1H NMR Spectra

Spectra ID	1484
Instrument Type	Varian
Frequency	500 MHz
Solvent	Water
pH	7.00
Shifts [ppm]:Intensity	2.07:1.26, 2.09:3.48, 2.10:5.92, 2.12:100.00, 2.12:9.80, 2.15:2.58, 2.15:3.07, 2.17:2.90, 2.17:5.22, 2.18:5.50, 2.19:3.78, 2.20:3.73, 2.21:1.68, 2.21:2.29, 2.23:1.38, 2.62:15.07, 2.63:25.65, 2.65:13.19, 3.84:6.93, 3.85:8.15, 3.85:8.22, 3.86:6.80
Thumbnail	

Human Metabolome Database (HMDB)

Spectra ID	4840
Instrument Type	Bruker
Solvent	D2O
pH	7.4
Shifts [ppm]:Intensity	2.09:0.69, 2.11:1.19, 2.12:15.00, 2.13:1.43, 2.14:0.49, 2.16:0.44, 2.17:0.54, 2.17:0.98, 2.18:1.06, 2.19:0.71, 2.19:0.72, 2.21:0.30, 2.21:0.47, 2.62:2.76, 2.63:4.75, 2.64:2.41, 3.84:0.96, 3.85:1.10, 3.85:1.12, 3.86:0.93
Thumbnail	

Human Metabolome Database (HMDB)

5.1.2 13C NMR Spectra

Showing 2 of 3 View More

13C NMR Spectra	13C NMR: 135 (Johnson and Jankowski, Carbon-13 NMR Spectra, John Wiley & Sons, New York) /Methionine (DL)/

Hazardous Substances Data Bank (HSDB)

Spectra ID	1254
Instrument Type	Bruker
Frequency	125 MHz
Solvent	Water

pH	7.00
Shifts [ppm]:Intensity	-0.00:5.63, 16.64:36.56, 176.96:19.01, 31.54:55.50, 32.53:54.72, 56.81:46.00
Thumbnail	

Human Metabolome Database (HMDB)

5.2 2D NMR Spectra

5.2.1 1H-1H NMR Spectra

2D NMR Spectra Type	1H-1H TOCSY
Spectra ID	1031
Shifts [ppm] (F2:F1)	2.13:2.08, 2.13:2.10, 2.13:2.12, 2.14:3.85, 2.16:2.17, 2.16:2.63, 2.17:2.08, 2.17:2.19, 2.17:2.62, 2.17:2.65, 2.18:2.10, 2.18:2.20, 2.30:2.30, 2.63:2.16, 2.63:2.19, 2.63:2.20, 2.63:2.22, 2.63:2.62, 2.64:2.08, 2.64:2.10, 2.64:2.12, 2.64:2.14, 2.64:2.63, 2.64:2.65, 2.64:3.85, 3.58:2.12, 3.86:2.14, 3.86:2.17, 3.86:2.19, 3.86:2.62, 3.86:2.63, 3.86:2.65, 3.86:3.84, 3.86:3.86
Thumbnail	

Human Metabolome Database (HMDB)

5.2.2 1H-13C NMR Spectra

2D NMR Spectra Type	1H-13C HSQC
Spectra ID	1430
Instrument Type	Bruker
Frequency	600 MHz
Solvent	Water
pH	7.00
Shifts [ppm] (F2:F1):Intensity	2.10:16.57:0.10, 2.18:32.72:0.35, 2.63:31.58:1.00, 3.85:56.84:0.60
Thumbnail	

Human Metabolome Database (HMDB)

5.3 Mass Spectrometry

5.3.1 GC-MS

Showing 2 of 15 View More

Spectra ID	1109
Instrument Type	GC-MS
SPLASH	splash10-0udi-1900000000-1a97567ce4f25c4e8263
Top 5 Peaks	104.0 1 131.0 0.22 130.0 0.18 221.0 0.12 116.0 0.11
Thumbnail	

Human Metabolome Database (HMDB)

Spectra ID	1204
Instrument Type	GC-MS
SPLASH	splash10-004i-0910000000-1b0477118cb20549bf4d
Top 5 Peaks	176.0 1 128.0 0.88 177.0 0.15 129.0 0.12 100.0 0.12
Thumbnail	

Human Metabolome Database (HMDB)

5.3.2 MS-MS

Showing 2 of 8 View More

Spectra ID	2227227
Ionization Mode	Positive
SPLASH	splash10-08fr-9000000000-15d18c8b69363f5fd070
Top 5 Peaks	61.01049 100 56.04918 97 74.02289 13.30 44.97952 9.20 102.05554 5.50
Thumbnail	

Human Metabolome Database (HMDB)

Spectra ID	2227290
Ionization Mode	Negative
SPLASH	splash10-0002-9000000000-fb25da28b5032f561ea6
Top 5 Peaks	46.99551 100 57.72199 2.40
Thumbnail	

Human Metabolome Database (HMDB)

5.3.3 LC-MS

Showing 2 of 27 View More

Accession ID	MSBNK-BGC_Munich-RP001901
Authors	BGC, Helmholtz Zentrum Muenchen
Instrument	maXis plus UHR-ToF-MS, Bruker Daltonics
Instrument Type	LC-ESI-QTOF
MS Level	MS2
Ionization Mode	POSITIVE
Ionization	ESI
Collision Energy	10
Fragmentation Mode	CID
Column Name	BEH C18 1.7um, 2.1x100mm, Waters
Retention Time	0.698 min
Precursor m/z	150.0583
Precursor Adduct	[M+H]+
Top 5 Peaks	104.0527 999 150.0582 264 133.0318 194 102.0549 154 74.0595 46
SPLASH	splash10-0udi-0900000000-7739b5e1721763636a0a
Thumbnail	

License	CC BY

MassBank Europe

Accession ID	MSBNK-BGC_Munich-RP001902
Authors	BGC, Helmholtz Zentrum Muenchen
Instrument	maXis plus UHR-ToF-MS, Bruker Daltonics
Instrument Type	LC-ESI-QTOF
MS Level	MS2
Ionization Mode	POSITIVE
Ionization	ESI
Collision Energy	20
Fragmentation Mode	CID
Column Name	BEH C18 1.7um, 2.1x100mm, Waters
Retention Time	0.698 min
Precursor m/z	150.0583
Precursor Adduct	[M+H]+
Top 5 Peaks	74.023 999 104.0526 962 87.0258 944 74.0595 741 102.0547 565
SPLASH	splash10-0fki-9400000000-103ca2cc7e18aabe73e4
Thumbnail	
License	CC BY

MassBank Europe

5.3.4 Other MS

Showing 2 of 8 View More

Other MS	MASS: 442 (National Bureau of Standards EPA-NIH Mass Spectra Data Base, NSRDS-NBS-63) /Methionine (DL)/
Other MS	MASS: 54346 (NIST/EPA/MSDC Mass Spectral Database, 1990 version)

Hazardous Substances Data Bank (HSDB)

Accession ID	MSBNK-GL_Sciences_Inc-GLS00029
Authors	Miyagawa H, Akimoto S, Yamasaki K, GL Sciences Inc.
Instrument	GCMS-2010 Plus, Shimadzu
Instrument Type	EI-B
MS Level	MS
Ionization Mode	POSITIVE
Column Name	InertCap 5MS/NP 0.25 mmI.D. x 30 m, df=0.25 um
Retention Time	596.79
Top 5 Peaks	176.1 999 128.1 647

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

	147.1 152 177.1 135 219.1 117
SPLASH	splash10-004i-0920000000-8ffae5d87508e0704903
Thumbnail	
License	CC BY-SA

MassBank Europe

5.4 UV Spectra

MAX ABSORPTION (0.01 N HCL): 208 NM (SHOULDER) (LOG E= 3.2)

Weast, R.C. (ed.). Handbook of Chemistry and Physics. 60th ed. Boca Raton, Florida: CRC Press Inc., 1979., p. C-378

Hazardous Substances Data Bank (HSDB)

5.5 IR Spectra

IR Spectra	IR: 2549 (Coblentz Society Spectral Collection) /Methionine (DL)/

Hazardous Substances Data Bank (HSDB)

5.5.1 ATR-IR Spectra

Source of Sample	Aldrich
Catalog Number	151696
Copyright	Copyright © 2018-2021 Sigma-Aldrich Co. LLC. - Database Compilation Copyright © 2018-2021 John Wiley & Sons, Inc. All Rights Reserved.
Thumbnail	

SpectraBase

5.6 Raman Spectra

Technique	FT-Raman
Source of Spectrum	Forensic Spectral Research
Source of Sample	Sigma-Aldrich Company LLC
Catalog Number	M9625
Lot Number	108K01611
Copyright	Copyright © 2015-2021 John Wiley & Sons, Inc. All Rights Reserved.
Thumbnail	

SpectraBase

Catalog Number	151696
Copyright	Copyright © 2017-2021 Sigma-Aldrich Co. LLC. - Database Compilation Copyright © 2017-2021 John Wiley & Sons, Inc. All Rights Reserved.
Thumbnail	

SpectraBase

6 Related Records

6.1 Related Compounds with Annotation

PubChem

6.2 Related Compounds

Same Connectivity	88 Records
Same Stereo	60 Records
Same Isotope	3 Records
Same Parent, Connectivity	413 Records
Same Parent, Stereo	208 Records
Same Parent, Isotope	326 Records
Same Parent, Exact	148 Records
Mixtures, Components, and Neutralized Forms	755 Records
Similar Compounds	680 Records
Similar Conformers	3,734 Records

PubChem

6.3 Substances

6.3.1 Related Substances

All	2,052 Records
Same	806 Records
Mixture	1,246 Records

PubChem

6.3.2 Substances by Category

PubChem

6.4 Entrez Crosslinks

PubMed	1,428 Records

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

Protein Structures	164 Records
Taxonomy	4 Records
OMIM	51 Records
Gene	3,658 Records

PubChem

6.5 Associated Chemicals

Methionine (DL);59-51-8

Hazardous Substances Data Bank (HSDB)

d-Methionine;657-27-2

Hazardous Substances Data Bank (HSDB)

6.6 NCBI LinkOut

NCBI

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

7 Chemical Vendors

PubChem

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

8 Drug and Medication Information

8.1 Drug Indication

Used for protein synthesis including the formation of SAMe, L-homocysteine, L-cysteine, taurine, and sulfate.

DrugBank

8.2 FDA National Drug Code Directory

METHIONINE is an active ingredient in 26 products including: 'AMINOSYN II', 'CLINIMIX E', and 'FREAMINE III'.

National Drug Code (NDC) Directory

National Drug Code (NDC) Directory

8.3 Clinical Trials

8.3.1 ClinicalTrials.gov

ClinicalTrials.gov

8.3.2 EU Clinical Trials Register

EU Clinical Trials Register

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

8.3.3 NIPH Clinical Trials Search of Japan

NIPH Clinical Trials Search of Japan

8.4 Therapeutic Uses

A sulfur containing essential amino acid that is important in many body functions. It is a chelating agent for heavy metals

National Library of Medicine's Medical Subject Headings online file (MeSH, 1999)

Hazardous Substances Data Bank (HSDB)

Methionine ... enhances the synthesis of glutathione and is used as an alternative to acetylcysteine in the treatment of paracetamol poisoning.

Sweetman SC (ed), Martindale: The Complete Drug Reference. London: Pharmaceutical Press (2009), p.1450.

Hazardous Substances Data Bank (HSDB)

... Many of signs of toxicity /of selenium poisoning/ can be prevented by high-protein diets, and by methionine in the presence of Vitamin E.

Doull, J., C.D. Klaassen, and M. D. Amdur (eds.). Casarett and Doull's Toxicology. 2nd ed. New York: Macmillan Publishing Co., 1980., p. 456

Hazardous Substances Data Bank (HSDB)

In Europe, oral methionine (10 g over 12 hours) is approved as an agent to restore depleted glutathione stores and prevent hepatotoxicity after large acetaminophen ingestions. N-Acetyl-L-cysteine remains the preferred antidote for acetaminophen overdose in the United States, Canada, Scotland, and most of England.

Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988., p. 80

Hazardous Substances Data Bank (HSDB)

For more Therapeutic Uses (Complete) data for (L)-Methionine (9 total), please visit the HSDB record page.

Hazardous Substances Data Bank (HSDB)

8.5 Drug Warnings

Methionine may cause nausea, vomiting, drowsiness, and irritability. It should not be used in patients with acidosis. Methionine may aggravate hepatic encephalopathy in patients with established liver damage; it should be used with caution in patients with severe liver disease.

Sweetman SC (ed), Martindale: The Complete Drug Reference. London: Pharmaceutical Press (2009), p. 1450.

Hazardous Substances Data Bank (HSDB)

Vomiting is a common adverse effect.

Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988., p. 163

Hazardous Substances Data Bank (HSDB)

Methionine ... may exacerbate hepatic encephalopathy when administered more than 10 hours postingestion.

Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988., p. 163

Hazardous Substances Data Bank (HSDB)

The death of a control subject after an oral load of methionine for a study of the possible relationship between homocysteine and Alzheimer's disease is reported. The subject developed postload plasma concentrations of methionine far beyond those reported previously in humans given the usual oral loading dose of methionine (100 mg/kg body wt). Her preload plasma metabolite values rule out known genetic diseases that might predispose one to unusually high methionine concentrations. The most likely explanation for these events is that the subject received a substantial overdose of methionine. The possibility that extremely high methionine concentrations may lead to severe cerebral effects is discussed, and it is recommended that any move to increase the sensitivity of the usual methionine loading test by increasing the dose of methionine either not be undertaken or be taken only with extreme care.

PMID:12067919

Cottington EM et al; Arterioscler Thromb Vasc Biol 22 (6): 1046-50 (2002).

Hazardous Substances Data Bank (HSDB)

When studying genetic factors in arteriosclerosis /the authors/ recorded acute complications during a standard methionine loading test (with a dose of 100 mg/kg bw) and assessed a 30-day mortality in a group of 296 patients with coronary artery or peripheral arterial disease and in 591 controls. Acute complications were observed in 33% of the women and 16.5% of the men. For each sex, the patients and controls exhibited the same proportion of complications. The most common symptom, dizziness, was attributable to methionine loading. In addition, isolated sleepiness, nausea, polyuria and decreased or increased blood pressure were observed in part of the subjects. None of the 887 individuals died within the 30-day period following the test...

PMID:12056788

Krupkova-Meixerova L et al; Clin Nutr 21 (2): 151-6 (2002).

- Hazardous Substances Data Bank (HSDB)

8.6 Biomarker Information

- MarkerDB

9 Food Additives and Ingredients

9.1 Food Additive Classes

Flavoring Agents

- EU Food Improvement Agents

9.2 FDA Substances Added to Food

Substance	L-METHIONINE
Used for (Technical Effect)	NUTRIENT SUPPLEMENT
Document Number (21 CFR)	172.320

- FDA Center for Food Safety and Applied Nutrition (CFSAN)

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

10 Pharmacology and Biochemistry

10.1 Pharmacodynamics

L-Methionine is a principle supplier of sulfur which prevents disorders of the hair, skin and nails; helps lower cholesterol levels by increasing the liver's production of lecithin; reduces liver fat and protects the kidneys; a natural chelating agent for heavy metals; regulates the formation of ammonia and creates ammonia-free urine which reduces bladder irritation; influences hair follicles and promotes hair growth. L-methionine may protect against the toxic effects of hepatotoxins, such as acetaminophen. Methionine may have antioxidant activity.

DrugBank

10.2 ATC Code

V - Various

V03 - All other therapeutic products

V03A - All other therapeutic products

V03AB - Antidotes

V03AB26 - Methionine

WHO Anatomical Therapeutic Chemical (ATC) Classification

10.3 Bionecessity

Plays an important role in biological methylation. Both l- and d-forms are effective in rat and man. D-form undergoes deamination, and the keto compound is then transaminated with the resultant inversion of the natural l-form.

The Merck Index. 9th ed. Rahway, New Jersey: Merck & Co., Inc., 1976., p. 780

Hazardous Substances Data Bank (HSDB)

Methionine restriction (MR) limits age-related adiposity in Fischer 344 (F344) rats. To assess the mechanism of adiposity resistance, the effect of MR on adipose tissue (AT) 11beta-hydroxysteroid dehydrogenase-1 (11beta-HSD1) was examined. MR induced 11beta-HSD1 activity in all ATs, correlating with increased tissue corticosterone. However, an inverse relationship between 11beta-HSD1 activity and adipocyte size was observed. Because dietary restriction controls lipogenic and lipolytic rates, MR's effects on lipogenic and lipolytic enzymes were evaluated. MR increased adipose triglyceride lipase and acetyl-coenzyme A carboxylase (ACC) protein levels but induced ACC phosphorylation at serine residues that render the enzyme inactive, suggesting alterations of basal lipolysis and lipogenesis. In contrast, no changes in basal or phosphorylated hormone-sensitive lipase levels were observed. ACC-phosphorylated sites were specific for AMP-activated protein kinase (AMPK); therefore, AMPK activation was evaluated. Significant differences in AMPKalpha protein, phosphorylation, and activity levels were observed only in retroperitoneal fat from MR rats. No differences in protein kinase A phosphorylation and intracellular cAMP levels were detected. In vitro studies revealed increased lipid degradation and a trend toward increased lipid synthesis, suggesting the presence of a futile cycle. In conclusion, MR disrupts the lipogenic/lipolytic balance, contributing importantly to adiposity resistance in F344 rats.

Perrone CE et al; J Lipid Res 49 (1): 12-23 (2008). Available from, as of March 17, 2010: https://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=17909224

Hazardous Substances Data Bank (HSDB)

The methionine choline-deficient (MCD) diet results in liver injury similar to human nonalcoholic steatohepatitis (NASH). The aims of this study were to define mechanisms of MCD-induced steatosis in insulin-resistant db/db and insulin-sensitive db/m mice. MCD-fed db/db mice developed more hepatic steatosis and retained more insulin resistance than MCD-fed db/m mice. Both subcutaneous and gonadal fat were reduced by MCD feeding: gonadal fat decreased by 23% in db/db mice and by 90% in db/m mice. Weight loss was attenuated in the db/db mice, being only 13% compared with 35% in MCD-fed db/db and db/m mice, respectively. Both strains had upregulation of hepatic fatty acid transport proteins as well as increased hepatic uptake of [14C]oleic acid: 3-fold in db/m mice ($P < 0.001$) and 2-fold in db/db mice ($P < 0.01$) after 4 weeks of MCD feeding. In both murine strains, the MCD diet reduced triglyceride secretion and downregulated genes involved in triglyceride synthesis. Therefore, increased fatty acid uptake and decreased VLDL secretion represent two important mechanisms by which the MCD diet promotes intrahepatic lipid accumulation in this model...

Rinella ME et al; J Lipid Res 49 (5): 1068-76 (2008). Available from, as of March 17, 2010: https://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=18227531

Hazardous Substances Data Bank (HSDB)

In women whose average daily intake of methionine was above the lowest quartile of intake (greater than 1.34 g/day), a 30 to 40% reduction in neural tube defect-affected pregnancies was observed. These reductions were observed for both anencephaly and spina bifida.

NAS, Food and Nutrition Board, Institute of Medicine; Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients). National Academy Press, Washington, D.C., pg. 726, 2009. Available from, as of March 10, 2010: https://www.nap.edu/catalog/10490.html

Hazardous Substances Data Bank (HSDB)

For more Bionecessity (Complete) data for (L)-Methionine (20 total), please visit the HSDB record page.

Hazardous Substances Data Bank (HSDB)

10.4 Absorption, Distribution and Excretion

Absorption

Absorbed from the lumen of the small intestine into the enterocytes by an active transport process.

DrugBank

... Rats were fed diets containing [(14)C-methyl]l-methionine ... with 6% of sodium formate, and conversion of (14)C into [(14)C]formate was measured in urine and exhaled air (as (14)CO2) ... Total oxidation of [(14)C-methyl] into CO2, amounted to 60-87% for methionine ...

The Chemical Society. Foreign Compound Metabolism in Mammals. Volume 5: A Review of the Literature Published during 1976 and 1977. London: The Chemical Society, 1979., p. 435

Hazardous Substances Data Bank (HSDB)

Although the free amino acids dissolved in the body fluids are only a very small proportion of the body's total mass of amino acids, they are very important for the nutritional and metabolic control of the body's proteins. ... Although the plasma compartment is most easily sampled, the concentration of most amino acids is higher in tissue intracellular pools. Typically, large neutral amino acids, such

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

as leucine and phenylalanine, are essentially in equilibrium with the plasma. Others, notably glutamine, glutamic acid, and glycine, are 10- to 50-fold more concentrated in the intracellular pool. Dietary variations or pathological conditions can result in substantial changes in the concentrations of the individual free amino acids in both the plasma and tissue pools. /Amino acids/

NAS, Food and Nutrition Board, Institute of Medicine; Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients). National Academy Press, Washington, D.C., pg. 596, 2009. Available from, as of March 10, 2010: https://www.nap.edu/catalog/10490.html

Hazardous Substances Data Bank (HSDB)

After ingestion, proteins are denatured by the acid in the stomach, where they are also cleaved into smaller peptides by the enzyme pepsin, which is activated by the increase in stomach acidity that occurs on feeding. The proteins and peptides then pass into the small intestine, where the peptide bonds are hydrolyzed by a variety of enzymes. These bond-specific enzymes originate in the pancreas and include trypsin, chymotrypsins, elastase, and carboxypeptidases. The resultant mixture of free amino acids and small peptides is then transported into the mucosal cells by a number of carrier systems for specific amino acids and for di- and tri-peptides, each specific for a limited range of peptide substrates. After intracellular hydrolysis of the absorbed peptides, the free amino acids are then secreted into the portal blood by other specific carrier systems in the mucosal cell or are further metabolized within the cell itself. Absorbed amino acids pass into the liver, where a portion of the amino acids are taken up and used; the remainder pass through into the systemic circulation and are utilized by the peripheral tissues. /Amino acids/

NAS, Food and Nutrition Board, Institute of Medicine; Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients). National Academy Press, Washington, D.C., pg. 599, 2009. Available from, as of March 10, 2010: https://www.nap.edu/catalog/10490.html

Hazardous Substances Data Bank (HSDB)

Protein secretion into the intestine continues even under conditions of protein-free feeding, and fecal nitrogen losses (ie, nitrogen lost as bacteria in the feces) may account for 25% of the obligatory loss of nitrogen. Under this dietary circumstance, the amino acids secreted into the intestine as components of proteolytic enzymes and from sloughed mucosal cells are the only sources of amino acids for the maintenance of the intestinal bacterial biomass. ... Other routes of loss of intact amino acids are via the urine and through skin and hair loss. These losses are small by comparison with those described above, but nonetheless may have a significant impact on estimates of requirements, especially in disease states. /Amino acids/

NAS, Food and Nutrition Board, Institute of Medicine; Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients). National Academy Press, Washington, D.C., pg. 600-601, 2009. Available from, as of March 10, 2010: https://www.nap.edu/catalog/10490.html

Hazardous Substances Data Bank (HSDB)

For more Absorption, Distribution and Excretion (Complete) data for (L)-Methionine (11 total), please visit the HSDB record page.

Hazardous Substances Data Bank (HSDB)

10.5 Metabolism/Metabolites

Hepatic

DrugBank

Product of oxidative deamination or transamination--alpha-keto-gamma-methiolbutyric acid. /From table/

Furia, T.E. (ed.). CRC Handbook of Food Additives. 2nd ed. Cleveland: The Chemical Rubber Co., 1972., p. 831

Hazardous Substances Data Bank (HSDB)

... Oxidation of methionine (S-methyl-l-cysteine and sarcosine) methyl group in vivo proceeds primarily by way of free formate, and that conversion to formate is probably not catalysed by tetrahydrofolic acid.

The Chemical Society. Foreign Compound Metabolism in Mammals. Volume 5: A Review of the Literature Published during 1976 and 1977. London: The Chemical Society, 1979., p. 435

Hazardous Substances Data Bank (HSDB)

... Methionine ... is catabolized to a large extent independently of initial activation to S-adenosyl-l-methionine. The system for catabolism ... appears analogous to one that catalyses oxidation of S-methyl-l-cysteine methyl group ... The methyl group of methionine ... /has been/ shown ... to yield formate in vitro and in vivo.

The Chemical Society. Foreign Compound Metabolism in Mammals. Volume 5: A Review of the Literature Published during 1976 and 1977. London: The Chemical Society, 1979., p. 435

Hazardous Substances Data Bank (HSDB)

Infants more rapidly metabolized methionine than adults.

NAS, Food and Nutrition Board, Institute of Medicine; Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients). National Academy Press, Washington, D.C., pg. 726, 2009. Available from, as of March 10, 2010: https://www.nap.edu/catalog/10490.html

Hazardous Substances Data Bank (HSDB)

For more Metabolism/Metabolites (Complete) data for (L)-Methionine (7 total), please visit the HSDB record page.

Hazardous Substances Data Bank (HSDB)

10.6 Mechanism of Action

The mechanism of the possible anti-hepatotoxic activity of L-methionine is not entirely clear. It is thought that metabolism of high doses of acetaminophen in the liver lead to decreased levels of hepatic glutathione and increased oxidative stress. L-methionine is a precursor to L-cysteine. L-cysteine itself may have antioxidant activity. L-cysteine is also a precursor to the antioxidant glutathione. Antioxidant activity of L-methionine and metabolites of L-methionine appear to account for its possible anti-hepatotoxic activity. Recent research suggests that methionine itself has free-radical scavenging activity by virtue of its sulfur, as well as its chelating ability.

DrugBank

Amino acids are selected for protein synthesis by binding with transfer RNA (tRNA) in the cell cytoplasm. The information on the amino acid sequence of each individual protein is contained in the sequence of nucleotides in the messenger RNA (mRNA) molecules, which are synthesized in the nucleus from regions of DNA by the process of transcription. The mRNA molecules then interact with various tRNA molecules attached to specific amino acids in the cytoplasm to synthesize the specific protein by linking together individual amino acids; this process, known as translation, is regulated by amino acids (e.g., leucine), and hormones. Which specific proteins are expressed in any particular cell and the relative rates at which the different cellular proteins are synthesized, are determined by the relative abundances of the different mRNAs and the availability of specific tRNA-amino acid combinations, and hence by the rate of transcription and the stability of the messages. From a nutritional and metabolic point of view, it is important to recognize that protein synthesis is a continuing process that takes place in most cells of the body. In a steady state, when neither net growth nor protein loss is occurring, protein synthesis is balanced by an equal amount of protein degradation. The major consequence of inadequate protein intakes, or diets low or lacking in specific indispensable amino acids relative to other amino acids (often termed limiting amino acids), is a shift in this balance so that rates of synthesis of some body proteins decrease while protein degradation continues, thus providing an endogenous source of those amino acids most in need. /Protein synthesis/

NAS, Food and Nutrition Board, Institute of Medicine; Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients). National Academy Press, Washington, D.C., pg. 601-602, 2009. Available from, as of March 10, 2010: https://www.nap.edu/catalog/10490.html

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

Hazardous Substances Data Bank (HSDB)

The mechanism of intracellular protein degradation, by which protein is hydrolyzed to free amino acids, is more complex and is not as well characterized at the mechanistic level as that of synthesis. A wide variety of different enzymes that are capable of splitting peptide bonds are present in cells. However, the bulk of cellular proteolysis seems to be shared between two multienzyme systems: the lysosomal and proteasomal systems. The lysosome is a membrane-enclosed vesicle inside the cell that contains a variety of proteolytic enzymes and operates mostly at acid pH. Volumes of the cytoplasm are engulfed (autophagy) and are then subjected to the action of the protease enzymes at high concentration. This system is thought to be relatively unselective in most cases, although it can also degrade specific intracellular proteins. The system is highly regulated by hormones such as insulin and glucocorticoids, and by amino acids. The second system is the ATP-dependent ubiquitin-proteasome system, which is present in the cytoplasm. The first step is to join molecules of ubiquitin, a basic 76-amino acid peptide, to lysine residues in the target protein. Several enzymes are involved in this process, which selectively targets proteins for degradation by a second component, the proteasome. /Protein degradation/

NAS, Food and Nutrition Board, Institute of Medicine; Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients). National Academy Press, Washington, D.C., pg. 602, 2009. Available from, as of March 10, 2010: https://www.nap.edu/catalog/10490.html

Hazardous Substances Data Bank (HSDB)

Methionine dependence, the inability of cells to grow when the amino acid methionine is replaced in culture medium by its metabolic precursor homocysteine, is characteristic of many cancer cell lines and some tumors in situ. Most cell lines proliferate normally under these conditions. The methionine dependent tumorigenic human melanoma cell line MeWo-LC1 was derived from the methionine independent non-tumorigenic line, MeWo. MeWo-LC1 has a cellular phenotype identical to that of cells from patients with the cblC inborn error of cobalamin metabolism, with decreased synthesis of cobalamin coenzymes and decreased activity of the cobalamin-dependent enzymes methionine synthase and methylmalonylCoA mutase. Inability of cblC cells to complement the defect in MeWo-LC1 suggested that it was caused by decreased activity of the MMACHC gene. However, no potentially disease causing mutations were detected in the coding sequence of MMACHC in MeWo-LC1. No MMACHC expression was detected in MeWo-LC1 by quantitative or non-quantitative PCR. There was virtually complete methylation of a CpG island at the 5'-end of the MMACHC gene in MeWo-LC1, consistent with inactivation of the gene by methylation. The CpG island was partially methylated (30-45%) in MeWo and only lightly methylated (2-11%) in control fibroblasts. Infection of MeWo-LC1 with wild type MMACHC resulted in correction of the defect in cobalamin metabolism and restoration of the ability of cells to grow in medium containing homocysteine. /It was concluded/ that epigenetic inactivation of the MMACHC gene is responsible for methionine dependence in MeWo-LC1.

Loewy AD et al; Mol Genet Metab 96 (4): 261-7 (2009). Available from, as of March 17, 2010: https://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=19200761

Hazardous Substances Data Bank (HSDB)

10.7 Human Metabolite Information

10.7.1 Tissue Locations

Fibroblasts
Kidney
Liver
Pancreas
Placenta
Prostate
Skeletal Muscle
Spleen

Human Metabolome Database (HMDB)

10.7.2 Cellular Locations

Extracellular

Human Metabolome Database (HMDB)

10.7.3 Metabolite Pathways

3-Phosphoglycerate dehydrogenase deficiency
Amikacin Action Pathway
Arbekacin Action Pathway
Azithromycin Action Pathway
Chloramphenicol Action Pathway
Clarithromycin Action Pathway
Clindamycin Action Pathway
Clomocycline Action Pathway
Cystathionine Beta-Synthase Deficiency
Demeclocycline Action Pathway
Total 50 pathways, visit the HMDB page for details

Human Metabolome Database (HMDB)

10.8 Biochemical Reactions

PubChem

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

11 Use and Manufacturing

11.1 Uses

EPA CPDat Chemical and Product Categories

The Chemical and Products Database, a resource for exposure-relevant data on chemicals in consumer products, Scientific Data, volume 5, Article number: 180125 (2018), DOI:10.1038/sdata.2018.125

- EPA Chemical and Products Database (CPDat)

Sources/Uses

An essential amino acid; Used therapeutically as an antidote for acetaminophen poisoning and a urinary acidifier; [Merck Index] Chelating agent for heavy metals; [ChemIDplus] Used as a flavoring agent and nutritional supplement for foods; [FDA] Used in pharmaceuticals, as a feed additive, for vegetable oil enrichment, and as single cell protein; [NTP] Permitted for use as an inert ingredient in non-food pesticide products; [EPA]

Merck Index - O'Neil MJ, Heckelman PE, Dobbelaar PH, Roman KJ (eds). The Merck Index, An Encyclopedia of Chemicals, Drugs, and Biologicals, 15th Ed. Cambridge, UK: The Royal Society of Chemistry, 2013.

- Haz-Map, Information on Hazardous Chemicals and Occupational Diseases

Industrial Processes with risk of exposure

Farming (Feed Additives) [Category: Industry]

- Haz-Map, Information on Hazardous Chemicals and Occupational Diseases

Feed additive; vegetable oil enrichment; single-cell protein /DL-Methionine/

Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 12th ed. New York, NY: Van Nostrand Rheinhold Co., 1993, p. 752

- Hazardous Substances Data Bank (HSDB)

Nutrient

FCC; Food Chemicals Codex. Committee on Food Chemicals Codex, Food and Nutrition Board, Institute of Medicine. 5th. Washington, DC: National Academy Press p. 286 (2003)

- Hazardous Substances Data Bank (HSDB)

BIOLOGICAL ACTIVITIES: Anticataract; antidote (acteaminophen, paracetamol); antieczemic; antihepatotic; antioxidant; antiparkinsonian; cancer-preventive; emetic; essential; glutathionigenic; heptoprotective; lioptropic; urine-acidifier, urine-deodorant

USDA; Dr. Duke's Phytochemical and Ethnobotanical Databases. Plants with a chosen chemical. Methionine. Washington, DC: US Dept Agric, Agric Res Service. Available from, as of August 17, 2010: https://www.ars-grin.gov/duke/

- Hazardous Substances Data Bank (HSDB)

THERAPEUTIC CATEGORY: Hepatoprotectant; antidote (acetaminophen poisoning); urinary acidifier

O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 2006., p. 1032

- Hazardous Substances Data Bank (HSDB)

For more Uses (Complete) data for (L)-Methionine (6 total), please visit the HSDB record page.

- Hazardous Substances Data Bank (HSDB)

11.1.1 Use Classification

EPA Safer Chemical Functional Use Classes -> Skin Conditioning Agents

- EPA Safer Choice

Safer Chemical Classes -> Green half-circle - The chemical is expected to be of low concern

- EPA Safer Choice

Food additives -> Flavoring Agents

- EU Food Improvement Agents

Cosmetics -> Antistatic; Hair conditioning; Skin conditioning

S13 | EUCOSMETICS | Combined Inventory of Ingredients Employed in Cosmetic Products (2000) and Revised Inventory (2006) | DOI:10.5281/zenodo.2624118

NORMAN Suspect List Exchange

11.1.2 Household Products

Household & Commercial/Institutional Products

Information on 5 consumer products that contain Methionine in the following categories is provided:

• Personal Care

Consumer Product Information Database (CPID)

11.2 Methods of Manufacturing

The production method of choice for L-methionine is still the enzymatic resolution of racemic N-acetyl-methionine using acylase from Aspergillus oryzae. The production is carried out in a continuously operated fixed-bed or enzyme membrane reactor. Alternatively, L-methionine may be produced by microbial conversion of the corresponding 5-substituted hydantoin. With growing cells of Pseudomonas sp. strain NS671, D,L-5-(2-methylthioethyl)hydantoin was converted to L-methionine; a final concentration of 34 g/L and a molar yield of 93% have been obtained.

Eggersdorfer M et al; Ullmann's Encyclopedia of Industrial Chemistry 7th ed. (2008). New York, NY: John Wiley & Sons; Vitamins. Online Posting Date: June 15, 2000

Hazardous Substances Data Bank (HSDB)

The most economic way for production of D,L-methionine is the chemical process based on acrolein, methyl mercaptan, hydrogen cyanide, and ammonium carbonate. beta-Methylthiopropionaldehyde, formed by addition of methyl mercaptan to acrolein, is the intermediate that reacts with hydrogen cyanide to give alpha-hydroxy-gamma-methylthiobutyronitrile. Treatment with ammonium carbonate leads to 5-(beta-methylthioethyl)hydantoin that is saponified by potassium carbonate giving D,L-methionine in up to 95% yield, calculated on acrolein. /D,L-Methionine/

Eggersdorfer M et al; Ullmann's Encyclopedia of Industrial Chemistry 7th ed. (2008). New York, NY: John Wiley & Sons; Vitamins. Online Posting Date: June 15, 2000

Hazardous Substances Data Bank (HSDB)

11.3 Formulations/Preparations

NF, feed 98%

Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 12th ed. New York, NY: Van Nostrand Rheinhold Co., 1993, p. 752

Hazardous Substances Data Bank (HSDB)

USP and FCC grades; 99% feed grade

Kuney, J.H., J.M. Mullican (eds.). Chemcyclopedia. Washington, DC: American Chemical Society, 1994., p. 286

Hazardous Substances Data Bank (HSDB)

Racemate mixture of D- and L- methionine

Gerhartz, W. (exec ed.). Ullmann's Encyclopedia of Industrial Chemistry. 5th ed.Vol A1: Deerfield Beach, FL: VCH Publishers, 1985 to Present., p. VA2: 71 (1985)

Hazardous Substances Data Bank (HSDB)

11.4 Consumption Patterns

Used almost exclusively to improve the nutritive value of animal feeds /DL-Methionine/

Gerhartz, W. (exec ed.). Ullmann's Encyclopedia of Industrial Chemistry. 5th ed.Vol A1: Deerfield Beach, FL: VCH Publishers, 1985 to Present., p. VA2: 91 (1985)

Hazardous Substances Data Bank (HSDB)

11.5 U.S. Production

(1992) No data

United States International Trade Commission. Synthetic Organic Chemicals - United States Production and Sales, 1992. USITC Publication 2720, Feb. 1994 Washington, D.C.: United States Trade Commission, 1994.

Hazardous Substances Data Bank (HSDB)

World market for L-methionine in 1982: 150 tons; World market for DL-methionine in 1982: 110,000 tons

Gerhartz, W. (exec ed.). Ullmann's Encyclopedia of Industrial Chemistry. 5th ed.Vol A1: Deerfield Beach, FL: VCH Publishers, 1985 to Present., p. VA2: 90 (1985)

Hazardous Substances Data Bank (HSDB)

Production volumes for non-confidential chemicals reported under the Inventory Update Rule.

Year	Production Range (pounds)
1986	10 thousand - 500 thousand
1990	No Reports
1994	No Reports
1998	No Reports
2002	No Reports

US EPA; Non-confidential Production Volume Information Submitted by Companies for Chemicals Under the 1986-2002 Inventory Update Rule (IUR). L-Methionine (63-68-3). Available from, as of March 23, 2010: https://www.epa.gov/oppt/iur/tools/data/2002-vol.html

Hazardous Substances Data Bank (HSDB)

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

11.6 General Manufacturing Information

EPA TSCA Commercial Activity Status

L-Methionine: ACTIVE

https://www.epa.gov/tsca-inventory

EPA Chemicals under the TSCA

... Available as d,l-methionine and as calcium salt of hydroxy analog of methionine. These products are used ... in animal feeds ... Relative biological value of these compared to l-methionine ... evidence suggests equivalency on mole basis both in rats and man.

Furia, T.E. (ed.). CRC Handbook of Food Additives. 2nd ed. Cleveland: The Chemical Rubber Co., 1972., p. 109

Hazardous Substances Data Bank (HSDB)

The D-form of methionine is as equally nutritive as the L-form, so that DL-methionine which is inexpensively produced by the chemical synthesis is primarily used as a feed supplement

Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present., p. V2: 556 (1992)

Hazardous Substances Data Bank (HSDB)

The amino acids that are incorporated into mammalian protein are alpha-amino acids, with the exception of proline, which is an alpha-imino acid. This means that they have a carboxyl group, an amino nitrogen group, and a side chain attached to a central alpha-carbon. Functional differences among the amino acids lie in the structure of their side chains. In addition to differences in size, these side groups carry different charges at physiological pH (e.g., nonpolar, uncharged but polar, negatively charged, positively charged); some groups are hydrophobic (e.g., branched chain and aromatic amino acids) and some hydrophilic (most others). These side chains have an important bearing on the ways in which the higher orders of protein structure are stabilized and are intimate parts of many other aspects of protein function.

NAS, Food and Nutrition Board, Institute of Medicine; Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients). National Academy Press, Washington, D.C., pg. 592, 2009. Available from, as of March 10, 2010: https://www.nap.edu/catalog/10490.html

Hazardous Substances Data Bank (HSDB)

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

12 Identification

12.1 Analytic Laboratory Methods

Method: AOAC 960.47; Procedure: microbiological, turbidimetric and titrimetric methods; Analyte: methionine; Matrix: vitamin preparations; Detection Limit: not provided.

Official Methods of Analysis of AOAC International, 18th Edition Online. Methionine (63-68-3). Available from, as of March 25, 2010: https://www.aoac.org

Hazardous Substances Data Bank (HSDB)

Method: AOAC 994.12; Procedure: performic acid oxidation with acid hydrolysis-sodium metabisulfite method; Analyte: methionine; Matrix: feeds; Detection Limit: not provided.

Official Methods of Analysis of AOAC International, 18th Edition Online. Methionine (63-68-3). Available from, as of March 25, 2010: https://www.aoac.org

Hazardous Substances Data Bank (HSDB)

Method: AOAC 999.13; Procedure: high performance liquid chromatography post-column derivatization; Analyte: methionine; Matrix: feed grade amino acid trade products or in premixes with more than 10% individual amino acid content; Detection Limit: not provided.

Official Methods of Analysis of AOAC International, 18th Edition Online. Methionine (63-68-3). Available from, as of March 25, 2010: https://www.aoac.org

Hazardous Substances Data Bank (HSDB)

SIMPLE PROCEDURE IN WHICH SILVER LIGAND CHROMATOGRAPHY IS USED TO ISOLATE METHIONINE FROM AMINO ACID MIXTURES IS DESCRIBED.

SHAW DC, WEST CE; J CHROMATOGR 200(0) 185 (1980)

Hazardous Substances Data Bank (HSDB)

The following methods have been developed for the analysis of free amino acids in blood, food, and feedstocks: (1) Protein hydrolysis, (2) Chromatographic methods that include high performance liquid chromatography (HPLC), gas chromatography (GC) and thin-layer chromatography (TLC), (3) Colorimetric and Fluorimetric Analysis, (4) Spectrometric Analysis, and (5) Enzymatic Determination and Microbial Assay /amino acids/

Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present., p. V2 531-4

Hazardous Substances Data Bank (HSDB)

12.2 Clinical Laboratory Methods

GC-MS determination in biological fluids

O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 2006., p. 1032

Hazardous Substances Data Bank (HSDB)

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

13 Safety and Hazards

13.1 Hazards Identification

13.1.1 GHS Classification

GHS Hazard Statements	Not Classified Reported as not meeting GHS hazard criteria by 205 of 209 companies (only ~ 1.9% companies provided GHS information). For more detailed information, please visit ECHA C&L website.

European Chemicals Agency (ECHA)

13.1.2 EPA Safer Chemical

Chemical: L-Methionine

Green half-circle - The chemical is expected to be of low concern based on experimental and modeled data. Additional data would strengthen EPA's confidence in the chemical's safer status.

EPA Safer Choice

13.1.3 Health Hazards

ACUTE/CHRONIC HAZARDS: This material is dangerous when heated to decomposition; it emits dangerous and highly toxic fumes. (NTP, 1992)

National Toxicology Program, Institute of Environmental Health Sciences, National Institutes of Health (NTP). 1992. National Toxicology Program Chemical Repository Database. Research Triangle Park, North Carolina.

CAMEO Chemicals

13.1.4 Fire Hazards

Flash point data for this material is not available, but it is probably combustible. (NTP, 1992)

National Toxicology Program, Institute of Environmental Health Sciences, National Institutes of Health (NTP). 1992. National Toxicology Program Chemical Repository Database. Research Triangle Park, North Carolina.

CAMEO Chemicals

13.1.5 Hazards Summary

Reacts with water evolving hydrogen sulfide (toxic and flammable); [CAMEO] May cause irritation; [Sigma-Aldrich MSDS] See Hydrogen sulfide.

Haz-Map, Information on Hazardous Chemicals and Occupational Diseases

13.2 First Aid Measures

13.2.1 First Aid

EYES: First check the victim for contact lenses and remove if present. Flush victim's eyes with water or normal saline solution for 20 to 30 minutes while simultaneously calling a hospital or poison control center. Do not put any ointments, oils, or medication in the victim's eyes without specific instructions from a physician. IMMEDIATELY transport the victim after flushing eyes to a hospital even if no symptoms (such as redness or irritation) develop. SKIN: IMMEDIATELY flood affected skin with water while removing and isolating all contaminated clothing. Gently wash all affected skin areas thoroughly with soap and water. If symptoms such as redness or irritation develop, IMMEDIATELY call a physician and be prepared to transport the victim to a hospital for treatment. INHALATION: IMMEDIATELY leave the contaminated area; take deep breaths of fresh air. If symptoms (such as wheezing, coughing, shortness of breath, or burning in the mouth, throat, or chest) develop, call a physician and be prepared to transport the victim to a hospital. Provide proper respiratory protection to rescuers entering an unknown atmosphere. Whenever possible, Self-Contained Breathing Apparatus (SCBA) should be used; if not available, use a level of protection greater than or equal to that advised under Protective Clothing. INGESTION: DO NOT INDUCE VOMITING. If the victim is conscious and not convulsing, give 1 or 2 glasses of water to dilute the chemical and IMMEDIATELY call a hospital or poison control center. Be prepared to transport the victim to a hospital if advised by a physician. If the victim is convulsing or unconscious, do not give anything by mouth, ensure that the victim's airway is open and lay the victim on his/her side with the head lower than the body. DO NOT INDUCE VOMITING. IMMEDIATELY transport the victim to a hospital. (NTP, 1992)

National Toxicology Program, Institute of Environmental Health Sciences, National Institutes of Health (NTP). 1992. National Toxicology Program Chemical Repository Database. Research Triangle Park, North Carolina.

CAMEO Chemicals

13.3 Fire Fighting

Fires involving this material can be controlled using a CO2, foam, and/or Halon extinguisher. (NTP, 1992)

National Toxicology Program, Institute of Environmental Health Sciences, National Institutes of Health (NTP). 1992. National Toxicology Program Chemical Repository Database. Research Triangle Park, North Carolina.

CAMEO Chemicals

13.4 Accidental Release Measures

13.4.1 Disposal Methods

SRP: Expired or waste pharmaceuticals shall carefully take into consideration applicable DEA, EPA, and FDA regulations. It is not appropriate to dispose by flushing the pharmaceutical down the toilet or discarding to trash. If possible return the pharmaceutical to the manufacturer for proper disposal being careful to properly label and securely package the material. Alternatively, the waste pharmaceutical shall be labeled, securely packaged and transported by a state licensed medical waste contractor to dispose by burial in a licensed hazardous or toxic waste landfill or incinerator.

Hazardous Substances Data Bank (HSDB)

SRP: At the time of review, regulatory criteria for small quantity disposal are subject to significant revision, however, household quantities of waste pharmaceuticals may be managed as follows: Mix with wet cat litter or coffee grounds, double bag in plastic, discard in trash.

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

Hazardous Substances Data Bank (HSDB)

SRP: Criteria for land treatment or burial (sanitary landfill) disposal practices are subject to significant revision. Prior to implementing land disposal of waste residue (including waste sludge), consult with environmental regulatory agencies for guidance on acceptable disposal practices.

Hazardous Substances Data Bank (HSDB)

13.5 Handling and Storage

13.5.1 Nonfire Spill Response

SMALL SPILLS AND LEAKAGE: If you spill this chemical, you should dampen the solid spill material with water, then transfer the dampened material to a suitable container. Use absorbent paper dampened with water to pick up any remaining material. Seal your contaminated clothing and the absorbent paper in a vapor-tight plastic bag for eventual disposal. Wash all contaminated surfaces with a soap and water solution. Do not reenter the contaminated area until the Safety Officer (or other responsible person) has verified that the area has been properly cleaned. STORAGE PRECAUTIONS: You should keep this material in a tightly-closed container under an inert atmosphere, and store it at refrigerated temperatures. (NTP, 1992)

National Toxicology Program, Institute of Environmental Health Sciences, National Institutes of Health (NTP). 1992. National Toxicology Program Chemical Repository Database. Research Triangle Park, North Carolina.

CAMEO Chemicals

13.6 Exposure Control and Personal Protection

13.6.1 Personal Protective Equipment (PPE)

RECOMMENDED RESPIRATOR: Where the neat test chemical is weighed and diluted, wear a NIOSH-approved half face respirator equipped with an organic vapor/acid gas cartridge (specific for organic vapors, HCl, acid gas and SO2) with a dust/mist filter. (NTP, 1992)

National Toxicology Program, Institute of Environmental Health Sciences, National Institutes of Health (NTP). 1992. National Toxicology Program Chemical Repository Database. Research Triangle Park, North Carolina.

CAMEO Chemicals

13.7 Stability and Reactivity

13.7.1 Air and Water Reactions

Reacts with water, steam, and/or acids to produce toxic and flammable vapors of hydrogen sulfide (NTP, 1992). Water soluble (NTP, 1992). pH of 1% aqueous solution is 5.6-6.0.

National Toxicology Program, Institute of Environmental Health Sciences, National Institutes of Health (NTP). 1992. National Toxicology Program Chemical Repository Database. Research Triangle Park, North Carolina.

CAMEO Chemicals

13.7.2 Reactive Group

Sulfides, Organic

Salts, Acidic

CAMEO Chemicals

13.7.3 Reactivity Profile

An organosulfide and amine derivative, carboxylic acid. Look at Reactive Groups 20 (organosulfides), 7 (amines), and 3 (carboxylic acids) may give indications about reactive tendencies. It is an amino acid essential in human nutrition.

CAMEO Chemicals

13.8 Regulatory Information

13.8.1 FDA Requirements

L-Methionine is a food additive permitted for direct addition to food for human consumption, as long as 1) the quantity of the substance added to food does not exceed the amount reasonably required to accomplish its intended physical, nutritive, or other technical effect in food, and 2) any substance intended for use in or on food is of appropriate food grade and is prepared and handled as a food ingredient.

*21 CFR 172.320 (USFDA); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of March 19, 2010: **https://www.ecfr.gov***

Hazardous Substances Data Bank (HSDB)

Drug products containing certain active ingredients offered over-the-counter (OTC) for certain uses. A number of active ingredients have been present in OTC drug products for various uses, as described below. However, based on evidence currently available, there are inadequate data to establish general recognition of the safety and effectiveness of these ingredients for the specified uses: methionine is included in weight control drug products.

*21 CFR 310.545(a)(20) (USFDA); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of March 22, 2010: **https://www.ecfr.gov***

Hazardous Substances Data Bank (HSDB)

Methionine used as a nutrient and/or dietary supplement in animal drugs, feeds, and related products is generally recognized as safe when used in accordance with good manufacturing or feeding practice.

*21 CFR 582.5475 (USFDA); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of March 3, 2010: **https://www.ecfr.gov***

Hazardous Substances Data Bank (HSDB)

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

13.9 Other Safety Information

13.9.1 Special Reports

NAS, Food and Nutrition Board, Institute of Medicine; Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, **Cholesterol**, Protein, and Amino Acids (Macronutrients). National Academy Press, Washington, D.C. (2009).[Available from, as of March 10, 2010: http://www.nap.edu/catalog/10490.html]

- Hazardous Substances Data Bank (HSDB)

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

14 Toxicity

14.1 Toxicological Information

14.1.1 Toxicity Summary

Doses of L-methionine of up to 250 mg daily are generally well tolerated. Higher doses may cause nausea, vomiting and headache. Healthy adults taking 8 grams of L-methionine daily for four days were found to have reduced serum folate levels and leucocytosis. Healthy adults taking 13.9 grams of L-methionine daily for five days were found to have changes in serum pH and potassium and increased urinary calcium excretion. Schizophrenic patients given 10 to 20 grams of L-methionine daily for two weeks developed functional psychoses. Single doses of 8 grams precipitated encephalopathy in patients with cirrhosis.

DrugBank

14.1.2 Drug Induced Liver Injury

Compound	l-methionine
DILI Annotation	No-DILI-Concern
Label Section	No match
References	M Chen, V Vijay, Q Shi, Z Liu, H Fang, W Tong. FDA-Approved Drug Labeling for the Study of Drug-Induced Liver Injury, Drug Discovery Today, 16(15-16):697-703, 2011. PMID:21624500 DOI:10.1016/j.drudis.2011.05.007 M Chen, A Suzuki, S Thakkar, K Yu, C Hu, W Tong. DILIrank: the largest reference drug list ranked by the risk for developing drug-induced liver injury in humans. Drug Discov Today 2016, 21(4): 648-653. PMID:26948801 DOI:10.1016/j.drudis.2016.02.015

Drug Induced Liver Injury Rank (DILIrank) Dataset

14.1.3 Acute Effects

ChemIDplus

14.1.4 Interactions

The adverse effects of methionine are alleviated by supplements of glycine or serine ... Vit B6 deficiency reduces the tolerance of the rat for methionine.

Toxicants Occurring Naturally In Foods, 2nd Ed NAS/NRC Wash DC, 134 (1973)

Hazardous Substances Data Bank (HSDB)

Pretreatment of young male rats with excess retinol (800 IU/g diet for 10 days) partially counteracted the adverse effects caused by a high methionine intake.

Peng Y-S et al; Nutr Rep Int 23(2) 303 (1981)

Hazardous Substances Data Bank (HSDB)

Methionine provided in the drinking water of pregnant rats injected with sodium valproate reduced the frequency of resorptions but did not improve embryo growth. Rats drinking methionine supplemented water had approx twice the level of serum free methionine and consumed only one half the volume of water as controls. Using whole rat embryo cultures, the simultaneous addition of methionine and sodium valproate to the medium provided no protection from the teratogenic effects of sodium valproate ... Protection from the teratogenic effects of sodium valproate was afforded by methionine and was particularly striking when embryos for culture were taken from pregnant rats that had been consuming methionine.

PMID:1462254

Nosel PG, Klein NW; Teratology 46 (5): 499-507 (1992).

Hazardous Substances Data Bank (HSDB)

This study showed that short-term vitamin administration /(folic acid, vitamins B6 and B12)/ effectively reduced post-methionine load homocysteine levels and thereby ameliorated endothelium-dependent flow-mediated vasodilation in 16 healthy adults. Post-methionine load homocysteine levels decreased from 22.7+/-3.8 to 17.0+/-2.1 micromol/L (p <0.001), and flow-mediated vasodilation after methionine load increased from 8.6+/-3.6% to 13.8+/-2.9% (p <0.001) after vitamin administration.

PMID:10614808

Chao CL et al; Am J Cardiol 84 (11): 1359-61, A8 (1999).

Hazardous Substances Data Bank (HSDB)

For more Interactions (Complete) data for (L)-Methionine (18 total), please visit the HSDB record page.

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

Hazardous Substances Data Bank (HSDB)

14.1.5 Antidote and Emergency Treatment

/SRP:/ Immediate first aid: Ensure that adequate decontamination has been carried out. If patient is not breathing, start artificial respiration, preferably with a demand valve resuscitator, bag-valve-mask device, or pocket mask, as trained. Perform CPR if necessary. Immediately flush contaminated eyes with gently flowing water. Do not induce vomiting. If vomiting occurs, lean patient forward or place on the left side (head-down position, if possible) to maintain an open airway and prevent aspiration. Keep patient quiet and maintain normal body temperature. Obtain medical attention. /Poisons A and B/

Currance, P.L. Clements, B., Bronstein, A.C. (Eds).; Emergency Care For Hazardous Materials Exposure. 3Rd edition, Elsevier Mosby, St. Louis, MO 2005, p. 160

Hazardous Substances Data Bank (HSDB)

/SRP:/ Basic treatment: Establish a patent airway (oropharyngeal or nasopharyngeal airway, if needed). Suction if necessary. Watch for signs of respiratory insufficiency and assist ventilations if needed. Administer oxygen by nonrebreather mask at 10 to 15 L/min. Monitor for pulmonary edema and treat if necessary ... . Monitor for shock and treat if necessary ... . Anticipate seizures and treat if necessary ... . For eye contamination, flush eyes immediately with water. Irrigate each eye continuously with 0.9% saline (NS) during transport ... . Do not use emetics. For ingestion, rinse mouth and administer 5 mL/kg up to 200 mL of water for dilution if the patient can swallow, has a strong gag reflex, and does not drool ... . Cover skin burns with dry sterile dressings after decontamination ... . /Poisons A and B/

Currance, P.L. Clements, B., Bronstein, A.C. (Eds).; Emergency Care For Hazardous Materials Exposure. 3Rd edition, Elsevier Mosby, St. Louis, MO 2005, p. 160

Hazardous Substances Data Bank (HSDB)

/SRP:/ Advanced treatment: Consider orotracheal or nasotracheal intubation for airway control in the patient who is unconscious, has severe pulmonary edema, or is in severe respiratory distress. Positive-pressure ventilation techniques with a bag valve mask device may be beneficial. Consider drug therapy for pulmonary edema ... . Consider administering a beta agonist such as albuterol for severe bronchospasm ... . Monitor cardiac rhythm and treat arrhythmias as necessary ... . Start IV administration of D5W /SRP: "To keep open", minimal flow rate/. Use 0.9% saline (NS) or lactated Ringer's if signs of hypovolemia are present. For hypotension with signs of hypovolemia, administer fluid cautiously. Watch for signs of fluid overload ... . Treat seizures with diazepam or lorazepam ... . Use proparacaine hydrochloride to assist eye irrigation ... . /Poisons A and B/

Currance, P.L. Clements, B., Bronstein, A.C. (Eds).; Emergency Care For Hazardous Materials Exposure. 3Rd edition, Elsevier Mosby, St. Louis, MO 2005, p. 160-1

Hazardous Substances Data Bank (HSDB)

14.1.6 Human Toxicity Excerpts

/HUMAN EXPOSURE STUDIES/ Methionine was administered to 17 adults with liver disease 8-20 g/day in divided doses for 3-9 days. In 7 patients with portal cirrhosis, neurological deterioration occurred from 1-4 days after total doses of 11-46 g. Methionine was tolerated in 10 controls.

Toxicants Occurring Naturally In Foods, 2nd Ed NAS/NRC Wash DC: 141 (1973)

Hazardous Substances Data Bank (HSDB)

/HUMAN EXPOSURE STUDIES/ Oral methionine supplements (8.0 g daily for 4 days) were given to five normal volunteers who continued to eat their usual diet. This treatment resulted in a significant fall in serum folate concentration. Three days after the end of treatment concentrations had not completely returned to control values. The fall in concentration was prevented by giving oral folic acid supplements.

PMID:97644
*Full text: **https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2425156***
Connor H; Postgrad med J 54 (631): 318-20 (1978).

Hazardous Substances Data Bank (HSDB)

/HUMAN EXPOSURE STUDIES/ ... The aim of the study was to investigate if methionine supplementation causes changes in endothelial function, plasma homocysteine, or lipid peroxidation which may be associated with atherosclerosis. Sixteen healthy volunteers were studied. Forearm blood flow in response to local intra-arterial infusion of acetylcholine to assess endothelium-dependent vasodilatation and sodium nitroprusside to assess endothelium-independent vasodilatation was measured by venous occlusion plethysmography. Plasma homocysteine and lipid peroxidation, measured as thiobarbituric acid reactive substances, were measured using high-performance liquid chromatography. Forearm vascular responses, plasma homocysteine concentrations, and thiobarbituric acid reactive substances were measured at baseline and following methionine supplementation. RESULTS: There was no significant difference in endothelial-dependent vascular responses after acute (methionine 250 mg orally, $p > 0.05$), 1 month of low-dose (methionine 250 mg daily, $p > 0.05$), or 1 week of high-dose (methionine 100 mg/kg daily, $p > 0.05$) methionine administration. There was no significant difference in plasma homocysteine concentrations after acute ($p > 0.05$) or 1 month of low-dose ($p > 0.05$) methionine administration. However, 1 week of high-dose methionine (100 mg/kg) administration daily significantly increased homocysteine concentrations ($p < 0.0015$). Thiobarbituric acid reactive substances were unchanged during the period of study ($p > 0.05$)...

PMID:10465239
McAuley DF et al; J Toxicol Clin Toxicol 37 (4): 435-40 (1999).

Hazardous Substances Data Bank (HSDB)

/HUMAN EXPOSURE STUDIES/ Prolonged exposure to nitrous oxide causes adverse effects mimicking those of cobalamin deficiency. This is explained by irreversible oxidation of cobalamin bound to the enzyme methionine synthase. The inactivation of methionine synthase by nitrous oxide in cultured human fibroblasts is decreased at high concentrations of methionine in culture medium. ... The possible protection against cobalamin inactivation by preoperative methionine loading /was investigated/ in patients undergoing nitrous oxide anesthesia. Fourteen patients receiving anesthesia for 75-230 min were included. Half of these patients received a peroral methionine loading dose 2 hr before anesthesia. After nitrous oxide exposure, a considerable inactivation of methionine synthase in mononuclear white blood cells was seen in all patients, reaching a nadir after 5-48 hr. In the patients not subjected to a methionine load, recovery of enzyme activity was not complete within 7 days. In the patients receiving a methionine load, the kinetics of inactivation of methionine synthase were similar, but the rate and extent of enzyme recovery was higher than in patients not receiving methionine, and in four patients, the enzyme activity even exceeded the preoperative level. The inactivation of methionine synthase was associated with a transient increase in plasma homocysteine, and the homocysteine concentration was still increased (mean 28.7%) 7 days after anesthesia in the patients not receiving methionine. A marked peak in homocysteine concentration was observed immediately after anesthesia in the methionine-loaded patients, but the homocysteine level was still increased (mean of 30.5%) after 7 days. The activity of the other cobalamin-dependent enzyme, methylmalonyl coenzyme A mutase, in the mononuclear white blood cells, and the serum concentration of the cobalamin marker methylmalonic acid, were not altered after nitrous oxide anesthesia or methionine loading or both...

PMID:8017644
Christensen B et al; Anesthesiology 80 (5): 1046-56 (1994).

Hazardous Substances Data Bank (HSDB)

For more Human Toxicity Excerpts (Complete) data for (L)-Methionine (19 total), please visit the HSDB record page.

Hazardous Substances Data Bank (HSDB)

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

14.1.7 Non-Human Toxicity Excerpts

/LABORATORY ANIMALS: Acute Exposure/ A single dietary dose (2.7% of the diet) of L-methionine decreased body growth and also reduced food intake in rats.

NAS, Food and Nutrition Board, Institute of Medicine; Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients). National Academy Press, Washington, D.C., pg. 725, 2009. Available from, as of March 10, 2010: https://www.nap.edu/catalog/10490.html

Hazardous Substances Data Bank (HSDB)

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ Feeding excess dietary DL-methionine to broiler chicks at 1.5% significantly depressed ($p < 0.01$) gain in body wt, hematocrit, and hemoglobin concentrations, increased ($p < 0.05$) iron level in liver and spleen, caused pancreatic damage and neurological changes.

PMID:7271665
Ekperigin HE, Vohra P; Avian Dis 25(1) 82 (1981).

Hazardous Substances Data Bank (HSDB)

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ Dietary excesses of L-methionine (2.7% of the diet) for 6, 13, or 20 days have been associated with erythrocyte engorgement and accumulation of hemosiderine in rats, and there was a depression of growth and splenic damage.

NAS, Food and Nutrition Board, Institute of Medicine; Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients). National Academy Press, Washington, D.C., pg. 725, 2009. Available from, as of March 10, 2010: https://www.nap.edu/catalog/10490.html

Hazardous Substances Data Bank (HSDB)

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ Dietary intakes of 2 to 4% of L-methionine caused slight changes in liver cells in rats and slight decreases in liver iron content. Darkened spleens caused by increases in iron deposition have been observed in weanling rats fed 1.8% methionine diets for 28 days.

NAS, Food and Nutrition Board, Institute of Medicine; Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients). National Academy Press, Washington, D.C., pg. 725, 2009. Available from, as of March 10, 2010: https://www.nap.edu/catalog/10490.html

Hazardous Substances Data Bank (HSDB)

For more Non-Human Toxicity Excerpts (Complete) data for (L)-Methionine (18 total), please visit the HSDB record page.

Hazardous Substances Data Bank (HSDB)

14.1.8 Non-Human Toxicity Values

LD50 Rat oral 36,000 mg/kg

Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 2334

Hazardous Substances Data Bank (HSDB)

LD50 Rat ip 4238 mg/kg

Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 2334

Hazardous Substances Data Bank (HSDB)

14.1.9 Ecotoxicity Values

LC50; Species: Eisenia fetida (earthworm, mature, weight 370-450 mg) direct application using filter paper >1000 AI ug/sq cm for 48 hr

Roberts BL, Dorough HW; Environ Toxicol Chem 3 (1): 67-78 (1984) as cited in the ECOTOX database. Available from, as of December 31, 2009

Hazardous Substances Data Bank (HSDB)

14.1.10 Populations at Special Risk

This case-controlled, monocenter association study included 290 patients of Caucasian origin undergoing surgical resection for intracranial meningioma (World Health Organization [WHO] Grade I, 190 cases; WHO Grade II, 82 cases; WHO Grade III, 18 cases) and 287 age- and sex-matched local controls. The authors analyzed the following genetic variants: dihydrofolate reductase c.594+59del19, 5,10-methylenetetrahydrofolate reductase c.677C > T and c.1298A > C, 5-methyltetrahydrofolate-homocysteine S-methyltransferase (MTR) c.2756A > G, reduced folate carrier 1 c.80G > A, cystathionine beta-synthase (CBS) c.844_855ins68 and transcobalamin 2 c.776C > G. RESULTS: The variant CBS c.844_855ins68 -- that is, the allele carrying the insertion ("ins" or "i") as opposed to the wild-type allele designated as deletion ("del" or "d") -- was significantly overrepresented in meningioma patients (dd/ id/ii: 0.81/0.18/0.01) in comparison with the controls (dd/id/ii: 0.88/0.12/0; 2 df, chi-square 8.97, p = 0.011; multiple nominal regression with age and sex as covariables). In addition, explorative analyses revealed an association of the MTR c.2756A > G variant with meningioma WHO Grade III (AA/AG/GG: patients, 1.0/0/0; controls, 0.64/0.32/0.04; 2 df, chi-square 14.44, p = 0.001). CONCLUSIONS: The results of this study suggest that genetic variants of methionine metabolism are associated with meningioma formation.

Semmler A et al; J Neurosurg 108 (5): 999-1004 (2008). Available from, as of March 17, 2010: https://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=18447718

Hazardous Substances Data Bank (HSDB)

14.2 Ecological Information

14.2.1 Environmental Fate/Exposure Summary

(L)-Methionine's production and use as a nutritional supplement in animal feeds may result in its release to the environment through various waste streams. (L)-Methionine is formed in natural waters through metabolism of naturally occurring proteins and is a naturally occurring amino acid, being present in foods such as maize, rice, wheat, potato, soybeans, lettuce, apples, oranges, beef, fish, milk, cheese and eggs. If released to air, an estimated vapor pressure of 8.1X10-8 mm Hg at 25 °C indicates (L)-methionine will exist in both the vapor and particulate phases in the atmosphere. Vapor-phase (L)-methionine will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 7.5 hours. Particulate-phase (L)-methionine will be removed from the atmosphere by wet or dry deposition. (L)-Methionine does not contain chromophores that absorb at wavelengths >290 nm and therefore is not expected to be susceptible to direct photolysis by sunlight. If released to soil, (L)-methionine is expected to have very high mobility based upon an estimated Koc of 8. The pKa values of (L)-methionine are 2.28 and 9.21, which indicate that this compound will exist as a zwitterion which may affect its adsorption to soils and sediments. Volatilization from moist soil is not expected because ions do not volatilize. (L)-Methionine may not volatilize from dry soil surfaces based upon its vapor pressure. Using a laboratory activated sludge system, (L)-methionine exhibited an 80% theoretical BOD reduction in 16 days, producing 3-mercaptopropionate, methanethiol and dimethylsulfide; this suggests that biodegradation may be an important environmental fate process. If released into water, (L)-methionine is not expected to adsorb to suspended solids and sediment based upon the estimated Koc. The pKa values of 2.28 and 9.21 indicate (L)-methionine will exist as a zwitterion at pH values of 5 to 9 and therefore volatilization from water surfaces is not expected to be an important fate process. An estimated BCF of 3 suggests the potential for bioconcentration in aquatic

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

organisms is low. Hydrolysis is not expected to be an important environmental fate process since this compound lacks functional groups that hydrolyze under environmental conditions. (L)-Methionine has been shown to degrade in sunlit natural water through photo-sensitized oxidation involving singlet oxygen. Occupational exposure to (L)-methionine may occur through inhalation and dermal contact with this compound at workplaces where (L)-methionine is produced or used. Monitoring data indicate that the general population may be exposed to (L)-methionine via ingestion of food. (SRC)

Hazardous Substances Data Bank (HSDB)

14.2.2 Natural Pollution Sources

(L)-Methionine is formed in natural waters through metabolism of naturally occurring proteins(1). It is one of the nine indispensable amino acids that cannot be synthesized to meet body needs in animals and therefore must be provided in the diet(2). (L)-Methionine is a naturally occurring amino acid constituent of egg albumin, casein, and beta-lactoglobulin proteins(3); (L)-methionine occurs naturally in foods such as maize, rice, wheat, potato, soybeans, lettuce, bean, tomato, apples, oranges, beef, veal, fish, milk, cheese and eggs(3).

(1) Kiene RP, Visscher PT; Appl Environ Microbiol 53: 2426-34 (1987) (2) NAS, Food and Nutrition Board, Institute of Medicine; Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients). National Academy Press, Washington, D.C. (2005). Available from, as of August 17, 2010: https://books.nap.edu/openbook.php?record_id=10490&page=589 (3) Drauz K et al; Ullmann's Encyclopedia of Industrial Chemistry. 7th ed. (2008). New York, NY: John Wiley & Sons; Amino Acids. Online Posting Date: Apr 15, 2007.

Hazardous Substances Data Bank (HSDB)

14.2.3 Artificial Pollution Sources

(L)-Methionine's production and use as nutritional supplement in animal feeds(1) may result in its release to the environment through various waste streams(SRC).

(1) Drauz K et al; Ullmann's Encyclopedia of Industrial Chemistry. 7th ed. (2008). New York, NY: John Wiley & Sons; Amino Acids. Online Posting Date: Apr 15, 2007.

Hazardous Substances Data Bank (HSDB)

14.2.4 Environmental Fate

TERRESTRIAL FATE: Based on a classification scheme(1), an estimated Koc value of 8(SRC), determined from a log Kow of -1.87(2) and a regression-derived equation(3), indicates that (L)-methionine is expected to have very high mobility in soil(SRC). The pKa values of (L)-methionine are 2.28 and 9.21(4), indicate that this compound will exist as a zwitterion which may affect its adsorption to soils and sediments(SRC). Volatilization from moist soil is not expected because ions do not volatilize(SRC). (L)-Methionine is not expected to volatilize from dry soil surfaces(SRC) based upon an estimated vapor pressure of 8.1X10-8 mm Hg at 25 °C(SRC), determined from a fragment constant method(5). Using a laboratory activated sludge system, (L)-methionine exhibited an 80% theoretical BOD reduction in 16 days, producing 3-mercaptopropionate, methanethiol and dimethylsulfide(6); this suggests that biodegradation may be an important environmental fate process in soil(SRC).

(1) Swann RL et al; Res Rev 85: 17-28 (1983) (2) Hansch C et al; Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. ACS Prof Ref Book. Heller SR, consult. ed., Washington, DC: Amer Chem Soc p. 15 (1995) (3) US EPA; Estimation Program Interface (EPI) Suite. Ver. 4.0. Jan, 2009. Available from https://www.epa.gov/oppt/exposure/pubs/episuitedl.htm as of Feb 19, 2010. (4) Drauz K et al; Ullmann's Encyclopedia of Industrial Chemistry. 7th ed. (2008). New York, NY: John Wiley & Sons; Amino Acids. Online Posting Date: Apr 15, 2007. (5) Lyman WJ; p. 31 in Environmental Exposure From Chemicals Vol I, Neely WB, Blau GE, eds, Boca Raton, FL: CRC Press (1985) (6) Engelbrecht RS, McKinney RE; Sew Indust Wastes 29: 1350-62 (1957)

Hazardous Substances Data Bank (HSDB)

AQUATIC FATE: Based on a classification scheme(1), an estimated Koc value of 8(SRC), determined from a log Kow of -1.87(2) and a regression-derived equation(3), indicates that (L)-methionine is not expected to adsorb to suspended solids and sediment(SRC). The pKa values of 2.28 and 9.21(4) indicates (L)-methionine will exist as a zwitterion at pH values of 5 to 9 and therefore volatilization from water surfaces is not expected to be an important fate process(5). According to a classification scheme(6), an estimated BCF of 3(SRC), from its log Kow(2) and a regression-derived equation(7), suggests the potential for bioconcentration in aquatic organisms is low(SRC). Using a laboratory activated sludge system, (L)-methionine exhibited an 80% theoretical BOD reduction in 16 days, producing 3-mercaptopropionate, methanethiol and dimethylsulfide(8); this suggests that biodegradation may be an important environmental fate process in water(SRC).

(1) Swann RL et al; Res Rev 85: 17-28 (1983) (2) Hansch C et al; Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. ACS Prof Ref Book. Heller SR, consult. ed., Washington, DC: Amer Chem Soc p. 15 (1995) (3) US EPA; Estimation Program Interface (EPI) Suite. Ver. 4.0. Jan, 2009. Available from https://www.epa.gov/oppt/exposure/pubs/episuitedl.htm as of Feb 19, 2010. (4) Drauz K et al; Ullmann's Encyclopedia of Industrial Chemistry. 7th ed. (2008). New York, NY: John Wiley & Sons; Amino Acids. Online Posting Date: Apr 15, 2007. (5) Doucette WJ; pp. 141-188 in Handbook of Property Estimation Methods for Chemicals. Boethling RS, Mackay D, eds, Boca Raton, FL: Lewis Publ (2000) (6) Franke C et al; Chemosphere 29: 1501-14 (1994) (7) Meylan WM et al; Environ Toxicol Chem 18: 664-72 (1999) (8) Engelbrecht RS, McKinney RE; Sew Indust Wastes 29: 1350-62 (1957)

Hazardous Substances Data Bank (HSDB)

AQUATIC FATE: (L)-Methionine has been shown to degrade in sunlit natural water through a photo-sensitized oxidation involving singlet oxygen(1,2); assuming that the top meter of sunlit natural water has a singlet oxygen concn of 4X10-14 M, the photooxidation half-life for the reaction (L)-methionine with singlet oxygen has been estimated to be about 200 hr at pH 6-11(1); the near-surface photooxidation rate (via singlet oxygen) of (L)-methionine in Okefenokee Swamp water from Georgia is predicted to be about 3 hr(2). Bioconcentration and volatilization are not expected to important fate processes because of its high water solubility(SRC).

(1) Haag WR, Holgne J; Environ Sci Technol 20: 341-8 (1986) (2) Zepp RG et al; Nature 267: 421-3 (1977)

Hazardous Substances Data Bank (HSDB)

ATMOSPHERIC FATE: According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere(1), (L)-methionine, which has an estimated vapor pressure of 8.1X10-8 mm Hg at 25 °C(SRC), determined from a fragment constant method(2), will exist in both the vapor and particulate phases in the ambient atmosphere. Vapor-phase (L)-methionine is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals(SRC); the half-life for this reaction in air is estimated to be 7.5 hours(SRC), calculated from its rate constant of 5.1X10-11 cu cm/molecule-sec at 25 °C(SRC) that was derived using a structure estimation method(3). (L)-Methionine does not contain chromophores that absorb at wavelengths >290 nm(4) and therefore is not expected to be susceptible to direct photolysis by sunlight(SRC).

(1) Bidleman TF; Environ Sci Technol 22: 361-367 (1988) (2) Lyman WJ; p. 31 in Environmental Exposure From Chemicals Vol I, Neely WB, Blau GE, eds, Boca Raton, FL: CRC Press (1985) (3) Meylan WM, Howard PH; Chemosphere 26: 2293-99 (1993) (4) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 8-12 (1990)

Hazardous Substances Data Bank (HSDB)

14.2.5 Environmental Biodegradation

AEROBIC: In a laboratory activated sludge system, (L)-methionine had an 80% theoretical BOD reduction after 16 days of incubation(1). In a Warburg respirometer study using activated sludge, (L)-methionine (at a concn of 500 mg/L) had a theoretical BOD of 2.6% over a 24-hr incubation period(2). In an activated sludge system that had been acclimated to phenol, (L)-methionine had a theoretical oxidation of 16% after 12 hrs of aeration(3).

(1) Engelbrecht RS, McKinney RE; Sew Indust Wastes 29: 1350-62 (1957) (2) Malaney GW, Gerhold RM; J Water Pollut Control Fed 41: R18-R33 (1969) (3) McKinney RE et al; Sew Indust Wastes 28: 547-57 (1956)

Hazardous Substances Data Bank (HSDB)

ANAEROBIC: The biotransformation of (L)-methionine in anoxic sediment slurries was found to produce 3-mercaptopropionate(1). In salt marsh sediment slurries, microbial metabolism of (L)-methionine yielded methanethiol as the major volatile organosulfur product, with the formation of lesser amounts of dimethylsulfide(2); the decomposition of (L)-methionine occurred rapidly in anoxic salt marsh sediments(2). (L)-Methionine was highly bioconvertible (68-90% CO2 evolution) in 35-78 day anaerobic degradation studies using waste activated sludge from the San Jose-Santa Clara Water Pollution Control Plant(3).

(1) Kiene RP, Taylor BF; Nature 332: 148-50 (1988) (2) Kiene RP, Visscher PT; Appl Environ Microbiol 53: 2426-34 (1987) (3) Stuckey DC, McCarty PL; Water Res 18: 1343-53 (1984)

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

Hazardous Substances Data Bank (HSDB)

14.2.6 Environmental Abiotic Degradation

The rate constant for the vapor-phase reaction of (L)-methionine with photochemically-produced hydroxyl radicals has been estimated as 6.1X10-11 cu cm/molecule-sec at 25 °C(SRC) using a structure estimation method(1). This corresponds to an atmospheric half-life of about 7.5 hours at an atmospheric concentration of 5X10+5 hydroxyl radicals per cu cm(1). (L)-Methionine is not expected to undergo hydrolysis in the environment due to the lack of functional groups that hydrolyze under environmental conditions(3). (L)-Methionine does not contain chromophores that absorb at wavelengths >290 nm(3) and therefore is not expected to be susceptible to direct photolysis by sunlight(SRC).

(1) Meylan WM, Howard PH; Chemosphere 26: 2293-99 (1993) (3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 7-4, 7-5, 8-12 (1990)

Hazardous Substances Data Bank (HSDB)

14.2.7 Environmental Bioconcentration

An estimated BCF of 3 was calculated in fish for (L)-methionine(SRC), using a log Kow of -1.87(1) and a regression-derived equation(2). According to a classification scheme(3), this BCF suggests the potential for bioconcentration in aquatic organisms is low(SRC).

(1) Hansch C et al; Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. ACS Prof Ref Book. Heller SR, consult. ed., Washington, DC: Amer Chem Soc p. 125 (1995) (2) US EPA; Estimation Program Interface (EPI) Suite. Ver. 4.0. Jan, 2009. Available from https://www.epa.gov/oppt/exposure/pubs/episuitedl.htm as of Feb 19, 2010. (3) Franke C et al; Chemosphere 29: 1501-14 (1994)

Hazardous Substances Data Bank (HSDB)

14.2.8 Soil Adsorption/Mobility

The Koc of (L)-methionine is estimated as 8(SRC), using a log Kow of -1.87(1) and a regression-derived equation(2). According to a classification scheme(3), this estimated Koc value suggests that (L)-methionine is expected to have very mobility in soil. The pKa values of (L)-methionine are 2.28 and 9.21(4), indicate that this compound will exist as a zwitterion which may affect its adsorption to soils and sediments(SRC). One study found that (L)-methionine was one of many amino acids that sorbed to carbonate sediments in seawater(5); a positive correlation between surface area (of the sediment) and the amount of sorbed amino acids indicated that sorption from solution (partitioning from the water column to sediment) was a likely mechanism(5).

(1) Hansch C et al; Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. ACS Prof Ref Book. Heller SR, consult. ed., Washington, DC: Amer Chem Soc p. 15 (1995) (2) US EPA; Estimation Program Interface (EPI) Suite. Ver. 4.0. Jan, 2009. Available from https://www.epa.gov/oppt/exposure/pubs/episuitedl.htm as of Feb 19, 2010. (3) Swann RL et al; Res Rev 85: 17-28 (1983) (4) Drauz K et al; Ullmann's Encyclopedia of Industrial Chemistry. 7th ed. (2008). New York, NY: John Wiley & Sons; Amino Acids. Online Posting Date: Apr 15, 2007. (5) Muller PJ, Suess E; Geochim Casmochim Acta 41: 941-9 (1977)

Hazardous Substances Data Bank (HSDB)

14.2.9 Volatilization from Water/Soil

The pKa values of 2.28 and 9.21(1) indicate (L)-methionine will exist as a zwitterion at pH values of 5 to 9 and therefore volatilization from water surfaces is not expected to be an important fate process(2). (L)-Methionine is not expected to volatilize from dry soil surfaces(SRC) based upon an estimated vapor pressure of 8.1X10-8 mm Hg(SRC), determined from a fragment constant method(3).

(1) Drauz K et al; Ullmann's Encyclopedia of Industrial Chemistry. 7th ed. (2008). New York, NY: John Wiley & Sons; Amino Acids. Online Posting Date: Apr 15, 2007. (2) Doucette WJ; pp. 141-188 in Handbook of Property Estimation Methods for Chemicals. Boethling RS, Mackay D, eds. Boca Raton, FL: Lewis Publ (2000) (3) Lyman WJ; p. 31 in Environmental Exposure From Chemicals Vol I, Neely WB, Blau GE, eds, Boca Raton, FL: CRC Press (1985)

Hazardous Substances Data Bank (HSDB)

14.2.10 Sediment/Soil Concentrations

SOIL: (L)-Methionine concentrations in three soil horizons of an active landfill, the Conica Montemarte outside of Seville, Spain, were reported as 0.5 nmol/g (1.0-1.5 meters), 19.9 nmol/g (3.0-3.5 meters), and 38.2 nmol/g (6.5-7.0 meters), 6, 18, and 24 months after deposition respectively(1).

(1) Gonzalez-Vila, FJ et al; Chemosphere 31: 2817-25 (1995)

Hazardous Substances Data Bank (HSDB)

SEDIMENT: (L)-Methionine concentrations of 0.46 to 0.055 umol/g were detected in carbonate sediment samples collected from a lagoon of Fanning Island, an atoll in the Line Islands of the Central Pacific Ocean(1).

(1) Muller PJ, Suess E; Geochim Casmochim Acta 41: 941-9 (1977)

Hazardous Substances Data Bank (HSDB)

14.2.11 Food Survey Values

The average methionine content of some foodstuffs (in mg/100g) has been reported as follows: maize, grain: 182; rice, husked: 183; wheat, whole grain: 196; potato: 26; bean (Phaselous vulgaris): 234; soybean, milk: 50; soy protein, isolate: 1008; tomato: 7; apple: 3; orange: 12; beef, veal, edible flesh: 478; fish: 220; cheese: 530; egg, whole: 416(1).

(1) Drauz K et al; Ullmann's Encyclopedia of Industrial Chemistry. 7th ed. (2008). New York, NY: John Wiley & Sons; Amino Acids. Online Posting Date: Apr 15, 2007.

Hazardous Substances Data Bank (HSDB)

14.2.12 Plant Concentrations

Plants with the highest amount of Methionine(1).

Genus species	Commone name(s)	Concentration	Area of Plant
Helianthus annuus L.	Girasol, Sunflower	5,220 - 20,500 ppm	Seed
Cucurbita foetidissima HBK.	Buffalo Gourd	2,610 - 19,000 ppm	Seed
Nigella sativa L.	Black Caraway, Black Cumin, Fennel-Flower, Nutmeg-Flower, Roman Coriander	13,100 - 16,750 ppm	Seed
Bertholletia excelsa BONPL.	Brazilnut, Brazilnut-Tree, Creamnut, Paranut	10,140 - 10,346 ppm	Seed

Genus species	Commone name(s)	Concentration	Area of Plant
Sesamum indicum L.	Ajonjoli (Sp.), Beni, Benneseed, Sesame, Sesamo (Sp.)	3,120 - 9,413 ppm	Seed
Trigonella foenum-graecum L.	Alholva (Sp.), Bockshornklee (Ger.), Fenugreek, Greek Clover, Greek Hay	120 - 8,830 ppm	Leaf
Juglans cinerea L.	Butternut	6,111 - 6,321 ppm	Seed
Spinacia oleracea L.	Spinach	530 - 6,294 ppm	Plant
Pinus pinea L.	Italian Stone Pine, Pignolia	4,300 - 6,050 ppm	Seed
Cucurbita pepo L.	Pumpkin	5,510 - 5,920 ppm	Seed
Ipomoea aquatica FORSSKAL	Swamp Cabbage, Water Spinach	440 - 5,845 ppm	Leaf
Moringa oleifera LAM.	Ben Nut, Benzolive Tree, Drumstick Tree, Horseradish Tree, Jacinto (Sp.), Moringa, West Indian Ben	1,230 - 5,765 ppm	Shoot
Oenothera biennis L.	Evening-Primrose	5,400 - 5,763 ppm	Seed
Citrullus lanatus (THUNB.) MATSUM. & NAKAI	Watermelon	5,742 ppm	Seed
Colocasia esculenta (L.) SCHOTT	Taro	790 - 5,510 ppm	Leaf
Glycine max (L.) MERR.	Soybean	4,920 - 5,380 ppm	Seed
Corchorus olitorius L.	Jew's Mallow, Mulukiya, Nalta Jute	460 - 5,290 ppm	Leaf
Sinapis alba L.	White Mustard	4,800 - 5,136 ppm	Seed
Papaver bracteatum L.	Great Scarlet Poppy	4,500 - 5,050 ppm	Seed
Papaver somniferum L.	Opium Poppy, Poppyseed Poppy	4,700 - 5,042 ppm	Seed
Opuntia ficus-indica (L.) MILL.	Indian Fig, Nopal, Nopalito, Prickly Pear	4,830 ppm	Seed
Phaseolus vulgaris subsp. var. vulgaris	Black Bean, Dwarf Bean, Field Bean, Flageolet Bean, French Bean, Garden Bean, Green Bean, Haricot, Haricot Bean, Haricot Vert, Kidney Bean, Navy Bean, Pop Bean, Popping Bean, Snap Bean, String Bean, Wax Bean	440 - 4,731 ppm	Sprout Seedling
Ceratonia siliqua L.	Carob, Locust Bean, St.John's-Bread	4,700 ppm	Seed
Amaranthus sp.	Pigweed	360 - 4,331 ppm	Leaf
Avena sativa L.	Oats	1,000 - 4,000 ppm	Seed
Hordeum vulgare L.	Barley, Barleygrass	1,000 - 4,000 ppm	Seed
Nasturtium officinale R. BR.	Berro, Watercress	200 - 4,000 ppm	Herb
Triticum aestivum L.	Wheat	1,000 - 4,000 ppm	Seed
Mucuna pruriens (L.) DC.	Cowage, Velvetbean	1,875 - 3,975 ppm	Seed
Pistacia vera L.	Pistachio	3,810 - 3,963 ppm	Seed

*(1) USDA; Dr. Duke's Phytochemical and Ethnobotanical Databases. Plants with a chosen chemical. Methionine. Washington, DC: US Dept Agric, Agric Res Service. Available from, as of August 17, 2010: **https://www.ars-grin.gov/duke/***

Hazardous Substances Data Bank (HSDB)

14.2.13 Animal Concentrations

Zebra mussels and clams sampled in November 1991 from Oneida Lake in NY State were found to have (L)-methionine levels of 1.66 and 1.58 g/100 g dry wt, respectively(1).

(1) Secor CL et al; Chemosphere 26: 1559-75 (1993)

Hazardous Substances Data Bank (HSDB)

14.2.14 Milk Concentrations

ENVIRONMENTAL: The average (L)-methionine content of cows milk is reported as 86 mg/100 g(1). The average (L)-methionine content of human milk is reported as 19 mg/100 g(1).

(1) Drauz K et al; Ullmann's Encyclopedia of Industrial Chemistry. 7th ed. (2008). New York, NY: John Wiley & Sons; Amino Acids. Online Posting Date: Apr 15, 2007.

Hazardous Substances Data Bank (HSDB)

14.2.15 Probable Routes of Human Exposure

NIOSH (NOES Survey 1981-1983) has statistically estimated that 28,250 workers (17,038 of these were female) were potentially exposed to (L)-methionine in the US(1). Occupational exposure to (L)-methionine may occur through inhalation and dermal contact with this compound at workplaces where (L)-methionine is produced or used. Monitoring and use data indicate that the general population may be exposed to (L)-methionine via ingestion of food or other consumer products containing (L)-methionine(SRC).

*(1) NIOSH; NOES. National Occupational Exposure Survey conducted from 1981-1983. Estimated numbers of employees potentially exposed to specific agents by 2-digit standard industrial classification (SIC). Available from, as of Feb 19, 2010: **https://www.cdc.gov/noes/***

Hazardous Substances Data Bank (HSDB)

14.2.16 Body Burden

The average (L)-methionine content of human milk is reported as 19 mg/100 g(1).

(1) Drauz K et al; Ullmann's Encyclopedia of Industrial Chemistry. 7th ed. (2008). NY, NY: John Wiley & Sons; Amino Acids. Online Posting Date: Apr 15, 2007.

Hazardous Substances Data Bank (HSDB)

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

15 Associated Disorders and Diseases

Comparative Toxicogenomics Database (CTD)

Disease	References
Epilepsy	PubMed: 14992292, 7869898, 12121313, 10534261, 6198481, 1705463, 7126379, 15993662, 803305, 10577274, 19817812, 10688964, 436860
Heart failure	PubMed: 16789974, 11532681, 11897434, 17482886, 21167146
Homocystinuria	PubMed: 14264314, 8745393 MetaGene: Metabolic & Genetic Information Center (MIC: http://www.metagene.de)
Colorectal cancer	PubMed: 7482520, 19006102, 23940645, 24424155, 20156336, 19678709, 22148915, 25105552, 21773981, 25037050, 27015276, 27107423, 27275383, 28587349 Silke Matysik, Caroline Ivanne Le Roy, Gerhard Liebisch, Sandrine Paule Claus. Metabolomics of fecal samples: A practical consideration. Trends in Food Science & Technology. Vol. 57, Part B, Nov. 2016, p.244-255: http://www.sciencedirect.com/science/article/pii/S0924224416301984
Early preeclampsia	PubMed: 22494326
Pregnancy	PubMed: 3252730, 663967, 12833386, 2994907, 17704099, 12698507, 17061063, 16925883, 22420377, 18059417, 22494326, 23159745, 23313728, 23535240, 24704061 The Merck Manual, 17th ed. Mark H. Beers, MD, Robert Berkow, MD, eds. Whitehouse Station, NJ: Merck Research Labs, 1999.
Late-onset preeclampsia	PubMed: 23159745
Fumarase deficiency	PubMed: 26078636, 20549362, 24182348, 6616883, 16972175 MetaGene: Metabolic & Genetic Information Center (MIC: http://www.metagene.de)
Tyrosinemia	PubMed: 16414314, 15168722
Methylenetetrahydrofolate reductase deficiency	PubMed: 8456826 MetaGene: Metabolic & Genetic Information Center (MIC: http://www.metagene.de)
Hypermethioninemia	PubMed: 2380820, 27671891, 15024124
Glycine N-methyltransferase deficiency	PubMed: 27207470
Methionine adenosyltransferase deficiency	PubMed: 7229751, 15996001
Obesity	PubMed: 15899597, 16253646, 2401584, 17264178, 1783639, 26505825, 17408529, 18997681, 24740590, 23108202, 26910390 Metabolomics reveals determinants of weight loss during lifestyle intervention in obese children
Homocystinuria-megaloblastic anemia due to defect in cobalamin metabolism, cblG complementation type	PubMed: 21559159
Citrullinemia type II, neonatal-onset	PubMed: 11281457
Cobalamin F disease (cblF)	PubMed: 21910240
Leukemia	PubMed: 9464484, 1184685, 15911239, 7482520, 11129502
Schizophrenia	PubMed: 115032, 7126379, 2480613, 17276036, 11877547, 12796220, 7595563, 20814316, 25004141, 24713860, 23823132, 2415198, 1694425, 7711000, 19390223, 22024767, 22007635, 21483431, 3741918, 11979513, 20206656, 436860, 19401681, 6184954, 26952797, 22800120, 24789758, 22944140, 22892715, 17440431, 25729574, 22257447
Adenosine kinase deficiency	PubMed: 21963049
Irritable bowel syndrome	PubMed: 9505884, 8723414, 21330412, 21761941, 21494186, 23867873, 27662586
Ulcerative colitis	PubMed: 21059682, 1740537, 17269711, 17314143, 21761941, 23516449, 23867873, 24811995, 25598765, 26806034, 26848182, 27609529, 28842642
Celiac disease	PubMed: 3816078, 16425363, 10063930, 6182605, 6182788, 24657864, 21970810, 27452636
Autism	PubMed: 20423563, 7687150, 6150139, 15585776, 3410814, 12205654, 24130822
Crohn's disease	PubMed: 16440420, 11418788, 8723414, 19491857, 17269711, 23516449, 23867873, 24811995, 25598765, 26806034, 26848182, 27609529, 28842642
Diverticular disease	PubMed: 8723414, 27622378
Rheumatoid arthritis	PubMed: 6589104, 16277678, 15338487, 10361015, 15249323 Tie-juan ShaoZhi-xing HeZhi-jun XieHai-chang LiMei-jiao WangCheng-ping Wen. Characterization of ankylosing spondylitis and rheumatoid arthritis using 1H NMR-based metabolomics of human fecal extracts. Metabolomics. April 2016, 12:70: https://link.springer.com/article/10.1007/s11306-016-1000-2

Disease	References
Eosinophilic esophagitis	Mordechai, Hien, and David S. Wishart

Human Metabolome Database (HMDB)

16 Literature

16.1 Coronavirus Studies

PubChem

16.2 NLM Curated PubMed Citations

PubChem

16.3 Springer Nature References

Springer Nature

16.4 Thieme References

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

- Thieme Chemistry

16.5 Wiley References

- Wiley

16.6 Depositor Provided PubMed Citations

- PubChem

16.7 Synthesis References

Clyde Eugene Stauffer, "Process for producing N-acyl-L-methionine." U.S. Patent US3963573, issued June, 1950.

- DrugBank

Boy, Matthias; Klein, Daniela; Schroeder, Hartwig. Method for the production and recovery of methionine. PCT Int. Appl. (2005), 34 pp.

- Human Metabolome Database (HMDB)

16.8 Metabolite References

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

- Human Metabolome Database (HMDB)

16.9 General References

Jie Yuan, William U. Fowler, Elizabeth Kimball, Wenyun Lu, Joshua D. Rabinowitz Kinetic flux profiling of nitrogen assimilation in Escherichia coli 10.1038/nchembio816

- Nature Chemical Biology

Eust quio et al. Discovery and characterization of a marine bacterial SAM-dependent chlorinase Nature Chemical Biology, doi: 10.1038/NChemBio.2007.56, published online 2 December 2007. http://www.nature.com/naturechemicalbiology

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Chatterjee et al. Reconstitution of ThiC in thiamine pyrimidine biosynthesis expands the radical SAM superfamily Nature Chemical Biology, doi: 10.1038/nchembio.121, published online 26 October 2008 http://www.nature.com/naturechemicalbiology

- Nature Chemical Biology

Gutierrez et al. Transition state analogs of 5\'-methylthioadenosine nucleosidase disrupt quorum sensing Nature Chemical Biology, doi: 10.1038/nchembio.153, published online 8 March 2009 http://www.nature.com/naturechemicalbiology

- Nature Chemical Biology

Yuan et al. Absolute Metabolite Concentrations and Implied Enzyme Active Site Occupancy in Escherichia coli Nature Chemical Biology, doi: 10.1038/nchembio.186, published online 28 June 2009 http://www.nature.com/naturechemicalbiology

- Nature Chemical Biology

Ngo et al. Cell-Selective Metabolic Labeling of Proteins. Nature Chemical Biology, doi: 10.1038/nchembio.200, published online 09 August 2009 http://www.nature.com/naturechemicalbiology

- Nature Chemical Biology

Cellitti et al. D-Ornithine coopts pyrrolysine biosynthesis to make and insert pyrroline-carboxy-lysine. Nature Chemical Biology, doi: 10.1038/nchembio.586, published online 3 May 2011 http://www.nature.com/naturechemicalbiology

- Nature Chemical Biology

Shu et al. A metabolic labeling method detects m6A transcriptome-wide at single base resolution. Nature Chemical Biology, DOI: 10.1038/s41589-020-0526-9, published online 27 April 2020

- Nature Chemical Biology

Hein et al. A route to enantiopure RNA precursors from nearly racemic starting materials. Nature Chemistry, doi: 10.1038/nchem.1108, published online 7 August 2011 http://www.nature.com/nchem

- Nature Chemistry

16.10 Chemical Co-Occurrences in Literature

- PubChem

16.11 Chemical-Gene Co-Occurrences in Literature

PubChem

16.12 Chemical-Disease Co-Occurrences in Literature

PubChem

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

17 Patents

17.1 Depositor-Supplied Patent Identifiers

PubChem

Link to all deposited patent identifiers

PubChem

17.2 WIPO PATENTSCOPE

Patents are available for this chemical structure:

https://patentscope.wipo.int/search/en/result.jsf?inchikey=FFEARJCKVFRZRR-BYPYZUCNSA-N

PATENTSCOPE (WIPO)

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

18 Interactions and Pathways

18.1 Protein Bound 3D Structures

RCSB Protein Data Bank (RCSB PDB)

View 164 proteins in NCBI Structure

PubChem

18.1.1 Ligands from Protein Bound 3D Structures

PDBe Ligand Code	MET
PDBe Conformer	

Protein Data Bank in Europe (PDBe)

18.2 Chemical-Target Interactions

Comparative Toxicogenomics Database (CTD)

Drug Gene Interaction database (DGIdb)

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

DrugBank

18.3 Drug-Drug Interactions

DrugBank

18.4 Drug-Food Interactions

Take with food.

DrugBank

18.5 Pathways

PubChem

19 Biological Test Results

19.1 BioAssay Results

PubChem

20 Taxonomy

L-Methionine is a metabolite found in or produced by Escherichia coli (strain K12, MG1655).

- E. coli Metabolome Database (ECMDB)

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

21 Classification

21.1 MeSH Tree

Medical Subject Headings (MeSH)

21.2 NCI Thesaurus Tree

NCI Thesaurus (NCIt)

21.3 ChEBI Ontology

ChEBI

21.4 KEGG: Metabolite

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

KEGG

21.5 KEGG: ATC

KEGG

21.6 KEGG: JP15

KEGG

21.7 KEGG: Risk Category of Japanese OTC Drugs

KEGG

21.8 WHO ATC Classification System

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

WHO Anatomical Therapeutic Chemical (ATC) Classification

21.9 EPA Safer Choice

EPA Safer Choice

21.10 ChemIDplus

ChemIDplus

21.11 CAMEO Chemicals

CAMEO Chemicals

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

21.12 ChEMBL Target Tree

ChEMBL

21.13 UN GHS Classification

UN Globally Harmonized System of Classification and Labelling of Chemicals (GHS)

21.14 EPA CPDat Classification

EPA Chemical and Products Database (CPDat)

21.15 NORMAN Suspect List Exchange Classification

NORMAN Suspect List Exchange

21.16 CCSBase Classification

CCSbase

21.17 EPA DSSTox Classification

EPA DSSTox

21.18 Consumer Product Information Database Classification

Consumer Product Information Database (CPID)

21.19 LOTUS Tree

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

- LOTUS - the natural products occurrence database

21.20 FDA Drug Type and Pharmacologic Classification

- National Drug Code (NDC) Directory

21.21 EPA Substance Registry Services Tree

- EPA Substance Registry Services

22 Information Sources

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L-METHIONINE
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CAMEO Chemical Reactivity Classification
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l-Methionine
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Methionine [USAN:USP:INN:BAN]
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ChemIDplus Chemical Information Classification
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Methionine
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L-Methionine
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L-methionine
https://echa.europa.eu/substance-information/-/substanceinfo/100.000.512

L-methionine
https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/68133

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METHIONINE
https://gsrs.ncats.nih.gov/ginas/app/beta/substances/AE28F7PNPL

10. **Hazardous Substances Data Bank (HSDB)**

(L)-Methionine
https://pubchem.ncbi.nlm.nih.gov/source/hsdb/4317

11. **Human Metabolome Database (HMDB)**

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Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

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L-Methionine
http://www.hmdb.ca/metabolites/HMDB0000696

HMDB0000696_nmr_one_1254
https://hmdb.ca/metabolites/HMDB0000696#spectra

12. ## Wikipedia

methionine
https://en.wikipedia.org/wiki/Methionine

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https://haz-map.com/About

Methionine
https://haz-map.com/Agents/15470

14. ## ChEBI

L-methionine
http://www.ebi.ac.uk/chebi/searchId.do?chebiId=CHEBI:16643

ChEBI Ontology
http://www.ebi.ac.uk/chebi/userManualForward.do#ChEBI%20Ontology

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NCI Thesaurus Tree
https://ncit.nci.nih.gov

17. ## West Coast Metabolomics Center-UC Davis

Methionine

18. ## CCSbase

L-Methionine

CCSbase Classification
https://ccsbase.net/

19. ## NORMAN Suspect List Exchange

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Methionine
https://ctdbase.org/detail.go?type=chem&acc=D008715

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METHIONINE
https://www.dgidb.org/drugs/METHIONINE

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https://www.whatsinproducts.com/contents/view/1/6

Methionine
https://www.whatsinproducts.com/chemicals/view/1/965/007005-18-7

Consumer Products Category Classification
https://www.whatsinproducts.com/

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l-methionine
https://www.fda.gov/science-research/liver-toxicity-knowledge-base-ltkb/drug-induced-liver-injury-rank-dilirank-dataset

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EPA CPDat Classification
https://www.epa.gov/chemical-research/chemical-and-products-database-cpdat

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L-Methionine
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L-METHIONINE
https://www.cfsanappsexternal.fda.gov/scripts/fdcc/index.cfm?set=FoodSubstances&id=METHIONINEL

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33. **Kruve Lab, Ionization & Mass Spectrometry, Stockholm University**
methionine

34. **MarkerDB**

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METHIONINE
https://www.fda.gov/drugs/drug-approvals-and-databases/national-drug-code-directory

36. **Nature Chemical Biology**
https://pubchem.ncbi.nlm.nih.gov/substance/14710667
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https://pubchem.ncbi.nlm.nih.gov/substance/84974939
https://pubchem.ncbi.nlm.nih.gov/substance/118111075
https://pubchem.ncbi.nlm.nih.gov/substance/404860012

37. **Nature Chemistry**
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https://www.nlm.nih.gov/research/umls/rxnorm/docs/termsofservice.html

methionine
https://rxnav.nlm.nih.gov/id/rxnorm/6837

40. **NMRShiftDB**
https://pubchem.ncbi.nlm.nih.gov/substance/840774

41. **Protein Data Bank in Europe (PDBe)**
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L-Methionine
https://spectrabase.com/spectrum/HPoQZUMJfDb

L-Methionine
https://spectrabase.com/spectrum/2KIBnW16jPT

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https://www.whocc.no/atc_ddd_index/

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MeSH Tree
http://www.nlm.nih.gov/mesh/meshhome.html

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Compounds with biological roles
http://www.genome.jp/kegg-bin/get_htext?br08001.keg

Anatomical Therapeutic Chemical (ATC) classification
http://www.genome.jp/kegg-bin/get_htext?br08303.keg

Drugs listed in the Japanese Pharmacopoeia
http://www.genome.jp/kegg-bin/get_htext?br08311.keg

Risk category of Japanese OTC drugs
http://www.genome.jp/kegg-bin/get_htext?br08312.keg

Case No.: IPR2023-00208
U.S. Patent No. 11,013,250

53. **UN Globally Harmonized System of Classification and Labelling of Chemicals (GHS)**

GHS Classification Tree
http://www.unece.org/trans/danger/publi/ghs/ghs_welcome_e.html

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56. **EPA Substance Registry Services**

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EPA SRS List Classification
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57. **PATENTSCOPE (WIPO)**

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58. **NCBI**

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