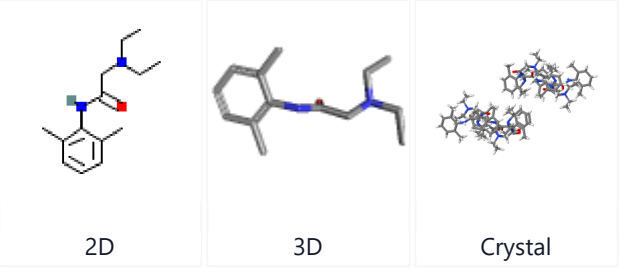
PubChem

COMPOUND SUMMARY

# Lidocaine

Cite | Download

| | |
|---|---|
| **PubChem CID** | 3676 |
| **Structure** |  2D 3D Crystal |
| **Chemical Safety** |  Irritant<br>Laboratory Chemical Safety Summary (LCSS) Datasheet |
| **Molecular Formula** | $C_{14}H_{22}N_2O$ |
| **Synonyms** | lidocaine<br>137-58-6<br>Lignocaine<br>Xylocaine<br>2-(Diethylamino)-N-(2,6-dimethylphenyl)acetamide<br>View More... |
| **Molecular Weight** | 234.34 g/mol<br>*Computed by PubChem 2.2 (PubChem release 2021.10.14)* |
| **Dates** | Create: 2005-03-25 Modify: 2024-11-16 |
| **Description** | Lidocaine is the monocarboxylic acid amide resulting from the formal condensation of N,N-diethylglycine with 2,6-dimethylaniline. It has a role as a local anaesthetic, an anti-arrhythmia drug, an environmental contaminant, a xenobiotic and a drug allergen. It is a monocarboxylic acid amide, a tertiary amino compound and a member of benzenes. It is functionally related to a glycinamide.<br>▸ ChEBI |

Ever since its discovery and availability for sale and use in the late 1940s, lidocaine has become an exceptionally commonly used medication. In particular, lidocaine's principal mode of action in acting as a local anesthetic that numbs the sensations of tissues means the agent is indicated for facilitating local anesthesia for a large variety of surgical procedures. It ultimately elicits its numbing activity by blocking sodium channels so that the neurons of local tissues that have the medication applied on are transiently incapable of signaling the brain regarding sensations. In doing so, however, it can block or decrease muscle contractile, resulting in effects like vasodilation, hypotension, and irregular heart rate, among others. As a result, lidocaine is also considered a class Ib anti-arrhythmic agent. Nevertheless, lidocaine's local anesthetic action sees its use in many medical situations or circumstances that may benefit from its action, including the treatment of premature ejaculation. Regardless, lidocaine is currently available as a relatively non-expensive generic medication that is written for in millions of prescriptions internationally on a yearly basis. It is even included in the World Health Organization's List of Essential Medicines.

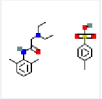
▸ DrugBank

Lidocaine is an Amide Local Anesthetic and Antiarrhythmic. The physiologic effect of lidocaine is by means of Local Anesthesia.

▸ FDA Pharm Classes

View More...

See also:  Lidocaine Hydrochloride (has salt form); Lidocaine; Tetracaine (component of);

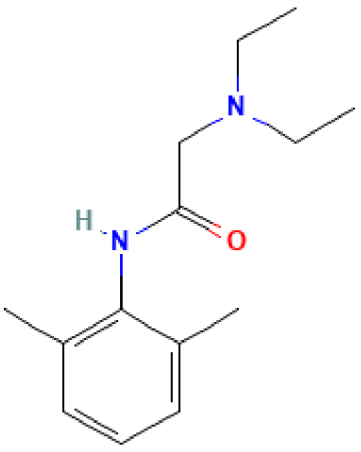
 Lidocaine tosylate (is active moiety of) ... View More ...

## Contents

# 1 Structures

## 1.1 2D Structure

Chemical Structure Depiction

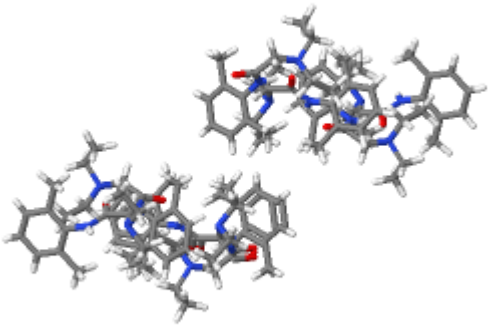


PubChem

## 1.2 3D Conformer

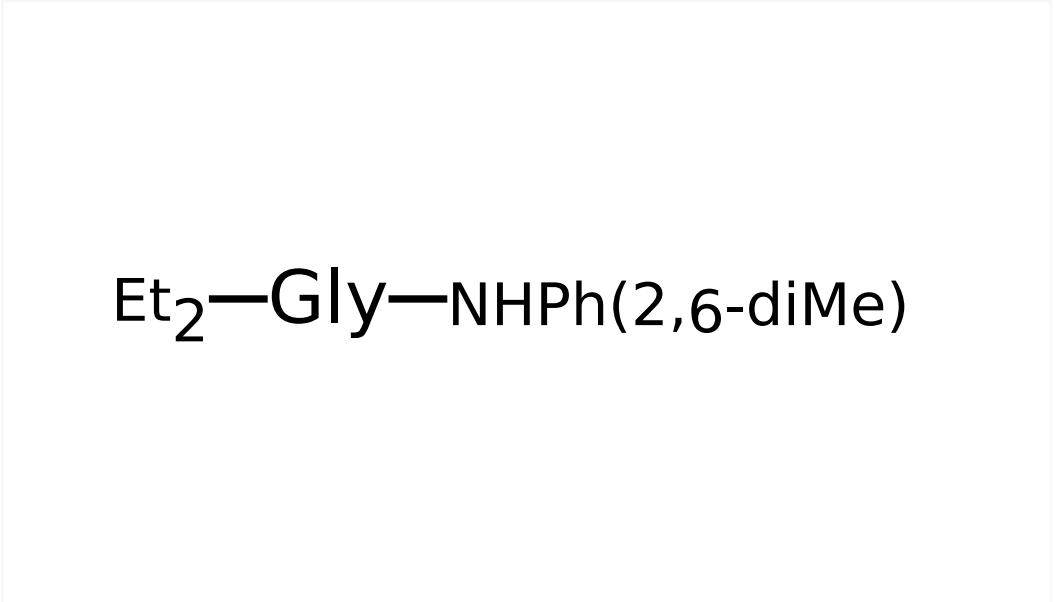
PubChem

## 1.3 Crystal Structures

| 1 of 2 | View All |
|---|---|
| CCDC Number | 636633 |
| Associated Article | DOI:10.1107/S1600536807001523 |
| Crystal Structure Data | DOI:10.5517/ccpcgk1 |
| Crystal Structure Depiction |  |

The Cambridge Structural Database

## 2 Biologic Description

| | |
|---|---|
| SVG Image |  |
| IUPAC Condensed | N(Et2)Gly-NHPh(2,6-diMe) |
| Sequence | G |



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## 3 Names and Identifiers

### 3.1 Computed Descriptors

#### 3.1.1 IUPAC Name

2-(diethylamino)-*N*-(2,6-dimethylphenyl)acetamide

*Computed by Lexichem TK 2.7.0 (PubChem release 2021.10.14)*

PubChem

#### 3.1.2 InChI

InChI=1S/C14H22N2O/c1-5-16(6-2)10-13(17)15-14-11(3)8-7-9-12(14)4/h7-9H,5-6,10H2,1-4H3,(H,15,17)

*Computed by InChI 1.0.6 (PubChem release 2021.10.14)*

PubChem

#### 3.1.3 InChIKey

NNJVILVZKWQKPM-UHFFFAOYSA-N

*Computed by InChI 1.0.6 (PubChem release 2021.10.14)*

PubChem

### 3.1.4 SMILES

CCN(CC)CC(=O)NC1=C(C=CC=C1C)C

*Computed by OEChem 2.3.0 (PubChem release 2021.10.14)*

PubChem

## 3.2 Molecular Formula

$C_{14}H_{22}N_2O$

*Computed by PubChem 2.2 (PubChem release 2021.10.14)*

PubChem

## 3.3 Other Identifiers

### 3.3.1 CAS

137-58-6

Australian Industrial Chemicals Introduction Scheme (AICIS); CAS Common Chemistry; ChemIDplus; Drug...

6108-05-0

New Zealand Environmental Protection Authority (EPA)

### 3.3.2 Related CAS

6108-05-0 (mono-hydrochloride, mono-hydrate)

73-78-9 (mono-hydrochloride)

ChemIDplus

### 3.3.3 Deprecated CAS

8059-42-5, 8059-66-3, 91484-71-8

ChemIDplus; EPA Chemicals under the TSCA

8059-66-3, 91484-71-8

- EPA DSSTox

## 3.3.4 European Community (EC) Number

205-302-8

- European Chemicals Agency (ECHA)

684-578-5

- European Chemicals Agency (ECHA)

## 3.3.5 UNII

98PI200987

- FDA Global Substance Registration System (GSRS)

## 3.3.6 ChEBI ID

CHEBI:6456

- ChEBI

## 3.3.7 ChEMBL ID

CHEMBL79

- ChEMBL

## 3.3.8 DrugBank ID

DB00281

- DrugBank

## 3.3.9 DSSTox Substance ID

DTXSID1045166

- EPA DSSTox

## 3.3.10 HMDB ID

HMDB0014426

- Human Metabolome Database (HMDB)

## 3.3.11 KEGG ID

C07073

- KEGG

D00358

- KEGG

## 3.3.12 Metabolomics Workbench ID

42673

- Metabolomics Workbench

## 3.3.13 NCI Thesaurus Code

C614

- NCI Thesaurus (NCIt)

## 3.3.14 Nikkaji Number

J5.631F

- Japan Chemical Substance Dictionary (Nikkaji)

## 3.3.15 NSC Number

40030

- DTP/NCI

## 3.3.16 PharmGKB ID

PA450226

- PharmGKB

### 3.3.17 Pharos Ligand ID

8NFQNG6H36UD

- Pharos

### 3.3.18 RXCUI

6387

- NLM RxNorm Terminology

### 3.3.19 Wikidata

Q216935

- Wikidata

### 3.3.20 Wikipedia

Lidocaine

- Wikipedia

## 3.4 Synonyms

### 3.4.1 MeSH Entry Terms

2-(Diethylamino)-N-(2,6-Dimethylphenyl)Acetamide
2-2EtN-2MePhAcN
Dalcaine
Lidocaine
Lidocaine Carbonate
Lidocaine Carbonate (2:1)
Lidocaine Hydrocarbonate
Lidocaine Hydrochloride
Lidocaine Monoacetate
Lidocaine Monohydrochloride
Lidocaine Monohydrochloride, Monohydrate
Lidocaine Sulfate (1:1)
Lignocaine
Octocaine
Xylesthesin
Xylocaine
Xylocitin
Xyloneural

- Medical Subject Headings (MeSH)

### 3.4.2 Depositor-Supplied Synonyms

lidocaine
137-58-6
Lignocaine
Xylocaine
2-(Diethylamino)-N-(2,6-dimethylphenyl)acetamide
Lidoderm
Duncaine
Esracaine
Xylestesin
Alphacaine
Cappicaine
Gravocain
Leostesin
Maricaine
Solarcaine
Isicaina
Solcain
Xylocain
L-Caine
Isicaine
Xylocitin
Rucaina
Xilina
Xycaine
Cito optadren
Anestacon
Lida-Mantle
Dentipatch
Xylotox
2-(Diethylamino)-2',6'-acetoxylidide
Lidoca
Lignoc
Cuivas
Jetoca
Remic
Xiloca
Xylon
Dalcai
2-Diet
Lidoca

PubChem

# 4 Chemical and Physical Properties

## 4.1 Computed Properties

| Property Name | Property Value | Reference |
|---|---|---|
| Molecular Weight | 234.34 g/mol | Computed by PubChem 2.2 (PubChem release 2021.10.14) |
| XLogP3 | 2.3 | Computed by XLogP3 3.0 (PubChem release 2021.10.14) |
| Hydrogen Bond Donor Count | 1 | Computed by Cactvs 3.4.8.18 (PubChem release 2021.10.14) |
| Hydrogen Bond Acceptor Count | 2 | Computed by Cactvs 3.4.8.18 (PubChem release 2021.10.14) |
| Rotatable Bond Count | 5 | Computed by Cactvs 3.4.8.18 (PubChem release 2021.10.14) |
| Exact Mass | 234.173213330 g/mol | Computed by PubChem 2.2 (PubChem release 2021.10.14) |
| Monoisotopic Mass | 234.173213330 g/mol | Computed by PubChem 2.2 (PubChem release 2021.10.14) |
| Topological Polar Surface Area | 32.3Å$^2$ | Computed by Cactvs 3.4.8.18 (PubChem release 2021.10.14) |
| Heavy Atom Count | 17 | Computed by PubChem |
| Formal Charge | 0 | Computed by PubChem |
| Complexity | 228 | Computed by Cactvs 3.4.8.18 (PubChem release 2021.10.14) |

| | | |
|---|---|---|
| Isotope Atom Count | 0 | Computed by PubChem |
| Defined Atom Stereocenter Count | 0 | 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 2021.10.14) |

▸ PubChem

## 4.2 Experimental Properties

### 4.2.1 Physical Description

Solid

▸ Human Metabolome Database (HMDB)

### 4.2.2 Color / Form

Needles from benzene or alcohol

*Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 1239*

▸ Hazardous Substances Data Bank (HSDB)

Yellow needles from water

*Haynes, W.M. (ed.). CRC Handbook of Chemistry and Physics. 94th Edition. CRC Press LLC, Boca Raton: FL 2013-2014, p. 3-172*

▸ Hazardous Substances Data Bank (HSDB)

White or slightly yellow, crystalline powder

*Lewis, R.J. Sr.; Hawley's Condensed Chemical Dictionary 15th Edition. John Wiley & Sons, Inc. New York, NY 2007., p. 754*

▸ Hazardous Substances Data Bank (HSDB)

### 4.2.3 Odor

Characteristic odor

*Lewis, R.J. Sr.; Hawley's Condensed Chemical Dictionary 15th Edition. John Wiley & Sons, Inc. New York, NY 2007., p. 754*

▸ **Hazardous Substances Data Bank (HSDB)**

## 4.2.4 Boiling Point

159-160 °C at 2.00E+00 mm Hg

*PhysProp*

▸ **DrugBank**

BP: 180-182 °C at 4 mm Hg; 159-160 °C at 2 mm Hg

*O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Cambridge, UK: Royal Society of Chemistry, 2013., p. 1019*

▸ **Hazardous Substances Data Bank (HSDB)**

181 °C

▸ **Human Metabolome Database (HMDB)**

## 4.2.5 Melting Point

68.5°C

*PhysProp*

▸ **DrugBank**

68 °C

*Haynes, W.M. (ed.). CRC Handbook of Chemistry and Physics. 94th Edition. CRC Press LLC, Boca Raton: FL 2013-2014, p. 3-172*

▸ **Hazardous Substances Data Bank (HSDB)**

68.5 °C

▸ **Human Metabolome Database (HMDB)**

## 4.2.6 Solubility

>35.2 [ug/mL] (The mean of the results at pH 7.4)

▸ **Burnham Center for Chemical Genomics**

4100mg/L (at 30 °C)

*YALKOWSKY,SH & DANNENFELSER,RM (1992)*

▸ **DrugBank**

VERY SOL IN ALC; SOL IN CHLOROFORM; INSOL IN ETHER; WHITE CRYSTALLINE POWDER /LIDOCAINE HYDROCHLORIDE/

*Osol, A. (ed.). Remington's Pharmaceutical Sciences. 16th ed. Easton, Pennsylvania: Mack Publishing Co., 1980., p. 995*

▸ **Hazardous Substances Data Bank (HSDB)**

In water, 410 mg/L at 30 °C

*Yalkowsky, S.H., He, Yan, Jain, P. Handbook of Aqueous Solubility Data Second Edition. CRC Press, Boca Raton, FL 2010, p. 1030*

▸ **Hazardous Substances Data Bank (HSDB)**

Very soluble in alcohol, chloroform; freely soluble in ether, benzene. Dissolves in oils

*O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Cambridge, UK: Royal Society of Chemistry, 2013., p. 1019*

▸ **Hazardous Substances Data Bank (HSDB)**

Soluble in alcohol, ether, or chloroform

*Lewis, R.J. Sr.; Hawley's Condensed Chemical Dictionary 15th Edition. John Wiley & Sons, Inc. New York, NY 2007., p. 754*

▸ **Hazardous Substances Data Bank (HSDB)**

Very soluble in benzene, ethyl ether, ethanol, and chloroform

*Haynes, W.M. (ed.). CRC Handbook of Chemistry and Physics. 94th Edition. CRC Press LLC, Boca Raton: FL 2013-2014, p. 3-172*

▸ **Hazardous Substances Data Bank (HSDB)**

5.93e-01 g/L

▸ **Human Metabolome Database (HMDB)**

### 4.2.7 LogP

2.44

*AVDEEF,A (1997)*

▸ **DrugBank**

log Kow = 2.26 at pH 7.4

*Hansch, C., Leo, A., D. Hoekman. Exploring QSAR - Hydrophobic, Electronic, and Steric Constants. Washington, DC: American Chemical Society., 1995., p. 126*

▸ **Hazardous Substances Data Bank (HSDB)**

2.1

▸ Human Metabolome Database (HMDB)

## 4.2.8 LogS

-1.76

*ADME Research, USCD*

▸ DrugBank

## 4.2.9 Stability / Shelf Life

Commercially available solutions of **lidocaine hydrochloride** in 5% dextrose usually are stable for 18 months after the date of manufacture. Commercially available solutions of **lidocaine hydrochloride** in 5% dextrose may be provided in plastic containers.

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 1698*

▸ Hazardous Substances Data Bank (HSDB)

Stable under recommended storage conditions.

*Sigma-Aldrich; Material Safety Data Sheet for Lidocaine. Product Number: L1026, Version 5.2 (Revision Date 06/28/2014). Available from, as of October 8, 2014: **https://www.sigmaaldrich.com/safety-center.html***

▸ Hazardous Substances Data Bank (HSDB)

## 4.2.10 Decomposition

When heated to decomposition it emits toxic fumes of /nitrogen oxides/.

*Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 1239*

▸ Hazardous Substances Data Bank (HSDB)

## 4.2.11 Ionization Efficiency

| | |
|---|---|
| **Ionization mode** | Positive |
| **logIE** | 5.12 |
| **pH** | 2.7 |
| **Instrument** | Agilent XCT |
| **Ion source** | Electrospray ionization |
| **Additive** | formic acid (5.3nM) |

| | |
|---|---|
| Organic modifier | MeCN (80%) |
| Reference | DOI:10.1038/s41598-020-62573-z |

▸ Kruve Lab, Ionization & Mass Spectrometry, Stockholm University

## 4.2.12 Caco2 Permeability

-4.21

*ADME Research, USCD*

▸ DrugBank

## 4.2.13 Dissociation Constants

### Basic pKa

7.928

*Tested as SID 103169867 in AID 781325: **https://pubchem.ncbi.nlm.nih.gov/bioassay/781325#sid=103169867***

*Comparison of the accuracy of experimental and predicted pKa values of basic and acidic compounds. Pharm Res. 2014; 31(4):1082-95. **DOI:10.1007/s11095-013-1232-z**. **PMID:24249037***

▸ ChEMBL

### Basic pKa

7.95

*Tested as SID 103169867 in AID 781326: **https://pubchem.ncbi.nlm.nih.gov/bioassay/781326#sid=103169867***

*Comparison of the accuracy of experimental and predicted pKa values of basic and acidic compounds. Pharm Res. 2014; 31(4):1082-95. **DOI:10.1007/s11095-013-1232-z**. **PMID:24249037***

▸ ChEMBL

### Basic pKa

7.94

*Tested as SID 103169867 in AID 781328: **https://pubchem.ncbi.nlm.nih.gov/bioassay/781328#sid=103169867***

*Comparison of the accuracy of experimental and predicted pKa values of basic and acidic compounds. Pharm Res. 2014; 31(4):1082-95. **DOI:10.1007/s11095-013-1232-z**. **PMID:24249037***

▸ ChEMBL

### pKa

8.01

*SANGSTER (1994)*

▸ DrugBank

pKa = 7.86

*Osol, A. (ed.). Remington's Pharmaceutical Sciences. 16th ed. Easton, Pennsylvania: Mack Publishing Co., 1980., p. 994*

▸ Hazardous Substances Data Bank (HSDB)

## 4.2.14 Collision Cross Section

150.66 Å$^2$ [M+H-H2O]$^+$ [CCS Type: TW; Method: calibrated with polyalanine and drug standards]

154.82 Å$^2$ [M+H]$^+$ [CCS Type: TW; Method: calibrated with polyalanine and drug standards]

159.47 Å$^2$ [M+K]$^+$ [CCS Type: TW; Method: calibrated with polyalanine and drug standards]

161.82 Å$^2$ [M+Na]$^+$ [CCS Type: TW; Method: calibrated with polyalanine and drug standards]

*Ross et al. JASMS 2022; 33; 1061-1072.* ***DOI:10.1021/jasms.2c00111***

▸ CCSbase

157.7 Å$^2$ [M+H]$^+$ [CCS Type: TW; Method: Major Mix IMS/Tof Calibration Kit (Waters)]

***https://www.sciencedirect.com/science/article/pii/S0021967318301894***

▸ CCSbase

158.92 Å$^2$ [M+H]$^+$

*S61 | UJICCSLIB | Collision Cross Section (CCS) Library from UJI |* ***DOI:10.5281/zenodo.3549476***

▸ NORMAN Suspect List Exchange

## 4.2.15 Kovats Retention Index

| | |
|---|---|
| **Standard non-polar** | 1870, 1881, 1884, 1838, 1857, 1865, 1875, 1875, 1875, 1875, 1875, 1880, 1880, 1880, 1880, 1880, 1880, 1880, 1881, 1882, 1882, 1882, 1882, 1882, 1885, 1885, 1885, 1885, 1885, 1885, 1885, 1885, 1890, 1890, 1890, 1890, 1890, 1892, 1893, 1895, 1895, 1895, 1854, 1852, 1848, 1854, 1860, 1863, 1842, 1865, 1875, 1875, 1882, 1875, 1850, 1900, 1869, 1859, 1866, 1860, 1885, 1875, 1876.9, 1841, 1842, 1870, 1856, 1844, 1842, 1852, 1854, 1856, 1857, 1857, 1858, 1858, 1860, 1860, 1870, 1865, 1865 |
| **Semi-standard non-polar** | 1924, 1924, 1885.9, 1875.2, 1872.7, 1881.1, 1842, 1871.3 |

▸ NIST Mass Spectrometry Data Center

## 4.2.16 Other Experimental Properties

ODORLESS; SLIGHTLY BITTER TASTE /LIDOCAINE HYDROCHLORIDE/

*Osol, A. (ed.). Remington's Pharmaceutical Sciences. 16th ed. Easton, Pennsylvania: Mack Publishing Co., 1980., p. 994*

▸ Hazardous Substances Data Bank (HSDB)

White crystals, mp 127-129 °C; monohydrate mp 77-78 °C. Very soluble in water, alcohol; soluble in chloroform. Insoluble in ether. /Lidocaine hydrochloride/

*O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Cambridge, UK: Royal Society of Chemistry, 2013., p. 1019*

- Hazardous Substances Data Bank (HSDB)

## 4.3 SpringerMaterials Properties

Nuclear quadrupole resonance spectroscopy
Quadrupole coupling

- SpringerMaterials

## 4.4 Chemical Classes

Pharmaceutical

- USGS Health-Based Screening Levels for Evaluating Water-Quality Data

### 4.4.1 Drugs

Pharmaceutical

*S120 | DUSTCT2024 | Substances from Second NORMAN Collaborative Dust Trial |* ***DOI:10.5281/zenodo.13835254***

- NORMAN Suspect List Exchange

#### 4.4.1.1 Human Drugs

Breast Feeding; Lactation; Milk, Human; Antiarrhythmics; Local Anesthetics

- Drugs and Lactation Database (LactMed)

Human drug -> Prescription

- Drugs@FDA

Human drug -> Discontinued

- Drugs@FDA

Human drug -> Prescription; Discontinued

- Drugs@FDA

Human drug -> Prescription; Discontinued; Active ingredient (LIDOCAINE)

- Drugs@FDA

Antiarrhythmic medicines

Local anaesthetics

- WHO Model Lists of Essential Medicines

### 4.4.1.2 Animal Drugs

Active Ingredients (Lidocaine) -> FDA Greenbook

- FDA Approved Animal Drug Products (Green Book)

Pharmaceuticals -> Animal Drugs -> Approved in Taiwan

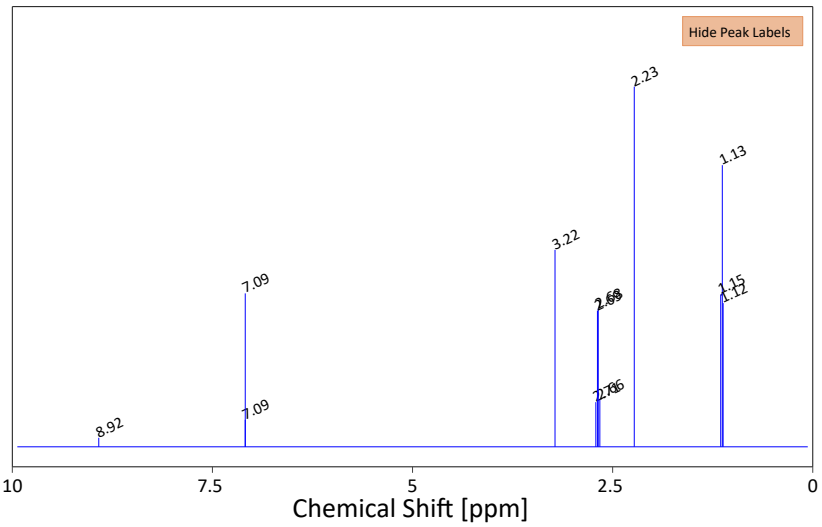
*S72 | NTUPHTW | Pharmaceutically Active Substances from National Taiwan University |*
*DOI:10.5281/zenodo.3955664*

- NORMAN Suspect List Exchange

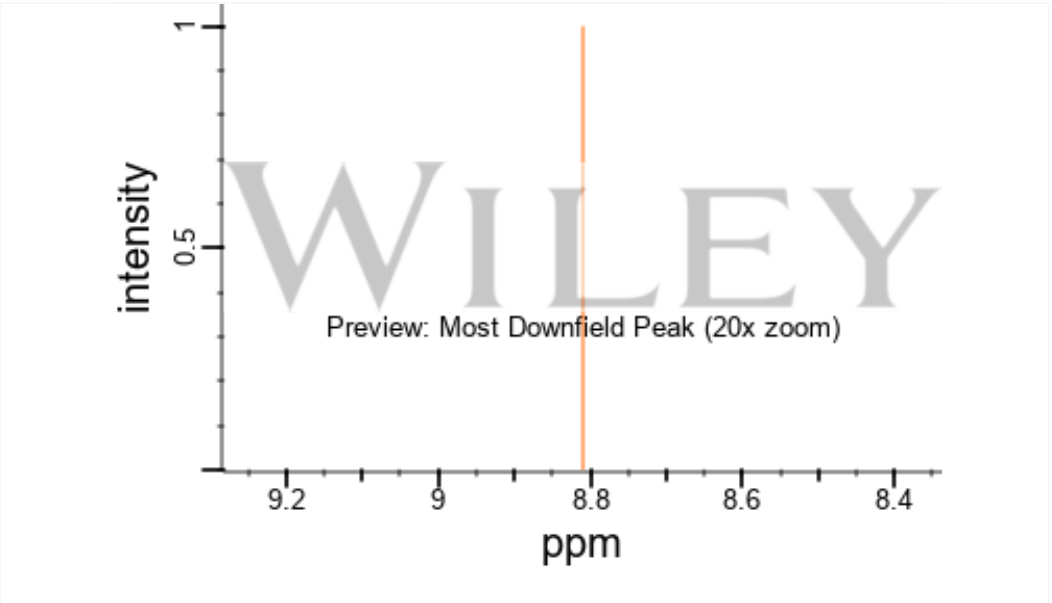
# 5 Spectral Information

## 5.1 1D NMR Spectra

### 5.1.1 1H NMR Spectra

| 1 of 2 | |
|---|---|
| **Spectra ID** | 2235 |
| **Instrument Type** | JEOL |
| **Frequency** | 400 MHz |
| **Solvent** | CDCl3 |
| **Shifts [ppm]:Intensity** | 1.12:399.00, 2.71:124.00, 2.66:131.00, 7.09:75.00, 2.68:384.00, 7.09:426.00, 1.13:782.00, 2.69:378.00, 8.92:25.00, 2.23:1000.00, 1.15:423.00, 3.22:547.00 |
| **Thumbnail** |  |

Human Metabolome Database (HMDB)

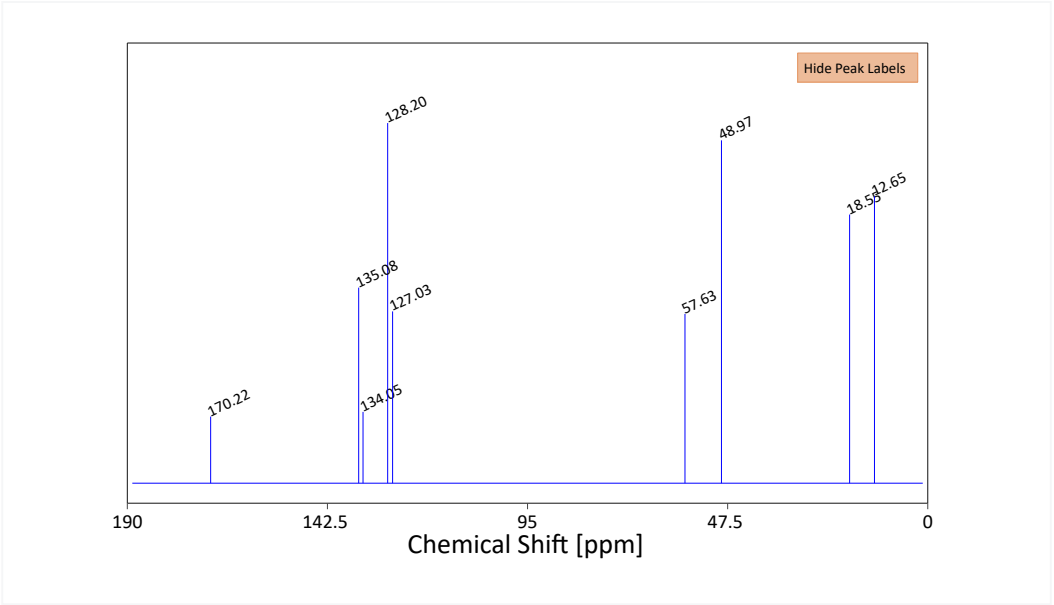
| 2 of 2 | |
|---|---|
| **Instrument Name** | Varian A-60D |
| **Copyright** | Copyright © 2009-2024 John Wiley & Sons, Inc. All Rights Reserved. |
| **Thumbnail** |  |



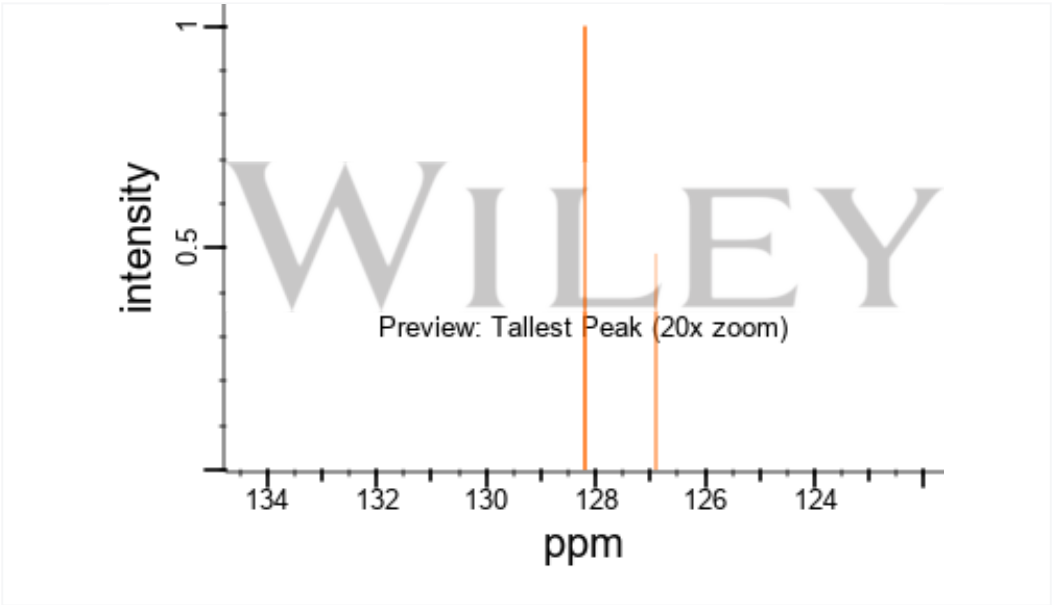
SpectraBase

## 5.1.2 13C NMR Spectra

| 1 of 3 | View All |
|---|---|
| **Spectra ID** | 2930 |
| **Instrument Type** | JEOL |
| **Frequency** | 22.53 MHz |
| **Solvent** | CDCl3 |
| **Shifts [ppm]:Intensity** | 134.05:198.00, 57.63:470.00, 48.97:952.00, 128.20:1000.00, 135.08:543.00, 170.22:185.00, 18.55:746.00, 127.03:477.00, 12.65:797.00 |

| | |
|---|---|
| Thumbnail |  |

▸ Human Metabolome Database (HMDB)

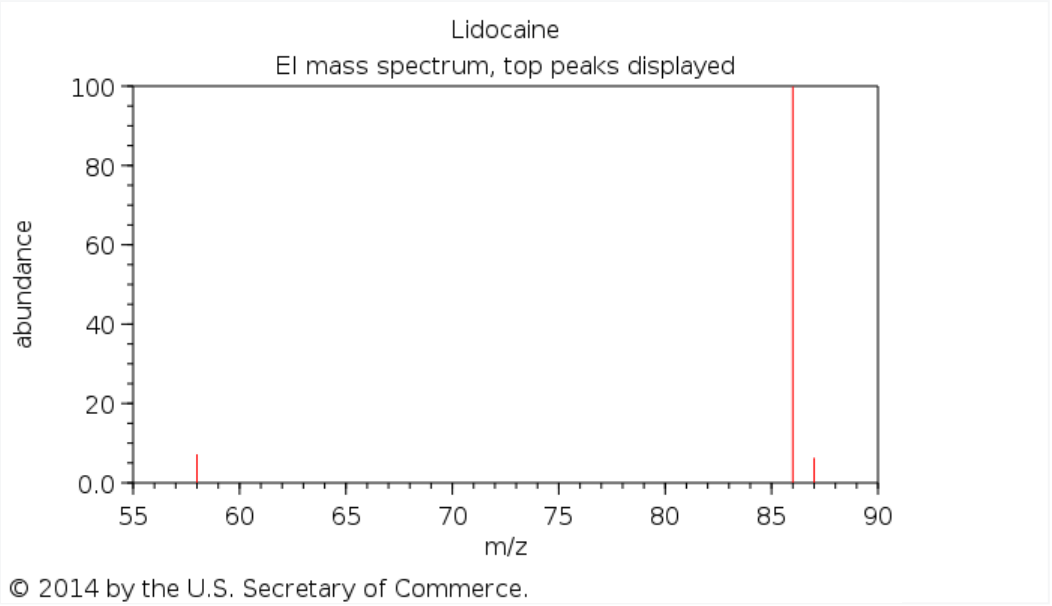
| 2 of 3 | View All |
|---|---|
| Source of Sample | Aldrich Chemical Company, Inc., Milwaukee, Wisconsin |
| Copyright | Copyright © 1980, 1981-2024 John Wiley & Sons, Inc. All Rights Reserved. |
| Thumbnail |  |

▸ SpectraBase

## 5.2 Mass Spectrometry

### 5.2.1 GC-MS

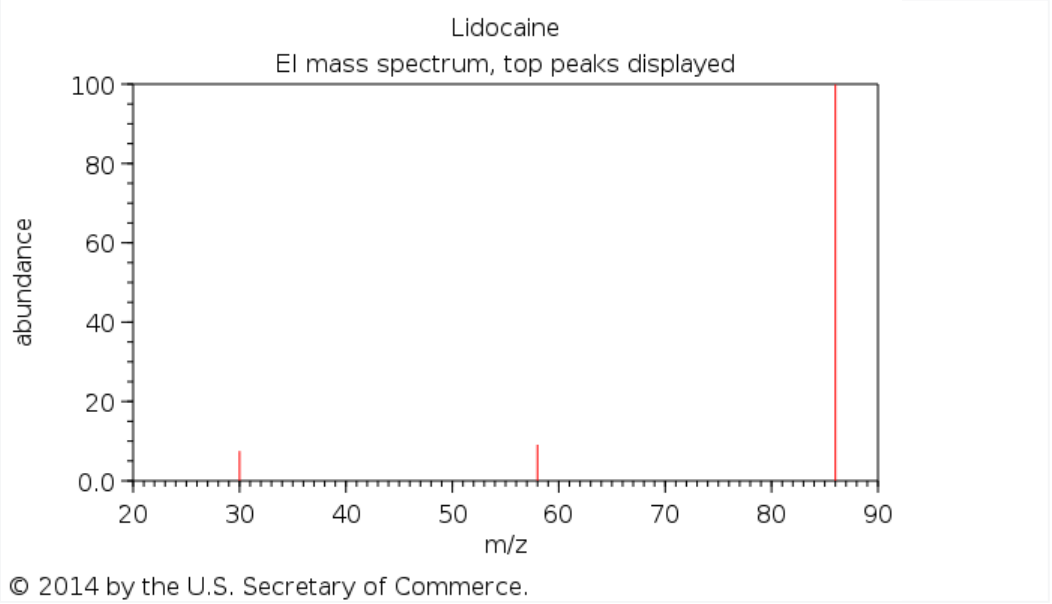
| 1 of 8 | View All |
|---|---|
| NIST Number | 408610 |
| Library | Main library |

| | |
|---|---|
| **Total Peaks** | 85 |
| **m/z Top Peak** | 86 |
| **m/z 2nd Highest** | 58 |
| **m/z 3rd Highest** | 87 |
| **Thumbnail** |  |



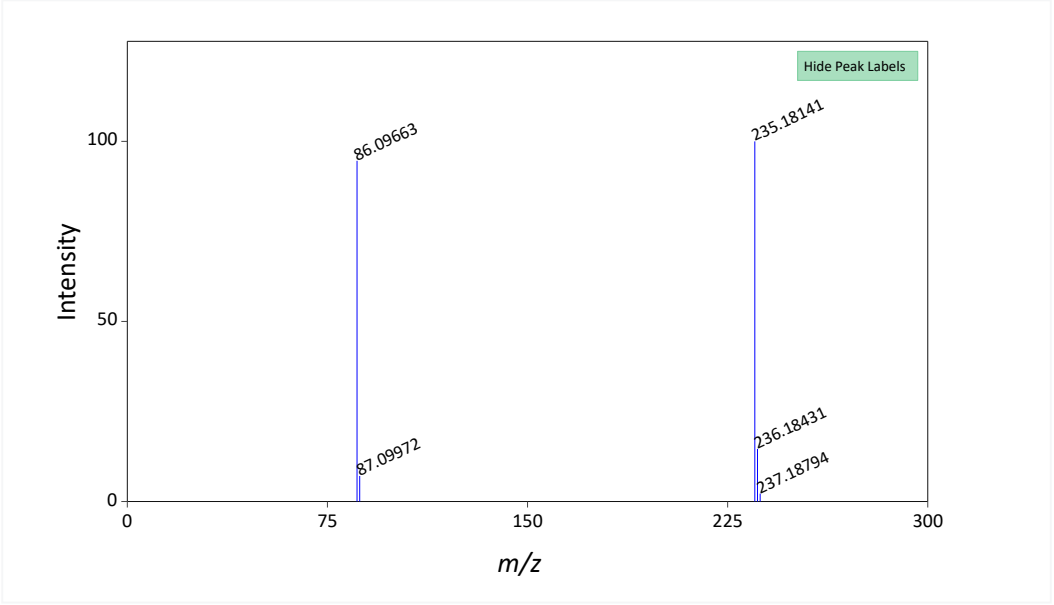


▸ NIST Mass Spectrometry Data Center

| 2 of 8 | View All |
|---|---|
| **NIST Number** | 250604 |
| **Library** | Replicate library |
| **Total Peaks** | 121 |
| **m/z Top Peak** | 86 |
| **m/z 2nd Highest** | 58 |
| **m/z 3rd Highest** | 30 |
| **Thumbnail** |  |

NIST Mass Spectrometry Data Center

## 5.2.2 MS-MS

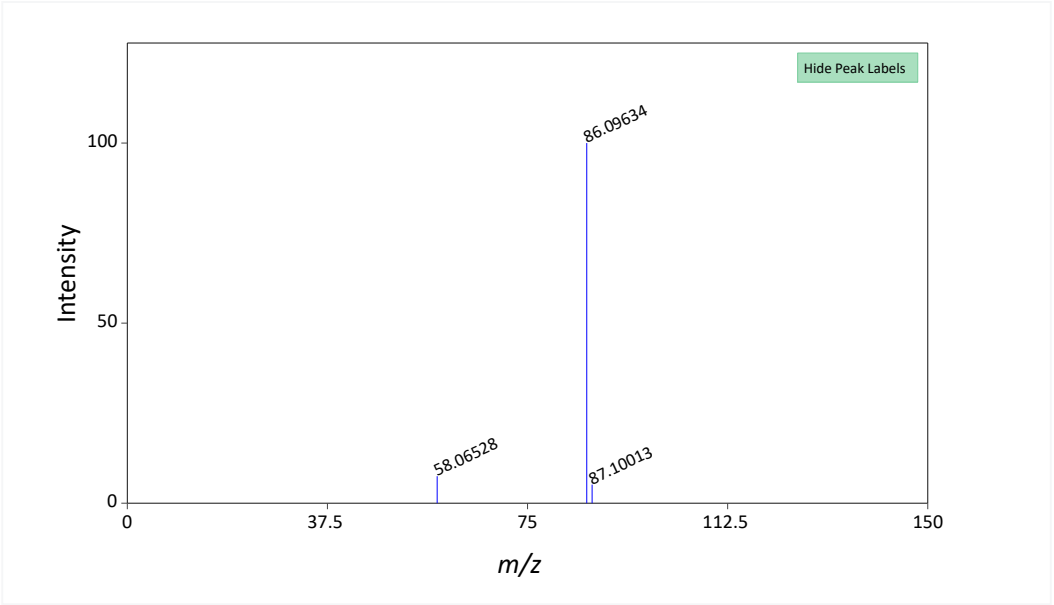
| 1 of 10 | View All |
|---|---|
| Spectra ID | 2226303 |
| Ionization Mode | Positive |
| SPLASH | splash10-000i-7090000000-fe49bdebdd5cc9ef64dc |
| Top 5 Peaks | 235.18141 100<br>86.09663 94.60<br>236.18431 14.60<br>87.09972 7.10<br>237.18794 2.20 |
| Thumbnail |  |



Human Metabolome Database (HMDB)

| 2 of 10 | View All |
|---|---|
| Spectra ID | 2228425 |
| Ionization Mode | Positive |
| SPLASH | splash10-000i-9000000000-55829c2fc7506b352c59 |
| Top 5 Peaks | 86.09634 100<br>58.06528 7.49<br>87.10013 5.16 |

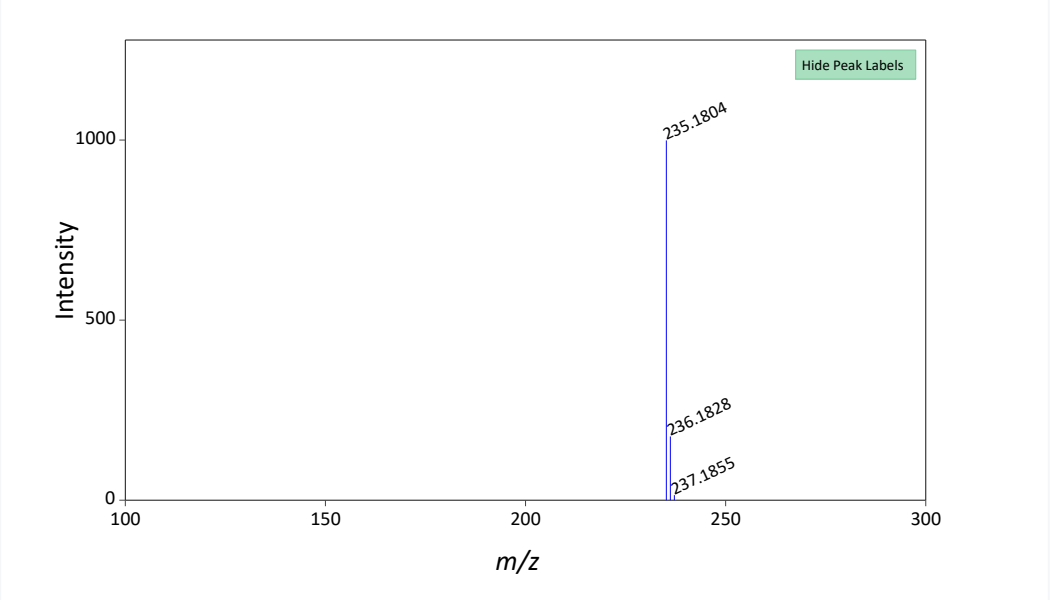
Thumbnail




▸ Human Metabolome Database (HMDB)

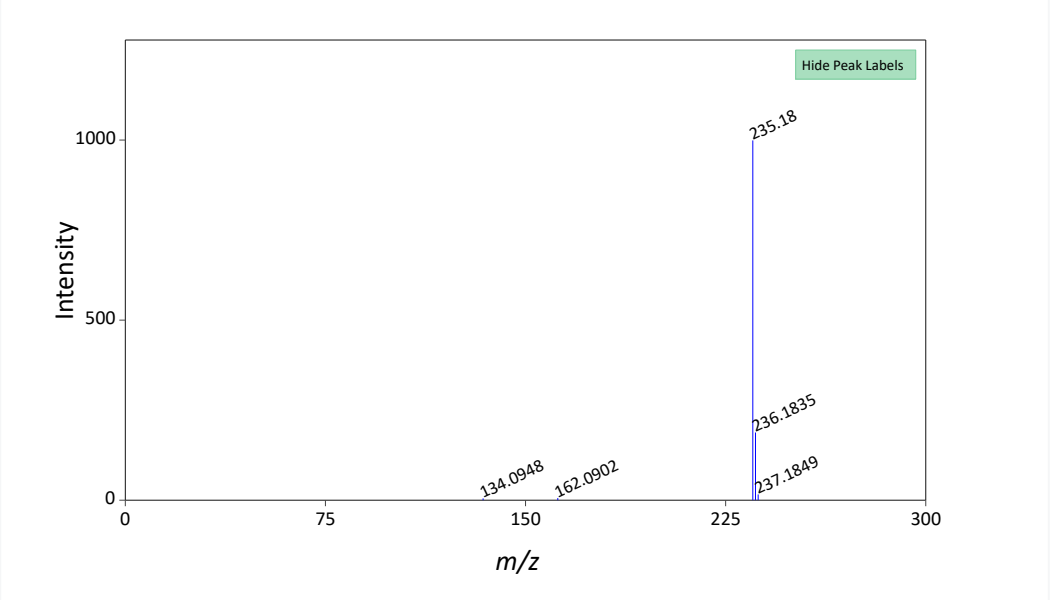
## 5.2.3 LC-MS

| 1 of 59 | View All |
|---|---|
| **Accession ID** | MSBNK-Athens_Univ-AU121201 |
| **Authors** | Nikiforos Alygizakis, Katerina Galani, Nikolaos Thomaidis, University of Athens |
| **Instrument** | Bruker maXis Impact |
| **Instrument Type** | LC-ESI-QTOF |
| **MS Level** | MS2 |
| **Ionization Mode** | POSITIVE |
| **Ionization** | ESI |
| **Collision Energy** | 10 eV |
| **Fragmentation Mode** | CID |
| **Column Name** | Acclaim RSLC C18 2.2um, 2.1x100mm, Thermo |
| **Retention Time** | 4.429 min |
| **Precursor m/z** | 235.1805 |
| **Precursor Adduct** | [M+H]+ |
| **Top 5 Peaks** | 235.1804 999<br>236.1828 177<br>237.1855 14 |
| **SPLASH** | splash10-000i-0090000000-5b8ffe7ee65749bd1b4d |

| | |
|---|---|
| Thumbnail |  |
| License | CC BY |

▸ MassBank Europe

| 2 of 59 | View All |
|---|---|
| Accession ID | MSBNK-Athens_Univ-AU121202 |
| Authors | Nikiforos Alygizakis, Katerina Galani, Nikolaos Thomaidis, University of Athens |
| Instrument | Bruker maXis Impact |
| Instrument Type | LC-ESI-QTOF |
| MS Level | MS2 |
| Ionization Mode | POSITIVE |
| Ionization | ESI |
| Collision Energy | 20 eV |
| Fragmentation Mode | CID |
| Column Name | Acclaim RSLC C18 2.2um, 2.1x100mm, Thermo |
| Retention Time | 4.386 min |
| Precursor m/z | 235.1805 |
| Precursor Adduct | [M+H]+ |
| Top 5 Peaks | 235.18 999<br>236.1835 188<br>237.1849 16<br>162.0902 6<br>134.0948 5 |
| SPLASH | splash10-000i-0090000000-209a26396e082040c335 |

| | |
|---|---|
| **Thumbnail** |  |
| **License** | CC BY |

▸ MassBank Europe

## 5.2.4 Other MS

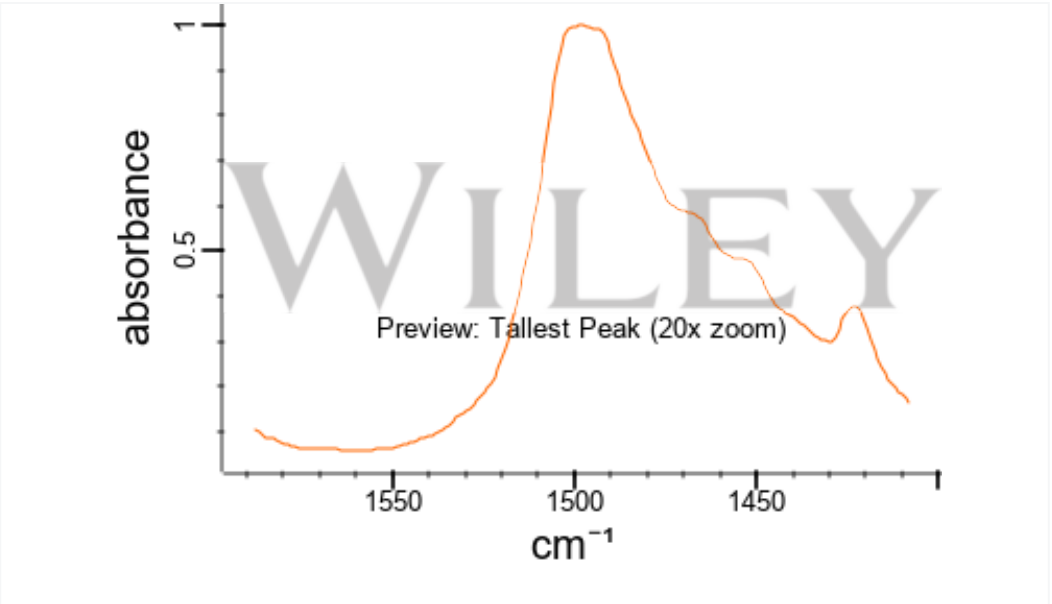
| | |
|---|---|
| **Other MS** | MASS: 35696 (NITS/EPA/MSDC Mass Spectral database, 1990 version) |

▸ Hazardous Substances Data Bank (HSDB)

## 5.3 IR Spectra

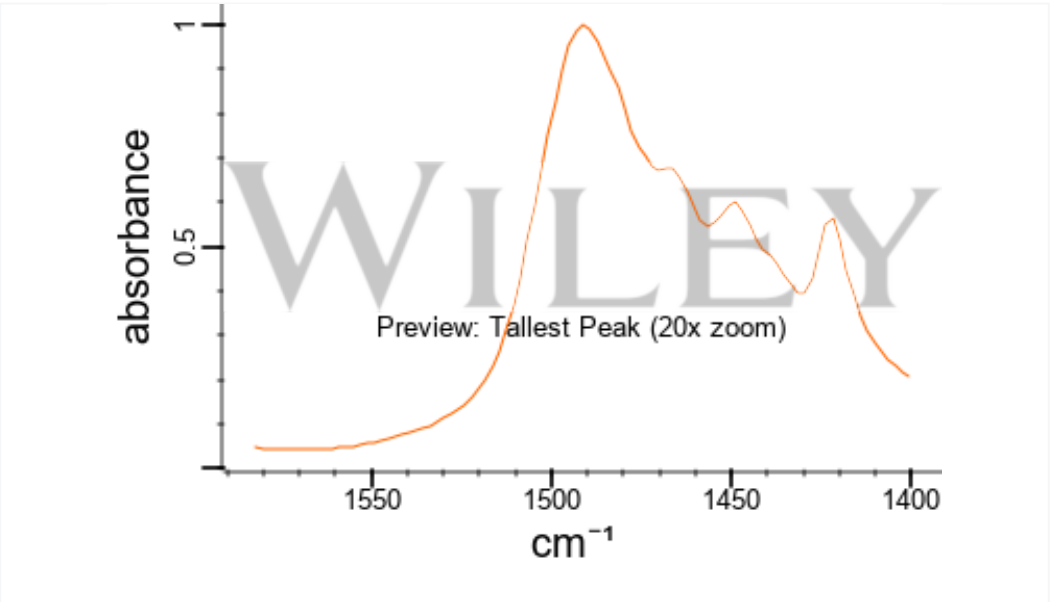
### 5.3.1 FTIR Spectra

| | |
|---|---|
| **Technique** | KBr WAFER |
| **Source of Sample** | Astra Pharmaceutical Products, Inc., Worcester, Massachusetts |
| **Copyright** |  |

| | |
|---|---|
| **Thumbnail** |  |

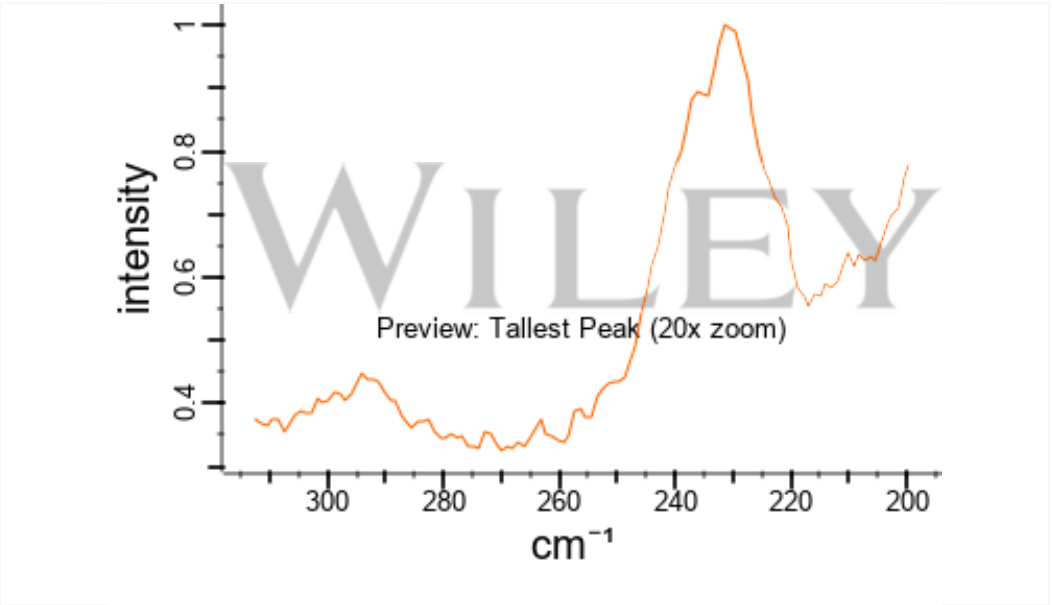
▸ SpectraBase

## 5.3.2 ATR-IR Spectra

| | |
|---|---|
| **Instrument Name** | Bio-Rad FTS |
| **Technique** | ATR-Neat (DuraSamplIR II) |
| **Source of Spectrum** | Forensic Spectral Research |
| **Source of Sample** | Alltech Associates, Inc., Grace Davison Discovery Sciences |
| **Catalog Number** | 01842 |
| **Lot Number** | 132 |
| **Copyright** |  |
| **Thumbnail** |  |

▸ SpectraBase

## 5.4 Raman Spectra

| | |
|---|---|
| **Technique** | FT-Raman |
| **Source of Spectrum** | Forensic Spectral Research |
| **Source of Sample** | Alltech Associates, Inc., Grace Davison Discovery Sciences |
| **Catalog Number** | 01842 |
| **Lot Number** | 132 |
| **Copyright** | Copyright © 2012-2024 John Wiley & Sons, Inc. All Rights Reserved. |
| **Thumbnail** |  |



▸ SpectraBase

## 5.5 Other Spectra

Intense mass spectral peaks: 58 m/z, 72 m/z, 86 m/z, 234 m/z

*Pfleger, K., H. Maurer and A. Weber. Mass Spectral and GC Data of Drugs, Poisons and their Metabolites. Parts I and II. Mass Spectra Indexes. Weinheim, Federal Republic of Germany. 1985., p. 381*

▸ Hazardous Substances Data Bank (HSDB)

# 6 Related Records

## 6.1 Related Compounds with Annotation

Follow these links to do a live 2D search or do a live 3D search for this compound, sorted by annotation score. This section is deprecated (see here for details), but these live search links provide equivalent functionality to the table that was previously shown here.

▸ PubChem

## 6.2 Related Compounds

| | |
|---|---|
| Same Connectivity Count | 10 |
| Same Parent, Connectivity Count | 58 |
| Same Parent, Exact Count | 46 |
| Mixtures, Components, and Neutralized Forms Count | 310 |
| Similar Compounds (2D) | View in PubChem Search |
| Similar Conformers (3D) | View in PubChem Search |

PubChem

## 6.3 Substances

### 6.3.1 PubChem Reference Collection SID

481107795

PubChem

### 6.3.2 Related Substances

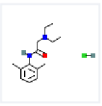
| | |
|---|---|
| All Count | 1252 |
| Same Count | 319 |
| Mixture Count | 933 |

PubChem

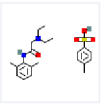
### 6.3.3 Substances by Category

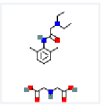
PubChem

## 6.4 Other Relationships


Lidocaine Hydrochloride (has salt form)

Lidocaine; Tetracaine (component of)


Lidocaine tosylate (is active moiety of)


Lidocaine iminodiacetic acid (is active moiety of)

Ceftriaxone sodium; lidocaine (component of)

Allantoin; Lidocaine (component of)
Glycerin; lidocaine (component of)
Dibucaine; lidocaine (component of)
Alcohol; lidocaine (component of)
Lidocaine; phenylephrine (component of)
Diclofenac sodium; lidocaine (component of)
Lidocaine; mupirocin (component of)
Capsicum; lidocaine (component of)
Lidocaine; petrolatum (component of)
Benzalkonium chloride; lidocaine (component of)

PubChem

## 6.5 Entrez Crosslinks

| | |
|---|---|
| PubMed Count | 2512 |
| Protein Structures Count | 3 |
| Taxonomy Count | 5 |
| OMIM Count | 14 |
| Gene Count | 686 |

PubChem

## 6.6 Associated Chemicals

Lidocaine hydrochloride; 73-78-9

Hazardous Substances Data Bank (HSDB)

## 6.7 NCBI LinkOut

NCBI

## 7 Chemical Vendors

PubChem

## 8 Drug and Medication Information

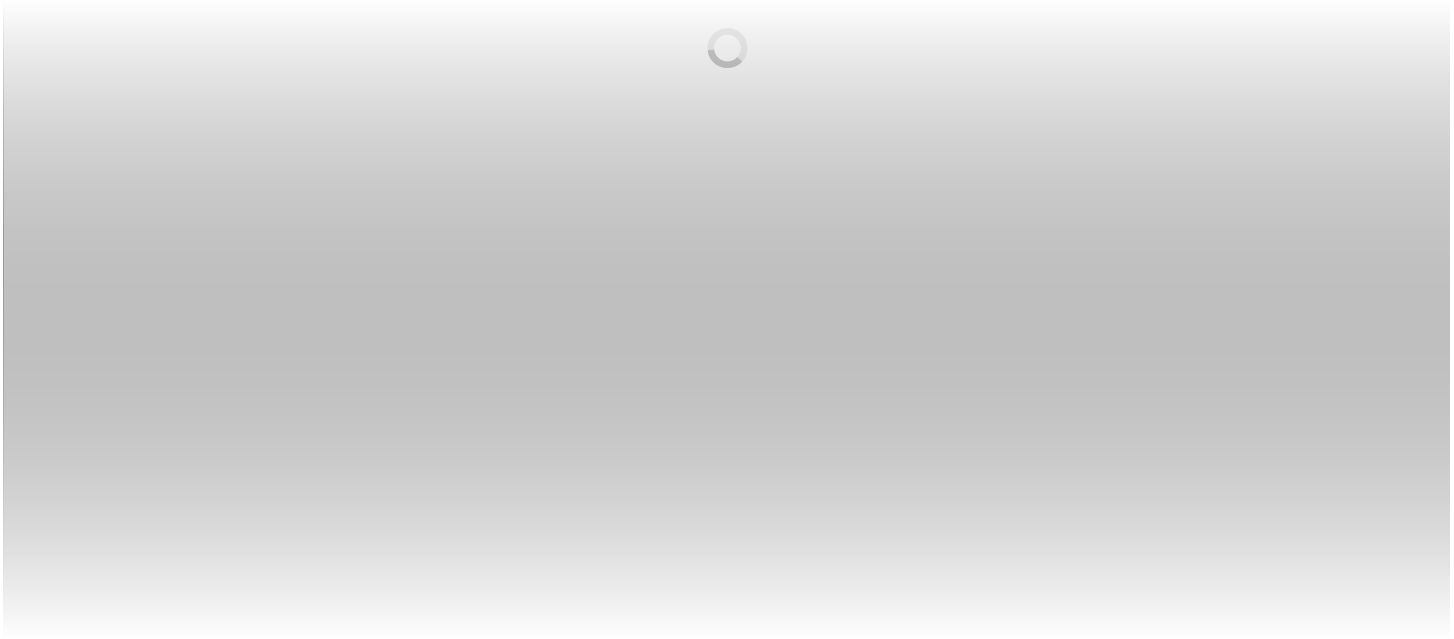
### 8.1 Drug Indication

Lidocaine is an anesthetic of the amide group indicated for production of local or regional anesthesia by infiltration techniques such as percutaneous injection and intravenous regional anesthesia by peripheral nerve block techniques such as brachial plexus and intercostal and by central neural techniques such as lumbar and caudal epidural blocks.

DrugBank

FDA Label

▸ DrugBank



▸ Open Targets

## 8.2 Drug Classes

Breast Feeding; Lactation; Milk, Human; Antiarrhythmics; Local Anesthetics

▸ Drugs and Lactation Database (LactMed)

## 8.3 Drug Transformations

Lidocaine has known transformation products that include Lidocaine-N-oxide and Norlidocaine.

Lidocaine is a known transformation product of Lidocaine-N-oxide.

*S66 | EAWAGTPS | Parent-Transformation Product Pairs from Eawag |* ***DOI:10.5281/zenodo.3754448***

▸ NORMAN Suspect List Exchange

## 8.4 WHO Essential Medicines

| Drug | Drug Classes | Formulation | Indication |
|---|---|---|---|
| Lidocaine | Antiarrhythmic medicines | Parenteral - General injections - IV: 20 mg per mL in 5 mL ampoule (hydrochloride) | Ventricular tachyarrhythmia |
| Lidocaine | Local anaesthetics | (1) Parenteral - Locoregional injections - Spinal anaesthesia: 5% in 2 mL ampoule (hydrochloride) + 7.5% glucose solution; (2) Parenteral - Locoregional injections - Other: 1% in vial (hydrochloride); 2% in vial (hydrochloride); (3) Local - Topical - unspecified: 2 to 4% (hydrochloride) | Local anaesthetics |

▸ WHO Model Lists of Essential Medicines

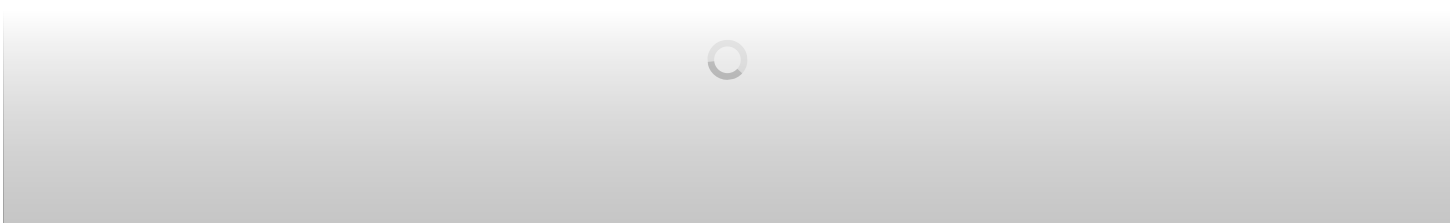
## 8.5 FDA Approved Drugs

▸ Drugs@FDA

## 8.6 FDA Orange Book

▸ FDA Orange Book

## 8.7 FDA National Drug Code Directory



▸ National Drug Code (NDC) Directory

▸ National Drug Code (NDC) Directory

## 8.8 FDA Green Book

▸ FDA Approved Animal Drug Products (Green Book)

## 8.9 Drug Labels

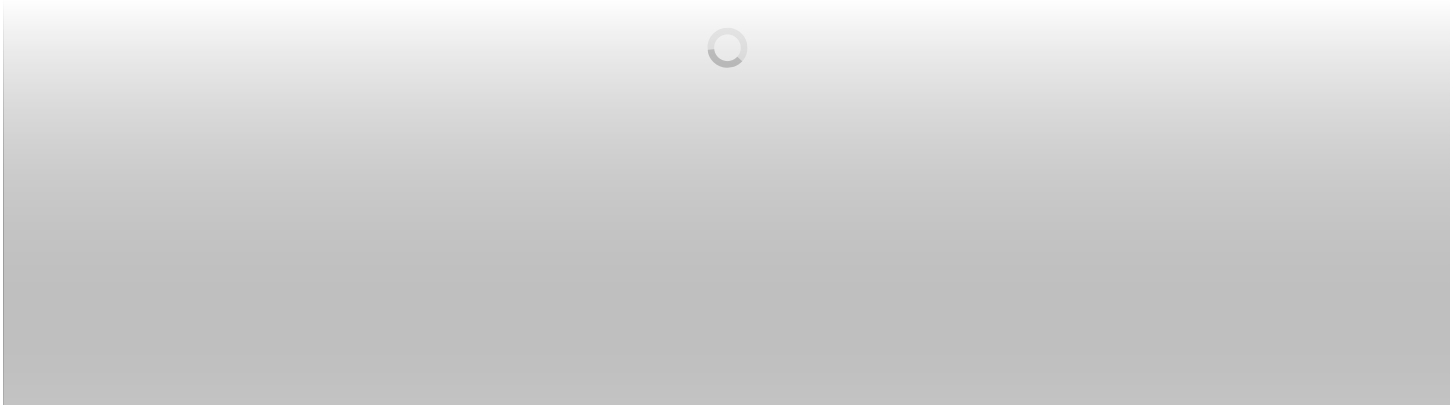
### Drug and label

DailyMed

### Active ingredient and drug

DailyMed

### Drug and label



DailyMed

## 8.10 Clinical Trials

### 8.10.1 ClinicalTrials.gov

ClinicalTrials.gov

### 8.10.2 EU Clinical Trials Register

EU Clinical Trials Register

### 8.10.3 NIPH Clinical Trials Search of Japan

NIPH Clinical Trials Search of Japan

## 8.11 Therapeutic Uses

Anesthetics, Local; Anti-Arrhythmia Agents; Voltage-Gated Sodium Channel Blockers

*National Library of Medicine's Medical Subject Headings. Lidocaine. Online file (MeSH, 2014). Available from, as of August 28, 2014: https://www.nlm.nih.gov/mesh/2014/mesh_browser/MBrowser.html*

Hazardous Substances Data Bank (HSDB)

Lidocaine hydrochloride is used for infiltration anesthesia and for nerve block techniques including peripheral, sympathetic, epidural (including caudal), and spinal block anesthesia. /Included in US product label/

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 3340*

Hazardous Substances Data Bank (HSDB)

Lidocaine has been administered intraperitoneally for anesthesia of the peritoneum and pelvic viscera. /NOT included in US product label/

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 3340*

Hazardous Substances Data Bank (HSDB)

Lidocaine is considered an alternative antiarrhythmic agent to amiodarone in the treatment of cardiac arrest secondary to ventricular fibrillation or pulseless ventricular tachycardia resistant to cardiopulmonary resuscitation (CPR), electrical cardioversion (e.g., after 2 to 3 shocks) and a vasopressor (epinephrine, vasopressin). /Included in US product label/

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 1694*

▸ Hazardous Substances Data Bank (HSDB)

For more Therapeutic Uses (Complete) data for LIDOCAINE (21 total), please visit the HSDB record page.

▸ Hazardous Substances Data Bank (HSDB)

## 8.12 Drug Warnings

WARNING: Life-threatening and fatal events in infants and young children. Postmarketing cases of seizures, cardiopulmonary arrest, and death in patients under the age of 3 years have been reported with use of Xylocaine 2% Viscous Solution when it was not administered in strict adherence to the dosing and administration recommendations. In the setting of teething pain, Xylocaine 2% Viscous Solution should generally not be used. For other conditions, the use of the product in patients less than 3 years of age should be limited to those situations where safer alternatives are not available or have been tried but failed. To decrease the risk of serious adverse events with use of Xylocaine 2% Viscous Solution, instruct caregivers to strictly adhere to the prescribed dose and frequency of administration and store the prescription bottle safely out of reach of children.

*FDA; Prescribing Information for 2% Xylocaine Viscous (Lidocaine Hydrochloride) Solution (September 2014). Available from, as of November 2014:* ***https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/009470s025lbl.pdf***

▸ Hazardous Substances Data Bank (HSDB)

Life-threatening adverse effects (e.g., irregular heart beat, seizures, breathing difficulties, coma, death) may occur when topical anesthetics are applied to a large area of skin, when the area of application is covered with an occlusive dressing, if a large amount of topical anesthetic is applied, if the anesthetic is applied to irritated or broken skin, or if the skin temperature increases (from exercise or use of a heating pad).101 102 When applied in such a manner, the amount of anesthetic that is absorbed systemically is unpredictable and the plasma concentrations achieved may be high enough to cause life-threatening adverse effects.

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 3341-2*

▸ Hazardous Substances Data Bank (HSDB)

The Food and Drug Administration (FDA) has reviewed 35 reports of chondrolysis (necrosis and destruction of cartilage) in patients given continuous intra-articular infusions of local anesthetics with elastomeric infusion devices to control post-surgical pain. The significance of this injury to otherwise healthy young adults warrants notification to health care professionals. The local anesthetics (with and without epinephrine) were infused for extended periods of time (48 to 72 hours) directly into the intra-articular space using an elastomeric pump. Chondrolysis was diagnosed within a median of 8.5 months after the infusion. Almost all of the reported cases of chondrolysis (97%) occurred following shoulder surgeries. Joint pain, stiffness, and loss of motion were reported as early as the second month after receiving the infusion. In more than half of these reports, the patients required additional surgery, including arthroscopy or arthroplasty (joint replacement). It is not known which specific factor or combination of factors contributed to the development of chondrolysis in these cases. The infused local anesthetic drugs, the device materials, and/or other sources may have resulted in the

development of chondrolysis. It is important to note that single intra-articular injections of local anesthetics in orthopedic procedures have been used for many years without any reported occurrence of chondrolysis. Local anesthetics are approved as injections for the production of local or regional anesthesia or analgesia. Neither local anesthetics nor infusion devices are approved for an indication of continuous intra-articular infusion.

*FDA; Information for Healthcare Professionals: Chondrolysis Reported with Continuously Infused Local Anesthetics (Marketed as Bupivacaine, Chlorprocaine, Lidocaine, Mepivacaine, Procaine and Ropivacaine) (February 16, 2010). Available from, as of November 24, 2014:* ***https://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm190302.htm***

▸ **Hazardous Substances Data Bank (HSDB)**

Local anesthetics should only be administered by clinicians who are experienced in the diagnosis and management of dose-related toxicities and other acute emergencies associated with these agents. Resuscitative equipment, **oxygen**, drugs, and personnel required for treatment of adverse reactions should be immediately available when lidocaine is administered. Proper positioning of the patient is extremely important in spinal anesthesia.

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 3341*

▸ **Hazardous Substances Data Bank (HSDB)**

For more Drug Warnings (Complete) data for LIDOCAINE (31 total), please visit the **HSDB record page**.

▸ **Hazardous Substances Data Bank (HSDB)**

## 8.13 Reported Fatal Dose

Two fatal cases of deliberate self poisoning with lignocaine are reported, one by oral ingestion and one by iv injection. Post-mortem blood lignocaine concn were 40 and 53 mg/L, respectively.

***PMID:2680899***

*Dawling S et al; Hum Toxicol 8 (5): 389-92 (1989)*

▸ **Hazardous Substances Data Bank (HSDB)**

Topical application of 25 g of lidocaine base twice daily led to death from cardiorespiratory arrest.

*Ellenhorn, M.J., S. Schonwald, G. Ordog, J. Wasserberger. Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. 2nd ed. Baltimore, MD: Williams and Wilkins, 1997., p. 1199*

▸ **Hazardous Substances Data Bank (HSDB)**

# 9 Pharmacology and Biochemistry

## 9.1 Pharmacodynamics

Excessive blood levels of lidocaine can cause changes in cardiac output, total peripheral resistance, and mean arterial pressure. With central neural blockade these changes may be attributable to the

block of autonomic fibers, a direct depressant effect of the local anesthetic agent on various components of the cardiovascular system, and/or the beta-adrenergic receptor stimulating action of epinephrine when present. The net effect is normally a modest hypotension when the recommended dosages are not exceeded. In particular, such cardiac effects are likely associated with the principal effect that lidocaine elicits when it binds and blocks sodium channels, inhibiting the ionic fluxes required for the initiation and conduction of electrical action potential impulses necessary to facilitate muscle contraction. Subsequently, in cardiac myocytes, lidocaine can potentially block or otherwise slow the rise of cardiac action potentials and their associated cardiac myocyte contractions, resulting in possible effects like hypotension, bradycardia, myocardial depression, cardiac arrhythmias, and perhaps cardiac arrest or circulatory collapse. Moreover, lidocaine possesses a dissociation constant (pKa) of 7.7 and is considered a weak base. As a result, about 25% of lidocaine molecules will be un-ionized and available at the physiological pH of 7.4 to translocate inside nerve cells, which means lidocaine elicits an onset of action more rapidly than other local anesthetics that have higher pKa values. This rapid onset of action is demonstrated in about one minute following intravenous injection and fifteen minutes following intramuscular injection. The administered lidocaine subsequently spreads rapidly through the surrounding tissues and the anesthetic effect lasts approximately ten to twenty minutes when given intravenously and about sixty to ninety minutes after intramuscular injection. Nevertheless, it appears that the efficacy of lidocaine may be minimized in the presence of inflammation. This effect could be due to acidosis decreasing the amount of un-ionized lidocaine molecules, a more rapid reduction in lidocaine concentration as a result of increased blood flow, or potentially also because of increased production of inflammatory mediators like peroxynitrite that elicit direct actions on sodium channels.

▸ DrugBank

## 9.2 MeSH Pharmacological Classification

### Voltage-Gated Sodium Channel Blockers

A class of drugs that inhibit the activation of VOLTAGE-GATED SODIUM CHANNELS. (See all compounds classified as Voltage-Gated Sodium Channel Blockers.)

▸ Medical Subject Headings (MeSH)

### Anti-Arrhythmia Agents

Agents used for the treatment or prevention of cardiac arrhythmias. They may affect the polarization-repolarization phase of the action potential, its excitability or refractoriness, or impulse conduction or membrane responsiveness within cardiac fibers. Anti-arrhythmia agents are often classed into four main groups according to their mechanism of action: sodium channel blockade, beta-adrenergic blockade, repolarization prolongation, or calcium channel blockade. (See all compounds classified as Anti-Arrhythmia Agents.)

▸ Medical Subject Headings (MeSH)

### Anesthetics, Local

Drugs that block nerve conduction when applied locally to nerve tissue in appropriate concentrations. They act on any part of the nervous system and on every type of nerve fiber. In contact with a nerve

trunk, these anesthetics can cause both sensory and motor paralysis in the innervated area. Their action is completely reversible. (From Gilman AG, et. al., Goodman and Gilman's The Pharmacological Basis of Therapeutics, 8th ed) Nearly all local anesthetics act by reducing the tendency of voltage-dependent sodium channels to activate. (See all compounds classified as Anesthetics, Local.)

▸ Medical Subject Headings (MeSH)

## 9.3 FDA Pharmacological Classification

| 1 of 29 | |
|---|---|
| **FDA UNII** | 98PI200987 |
| **Active Moiety** | LIDOCAINE |
| **Pharmacological Classes** | Established Pharmacologic Class [EPC] - Amide Local Anesthetic |
| **Pharmacological Classes** | Chemical Structure [CS] - Amides |
| **Pharmacological Classes** | Established Pharmacologic Class [EPC] - Antiarrhythmic |
| **Pharmacological Classes** | Physiologic Effects [PE] - Local Anesthesia |
| **FDA Pharmacology Summary** | Lidocaine is an Amide Local Anesthetic and Antiarrhythmic. The physiologic effect of lidocaine is by means of Local Anesthesia. |

▸ FDA Pharm Classes

| 2 of 29 | |
|---|---|
| **Non-Proprietary Name** | 4% LIDOCAINE |
| **Pharmacological Classes** | Amides [CS]; Local Anesthesia [PE]; Antiarrhythmic [EPC]; Amide Local Anesthetic [EPC] |

▸ National Drug Code (NDC) Directory

| 3 of 29 | |
|---|---|
| **Non-Proprietary Name** | 5% LIDOCAINE |
| **Pharmacological Classes** | Antiarrhythmic [EPC]; Amide Local Anesthetic [EPC]; Amides [CS]; Local Anesthesia [PE] |

▸ National Drug Code (NDC) Directory

| 4 of 29 | |
|---|---|
| **Non-Proprietary Name** | BURN RELIEF SPRAY |
| **Pharmacological Classes** | Antiarrhythmic [EPC]; Amide Local Anesthetic [EPC]; Amides [CS]; Local Anesthesia [PE] |

▸ National Drug Code (NDC) Directory

| 5 of 29 | |
|---|---|
| **Non-Proprietary Name** | LIDICAINE |
| **Pharmacological Classes** | Local Anesthesia [PE]; Amides [CS]; Amide Local Anesthetic [EPC]; Antiarrhythmic [EPC] |

▸ National Drug Code (NDC) Directory

| 6 of 29 | |
|---|---|
| **Non-Proprietary Name** | LIDOCAIN 5% |
| **Pharmacological Classes** | Amides [CS]; Local Anesthesia [PE]; Antiarrhythmic [EPC]; Amide Local Anesthetic [EPC] |

▸ National Drug Code (NDC) Directory

| 7 of 29 | |
|---|---|
| **Non-Proprietary Name** | LIDOCAINE |
| **Pharmacological Classes** | Amides [CS]; Local Anesthesia [PE]; Antiarrhythmic [EPC]; Amide Local Anesthetic [EPC] |

▸ National Drug Code (NDC) Directory

| 8 of 29 | |
|---|---|
| **Non-Proprietary Name** | LIDOCAINE 0.5% |
| **Pharmacological Classes** | Local Anesthesia [PE]; Amides [CS]; Amide Local Anesthetic [EPC]; Antiarrhythmic [EPC] |

▸ National Drug Code (NDC) Directory

| 9 of 29 | |
|---|---|
| **Non-Proprietary Name** | LIDOCAINE 3 PERCENT |
| **Pharmacological Classes** | Local Anesthesia [PE]; Amides [CS]; Amide Local Anesthetic [EPC]; Antiarrhythmic [EPC] |

▸ National Drug Code (NDC) Directory

| 10 of 29 | |
|---|---|
| **Non-Proprietary Name** | LIDOCAINE 4% CREAM |

| | |
|---|---|
| **Pharmacological Classes** | Antiarrhythmic [EPC]; Amide Local Anesthetic [EPC]; Amides [CS]; Local Anesthesia [PE] |

▸ National Drug Code (NDC) Directory

| 11 of 29 | |
|---|---|
| **Non-Proprietary Name** | LIDOCAINE 4% FABRIC TAPE |
| **Pharmacological Classes** | Amides [CS]; Local Anesthesia [PE]; Antiarrhythmic [EPC]; Amide Local Anesthetic [EPC] |

▸ National Drug Code (NDC) Directory

| 12 of 29 | |
|---|---|
| **Non-Proprietary Name** | LIDOCAINE 4% GEL PATCH |
| **Pharmacological Classes** | Amide Local Anesthetic [EPC]; Antiarrhythmic [EPC]; Local Anesthesia [PE]; Amides [CS] |

▸ National Drug Code (NDC) Directory

| 13 of 29 | |
|---|---|
| **Non-Proprietary Name** | LIDOCAINE 5% |
| **Pharmacological Classes** | Amide Local Anesthetic [EPC]; Antiarrhythmic [EPC]; Local Anesthesia [PE]; Amides [CS] |

▸ National Drug Code (NDC) Directory

| 14 of 29 | |
|---|---|
| **Non-Proprietary Name** | LIDOCAINE 5% ANORECTAL |
| **Pharmacological Classes** | Amides [CS]; Local Anesthesia [PE]; Antiarrhythmic [EPC]; Amide Local Anesthetic [EPC] |

▸ National Drug Code (NDC) Directory

| 15 of 29 | |
|---|---|
| **Non-Proprietary Name** | LIDOCAINE 5% TOPICAL ANORECTAL CREAM |
| **Pharmacological Classes** | Antiarrhythmic [EPC]; Amide Local Anesthetic [EPC]; Amides [CS]; Local Anesthesia [PE] |

▸ National Drug Code (NDC) Directory

| 16 of 29 |
|---|

| | |
|---|---|
| **Non-Proprietary Name** | LIDOCAINE GEL PATCH |
| **Pharmacological Classes** | Amides [CS]; Local Anesthesia [PE]; Antiarrhythmic [EPC]; Amide Local Anesthetic [EPC] |

▸ National Drug Code (NDC) Directory

| 17 of 29 | |
|---|---|
| **Non-Proprietary Name** | LIDOCAINE LOTION |
| **Pharmacological Classes** | Local Anesthesia [PE]; Amides [CS]; Amide Local Anesthetic [EPC]; Antiarrhythmic [EPC] |

▸ National Drug Code (NDC) Directory

| 18 of 29 | |
|---|---|
| **Non-Proprietary Name** | LIDOCAINE PAIN RELIEF |
| **Pharmacological Classes** | Antiarrhythmic [EPC]; Amide Local Anesthetic [EPC]; Amides [CS]; Local Anesthesia [PE] |

▸ National Drug Code (NDC) Directory

| 19 of 29 | |
|---|---|
| **Non-Proprietary Name** | LIDOCAINE PATCH 5% |
| **Pharmacological Classes** | Antiarrhythmic [EPC]; Amide Local Anesthetic [EPC]; Amides [CS]; Local Anesthesia [PE] |

▸ National Drug Code (NDC) Directory

| 20 of 29 | |
|---|---|
| **Non-Proprietary Name** | LIDOCAINE SPRAY |
| **Pharmacological Classes** | Amide Local Anesthetic [EPC]; Antiarrhythmic [EPC]; Local Anesthesia [PE]; Amides [CS] |

▸ National Drug Code (NDC) Directory

| 21 of 29 | |
|---|---|
| **Non-Proprietary Name** | LIDOCAINE, 0.5% |
| **Pharmacological Classes** | Local Anesthesia [PE]; Amides [CS]; Amide Local Anesthetic [EPC]; Antiarrhythmic [EPC] |

▸ National Drug Code (NDC) Directory

| 22 of 29 | |
|---|---|
| **Non-Proprietary Name** | LIDOCANE |
| **Pharmacological Classes** | Antiarrhythmic [EPC]; Amide Local Anesthetic [EPC]; Amides [CS]; Local Anesthesia [PE] |

▸ National Drug Code (NDC) Directory

| 23 of 29 | |
|---|---|
| **Non-Proprietary Name** | MAXIMUM STRENGTH PAIN RELIEVER |
| **Pharmacological Classes** | Antiarrhythmic [EPC]; Amide Local Anesthetic [EPC]; Amides [CS]; Local Anesthesia [PE] |

▸ National Drug Code (NDC) Directory

| 24 of 29 | |
|---|---|
| **Non-Proprietary Name** | TATTOO NUMBING CREAM |
| **Pharmacological Classes** | Local Anesthesia [PE]; Amides [CS]; Amide Local Anesthetic [EPC]; Antiarrhythmic [EPC] |

▸ National Drug Code (NDC) Directory

| 25 of 29 | |
|---|---|
| **Non-Proprietary Name** | XYLOCAINE |
| **Pharmacological Classes** | Antiarrhythmic [EPC]; Amide Local Anesthetic [EPC]; Amides [CS]; Local Anesthesia [PE] |

▸ National Drug Code (NDC) Directory

| 26 of 29 | |
|---|---|
| **Non-Proprietary Name** | LIDOCAINE NUMBING CREAM |
| **Pharmacological Classes** | Local Anesthesia [PE]; Amides [CS]; Amide Local Anesthetic [EPC]; Antiarrhythmic [EPC] |

▸ National Drug Code (NDC) Directory

| 27 of 29 | |
|---|---|
| **Non-Proprietary Name** | LIDOCAINE 4% PATCH |
| **Pharmacological Classes** | Antiarrhythmic [EPC]; Amide Local Anesthetic [EPC]; Amides [CS]; Local Anesthesia [PE] |

▸ National Drug Code (NDC) Directory

| 28 of 29 | |
|---|---|
| **Non-Proprietary Name** | LIDOCAINE 5% CREAM |
| **Pharmacological Classes** | Antiarrhythmic [EPC]; Amide Local Anesthetic [EPC]; Amides [CS]; Local Anesthesia [PE] |

▸ National Drug Code (NDC) Directory

| 29 of 29 | |
|---|---|
| **Non-Proprietary Name** | LIDOCAINE PAIN RELIEF GEL-PATCH |
| **Pharmacological Classes** | Antiarrhythmic [EPC]; Amide Local Anesthetic [EPC]; Amides [CS]; Local Anesthesia [PE] |

▸ National Drug Code (NDC) Directory

## 9.4 ATC Code

N01BB02

*S76 | LUXPHARMA | Pharmaceuticals Marketed in Luxembourg | Pharmaceuticals marketed in Luxembourg, as published by d'Gesondheetskeess (CNS, la caisse nationale de sante, www.cns.lu), mapped by name to structures using CompTox by R. Singh et al. (in prep.). List downloaded from **https://cns.public.lu/en/legislations/textes-coordonnes/liste-med-comm.html**. Dataset **DOI:10.5281/zenodo.4587355***

*S66 | EAWAGTPS | Parent-Transformation Product Pairs from Eawag | **DOI:10.5281/zenodo.3754448***

▸ NORMAN Suspect List Exchange

S - Sensory organs
S02 - Otologicals
S02D - Other otologicals
S02DA - Analgesics and anesthetics
S02DA01 - Lidocaine

▸ WHO Anatomical Therapeutic Chemical (ATC) Classification

R - Respiratory system
R02 - Throat preparations
R02A - Throat preparations
R02AD - Anesthetics, local
R02AD02 - Lidocaine

▸ WHO Anatomical Therapeutic Chemical (ATC) Classification

C - Cardiovascular system

C01 - Cardiac therapy

C01B - Antiarrhythmics, class i and iii

C01BB - Antiarrhythmics, class ib

C01BB01 - Lidocaine

▸ WHO Anatomical Therapeutic Chemical (ATC) Classification

C - Cardiovascular system

C05 - Vasoprotectives

C05A - Agents for treatment of hemorrhoids and anal fissures for topical use

C05AD - Local anesthetics

C05AD01 - Lidocaine

▸ WHO Anatomical Therapeutic Chemical (ATC) Classification

N - Nervous system

N01 - Anesthetics

N01B - Anesthetics, local

N01BB - Amides

N01BB02 - Lidocaine

▸ WHO Anatomical Therapeutic Chemical (ATC) Classification

S - Sensory organs

S01 - Ophthalmologicals

S01H - Local anesthetics

S01HA - Local anesthetics

S01HA07 - Lidocaine

▸ WHO Anatomical Therapeutic Chemical (ATC) Classification

D - Dermatologicals

D04 - Antipruritics, incl. antihistamines, anesthetics, etc.

D04A - Antipruritics, incl. antihistamines, anesthetics, etc.

D04AB - Anesthetics for topical use

D04AB01 - Lidocaine

▸ WHO Anatomical Therapeutic Chemical (ATC) Classification

N01BB02; C01BB01

▸ WHO Model Lists of Essential Medicines

## 9.5 Absorption, Distribution and Excretion

**Absorption**

In general, lidocaine is readily absorbed across mucous membranes and damaged skin but poorly through intact skin. The agent is quickly absorbed from the upper airway, tracheobronchial tree, and alveoli into the bloodstream. And although lidocaine is also well absorbed across the gastrointestinal tract the oral bioavailability is only about 35% as a result of a high degree of first-pass metabolism. After injection into tissues, lidocaine is also rapidly absorbed and the absorption rate is affected by both vascularity and the presence of tissue and fat capable of binding lidocaine in the particular tissues. The concentration of lidocaine in the blood is subsequently affected by a variety of aspects, including its rate of absorption from the site of injection, the rate of tissue distribution, and the rate of metabolism and excretion. Subsequently, the systemic absorption of lidocaine is determined by the site of injection, the dosage given, and its pharmacological profile. The maximum blood concentration occurs following intercostal nerve blockade followed in order of decreasing concentration, the lumbar epidural space, brachial plexus site, and subcutaneous tissue. The total dose injected regardless of the site is the primary determinant of the absorption rate and blood levels achieved. There is a linear relationship between the amount of lidocaine injected and the resultant peak anesthetic blood levels. Nevertheless, it has been observed that **lidocaine hydrochloride** is completely absorbed following parenteral administration, its rate of absorption depending also on lipid solubility and the presence or absence of a vasoconstrictor agent. Except for intravascular administration, the highest blood levels are obtained following intercostal nerve block and the lowest after subcutaneous administration. Additionally, lidocaine crosses the blood-brain and placental barriers, presumably by passive diffusion.

▸ DrugBank

### Route of Elimination

The excretion of unchanged lidocaine and its metabolites occurs predominantly via the kidney with less than 5% in the unchanged form appearing in the urine. The renal clearance is inversely related to its protein binding affinity and the pH of the urine. This suggests by the latter that excretion of lidocaine occurs by non-ionic diffusion.

▸ DrugBank

### Volume of Distribution

The volume of distribution determined for lidocaine is 0.7 to 1.5 L/kg. In particular, lidocaine is distributed throughout the total body **water**. Its rate of disappearance from the blood can be described by a two or possibly even three-compartment model. There is a rapid disappearance (alpha phase) which is believed to be related to uptake by rapidly equilibrating tissues (tissues with high vascular perfusion, for example). The slower phase is related to distribution to slowly equilibrating tissues (beta phase) and to its metabolism and excretion (gamma phase). Lidocaine's distribution is ultimately throughout all body tissues. In general, the more highly perfused organs will show higher concentrations of the agent. The highest percentage of this drug will be found in skeletal muscle, mainly due to the mass of muscle rather than an affinity.

▸ DrugBank

### Clearance

The mean systemic clearance observed for intravenously administered lidocaine in a study of 15 adults was approximately 0.64 +/- 0.18 L/min.

▸ DrugBank

Binding of lidocaine to plasma proteins is variable and concentration dependent. At concentrations of 1-4 ug/mL, the drug is approximately 60-80% bound to plasma proteins. Lidocaine is partially bound to a1-acid glycoprotein (a1-AGP), and the extent of binding to a1-AGP depends on the plasma concentration of the protein. In patients with myocardial infarction, increases in plasma a1-AGP concentration are associated with increased lidocaine binding and increased total plasma concentrations of the drug, but only small increases in plasma concentration of free drug; these changes in a1-AGP concentration and lidocaine binding are believed to account in part for accumulation of the drug observed in patients with myocardial infarction receiving prolonged infusions.

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 1697*

▸ Hazardous Substances Data Bank (HSDB)

The volume of distribution is decreased in patients with congestive heart failure and increased in patients with liver disease.

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 1697*

▸ Hazardous Substances Data Bank (HSDB)

Lidocaine is widely distributed into body tissues. After an IV bolus, there is an early, rapid decline in plasma concentrations of the drug, principally associated with distribution into highly perfused tissues such as the kidneys, lungs, liver, and heart, followed by a slower elimination phase in which metabolism and redistribution into skeletal muscle and adipose tissue occur. Lidocaine has a high affinity for fat and adipose tissue. As plasma concentrations of the drug fall, the diffusion gradient from tissue to blood increases and the lidocaine that initially entered the highly perfused tissues and fat diffuses back into the blood.

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 1697*

▸ Hazardous Substances Data Bank (HSDB)

Plasma lidocaine concentrations of approximately 1-5 ug/mL are required to suppress ventricular arrhythmias. Toxicity has been associated with plasma lidocaine concentrations greater than 5 ug/mL. Following IV administration of a bolus dose of 50-100 mg of **lidocaine hydrochloride**, the drug has an onset of action within 45-90 seconds and a duration of action of 10-20 minutes. If an IV infusion is begun without an initial bolus dose, the attainment of therapeutic plasma concentrations is relatively slow. For example, therapeutic plasma concentrations are achieved in 30-60 minutes after the start of a continuous infusion of 60-70 ug/kg per minute when no loading dose is given. Plasma concentrations of 1.5-5.5 ug/mL have been reported to be maintained with an initial IV bolus of 1.5 mg/kg followed by infusion of 50 ug/kg per minute in patients with heart disease.

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 1697*

▸ Hazardous Substances Data Bank (HSDB)

For more Absorption, Distribution and Excretion (Complete) data for LIDOCAINE (17 total), please visit the **HSDB record page**.

▸ Hazardous Substances Data Bank (HSDB)

## 9.6 Metabolism / Metabolites

Lidocaine is metabolized predominantly and rapidly by the liver, and metabolites and unchanged drug are excreted by the kidneys. Biotransformation includes oxidative N-dealkylation, ring hydroxylation, cleavage of the amide linkage, and conjugation. N-dealkylation, a major pathway of biotransformation, yields the metabolites **monoethylglycinexylidide** and **glycinexylidide**. The pharmacological/toxicological actions of these metabolites are similar to, but less potent than, those of **lidocaine HCl**. Approximately 90% of **lidocaine HCl** administered is excreted in the form of various metabolites, and less than 10% is excreted unchanged. The primary metabolite in urine is a conjugate of **4-hydroxy-2,6-dimethylaniline**.

▸ DrugBank

Approximately 90% of a parenteral dose of lidocaine is rapidly metabolized in the liver by de-ethylation to form **MEGX** and GX followed by cleavage of the amide bond to form **xylidine** and 4-hydroxyxylidine which are excreted in urine. Less than 10% of a dose is excreted unchanged in urine.

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 1697*

▸ Hazardous Substances Data Bank (HSDB)

The rate of lidocaine metabolism may also be decreased in patients with liver disease, possibly because of altered perfusion in the liver or hepatic tissue necrosis. Distribution and elimination of lidocaine and /**monoethylglycinexylidide**/ **MEGX** appear to remain normal in patients with renal failure, but /**glycinexylidide**/ GX may accumulate in these patients when lidocaine is administered IV for several days.

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 1697*

▸ Hazardous Substances Data Bank (HSDB)

... The purpose of this study is to determine the amount of lidocaine and its metabolite **monoethyl-glycinexylidide** (**MEGX**) in breast milk after local anesthesia during dental procedures. The study population consisted of seven nursing mothers (age, 23-39 years) who received 3.6 to 7.2 mL 2% lidocaine without **adrenaline**. Blood and milk concentrations of lidocaine and its metabolite **MEGX** were assayed using high-performance liquid chromatography. The milk-to-plasma ratio and the possible daily doses in infants for both lidocaine and **MEGX** were calculated. The lidocaine concentration in maternal plasma 2 hours after injection was 347.6 +/- 221.8 ug/L, the lidocaine concentration in maternal milk ranged from 120.5 +/- 54.1 ug/L (3 hours after injection) to 58.3 +/- 22.8 ug/L (6 hours after injection), the **MEGX** concentration in maternal plasma 2 hours after injection was 58.9 +/- 30.3 ug/L, and the **MEGX** concentration in maternal milk ranged from 97.5 +/- 39.6 ug/L (3 hours after injection) to 52.7 +/- 23.8 ug/L (6 hours after injection). According to these data and considering an intake of 90 mL breast milk every 3 hours, the daily infant dosages of lidocaine and **MEGX** were 73.41 +/- 38.94 ug/L/day and 66.1 +/- 28.5 ug/L/day respectively. This study suggests that even if a nursing mother undergoes dental treatment with local anesthesia using lidocaine without **adrenaline**, she can safely continue breastfeeding.

*PMID:11321382*

*Giuliani M et al; J Pediatr Gastroenterol Nutr. 32(2):142-4. (2001).*

▸ Hazardous Substances Data Bank (HSDB)

... To determine the time/concentration profile of lidocaine and its active metabolites glycinexylidide (GX) and monoethylglycinexylidide (MEGX) during a 96 hr lidocaine infusion. lidocaine was administered to 8 mature healthy horses as a continuous rate infusion (0.05 mg/kg bwt/min) for 96 hr. Blood concentrations of lidocaine, GX and MEGX were determined using high performance liquid chromatography during and after discontinuation of the infusion. Serum lidocaine concentrations reached steady state by 3 hr and did not accumulate thereafter. Concentrations were above the target therapeutic concentration (980 ng/mL) only at 6 and 48 hr, and did not reach the range described as potentially causing toxicity (>1850 ng/mL) at any time. MEGX did not accumulate over time, while the GX accumulated significantly up to 48 hr and then remained constant. The serum concentrations of lidocaine, MEGX and GX were below the limit of detection within 24 hr of discontinuation of the infusion. None of the horses developed any signs of lidocaine toxicity during the study. The metabolism of lidocaine was not significantly impaired by prolonged infusion and no adverse effects were observed. Prolonged infusions appear to be safe in normal horses but the accumulation of GX, a potentially toxic active metabolite, is cause for concern.

***PMID:18267881***

*Dickey EJ et al; Equine Vet J 40 (4): 348-52 (2008)*

▸ Hazardous Substances Data Bank (HSDB)

For more Metabolism/Metabolites (Complete) data for LIDOCAINE (11 total), please visit the HSDB record page.

▸ Hazardous Substances Data Bank (HSDB)

Lidocaine has known human metabolites that include 3-Hydroxylidocaine and Monoethylglycinexylidide.

*S73 | METXBIODB | Metabolite Reaction Database from BioTransformer | **DOI:10.5281/zenodo.4056560***

▸ NORMAN Suspect List Exchange

Primarily hepatic. Route of Elimination: Lidocaine and its metabolites are excreted by the kidneys. Half Life: 109 minutes

▸ Toxin and Toxin Target Database (T3DB)

## 9.7 Biological Half-Life

The elimination half-life of lidocaine hydrochloride following an intravenous bolus injection is typically 1.5 to 2.0 hours. Because of the rapid rate at which lidocaine hydrochloride is metabolized, any condition that affects liver function may alter lidocaine HCl kinetics. The half-life may be prolonged two-fold or more in patients with liver dysfunction.

▸ DrugBank

... In 30 patients (aged 18-70 yr) undergoing surgery ... mean half-life ... lidocaine was ... 94 min.

*Sanchez Alcaraz A et al; Farmacia Hosp 15 (Jul-Aug): 211-5 (1991)*

▸ **Hazardous Substances Data Bank (HSDB)**

... In patients with myocardial infarction (with or without cardiac failure), the half-lives of lidocaine and **MEGX** have been reported to be prolonged; the half-life of GX is reportedly prolonged in patients with cardiac failure secondary to myocardial infarction. The half-life of lidocaine is reportedly also prolonged in patients with congestive heart failure or liver disease and may be prolonged following continuous IV infusions lasting longer than 24 hours.

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 1697*

▸ **Hazardous Substances Data Bank (HSDB)**

Lidocaine has an initial half-life of 7-30 minutes and a terminal half-life of 1.5-2 hours. In healthy individuals, the elimination half-lives of the active metabolites, **monoethylglycinexylidide** (**MEGX**) and **glycinexylidide** (GX) are 2 hours and 10 hours, respectively...

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 1697*

▸ **Hazardous Substances Data Bank (HSDB)**

Lidocaine is extensively metabolized by the liver; heaptic disease and reduced hepatic blood flow prolong the half life, which is normally < 1 hr in dogs.

*National Fire Protection Association; Fire Protection Guide to Hazardous Materials. 14TH Edition, Quincy, MA 2010, p. 2162*

▸ **Hazardous Substances Data Bank (HSDB)**

The elimination half-life of lidocaine in the newborn following maternal epidual anesthesia averaged 3 hr.

*Briggs, G.G., Freeman, R.K., Yaffee, S.J.; Drugs in Pregancy and Lactation Nineth Edition. Wolters Kluwer/Lippincott Williams & Wilkins, Philadelphia, PA. 2011, p. 832*

▸ **Hazardous Substances Data Bank (HSDB)**

## 9.8 Mechanism of Action

Lidocaine is a local anesthetic of the amide type. It is used to provide local anesthesia by nerve blockade at various sites in the body. It does so by stabilizing the neuronal membrane by inhibiting the ionic fluxes required for the initiation and conduction of impulses, thereby effecting local anesthetic action. In particular, the lidocaine agent acts on **sodium ion** channels located on the internal surface of nerve cell membranes. At these channels, neutral uncharged lidocaine molecules diffuse through neural sheaths into the axoplasm where they are subsequently ionized by joining with **hydrogen** ions. The resultant lidocaine cations are then capable of reversibly binding the **sodium** channels from the inside, keeping them locked in an open state that prevents nerve depolarization. As a result, with sufficient blockage, the membrane of the postsynaptic neuron will ultimately not depolarize and will thus fail to transmit an action potential. This facilitates an anesthetic effect by not merely preventing pain signals from propagating to the brain but by aborting their generation in the

first place. In addition to blocking conduction in nerve axons in the peripheral nervous system, lidocaine has important effects on the central nervous system and cardiovascular system. After absorption, lidocaine may cause stimulation of the CNS followed by depression and in the cardiovascular system, it acts primarily on the myocardium where it may produce decreases in electrical excitability, conduction rate, and force of contraction.

▸ DrugBank

Abnormal, repetitive impulse firing arising from incomplete inactivation of Na+ channels may be involved in several diseases of muscle and nerve, including familial myotonias and neuropathic pain syndromes. Systemic local anesthetics have been shown to have clinical efficacy against myotonias and some forms of neuropathic pain, so we sought to develop an in vitro model to examine the cellular basis for these drugs' effects. In frog sciatic nerves, studied in vitro by the sucrose-gap method, peptide alpha-toxins from sea anemone (ATXII) or scorpion (LQIIa) venom, which inhibit Na+ channel inactivation, induced repetitively firing compound action potentials (CAPs) superimposed on a plateau depolarization lasting several seconds. The initial spike of the CAP was unaffected, but the plateau and repetitive firing were strongly suppressed by 5-30 uM lidocaine. Lidocaine caused a rapid, concentration-dependent decay of the plateau, quantitatively consistent with blockade of open Na(+) channels. Early and late repetitive firing were equally suppressed by lidocaine with IC50 = 10 uM. After washout of lidocaine and LQIIa, the plateau and repetitive firing remained for > 1 hr, showing that lidocaine had not caused dissociation of channel-bound alpha-toxin. These findings indicate that therapeutic concentrations of lidocaine can reverse the "abnormal" features of action potentials caused by non-inactivating Na+ channels without affecting the normal spike component.

*PMID:11317273*

*Khodorova A et al; Muscle Nerve 24 (5): 634-47 (2001)*

▸ Hazardous Substances Data Bank (HSDB)

Lidocaine controls ventricular arrhythmias by suppressing automaticity in the His-Purkinje system and by suppressing spontaneous depolarization of the ventricles during diastole. These effects occur at lidocaine concentrations that do not suppress automaticity of the sinoatrial (SA) node. At therapeutic plasma concentrations, lidocaine has little effect on atrioventricular (AV) node conduction and His-Purkinje conduction in the normal heart. Specialized conducting tissues of the atria are less sensitive to the effects of lidocaine than are those of ventricular tissues. Lidocaine has a variable effect on the effective refractory period (ERP) of the AV node; the drug shortens the ERP and the action potential duration of the His-Purkinje system. Lidocaine does not appear to affect excitability of normal cardiac tissue.

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 1697*

▸ Hazardous Substances Data Bank (HSDB)

Prilocaine and lidocaine are classified as amide-type local anesthetics for which serious adverse effects include methemoglobinemia. Although the hydrolyzed metabolites of prilocaine (o-toluidine) and lidocaine (2,6-xylidine) have been suspected to induce methemoglobinemia, the metabolic enzymes that are involved remain uncharacterized. In the present study, we aimed to identify the human enzymes that are responsible for prilocaine- and lidocaine-induced methemoglobinemia. Our experiments revealed that prilocaine was hydrolyzed by recombinant human carboxylesterase (CES)

1A and CES2, whereas lidocaine was hydrolyzed by only human CES1A. When the parent compounds (prilocaine and lidocaine) were incubated with human liver microsomes (HLM), methemoglobin (Met-Hb) formation was lower than when the hydrolyzed metabolites were incubated with HLM. In addition, Met-Hb formation when prilocaine and o-toluidine were incubated with HLM was higher than that when lidocaine and 2,6-xylidine were incubated with HLM. Incubation with diisopropyl fluorophosphate and bis-(4-nitrophenyl) phosphate, which are general inhibitors of CES, significantly decreased Met-Hb formation when prilocaine and lidocaine were incubated with HLM. An anti-CYP3A4 antibody further decreased the residual formation of Met-Hb. Met-Hb formation after the incubation of o-toluidine and 2,6-xylidine with HLM was only markedly decreased by incubation with an anti-CYP2E1 antibody. o-Toluidine and 2,6-xylidine were further metabolized by CYP2E1 to 4- and 6-hydroxy-o-toluidine and 4-hydroxy-2,6-xylidine, respectively, and these metabolites were shown to more efficiently induce Met-Hb formation than the parent compounds. Collectively, we found that the metabolites produced by human CES-, CYP2E1-, and CYP3A4-mediated metabolism were involved in prilocaine- and lidocaine-induced methemoglobinemia.

*PMID:23530020*

*Higuchi R et al; Drug Metab Dispos 41 (6): 1220-30 (2013)*

▸ Hazardous Substances Data Bank (HSDB)

Lidocaine acts primarily to inhibit sodium movement across cell membranes. In peripheral nerves, this action results in a decreased rate and degree of depolarization of nerve cells and failure to achieve the threshold potential necessary to propagate action potentials, resulting in conduction blockade and anesthesia. In the heart, lidocaine also inhibits sodium conductance, decreasing the maximal rate of depolarization of myocardial conducting cells. This effect is more prominent in cells that are ischemic and at rapid heart rates. For this reason lidocaine is most effective in the termination of rapid ventricular tachycardia, especially during acute ischemia or after myocardial infarction. Lidocaine may also increase the ventricular fibrillation threshold. At therapeutic doses, lidocaine has minimal electrophysiologic effects on normal cells.

*Haddad, L.M., Clinical Management of Poisoning and Drug Overdose. 2nd ed. Philadelphia, PA: W.B. Saunders Co., 1990., p. 1372*

▸ Hazardous Substances Data Bank (HSDB)

## 9.9 Human Metabolite Information

### 9.9.1 Tissue Locations

Placenta

▸ Human Metabolome Database (HMDB)

### 9.9.2 Cellular Locations

Extracellular
Membrane

Human Metabolome Database (HMDB)

### 9.9.3 Metabolite Pathways

Lidocaine (Antiarrhythmic) Action Pathway
Lidocaine (Local Anaesthetic) Action Pathway
Lidocaine (Local Anaesthetic) Metabolism Pathway

Human Metabolome Database (HMDB)

## 9.10 Biochemical Reactions

PubChem

## 9.11 Transformations

▸ NORMAN Suspect List Exchange

# 10 Use and Manufacturing

## 10.1 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)

THERAPEUTIC CATEGORY (VETERINARY): Anesthetic (local)

*O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Cambridge, UK: Royal Society of Chemistry, 2013., p. 1019*

▸ Hazardous Substances Data Bank (HSDB)

MEDICATION

▸ Hazardous Substances Data Bank (HSDB)

MEDICATION (VET)

▸ Hazardous Substances Data Bank (HSDB)

Anesthetics, Local; Anti-Arrhythmia Agents; Voltage-Gated Sodium Channel Blockers

*National Library of Medicine's Medical Subject Headings. Lidocaine. Online file (MeSH, 2014). Available from, as of August 28, 2014:* ***https://www.nlm.nih.gov/mesh/2014/mesh_browser/MBrowser.html***

▸ Hazardous Substances Data Bank (HSDB)

For production of local or regional anesthesia by infiltration techniques such as percutaneous injection and intravenous regional anesthesia by peripheral nerve block techniques such as brachial plexus and

intercostal and by central neural techniques such as lumbar and caudal epidural blocks.

- Toxin and Toxin Target Database (T3DB)

### 10.1.1 Use Classification

Animal Drugs -> FDA Approved Animal Drug Products (Green Book) -> Active Ingredients

- FDA Approved Animal Drug Products (Green Book)

Human Drugs -> FDA Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book) -> Active Ingredients

- FDA Orange Book

Pharmaceuticals -> Animal Drugs -> Approved in Taiwan

*S72 | NTUPHTW | Pharmaceutically Active Substances from National Taiwan University | **DOI:10.5281/zenodo.3955664***

- NORMAN Suspect List Exchange

Pharmaceuticals -> Nervous System -> Anaesthetics -> Local anaesthetics -> Amides

*S66 | EAWAGTPS | Parent-Transformation Product Pairs from Eawag | **DOI:10.5281/zenodo.3754448***

- NORMAN Suspect List Exchange

## 10.2 Methods of Manufacturing

Prepared by acylation of **2,6-dimethylaniline** with **chloroacetyl chloride** and subsequent reaction with **diethylamine**.

*Kleemann A; Cardiovascular Drugs. Ullmann's Encyclopedia of Industrial Chemistry 7th ed. (1999-2014). NY, NY: John Wiley & Sons. Online Posting Date: January 15, 2008*

- Hazardous Substances Data Bank (HSDB)

By action of **diethylamine** on chloroacetylxylidide.

*Lewis, R.J. Sr.; Hawley's Condensed Chemical Dictionary 15th Edition. John Wiley & Sons, Inc. New York, NY 2007., p. 754*

- Hazardous Substances Data Bank (HSDB)

Preparation: N. M. Lofgren, B. J. Lundqvist, United States of America patent 2441498 (1948 to Astra); A. D. H. Self, A. P. T. Easson, United Kingdom patent 706409 (1954 to May & Baker); I. P. S. Hardie, E. S. Stern, United Kingdom patent 758224 (1956 to J. F. MacFarlane & Co.)

*O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Cambridge, UK: Royal Society of Chemistry, 2013., p. 1019*

- Hazardous Substances Data Bank (HSDB)

... Synthesized by reacting 2,6-dimethylaniline with chloroacetyl chloride in glacial acetic acid and adding sodium acetate. The product (chloroacetyl-2,6-dimethylanilide) is boiled with diethylamine in an inert solvent (e.g., benzene). The hydrochloride crystallizes with one molecule of water which can be removed by careful drying. /Lidocaine hydrochloride/

*Rippel R; Local Anesthetics. Ullmann's Encyclopedia of Industrial Chemistry 7th ed. (1999-2014). NY, NY: John Wiley & Sons. Online Posting Date: June 15, 2000*

▸ Hazardous Substances Data Bank (HSDB)

## 10.3 Formulations / Preparations

Table: Lidocaine Hydrochloride Preparations

| Route of Administration | Dosage Form | Strength | Brand or Generic Name (Manufacturer) |
|---|---|---|---|
| Parenteral | Injection, for direct IV injection | 10 mg/mL | Lidocaine Hydrochloride injectin for Carciac Arrhythmias (Available from one or more manufacturer, distributor, and/or repackager by generic (nonproprietary) name) |
| Parenteral | Injection, for direct IV injection | 20 mg/mL | Lidocaine Hydrochloride injectin for Carciac Arrhythmias (Available from one or more manufacturer, distributor, and/or repackager by generic (nonproprietary) name) |
| Parenteral | Injection, for preparation of IV infusion only | 100 mg/mL (1 g) | Lidocaine Hydrochloride injectin for Carciac Arrhythmias (Available from one or more manufacturer, distributor, and/or repackager by generic (nonproprietary) name) |
| Parenteral | Injection, for preparation of IV infusion only | 200 mg/mL (1 or 2 g) | Lidocaine Hydrochloride injectin for Carciac Arrhythmias (Available from one or more manufacturer, distributor, and/or repackager by generic (nonproprietary) name) |

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 1698*

▸ Hazardous Substances Data Bank (HSDB)

Table: Lidocaine Hydrochloride in Dextrose Preparations

| Route of Administration | Dosage Form | Strength | Brand or Generic Name (Manufacturer) |
|---|---|---|---|
| Parenteral | Injection, for IV infusion | 4 mg/mL (1 or2 g) Lidocaine Hydrochloride in 5% Dextrose | 0.4% Lidocaine Hydrochloride and 5% Dextrose Injection (LifeCare and glass containers (Hospira), Viaflex (Baxter), Excel (Braun)) |
| Parenteral | Injection, for IV infusion | 8 mg/mL (2 or 4 g) Lidocaine Hydrochloride in 5% Dextrose | 0.8% Lidocaine Hydrochloride and 5% Dextrose Injection (LifeCare (Hospira), Viaflex (Baxter), Excel (Braun)) |

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 1698*

▸ Hazardous Substances Data Bank (HSDB)

Table: Lidocaine Hydrochloride in Dextrose Preparations

| Route of Administration | Dosage Form | Strength | Brand or Generic Name (Manufacturer) |
|---|---|---|---|
| Parenteral | Injection | 5% Lidocaine Hydrochloride in 7.5% Dextrose | Lidocaine Hydrochloride Injection in Dextrose (Available from one or more manufacturer, distributor, and/or repackager by generic (nonproprietary) name) |

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 3342*

▸ Hazardous Substances Data Bank (HSDB)

Table: Lidocaine Hydrochloride Preparations

| Route of Administration | Dosage Form | Strength | Brand or Generic Name (Manufacturer) |
|---|---|---|---|
| Parenteral | Injection | 0.5% | Lidocaine Hydrochloride Injection (Available from one or more manufacturer, distributor, and/or repackager by generic (nonproprietary) name) |
| Parenteral | Injection | 0.5% | Xylocaine (APP Pharmaceuticals) |
| Parenteral | Injection | 0.5% | Xylocaine-MPF (APP Pharmaceuticals) |
| Parenteral | Injection | 1% | Lidocaine Hydrochloride Injection (Available from one or more manufacturer, distributor, and/or repackager by generic (nonproprietary) name) |
| Parenteral | Injection | 1% | Xylocaine (APP Pharmaceuticals) |
| Parenteral | Injection | 1% | Xylocaine-MPF (APP Pharmaceuticals) |
| Parenteral | Injection | 1.5% | Lidocaine Hydrochloride Injection (Available from one or more manufacturer, distributor, and/or repackager by generic (nonproprietary) name) |
| Parenteral | Injection | 1.5% | Xylocaine-MPF (APP Pharmaceuticals) |
| Parenteral | Injection | 2% | Lidocaine Hydrochloride Injection (Available from one or more manufacturer, distributor, and/or repackager by generic (nonproprietary) name) |
| Parenteral | Injection | 2% | Xylocaine (APP Pharmaceuticals) |
| Parenteral | Injection | 2% | Xylocaine-MPF (APP Pharmaceuticals) |
| Parenteral | Injection | 2% | Xylocaine Dental, available as dental cartridge (Dentsply) |
| Parenteral | Injection | 4% | Lidocaine Hydrochloride Injection (Available from one or more manufacturer, distributor, and/or repackager by generic (nonproprietary) name) |
| Parenteral | Injection | 4% | Xylocaine-MPF Sterile Solution (APP Pharmaceuticals) |

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 3342*

▸ Hazardous Substances Data Bank (HSDB)

For more Formulations/Preparations (Complete) data for LIDOCAINE (7 total), please visit the HSDB record page.

▸ Hazardous Substances Data Bank (HSDB)

## 10.4 General Manufacturing Information

**EPA TSCA Commercial Activity Status**

Acetamide, 2-(diethylamino)-N-(2,6-dimethylphenyl)-: ACTIVE

▸ EPA Chemicals under the TSCA

List of Essential Medicines: The core list presents a list of minimum medicine needs for a basic health-care system, listing the most efficacious, safe and cost-effective medicines for priority conditions. Priority conditions are selected on the basis of current and estimated future public health relevance, and potential for safe and cost-effective treatment. Lidocaine is included on this list.

*WHO; WHO Model List of Essential Medicines 18th List p.1 (April 2013). Available from, as of January 29, 2015: https://www.who.int/medicines/publications/essentialmedicines/en/*

▸ Hazardous Substances Data Bank (HSDB)

... Synthetic nonnarcotic substitutes for cocaine, the first anesthetic ever used. ... Lidocaine is preferred in veterinary medicine.

*Veterinary Drugs. Kirk-Othmer Encyclopedia of Chemical Technology (1999-2014). John Wiley & Sons, Inc. Online Posting Date: December 4, 2000*

▸ Hazardous Substances Data Bank (HSDB)

# 11 Identification

## 11.1 Analytic Laboratory Methods

DETERMINATION OF LIDOCAINE BY HPLC.

*SMITH FM, NUESSLE NO; ANAL LETT 14 (B8): 567 (1981)*

▸ Hazardous Substances Data Bank (HSDB)

Charcoal is used to adsorb the lidocaine, which is then eluted with chloroform. The concentrated eluate is then gas chromatographed. Methadone is added as an internal standard ... to the alkalinized sample which is then extracted with ether. The concn of lidocaine in the original samples is determined by GC analysis of an aliquot of the chloroform layer. Sensitivity for lidocaine is 0.5 mg/dl. The coefficient of variation for ten replicate analyses of samples containing 0.4 mg/100 ml was 1.7%.

*Sunshine, Irving (ed.) Methodology for Analytical Toxicology. Cleveland: CRC Press, Inc., 1975., p. VI 211*

▸ Hazardous Substances Data Bank (HSDB)

A lidocaine test system is a device intended to measure lidocaine, an antiarrythmic and anticonvulsant drug, in serum and plasma. Measurements obtained by this device are used in the diagnosis and treatment of lidocaine overdose or in monitoring levels of lidocaine to ensure appropriate therapy.

*21 CFR 862.355 (USFDA); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of November 11, 2014:* ***https://www.ecfr.gov***

▸ **Hazardous Substances Data Bank (HSDB)**

## 11.2 Clinical Laboratory Methods

QUANTIFICATION OF LIDOCAINE AND SEVERAL METABOLITES UTILIZING CHEMICAL IONIZATION MS AND STABLE ISOTOPE LABELING IN HUMAN PLASMA AND URINE SAMPLES.

***PMID:408479***

*NELSON SD ET AL; J PHARM SCI 66 (AUG): 1180 (1977)*

▸ **Hazardous Substances Data Bank (HSDB)**

A METHOD OF RAPIDLY MEASURING BLOOD LEVELS OF LIDOCAINE BY ENZYME IMMUNOASSAY IS PRESENTED.

***PMID:7015581***

*MILLER E ET AL; THER DRUG MONIT 3 (1): 85 (1981)*

▸ **Hazardous Substances Data Bank (HSDB)**

GLC ASSAY FOR LIDOCAINE IN PLASMA.

***PMID:660486***

*KLINE BJ, MARTIN MF; J PHARM SCI 67 (JUN): 887 (1978)*

▸ **Hazardous Substances Data Bank (HSDB)**

The drug and its metabolites are effectively extracted from alkalinized plasma (serum) by a mixture of organic solvents. An aliquot is evaporated to dryness under a slow stream of **nitrogen** and the residue is dissolved in **methanol** containing the internal standard. An aliquot is determined by high performance liquid chromatography on a reversed-phase column with ultraviolet detection and quantitation at 210 nm. Flow rate is 2 ml/min, sensitivity is 0.05 mg/ml and recovery is 94% respectively.

*Sunshine, Irving (ed.) Methodology for Analytical Toxicology. Cleveland: CRC Press, Inc., 1975., p. V2 159*

▸ **Hazardous Substances Data Bank (HSDB)**

# 12 Safety and Hazards

## 12.1 Hazards Identification

### 12.1.1 GHS Classification

| 1 of 4 | View All |
|---|---|
| **Note** | *Pictograms displayed are for 98.8% (165 of 167) of reports that indicate hazard statements. This chemical does not meet GHS hazard criteria for 1.2% (2 of 167) of reports.* |
| **Pictogram(s)** |  Irritant |
| **Signal** | Warning |
| **GHS Hazard Statements** | H302 (98.2%): Harmful if swallowed [**Warning** Acute toxicity, oral] |
| **Precautionary Statement Codes** | P264, P270, P301+P317, P330, and P501 (The corresponding statement to each P-code can be found at the GHS Classification page.) |
| **ECHA C&L Notifications Summary** | *Aggregated GHS information provided per 167 reports by companies from 10 notifications to the ECHA C&L Inventory.* *Reported as not meeting GHS hazard criteria per 2 of 167 reports by companies. For more detailed information, please visit ECHA C&L website.* *There are 9 notifications provided by 165 of 167 reports by companies with hazard statement code(s).* *Information may vary between notifications depending on impurities, additives, and other factors. The percentage value in parenthesis indicates the notified classification ratio from companies that provide hazard codes. Only hazard codes with percentage values above 10% are shown.* |

▸ European Chemicals Agency (ECHA)

### 12.1.2 Hazard Classes and Categories

Acute Tox. 4 (98.2%)

▸ European Chemicals Agency (ECHA)

Acute Tox. 4 (100%)

▸ European Chemicals Agency (ECHA)

View More...

## 12.2 Fire Fighting

### 12.2.1 Fire Fighting Procedures

Suitable extinguishing media: Use water spray, alcohol-resistant foam, dry chemical or carbon dioxide.

*Sigma-Aldrich; Material Safety Data Sheet for Lidocaine. Product Number: L1026, Version 5.2 (Revision Date 06/28/2014). Available from, as of October 8, 2014: **https://www.sigmaaldrich.com/safety-center.html***

▸ Hazardous Substances Data Bank (HSDB)

Advice for firefighters: Wear self contained breathing apparatus for fire fighting if necessary.

*Sigma-Aldrich; Material Safety Data Sheet for Lidocaine. Product Number: L1026, Version 5.2 (Revision Date 06/28/2014). Available from, as of October 8, 2014: **https://www.sigmaaldrich.com/safety-center.html***

▸ Hazardous Substances Data Bank (HSDB)

### 12.2.2 Firefighting Hazards

Special hazards arising from the substance or mixture: Carbon oxides, nitrogen oxides (NOx).

*Sigma-Aldrich; Material Safety Data Sheet for Lidocaine. Product Number: L1026, Version 5.2 (Revision Date 06/28/2014). Available from, as of October 8, 2014: **https://www.sigmaaldrich.com/safety-center.html***

▸ Hazardous Substances Data Bank (HSDB)

## 12.3 Accidental Release Measures

### 12.3.1 Cleanup Methods

Accidental Release Measures. Personal precautions, protective equipment and emergency procedures: Use personal protective equipment. Avoid dust formation. Avoid breathing vapours, mist or gas. Ensure adequate ventilation. Avoid breathing dust. Environmental precautions: Do not let product enter drains. Methods and materials for containment and cleaning up: Pick up and arrange disposal without creating dust. Sweep up and shovel. Keep in suitable, closed containers for disposal.

*Sigma-Aldrich; Material Safety Data Sheet for Lidocaine. Product Number: L1026, Version 5.2 (Revision Date 06/28/2014). Available from, as of October 8, 2014: **https://www.sigmaaldrich.com/safety-center.html***

▸ Hazardous Substances Data Bank (HSDB)

### 12.3.2 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)

Waste treatment methods. Product: Offer surplus and non-recyclable solutions to a licensed disposal company. Contact a licensed professional waste disposal service to dispose of this material. Dissolve

or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber. Contaminated packaging: Dispose of as unused product.

*Sigma-Aldrich; Material Safety Data Sheet for Lidocaine. Product Number: L1026, Version 5.2 (Revision Date 06/28/2014). Available from, as of October 8, 2014:* ***https://www.sigmaaldrich.com/safety-center.html***

▸ **Hazardous Substances Data Bank (HSDB)**

### 12.3.3 Preventive Measures

Precautions for safe handling: Avoid contact with skin and eyes. Avoid formation of dust and aerosols. Provide appropriate exhaust ventilation at places where dust is formed. Normal measures for preventive fire protection.

*Sigma-Aldrich; Material Safety Data Sheet for Lidocaine. Product Number: L1026, Version 5.2 (Revision Date 06/28/2014). Available from, as of October 8, 2014:* ***https://www.sigmaaldrich.com/safety-center.html***

▸ **Hazardous Substances Data Bank (HSDB)**

Appropriate engineering controls: Handle in accordance with good industrial hygiene and safety practice. Wash hands before breaks and at the end of workday.

*Sigma-Aldrich; Material Safety Data Sheet for Lidocaine. Product Number: L1026, Version 5.2 (Revision Date 06/28/2014). Available from, as of October 8, 2014:* ***https://www.sigmaaldrich.com/safety-center.html***

▸ **Hazardous Substances Data Bank (HSDB)**

Gloves must be inspected prior to use. Use proper glove removal technique (without touching glove's outer surface) to avoid skin contact with this product. Dispose of contaminated gloves after use in accordance with applicable laws and good laboratory practices. Wash and dry hands.

*Sigma-Aldrich; Material Safety Data Sheet for Lidocaine. Product Number: L1026, Version 5.2 (Revision Date 06/28/2014). Available from, as of October 8, 2014:* ***https://www.sigmaaldrich.com/safety-center.html***

▸ **Hazardous Substances Data Bank (HSDB)**

## 12.4 Handling and Storage

### 12.4.1 Storage Conditions

Lidocaine hydrochloride injections and commercially available solutions of the drug in 5% dextrose should be stored at 25 °C but may be exposed to temperatures up to 40 °C; the injection and solutions should not be frozen, and the solutions should be protected from excessive heat.

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 1698*

▸ **Hazardous Substances Data Bank (HSDB)**

Conditions for safe storage, including any incompatibilities: Keep container tightly closed in a dry and well-ventilated place.

*Sigma-Aldrich; Material Safety Data Sheet for Lidocaine. Product Number: L1026, Version 5.2 (Revision Date 06/28/2014). Available from, as of October 8, 2014:* ***https://www.sigmaaldrich.com/safety-center.html***

▸ Hazardous Substances Data Bank (HSDB)

Lidocaine hydrochloride injections should be stored at a 20-25 °C; solutions containing epinephrine should be protected from light.

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 3342*

▸ Hazardous Substances Data Bank (HSDB)

## 12.5 Exposure Control and Personal Protection

### 12.5.1 Personal Protective Equipment (PPE)

Eye/face protection: Safety glasses with side-shields conforming to EN166 Use equipment for eye protection tested and approved under appropriate government standards such as NIOSH (US) or EN 166(EU).

*Sigma-Aldrich; Material Safety Data Sheet for Lidocaine. Product Number: L1026, Version 5.2 (Revision Date 06/28/2014). Available from, as of October 8, 2014: **https://www.sigmaaldrich.com/safety-center.html***

▸ Hazardous Substances Data Bank (HSDB)

Skin protection: Handle with gloves.

*Sigma-Aldrich; Material Safety Data Sheet for Lidocaine. Product Number: L1026, Version 5.2 (Revision Date 06/28/2014). Available from, as of October 8, 2014: **https://www.sigmaaldrich.com/safety-center.html***

▸ Hazardous Substances Data Bank (HSDB)

Body Protection: Complete suit protecting against chemicals, The type of protective equipment must be selected according to the concentration and amount of the dangerous substance at the specific workplace.

*Sigma-Aldrich; Material Safety Data Sheet for Lidocaine. Product Number: L1026, Version 5.2 (Revision Date 06/28/2014). Available from, as of October 8, 2014: **https://www.sigmaaldrich.com/safety-center.html***

▸ Hazardous Substances Data Bank (HSDB)

Respiratory protection: For nuisance exposures use type P95 (US) or type P1 (EU EN 143) particle respirator. For higher level protection use type OV/AG/P99 (US) or type ABEK-P2 (EU EN 143) respirator cartridges. Use respirators and components tested and approved under appropriate government standards such as NIOSH (US) or CEN (EU).

*Sigma-Aldrich; Material Safety Data Sheet for Lidocaine. Product Number: L1026, Version 5.2 (Revision Date 06/28/2014). Available from, as of October 8, 2014: **https://www.sigmaaldrich.com/safety-center.html***

▸ Hazardous Substances Data Bank (HSDB)

## 12.6 Stability and Reactivity

### 12.6.1 Hazardous Reactivities and Incompatibilities

Incompatible materials: Strong oxidizing agents.

*Sigma-Aldrich; Material Safety Data Sheet for Lidocaine. Product Number: L1026, Version 5.2 (Revision Date 06/28/2014). Available from, as of October 8, 2014:* ***https://www.sigmaaldrich.com/safety-center.html***

▸ Hazardous Substances Data Bank (HSDB)

## 12.7 Regulatory Information

### REACH Registered Substance

Status: Active Update: 11-07-2019 **https://echa.europa.eu/registration-dossier/-/registered-dossier/24208**

▸ European Chemicals Agency (ECHA)

### New Zealand EPA Inventory of Chemical Status

Lidocaine: Does not have an individual approval but may be used under an appropriate group standard

▸ New Zealand Environmental Protection Authority (EPA)

### New Zealand EPA Inventory of Chemical Status

Lignocaine: Does not have an individual approval but may be used under an appropriate group standard

▸ New Zealand Environmental Protection Authority (EPA)

## 12.7.1 FDA Requirements

External analgesic drug products for over-the-counter human use. Analgesic, anesthetic, and antipruritic active ingredients. The active ingredient of the product consists of any of the following within the specified concentration established for each ingredient: (a) Male genital desensitizers. ... Lidocaine in a metered spray with approximately 10 milligrams per spray.

*21 CFR 348.10 (USFDA); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of November 11, 2014:* ***https://www.ecfr.gov***

▸ Hazardous Substances Data Bank (HSDB)

Anorectal drug products for over-the-counter human use. Local anesthetic active ingredients. The active ingredient of the product consists of any of the following when used in the concentration or within the concentration range established for each ingredient: Lidocaine 2 to 5 percent.

*21 CFR 346.10 (USFDA); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of November 11, 2014:* ***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: lidocaine is included in oral health care drug products.

*21 CFR 310.545(a) (14); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of November 11, 2014:* ***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: **lidocaine hydrochloride** is included in oral health care drug products. /**Lidocaine hydrochloride**/

*21 CFR 310.545(a) (14); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of November 11, 2014:* ***https://www.ecfr.gov***

▸ Hazardous Substances Data Bank (HSDB)

For more FDA Requirements (Complete) data for LIDOCAINE (7 total), please visit the **HSDB record page**.

▸ Hazardous Substances Data Bank (HSDB)

## 12.8 Other Safety Information

**Chemical Assessment**

IMAP assessments - **Acetamide**, 2-(diethylamino)-N-(2,6-dimethylphenyl)-: Human health tier I assessment

IMAP assessments - **Acetamide**, 2-(diethylamino)-N-(2,6-dimethylphenyl)-: Environment tier I assessment

▸ Australian Industrial Chemicals Introduction Scheme (AICIS)

### 12.8.1 Special Reports

GREEN L ET AL; LIDOCAINE: COUNTERPOINT DISCUSSION; APPL PHARMACOKINET 392 (1980). A REVIEW ON METABOLISM AND PHARMACOKINETICS OF LIDOCAINE IN RELATION TO THERAPEUTIC & TOXIC EFFECTS.

▸ Hazardous Substances Data Bank (HSDB)

RODMAN JH; LIDOCAINE; APPL PHARMACOKINET 350 (1980). A REVIEW OF METABOLISM AND PHARMACOKINETICS OF LIDOCAINE.

▸ Hazardous Substances Data Bank (HSDB)

WALLER ES; PHARMACOKINETIC PRINCIPLES OF LIDOCAINE DOSING IN RELATION TO DISEASE STATE; J CLIN PHARMACOL 21 (4):1 81 (1981). PRINCIPLES OF DOSING WITH LIDOCAINE.

- Hazardous Substances Data Bank (HSDB)

ASTRUP J, SORENSEN HR; INHIBITION OF CEREBRAL METABOLISM BY LIDOCAINE; EUR NEUROL 20 (3): 221 (1981). REVIEW ON EFFECTS IN HIGH DOSES (HIGHER THAN THOSE THAT INDUCE SEIZURES) ON CEREBRAL FUNCTION & METABOLISM.

- Hazardous Substances Data Bank (HSDB)

BRUGUEROLLE B ET AL; FACTORS AFFECTING LIDOCAINE PHARMACOKINETICS; THERAPIE 38 (1): 27 (1983). A REVIEW WITH 69 REFERENCES OF PHYSIOLOGICAL, PHARMACOLOGICAL, AND PATHOLOGICAL FACTORS AFFECTING THE PHARMACOKINETICS OF LIDOCAINE.

- Hazardous Substances Data Bank (HSDB)

# 13 Toxicity

## 13.1 Toxicological Information

### 13.1.1 Toxicity Summary

IDENTIFICATION AND USE: Lidocaine is a white or slightly yellow, crystalline powder or needle with a characteristic odor. It is commonly used as a medication including for local anesthetics, anti-arrhythmia agent, or as a voltage-gated **sodium** channel blocker. Lidocaine may also be used in the treatment of hypertensive emergencies, or acute coronary syndrome associated with the toxicity of various stimulants and antiarrhythmic agents. A lidocaine transdermal patch is used for relief of pain associated with postherpetic neuralgia. An oral patch is available for application to accessible mucous membranes of the mouth prior to superficial dental procedures. The combination of lidocaine (2.5%) and **prilocaine** (2.5%) in an occlusive dressing is used as an anesthetic prior to venipuncture, skin graft harvesting, and infiltration of anesthetics into genitalia. Lidocaine in combination with **tetracaine** in a formulation that generates a "peel" is approved for topical local analgesia prior to superficial dermatological procedures. HUMAN EXPOSURE AND TOXICITY: Adverse effects of the drug mainly involve the CNS because of its rapid entry in the brain. Adverse CNS reactions may be manifested by drowsiness; dizziness; disorientation; confusion; lightheadedness; tremulousness; psychosis; nervousness; apprehension; agitation; euphoria; tinnitus; visual disturbances including blurred or double vision; nausea; vomiting; paresthesia; sensations of neat, cold or numbness; difficulty swallowing; dyspnea; and slurred speech. Muscle twitching or tremors, seizures, unconsciousness, coma, and respiratory depression and arrest may also occur. Shortly following the CNS effects, patients with lidocaine toxicity may also experience cardiovascular effects. If the patient is supported through this period, the drug rapidly distributes away from the heart, and spontaneous cardiac function returns. Lidocaine, when administered to a baby may induce convulsions. Lidocaine intoxication in the neonate, occurring as a result of inadvertent injection into the fetal scalp or cranium during local anesthesia (caudal or paracervical block or episiotomy), produces apnea, hypotonia, and seizures. Dilated pupils and loss of the oculocephalic reflex may also be observed. The more severe of these effects develop when serum lidocaine concentrations exceed 5 ug/mL and are often preceded

by paresthesias or somnolence. Continuous application for 72 hours of four lidocaine patches 5%, changed every 12 or 24 hours, produced mild application-site erythema in most patients, but no systemic adverse reactions. No loss in sensation at the application site was reported. Systemic exposure to lidocaine and **monoethylglycinexylidide** (**MEGX**), the primary active metabolite of lidocaine, after application of lidocaine gel or patches was minimal in normal volunteers, patients with post-herpetic neuralgia, and patients with acute herpes zoster. In human SH-SY5Y neuroblastoma cells, local anesthesia caused rapid cell death, which was primarily due to necrosis. Lidocaine can trigger apoptosis with either increased time of exposure or increased concentration. ANIMAL STUDIES: In rats persistent functional impairment and histologic damage in the nerve roots and the spinal cord was less severe after epidural lidocaine than after intrathecal lidocaine. In 8 New Zealand Rabbits receiving 0.2 mL 1% **lidocaine hydrochloride** applied intracamerally to the lenses, had morphological abnormalities in both cornea and iris of the lidocaine injected eyes. Another experiment in rabbits with 2% **lidocaine HCl** applied intracamerally on the corneal endothelium found that lidocaine caused statistically significant corneal thickening and clinically significant corneal opacification. Lidocaine injection into the dorsal root ganglion of rats produced hyperalgesia, possibly due to activation of resident satellite glial cells. One-hour exposure of primary rabbit urothelial cells (PRUC) culture to 0.5 or 1.0% lidocaine decreased cell viability. Lidocaine rapidly crosses the placenta in pregnant guinea pigs. High concentrations are found in the fetal liver, heart, and brain. High myocardial levels of drug in the fetus may possibly account for marked depressant effects that local anesthetics produce. In another study, no significant effects were observed in offspring of rats administered lidocaine at by constant infusion for 2 weeks before mating and throughout pregnancy. Additionally, pregnancy did not enhance the CNS and cardiovascular toxic effects of lidocaine when studied in pregnant sheep receiving continuous IV drug infusion and compared to data from nonpregnant ewes. Lidocaine did not induce genotoxicity in the wing somatic mutation and recombination test in Drosophila melanogaster, which detects point and chromosomal mutations as well as recombination induced by the activity of genotoxins of direct and indirect action. Lidocaine 0.25% did decrease cell viability and caused DNA degradation in murine fibroblasts 3T6. Lidocaine was not oncogenic when administered topically weekly to the dorsal skin of mice for 26 weeks.

▸ Hazardous Substances Data Bank (HSDB)

Lidocaine stabilizes the neuronal membrane by inhibiting the ionic fluxes required for the initiation and conduction of impulses thereby effecting local anesthetic action. Lidocaine alters signal conduction in neurons by blocking the fast voltage gated **sodium** (Na+) channels in the neuronal cell membrane that are responsible for signal propagation. With sufficient blockage the membrane of the postsynaptic neuron will not depolarize and will thus fail to transmit an action potential. This creates the anaesthetic effect by not merely preventing pain signals from propagating to the brain but by aborting their birth in the first place.

▸ Toxin and Toxin Target Database (T3DB)

## 13.1.2 USGS Health-Based Screening Levels for Evaluating Water-Quality

| | |
|---|---|
| **Chemical** | Lidocaine |
| **Chemical Classes** | Pharmaceutical |

| | |
|---|---|
| **Reference** | Smith, C.D. and Nowell, L.H., 2024. Health-Based Screening Levels for evaluating water-quality data (3rd ed.). DOI:10.5066/F71C1TWP |

▸ USGS Health-Based Screening Levels for Evaluating Water-Quality Data

### 13.1.3 Drug Induced Liver Injury

| | |
|---|---|
| **Compound** | lidocaine |
| **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<br>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

### 13.1.4 Carcinogen Classification

| | |
|---|---|
| **Carcinogen Classification** | No indication of carcinogenicity to humans (not listed by IARC). |

▸ Toxin and Toxin Target Database (T3DB)

### 13.1.5 Health Effects

Systemic exposure to excessive quantities of lidocaine mainly result in central nervous system (CNS) and cardiovascular effects. CNS effects may include CNS excitation(nervousness, tingling around the mouth) followed by depression. [Wikipedia]

▸ Toxin and Toxin Target Database (T3DB)

### 13.1.6 Effects During Pregnancy and Lactation

◉ Summary of Use during Lactation

Lidocaine concentrations in milk during continuous IV infusion, epidural administration and in high doses as a local anesthetic are low and the lidocaine is poorly absorbed by the infant. Lidocaine is not expected to cause any adverse effects in breastfed infants. No special precautions are required.

Lidocaine during labor and delivery with other anesthetics and analgesics has been reported by some to interfere with breastfeeding. However, this assessment is controversial and complex because of the many different combinations of drugs, dosages and patient populations studied as well as the variety

of techniques used and deficient design of many of the studies. Overall it appears that with good breastfeeding support epidural lidocaine with or without **fentanyl** or one of its derivatives has little or no adverse effect on breastfeeding success. Labor pain medication may delay the onset of lactation.

◉ Effects in Breastfed Infants

Lidocaine in doses ranging from 60 to 500 mg administered to the mother by intrapleural or epidural routes during delivery had no effect on their 14 infants who were either breastfed or received their mother's breastmilk by bottle.

A neurology group reported using 1% lidocaine for peripheral nerve blocks in 14 nursing mothers with migraine. They reported no infant side effects and considered the procedure safe during breastfeeding.

◉ Effects on Lactation and Breastmilk

A randomized study compared three groups of women undergoing elective cesarean section who received subcutaneous infusion of 20 mL of lidocaine 1% plus **epinephrine** 1:100:000 at the incision site. One group received the lidocaine before incision, one group received the lidocaine after the incision, and the third received 10 mL before the incision and 10 mL after. Women in the pre-and post-incision administration group initiated breastfeeding earlier than those in the pre-incision administration (3.4 vs 4.1 hours). There was no difference between the post-incision administration group and the other groups in time to breastfeeding initiation.

A national survey of women and their infants from late pregnancy through 12 months postpartum compared the time of lactogenesis II in mothers who did and did not receive pain medication during labor. Categories of medication were spinal or epidural only, spinal or epidural plus another medication, and other pain medication only. Women who received medications from any of the categories had about twice the risk of having delayed lactogenesis II (>72 hours) compared to women who received no labor pain medication.

An Egyptian study compared lidocaine 2% (n = 75) to lidocaine 2% plus **epinephrine** 1:200,000 (n = 70) as a wound infiltration following cesarean section. Patients who received **epinephrine** in combination with lidocaine began breastfeeding at 89 minutes following surgery compared to 132 minutes for those receiving lidocaine alone. The difference was statistically significant.

▸ **Drugs and Lactation Database (LactMed)**

◈ What is lidocaine?

Lidocaine is a local anesthetic. Local anesthetics are used to numb areas of the body for short periods of time. Lidocaine has been used as an injection (given by shot), intravenously (by I.V.) and topically (rubbed on the body). Lidocaine can be found in some over-the-counter pain-relieving creams and patches. Lidocaine I.V. has also been used to treat ventricular arrhythmia (abnormal heart rhythm). Injected lidocaine has also be used in some medical or dental procedures or as a therapeutic nerve block to numb a part of the body and relieve pain. Lidocaine is sometimes injected into spinal fluid or the space around the spinal cord ('epidural') to provide pain relief during labor or for a surgical delivery ('cesarian section').Lidocaine is also found in a topical cream called **EMLA®**. **EMLA®** cream also contains the medication **prilocaine**. For more information on **prilocaine**, please see the MotherToBaby fact sheet at: https://mothertobaby.org/fact-sheets/**prilocaine**.

◈ I take lidocaine. Can it make it harder for me to get pregnant?

Studies have not been done to see if lidocaine could make it harder to get pregnant. An experimental animal study did not find that lidocaine would affect fertility (ability to get pregnant).

◈ Does taking lidocaine increase the chance for miscarriage?

Miscarriage is common and can occur in any pregnancy for many different reasons. Studies have not been done to see if lidocaine increases the chance for miscarriage.

◈ Does taking lidocaine increase the chance of birth defects?

Every pregnancy starts out with a 3-5% chance of having a birth defect. This is called the background risk. One study involving lidocaine as a local anesthetic did not find a higher chance for birth defects. Also, human case reports and experimental animal studies do not suggest that lidocaine would significantly increase the chance of birth defects.

◈ Does taking lidocaine in pregnancy increase the chance of other pregnancy related problems?

There are a few case reports of side effects in newborns of pregnant persons who received lidocaine at the time of delivery. The infants in these case reports needed treatment for symptoms that included low muscle tone ("floppy"), dilated pupils, difficulty breathing, apnea, and/or seizures. There are also case reports without health concerns in the newborn when lidocaine was used at the time of delivery.

◈ Does taking lidocaine in pregnancy affect future behavior or learning for the child?

Studies have not been done to see if lidocaine can cause behavior or learning issues for the child.

◈ Breastfeeding while taking lidocaine:

Lidocaine can get into breastmilk at low levels. However, when swallowed, it is not well absorbed by the baby. Breastfeeding after receiving lidocaine is unlikely to cause problems for a nursing child. Be sure to talk to your healthcare provider about all your breastfeeding questions.

◈ If a male takes lidocaine, could it affect fertility (ability to get partner pregnant) or increase the chance of birth defects?

Studies have not been done to see if lidocaine could affect fertility. In general, exposures that fathers or sperm donors have are unlikely to increase the risks to a pregnancy. For more information, please see the MotherToBaby fact sheet Paternal Exposures at https://mothertobaby.org/fact-sheets/paternal-exposures-pregnancy/.

▸ **Mother To Baby Fact Sheets**

## 13.1.7 Exposure Routes

Intravenous, Topical, Oral, Buccal, Dental, Intramuscular, or Urethral injection , Infiltration. Information derived from diverse formulations, concentrations and usages reveals that lidocaine is completely absorbed following parenteral administration, its rate of absorption depending, for example, upon various factors such as the site of administration and the presence or absence of a vasoconstrictor agent.

▸ **Toxin and Toxin Target Database (T3DB)**

## 13.1.8 Symptoms

Symptoms of overdose include convulsions, hypoxia, acidosis, bradycardia, arrhythmias and cardiac arrest.

Toxin and Toxin Target Database (T3DB)

## 13.1.9 Acute Effects

ChemIDplus

## 13.1.10 Toxicity Data

LD50: 459 (346-773) mg/kg (oral, non-fasted female rats) LD50: 214 (159-324) mg/kg (oral, fasted female rats)

Toxin and Toxin Target Database (T3DB)

## 13.1.11 Treatment

The first step in the management of systemic toxic reactions consists of immediate attention to the establishment and maintenance of a patent airway and assisted or controlled ventilation with **oxygen** and a delivery system capable of permitting immediate positive airway pressure by mask. If convulsions occur, the objective of the treatment is to maintain ventilation and oxygenation and support the circulation. **Oxygen** must be given and ventilation assisted if necessary (mask and bag or tracheal intubation). Should convulsions not stop spontaneously after 15-20 seconds, an anticonvulsant should be given i.v. to facilitate adequate ventilation and oxygenation. **Thiopental sodium** 1-3 mg/kg i.v. is the first choice. Alternatively **diazepam** 0.1 mg/kg bw i.v. may be used, although its action will be slow. Prolonged convulsions may jeopardise the patient's ventilation and oxygenation. If so, injection of a muscle relaxant (e.g. **succinylcholine** 1 mg/kg bw) will facilitate ventilation, and oxygenation can be controlled. Early endotracheal intubation must be considered in such situations. If cardiovascular depression is evident (hypotension, bradycardia), **ephedrine** 5-10 mg i.v. should be given and may be repeated, if necessary, after 2-3 minutes. Should circulatory arrest occur, immediate cardiopulmonary resuscitation should be instituted. Continual oxygenation and ventilation and circulatory support as well as treatment of acidosis are of vital importance. (L1712)

*L1712: RxList: The Internet Drug Index (2009).* ***http://www.rxlist.com/***

▸ **Toxin and Toxin Target Database (T3DB)**

## 13.1.12 Interactions

EMLA cream is a topical formulation based upon the eutectic mixture of lidocaine and **prilocaine** and is used in clinical settings to produce local analgesia after application under occlusive dressing. A blanching reaction has been reported to occur locally after application, but it is not clear whether this reaction is caused by the anesthetic mixture, by the vehicle or the occlusion. This blanching reaction was studied in 50 healthy volunteers in a double-blind randomized assay: **EMLA** versus placebo, under occlusive dressing for 1 hr, each subject being his own control. 33 Cases (66%) of blanching after application of EMLA cream were observed versus 3 cases (6%) after placebo, this difference being highly significant. Blanching was observed without delay, after removal of the dressing, and was very transient, disappearing in less than 3 hr in all cases. It is concluded that the blanching reaction is (1) frequent but very transient, and (2) determined by the anesthetic mixture included in EMLA cream and not by the vehicle alone, nor by the occlusion, since it is not found with the placebo. The precise mechanism of this reaction is unknown.

***PMID:2394302***

*Villada G et al; Dermatologica 181 (1): 38-40 (1990)*

▸ **Hazardous Substances Data Bank (HSDB)**

Recent studies have suggested that cytochrome P-450 isoenzyme 1A2 has an important role in lidocaine biotransformation. /This research/ studied the effect of a cytochrome P-450 1A2 inhibitor, **ciprofloxacin**, on the pharmacokinetics of lidocaine. In a randomized, double-blinded, cross-over study, nine healthy volunteers ingested for 2.5 days 500 mg oral **ciprofloxacin** or placebo twice daily. On day 3, they received a single dose of 1.5 mg/kg lidocaine intravenously over 60 min. Plasma concentrations of lidocaine, **3-hydroxylidocaine** and **monoethylglycinexylidide** were determined for 11 hr after the start of the lidocaine infusion. **Ciprofloxacin** increased the mean peak concentration and area under plasma concentration-time curve of lidocaine by 12% (range [-6] to 46%; P<0.05) and 26% (8 to 59%; P 0.01), respectively. The mean plasma clearance of lidocaine was decreased by ciprofloxacin by 22% (7 to 38%; P<0.01). Ciprofloxacin decreased the area under the plasma concentration-time curve of monoethylglycinexylidide by 21% (P<0.01) and that of 3-hydroxylidocaine by 14% (P< 0.01). The plasma decay of intravenously administered lidocaine is modestly delayed by concomitantly administered ciprofloxacin. Ciprofloxacin may increase the systemic toxicity of lidocaine.

***PMID:16211753***

*Isohanni MH et al; Eur J Anaesthesiol 22 (10): 795-9 (2005)*

▸ **Hazardous Substances Data Bank (HSDB)**

**Epinephrine** is commonly added to lidocaine solutions to increase the duration of spinal anesthesia. Despite this common usage, the effect of **epinephrine** on the neurotoxic potential of this anesthetic is not known. The current experiments investigated whether adding **epinephrine** increases functional impairment or histologic damage induced by spinal administration of lidocaine in the rat. Eighty rats were divided into four groups to receive an intrathecal injection of **normal saline** containing either 5% lidocaine, 5% lidocaine with 0.2 mg/mL of **epinephrine**, 0.2 mg/mL of **epinephrine**, or **normal saline**

alone. Animals were assessed for persistent sensory impairment using the tail-flick test administered 4 and 7 days after infusion. Animals were then killed, and the spinal cord and nerve roots were prepared for neuropathologic evaluation. Rats given 5% lidocaine developed persistent sensory impairment and histologic damage, and the addition of **epinephrine** resulted in a further significant increase in injury. Sensory function in animals given **epinephrine** without anesthetic was similar to baseline and did not differ from saline. Histologic changes in animals treated with **epinephrine** alone did not differ significantly from saline controls. The neurotoxicity of intrathecally administered lidocaine is increased by the addition of **epinephrine**. When making clinical recommendations for maximum safe intrathecal dose of this anesthetic, one may need to consider whether the solution contains **epinephrine**.

*PMID:11388541*

*Hashimoto K et al; Anesthesiology 94 (5): 876-81 (2001)*

▸ **Hazardous Substances Data Bank (HSDB)**

PURPOSE: During continuous epidural anesthesia with lidocaine, plasma **monoethylglycinexylidide** (**MEGX**), an active metabolite of lidocaine, increases continuously. /This study/ assessed the effect of **epinephrine** on the absorption of lidocaine and the accumulation of **MEGX** during continuous epidural anesthesia in children. Anesthesia was administered as an initial bolus of 5 mg/kg of 1% lidocaine solution followed by continuous infusion at 2.5 mg/kg/hr. Patients in the control group (n = 8) received lidocaine alone, while patients in the **epinephrine** group (n = 8) received lidocaine + **epinephrine** (5 ug/mL). Concentrations of lidocaine and its active metabolite, **MEGX**, were measured in plasma samples obtained after 15 min, 30 min, and one, two, three, four, and five hours of infusion using high-performance liquid chromatography with ultraviolet detection. Plasma lidocaine concentrations were higher in samples from the control group for the first hour; however, after two hours the levels were the same in all samples. Plasma **MEGX** levels increased continuously in both groups and were significantly higher in the control group samples. The sum of lidocaine + **MEGX** was higher in the control group for the first two hours but there was no significant difference between groups after three hours. Reduction of the potential for systemic toxicity by the addition of **epinephrine** to lidocaine is limited, because the reduction of the sum of the plasma concentrations of lidocaine and its active metabolite **MEGX** is small and limited to the initial phase of infusion.

*PMID:12193490*

*Miyabe M et al; Can J Anaesth 49 (7): 706-10 (2002)*

▸ **Hazardous Substances Data Bank (HSDB)**

For more Interactions (Complete) data for LIDOCAINE (33 total), please visit the **HSDB record page**.

▸ **Hazardous Substances Data Bank (HSDB)**

## 13.1.13 Antidote and Emergency Treatment

Demonstrate a case report involving successful use of lipid emulsion therapy for intractable cardiac arrest due to lidocaine toxicity. ... The mechanism of action of lipid emulsion therapy is not well defined and has been postulated to work by both a "lipid sink," decreasing circulating amounts of drugs to the periphery, or through a direct "energy source" to the myocardium. We present a case report of a patient successfully resuscitated with lipid emulsion therapy after prolonged and

intractable lidocaine toxicity. Lidocaine is generally considered much less cardiotoxic than other local anesthetics and is used commonly as infusions for intractable ventricular arrhythmias. This case demonstrates the need to consider lipid emulsion therapy in the advanced cardiac life support algorithm for lidocaine toxicity as well as other lipid soluble drug intoxications.

*PMID:21263316*

*Dix SK et al; Crit Care Med 39 (4): 872-4 (2011)*

▸ **Hazardous Substances Data Bank (HSDB)**

The focus of the initial management for IV lidocaine-induced cardiac arrest is continuous cardiopulmonary resuscitation to allow lidocaine to redistribute away from the heart. Apart from this setting, management of hemodynamic compromise incudes fluid replacement and other conventional strategies. Resistant hypotension may require **dopamine** or **norepinephrine** administration, insertin of an intraaortic balloon assist pump, or bypass. Cardiopulmonary bypass, which does not direcly enhance elimination, maintains hepatic perfusion, thereby allowing the lidocaine to be metabolized. bradytachyarrhythmias typically do not respond to **atropine**, requiring the administration of a chronotrope such as **dopamine**, **norepinephrine**, or **isoproterenol**. External pacing or insertion of a transvenous pacemaker may be useful, but the myocardium is often refractory to electrical capture. lidocaine-induced seizures and those related to lidocaine analogs are generally brief in nature and do not require specific therapy. for patients requiring treatment, an IV **benzodiazepine** generally suffices; rarely, a barbiturate is required. Similarly, although IV lipid emulsion is often described as useful for the resuscitation of patients with life-threatening local anesthetic overdose, its use for lidocaine-poisoned patients is unstudied and likely unnecessary given the rapid time course of recovery. Enhanced elimination techniques are limited after IV poisoning because of the rapid time course of poisoning.

*Goldfrank, L.R., Goldfrank's Toxicologic Emergencies 9th Ed. 2011., McGraw-Hill, New York, N.Y., p. 931*

▸ **Hazardous Substances Data Bank (HSDB)**

Emergency and supportive measures. 1. Maintain an open airway and assist ventilation if necessary. 2. Treat coma, seizures, hypotension, and arrhythmias if they occur. ... Continuously monitor vital signs and ECG for a minimum of 6 hours after exposure, and admit the patient for 24 hours of intensive monitoring if there is evidence of toxicity. /Antiarrhythmic drugs/

*OLSON, K.R. (Ed). Poisoning and Drug Overdose, Sixth Edition. McGraw-Hill, New York, NY 2012, p. 86*

▸ **Hazardous Substances Data Bank (HSDB)**

Specific drugs and antidotes. In patients with intoxication by type Ia or type Ic drugs, QRS prolongation, bradyarrhythmias, and hypotension may respond to **sodium bicarbonate**, ... . The **sodium bicarbonate** reverses cardiac-depressant effects caused by inhibition of the fast **sodium** channel. Torsade de pointes should be treated with IV **magnesium**, repletion of **potassium**, and, if necessary, overdrive cardiac pacing. /Antiarrhythmic drugs/

*OLSON, K.R. (Ed). Poisoning and Drug Overdose, Sixth Edition. McGraw-Hill, New York, NY 2012, p. 86*

▸ **Hazardous Substances Data Bank (HSDB)**

For more Antidote and Emergency Treatment (Complete) data for LIDOCAINE (10 total), please visit the **HSDB record page**.

Hazardous Substances Data Bank (HSDB)

## 13.1.14 Human Toxicity Excerpts

/SIGNS AND SYMPTOMS/ Some commercially available formulations of **lidocaine hydrochloride** contain **sodium metabisulfite**, a **sulfite** that may cause allergic-type reactions, including anaphylaxis and life-threatening or less severe asthmatic episodes, in certain susceptible individuals. The overall prevalence of **sulfite** sensitivity in the general population is unknown but probably low; such sensitivity appears to occur more frequently in asthmatic than in nonasthmatic individuals.

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 3341*

Hazardous Substances Data Bank (HSDB)

/SIGNS AND SYMPTOMS/ Adverse CNS reactions may be manifested by drowsiness; dizziness; disorientation; confusion; lightheadedness; tremulousness; psychosis; nervousness; apprehension; agitation; euphoria; tinnitus; visual disturbances including blurred or double vision; nausea; vomiting; paresthesia; sensations of heat, cold, or numbness; difficulty swallowing; dyspnea; and slurred speech. Muscle twitching or tremors, seizures, unconsciousness or altered consciousness, coma, and respiratory depression and arrest may also occur.

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 1696*

Hazardous Substances Data Bank (HSDB)

/SIGNS AND SYMPTOMS/ The side effects of lidocaine seen with increasing dose include drowsiness, tinnitus, dysgeusia, dizziness, and twitching. As the dose increases, seizures, coma, and respiratory depression and arrest will occur.

*Brunton, L. Chabner, B, Knollman, B. Goodman and Gillman's The Pharmaceutical Basis of Therapeutics, Twelth Edition, McGraw Hill Medical, New York, NY. 2011, p. 573*

Hazardous Substances Data Bank (HSDB)

/CASE REPORTS/ ...Rare cases of lidocaine-associated exacerbations of heart failure have been reported, especially in patients with very poor ventricular function.

*Brunton, L. Chabner, B, Knollman, B. Goodman and Gillman's The Pharmaceutical Basis of Therapeutics, Twelth Edition, McGraw Hill Medical, New York, NY. 2011, p. 841*

Hazardous Substances Data Bank (HSDB)

For more Human Toxicity Excerpts (Complete) data for LIDOCAINE (42 total), please visit the **HSDB record page**.

Hazardous Substances Data Bank (HSDB)

## 13.1.15 Non-Human Toxicity Excerpts

/ALTERNATIVE and IN VITRO TESTS/ All local anesthetics (LAs) are, to some extent, neurotoxic. Toxicity studies have been performed in dissociated neuron cultures, immersing both axon and soma in LA.

This approach, however, does not accurately reflect the in vivo situation for peripheral nerve blockade, where LA is applied to the axon alone. /This study/ investigated lidocaine neurotoxicity in compartmental sensory neuron cultures, which are composed of one central compartment containing neuronal cell bodies and a peripheral compartment containing their axons, allowing for selective incubation. We applied lidocaine +/- neuroprotective drugs to neuronal somata or axons, and assessed neuron survival and axonal outgrowth. Lidocaine applied to the peripheral compartment led to a decreased number of axons (to 59% +/- 9%), without affecting survival of cell bodies. During axonal incubation with lidocaine, the p38 mitogen-activated protein kinase inhibitor **SB203580** (10 uM) attenuated axonal injury when applied to the axon (insignificant reduction of maximal axonal distance to 93% +/- 9%), but not when applied to the cell body (deterioration of maximal axonal length to 48% +/- 6%). Axonal co-incubation of lidocaine with the caspase inhibitor z-vad-fmk (20 microM) was not protective. Whereas inhibition of either p38 mitogen-activated protein kinase or caspase activity promote neuronal survival after LA treatment of dissociated neuronal cultures, axonal degeneration induced by lidocain (40 mM) is prevented by p38 MAP kinase but not by caspase inhibition. /It is concluded/ that processes leading to LA-induced neurotoxicity in dissociated neuronal culture may be different from those observed after purely axonal application.

*PMID:18042864*

*Lirk P et al; Anesth Analg 105 (6): 1657-64 (2007)*

▸ **Hazardous Substances Data Bank (HSDB)**

/ALTERNATIVE and IN VITRO TESTS/ Pharmacologic inhibition of the p38 mitogen-activated protein kinase (MAPK) leads to a reduction in lidocaine neurotoxicity in vitro and in vivo. The current study investigated in vitro the hypotheses that lidocaine neurotoxicity is specific for dorsal root ganglion cells of different size or phenotype, involves time-dependent and specific activation of the p38 MAPK, that p38 MAPK inhibitors are only effective if applied with local anesthetic, and that p38 MAPK activation triggers activation of lipoxygenase pathways. /This study/ used primary sensory neuron cultures and pheochromocytoma cell line cultures to detect time-dependent activation of the p38 MAPK or related pathways such as extracellular signal-regulated kinases and c-jun N-terminal kinases. Cells were divided by size or by immunoreactivity for calcitonin gene-related peptide or isolectin B4, indicative of nociceptive phenotype. The authors also investigated whether **arachidonic acid** pathways represent a downstream effector of the p38 MAPK in local anesthetic-induced neurotoxicity. All types of dorsal root ganglion cells were subject to neurotoxic effects of lidocaine, which were mediated by specific activation of the p38 MAPK but not extracellular signal-regulated kinases or c-jun N-terminal kinases. Neuroprotective efficacy of p38 MAPK inhibitors declined significantly when administered more than 1 hr after lidocaine exposure. Activation of p38 MAPK preceded activation of **arachidonic acid** pathways. Neurotoxicity of lidocaine, specific activation of p38 MAPK, and neuroprotective effects of a p38 MAPK inhibitor were further confirmed in pheochromocytoma cell line cultures. Specific and time-dependent activation of the p38 MAPK is involved in lidocaine-induced neurotoxicity, most likely followed by activation of lipoxygenase pathways.

*PMID:17065898*

*Haller I et al; Anesthesiology. 105(5):1024-33. (2006).*

▸ **Hazardous Substances Data Bank (HSDB)**

/ALTERNATIVE and IN VITRO TESTS/ Local anesthetic-induced neurotoxicity is one of the potential causes of postspinal anesthesia neurologic injury. Many experimental and clinical studies have

demonstrated that lidocaine is more neurotoxic than **bupivacaine**. The mechanisms of local anesthetic-induced neurotoxicity remain unclear. **Glutamate** is an excitatory amino acid and widely exists in the central nervous system. Overstimulation of the **glutamate** receptors may produce neuronal toxic effect. In this study, we used in vivo microdialysis to examine the **glutamate** release in cerebrospinal fluid (CSF) after intrathecal lidocaine and **bupivacaine** injection. Male Wistar rats were used. Administration of lidocaine (5 groups: **normal saline**, 2.5%, 5%, 10%, and 10% + **MK-801** intrathecally injected) and **bupivacaine** (4 groups: **normal saline**, 0.25%, 0.5%, and 1% intrathecally injected) was performed in both microdialysis and postinjection neurologic sequelae studies. After intrathecal injection of the studied agents, the CSF dialysates were collected in 10-minute intervals for 2 hours. Cerebrospinal fluid **glutamate** concentrations were measured by high-performance liquid chromatography. In addition, tail-flick latencies were examined daily before and after microdialysis for 4 days. Intrathecal lidocaine concentration-dependently elevated **glutamate** release in CSF. Pretreatment with **MK-801** significantly inhibited the **glutamate** release induced by 10% lidocaine. Intrathecal **bupivacaine** has no influence on **glutamate** release in CSF. The tail-flick latencies were significantly prolonged for 4 days after intrathecal lidocaine injection, and these effects were in a concentration-dependent manner. Pretreatment with **MK-801** significantly reversed the 10% lidocaine-induced prolonged tail-flick latencies. There was no difference of the tail-flick latencies among the **bupivacaine**-treated groups. Intrathecal lidocaine caused a concentration-dependent increase of the CSF **glutamate** release and postinjection neurologic impairment; these effects can be reversed by **MK-801**. However, intrathecal **bupivacaine** shows no influence. /It is suggested/ that **glutamate** may be involved in the pathogenesis of lidocaine-induced spinal neurotoxicity.

***PMID:21857271***

*Cherng CH et al; Reg Anesth Pain Med 36 (5): 452-6 (2011)*

▸ **Hazardous Substances Data Bank (HSDB)**

/ALTERNATIVE and IN VITRO TESTS/ Although lidocaine-induced cell toxicity has been reported, its mechanism is unclear. Cell size, morphological change, and membrane resistance are related to homeostasis and damage to the cell membrane; however, the effects of lidocaine on these factors are unclear. Using an identified LPeD1 neuron from Lymnaea stagnalis, /this study/ sought to determine how lidocaine affects these factors and how lidocaine is related to damage of the cell membrane. Cell size and morphological form were measured by a micrograph and imaging analysis system. Membrane potential and survival rate were obtained by intracellular recording. Membrane resistance and capacitance were measured by whole-cell patch clamp. Phosphatidyl serine and nucleic acid were double stained and simultaneously measured by annexin V and **propidium iodide**. Lidocaine at a clinical dose (5-20 mM) induced morphological change (bulla and bleb) in the neuron and increased cell size in a concentration-dependent manner. Membrane potential was depolarized in a concentration-dependent manner. At perfusion of more than 5 mM lidocaine, the depolarized membrane potential was irreversible. Lidocaine decreased membrane resistance and increased membrane capacitance in a concentration-dependent manner. Both phosphatidyl serine and nucleic acid were stained under lidocaine exposure in a concentration-dependent manner. A clinical dose of lidocaine greater than 5 mM destroys the cell membrane and induces both necrosis and apoptosis in an identified Lymnaea neuron.

***PMID:22038615***

*Onizuka S et al; J Anesth 26 (1): 54-61 (2012)*

Hazardous Substances Data Bank (HSDB)

For more Non-Human Toxicity Excerpts (Complete) data for LIDOCAINE (47 total), please visit the HSDB record page.

Hazardous Substances Data Bank (HSDB)

## 13.1.16 Non-Human Toxicity Values

LD50 Mouse oral 292 mg/kg

*O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Cambridge, UK: Royal Society of Chemistry, 2013., p. 1019*

Hazardous Substances Data Bank (HSDB)

LD50 Mouse ip 105 mg/kg

*O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Cambridge, UK: Royal Society of Chemistry, 2013., p. 1019*

Hazardous Substances Data Bank (HSDB)

LD50 Mouse iv 19.5 mg/kg

*O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Cambridge, UK: Royal Society of Chemistry, 2013., p. 1019*

Hazardous Substances Data Bank (HSDB)

LD50 Rat oral 317 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. 1239*

Hazardous Substances Data Bank (HSDB)

For more Non-Human Toxicity Values (Complete) data for LIDOCAINE (8 total), please visit the HSDB record page.

Hazardous Substances Data Bank (HSDB)

## 13.1.17 Populations at Special Risk

Although some manufacturers state that lidocaine is contraindicated in patients with Wolff-Parkinson-White syndrome, some clinicians have used the drug for the treatment of tachyarrhythmias in patients with this syndrome.

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 1696*

Hazardous Substances Data Bank (HSDB)

In general lidocaine should not be given to patients with hypovolemia, heart block or other conduction disturbances, and should be used with caution in patients with congestive heart failure, bradycardia, or respiratory depression. Lidocaine is metabolized in the liver and must be given with caution to patients with hepatic impairment. The plasma half life of lidocaine may be prolonged in conditions that reduce hepatic blood flow such as cardiac and circulatory failure. Metabolites of lidocaine may accumulate in patients with renal impairment.

*SWEETMAN, S.C. (ed.) Martindale-The Complete Drug Reference. 36th ed. London: The Pharmaceutical Press, 2009., p. 1863*

▸ **Hazardous Substances Data Bank (HSDB)**

...Although lidocaine usually has little effect on heart rate, patients with a diseased or abnormal sinus node may be especially sensitive to the cardiac depressant effects of the drug. Lidocaine may increase coronary blood flow in patients with recent myocardial infarction.

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 1697*

▸ **Hazardous Substances Data Bank (HSDB)**

### 13.1.18 Protein Binding

The protein binding recorded for lidocaine is about 60 to 80% and is dependent upon the plasma concentration of alpha-1-acid glycoprotein. Such percentage protein binding bestows lidocaine with a medium duration of action when placed in comparison to other local anesthetic agents.

▸ **DrugBank**

## 13.2 Ecological Information

### 13.2.1 Ecotoxicity Values

EC50; Species: Chlorella **fusca** var. vacuolata (Green Algae) strain 211-15; Conditions: freshwater, static, 25 °C, pH 9.5-10.0; Concentration: 459 uM for 24 hr (95% confidence interval: 158-1333 uM); Effect: decreased population growth rate /formulation/

*Neuwoehner J, Escher BI; Aquat Toxicol 101 (1): 266-275 (2011) as cited in the ECOTOX database. Available from, as of October 3, 2014*

▸ **Hazardous Substances Data Bank (HSDB)**

EC50; Species: Chlorella **fusca** var. vacuolata (Green Algae) strain 211-15; Conditions: freshwater, static, 25 °C, pH 9.0; Concentration: 545 uM for 24 hr (95% confidence interval: 244-1217 uM); Effect: decreased population growth rate /formulation/

*Neuwoehner J, Escher BI; Aquat Toxicol 101 (1): 266-275 (2011) as cited in the ECOTOX database. Available from, as of October 3, 2014*

▸ **Hazardous Substances Data Bank (HSDB)**

EC50; Species: Chlorella fusca var. vacuolata (Green Algae) strain 211-15; Conditions: freshwater, static, 25 °C, pH 6.5-7.2; Concentration: 575 uM for 24 hr (95% confidence interval: 52-6365 uM); Effect: decreased population growth rate /formulation/

*Neuwoehner J, Escher BI; Aquat Toxicol 101 (1): 266-275 (2011) as cited in the ECOTOX database. Available from, as of October 3, 2014*

▸ **Hazardous Substances Data Bank (HSDB)**

EC50; Species: Chlorella fusca var. vacuolata (Green Algae) strain 211-15; Conditions: freshwater, static, 25 °C, pH 8.5-8.6; Concentration: 608 uM for 24 hr (95% confidence interval: 272-1360 uM); Effect: decreased population growth rate /formulation/

*Neuwoehner J, Escher BI; Aquat Toxicol 101 (1): 266-275 (2011) as cited in the ECOTOX database. Available from, as of October 3, 2014*

▸ **Hazardous Substances Data Bank (HSDB)**

EC50; Species: Chlorella fusca var. vacuolata (Green Algae) strain 211-15; Conditions: freshwater, static, 25 °C, pH 7.5-7.9; Concentration: 686 uM for 24 hr (95% confidence interval: 158-2982 uM); Effect: decreased population growth rate /formulation/

*Neuwoehner J, Escher BI; Aquat Toxicol 101 (1): 266-275 (2011) as cited in the ECOTOX database. Available from, as of October 5, 2014*

▸ **Hazardous Substances Data Bank (HSDB)**

### 13.2.2 Environmental Fate / Exposure Summary

Lidocaine's production and administration as an anesthetic and cardiac medication may result in its release to the environment through various waste streams. If released to air, an estimated vapor pressure of 6.8X10-6 mm Hg at 25 °C indicates lidocaine will exist in both the vapor and particulate phases in the atmosphere. Vapor-phase lidocaine 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 1.2 hours. Particulate-phase lidocaine will be removed from the atmosphere by wet and dry deposition. Lidocaine contains chromophores that absorb at wavelengths >290 nm and, therefore, may be susceptible to direct photolysis by sunlight. If released to soil, lidocaine is expected to have moderate mobility based upon an estimated Koc of 400. The estimated pKa of lidocaine is 7.75, indicating that this compound will exist partially in the cation form in the environment and cations generally adsorb more strongly to soils containing organic carbon and clay than their neutral counterparts. Volatilization from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry's Law constant of 1.3X10-10 atm-cu m/mole. Lidocaine is not expected to volatilize from dry soil surfaces based upon its vapor pressure. Biodegradation data in soil or water were not available. If released into water, lidocaine is expected to adsorb to suspended solids and sediment based upon the estimated Koc. Volatilization of the neutral species from water surfaces is not expected to be an important fate process based upon this compound's estimated Henry's Law constant. An estimated BCF of 3 suggests the potential for bioconcentration in aquatic 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 (pH 5 to 9). Occupational exposure to lidocaine may occur through inhalation and dermal contact with this compound at

workplaces where lidocaine is produced or used. Limited monitoring data indicate that the general population may be exposed to lidocaine via ingestion and dermal contact with contaminated water. Use data indicate exposure may occur via administration as a medication and dermal contact with consumer products containing lidocaine. (SRC)

▸ Hazardous Substances Data Bank (HSDB)

### 13.2.3 Artificial Pollution Sources

Lidocaine's production and administration an anesthetic and cardiac medication(1) may result in its release to the environment through various waste streams(SRC).

*(1) O'Neil MJ, ed; The Merck Index. 15th ed., Cambridge, UK: Royal Society of Chemistry, p. 1019 (2013)*

▸ Hazardous Substances Data Bank (HSDB)

### 13.2.4 Environmental Fate

TERRESTRIAL FATE: Based on a classification scheme(1), an estimated Koc value of 400(SRC), determined from a structure estimation method(2), indicates that lidocaine is expected to have moderate mobility in soil(SRC). The estimated pKa of lidocaine is 7.5(3), indicating that this compound will exist partially in the cation form in the environment and cations generally adsorb more strongly to soils containing organic carbon and clay than their neutral counterparts(4). Volatilization of the neutral species of lidocaine from moist soil surfaces is not expected to be an important fate process(SRC) given an estimated Henry's Law constant of 1.3X10-10 atm-cu m/mole(SRC), using a fragment constant estimation method(5). Lidocaine is not expected to volatilize from dry soil surfaces(SRC) based upon an estimated vapor pressure of 6.8X10-6 mm Hg at 25 °C(SRC), determined from a fragment constant method(2). Biodegradation data in soil were not available(SRC, 2014).

*(1) Swann RL et al; Res Rev 85: 17-28 (1983)*

*(2) US EPA; Estimation Program Interface (EPI) Suite. Ver. 4.1. Nov, 2012. Available from, as of Aug 26, 2014:* ***https://www.epa.gov/oppt/exposure/pubs/episuitedl.htm***

*(3) Royal Soc Chem; ChemSpider. Lignocaine. (137-58-6). Available from, as of Aug 25, 2014:* ***https://www.chemspider.com/Search.aspx***

*(4) Doucette WJ; pp. 141-188 in Handbook of Property Estimation Methods for Chemicals. Boethling RS, Mackay D, eds. Boca Raton, FL: Lewis Publ (2000)*

*(5) Meylan WM, Howard PH; Environ Toxicol Chem 10: 1283-93 (1991)*

▸ Hazardous Substances Data Bank (HSDB)

AQUATIC FATE: Based on a classification scheme(1), an estimated Koc value of 400(SRC), determined from a structure estimation method(2), indicates that lidocaine is expected to adsorb to suspended solids and sediment(SRC). Volatilization from water surfaces is not expected(3) based upon an estimated Henry's Law constant of 1.3X10-10 atm-cu m/mole(SRC), developed using a fragment constant estimation method(4). According to a classification scheme(5), an estimated BCF of 3(SRC), from its log Kow of 2.4467) and a regression-derived equation(2), suggests the potential for bioconcentration in aquatic organisms is low(SRC). Half-lives of 0.4 and 1.3 days for laboratory (Hg lamp) and field (natural sunlight), respectively, have been reported in river water media, which take

into account photodegradation and biotic degradation(7). Biodegradation data in water were not available(SRC, 2014).


*(1) Swann RL et al; Res Rev 85: 17-28 (1983)*

*(2) US EPA; Estimation Program Interface (EPI) Suite. Ver. 4.1. Nov, 2012. Available from, as of Aug 26, 2014: https://www.epa.gov/oppt/exposure/pubs/episuitedl.htm*

*(3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 15-1 to 15-29 (1990)*

*(4) Meylan WM, Howard PH; Environ Toxicol Chem 10: 1283-93 (1991)*

*(5) Franke C et al; Chemosphere 29: 1501-14 (1994)*

*(6) 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. 126 (1995)*

*(7) Rua-Gomez PC, Putnam W; Chemosphere 90: 1952-9 (2013)*


▸ **Hazardous Substances Data Bank (HSDB)**

ATMOSPHERIC FATE: According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere(1), lidocaine, which has an estimated vapor pressure of 6.8X10-6 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 lidocaine 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 1.2 hours(SRC), calculated from its rate constant of 1.1X10-10 cu cm/molecule-sec at 25 °C(SRC) that was derived using a structure estimation method(3). Particulate-phase lidocaine may be removed from the air by wet and dry deposition(SRC). Lidocaine contains chromophores that absorb at wavelengths >290 nm(4) and, therefore, may be susceptible to direct photolysis by sunlight(SRC).


*(1) Bidleman TF; Environ Sci Technol 22: 361-367 (1988)*

*(2) US EPA; Estimation Program Interface (EPI) Suite. Ver. 4.1. Nov, 2012. Available from, as of Aug 26, 2014: https://www.epa.gov/oppt/exposure/pubs/episuitedl.htm*

*(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)**

## 13.2.5 Environmental Biodegradation

AEROBIC: Half-lives of 92 and 110 days for laboratory and field experiments, respectively, have been reported using water collected from the river Nidda in Bad Vilbel, Germany; this river previously had been reported as receiving treated wastewater with high concentrations of lidocaine(1).


*(1) Rua-Gomez PC, Putnam W; Chemosphere 90(6): 1952-9 (2013)*


▸ **Hazardous Substances Data Bank (HSDB)**

## 13.2.6 Environmental Abiotic Degradation

The rate constant for the vapor-phase reaction of lidocaine with photochemically-produced hydroxyl radicals has been estimated as 1.1X10-10 cu cm/molecule-sec at 25 °C(SRC) using a structure estimation method(1). This corresponds to an atmospheric half-life of about 1.2 hours at an atmospheric concentration of 5X10+5 hydroxyl radicals per cu cm(1). Lidocaine is not expected to undergo hydrolysis in the environment due to the lack of functional groups that hydrolyze under environmental conditions(2). Lidocaine contains chromophores that absorb at wavelengths >290 nm(2) and, therefore, may be susceptible to direct photolysis by sunlight(SRC). Photodegradation half-lives have been measured using **water** from the river Nidda in Bad Vilbel, Germany; this river previously had been reported as receiving treated wastewater with high concentrations of lidocaine(3).

Table: Lidocaine (25 mg/L) photodegradation half-lives (days)(3)

| Media | Mercury lamp (200-350 nm) | Sunlight |
|---|---|---|
| Ultrapure water | 29.5 | 65.5 |
| Natural river water (pH 7.5) | 10.7 hours | 1.3 |
| Steril control | 17.3 hours | 1.7 |

*(1) Meylan WM, Howard PH; Chemosphere 26: 2293-99 (1993)*

*(2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 7-4, 7-5, 8-12 (1990)*

*(3) Rua-Gomez PC, Putnam W; Chemosphere 90(6): 1952-9 (2013)*

▸ **Hazardous Substances Data Bank (HSDB)**

PURPOSE: Some of the pharmaceuticals that are not extensively investigated in the aquatic environment are the anesthetic lidocaine (LDC), the analgesic **tramadol** (TRA), and the antidepressant **venlafaxine** (VEN). LDC metabolizes to **2,6-xylidine** (**2,6-DMA**) and monoethylglycinexylidine (**MEGX**), TRA to **O-desmethyltramadol** (ODT), and VEN to **O-desmethylvenlafaxine** (ODV). Within this study, the distribution and behavior of these compounds in German wastewater treatment plants (WWTPs) were investigated. METHODS: Samples of influents and effluents from WWTPs in Hesse, Germany were collected between January and September 2010. Analytes were extracted from wastewater samples by solid-phase extraction and from solid samples by sonication. Extracts were measured using gas chromatography/mass spectrometry. RESULTS: DC, TRA, VEN, ODT, and ODV were detected in all analyzed influent and effluent samples. **2,6-DMA** could not be identified. **MEGX** was not detected. TRA and ODV were present in untreated wastewater at the highest concentrations (max, 1,129 (TRA) and 3,302 ng/L (ODV)), while the concentrations of LDC and VEN were all significantly lower (mean, 135 (LDC) and 116 ng/L (VEN)). All of the analytes were only partially removed in the WWTPs. The mean ratios between the concentrations of the metabolites and their respective parent compounds in influents were 4.7 (ODV/VEN) and 0.7 (ODT/TRA). These values remain approximately constant comparing influents and effluents. CONCLUSIONS: LDC, TRA, VEN, ODT, and ODV are only partially removed from sewage **water** by WWTPs and thus are continuously discharged in respective recipient rivers. A further transformation of TRA and VEN into the known metabolites during treatment in the WWTPs is not observed.

***PMID:21909967***

*Rua-Gomez, Putnam W; Environ Sci Pollut Res 19(3): 689-99 (2012)*

▸ Hazardous Substances Data Bank (HSDB)

## 13.2.7 Environmental Bioconcentration

An estimated BCF of 3 was calculated in fish for lidocaine(SRC), using a log Kow of 2.44(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. 126 (1995)*

*(2) US EPA; Estimation Program Interface (EPI) Suite. Ver. 4.1. Nov, 2012. Available from, as of Aug 26, 2014:* ***https://www.epa.gov/oppt/exposure/pubs/episuitedl.htm/***

*(3) Franke C et al; Chemosphere 29: 1501-14 (1994)*

▸ Hazardous Substances Data Bank (HSDB)

## 13.2.8 Soil Adsorption / Mobility

Using a structure estimation method based on molecular connectivity indices(1), the Koc of lidocaine can be estimated to be 400(SRC). According to a classification scheme(2), this estimated Koc value suggests that lidocaine is expected to have moderate mobility in soil. The estimated pKa of lidocaine is 7.75(3), indicating that this compound will exist partially in the cation form in the environment and cations generally adsorb more strongly to soils containing organic **carbon** and clay than their neutral counterparts(4).

*(1) US EPA; Estimation Program Interface (EPI) Suite. Ver. 4.1. Nov, 2012. Available from, as of Aug 26, 2014:* ***https://www.epa.gov/oppt/exposure/pubs/episuitedl.htm***

*(2) Swann RL et al; Res Rev 85: 17-28 (1983)*

*(3) Royal Soc Chem; ChemSpider. Lignocaine. (137-58-6). Available from, as of Aug 25, 2014:* ***https://www.chemspider.com/Search.aspx***

*(4) Doucette WJ; pp. 141-188 in Handbook of Property Estimation Methods for Chemicals. Boethling RS, Mackay D, eds. Boca Raton, FL: Lewis Publ (2000)*

▸ Hazardous Substances Data Bank (HSDB)

## 13.2.9 Volatilization from Water / Soil

The Henry's Law constant for the neutral species of lidocaine is estimated as 1.3X10-10 atm-cu m/mole(SRC) using a fragment constant estimation method(1). This Henry's Law constant indicates that lidocaine is expected to be essentially nonvolatile from **water** and moist soil surfaces(2). Lidocaine is not expected to volatilize from dry soil surfaces(SRC) based upon an estimated vapor pressure of 6.8X10-6 mm Hg(SRC), determined from a fragment constant method(3).

*(1) Meylan WM, Howard PH; Environ Toxicol Chem 10: 1283-93 (1991)*

*(2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 15-1 to 15-29 (1990)*

*(3) US EPA; Estimation Program Interface (EPI) Suite. Ver. 4.1. Nov, 2012. Available from, as of Aug 26, 2104: **https://www.epa.gov/oppt/exposure/pubs/episuitedl.htm***

▸ **Hazardous Substances Data Bank (HSDB)**

## 13.2.10 Environmental Water Concentrations

SURFACE **WATER**: Lidocaine was present at a range of 0.6 to 15 ng/L in surface **water** of the Netherlands, sampled between 1996 and 2005. Concentrations of 100 to 1.0X10+5 ng/L were reported in Netherlands industrial waste waters sampled in 2002(1). It has been reported in German surface **water** samples at concentrations ranging from <16 to 176 ng/L(2).

*(1) Walraven N, Laane RWPM; Rev Environ Contam Toxicol 199: 1-18 (2008)*

*(2) Rua-Gomez PC, Putnam W; Chemosphere 90(6): 1952-9 (2013)*

▸ **Hazardous Substances Data Bank (HSDB)**

## 13.2.11 Effluent Concentrations

Lidocaine was present at a range of 16 to 102 ng/L in sewage **water** effluents of the Netherlands, sampled in 2002(1).

*(1) Walraven N, Laane RWPM; Rev Environ Contam Toxicol 199: 1-18 (2008)*

▸ **Hazardous Substances Data Bank (HSDB)**

## 13.2.12 Milk Concentrations

EXPERIMENTAL: Lidocaine ... is distributed into milk; in one lactating woman, milk lidocaine concentration was approximately 40% of the serum concentration (from a sample obtained 2 hours earlier).

*American Society of Health-System Pharmacists 2014; Drug Information 2014. Bethesda, MD. 2014, p. 1697*

▸ **Hazardous Substances Data Bank (HSDB)**

EXPERIMENTAL: ... The purpose of this study is to determine the amount of lidocaine and its metabolite **monoethyl-glycinexylidide** (**MEGX**) in breast milk after local anesthesia during dental procedures. The study population consisted of seven nursing mothers (age, 23-39 years) who received 3.6 to 7.2 mL 2% lidocaine without **adrenaline**. Blood and milk concentrations of lidocaine and its metabolite **MEGX** were assayed using high-performance liquid chromatography. The milk-to-plasma ratio and the possible daily doses in infants for both lidocaine and **MEGX** were calculated. The lidocaine concentration in maternal plasma 2 hours after injection was 347.6 +/- 221.8 ug/L, the lidocaine concentration in maternal milk ranged from 120.5 +/- 54.1 ug/L (3 hours after injection) to 58.3 +/- 22.8 ug/L (6 hours after injection), the **MEGX** concentration in maternal plasma 2 hours after injection was 58.9 +/- 30.3 ug/L, and the **MEGX** concentration in maternal milk ranged from 97.5 +/- 39.6 ug/L (3 hours after injection) to 52.7 +/- 23.8 ug/L (6 hours after injection). According to these data and considering an intake of 90 mL breast milk every 3 hours, the daily infant dosages of lidocaine and **MEGX** were 73.41 +/- 38.94 ug/L/day and 66.1 +/- 28.5 ug/L/day respectively. ...

PMID:11321382

*Giuliani M et al; J Pediatr Gastroenterol Nutr. 32(2):142-4. (2001).*

▸ Hazardous Substances Data Bank (HSDB)

### 13.2.13 Probable Routes of Human Exposure

NIOSH (NOES Survey 1981-1983) has statistically estimated that 51,880 workers (43,813 of these were female) were potentially exposed to lidocaine in the US(1). Occupational exposure to lidocaine may occur through inhalation and dermal contact with this compound at workplaces where lidocaine is produced or used. Limited monitoring data indicate that the general population may be exposed to lidocaine via ingestion and dermal contact with contaminated **water**. Use data indicate exposure may occur via administration as a medication and dermal contact with consumer products containing lidocaine(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 Aug 25, 2104:* ***https://www.cdc.gov/noes/***

▸ Hazardous Substances Data Bank (HSDB)

### 13.2.14 Body Burden

Lidocaine ... is distributed into milk; in one lactating women, milk lidocaine concentration was approximately 40% of the serum concentration (from a sample obtained 2 hours earlier).

*McEvoy, G.K. (ed.). American Hospital Formulary Service - Drug Information 92. Bethesda, MD: American Society of Hospital Pharmacists, Inc., 1992 (Plus Supplements 1992)., p. 295*

▸ Hazardous Substances Data Bank (HSDB)

## 14 Associated Disorders and Diseases

▸ Comparative Toxicogenomics Database (CTD); Open Targets; Therapeutic Target Database (TTD)

| Disease | References |
| --- | --- |
| Colorectal cancer | PubMed: 7482520, 22148915, 19006102, 23940645, 24424155, 20156336, 19678709, 25105552, 21773981, 25037050, 27015276, 27107423, 27275383, 28587349<br>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 |

▸ Human Metabolome Database (HMDB)

# 15 Literature

## 15.1 Consolidated References

▸ PubChem

## 15.2 NLM Curated PubMed Citations

PubChem

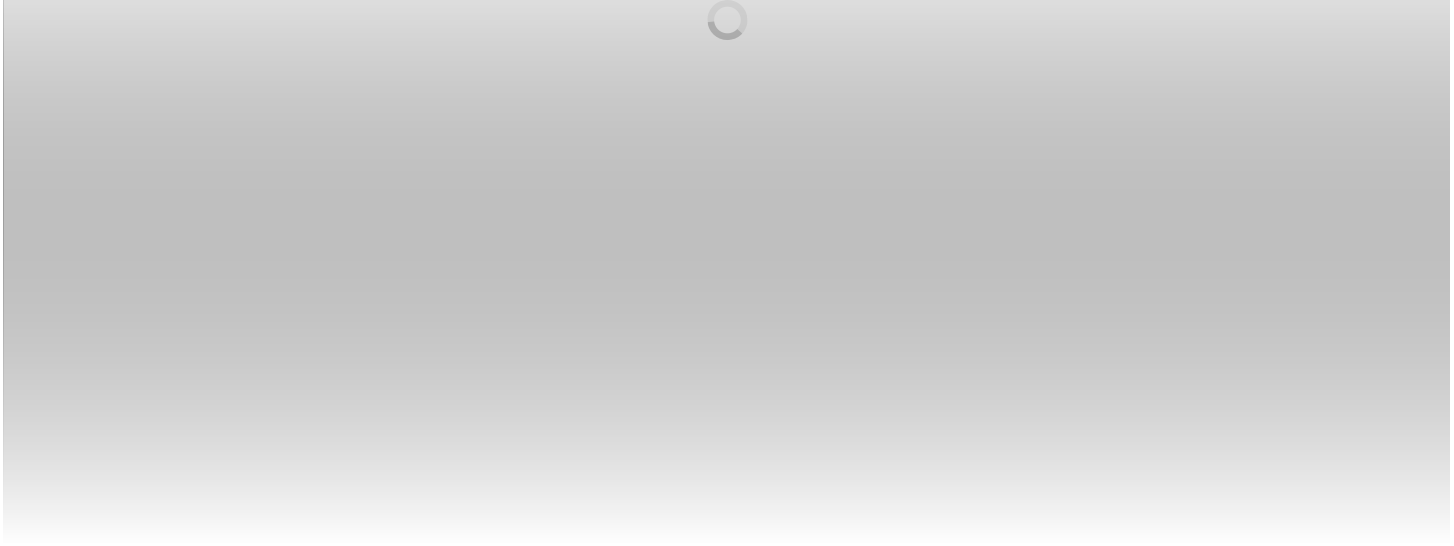
## 15.3 Springer Nature References

Springer Nature

## 15.4 Thieme References

Thieme Chemistry

## 15.5 Wiley References



Wiley

## 15.6 Nature Journal References

Feng et al. Small-molecule aggregates inhibit amyloid polymerization Nature Chemical Biology, doi: 10.1038/nchembio.65, published online 27 January 2008.
http://www.nature.com/naturechemicalbiology

Nature Chemical Biology

## 15.7 Chemical Co-Occurrences in Literature

PubChem

## 15.8 Chemical-Gene Co-Occurrences in Literature

PubChem

## 15.9 Chemical-Disease Co-Occurrences in Literature

PubChem

## 16 Patents

US5234957
US5827529
US8540665
US6881200
US6004286
US5899880
US6031007
US6629968
US6635045
US6546281
US5658583
US6465006
US6465709
US6780426
US6306431
US5919479
US6528086
US8759401
US9370622
US9358338
US9283174
US9925264
US9931403
US10350180
US10603293
US10765640
US10765749
US10751305
US11278623
US11786455
US11793766

DrugBank

## 16.1 Depositor-Supplied Patent Identifiers

PubChem

Link to all deposited patent identifiers

PubChem

## 16.2 WIPO PATENTSCOPE

Patents are available for this chemical structure:

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

PATENTSCOPE (WIPO)

## 16.3 FDA Orange Book Patents

FDA Orange Book

## 16.4 Chemical Co-Occurrences in Patents

PubChem

## 16.5 Chemical-Disease Co-Occurrences in Patents

PubChem

## 16.6 Chemical-Gene Co-Occurrences in Patents

PubChem

## 17 Interactions and Pathways

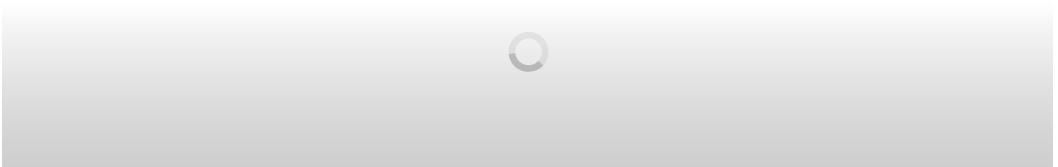
### 17.1 Protein Bound 3D Structures

RCSB Protein Data Bank (RCSB PDB)

View 3 proteins in NCBI Structure

PubChem

#### 17.1.1 Ligands from Protein Bound 3D Structures

| | |
|---|---|
| PDBe Ligand Code | LQZ |
| PDBe Structure Code | 3JQZ |
| PDBe Conformer |  |

Protein Data Bank in Europe (PDBe)

## 17.2 Chemical-Target Interactions

Comparative Toxicogenomics Database (CTD); Drug Gene Interaction database (DGIdb); IUPHAR/BPS Gui…

DrugBank

## 17.3 Drug-Drug Interactions

DrugBank

## 17.4 Pathways

PubChem

# 18 Biological Test Results

## 18.1 BioAssay Results

PubChem

## 19 Taxonomy

*A metabolome atlas of the aging mouse brain. Nat Commun. 2021 Oct 15;12(1):6021.* ***DOI:10.1038/s41467-021-26310-y****.* ***PMID:34654818****;* ***PMCID:PMC8519999****.*

*The Metabolome Atlas of the Aging Mouse Brain:* ***https://mouse.atlas.metabolomics.us***

West Coast Metabolomics Center-UC Davis

## 20 Classification

### 20.1 MeSH Tree

Medical Subject Headings (MeSH)

## 20.2 NCI Thesaurus Tree

NCI Thesaurus (NCIt)

## 20.3 ChEBI Ontology

ChEBI

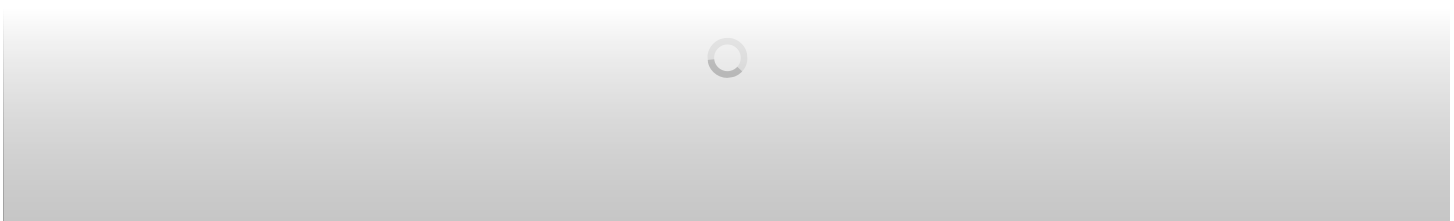
## 20.4 KEGG: Drug

KEGG

## 20.5 KEGG: USP

KEGG

## 20.6 KEGG: ATC



KEGG

## 20.7 KEGG: Target-based Classification of Drugs

KEGG

## 20.8 KEGG: JP15

KEGG

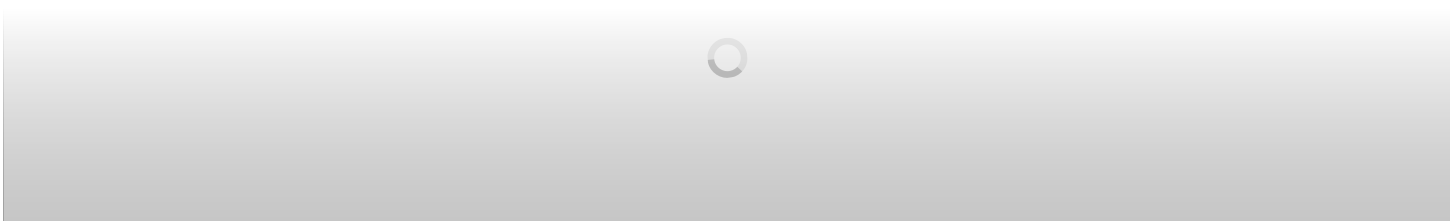
## 20.9 KEGG: Risk Category of Japanese OTC Drugs

KEGG

## 20.10 KEGG: OTC drugs

KEGG

## 20.11 KEGG: Drug Groups



KEGG

## 20.12 KEGG: Drug Classes

KEGG

## 20.13 WHO ATC Classification System

WHO Anatomical Therapeutic Chemical (ATC) Classification

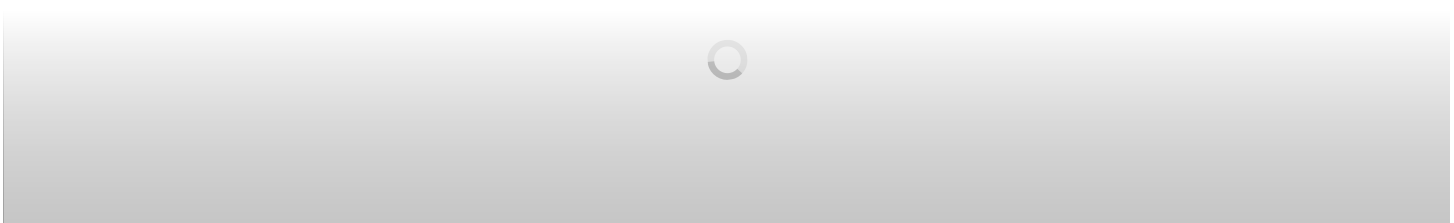
## 20.14 FDA Pharm Classes

FDA Pharm Classes

## 20.15 ChemIDplus

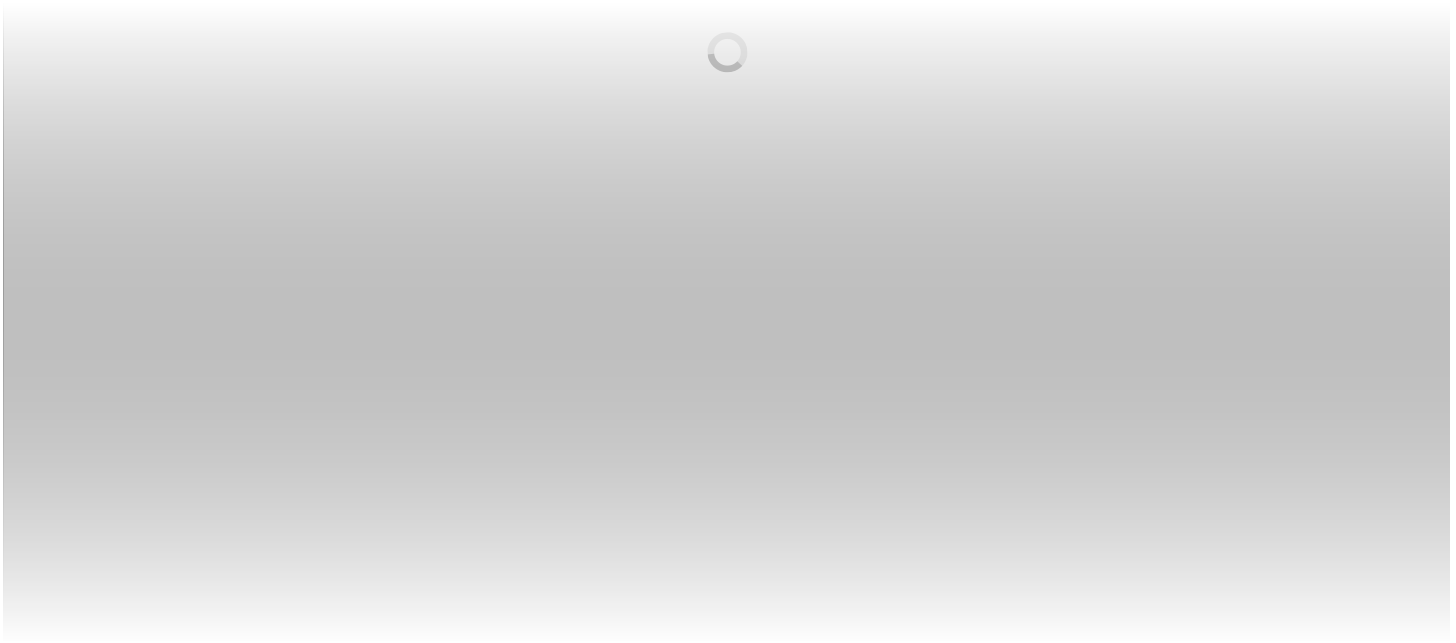
ChemIDplus

## 20.16 IUPHAR / BPS Guide to PHARMACOLOGY Target Classification



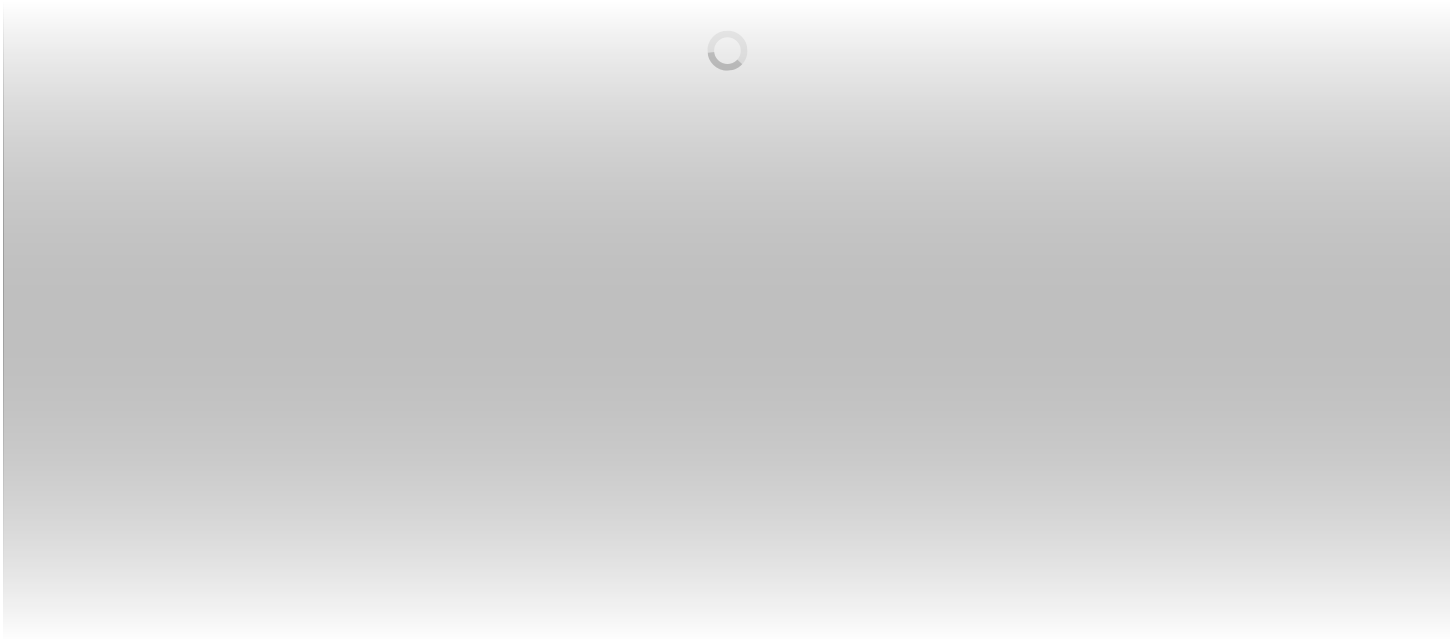
▸ IUPHAR/BPS Guide to PHARMACOLOGY

## 20.17 ChEMBL Target Tree



▸ ChEMBL

## 20.18 UN GHS Classification



GHS Classification (UNECE)

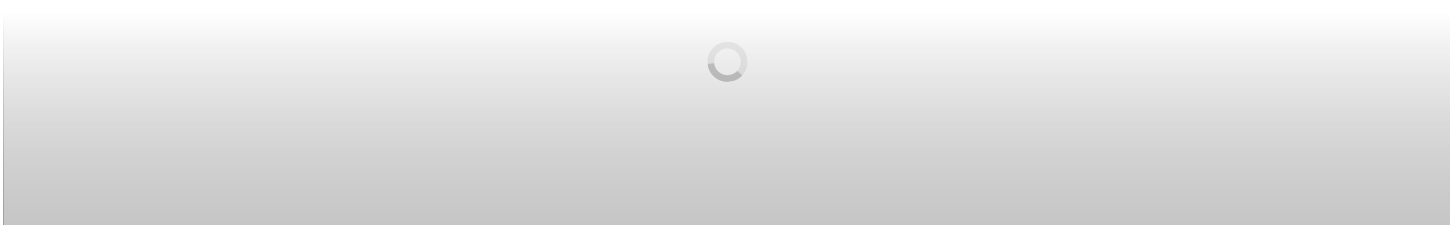
## 20.19 EPA CPDat Classification

EPA Chemical and Products Database (CPDat)

## 20.20 NORMAN Suspect List Exchange Classification

NORMAN Suspect List Exchange

## 20.21 CCSBase Classification



CCSbase

## 20.22 EPA DSSTox Classification

EPA DSSTox

## 20.23 EPA TSCA and CDR Classification

EPA Chemicals under the TSCA

## 20.24 FDA Drug Type and Pharmacologic Classification

National Drug Code (NDC) Directory

## 20.25 EPA Substance Registry Services Tree

EPA Substance Registry Services

# 21 Information Sources

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ALL SOURCES

1. Australian Industrial Chemicals Introduction Scheme (AICIS)

**LICENSE**
https://www.industrialchemicals.gov.au/copyright

*Acetamide, 2-(diethylamino)-N-(2,6-dimethylphenyl)-*

***https://services.industrialchemicals.gov.au/search-assessments/***

## 2. CAS Common Chemistry

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*Lidocaine*

***https://commonchemistry.cas.org/detail?cas_rn=137-58-6***

## 3. ChemIDplus

**LICENSE**
https://www.nlm.nih.gov/copyright.html

*Lidocaine [USP:INN:BAN:JAN]*

***https://pubchem.ncbi.nlm.nih.gov/substance/?source=chemidplus&sourceid=0000137586***

*ChemIDplus Chemical Information Classification*

***https://pubchem.ncbi.nlm.nih.gov/source/ChemIDplus***

## 4. DrugBank

**LICENSE**
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https://www.drugbank.ca/legal/terms_of_use

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***https://www.drugbank.ca/drugs/DB00281***

## 5. DTP/NCI

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***https://dtp.cancer.gov/dtpstandard/servlet/dwindex?searchtype=NSC&outputformat=html&searchlist=40030***

## 6. EPA Chemicals under the TSCA

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https://www.epa.gov/privacy/privacy-act-laws-policies-and-resources

*Acetamide, 2-(diethylamino)-N-(2,6-dimethylphenyl)-*

***https://www.epa.gov/chemicals-under-tsca***

*EPA TSCA Classification*

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

## 7. EPA DSSTox

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*https://comptox.epa.gov/dashboard/DTXSID1045166*

*CompTox Chemicals Dashboard Chemical Lists*

*https://comptox.epa.gov/dashboard/chemical-lists/*

## 8. European Chemicals Agency (ECHA)



*Lidocaine*

*https://chem.echa.europa.eu/100.004.821*

*Lidocaine (EC: 205-302-8)*

*https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/14913*

*2-(Diethylamino)-N-(2,6-dimethylphenyl)acetamide (EC: 684-578-5)*

*https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/215042*

*2-(Diethylamino)-N-(2,6-dimethylphenyl)acetamide*

*https://echa.europa.eu/substance-information/-/substanceinfo/100.210.025*

## 9. FDA Global Substance Registration System (GSRS)



*LIDOCAINE*

*https://gsrs.ncats.nih.gov/ginas/app/beta/substances/98PI200987*

## 10. Hazardous Substances Data Bank (HSDB)



*LIDOCAINE*

*https://pubchem.ncbi.nlm.nih.gov/source/hsdb/3350*

## 11. Human Metabolome Database (HMDB)



*Lidocaine*

*http://www.hmdb.ca/metabolites/HMDB0014426*

*HMDB0014426_nmr_one_2235*

*https://hmdb.ca/metabolites/HMDB0014426#spectra*

## 12. New Zealand Environmental Protection Authority (EPA)

*Lidocaine*

***https://www.epa.govt.nz/industry-areas/hazardous-substances/guidance-for-importers-and-manufacturers/hazardous-substances-databases/***

## 13. Burnham Center for Chemical Genomics

*SID855682*

***https://pubchem.ncbi.nlm.nih.gov/bioassay/1996#section=Data-Table***

## 14. CCSbase

*CCSbase Classification*

***https://ccsbase.net/***

## 15. NORMAN Suspect List Exchange



*lidocaine*

*NORMAN Suspect List Exchange Classification*

***https://www.norman-network.com/nds/SLE/***

## 16. ChEBI

*Lidocaine*

***https://www.ebi.ac.uk/chebi/searchId.do?chebiId=CHEBI:6456***

*ChEBI Ontology*

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

## 17. FDA Pharm Classes



*LIDOCAINE*

***https://dailymed.nlm.nih.gov/dailymed/browse-drug-classes.cfm***

*FDA Pharmacological Classification*

***https://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/ucm162549.htm***

## 18. NCI Thesaurus (NCIt)



***https://ncithesaurus.nci.nih.gov/ncitbrowser/ConceptReport.jsp?dictionary=NCI_Thesaurus&ns=ncit&code=C614***

*NCI Thesaurus*

***https://ncit.nci.nih.gov***

## 19. Open Targets

**LICENSE**
Datasets generated by the Open Targets Platform are freely available for download.
https://platform-docs.opentargets.org/licence

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***https://platform.opentargets.org/drug/CHEMBL79***

## 20. Toxin and Toxin Target Database (T3DB)

**LICENSE**
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http://www.t3db.ca/downloads

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***http://www.t3db.ca/toxins/T3D2735***

## 21. ChEMBL

**LICENSE**
Access to the web interface of ChEMBL is made under the EBI's Terms of Use (http://www.ebi.ac.uk/Information/termsofuse.html). The ChEMBL data is made available on a Creative Commons Attribution-Share Alike 3.0 Unported License (http://creativecommons.org/licenses/by-sa/3.0/).
http://www.ebi.ac.uk/Information/termsofuse.html

***https://www.ebi.ac.uk/chembl/compound_report_card/CHEMBL79/***

*ChEMBL Protein Target Tree*

***https://www.ebi.ac.uk/chembl/g/#browse/targets***

## 22. ClinicalTrials.gov

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https://clinicaltrials.gov/ct2/about-site/terms-conditions#Use

***https://clinicaltrials.gov/***

## 23. Comparative Toxicogenomics Database (CTD)

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http://ctdbase.org/about/legal.jsp

*heparin-dihydergot*

***https://ctdbase.org/detail.go?type=chem&acc=C031388***

*Lidoderm*

***https://ctdbase.org/detail.go?type=chem&acc=C511998***

*Lidocaine*

***https://ctdbase.org/detail.go?type=chem&acc=D008012***

## 24. Therapeutic Target Database (TTD)

*Lidocaine*

***https://idrblab.net/ttd/data/drug/details/D0X4RN***

## 25. Drug Gene Interaction database (DGIdb)

**LICENSE**
The data used in DGIdb is all open access and where possible made available as raw data dumps in the downloads section.
http://www.dgidb.org/downloads

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***https://www.dgidb.org/drugs/rxcui:6387***

*CFT1946*

***https://www.dgidb.org/drugs/iuphar.ligand:12623***

## 26. IUPHAR/BPS Guide to PHARMACOLOGY

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https://www.guidetopharmacology.org/about.jsp#license

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***https://www.guidetopharmacology.org/GRAC/LigandDisplayForward?ligandId=2623***

*Guide to Pharmacology Target Classification*

***https://www.guidetopharmacology.org/targets.jsp***

## 27. Crystallography Open Database (COD)

**LICENSE**
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https://creativecommons.org/publicdomain/zero/1.0/

## 28. DailyMed

**LICENSE**
https://www.nlm.nih.gov/copyright.html

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***https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=all&query=LIDOCAINE***

*XYLOCAINE*

***https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=all&query=XYLOCAINE***

## 29. Drug Induced Liver Injury Rank (DILIrank) Dataset

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https://www.fda.gov/about-fda/about-website/website-policies#linking

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

## 30. Drugs and Lactation Database (LactMed)

**LICENSE**
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***https://www.ncbi.nlm.nih.gov/books/n/lactmed/LM363/***

## 31. Mother To Baby Fact Sheets



*lidocaine*

***https://www.ncbi.nlm.nih.gov/books/n/mtb/lidocaine-en/***

## 32. Drugs@FDA



*ZTLIDO*

***https://www.accessdata.fda.gov/scripts/cder/daf/***

## 33. WHO Model Lists of Essential Medicines



*Lidocaine*

***https://list.essentialmeds.org/medicines/8***

## 34. EPA Chemical and Products Database (CPDat)



***https://comptox.epa.gov/dashboard/DTXSID1045166#exposure***

*EPA CPDat Classification*

***https://www.epa.gov/chemical-research/chemical-and-products-database-cpdat***

## 35. EU Clinical Trials Register

***https://www.clinicaltrialsregister.eu/***

## 36. NITE-CMC

*Lidocaine - FY2011 (New/original classication)*

***https://www.nite.go.jp/chem/english/ghs/11-mhlw-0127e.html***

## 37. FDA Approved Animal Drug Products (Green Book)



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***https://www.fda.gov/animal-veterinary/products/approved-animal-drug-products-green-book***

## 38. FDA Orange Book

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***https://www.fda.gov/drugs/drug-approvals-and-databases/approved-drug-products-therapeutic-equivalence-evaluations-orange-book***

## 39. National Drug Code (NDC) Directory



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

## 40. SpectraBase

*2-(diethylamino)-2,6-acetoxylidine*

***https://spectrabase.com/spectrum/2B8pWzMXpVA***

*2-(DIETHYLAMINO)-2,6-ACETOXYLIDIDE*

***https://spectrabase.com/spectrum/2Jh7eSn4BPE***

*A-Diethylamino-2,6-dimethyl-acetanilide*

***https://spectrabase.com/spectrum/KJXn9QDHSwz***

*Lidocaine*

***https://spectrabase.com/spectrum/TmJ9eANUOp***

*Lidocaine*

***https://spectrabase.com/spectrum/1BW5fJOXXIF***

*Lidocaine (free base)*

***https://spectrabase.com/spectrum/I64oA7fcJph***

*Lidocaine*

***https://spectrabase.com/spectrum/8VK60SQQsm***

*2-(DIETHYLAMINO)-2',6'-ACETOXYLIDIDE*

***https://spectrabase.com/spectrum/wayCN0SGfX***

## 41. NIST Mass Spectrometry Data Center



*Lignocaine*

***http://www.nist.gov/srd/nist1a.cfm***

## 42. Japan Chemical Substance Dictionary (Nikkaji)

***http://jglobal.jst.go.jp/en/redirect?Nikkaji_No=J5.631F***

## 43. KEGG

*https://www.kegg.jp/entry/C07073*

*https://www.kegg.jp/entry/D00358*

*Therapeutic category of drugs in Japan*
*http://www.genome.jp/kegg-bin/get_htext?br08301.keg*

*USP drug classification*
*http://www.genome.jp/kegg-bin/get_htext?br08302.keg*

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

*Target-based classification of drugs*
*http://www.genome.jp/kegg-bin/get_htext?br08310.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*

*Classification of Japanese OTC drugs*
*http://www.genome.jp/kegg-bin/get_htext?br08313.keg*

*Drug Groups*
*http://www.genome.jp/kegg-bin/get_htext?br08330.keg*

*Drug Classes*
*http://www.genome.jp/kegg-bin/get_htext?br08332.keg*

## 44. Kruve Lab, Ionization & Mass Spectrometry, Stockholm University

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## 45. MassBank Europe

> **LICENSE**
> https://github.com/MassBank/MassBank-web/blob/main/MassBank-Project/LICENSE.txt

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*https://massbank.eu/MassBank/Result.jsp?inchikey=NNJVILVZKWQKPM-UHFFFAOYSA-N*

## 46. MassBank of North America (MoNA)

> **LICENSE**
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> https://mona.fiehnlab.ucdavis.edu/documentation/license

*Lidocaine*
*https://mona.fiehnlab.ucdavis.edu/spectra/browse?*
*query=exists(compound.metaData.name:%27InChIKey%27%20and%20compound.metaData.value:%27NNJVILVZKWQKPM-UHFFFAOYSA-N%27)*

## 47. Metabolomics Workbench

*Lidocaine*
*https://www.metabolomicsworkbench.org/data/StructureData.php?RegNo=42673*

## 48. Nature Chemical Biology

*https://pubchem.ncbi.nlm.nih.gov/substance/46499871*

## 49. NIPH Clinical Trials Search of Japan

*https://rctportal.niph.go.jp/en/*

## 50. NLM RxNorm Terminology



*lidocaine*

*https://rxnav.nlm.nih.gov/id/rxnorm/6387*

## 51. WHO Anatomical Therapeutic Chemical (ATC) Classification



*Lidocaine*

*https://www.whocc.no/atc_ddd_index/?code=S02DA01*

*Lidocaine*

*https://www.whocc.no/atc_ddd_index/?code=R02AD02*

*Lidocaine*

*https://www.whocc.no/atc_ddd_index/?code=C01BB01*

*Lidocaine*

*https://www.whocc.no/atc_ddd_index/?code=C05AD01*

*Lidocaine*

*https://www.whocc.no/atc_ddd_index/?code=N01BB02*

*Lidocaine*

*https://www.whocc.no/atc_ddd_index/?code=S01HA07*

*Lidocaine*

*https://www.whocc.no/atc_ddd_index/?code=D04AB01*

*ATC Code*

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

## 52. PharmGKB



*lidocaine*

*https://www.pharmgkb.org/chemical/PA450226*

## 53. Pharos



*lidocaine*

*https://pharos.nih.gov/ligands/8NFQNG6H36UD*

## 54. Protein Data Bank in Europe (PDBe)

*http://www.ebi.ac.uk/pdbe-srv/pdbechem/chemicalCompound/show/LQZ*

## 55. RCSB Protein Data Bank (RCSB PDB)



*https://www.rcsb.org/*

## 56. Springer Nature

*https://pubchem.ncbi.nlm.nih.gov/substance/?source=15745&sourceid=17045077-838876556*

## 57. SpringerMaterials

*Acetamide, 2-(diethylamino)-N-(2,6-dimethylphenyl)-*

*https://materials.springer.com/substanceprofile/docs/smsid_iasanilfftfecrpn*

## 58. The Cambridge Structural Database

*https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=636633*

## 59. Thieme Chemistry



*https://pubchem.ncbi.nlm.nih.gov/substance/?source=22163&sourceid=17045077-838876556*

## 60. USGS Health-Based Screening Levels for Evaluating Water-Quality Data



*Lidocaine*

*https://water.usgs.gov/water-resources/hbsl/index.html*

## 61. West Coast Metabolomics Center-UC Davis

*Lidocaine*

## 62. Wikidata



*lidocaine*

*https://www.wikidata.org/wiki/Q216935*

## 63. Wikipedia

*Lidocaine*

*https://en.wikipedia.org/wiki/Lidocaine*

## 64. Wiley

*https://pubchem.ncbi.nlm.nih.gov/substance/?source=wiley&sourceid=7398*

## 65. Medical Subject Headings (MeSH)



*Lidocaine*
***https://www.ncbi.nlm.nih.gov/mesh/68008012***

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

*Voltage-Gated Sodium Channel Blockers*
***https://www.ncbi.nlm.nih.gov/mesh/68061567***

*Anti-Arrhythmia Agents*
***https://www.ncbi.nlm.nih.gov/mesh/68000889***

*Anesthetics, Local*
***https://www.ncbi.nlm.nih.gov/mesh/68000779***

## 66. PubChem

***https://pubchem.ncbi.nlm.nih.gov***

## 67. GHS Classification (UNECE)

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

## 68. EPA Substance Registry Services



*EPA SRS List Classification*
***https://sor.epa.gov/sor_internet/registry/substreg/LandingPage.do***

## 69. PATENTSCOPE (WIPO)

*SID 403383613*
***https://pubchem.ncbi.nlm.nih.gov/substance/403383613***

## 70. NCBI

***https://www.ncbi.nlm.nih.gov/projects/linkout***