« Synapt G2 LC/MS »

Preparing the samples

1. Prepare the following samples:

Table 3: Sample composition

Sample	Composition
Blank	10:90 acetonitrile:water
Test Mixture	M.W. ~~acetaminophen~~ (151) caffeine (194) sulfadimethoxine (310) reserpine (608) terfenadine (471) (each 2 ng/µL in 10:90 acetonitrile:water)
Calibration	5 mM sodium formate solution (in 30-mL fluidics bottle)
Lock Mass	leucine enkephalin (2 ng/µL in 50:50 acetonitrile:water, in 30-mL fluidics bottle)

NOTE: *Theses samples are the same as those used in the SYNAPT G2 ACQUITY UPLC System performance test during installation. Stock solutions of the test mixture (p/n 700002741) and leucine enkephalin (p/n 700002456) are available from Waters.*

Paracetamol

From Wikipedia, the free encyclopedia

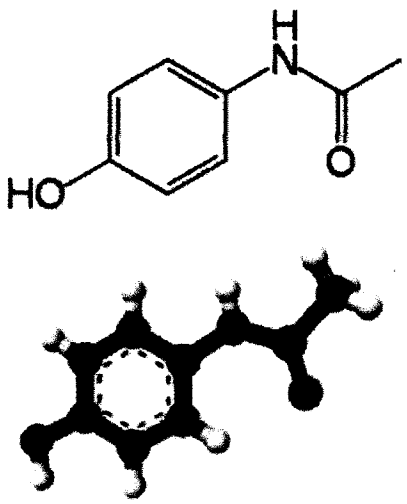
Paracetamol INN (/ˌpærəˈsiːtəmɒl/ or /ˌpærəˈsɛtəmɒl/), or **acetaminophen** USAN (/əˌsiːtəˈmɪnəfɪn/), is a widely used over-the-counter analgesic (pain reliever) and antipyretic (fever reducer). It is commonly used for the relief of headaches, other minor aches and pains, and is a major ingredient in numerous cold and flu remedies. In combination with opioid analgesics, paracetamol can also be used in the management of more severe pain such as post surgical pain and providing palliative care in advanced cancer patients.[4] The onset of analgesia is approximately 11 minutes after oral administration of paracetamol,[5] and its half-life is 1–4 hours.

While generally safe for use at recommended doses (1,000 mg per single dose and up to 4,000 mg per day for adults, up to 2,000 mg per day if drinking alcohol),[6] acute overdoses of paracetamol can cause potentially fatal liver damage and, in rare individuals, a normal dose can do the same; the risk is heightened by alcohol consumption. Paracetamol toxicity is the foremost cause of acute liver failure in the Western world, and accounts for most drug overdoses in the United States, the United Kingdom, Australia and New Zealand.[7][8][9][10]

It is the active metabolite of phenacetin, once popular as an analgesic and antipyretic in its own right, but unlike phenacetin and its combinations, paracetamol is not considered to be carcinogenic at therapeutic doses.[11] The words *acetaminophen* (used in the United States, Canada, Japan, South-Korea, Hong Kong, and Iran[12]) and *paracetamol* (used elsewhere) both come from chemical names for the compound: *para*-**acetyl**-**amino**-**phen**-**ol** and ***para***-**acetyl**-**amino**-**phen**-**ol**. In some contexts, it is simply abbreviated as **APAP**, for **a**cetyl-**p**ara-**a**minophenol.

Chemical data	
Formula	$C_8H_9NO_2$
Mol. mass	151.17 g/mol

Acetaminophen



Systematic (IUPAC) name

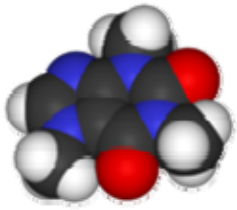
N-(4-hydroxyphenyl)ethanamide

N-(4-hydroxyphenyl)acetamide

Clinical data	
Trade names	Tylenol
AHFS/Drugs.com	monograph
MedlinePlus	a681004
Licence data	US FDA:link
Pregnancy cat.	A(AU) B(US) safe
Legal status	Unscheduled (AU) GSL (UK) OTC (US)
Routes	Oral, rectal, intravenous
Pharmacokinetic data	
Bioavailability	~100%
Metabolism	90 to 95% Hepatic
Half-life	1–4 h
Excretion	Renal
Identifiers	
CAS number	103-90-2
ATC code	N02BE01
PubChem	CID 1983
DrugBank	DB00316

Caffeine

From Wikipedia, the free encyclopedia

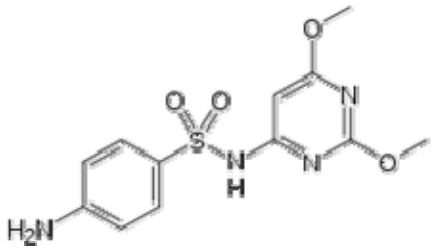
Caffeine	
	
	
IUPAC name 1,3,7-trimethyl-1*H*-purine-2,6(3*H*,7*H*)-dione 3,7-dihydro-1,3,7-trimethyl-1H-purine-2,6-dione	
Other names Caffein;[1] 1,3,7-Trimethylxanthine; Trimethylxanthine; Methyltheobromine; 7-Methyltheophylline; Mateine; Guaranine	
Identifiers	
CAS number	58-08-2 ✓
PubChem	2519
ChemSpider	2424 ✓
UNII	3G6A5W338E ✓
EC-number	200-362-1
DrugBank	DB00201
KEGG	D00528 ✓
ChEBI	CHEBI:27732 ✓
ChEMBL	CHEMBL113 ✓
IUPHAR ligand	407
RTECS number	EV6475000
Jmol-3D images	Image 1 (http://chemapps.stolaf.edu/jmol/jmol.php?model=O%3DC2N%28c1ncn%28c1C%28%3DO%29N2C%29C%29C) Image 2 (http://chemapps.stolaf.edu/jmol/jmol.php?model=Cn1cnc2c1c%28%3DO%29n%28c%28%3DO%29n2C%29C)
SMILES	
InChI	
Properties	
Molecular formula	$C_8H_{10}N_4O_2$
Molar mass	194.19 g mol^{-1}
Exact mass	194.080376 u

Sulfadimethoxine

From Wikipedia, the free encyclopedia

Sulfadimethoxine (trade name **Di-Methox**, Albon) is a sulfonamide antibiotic. Albon is produced by Pfizer Animal Health and is available as a oral suspension, tablet or bolus. It is used to treat many infections including treatment of respiratory, urinary tract, enteric, and soft tissue infections. [1]

Sulfadimethoxine



Systematic (IUPAC) name

4-amino-*N*-(2,6-dimethoxypyrimidin-4-yl) benzenesulfonamide

Clinical data	
AHFS/Drugs.com	FDA Professional Drug Information
Pregnancy cat.	?
Legal status	?
Identifiers	
CAS number	122-11-2
ATC code	J01ED02 QJ01EQ09 QP51AG02
PubChem	CID 5323
DrugBank	DB06150
ChemSpider	5132 ✓
UNII	30CPC5LDEX ✓
KEGG	D01142 ✓
ChEBI	CHEBI:32161 ✗
ChEMBL	CHEMBL62193 ✓
Chemical data	
Formula	$C_{12}H_{14}N_4O_4S$
Mol. mass	310.33 g/mol
SMILES	eMolecules & PubChem
InChI	

✗**(what is this?) (verify)**

(http://www.pfizerah.com/PAHimages/compliance_pdfs/US_EN_AO_compliance.pdf) It is most frequently used in veterinary medicine. Sulfadimethoxine inhibits bacterial synthesis of folic acid (pteroylglutamic acid) from para-aminobenzoic acid. It is also commonly used for the treatment of coccidiosis in many species.[2] (http://www.peteducation.com/article.cfm?c=0+1451&aid=1481)

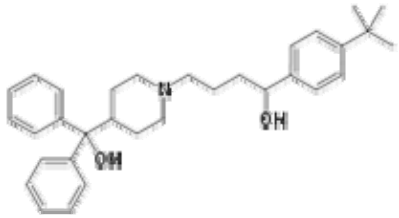
Terfenadine

From Wikipedia, the free encyclopedia

Terfenadine is an antihistamine formerly used for the treatment of allergic conditions. It was brought to market by Hoechst Marion Roussel (now Sanofi-Aventis) and marketed under various brand names including **Seldane** in the United States, **Triludan** in the United Kingdom, and **Teldane** in Australia. According to its manufacturer, terfenadine had been used by over 100 million patients worldwide as of 1990.[1] It was superseded by fexofenadine in the 1990s due to the risk of cardiac arrhythmia caused by QT interval prolongation.

Terfenadine is a prodrug, generally completely metabolised to the active form fexofenadine in the liver by the enzyme cytochrome P450 CYP3A4 isoform. Due to its near complete metabolism by the liver immediately after leaving the gut, terfenadine normally is not measurable in the plasma. Terfenadine itself, however, is cardiotoxic at higher doses while its major, active metabolite is not. Toxicity is possible after years of continued use with no previous problems as a result of an interaction with other medications such as erythromycin, or foods like grapefruit. The addition of, or dosage change in, these CYP3A4 inhibitors makes it harder for the body to metabolize and remove terfenadine. In larger plasma concentrations, terfenadine may lead to toxic effects on the heart's rhythm (e.g. ventricular tachycardia and *torsades de pointes*).

Terfenadine



Systematic (IUPAC) name

(*RS*)-1-(4-*tert*-butylphenyl)-4-{4-[hydroxy(diphenyl)methyl] piperidin-1-yl}-butan-1-ol

Clinical data

AHFS/Drugs.com	Multum Consumer Information
MedlinePlus	a600034
Pregnancy cat.	?
Legal status	Withdrawn

Pharmacokinetic data

Protein binding	70%
Half-life	3.5 hours

Identifiers

CAS number	50679-08-8
ATC code	R06AX12
PubChem	CID 5405
DrugBank	APRD00606
ChemSpider	5212 ✓
UNII	7BA5G9Y06Q ✓
KEGG	D00521 ✓
ChEMBL	CHEMBL17157 ✓

Chemical data

Formula	$C_{32}H_{41}NO_2$
Mol. mass	471.673 g/mol
SMILES	eMolecules & PubChem
InChI	

✗**(what is this?) (verify)**

History

In the United States, Seldane was brought to market in 1985 as the first non-sedating antihistamine for the treatment of allergic rhinitis.[1][2] In June 1990, evidence of serious ventricular arrhythmias among those taking Seldane prompted the FDA to issue a report on the risk factors associated with concomitant use of the drug with macrolide antibiotics and ketoconazole.[1] Two months later, the FDA required the manufacturer to send a letter to all physicians, alerting them to the problem; in July 1992 the existing precautions were elevated to a black box warning[1] and the issue attracted mass media attention in reports that people with liver disease or who took ketoconazole, an antifungal agent, or the antibiotic erythromycin, could suffer cardiac arrhythmia if they also took Seldane.[2]

In January 1997, the same month when the U.S. Food and Drug Administration (FDA) had earlier approved a generic version of Seldane made by IVAX Corporation of Miami, the FDA recommended that terfenadine-containing drugs be removed from the market and that physicians consider alternative medications for their patients.[2] Seldane (and Seldane-D, terfenadine combined

Reserpine

From Wikipedia, the free encyclopedia

Reserpine is an indole alkaloid[2] antipsychotic and antihypertensive drug that has been used for the control of high blood pressure and for the relief of psychotic symptoms, although because of the development of better drugs for these purposes and because of its numerous side-effects, it is rarely used today.[1] The antihypertensive actions of reserpine are a result of its ability to deplete catecholamines (among other monoamine neurotransmitters) from peripheral sympathetic nerve endings. These substances are normally involved in controlling heart rate, force of cardiac contraction and peripheral resistance.[3]

Reserpine mediated depletion of monoamine neurotransmitters in the synapses is often cited as evidence to the theory that depletion of the neurotransmitters causes subsequent depression in humans (c.f. monoamine hypothesis). However, this claim is not without controversy; Some have called reserpine-induced depression a myth, while others claim that teas made out of the plant roots containing reserpine have a calming, sedative action that can actually be considered **anti**depressant.[2] This remains to be demonstrated in the clinic.

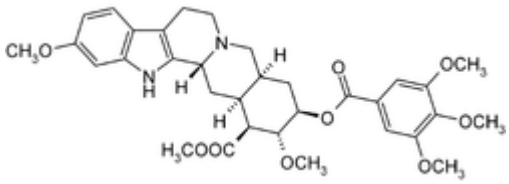
Moreover, reserpine has a peripheral action in many parts of the body, resulting in a preponderance of the cholinergic part of the nervous system (GI tract, smooth muscles vessels).

Contents

Mechanism of Action

Reserpine is an irreversible antagonist of VMAT. It acts by blocking the vesicular monoamine transporter VMAT.[3] This normally transports free norepinephrine, serotonin, and dopamine from the cytoplasm of the presynaptic nerve

Reserpine



Systematic (IUPAC) name

methyl-11,17α-dimethoxy-18β-[(3,4,5-trimethoxybenzoyl)

Clinical data	
AHFS/Drugs.com	Consumer Drug Information
MedlinePlus	a601107
Licence data	US FDA:link
Pregnancy cat.	D (fetotoxic)
Legal status	Rx-only (some countries banned/discontinued)
Routes	oral
Pharmacokinetic data	
Bioavailability	50%
Metabolism	gut/liver
Half-life	phase 1 = 4.5h, phase 2 = 271h, average = 33h
Excretion	62% feces / 8% urine
Identifiers	
CAS number	50-55-5
ATC code	C02AA02
PubChem	CID 5770
DrugBank	APRD00472
ChemSpider	5566 ✓
UNII	8B1QWR724A ✓
KEGG	D00197 ✓
ChEBI	CHEBI:28487 ✗
ChEMBL	CHEMBL772 ✓
Chemical data	
Formula	$C_{33}H_{40}N_2O_9$
Mol. mass	608.68 g/mol
SMILES	eMolecules & PubChem