Hypnotics:
Past, Present, and Future

Psychopharmacology Update
Maryland Psychiatric Society

November 17, 2018

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Johns Hopkins University
School of Medicine

Disclosures

- Consultant: Eisai Pharmaceuticals, Purdue Pharma
- All "off-label" and investigational use of medications will be clearly identified
- Product brand names and images are presented solely for educational purposes and do not represent endorsements or promotion for any medications

Learning Objectives

- Review the key pharmacologic characteristics of FDA-approved insomnia medications that allow customized therapy of patients with insomnia disorder
- Describe the mechanism of action of medications commonly prescribed for insomnia symptoms
- Discuss types of compounds being investigated as possible insomnia disorder treatments

PNAS PLUS

Early Neolithic wine of Georgia in the South Caucasus

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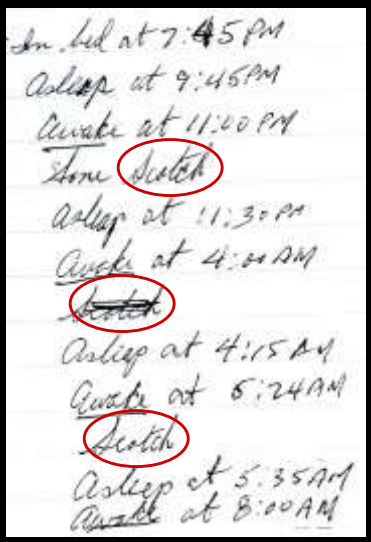
Contributed by David Lordkipanidze, October 7, 2017 (sent for review August 22, 2017; reviewed by A. Nigel Goring-Morris and Roald Hoffmann)

Sleep Diary – May, 2006



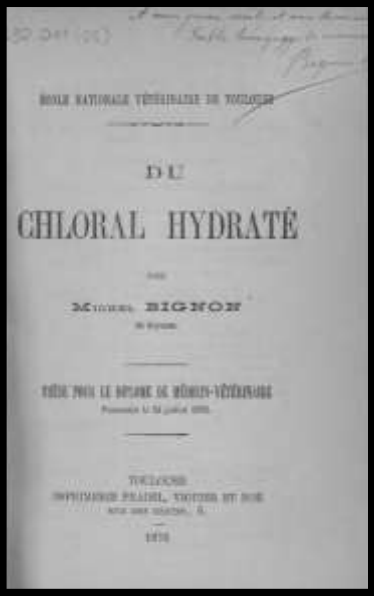
¶ Krafft vnd wirckung.

Die Bletter von allen Geschlechten deß Stechdorns/löschen S. Anthonius Feuwer/ vnd heilen die vmbfressenden Geschwer/ darauff gelegt. Die Zweige dieser Stechdorn vber die Thüren vnnd Fenster gehenckt/ vertreiben alle Gespenst vnd Zauberey/ schreibt Dioscorides.

Laudanumbaum/ Laudanum.

Cap. xcij.

Laudanumbaum/ Ladon oder Ledon, ist ein Geschlecht deß Cisthi, darvon droben gesagt/ nemlich das dritte/ darauß der Safft Ladanum bereitet wirdt. *Græcis, Λάδος. Italicè, Ladanifero arbuscello. Hispanicè, Xara.* Es ist dieser Strauch auch dem Cistho gleich/ hat aber länger vnd schwärtzere Bletter/ welche ein feuchtigkeit im Lentzen an sich ziehen/ auß welcher das Ladanum gemacht wirdt. Solcher Safft oder feyßtigkeit wirdt also gesamlet: Wann die Geyse vnnd Böcke seine Bletter abweyden/ so bleibet der feyßte Safft an jhrem Bart vnd Seiten kleben/ gleich wie ein Vogelleim / solcher Safft wirdt dann abgekemmet/ vnnd mit den Haren verwickelt vnnd vermenget



DU

CHLORAL HYDRATÉ

Michel BIGNON

TOULOUSE
IMPRIMERIE PLAISEL, VIGUIER ET SOIE

1878

1903

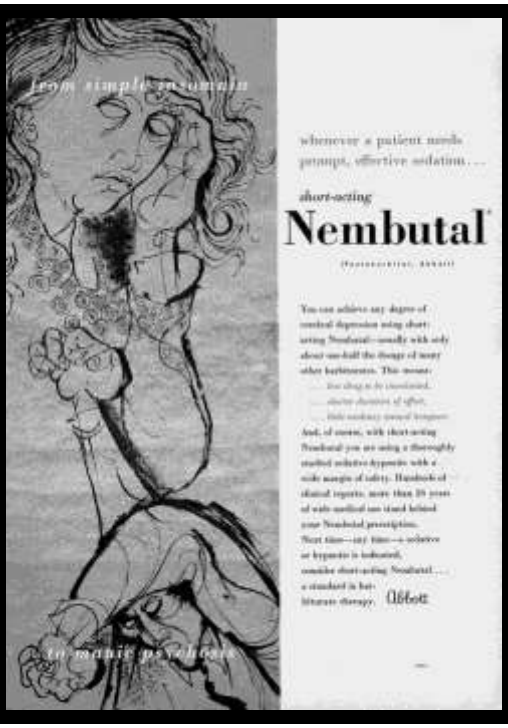

PROFESSIONAL SAMPLE
ALLONAL
'ROCHE'
A SAFE AND EFFECTIVE
NON-NARCOTIC REMEDY
for PAIN or INSOMNIA
Hoffmann-La Roche Inc.
NUTLEY,
DOSAGE:
SEDATIVE - 1 TABLET
FOR PAIN - 1 TO 2 TABLETS
FOR INSOMNIA - 1 TO 2 TABLETS

1920s

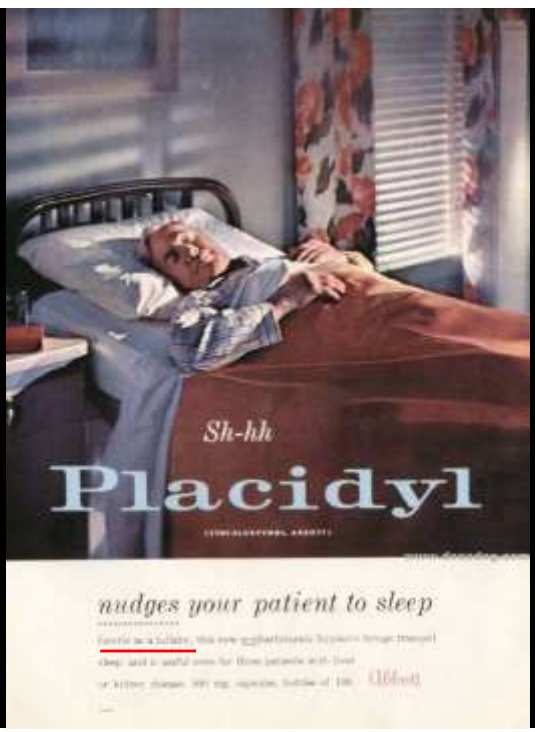

WHEN
Crisis
DEMANDS QUICK-ACTING HYPNOTICS
*Pentobarbital
*Phenobarbital
LAKESIDE

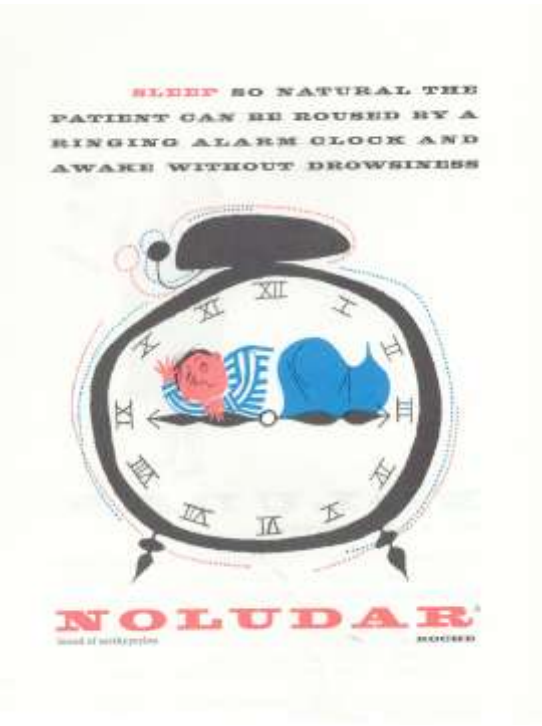
1944

1956


whenever a patient needs
prompt, effective sedation...
short-acting
Nembutal

1956


Sh-hh
Placidyl
nudges your patient to sleep


SLEEP SO NATURAL THE PATIENT CAN BE ROUSED BY A RINGING ALARM CLOCK AND AWAKE WITHOUT DROWSINESS
NOLUDAR

1957


GOOD NIGHT
Doriden
GOOD MORNING

1962


why resumption of interrupted sleep
is important to all your patients
Quaalude
(methaqualone)

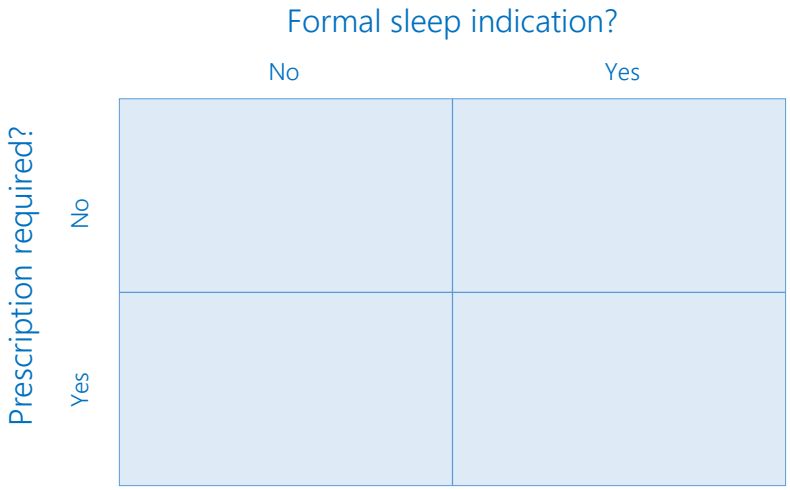
Insomnia does not result from a hypnotic deficiency

Insomnia Treatment Approaches

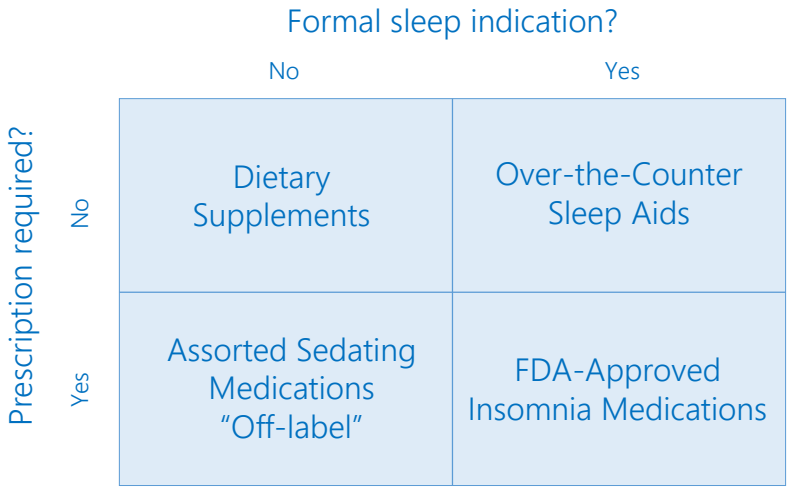
- Education about sleep and mental health
- Promote healthy sleep habits
  - Recommend regularity in sleep-wake timing
  - Discuss an environment conducive for sleep
  - Advise caution with caffeine, alcohol, and other drugs
- Optimize management of comorbid conditions
- Cognitive-behavioral therapy for insomnia (CBT-I)
- Light/dark exposure
- Head cooling
- Pharmacotherapy
  - Directly targeting sleep
  - Indirectly facilitating sleep

Schutte-Rodin S, et al. *J Clin Sleep Med*. 2008;4(5):487-504.

What People Take for Insomnia



What People Take for Insomnia



What People Take for Insomnia

Prescription required?	Formal sleep indication? No	Formal sleep indication? Yes
No	Dietary Supplements	Over-the-Counter Sleep Aids
Yes	Assorted Sedating Medications "Off-label"	FDA-Approved Insomnia Medications

Dietary Supplement Sleep Aids

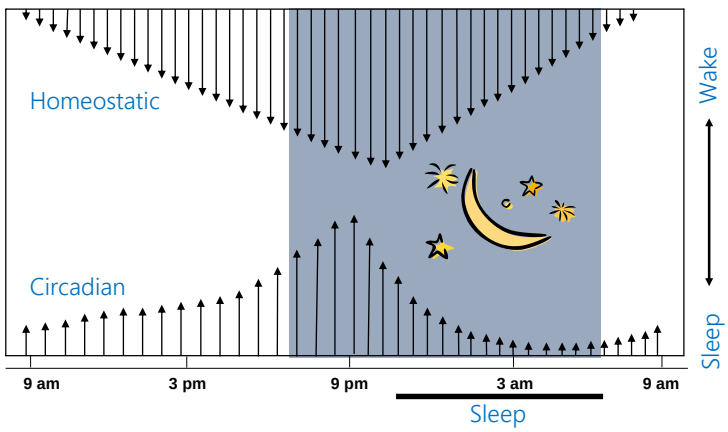
- Dietary supplements, herbal preparations, homeopathic formulations
- Often considered Complementary and Alternative Medicine
- Two broad types
  - Melatonin
  - Everything else (e.g., valerian)
- Limited efficacy data
- Few safety concerns
- Huge number of products marketed as sleep aids

Melatonin

- Hormone produced by the pineal gland with timing controlled by the circadian system
- Melatonin blood level:
  - Low throughout daytime
  - Gradually rises in the evening as bedtime approaches
  - Relatively high during the nighttime sleep period
  - Declines at the end of the normal sleep period in the morning
  - May free run in totally blind individuals or in people not exposed to the photoperiod or 24-hour routines
- Minimal efficacy for insomnia when taken at typical bedtime
- Strong evidence for selected circadian rhythm disorders

Buscemi N, et al. *J Gen Intern Med*. 2005;20(12):1151-1158.

Homeostatic and Circadian Sleep Regulation



Dietary Supplement Sleep Aids: Other Assorted Ingredients

- Valerian
- Kava-Kava
- Passion flower
- Skullcap
- Lavender
- Hops
- Glycine
- Hyoscyamus
- Stramonium
- L-Theanine
- Griffonia
- Wild jujube seeds
- Chamomile
- L-Tryptophan

Dietary Supplement Sleep Aids

- None are regulated by the FDA
- Safety questions
  - Purity
  - Concentration
  - Toxicity

Seeff LB, et al. *Gastroenterology*. 2015;148(3):517.e3-532.e3.

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Over-the-Counter Sleep Aids

- Regulated by FDA
  - Composition
  - Dosing
  - Manufacturing
  - Labeling
  - Marketing
- Antihistamines (Brand or generic)
- Sedating effect (tolerance possible)
- Available alone or combined with analgesics
- May be prescribed at higher doses

Over-the-Counter Sleep Aids

- All are antihistamines
  - Diphenhydramine (most products)
    - Peak concentration: 2 to 3 hours
    - Elimination half-life: 8.5 ± 3.2 hours (short in children; longer in elderly)
  - Doxylamine
    - Peak concentration: 2 to 4 hours
    - Elimination half-life: 10 to 12 hours (longer in elderly)
  - Pharmacodynamics
    - Histamine H_1 receptor antagonist
    - Muscarinic acetylcholine receptor antagonist
    - Tolerance to sedating effects may develop with daily use
  - Adverse effects: Sedation, anticholinergic symptoms

Antihistamines: Potential Adverse Effects

- Next day residual sedation - common
- Anticholinergic effects
  - Confusion and delirium
  - Urinary retention
  - Dry mouth
  - Blurred vision
  - Narrow angle glaucoma exacerbation
  - Greater risk:
    - Elderly individuals
    - Patients concomitantly taking other anticholingeric medications (e.g., antidepressants, antipsychotics)

Gerretsen P, Pollock BG. Drugs with anticholinergic properties: A current perspective on use and safety. *Expert Opin Drug Saf.* 2011;10(5):751-765

What People Take for Insomnia

Prescription required?	Formal sleep indication? No	Formal sleep indication? Yes
No	Dietary Supplements	Over-the-Counter Sleep Aids
Yes	Assorted Sedating Medications "Off-label"	FDA-Approved Insomnia Medications

"Off-Label" Prescriptions for Insomnia

- Antidepressants
- Antipsychotics
- Anxiolytics
- Antihistamines
- Anticonvulsants/mood stabilizers
- Antihypertensives
- Anesthetics

- Issues
  - Efficacy for insomnia
  - Safety in insomnia patients
  - Prescribing guidelines
  - Knowledge of sleep effects
- Is there comorbidity with an indicated condition?

Antidepressants Prescribed for Insomnia

- Question of psychiatric comorbidity
- Often prescribed in absence of mental health disorders
- Sedation from serotonergic, muscarinic, and histaminic receptor blockade
- Risk-benefit questions
- Commonly prescribed examples
  - Trazodone
  - Amitriptyline
  - Mirtazapine
  - Doxepin*

Trazodone

Biphasic $T_{½}$
- 3 – 6 hours
- 5 – 9 hours

Onset 30 – 120 minutes

Receptor effects
- 5-$HT_{2A,2B}$ receptor antagonist
- 5-HT_{1A} partial agonist
- α_1-receptor antagonist
- α_2-receptor antagonist
- Histamine H_1 antagonist
- Serotonin reuptake inhibition

Side effects
- Dizziness
- Hypotension
- Sedation
- Headache
- Sweating
- Arrhythmias
- Priapism
- Serotonin syndrome

Active metabolite: mCPP

Mendelson WB. *J Clin Psychiatry.* 2005;66(4):469-476. Mittur A. *Expert Rev Clin Pharmacol.* 2011;4(2):181-196. Trazodone Prescribing Information

Antipsychotics Prescribed for Insomnia

- Question of psychiatric comorbidity
- Occasionally prescribed solely for insomnia symptoms
- Sedation from serotonergic, muscarinic, and histaminic receptor blockade
- Major risk-benefit questions
- Most commonly prescribed example
  - Quetiapine

What People Take for Insomnia

Prescription required?	Formal sleep indication? No	Formal sleep indication? Yes
No	Dietary Supplements	Over-the-Counter Sleep Aids
Yes	Assorted Sedating Medications "Off-label"	FDA-Approved Insomnia Medications

Current FDA-Approved Insomnia Treatment Medications

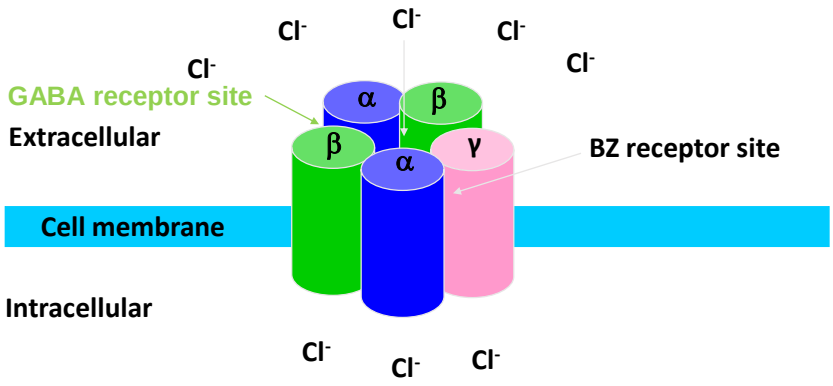
- Benzodiazepine receptor agonists
  - Benzodiazepine hypnotics
  - Nonbenzodiazepine hypnotics
- Selective melatonin receptor agonist
  - Ramelteon
- Selective histamine receptor antagonist
  - Low dose doxepin
- Dual orexin/hypocretin receptor antagonist
  - Suvorexant

FDA-Approved Insomnia Medications, Part 1

Generic name	Brand name	Available doses (mg)	Elimination half-life (hours)
Benzodiazepine Receptor Agonists			
Benzodiazepines Immediate Release			
Estazolam	ProSom	1, 2	10 to 24
Flurazepam	Dalmane	15, 30	2.3 (active metabolite: 48 - 160)
Quazepam	Doral	7.5, 15	39 (active metabolite 73)
Temazepam	Restoril	7.5, 15, 22.5, 30	3.5 to 18.4
Triazolam	Halcion	0.125, 0.25	1.5 to 5.5
Nonbenzodiazepines Immediate Release			
Eszopiclone	Lunesta	1, 2, 3	~6 (~9 in elderly)
Zaleplon	Sonata	5, 10	1
Zolpidem	Ambien	5, 10	~2.5
Nonbenzodiazepines Extended Release			
Zolpidem ER	Ambien CR	6.25, 12.5	2.8 in males (longer in females)
Nonbenzodiazepines Alternate Delivery			
Zolpidem oral spray	Zolpimist	5, 10	2.7 – 3.0
Zolpidem sublingual	Edluar	5, 10	~2.5
Zolpidem sublingual	Intermezzo	1.75, 3.5	~2.5

US Food and Drug Administration. Drugs@FDA. www.accessdata.fda.gov/scripts/cder/drugsatfda.

$GABA_A$ Receptor Complex



Möhler H, et al. *J Pharmacol Exp Ther*. 2002;300(1):2-8. Rowlett JK, et al. *CNS Spectr*. 2004;10(1):40-48.

Benzodiazepine Receptor Agonists
Benzodiazepines

- Pharmacodynamics
  - Positive allosteric modulators of GABA responses at the $GABA_A$ receptor complex
  - Multiple $GABA_A$ receptor α subunit subtypes
  - Targeted action in the hypothalamic sleep nuclei
  - Global CNS effects
- Pharmacokinetics
  - Relatively rapidly absorbed
  - Very wide range of elimination half-lives: hours to days
  - Expect prolonged half-life in older adults
  - Most efficacious for sleep onset and maintenance
  - Potential for residual daytime sedation

Walsh JK, Roth T. In: Kryger MH, Roth T, Dement WC, eds. *Principles and Practice of Sleep Medicine.* 5th ed. St. Louis, MO: Elsevier Saunders; 2011:905-915. Mohler H, Fritschy JM, Rudolph U. J Pharmacol Exp Ther 2002;300:2-8

Benzodiazepine Receptor Agonists
Non-Benzodiazepines

- Pharmacodynamics
  - Positive allosteric modulators of GABA responses at the $GABA_A$ receptor complex
  - Selected $GABA_A$ receptor α subunit subtypes
  - Targeted action in the hypothalamic sleep nuclei
  - Global CNS effects
- Pharmacokinetics
  - Relatively rapidly absorbed
  - Relatively shorter elimination half-lives: About 1 to 6 hours
  - Expect prolonged half-life in older adults and for zolpidem in women
  - Indications vary for sleep onset and maintenance
  - Limited potential for residual daytime sedation

Walsh JK, Roth T. In: Kryger MH, Roth T, Dement WC, eds. *Principles and Practice of Sleep Medicine*. 5th ed. St. Louis, MO: Elsevier Saunders; 2011:905-915. Mohler H, Fritschy JM, Rudolph U. J Pharmacol Exp Ther 2002;300:2-8

BZRA Hypnotics: Possible Adverse Effects

- Residual effects
- Dizziness
- Headache
- Somnolence
- Blurred vision
- Nausea/diarrhea
- Fatigue
- Ataxia
- Anterograde amnesia
- Somnambulism/complex sleep behaviors

US Food and Drug Administration. Drugs@FDA. www.accessdata.fda.gov/scripts/cder/drugsatfda.

Zolpidem: 2013 FDA Update

Drug Safety Communication

- Recommends lower doses for women due to slower metabolism and possible excessive blood levels the following morning
- Initial dose for women should be 5 mg (IR) or 6.25 mg (ER)
- Consider these lower doses for men as well since they often provide sufficient efficacy
- Exception: dissolvable middle-of-the-night formulation (1.75, 3.5 mg) already recommends lower dose for women

Eszopiclone: 2014 FDA Update

Drug Safety Communication

- Recommends lower initial dose for men and women to be 1 mg at bedtime
- "…the previously recommended dose of 3 mg can cause impairment to driving skills, memory, and coordination that can last more than 11 hours after receiving an evening dose "
- Dosage may be increased to 2 or 3 mg at bedtime with caution

FDA-Approved Insomnia Medications, Part 2

Generic name	Brand name	Available doses (mg)	Elimination half-life (hr)
Selective melatonin receptor agonist			
Ramelteon	Rozerem	8	1 – 2.6
Selective histamine H_1 receptor antagonist			
Doxepin	Silenor	3, 6	15.3
Dual orexin receptor antagonist			
Suvorexant	Belsomra	5, 10, 15, 20	12

US Food and Drug Administration. Drugs@FDA. www.accessdata.fda.gov/scripts/cder/drugsatfda.

Melatonin Receptor Agonist: Ramelteon

- Pharmacodynamics
  - Melatonin MT_1 and MT_2 receptor agonist
  - Targeted action in the hypothalamic suprachiasmatic nucleus (SCN)
  - Reduces evening circadian driven arousal
  - Reinforces circadian periodicity
  - Enhances sleep onset
- Pharmacokinetics
  - Relatively rapidly absorbed
  - Relatively short elimination half-life: 1 to 2.6 hours
  - Indication for sleep onset
  - Limited potential for residual daytime sedation

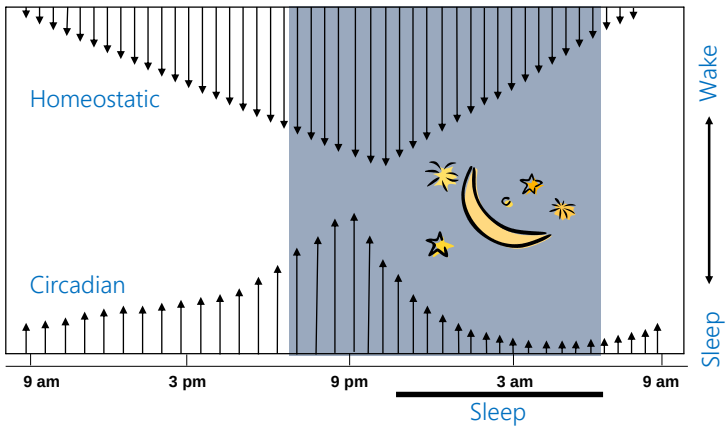
Kato K, et al. *Neuropharmacology.* 2005;48(2):301-310.

Melatonin Receptor Agonist:
Ramelteon

- Indicated for insomnia with sleep onset difficulty
- Adverse events
  - Somnolence (5%)
  - Dizziness (5%)
  - Fatigue (4%)
- No abuse liability
- Avoid with
  - Hepatic impairment (moderate to severe)
  - Fluvoxamine (Luvox) coadministration

Kato K, et al. *Neuropharmacology.* 2005;48(2):301-310.

Homeostatic and Circadian Sleep Regulation



Histamine Receptor Antagonist
Low-Dose Doxepin

- Pharmacodynamics
  - At very low doses primarily histamine receptor antagonist (avoiding receptor effects associated with higher doses)
  - Histamine is a potent wake-promoting neurotransmitter
  - Enhances sleep by reducing nighttime histamine arousal
- Pharmacokinetics
  - Relatively rapidly absorbed
  - Elimination half-life: About 15.3 hours
  - Indication for sleep maintenance
  - Limited potential for residual daytime sedation

Krystal AD, et al. *Sleep Med Rev.* 2013;17(4):263-272.

Histamine Receptor Antagonist
Low-Dose Doxepin

- Indicated for the treatment of insomnia characterized by difficulties with sleep maintenance
- Approved by the FDA (2010)
- Ultra-low dose (3 mg, 6 mg)
- No abuse liability
- Most common adverse effects
  - Somnolence/sedation
  - Nausea
  - Upper respiratory tract infection

US Food and Drug Administration. Drugs@FDA. www.accessdata.fda.gov/scripts/cder/drugsatfda.

Orexin/Hypocretin Receptor Antagonist
Suvorexant

- Pharmacodynamics
  - Dual orexin receptor (OX_1 and OX_2) antagonist
  - Hypothalamic neurons with peptides orexin-A and orexin-B project to cortex and wake-promoting nuclei to reinforce and stabilize wakefulness
  - Suvorexant promotes sleep by decreasing orexin-associated CNS arousal
- Pharmacokinetics
  - Relatively rapidly absorbed
  - Elimination half-life: About 12 hours
  - Dose-dependent potential for residual daytime sedation

Winrow CJ, et al. *J Neurogenet.* 2011;25(1-2):52-61.

Orexin/Hypocretin Receptor Antagonist
Suvorexant

- Indication: For the treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance
- FDA approved in 2014
- Contraindication: narcolepsy
- Adverse reactions: somnolence
- Schedule IV controlled substance

Medication	Unspecified Insomnia	Sleep Onset	Sleep Maintenance	Early Awakening
Estazolam		√	√	√
Flurazepam		√	√	√
Quazepam		√	√	√
Temazepam	√			
Triazolam	√			
Eszopiclone		√	√	
Zaleplon		√		
Zolpidem		√		
Zolpidem ER		√	√	
Zolpidem spray		√		
Zolpidem sublingual		√		
Zolpidem sublingual-MONT			√	
Ramelteon		√		
Low-dose doxepin			√	
Suvorexant		√	√	

US Food and Drug Administration. www.accessdata.fda.gov/scripts/cder/daf/.

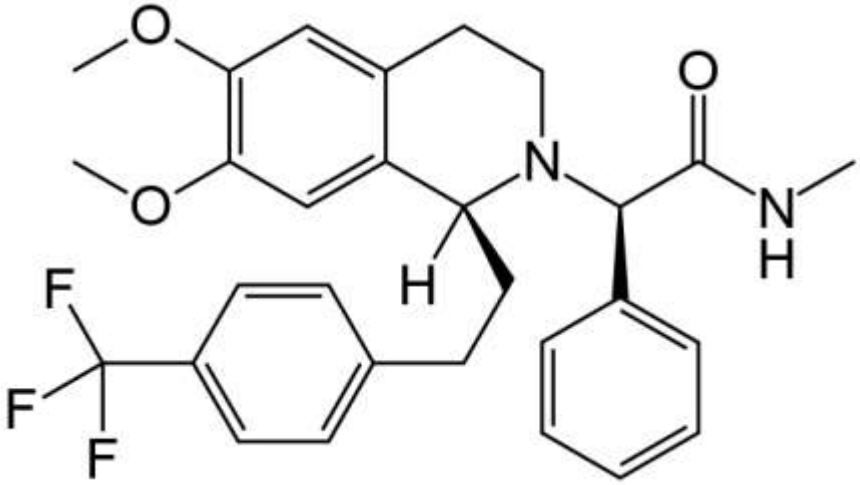
Medication	DEA Class	PC	Most Common Side Effects
Estazolam	IV	X	Somnolence, hypokinesia, dizziness, abnormal coordination
Flurazepam	IV	X	Dizziness, drowsiness, lightheadedness, loss of coordination, staggering, falling
Quazepam	IV	X	Drowsiness, headache
Temazepam	IV	X	Drowsiness, dizziness, lightheadedness, difficulty with coordination
Triazolam	IV	X	Drowsiness, headache, dizziness, "pins & needles," coordination difficulty, lightheadedness
Eszopiclone	IV	C	Unpleasant taste, headache, somnolence, rash, respiratory and viral infections, dizziness, dry mouth, anxiety, hallucinations
Zaleplon	IV	C	Drowsiness, lightheadedness, dizziness, "pins & needles," difficulty with coordination
Zolpidem	IV	C	Drowsiness, dizziness, diarrhea, drugged feeling
Zolpidem ER	IV	C	Headache, next-day somnolence, dizziness
Zolpidem spray	IV	C	Drowsiness, dizziness, diarrhea, drugged feeling
Zolpidem sublingual	IV	C	Drowsiness, dizziness, diarrhea, drugged feeling
Zolpidem sublingual-MONT	IV	C	Headache, nausea, fatigue
Ramelteon	---	C	Somnolence, dizziness, fatigue, nausea, exacerbated insomnia
Low-dose doxepin	---	C	Somnolence/sedation, nausea, upper respiratory tract infection
Suvorexant	IV	C	Somnolence

US Food and Drug Administration. www.accessdata.fda.gov/scripts/cder/daf/. PC = pregnancy category

What's new under the moon?

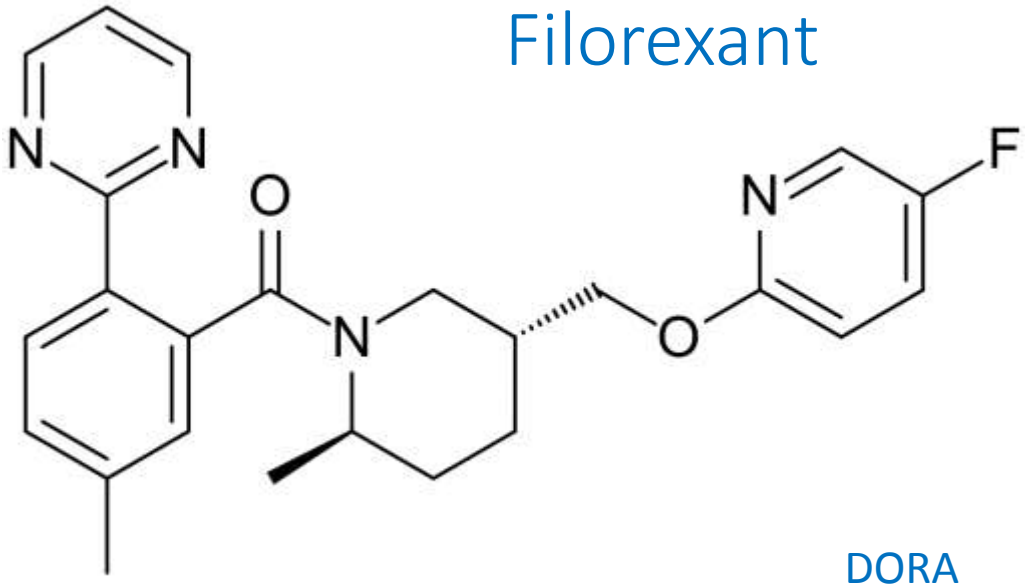
More Orexin Antagonists

Almorexant



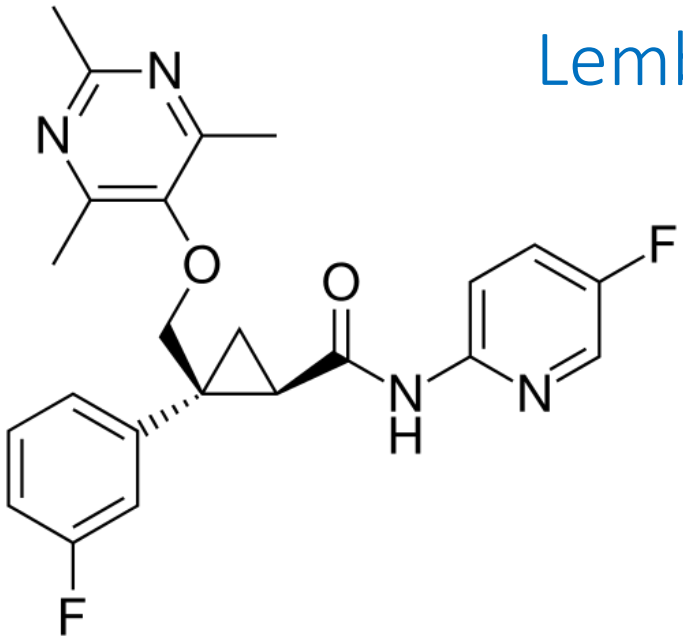
DORA

Filorexant



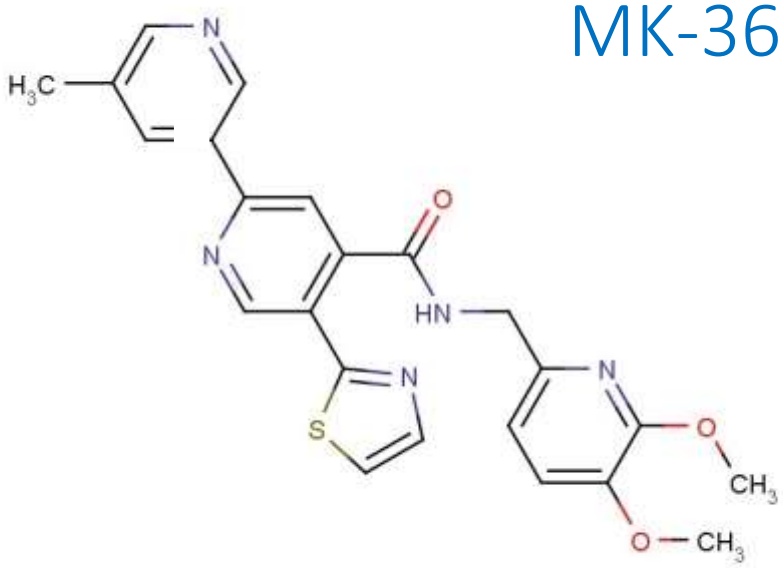
DORA

Lemborexant



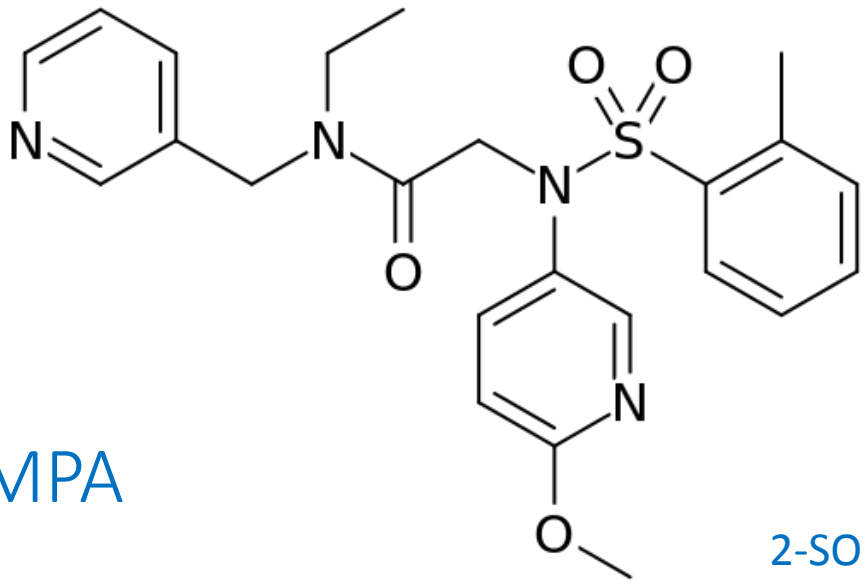
DORA

MK-3697



2-SORA

EMPA



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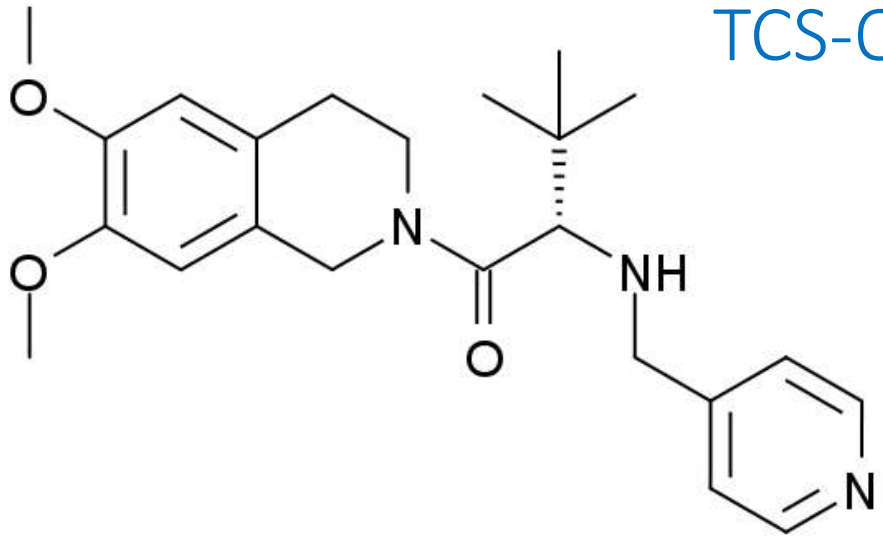

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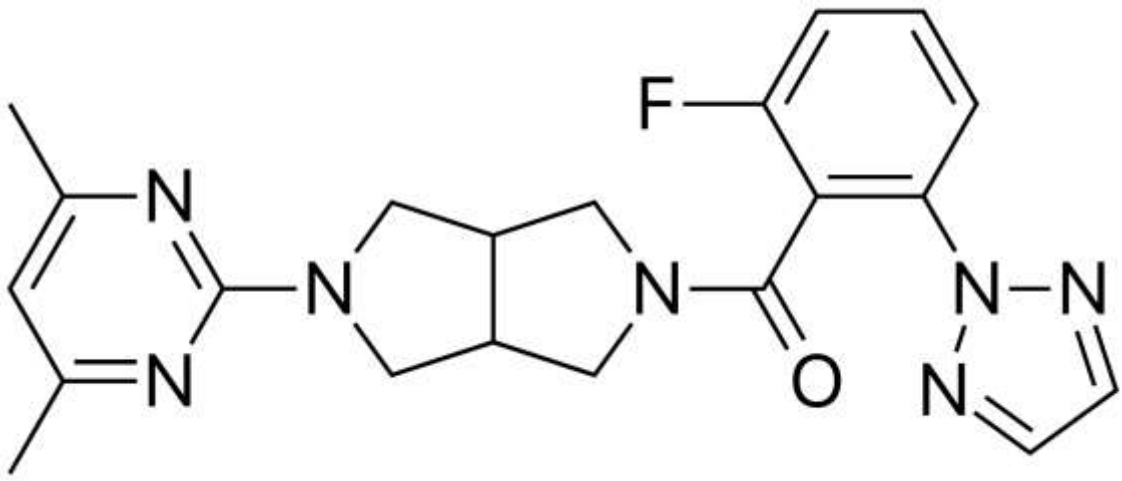

Seltorexant

2-SORA

What's new under the moon?

Benzodiazepine Receptor Agonists

What's new under the moon?

Controlled Release Zaleplon (Somnus Therapeutics)

What's new under the moon?

Inhaled Zaleplon (Alexza Pharmaceuticals)

What's new under the moon?

Avram MJ, Spyker DA, Kehne JH, Cassella JV. The Pharmacokinetics and Pharmacodynamics of Zaleplon Delivered as a Thermally Generated Aerosol in a Single Breath to Volunteers. *J Clin Pharmacol*. 2013.

What's new under the moon?

Indiplon
(Neurocrine Biosciences)

What's new under the moon?

Loredіplon
(Ferrer)

What's new under the moon?

EVT-201
(Evotec)

What's new under the moon?

Melatonin Agonists

What's new under the moon?

Controlled Release Melatonin (Neurim Pharmaceuticals)

What's new under the moon?

Tasimelteon Non-24 Hour Disorder (Vanda Pharmaceuticals)

What's new under the moon?

Piromelatine (Neu-P11)
MT, 5-HT_{1A}, 5-HT_{1D} Agonists
(Neurim Pharmaceuticals)

What's new under the moon?

TIK-301
(Tikvah Pharmaceuticals)

What's new under the moon?

UCM-765
Selective MT2 Agonist

What's new under the moon?

Beta Blockers

Use of a composition comprising at least one beta-blocker for the treatment of sleep disorders

WO 2009018824 A1

ABSTRACT

A composition comprising specific beta-blockers such as bisoprolol and nebivolol for the treatment of insomnia and/or another sleep disorder. The composition should be given in such an amount that it causes a less than 40 % decrease in the amount of aMT6s in complete nocturnal urin. The composition can be a combination treatment comprising a specific beta-blocker in combination with another known drug e.g., melatonin with similar effect for treatment of insomnia.

Publication number	WO2009018824 A1
Publication type	Application
Application number	PCT/DK2008/000249
Publication date	Feb 12, 2009
Filing date	Jul 4, 2008
Priority date ⓘ	Aug 3, 2007
Inventors	Søren TULLIN, Birger Jan Oslen
Applicant	Tullin Soeren, Birger Jan Oslen
Export Citation	BiBTeX, EndNote, RefMan

Patent Citations (5), Non-Patent Citations (1), Classifications (13), Legal Events (3)

External Links: Patentscope, Espacenet

What's new under the moon?

Histamine H1 Antagonist

What's new under the moon?

LY-2624803
(Eli Lilly)

What's new under the moon?

Histamine H3 Agonist

What's new under the moon?

Tetracyclic Antidepressant

What's new under the moon?

CB-2810 (Cennerv Pharma)

What's new under the moon?

5-HT_{2A} Receptor Antagonists

What's new under the moon?

A(2A) Adenosine Receptor Agonist

What's new under the moon?

CGS-21680

What's new under the moon?

Angiotensin II Receptor Type 1 (AT1) Antagonist

What's new under the moon?

Promoting sleep using at1 receptor blockers
WO 2013119605 A1

ABSTRACT

The present invention relates to the use of an Angiotensin II type 1 (AT1) receptor blocker for promoting sleep and/or the treatment of insomnia. It is based, at least in part, on the results of experiments performed using a validated rat model of stress-induced insomnia in which candesartan was found to ameliorate sleep disturbances induced by stress. Further, it was observed that this effect seems to be caused by blockade of AT1 receptors located in several brain regions that are key components of the neural circuitry activated during insomnia. In contrast to currently marketed treatments for insomnia, the AT1 receptor blocker was found to restore normal sleep without inhibiting REM sleep and/or inducing atypical wave components in the EEC

Publication number	WO2013119605 A1
Publication type	Application
Application number	PCT/US2013/024844
Publication date	Aug 15, 2013
Filing date	Feb 6, 2013
Priority date	Feb 7, 2012
Also published as	US20150150853
Inventors	Georgina CANO, Alan F. SVED
Applicant	University Of Pittsburgh - Of The Commonwealth System Of Higher Education
Export Citation	BiBTeX, EndNote, RefMan

Patent Citations (2), Non-Patent Citations (4), Referenced by (1), Classifications (10), Legal Events (3)

External Links: Patentscope, Espacenet

What's new under the moon?

CB1/CB2
Cannabinoid Agonist

What's new under the moon?

NEO-1940
Insomnia with cancer
(NEOMED)

2008 AASM Chronic Insomnia Clinical Guideline Consensus Recommendations

The choice of a specific pharmacologic agent within a class should be directed by:

- Symptom pattern
- Treatment goals
- Past treatment response
- Patient preference
- Cost
- Availability of other treatments
- Comorbid conditions
- Contraindications
- Concurrent medication interactions
- Side effects

AASM: American Academy of Sleep Medicine

2008 AASM Chronic Insomnia Clinical Guideline Consensus Recommendations

- Patient education to accompany pharmacologic treatment
  - Treatment goals and expectations
  - Safety concerns
  - Side effects/interactions
  - Alternate Rx modalities
  - Potential for dose escalation
  - Rebound insomnia

AASM: American Academy of Sleep Medicine

2008 AASM Chronic Insomnia Clinical Guideline Consensus Recommendations

- Patients should be followed on a regular basis, every few weeks in the initial period of treatment when possible
- Efforts should be made to employ the lowest effective maintenance dosage of medication and to taper medication when conditions allow
- Chronic hypnotic medication may be indicated for long-term use in those with severe or refractory insomnia or chronic comorbid illness
- Long-term use may be nightly, intermittent, or as needed

AASM: American Academy of Sleep Medicine

1968