

The pitfalls in Life Style Drugs

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-Life style drugs is a category of drugs with
diverse chemical formulae and mechanism of actions,
-the term has been introduced during the last 7-10 years

- they have common, but also uncommon characteristics
as compared to all other categories of drugs

- There are serious pitfalls associated with their use

LSD

LSD

- Some of their common and uncommon characteristics
- The pitfalls in their use
 - (a) for individual LSD (a little bit of pharmacology)
 - (b) common problems
- Actions (if any) to be taken

Characteristics of LSD

Drugs approved by official national or international drug agencies (e.g. FDA, EMEA)

- used to treat very common symptoms or habits that are associated with the way of life (life style) or with social prototypes

- smoking
- obesity
- androgen alopecia (baldness)
- hirsutism, (excessive hair growth)
- wrinkles
- male sexual dysfunction
- shyness, blushing, phobia etc
- old age syndrome
- contraception (pill)

- these symptoms are not associated with a disease
- the individual decides on his own that he requires treatment
- huge consumption (almost out of control)
- many pitfalls in their use

Pitfalls of LSD

The use of LSD comprises part of the "Threat to health, originating from the medical establishment" (iatrogenic threat)

They are drugs with low efficacy
In many cases, drugs with serious side-effects
In several cases, induce a form of addiction

There is often lack of quality control (fraudulence)

Tax evasion

LSD are a socio-economic burden to society
(expensive, who pays?)

Disorientation from "needed" drug research from
pharma-industry

Individual categories of LSD Evaluation of the risk/benefit ratio

- Be careful who you are talking to
- No mass media (distortion, grey advertisement)
- Only specialized audiences and state authorities

shyness, blushing:	- SSRIs
smoking:	- bupropione, Zyban®
drug addiction:	- Antabuse, Naltrexone
obesity:	- orlistat, Xenical®
baldness:	- minoxidil, Rogain® finasteride, Propecia®
hirsutism, hair growth:	- eflornithine, Vaniqa®
wrinkles:	- HA, Juvederm®, botulinum toxin, Botox®
♂ sexual dysfunction:	- PG, sildenafil, Viagra®, vardenafil, Levitra®, tadalafil, Cialis®, apomorphine, Uprima®
old age syndrome:	- growth hormone
contraception:	- the "pill"

LSD for sexual dysfunction

Pharmaceutical Industry is governed by men:

♂ : several drugs for improving male sexual performance

♀: contraception (pill)

- Avlimil: female sexual dysfunction
- an example of an LSD that has no official approval
- No known mechanism of action
- No proven efficacy
- Numerous side effects

- up to 43 % of women in the United States suffer from sexual dysfunction (Journal of the American Medical Association, 1999)

- ∴ has a big market

Avlimil Ingredients	Adverse effects
Sage leaf	Nausea, vomiting, abdominal pain, dizziness, agitation, and wheezing, may increase blood pressure of hypertensive patients, may cause seizures.
Red raspberry leaf	
Kudzu root extract	
Red clover extract	Rash-like reactions, muscle pain, headache, nausea, and vaginal spotting.
Capsicum pepper	Gastrointestinal irritation, sweating and flushing of the head and neck, lacrimation, runny nose, may decrease blood coagulation, may lead to gastroenteritis and hepatic or renal damage if taken in large amounts, may cause dermatitis in breastfed infants whose mothers eat food heavily spiced with capsicum.
Licorice root	Hypertension, sodium and water retention, edema, lethargy, amenorrhea, and headache with consumption of 50 grams per day or chronic use longer than 6 weeks. Higher levels of consumption may cause low potassium levels, muscle pain, muscle damage, myoglobinuria, severe congestive heart failure, pulmonary edema, lower extremity weakness, hypertensive encephalopathy, and quadriplegia, due to pseudoadosteronism and hypermineralcorticoidism. May cause decreased libido and sexual dysfunction in men.
Bayberry fruit	Gastrointestinal irritation, vomiting, liver damage, may act as an irritant and sensitizer.
Damiana leaf	
Valerian root	Headache, excitability, uneasiness, cardiac disturbances, insomnia, gastric discomfort, dry mouth, vivid dreams, morning drowsiness, impaired alertness and information processing (dose-dependent), may cause benzodiazepine-like withdrawal symptoms when treatment is discontinued.
Ginger root	Abdominal discomfort, heartburn, diarrhea, pepper-like irritant effect in the mouth and throat. Overdoses can cause central nervous system depression and cardiac arrhythmias.
Black cohosh root	Gastrointestinal upset, rash, headache, dizziness, weight gain, feeling of heaviness in the legs, and cramping. May cause jaundice and acute hepatitis.

Selective serotonin reuptake inhibitors, SSRIs

- fluoxetine Prozac®
- paroxetine Paxil®
- chloropramine Anafranil®
- fluvoxamine Luvox®
- sertraline Zoloft®
- citalopram Celexa®

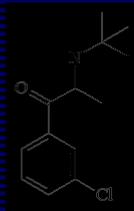
LSD for: shyness, blushing, timidity, social phobia, obligatory children

There are numerous articles written in scientific journals and mass media, arguing that these symptoms are quite normal for the human nature and should not be treated

Despite this, there is a huge consumption of SSRIs.
e.g., 1 in every 5 adults in USA takes SSRIs.

**-one of the biggest problems of drug abuse
-their use is in the limits of legal drug addiction**

LSD for giving up smoking



ZYBAN
bupropion HCl

Weak inhibitor of uptake I for monoamines:
Nor, DA and 5-HT in CNS

300 mg/day, (150 mg x 2/day, 7 to 12 weeks)

Helps, via an unknown mechanism, in reducing
withdrawal symptoms after giving up smoking



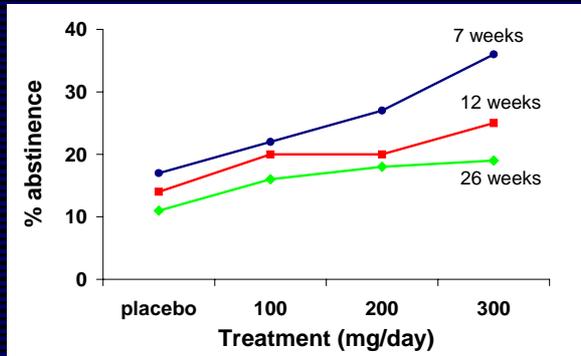
The argument from Pharma-Industry is that the cost should be covered by National Health systems

Otherwise, there would be excessive cost to National Health systems due to the effects of smoking in respiratory and cardiovascular systems

Side effects

Dry mouth	Headache	Anxiety
Insomnia	Nausea	Disturbed concentration
Tremor	Dizziness	Nervousness
Pruritis	Anorexia	Rhinitis
Skin Rash	Constipation	Pharyngitis
	Dysuria	Taste perversion
	Myalgia	Vision disturbances
	Arthralgia	Excessive perspiration
	Abdominal Pain	

Efficacy of bupropione is low



Effective, for short term (7-12 weeks) but not for long term (26 weeks)
Effective providing that the individual is really willing to cut smoking
- in which case he does not need any drug treatment

The spontaneous quit rate for smokers,
(people who just decide to quit smoking),
can be raised up to 25% with counselling

LSD for drug addiction

Drug addiction is a serious personal problem (failure)
(though not a disease)
-However, addicts should be treated as patients, at any cost
-Criticism for LSD does not apply for drug addiction

Alcoholism

- Antabuse (induces acetaldehyde syndrome, 1948)
- Naltrexone (antagonist of μ , κ , δ receptors)
- Acamprosate (↓ excitatory amino acids in CNS)
- Ondansetron (inhibits 5-HT_{3A} receptors)

Low efficacy

Addiction to opioids

- Methadone
- Naltrexone
- Buprenorphine

Addiction to Cocaine

- Vigabatrin, Sabril® (antidepressant) (↑ GABA)
- Baclofen (muscle relaxant) (↑ GABA)

Low efficacy



'Couple'
Fernando Botero



'Nude on a Divan'
Camille Bombois

Body weight

"normal" varies through different time periods

WHO

Body mass index
 $\text{Kg}/\text{height}(\text{m})^2$

Normal >25
Overweight: 25-30
Obese >30

- Obese in USA > 15%
- Overweight in USA > 45%
- " in Germany > 30%



'Woman Upright IV'
Alberto Giacometti



Despite the fact that obesity could be an advantage ...



Obesity is strongly associated with:

- Hypertension
- Dyslipidemia
- Type 2 diabetes
- Coronary heart disease
- Stroke
- Gallbladder disease
- Osteoarthritis
- Sleep apnea and respiratory problems
- Cancer of endometrium, breast and colon

∴ Obesity and Overweight
must be
seriously confronted

What is today's somatic prototype?
According to mass media we should look something
like this, or we are sick!!!



Obesity



78,200 prescriptions
in first 3 months after orlistat
was launched in Canada

➤ Approved 1998 (USA, Europe, Asia)

- Orlistat acts as a reversible inhibitor of gastric and pancreatic lipases, by forming a covalent bond with the active serine residue site of the enzymes (necessary for degradation of dietary lipids)
- It inhibits the hydrolysis of 1/3 of triglycerides
- ∴ the formation and absorption of 1/3 of absorbable free fatty acids and monoglycerides present in a meal
- ∴ non-hydrolysed lipids are excreted in the feces

Dosage: 120 mg x 3 daily, up to 1 h after meal

Side effects: not serious but very embarrassing

- Oily spotting
- Flatus with discharge
- Fecal urgency and incontinence
- Fatty/oily stool
- Oily evacuation
- Increased defecation

- Abdominal pain and cramps
- ▼ the absorption of some fat-soluble vitamins (Vitamin E, Vitamin A, Vitamin D) and beta-carotene
- ▼ blood pressure
- Possible association with breast cancer

Efficacy: recommended for BMI ≥ 30 kg/m²
but it is also administered to overweight people

The results in body weight loss:

- at best: 5-10%
 - but ONLY for diets rich in lipids
 - presumes adapting proper dietary habits
-
- It is not superior to simple diet
 - No evidence that orlistat is any more effective than diet alone in reducing the morbidity and mortality due to obesity
 - So, why get dependent (addicted) to a drug?



∴ Obesity and Overweight must be seriously confronted by each individual facing his problem and changing dietary and life style habits

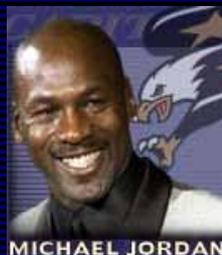
Androgenic alopecia (baldness)

Preferences for hair style may be of all kinds

Baldness may occasionally become a sign of recognition and success



Tellys Savalas



MICHAEL JORDAN



Androgenic alopecia (baldness)

Preferences for hair style may be of all kinds

skin-heads are fashionable, specially in show-business and sports



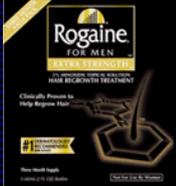
Affects 50-80% of man
20-40% of women after menopause

Depending on life-style and social pressure,
baldness can affect the personality and create
serious psychosomatic problems

Types of male baldness according to Hamilton

Types of female baldness according to Ebling-Rook

LSD for androgenic alopecia (baldness)




Minoxidil (Rogaine®, Regaine®) (local)
- antihypertensive (vasodilatation by activating K^+ channels)




Finasteride (Propecia®, Proscar®) (per os)
- benign prostate hyperplasia (inhibits 5 α reductase II, which mediates the conversion of testosterone to dihydrotestosterone, which is responsible for alopecia)

alopecia: 1- 5 mg/day (no dose/response effect)

Efficacy

Cost: \$600 per year

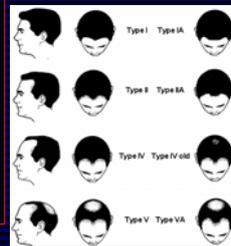
Probably due to presence of 30% of 5 α reductase I, which is not affected by finasteride, mediates the conversion of testosterone to dihydrotestosterone

prolonged treatment (>3 months)

-to observe in < 25% (minoxidil)
and in < 30% (finasteride) } of users

recovery of part of physiological hair growth

- better results in women
- better results in man with "mild" type I-V baldness
- better results if treatment starts early
- treatment must be continued to retain the effects



Side effects of minoxidil

- erythema
- scaling
- pruritus
- dermatitis
- itching or skin rash
- acne
- burning of the scalp
- increased hair loss
- inflammation at root of hair
- reddened skin
- swelling of the face

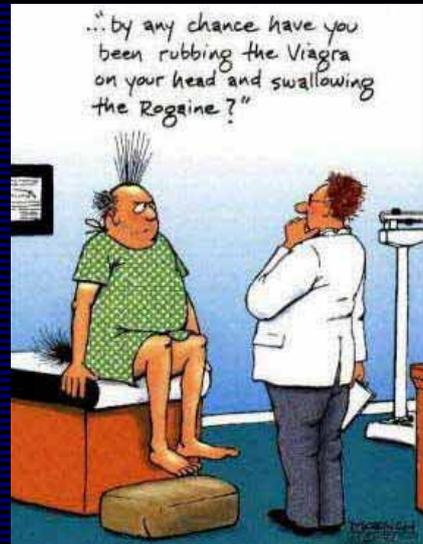
May also be absorbed systemically

- blurred vision
- chest pain
- ↓ of sexual ability or desire
- fast or irregular heartbeat
- flushing
- headache
- numbness: hands, feet, face
- swelling of face, hands, feet, legs
- rapid weight gain
- hair growth in other parts of body

Side effects of finasteride

- breast enlargement
- skin rashes
- swelling of the lips
- abdominal pain
- back pain
- diarrhoea
- dizziness
- headache
- ↓ volume of ejaculate
- ↓ libido
- impotence (inability to have or keep an erection)

So, you start bold and may end up bold with sexual dysfunction



Hirsutism (excessive hair growth)

Again, tastes may vary



Hirsutism (excessive hair growth)

- Endocrine disturbance
 - adrenal glands:
 - tumor (malignant)
 - Cushing syndrome
 - cognate hyperplasia of adrenals
 - ovaries
 - tumor (benign or malignant)
 - polycystic ovary syndrome
- Hereditary
- Idiopathic
- Drugs: Metoclopropamide
 - Methyldopa
 - Reserpine
 - Danazol (progesterone)
 - Phenothiazine
 - Progestins
 - testosterone

8-10% of women

LSD for hirsutism (excessive hair growth)

- eflornithine hydrochloride
Vaniqa®



Originally used for helminthiases (trypanosomiasis)

- inhibits ornithine decarboxylase
(which is necessary for cell division)
- Efficacy 32%
- has serious side effects

Side effects of eflornithine

- dry skin
- bleeding of the skin
- cheilitis
- dermatitis
- acne
- edema of the lips
- herpes simplex
- ↑ transaminases
- carcinogenic
- teratogenic
- sterility

It is wiser to retain
the traditional methods



LSD for wrinkles

- Hyaluronic acid,
Juvederm®
- lasts 1-3 years

- Collagen type I
- lasts 2-6 months

- Polygalactic acid
- (induces fibroblasts to
produce collagen)
- lasts 1-2 years

In all cases
danger for deformities

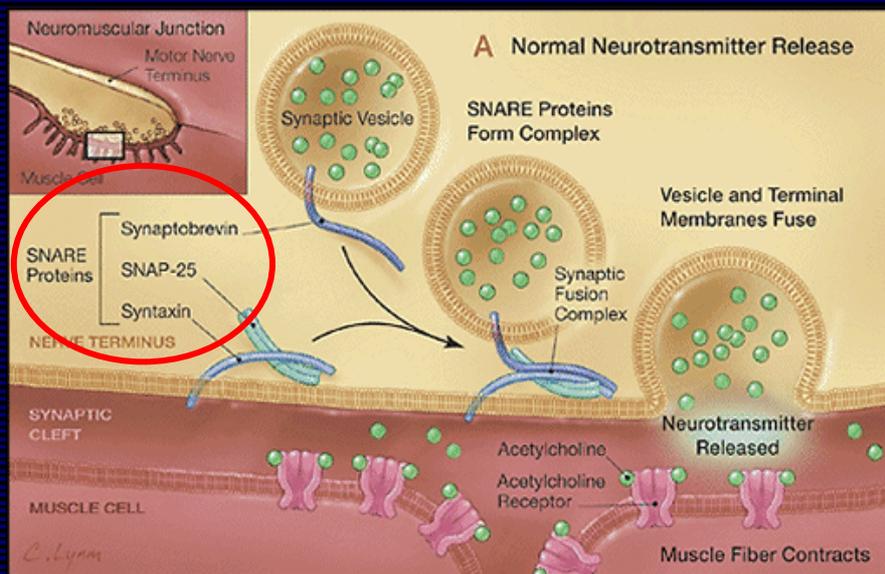


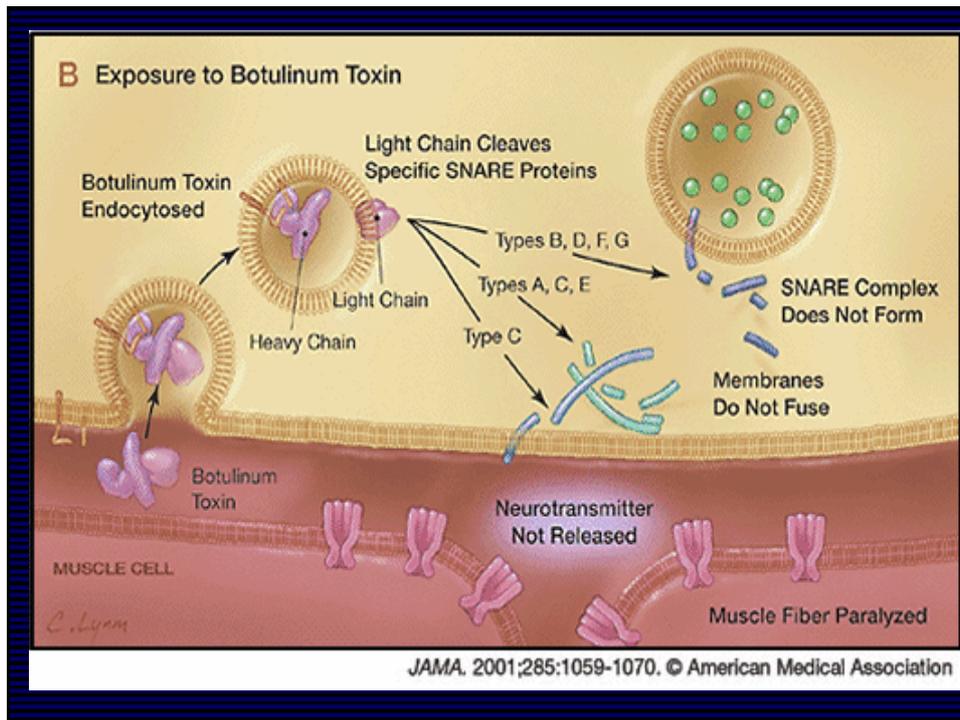
Botulinum toxin A (Botox®)

Clostridium botulinum
responsible for botulism (paralysis of the nervous system)

Produces 7 neurotoxins:
Allantotoxin A, B, C1, D, E, F, G

botulinum toxin A: mechanism of action



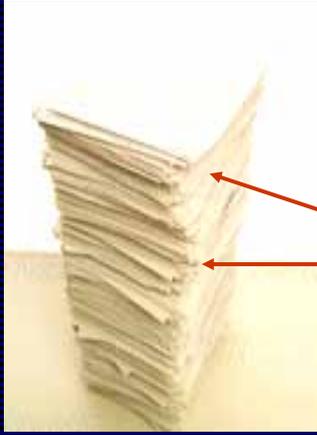


Efficacy - Side effects

- It is effective for upper part of the face
- Cost: 1000-2000 \$
- Lasts 1-8 months
- $LD_{50} = 1-2 \mu g$
 ∴ Danger of accidental systemic administration
- Pain
- Metallic taste
- Dropped eyelid (5%), if:
 - Patient with dermatochalasis
 - Infusion in wrong place
 - Higher dose
- Psychological problems ?
- Personality confusion ?
 (interchange between young look-old look)
- It is a form of addiction



LSD for old age syndrome



- abdominal obesity
- emaciation
- depression
- weakness
- reduced sociability
- reduced libido and sexual performance

Growth hormone (GH)

Central endocrine regulator
of body growth

Adolescence
gigantism

Robert Wadlow,
22 y., 2,73 m.



childhood

10 y., 1 m, dwarfism



Production of GH

Adulthood,
acromegaly



GH products

Extracts from human hypophysis

Recombinant human GH (Somatropin)

ZOMACTON[®]
GENOTROPIN[®]
HUMATROPE[®]
NORDITROPIN[®]
SAIZEN[®]

Analogues of GHRH

Somatorelin (ESFARASER[®])
Sermorelin (GEREFR[®])

Abuse of GH

- Athletes

- In normal children of small height

- Old age syndrome

- Old age syndrome

(0,125 iu/kg)

- Reduces visceral, or abdominal, obesity
- Improves emaciation
- Reduces depression
- Increases strength and endurance
- Improves sociability
- Increases libido and sexual performance

Miracle drug !!!

Tremendous use (abuse) in Europe and USA
- BUT has serious adverse effects

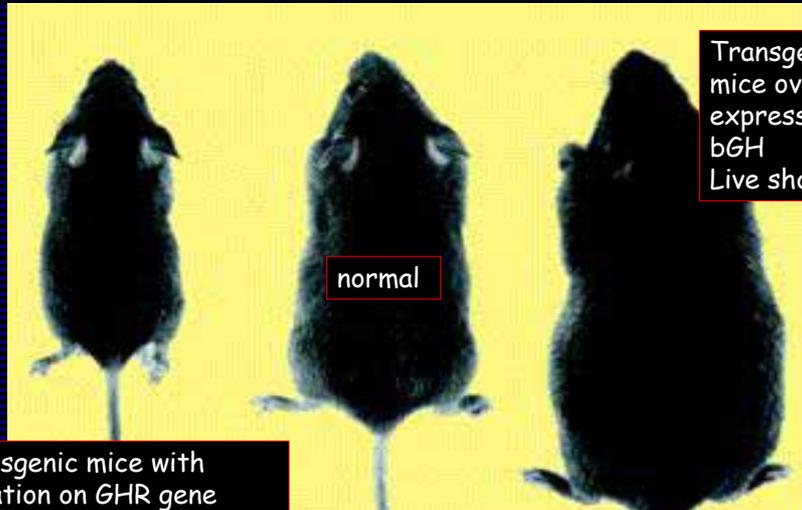
Side effects GH

- Retains body fluids and results to peripheral oedema
- Increases metabolism of carbohydrates and protein synthesis

Causes:

- Endocranial hypertension
- Diabetes mellitus type II
- Pro-inflammatory conditions
- Arthralgia
- Myalgia
- Hypothyroidism

GH increases mortality ???



Transgenic mice with mutation on GHR gene
- Fall short in development
- But live longer

- Genetics. 2005 Jan;169(1):265-74
- J Gerontol A Biol Sci Med Sci. 2003 Apr;58(4):291-6
- Mech Ageing Dev. 2002 Jan;123(2-3):121-30
- Biol Reprod. 1991 Jul;45(1):178-87

General Pitfalls (1)

ECONOMIC BURDEN

- - overall, LSD are very expensive drugs
- who will pay?
- the "patient" or national health systems, private health systems?
- LSD threaten the financial sustainability of current health systems

General Pitfalls (2)

LOW EFFICACY, SIDE EFFECTS, ETHICAL PROBELMS

overall

- LSD are of extremely low efficacy
- Have serious side effects
- Consist a form of legal addiction

General Pitfalls (3)

Pharmaceutical Industry

Cost for Promotion

- Pharma-Co spent \$ 325 m for promotion of only 4 LSD in 1999 in USA alone
 - Propecia [finasteride]
 - Viagra [sildenafil]
 - Xenical [orlistat]
 - Zyban [bupropion]

- Pharmaceutical companies make huge profits from LSD
- It is obvious that they will continue to invest on these lines
- Is this a temporary or a permanent trend?
- If permanent, who will produce new safe drugs for the real diseases?

Prof. Downey mentioned yesterday, for example, that Pharma-Industry is not interested in cardioprotective agents, even though people die from ischemia, because there is not a big market

General Pitfalls (4)

How LSD are sold
 - Tax evasion
 - Often, lack of quality control (fraudulence)

- Mainly sold via the e-commerce (the WEB)
- From International "Pharmacy" stores
- Is this legal?
- Is there a pharmacist there?
- Who controls the quality?
- Who controls their income?



Apparently, there is no control
 • Flooded every day with junk e-mails

RXONLINE
 Discount Medication Pharmacy

Generic Levitra 30 Pills x 20mg only \$171 identical to: LEVITRA <small>WARDENAFIL HCl</small>	Generic Soma 30 Pills x 350mg only \$59 identical to: SOMA TM	Generic Zocor 30 Pills x 20mg only \$105 identical to: ZOCOR <small>SIMVASTATIN</small>	Generic Lipitor 30 Pills x 20mg only \$99 identical to: LIPITOR <small>ATORVASTATIN</small>	Generic Propecia 30 Pills x 1mg only \$72 identical to: Propecia [®]
EDTM PACK 10 x Viagra 100mg pills + 10 x Cialis 20mg pills only \$109	Generic Cialis 30 Pills x 20mg only \$171 identical to: Cialis <small>Tadalafil</small>	Generic Viagra 30 Pills x 100mg only \$92 identical to: VIAGRA <small>Sildenafil</small>	Generic Ultram 30 Pills x 100mg only \$63 identical to: ultram [®]	

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- Discreet Packaging
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 Our shipping rates are the same no matter where you are ordering from: **FREE!**

Your Address	Shipping Time
Europe	14-24 business days
United States	14-24 business days

WE SHIP WITH

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The pitfalls of LSD: In conclusion

- The pharmaceutical industry takes advantage of very common symptoms and weakness of the human nature
- Sells drugs for non-health problems or for conditions that lie at the boundary between a health need and a life-style wish
- These drugs are expensive and threaten the financial sustainability of current health systems
- These drugs have low efficacy
- They may be dangerous to health

Propositions

- Traditional approaches to regulating medicines are not effective for LSD
- It is our duty, as pharmacologists and academics,
 - to protect the general public from the abuse of LSD
 - to re-establish priorities for drug development
 - to participate in coordinated actions for the management of pharmaceutical policy nationally and internationally