



Option D: Medicinal Chemistry

Part D.6

D.6 Environmental Impact of Medications



- ▶ Drugs produce side effects in the patient (and are monitored...)
- ▶ the pharmaceutical industry's side effects on the environment should be monitored too
- ▶ Green Chemistry! - 12 principles listed on 940-941

D.6 Environmental Impact of Medications

Solvent Waste

- ▶ 80% of chemicals used in the synthesis process are discarded
- ▶ often involves incineration, which releases toxins into the environment



D.6 Environmental Impact of Medications

Suitability of Solvents

- ▶ Assessed based on 3 factors
 - ▶ toxicity to workers - carcinogenic or other health issues?
 - ▶ safety of the process - flammable, explosive or toxic by-products?
 - ▶ harm to the environment - contaminate soil and ground water, cause ozone depletion, contribute to greenhouse gas formation when formed or burned?

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Preferred Solvents	Undesirable Solvents
Water	dichloromethane
Ethanol	methanal
2- Propanol	tetrachloromethane
propanone (acetone)	diethyl ether
ethyl ethanoate (ethyl acetate)	benzene

- ▶ chlorinated compounds, ethers and many aromatic compounds are not desirable and should be replaced if possible

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Nuclear Waste

- ▶ **high-level waste** - gives off large amounts of ionizing radiation for a long period of time - long half-lives
- ▶ **low-level waste** - gives off small amount of ionizing radiation for a short period of time - short half-lives
- ▶ Most waste generated in nuclear medicine is low-level
 - ▶ contains clothing, instruments, etc that have been in contact with the material and can be disposed of conventionally after a short isolation period

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Nuclear Waste

- ▶ Some waste is high-level, but far less than the nuclear energy industry - must be stored in reinforced cooling ponds for 5-10 years, then buried in a heavily shielded structure deep in the earth
- ▶ Innovations in Green Chemistry:
 - ▶ extracting enriched uranium from incinerator ash
 - ▶ reduce use of radioactive isotopes in diagnosis and replace them with fluorescent dyes



D.6 Environmental Impact of Medications

Antibiotics

- ▶ Many antibiotics are no longer effective against bacterial infections
- ▶ Antibiotic resistant bacteria - superbugs - are often a problem in hospitals
 - ▶ MRSA - methicillin resistant *Staphylococcus aureus*
 - ▶ carry several resistant genes and cause extremely difficult to treat



D.6 Environmental Impact of Medications

Antibiotic



- ▶ broad spectrum antibiotics
- ▶ extensive use has enabled some infections to thrive
- ▶ resistance to antibiotics arises from genetic mutations
- ▶ should be small number of bacterial population, but increased exposure to antibiotics increases the number of resistant organisms

D.6 Environmental Impact of Medications

Antibiotic Use

- ▶ Less than half of the world's antibiotics are used to treat human disease
 - ▶ aquaculture and household pets
 - ▶ growth and prophylactic use in livestock
 - ▶ pest control - agriculture
 - ▶ sanitizers in household products
 - ▶ sterilization and culture selection in research and industry



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Antibiotic waste



- ▶ Use in animals feeds
- ▶ given to livestock to lower incidence of disease as a precautionary measure (administered to healthy animals)
- ▶ pass through systems and out as waste - into the soil and water - and into human food chain

D.6 Environmental Impact of Medications

Antibiotic waste

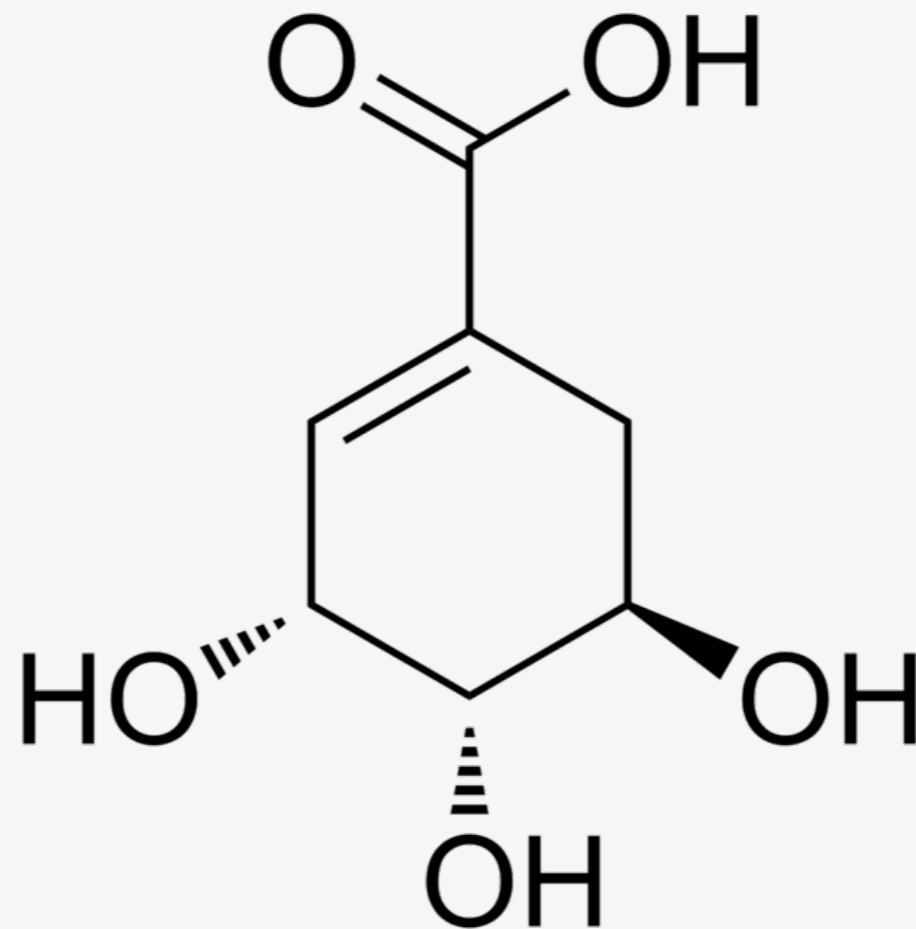
- ▶ Improper drug disposal
 - ▶ expired and unused antibiotics are often discarded by households and medical professionals
 - ▶ contaminates surface, ground and drinking water
 - ▶ effluent from some pharmaceutical plants are contaminated with antibiotics in some countries



D.6 Environmental Impact of Medications

Tamiflu

- ▶ only oral drug that was effective in cases of H5N1 (avian flu)
- ▶ Precursor to Tamiflu - shikimic acid, or its salt, shikimate:



D.6 Environmental Impact of Medications

Tamiflu

- ▶ Shikimate is found in Chinese star anise - can be extracted in a lengthy chemical process
- ▶ low yields caused shortages in 2005 and 2009
- ▶ Active efforts to find alternative sources of the precursor



D.6 Environmental Impact of Medications

Tamiflu

- ▶ Green chemistry options:
 - ▶ production of shikimate from fermentation reactions of genetically engineered bacteria
 - ▶ harvesting from needles of pine trees - even though yields are low, needles are plentiful
 - ▶ extraction from Indian sweetgum tree - inexpensive natural resource that does not involve genetic manipulation

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Green Chemistry Success for Pharmaceuticals

- ▶ Viagra by *Pfizer* - reaction route that creates a quarter of the waste - reduces amount of solvent and avoids toxic reagents
- ▶ ibuprofen - altered from a six step reaction to a three step - increased atom economy from 40% to 77% and decreased energy demand
- ▶ Lyrica - modified to use natural reagent with water as a solvent - eliminated 3 million tons of CO₂

