



Identification and Evaluation of Chemical Hazards

IGSS'09

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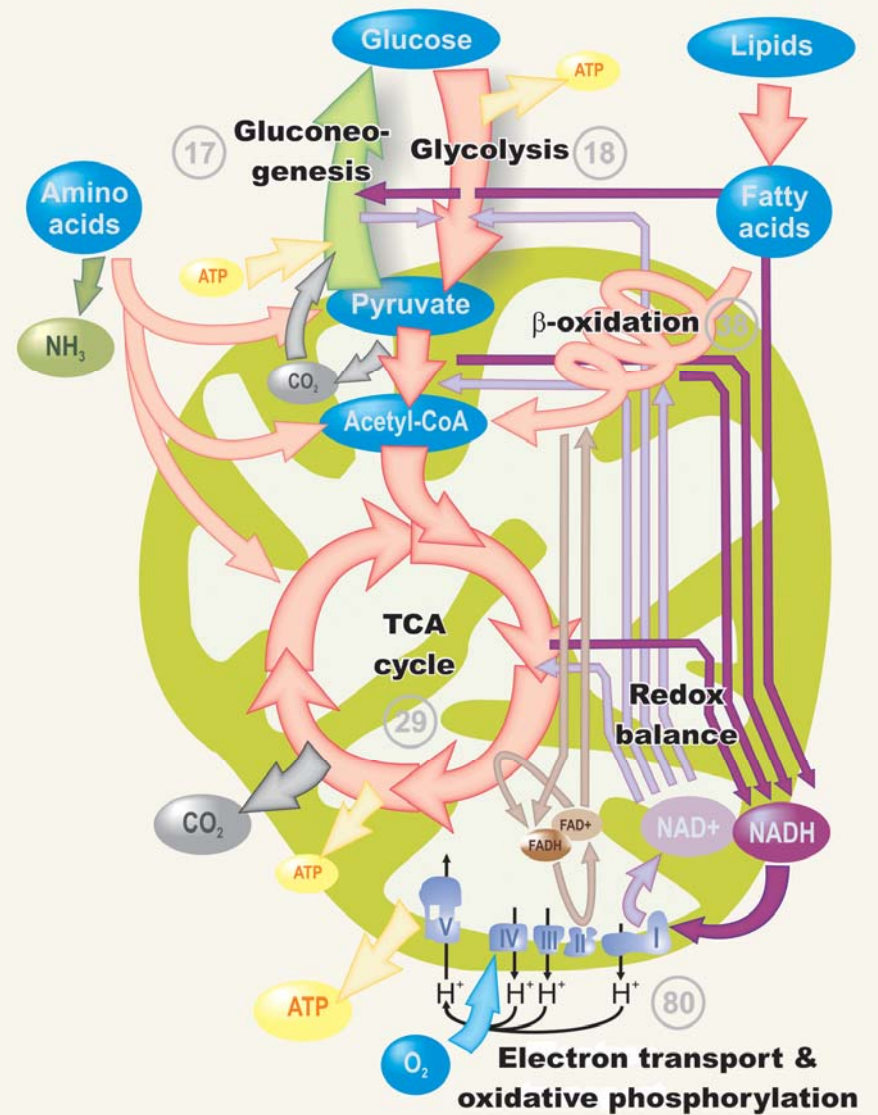
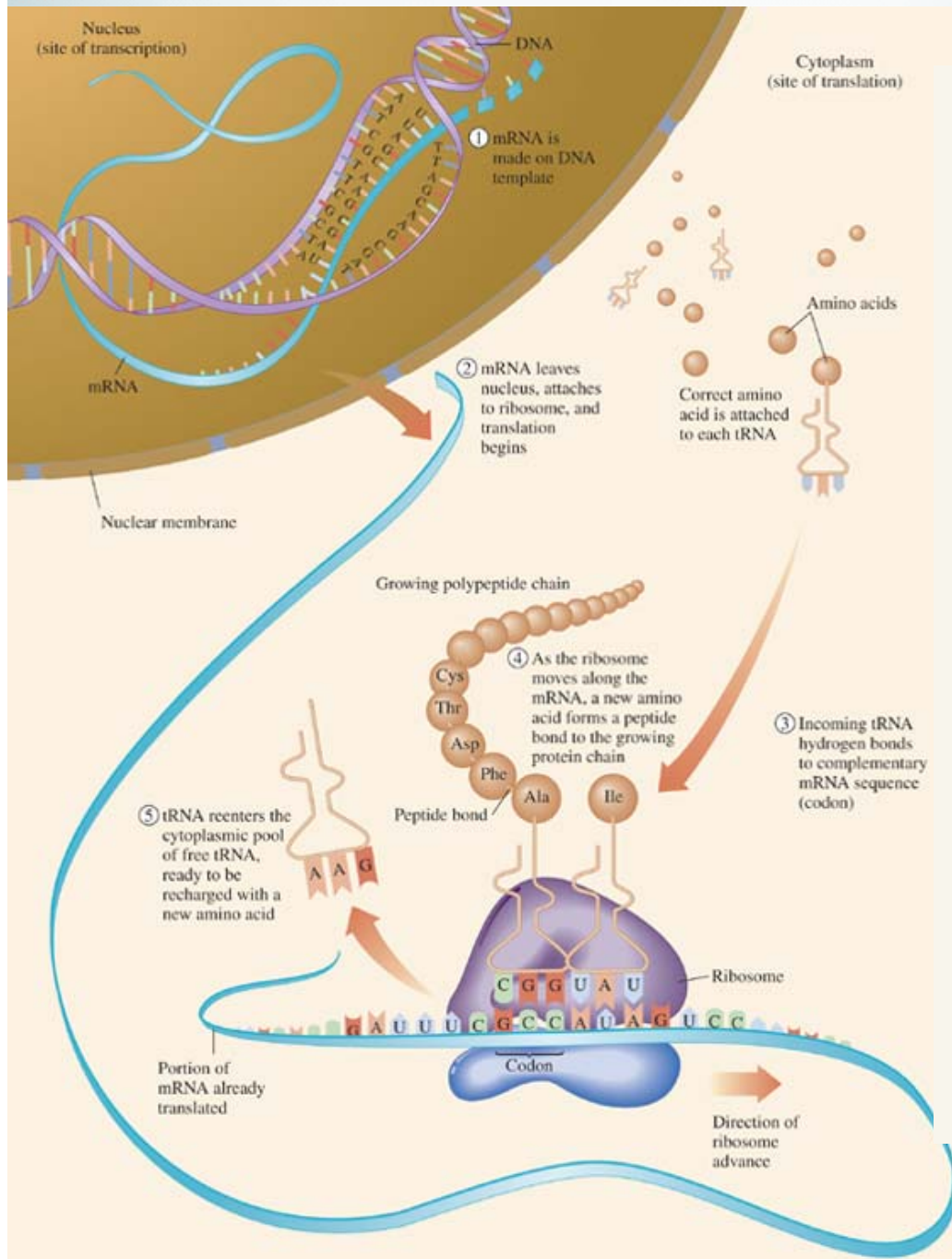
*Director of the Marian University
Institute for Green and Sustainable Science*

June 29th-July 31st, 2009

*Poison is in everything, and no thing is without poison.
The dose makes it either a poison or a remedy.*

Are chemicals hazardous?





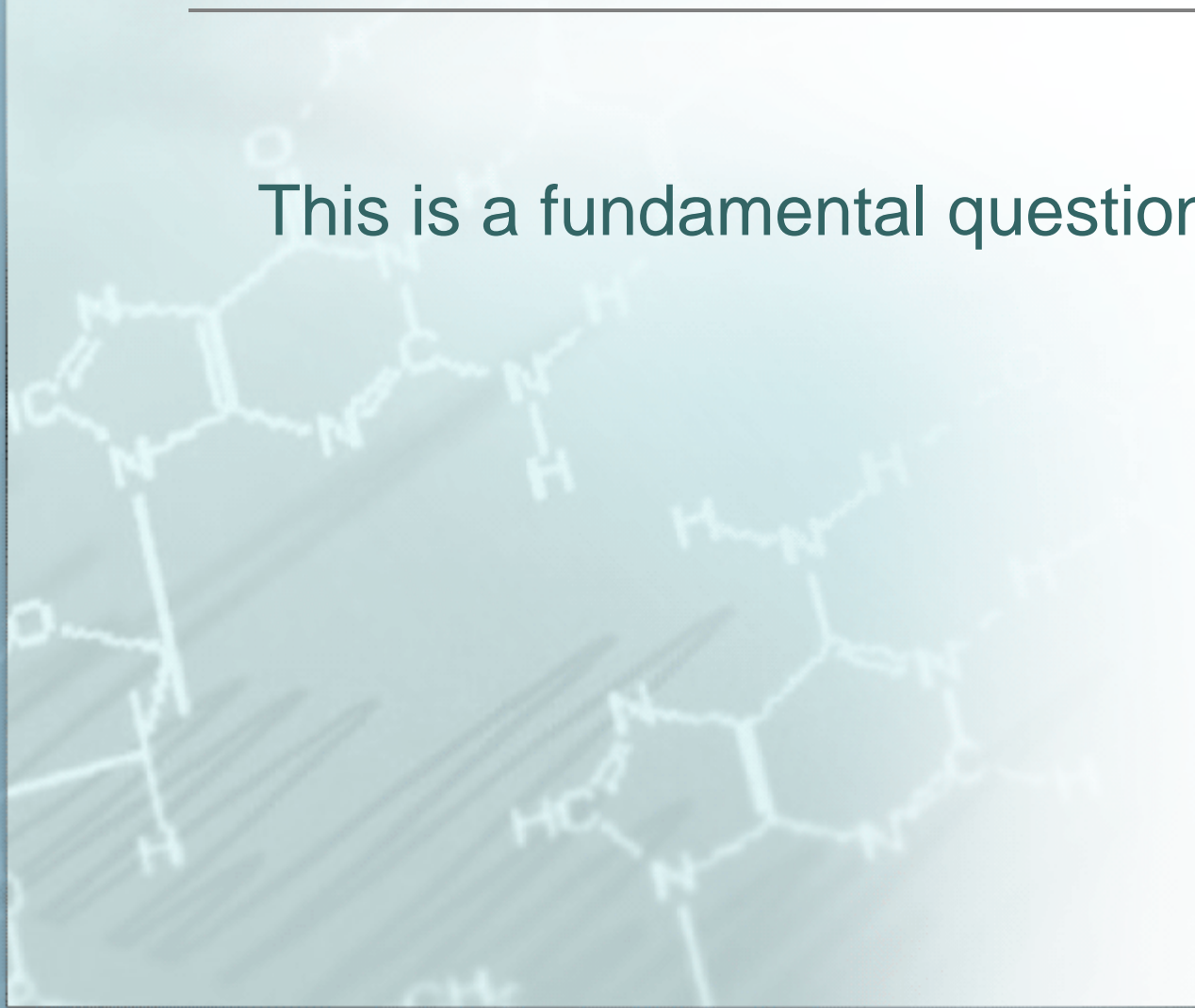
How do Green Chemists view Chemicals?

1. Not all chemical are hazardous, therefore we do not assume that all chemicals are hazards
2. We must not assume that any chemical is safe
3. We must learn about the hazards associated with a chemical and treat it appropriately
4. Natural does not equal safe



Why do molecules do what they do?

This is a fundamental question to ask!

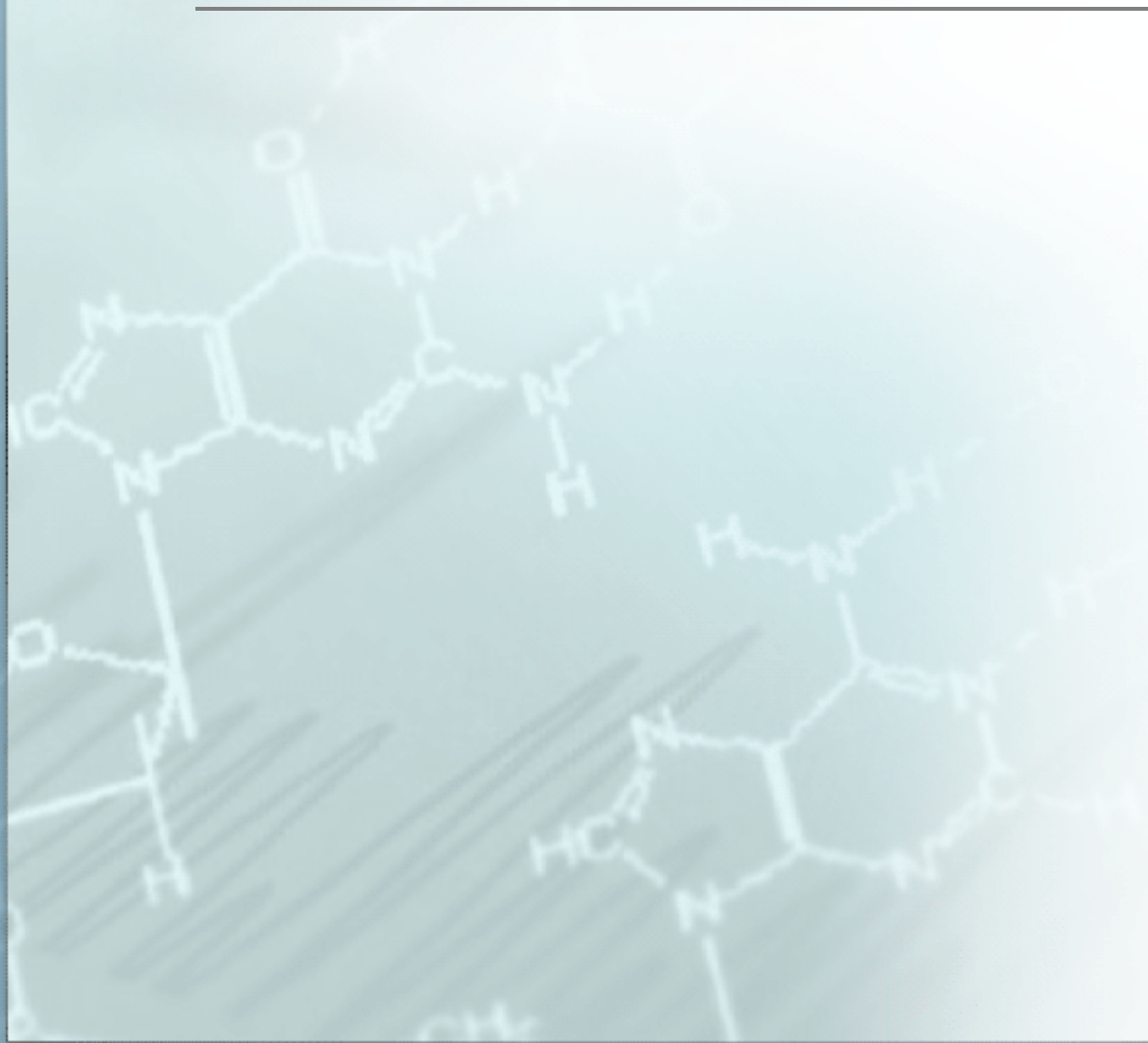


Structure-Activity Relationship (SAR)

The effect of a drug or toxic chemical on an animal, plant or the environment can be related to its molecular structure.

Used by the pharmaceutical industry to identify and optimize drug targets

What are the key features to a molecule?



What are the key features to a molecule?

organic or inorganic

neutral / cationic / anionic

shape and size

presence (and absence) functional groups

bond strengths

polarity

hydrophobic / hydrophilic

aromatic / aliphatic

hydrogen bond acceptor / donor

bp / mp / vapor pressure

solubility

Types of exposure: Chronic vs. acute



Quantitative evaluation of acute toxicity




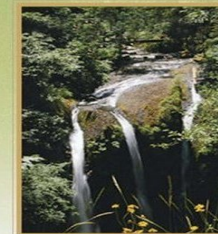
| Classification and Signal Wording | Pictorial Reference for Each Class | Acute LD ₅₀ for rat (mg/kg body weight) | | | |
|---|--|--|--------------|--------------|--------------|
| | | ORAL | | DERMAL | |
| | | Solid | Liquid | Solid | Liquid |
| Extremely Hazardous CLASS Ia "DANGER - POISON" |  | 5 or less | 20 or less | 10 or less | 40 or less |
| Highly Hazardous CLASS Ib "DANGER - POISON" |  | >5-50 | >20-200 | >10-100 | >40-400 |
| Moderately Hazardous CLASS II "WARNING" |  | >50-500 | >200-2000 | >100-1000 | >400-4000 |
| Slightly Hazardous CLASS III "CAUTION" | | >500 - 2000 | >2000 - 3000 | >1000 - 4000 | >4000 - 6000 |
| UNLIKELY TO PRESENT ACUTE HAZARD IN NORMAL USE "CAUTION" | | Over 2000 | Over 3000 | Over 4000 | Over 6000 |

Table 2.1. LD₅₀ values for various chemicals

| Substance | LD ₅₀ (grams/kilogram) |
|--------------------------------------|-----------------------------------|
| Water | 180 |
| Sugar | 35 |
| Sodium chloride | 3.75 |
| Caffeine | 0.13 |
| Sodium cyanide | 0.015 |
| Arsenic trioxide | 0.015 |
| Aflatoxin (moldy legumes and grains) | 0.010 |
| Sarin (nerve gas) | 4×10^{-4} |
| Tetanus toxin A | 5×10^{-9} |
| Botulinium toxin | 3×10^{-11} |



Classifying of Hazardous Substances

Carcinogens

Cancer-suspect Agents

Mutagens

Teratogens

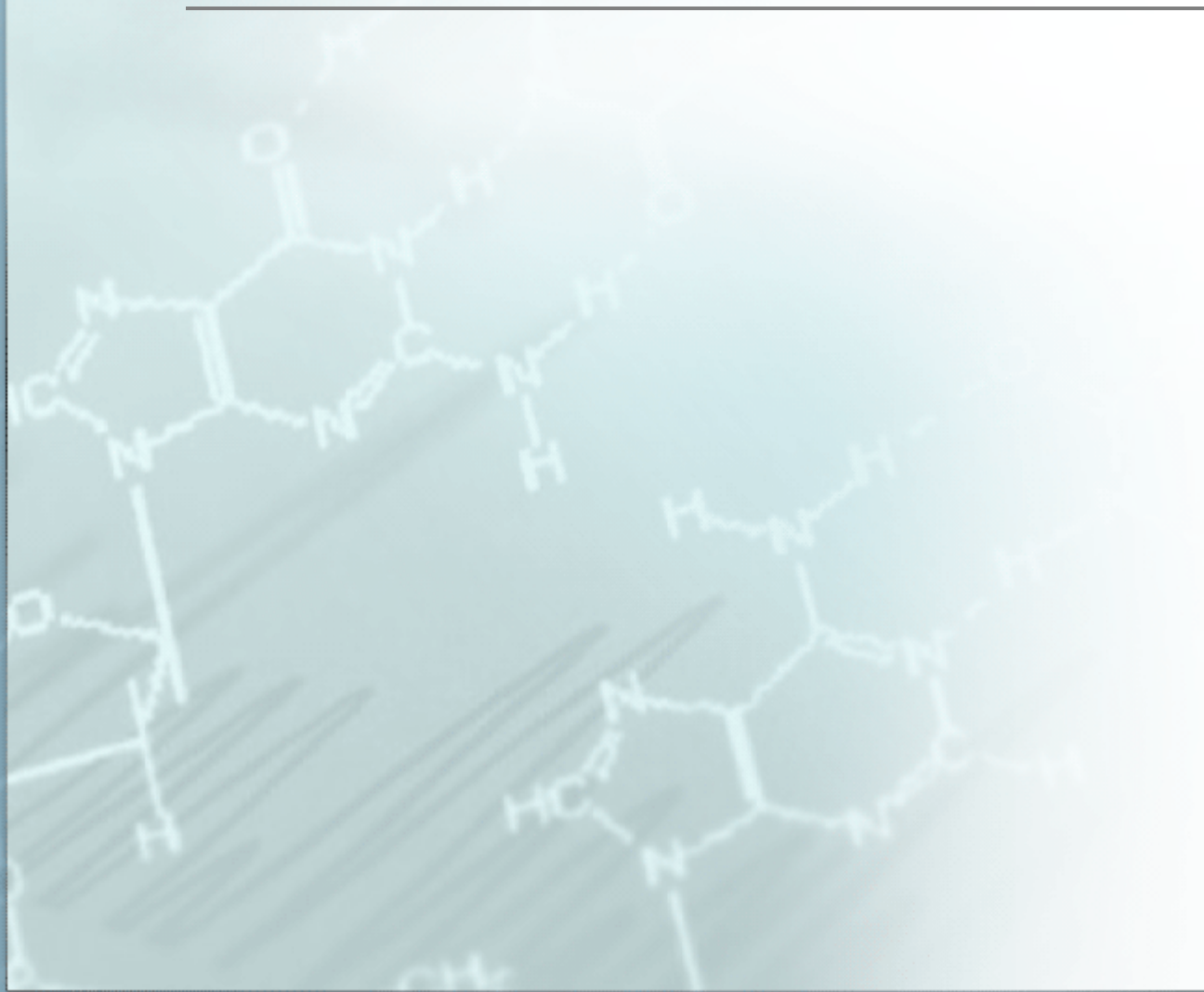
Tumor Promoters

Corrosives

Lachrymators

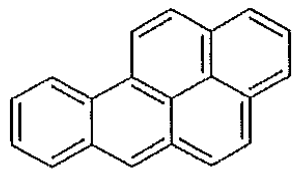
Unstable Compounds

What is a carcinogen?

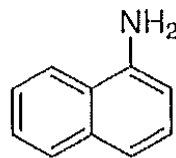


What is a carcinogen?

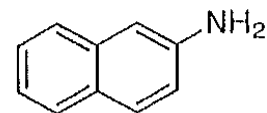
A compound that causes cancer in animals or humans



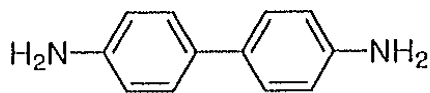
benzo[a]pyrene



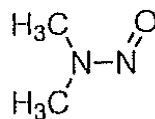
1-aminonaphthalene



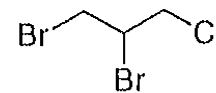
2-aminonaphthalene



benzidine



N-nitrosodimethylamine

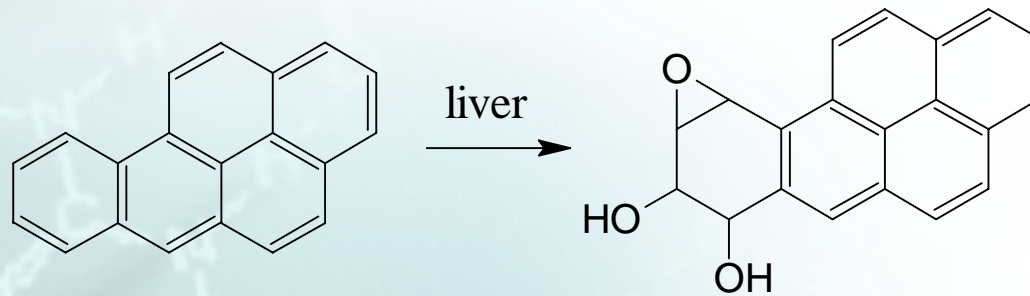


1,2-dibromo-3-chloropropane

Representative carcinogens



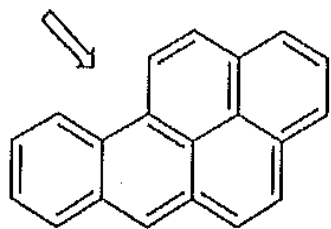
Is a carcinogen carcinogenic when it enters the body?



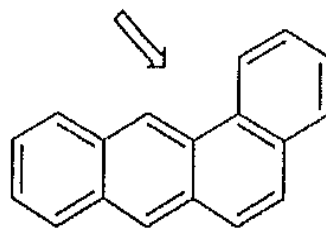
Conversion of benzo[α]pyrene to a highly carcinogenic diol epoxide

Why does the body do this?

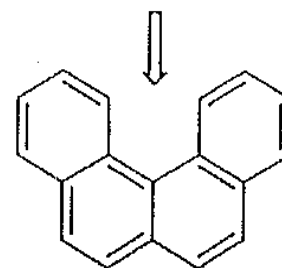
Cancer-Suspect Agents



benzo[a]pyrene

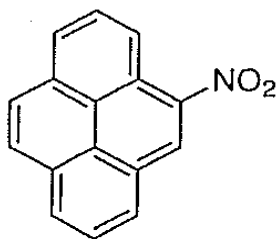


benz[a]anthracene

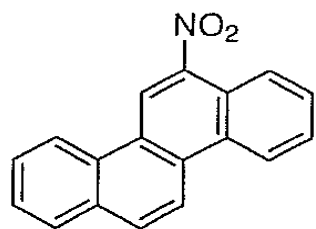


benzo[c]phenanthrene

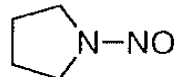
Polycyclic aromatic hydrocarbons with "bay region" indicated by arrow



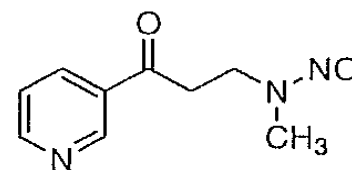
1-nitropyrene



6-nitrochrysene



1-nitrosopyrrolidine
(fried bacon)

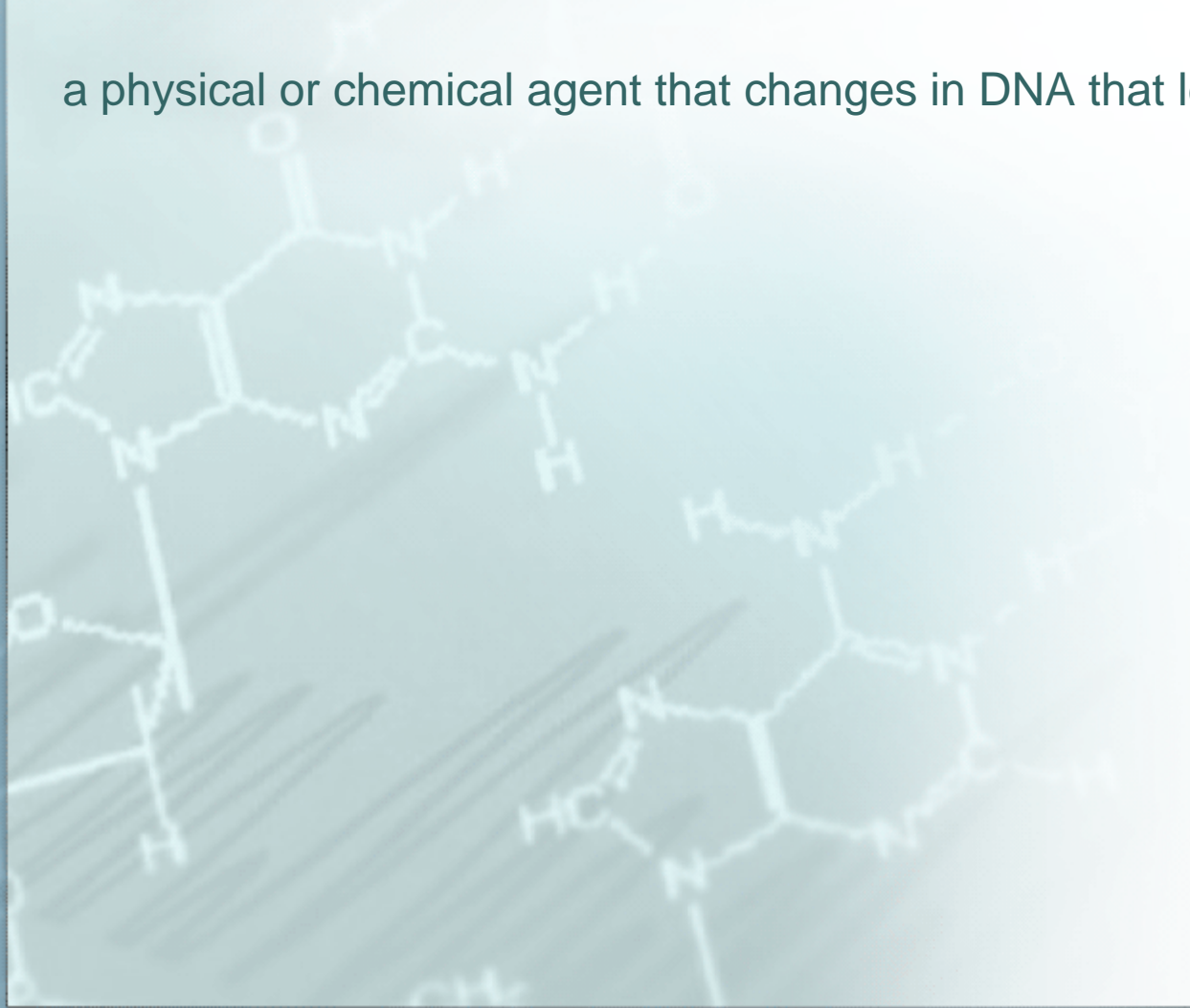


4-(methylnitrosoamino)-
1-(3-pyridyl)-1-butanone
(tobacco smoke)

Other cancer suspect agents

What is a mutagen?

a physical or chemical agent that changes in DNA that lead to genetic mutations



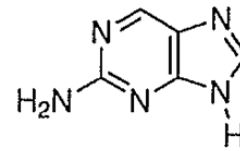
What sort of molecules can act as mutagens?

Base analogs

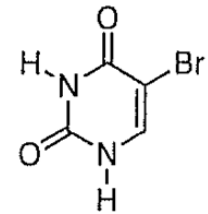
Alkylating agents

Deaminating agents

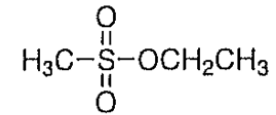
Intercalating agents



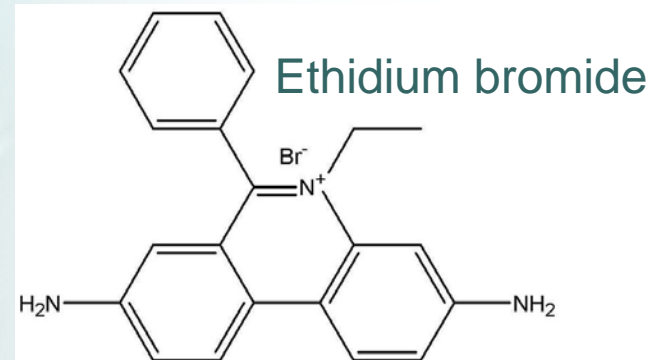
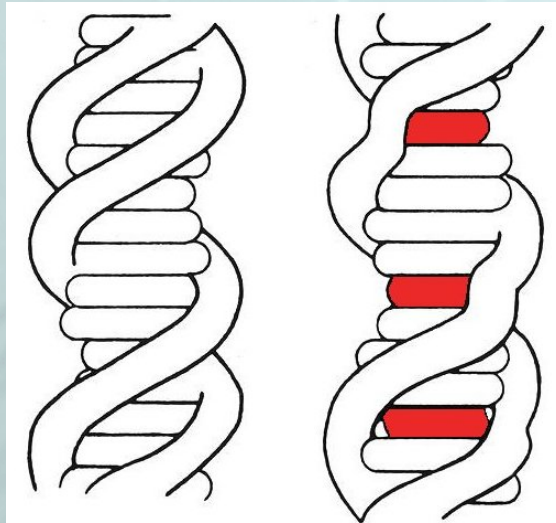
2-aminopurine



5-bromouracil

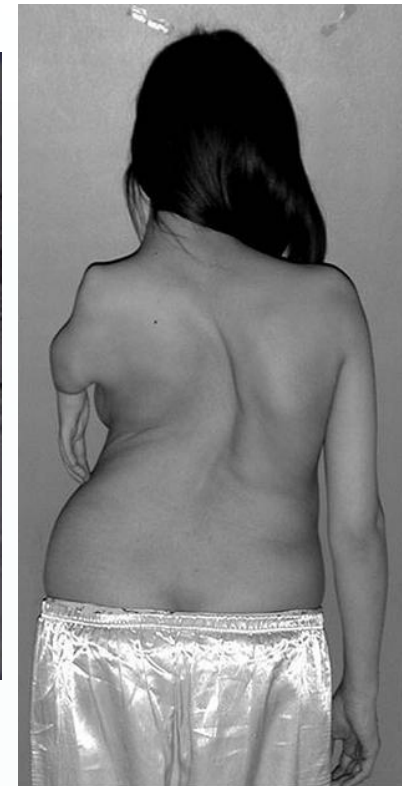


ethyl methanesulfonate



What is a teratogen?

a physical or chemical agent that causes developmental malformations



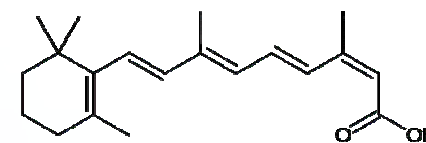
What sort of molecules can act as teratogens?

Inorganic materials

Organic solvents

Complex synthetic compounds

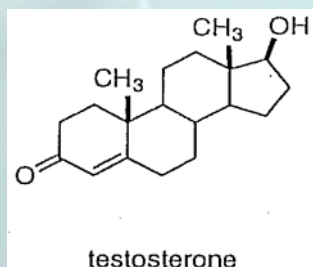
Biological compounds



Isotretinoin, used for the treatment of severe acne



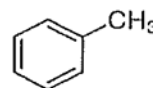
Cadmium



testosterone



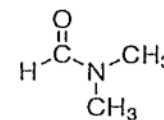
benzene



toluene

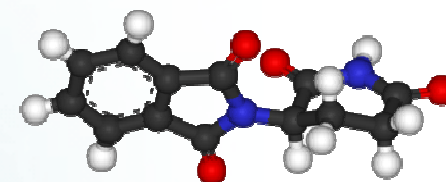
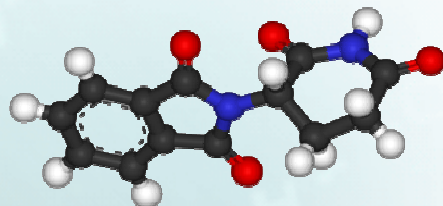
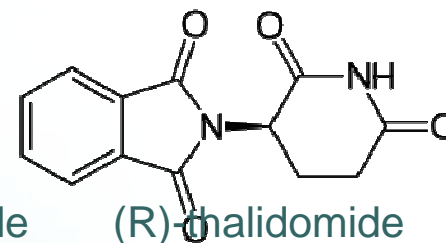
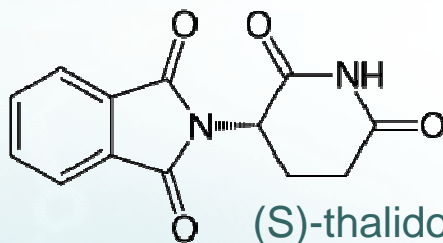


chloroform



N,N-dimethylformamide (DMF)

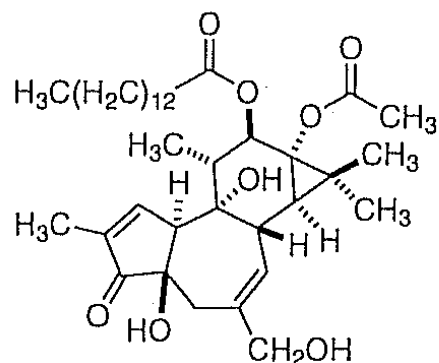
The Thalidomide Tragedy



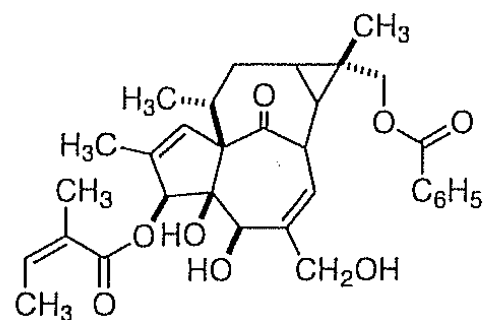
- Prescribed from 1957 to 1962 in UK, Canada, Germany, Japan - not FDA approved
- For the prevention of morning sickness
- Caused about 12,000 cases of phocomelia (flipper-like arms or legs)
- The mechanism of thalidomide's teratogenic action has led to over 2000 research papers and the proposal of at least fifteen plausible mechanisms

What is a tumor promoter?

a compounds that enhance the carcinogenicity of other compounds



tetradecanoyl phorbol acetate ("TPA")
(from *Croton tiglium*)



a 3,16-diester of 16-hydroxyingenol
(from *Euphorbia canariensis*)

Typical phorbol esters

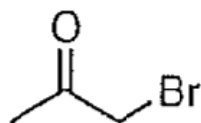
What is a lachrymator?

a physical or chemical agent that irritate mucous membranes and can cause severe eye watering

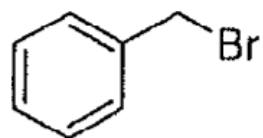
from Latin *lacrima*, for tear



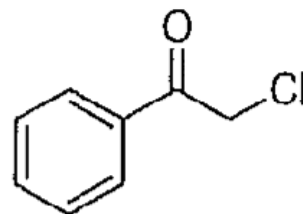
What sort of molecules can act as lachrymators?



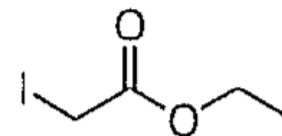
bromoacetone



benzyl bromide



chloroacetophenone



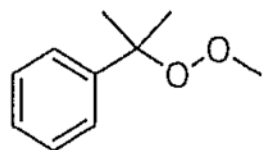
ethyl iodoacetate

What is an unstable compound?

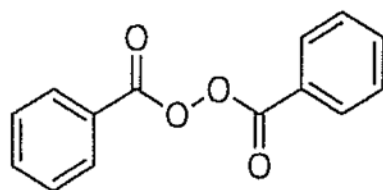
A compound that is shock sensitive or can explosively decompose



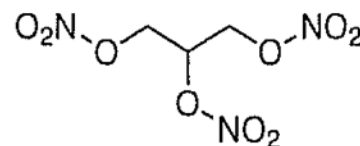
What sort of molecules are unstable?



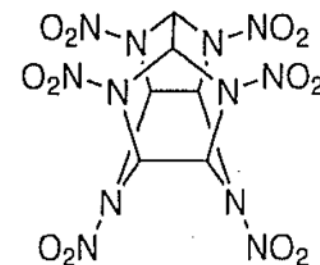
cumene hydroperoxide



dibenzoyl peroxide

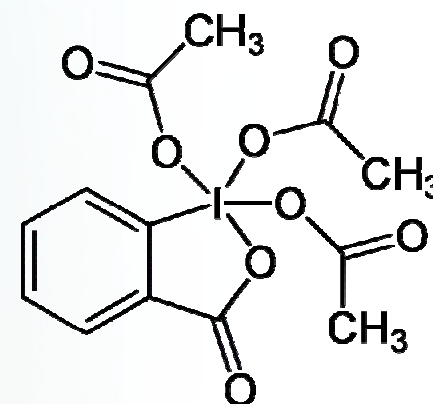


nitroglycerin



hexanitrohexaaza-
isowurtzitane

Organic peroxides
Polynitrated compounds
Inorganic perchlorates



Dess-Martin periodinane

What is a corrosive compound?

A compound that can cause severe skin and tissue damage



What sort of molecules are corrosive?

Strong acids such as H_2SO_4 , HNO_3 and HCl

Concentrated weak acids

Lewis acids

Strong bases (caustics)

Concentrated weak bases (ammonia)

Hydrides

X_2 : fluorine, chlorine, bromine and iodine