Xenobiotics in environment

1. Originated from greek word ‘xenos’= stranger/foreign, bios- life, tics-suffix
2. Xenobiotics is a compound that is foreign to the body.
3. The substances if present in higher concentration than usual are also grouped under xenobiotics.
4. Extremely stable in nature and insoluble in water.
5. Chemical compounds which are not naturally present or produced in organisms but still exist in their body is called xenobiotics.
6. Access to the body via the diet, air, drinking water, drug administration and lifestyle choices.
7. Compounds present in the higher concentration also called xenobiotics.

Man- made compound such as

1. Drugs(antibiotics)
2. Plastics(PVC)
3. Pesticides(DDT)
4. Heavy metals(arsenic)
5. Industrial chemicals(formalin)
6. Cosmetics(moisturizer)
7. Food additives(sodium nitrate)

a) Natural compound can also be xenobiotics
b) Industrial waste discharged into lakes, river, ponds and farms
c) Waste reach to plants
d) Plants store these harmful chemicals
e) From plants, transferred to human being and animals
f) Furthermore direct comsumption of water from these contaminated sites also the reason of xenobiotics in living being.
g) Xenobiotics detoxified in the liver remove from the body via urine, feces and sweat.

Xenobiotics can be-

Exogenous xenobiotics :-

The foreign molecules which are not normally ingested or utilized by the orgaism but they gain entry through dietary food stuffs, or in the form of certain medicines/ drugs used for a therapeutic cause or are inhaled through environment.

Example – drugs, food additive, pollutants, incesticides, chemical carcinogens etc

Endogenous xenobiotics :-

through they are not foreign substances but have effects similar to exogenous xenobotics. These are synthesized in the body or are produced as metabolites of various processes in the body.

Example- bilirubin, bile acids, steroids, eicosanoids and certain fatty acids.

Recalcitrant xenobiotics :-

A. halocarbons- halogens in diverse amounts viz. chlorine, bromine, fluorine or iodine instead of hydrogen atoms.

Used as propellants in spray cans of cosmetics, paints etc. and solvents such as chloroform.

They are also used in condenser units of cooling systems(ferons, CCL3F, CCL2F2 etc)

Chloroform and ferons which are basically volatile in nature and release into the atmosphere where they devastate protective ozone layer that leads to increased UV radiation.

B. polychlorinated biphenyls(PCBs) - these complexes are covalently linked with two benzene rings have halogens in the place of hydrogen. They are basically utilized as coolants in transformer or as exchange fluids for heat
C. synthetic polymers - synthesis polymers are those which are human- made polymers

Polymers are those which consists of repeated structural units known as monomers.

Polyethylene is one of the simplest polymer, it has ethylene as the monomer unit,

Example – nylon, polyvinyl chloride and polypropylene.

D. Alkylbenzyl sulphonates –are surface- active detergents that are superior as compared to soaps.

They are regarded as 'hard' detergents due to their resistance to biological degradation

Alkyl benzene sulfonate caused persistent foam in sewage treatment plants, streams and rivers and created environmental problems.

E. oil mixtures – oil is recalcitrant basically because it is not soluble in water and due to lethal nature of some of its compounds.

Biodegradation is used when there is small oil spillage but when large spill occurs these complexes become recalcitrant in nature

Biodegradation

Microorganisms on constant exposure to xenobiotics develop the capacity to degrade the same.

Mutation results in modifications of gene in microorganisms in order that the active site of enzyme is altered to show enhanced affinity of xenobiotics.

'Biodegradation' involves the breakdown of organic compounds by microorganisms, into biomass and less complex compounds, and ultimately to water, carbon dioxide and the oxides or mineral salts of other elements present.

Requirement for biodegrading xenobiotics

1. Avalibility of xenobiotic complex to microorganisms: compounds may be absorbed to particular matter in the soil, therefore prevent potential microbial attack.
2. Entry of a compound into an organism : absence of suitable extracellular enzymes and luck of penetration results in compound being resistant to biological degradation.

3. Induction of catabolic enxymes : the xenobiotics compound work as substrate or induce the synthesis of degradative enzymes for complete degradation of toxic compounds.
4. Aerobic or anaerobic environments : aerobic or anoxic environmant can bulid up some compounds that could be degraded by different conditions.

Biotransformation/detoxification reactions

All the biochemical reactions involved in the conversion of foreign, toxic and water insoluble molecules to non-toxic, water soluble and excretable forms are called detoxification/biotransformation reactions.

The overall purpose of the two phases of metabolism of xenobiotics is to increase their water solubility(polarity)and thus excretion from the body.

In certain situations these reactions may instead increase the toxicity of a foreign compound, then these are called entoxification reactions.

Occur in two phases of reaction –

1. **Phase 1 reactions** : phase 1 reaction alters the xenobiotic complex from lipophilic to polar so as to introduce one of following groups into the initial compounds :- OH, -COOH, -NH2 or –SH.
   A. Oxidation
   B. Reducation
   C. Hydrolysis reactions

   a) Oxidation – a large number of foreign substances are destroyed by oxidation in the body.
      Example – oxidative of methyl group containing compounds
      Methyl group- is oxidized to acid through formation of alcohol and aldehyde
   b) Reduction : azo/nitro compounds

It is supported by anaerobic conditions that most commonly occur in mammalian tissue.

Nitro reduction(nitro reductase)and azo reduction(azo reductase) are the two types of reductions(mercier, 2013) in which nitro reduction involves three important enzyme system that are:

a) Cytochrome P450(e.g in liver)
b) DT- diaphorase : cytosolic flavoprotein(in liver) = NAD(P)H quinone oxido reductase
c) Bacterial intestinal enzymes

Reduction of nitro compounds
p- nitrobenzene → p- amino benzene

p- nitro phenol → p- aminophenol

c) Hydrolysis - Breakdown of any bond in molecules using water. Hydrolytic enzymes are involved in biotransformation of xenobiotics through hydrolysis.

Substrates that are involved in hydrolysis are:

a) Phosphate ester (phosphoesterase)
b) Carboxylic acid ester, amides
c) Epoxide

Whereas the enzymes that are utilized are epoxide hydrolase(former names: epoxide hydrate, epoxide hydrase). Most of the enzymes are in microsomes or in cytosol. While the product formed at the end is always trans hydroxyls.

Phase II reactions:

Parent xenobiotics compound or their phase I metabolites which contains suitable reactions undergo conjugation reactions with the substrate to yield conjugates.

Conjugation is a process by which the foreign molecules and their metabolites are coupled with a conjugated agents and are converted to soluble, non toxic derivatives which are easily excreted in urine.Types of phase 2 reactions

A. Glucuronidation

Glucuronidation is the most frequent conjugation reaction. It raction characteristics are low affinity, high capability for catalysis and availability of proficient substrate conjugation. The enzyme that is utilized for glucuronidation is UDP glucuronosyl transferases(UGT).

B. Sulfation

Reaction characteristics are high- affinity, little capability and availability of competent substrate conjugation at low substrate concentrations.

The sulfate donor is adenosine 3'phosphosulfate(PAPS) this compound is called 'active sulfate'
The enzyme is sulfo transferase
Major subfamilies of cytosolic sulfotransferases are included as SULT 1, SLUT2 and SLUT3.
The end product released after sulfate conjugation involves the transfer of sulfonate(SO3-), not sulfate(SO4-) from PAPS to the xenobiotics

C. Acetylation

Two types of acetylation reactions occur. One involves xenobiotic compound and an activated conjugated intermediate, acetyl CoA. This reaction is called as acetylation
Acetylation is represented by :

X + acetyl- CoA → acetyl + CoA

X- xenobiotic
Acetyl-CoA(active acctate) is the acetyl donor
Compounds conjugated by acetylation
Sulphanilamide
PABA(para amino benzoic acid)

D. Methylation

Methylation is a ordinary but usually a insignificant pathway of xenobiotic metabolism.
Methylation is limited in the body.

S- Adenosyl methionine (active methionine)acts as a methyl group donor
Reactions are called transmethylation reactions
Enzymes catalyzing the reactions are methyl transferases
Compounds conjugated by methylation are-

1. Nicotinamide
   Nicotinamide →(CH3) N- methyl nicotinamide
2. p- methyl amino azo benzene →(CH3) p- Dimethyl amino azo benzene(hepatic carcinogen)

E. Conjugation with amino acids(glutathione conjugation)

Substrate that are involved in glutathione conjugation comprises an vast array of electrophilic xenobiotics, or xenobiotics bio transformed into electrophiles.

To act as substrate for glutathione S- transferase(GST), the compound should exhibit three general features 1)hydrophobic 2)electrophilic 3)react non enzymatically with glutathione(GSH)at a computable rate.

Hazards caused by xenobiotic compounds

1. they are identified to cause health hazards to mankind in various ways like skin problems, disrupt reproductive system and even may be the cause of triggering cancer.
2. These compounds have the property of bioaccumulation or bio magnification as they are persistent and remain in environment for many years.
3. They are also found in food chains and the concentration was found to be exceptionally high even in organisms that are not in direct contact with xenobiotics

a) Carcinogens – liver cancer, melanoma
b) Immune system- suppressed, swollen thymus gland infants
c) Reproductive system- reduced birth weight, decrease in gestational ages, abortions
d) Nervous system- short-term memory loss, learning
e) Endocrine system- thyroid health