SKF 4163 : Safety in Process Plant Design

Toxicology

Mohammad Fadil Abdul Wahab
Faculty of Petroleum and Renewable Energy Engineering

Norzita Ngadi
Faculty of Chemical Engineering

Toxicology

Is a study of:

- The way toxicants enter biological organism
- The effect of toxicants on biological organism
- The way toxicants are eliminated from biological organism

Fundamental principle of toxicology

- There are no harmless substance, only harmless ways of using substances

Definition of toxicology

- A qualitative and quantitative study of the adverse effects of toxicants on biological organism.

Toxicants

- Toxicants are hazardous materials
- A chemical agents
- A physical (dusts, fibers, noise, and radiation) agents, e.g. asbestos
- Toxicity is a property of toxicant that describe its effect on biological organism.
- Toxic hazards is the likelihood of damage to biological organism based on exposure resulting from the use/transport/storage of the toxicants.

Industrial Hygiene

- The toxicity however, cannot be changed.
- So we need methods to prevent or reduce the entry of toxicants into biological organism
- Toxic hazard can be reduced by the application of appropriate industrial hygiene techniques.
- Industrial hygiene is the identification, evaluation and control of occupational conditions that cause sickness and injury.

How toxicant enter biological organism?

- Injection: through cuts or hypodermic needles into the skin, usually result in highest blood level concentration.
- Inhalation: through mouth/nose into the lungs (respiratory system), most common in industry, 2nd highest blood level concentration.
- Ingestion: through mouth into stomach and gastrointestinal tract, 2nd lowest in blood level concentration.
- Dermal absorption: through skin membrane, lowest in blood level concentration, note: absorption of phenol could result in death

Entry routes for toxicants and methods of control

Entry route	Method of control
Ingestion	Enforcement of rules on eating and drinking
Inhalation	Proper ventilation, use of respirators, fume hood, and use of other PPE
Injection	Proper protection clothing and PPE
Dermal absorption	Proper protection clothing and PPE

Respiratory system

- Upper respiratory
- Lower respiratory

Upper respiratory system

- Nasal passages (nose, sinuses), Oral cavity (mouth), pharynx, larynx and trachea.
- Filtering, heating, and humidifying the air
- Affected by toxicants that are soluble in water
- These toxicants will react or dissolve in the mucus to form acids or bases
- E.g. hydrogen halides, oxides, hydroxides, sodium dusts

Lower respiratory system

- Lungs that contain bronchial tubes and alveoli for gas (O_2 and CO_2) exchange with blood.
- Toxicants affect the function of alveoli by blocking the transfer of gases or by reaction with alveoli wall to produce corrosive/toxic substances.
- e.g. of toxicants: monomers (acrylonitrile), halides (Chlorine), hydrogen sulfide, methyl cyanide etc

Respiratory system

- Effect of dust and insoluble materials
  - The smaller the dust particles, the farther it penetrates into respiratory system
  - Particles >5µm are filtered in the upper respiratory system.
  - 5µm>Particles>2µm can reach bronchial system
  - Particles<1µm can reach the alveoli

How toxicants are eliminated from biological organism

- Excretion- through kidneys (blood to urine), liver (selectively excrete certain chemicals indigestive tract to bile), lungs , skin (sweats), hair, nail or other organ
- Detoxification-change the chemical into something less harmful by biotransformation through liver, can also occur in blood, intestinal wall, skin, kidney
- Storage- in fatty tissue. Can create problem when fatty deposits are metabolized and released the toxic (e.g. during reduced food supply). Also store in bone, blood, liver, and kidney.

Note: Massive exposure to hazardous chemical can damage major organs (kidney, lung, liver), hence reduces their ability to excrete.

Your kidneys receive the blood from the **renal artery, process it, return the processed blood to the body through the renal vein and remove the wastes and other unwanted substances in the urine. Urine flows from the kidneys through the ureters to the bladder.**

Effects of Toxicant

- Irreversible
  - Carcinogen - cause cancer
  - Mutagen - cause chromosome damage (genetic changes in spermatozoa or ovum cells)
  - Teratogen - cause birth defects (deformation of fetus)
- May or may not be irreversible
  - Dermatotoxic – affects skin
  - Hemotoxic – affects blood
  - Hepatotoxic- affects liver
  - Nephrotoxic – affects kidneys
  - Neurotoxic – affects nervous system
  - Pulmonotoxic- affects lungs

Agent Orange

- To reduce the dense jungle foliage so that communist forces might not use it for cover and to deny them use of crops needed for subsistence - **Herbicidal warfare turns 'mutagenic warfare'**
- 78 million liters of Agent Orange was sprayed during Vietnam war
- Contain dioxins

Medical Test to Determine Exposure Before Symptoms Appears

- Compare results with a medical baseline results (usually done on new employees before employment)
  - Respiratory problem (using spirometer): asthma, bronchitis, emphysema
  - Nervous system disorder: mental status, motor system reflexes, sensory system
  - Skin texture, hair, nail, vascularity (blood vessel)
  - Blood count (red/white cell, hemoglobin, platelet count)
  - Kidney (test for quantity and for sugar and proteins in urine)
  - Liver (through chemical test on urine and blood)

Toxicological Studies

- To quantify the effects of toxicant on target organism (e.g. LD, LC etc.)
- Usually done on animals (lung, kidney, liver) and the results are extrapolated to human. For genetic effect, the study is on single-cell organism.
- Different routes requires different toxicological study

- Involve identifying,
  - The toxicant
  - The target or test organism
  - The effect or response to be monitored
  - The dose range
    - Ingestion and injection , *mg toxicant/kg of body weight*
    - Gaseous inhalation, *ppm or mg/m^3 air*.
    - Particle inhalation, *millions of particle per cubic foot* (mppcf) or *mg/m^3 air*.
  - The period of the test (mostly acute tocixity study)
    - Acute toxicity, single exposure or series of exposure in a short time
    - Chronic toxicity, multiple exposure over a long period of time. This is difficult and time consuming to perform.

Dose or Concentration vs Response

- Toxicological test are done on a target population.
- Individual target response different for the same dose (depends on age, sex, weight, diet, gen health).
- The results are statistically analyzed
- The results are reported as,
  - LD : lethal dose for ingestion or injection or skin absorption
  - TD : toxic dose for not lethal but irreversible
  - ED : effective dose for minor and reversible
  - LC : lethal concentration for gaseous inhalation

e.g. LD_{50} means lethal dose for 50% of the subjects or expt. animal population.

Hodge-Sterner Table for Degree of Toxicity

LD_{50} per kg of body weight	Degree of toxicity	Probable lethal dose for 70-kg human
<1.0 mg	Dangerously toxic	A taste
1.0 - 50 mg	Seriously toxic	A teaspoonful
50 – 500 mg	Highly toxic	An ounce (or 28 gm)
0.5 – 5 g	Moderately toxic	A pint (or 1/2 quart)
5 – 15 g	Slightly toxic	A quart (or 1.13 liter)
> 15 g	Extremely low toxicity	More than a quart

According CPLHC

LD_{50} per kg of body weight	Degree of toxicity
<25 mg	Very toxic
25 to 200 mg	Toxic
200 to 500 mg	Harmful

Threshold Limit Value (TLV)

- Refer to airborne concentrations that correspond to condition under which no adverse effects are normally expected during worker's lifetime.
- The body is able to detoxify and eliminate the agent without any detectable effects.
- Units:

  ppm (by volume), *mg/m*^{3},

  for dust *mg/m*^{3} or *mppcf* (*millions of particles per ft*^{3} *air*)
- The TLV assumes that workers are exposed only during normal eight-hour workday.

Threshold Limit Value (TLV)

– The American Conference of Governmental Industrial Hygienists (ACGIH) established 3 different types of TLV

TLV	PEL (OSHA 1994 , Malaysia)
– TLV-TWA (~OSHA PEL)	eight-hour TWA
– TLV-STEL (Short-Term Exposure Limit)	Maximum exposure limit?
– TLV-C	Ceiling limit

Note:

TLV definition is similar to PEL in OSHA 1994 (Malaysia)

Data for TLV-TWA is slightly more conservative than OSHA PEL.

TLV-TWA

- Time-weighted average (TWA) for a normal 8-hour workday or 40-hour work week, to which nearly all workers can be exposed, day after day, without adverse effects.
- PEL (Permissible exposure level) defined by OSHA (USA) generally follow closely TLV-TWA
- More TLV-TWA data are available than TLV-STEL and TLV-C
- See Table for variety of TLV-TWA and PEL for a variety of chemical substances.
- Compare with schedule 1 in USECHH (eight-hour TWA).

TLV-STEL

Short-Term Exposure Limit (STEL).

The maximum concentration to which workers can be exposed for a period of up to 15 minutes continuously without suffering,

(1) intolerable irritation

(2) chronic or irreversible tissue change

(3) narcosis of sufficient degree to increase accident proneness, impair self-rescue, or materially reduce worker efficiency,

provided that no more than 4 excursions per day are permitted, with at least 60 minutes between exposure periods, and provided that the daily TLV-TWA is not exceeded

- Compare with USECHH in OSHA 1994 (maximum exposure limit)?

TLV-C

- Ceiling limit. The concentration that should not be exceeded, even instantaneously.
- Some values are tabulated in Table
- Compare with ceiling limit in schedule 1 in USECHH, OSHA 1994 (Malaysia)?

Convert mg/m^3 to ppm

$$C_{ppm} = \text{Concentration in ppm} = 0.08205\left(\frac{T}{PM}\right)\left(C(mg/m^3)\right)$$

- T is in *Kelvin,* P is the absolute pressure in *atm*
- M is the molecular weight in *g/g-mol*
- For T=25^{o}C and P= 1atm,

$$C_{ppm} = 0.08205\left(\frac{298.15}{(1)M}\right)\left(C(mg/m^3)\right) = 24.46\frac{C(mg/m^3)}{M}$$

For example, Acetone with TLV 1780mg/m^3,

$$C_{ppm} = 24.46\frac{1780}{58.08} = 749.6\,ppm$$

Case study

- A group of 100 workers is exposed to phosgene in two consecutive periods as follows:

  10 ppm for 30 minutes and 1 ppm for 300 minutes.

- Check whether these exposures exceed the TLV?

- If so, determine the expected number of fatalities?

- The TLV-TWA for phosgene is 0.1 ppm.

  TWA=[0.5x10 +5x1+2.5x0]/8=10/8=1.25ppm >0.1ppm

  Also two-consecutive exposures at high concentration for 5½ hrs is definitely above the TLV-STEL.
- To determine the expected number of deaths, we need a correlation.
- Here we will use probit correlation.
- Probit stands for probability unit.

Probit Correlation

- If we plot percentage (of workers) affected vs magnitude of exposure(nat. log or log) (e.g. explosion peak overpressure, exposure to hazardous chemical) we typically get a sigmoid shape response.

Probit Correlation

- However, it is easier to work with straight line.
- We do that by converting the percentage (P) to a probit variable (Y) using,

$$P = 50\left[1 + \frac{Y-5}{|Y-5|}\,erf\left(\frac{|Y-5|}{\sqrt{2}}\right)\right]$$

Note: erf is error function.

Probit Correlation

- We could then tabulate percentage (P) and probit variable or probits (Y) for convenience.

Probit Correlation

- The relationship between probit variable Y and the causative variable (V) is given by

$$Y = k_1 + k_2 \ln V$$

- Where k_1 and k_2 are probit parameters.
- Probit parameters and the causative variable (V) for a variety of exposures are available.

Revisit our case study

- For deaths due to phosgene exposure, the values for k:

  k_1=-19.27 and k_2=3.69

  and V=ΣCT, where T is time in minutes, C is concentration in ppm.

  $Y=k_1+k_2 \ln V$

  $Y=k_1+k_2 \ln \Sigma CT=-19.27+3.69 \ln[10(30)+1(300)]$

  $Y=4.33$

So percentage = 25%

And the expected deaths= 0.25x100 workers = 25 workers

References

- Crowl, Daniels A. and Louvar, Joseph F., Chemical Process Safety: Fundamentals with Applications, Prentice Hall, 1990, New Jersey, USA.
- Occupational Safety and Health Act (OSHA) and Regulations, MDC Publishers Sdn Bhd, Malaysia