VOLATILE ORGANIC COMPOUNDS

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1 Basic principles of volatile organic compounds

1.1 Introduction to volatile organic compounds

The term volatile organic compounds refer to a class of liquid organic chemicals with variable lipophilicity and volatility, small molecular size and lack of change. Volatile organic compounds undergo ready absorption across the lung, skin and gastrointestinal tract. The lipophilicity of volatile organic compounds increases with increasing molecular weight, whereas volatility decreases. Volatile organic compounds frequently are used to dissolve, dilute or disperse materials that are insoluble in water. Everyone is exposed to volatile organic compounds during normal daily activities. Environmental exposure to volatile organic compounds in air or and groundwater have multiple exposure pathways. Household use of solvent contaminated water may result in solvent intake from inhalation and dermal and oral absorption. Most solvent exposures involve a mixture of chemicals rather than a single compound.

Although some volatile organic compounds are less hazardous than other, all volatile organic compounds have toxic effects. Most have the potential to induce narcosis and cause dermal and mucous membrane irritation.

1.2 Classification of volatile organic compounds

Volatile organic compounds are classified in accordance with the interests and needs. Volatile organic compounds can be discussed in terms of their target organs, use, source and effects. Volatile organic compounds can be classified in terms of their physical state, chemical stability or reactivity, general chemical structure and poisoning potential. Volatile organic compounds are the chemical or physical agent that produces adverse responses in the biological systems with which they interact. These responses span a broad physiologic spectrum, ranging from minor effects to a more serious response such as liver or kidney damage or causes permanent disabilities such as kidney failure or cancer.

1.3 Characteristics of exposure

A toxic response is dependant on the chemical and physical properties of the solvent, the exposure situation, how the solvent is metabolized by the system and the overall susceptibility of the biological system.

1.3.1 Route and site of exposure

The major routes by which volatile organic compounds gain access to the body are the gastrointestinal (ingestion), lungs (inhalation) and the skin (dermal).

1.3.2 Duration and frequency of exposure

A great variety of toxicities can result from chemical exposure from volatile organic compounds and it can be classified into categories such as:

i. Acute exposure: These volatile organic compounds have a sudden onset for a short period of time and have a reversible effect. Acute exposure by inhalation refers to continuous exposure for less than 24 hours, most frequently for 4 hours. Repeated exposure is divided into three categories; sub-acute, sub-chronic and chronic. Sub-active exposure refers to repeated exposure to a chemical for 1 month or less, sub-chronic for 1 to 3 months and chronic for more than 3 months.
ii. Chronic exposure: These volatile organic compounds have a long or permanent effect, constant or continuous, a permanent or irreversible effect.
iii. Local exposure: Occurs at the site of application or exposure between the toxicant and the biologic system.
iv. Systematic exposure: Requires absorption of the toxic solvent within the body and then distribution of the toxic solvent via the bloodstream to susceptible organs, which are the sites of action.

The other time related factor that is important in the temporal characterization of repeated exposure is the frequency of exposure. A chemical that produces severe effects with a single dose may have no effect if the same total dose is given at several different times.

1.4. Spectrum of undesired effects

Each solvent and drug produces a number of effects, but usually one effect is associated with the primary objective of the therapy. All the other effects are referred to as undesirable effects or side effects.

1.4.1 Allergic Reactions

Chemical allergy is an immunological mediated adverse reaction to a chemical resulting from previous sensitization to that chemical or to a similar one. Once sensitization has occurred, allergic reaction may result from exposure to relatively very low doses of chemicals. Sensitization reactions are sometimes very severe and may be fatal.

Most chemicals and their metabolic products are not sufficiently large to be recognized by the immune system as foreign substances and thus must first combine with an endogenous protein to form an immunogen, which is called a hapten. This hapten-protein complex is then capable of eliciting the formation of antibodies.

1.4.2 Immediate versus Delayed effects

Immediate effects occur rapidly after a single administration of a substance, whereas delayed effects occur after the lapse of some period of time. Carcinogenic effects of chemicals usually have long latency periods often 20 to 30 years after the initial exposure, before tumors are observed in humans.

1.4.3 Reversible versus Irreversible effects

Some effects of chemicals are reversible and others are irreversible. If a chemical causes pathological injury to a tissue, the ability of that tissue to regenerate largely determines whether the effect is reversible or irreversible. Carcinogenic and teratogenic effects of chemicals once they occur are usually considered irreversible effects.

1.4.4 Local versus Systemic Toxicity

Another distinction between types of effects is made on the basis of the general site of action. Local effects occur at the site of first contact between the biological system and the toxicant. Systemic effects require absorption and distribution of a solvent from its entry point to a distant site at which deleterious effects are produced. Most substances except highly reactive materials produce systemic effects. Most chemicals that produce systemic effects usually elicit their major toxicity in only one or two organs, which are the target organs of toxicity of a particular chemical. Target organs in order of frequency of involvement are the Central Nerve System, the circulatory system, the blood, visceral organs such as the liver, kidney, lung and the skin. Muscle and bone are seldom target tissues for systemic effects.

1.5 Interaction of chemicals

Because of the large number of chemicals an individual may come in contact with it at any time at the workplace, environment and medication. It is necessary to consider how different chemicals may interact with each other. Interactions can occur through various mechanisms such as absorption, protein binding and the biotransformation and excretion of one or both of the interacting toxicants. The response of the organism to combinations of toxicants may increase or decrease because of toxicological responses at the site of action.
Additive effect: occurs when the combined effect of two chemicals is equal to the sum of the effects of each agent given alone.

Synergistic effect: occurs when the combined effect of two chemicals is much greater than the sum of the effect of each agent given alone.

Potentiation effect: occurs when one substance does not have a toxic effect on a certain organ or system, but when added to another chemical makes that chemical much more toxic.

Antagonism effect: occurs when two chemicals administrated together interfere with each other’s actions or one interferes with the action of the other.

There are four major types of antagonism:

i. Functional antagonism: occurs when two chemicals counterbalance each other by producing opposite effects on the same physiologic function.

ii. Chemical antagonism or inactivation is a chemical reaction between two compounds that produces a less toxic product.
iii. Dispositional antagonism: occurs when the absorption, biotransformation, distribution or excretion of a chemical is altered so that the concentration or duration of the chemical at the target organ is diminished.
iv. Receptor antagonism: occurs when two chemicals that bind to the same receptor produce less of an effect when given together than the addition of their separate effects, or when one chemical antagonizes the effect of the second chemical. Receptor antagonists often are termed blockers.

1.6 Tolerance

Tolerance is a state of decreased responsiveness to a toxic effect of a chemical resulting from prior exposure to that chemical, or to a structurally related chemical. Two major mechanisms are responsible for tolerance. One is due to a decreased amount of toxicant reaching the site where the toxic effect is produced and the other is due to reduced responsiveness of a tissue to the chemical.

1.7 Dose Response

The characteristics of exposure and the spectrum of effects come together in a correlative relationship customarily referred to as the dose-response relationship. There are two types of dose-response relationships:
i. The individual dose-response relationship, which describes the response of an individual organism to varying doses of a chemical.
ii. A quanta-dose-response relationship, which characterizes the distribution of responses to different doses in a population of individual organisms.

1.8 Variation in substance responses

1.8.1 Selective toxicity

Selective toxicity means that a chemical produces injury to one kind of living matter without harming another form of live, even though the two may exist in intimate contact.

Some agents are lethal for some species and harmless to another. Such selective toxicity can be due to differences in distribution, absorption, biotransformation or excretion, or to differing biochemical processing of the toxicant by different organisms.

1.8.2 Species Differences

Experimental results in animals when properly qualified are applicable to humans, both quantitative and qualitative differences in the response to substances may occur among different species.

1.8.3 Individual Differences in Response

Even within a species there can be large inter-individual differences in response to a chemical because of subtitle genetic differences. These differences may be responsible for idiosyncratic reactions to chemicals and inter-individual differences in toxic responses.

2 Absorption of volatile organic compounds

Chemicals enter the human body by three main routes, the skin, the respiratory system and the gastrointestinal tract.

2.1 Volatile organic compounds and the body

The solvent is absorbed into the body and then into the blood. From the blood it is both eliminated and distributed to various tissues, including the target tissue. The target tissue is the tissue on which the toxicant solvent exerts its effect. In some cases the blood itself represents the target. Absorption can also take place from the gastrointestinal tract, from the lungs or through the skin.

2.2 Gastrointestinal tract

This route of absorption is a very important route, because toxic volatile organic compounds may be present in food, drinking water or if it is inhaled but as relatively large particulates which have been collected in the nasopharyngeal area, swallowed and then subjected through the transported processes in the gastrointestinal tract. The wall of the gastrointestinal tract is specialized not only for absorption but also for elimination. Another factor in gastrointestinal absorption is the rate at which foodstuffs pass through the gastrointestinal tract. If the rate of passage is slow the length of time during which the compound is available for absorption is increased. Another factor for absorption of volatile organic compounds includes the chemical and physical makeup of the compound, its solubility and its interactions with other compounds present in the gastrointestinal tract. Age and nutritional status of a person may also effects absorption from the gastrointestinal tract.

Several features of the gastrointestinal tract help to minimize toxicity by this route. Gastric and pancreatic juices can detoxify some substances by hydrolysis and reduction. Absorption into the bloodstream may be inefficient and selective. Food and liquid present in the gastrointestinal tract can dilute toxins and can form less soluble complexes with them. The portal circulation carries absorbed materials to the liver where metabolism can begin promptly. The gastrointestinal tract is not commonly a significant route of absorption. The first-pass metabolism remove (immediately) volatile organic compounds absorbed via the gastrointestinal tract. Only if the quantity of solvent ingested exceeds the capacity of the liver to metabolize it is the gastrointestinal tract route significant.

2.3 Absorption by skin

Skin absorption, the second most important route for solvent entry into the body, is at times much more toxic than inhalation. Absorption of organic solvent vapors by inhalation at the threshold limit value is insignificant and less than 2% of the amount absorbed through the skin under the same exposure conditions. Volatile organic compounds may be absorbed through the skin in significant amounts even below the threshold limit value. Factors that effect cutaneous absorption of volatile organic compounds include the composition of the skin, whether the skin is healthy or not, and the lipid solution of the solvent. A mixture of volatile organic compounds is more readily absorbed via the skin than a single solvent. Human skin consists of three layers; the epidermis, dermis and subcutaneous. The skin is a very effective barrier to absorption because of the outermost keratinized layer of thick-walled epidermal cells, the stratum corneum, which in general is not very permeable to toxicants. This layer consists mainly of thickened cell envelopes and a combination of sulfur-rich amorphous proteins and sulfur-poor fibrous proteins known as keratin.

There are two forms of absorption:

i. Trans-epidermal (through epidermal cells and
ii. Appendageal (through hair follicles and sebaceous glands).

The appendageal route offers greater permeability and plays an important role early in exposure, and in the diffusion of ions and polar non-electrolytes.

The trans-epidermal route is generally more prominent because of its far greater absorption surface. The blood vessels in the skin do not extend directly into the epidermis, but they terminate in the dermis. A toxic solvent that gets into the skin penetrates the dermis to be systemically carried to other organs. Once the solvent passes the stratum corneum, the epidermis poses little resistance to its further penetration into the dermis and dermal blood vessels.

Little absorption can happen through sweat glands or hair follicles, but these routes represent a very small percentage of the surface area and are not important in the absorption process. The stratum corneum is generally rate limiting in the process of absorption through the skin. Compared with the total thickness of the epidermis and dermis together the thickness of the stratum corneum is relatively slight. This barrier is important because many compounds or volatile organic compounds are unable to pass through it readily. Volatile organic compounds that penetrate the skin appear to do so by passive diffusion. The intracellular keratin matrix of the stratum corneum provides the main resistance to penetration by toxic substances.

There are mechanisms by which absorption through the skin can be increased. Abrasion, which damages or removes the stratum corneum, increases the permeability of the damaged area. The skin is normally partially hydrated; further increases in the degree of hydration increase permeability and promote absorption. Certain volatile organic compounds also increase skin permeability and facilitate absorption of toxicants. Certain volatile organic compounds can produce systematic injury by absorption through the skin. The skin acts as a reservoir. After exposure ceases, toxins could continue to enter the bloodstream from skin “stores”. A variety of factors can influence the extent of absorption, such as wetness, location on the body and vascularisation.

2.4 Absorption by lungs

Lungs are very important routes because gases and vapors of toxic volatile organic compounds, liquid or particulate aerosols can be absorbed through the lungs. The main route of absorption is pulmonary, and this depends on several factors, including the frequency of breathing, diffusion of solvent vapors across the alveolar membrane, partial pressure of solvent vapor in inspired air and blood, solubility of the solvent in the blood as the result of the blood-air partition coefficient, and blood flow through the lungs. Vapors can damage the respiratory tract; they can pass from the lungs to the bloodstream for distribution to other parts of the body. Vapors and mists that are fat-soluble can cross from the alveoli to the bloodstream and migrate from there to binding or storage sites, for which they have a special affinity. Less soluble vapors reach the bronchioles and alveoli where they dissolve slowly and may cause acute pneumonitis and pulmonary edema hours later. Long-term exposure at low concentrations may lead to chronic changes such as emphysema and fibrosis. Whether acute or chronic, the effects of irritant vapors are seen mainly in the respiratory tract.

The toxic action of some inhaled vapors may be considerably enhanced when they are absorbed to respirable particles. The particles transport the toxins to deep parts of the respiratory tree, which would otherwise be inaccessible. With rapid, deep breathing as occurs during strenuous exertion, the delivered dose increases.

2.4.1 Absorption of Solid and liquid particulates Are volatile organic compounds solids? If not delete what is not applicable

The lung consists of three basic regions, the:

i. Nasopharyngeal region
ii. Tracheobronchiolar region
iii. Alveolar region

i. Nasopharyngeal region

Particles that are roughly 5 diameter or greater in diameter are generally deposited in the nasopharyngeal region. If the particles are deposited very close to the surface it can be sneezed out, blown out or wiped away. If the particles are deposited farther back it can be picked up by the muscociliary escalator system and moved back up into the nasopharyngeal region where it may be swallowed and absorbed through the gastrointestinal tract in accordance with their solubility and absorption characteristics.

ii. Tracheobronchiolar region

Particles the size range of 2 to 5 diameter generally reach the tracheobronchiolar area before they impact the lung surface.

iii. Alveolar region

Particulars smaller than one diameter may reach the alveolar region of the lung. Absorption in the lung will most likely take place in the alveolar region, particularly if the material is soluble in the mucus.

Size is probably the most important single characteristic determining the efficiency of particulate absorption in the lung. Size determines the region of the lung in which aerosols is likely to be deposited, even within the range of very small particles that reach the alveolar region and may be absorbed there, size is inversely proportional to the magnitude of particle deposition. Absorption of vapors in the lung depends on solubility.

3 Excretion of volatile organic compounds

Elimination is made up of two kinds of processes, namely excretion and biotransformation, which occur usually at the same time, but if a substance is effectively excreted it will not be distributed into peripheral tissues to any great extent. Wide distribution of a substance may impede excretion. Biotransformation makes compounds more polar and less fat-soluble, and therefore toxins can be more readily excreted from the body. Excretion is the removal of xenobiotics from the blood and their return to the environment. Excretion is a physical mechanism, whereas biotransformation is a chemical mechanism for eliminating the toxicant. The route and speed of excretion depend largely on the physicochemical properties of the toxicant. There are no efficient elimination mechanisms for nonvolatile, highly lipophilic chemicals. If they are resistant to biotransformation, such chemicals are eliminated very slowly and tend to accumulate in the body after repeated exposure. The kidney is the most important excretory organ in terms of the number of compounds excreted, but the liver and lungs are of greater importance for certain kinds of compounds. The lungs are active in excretion of volatile compounds and gases. The liver may excrete metabolites before they have a change to reach the systematic circulation.

3.1 Excretion by kidney

The principal excretory organs in all vertebrates are the two kidneys. The primary function of the kidneys in humans is excreting waste from the blood in the form of urine. The kidneys are non-segmental and drain wastes only from the blood.

The major route of excretion of toxins and their metabolites is through the kidneys. The kidneys handle toxins in the same way that they handle any serum solutes, passive glomerular filtration, passive tubular diffusion and active tubular secretion. The kidney in the glomerular filtration process filters about 20 percent of all dissolved compounds of less than protein size. Glomerular filtration is a passive process and do not require energy input. Filtered compounds may be either excreted or reabsorbed. Passive re-absorption in the kidney is a diffusion process. Lipid-soluble compounds are subject to re-absorption after having been filtered by the kidney. The degree of re-absorption of electrolytes will be influenced by the pH of the urine, which determines the amount of the compound present in a non-ionized form. Active secretory and re-absorption processes also take place in the tubules of the kidney.

3.2 Excretion by liver

The liver is both the major metabolizing organ and a major excretory organ. A toxicant is absorbed from the gastro intestinal tract and eliminated in the liver by metabolism or excretion before it can reach the systemic circulation. Metabolites formed in the liver from compounds already present in the systemic circulation may be excreted into the bile before it themselves have had a change to circulate. Although it does not excrete as many different compounds as the kidneys do, the liver is in an advantage position with regard to excretion, particularly of metabolites.

There are three active systems for transport from the liver into the bile, one for organic bases, one for neutral organic compounds and one for organic acids. These transport processes are efficient and can extract protein-based as well as free compounds.
The liver occupies a strategic position, since the portal circulation promptly delivers compounds to it following gastrointestinal absorption. Furthermore, the generous perfusion of the liver and the discontinuous capillary structure within it facilitate its filtration of the blood. Excretion into the bile is potentially a rapid and efficient process. Toxins that are secreted with the bile enter the gastrointestinal tract and unless reabsorbed are secreted with the feces.

Certain factors influence the efficiency of liver excretion. Liver disease can reduce the excretory as well as the metabolic capacity of the liver. The liver is the largest gland in the body and is often the target organ of chemical-induced tissue injury. The liver maintains a unique position within the circulatory system and therefore receives a large portion of the venous return. It “filters” the blood coming from the lower body, kidneys, spleen and gastro intestinal tract before this blood is pumped through the lungs for re-oxygenation.

This unique position aids the liver in metabolize endogenous wastes and foreign chemicals and bile formation. The liver removes foreign chemicals that reach the bloodstream, regardless of the route of administration or exposure. The liver can be affected by chemicals ingested because it is the first organ perfumed by the blood containing the chemical. The liver removes and metabolizes almost all blood-transported substances. If removal and metabolism of a chemical is done rapidly and extensively by the liver it can dramatically decrease blood levels of the chemicals before the chemicals can reach other organs. The liver’s susceptibility to chemical attack is that it is the primary organ for the biotransformation of chemicals within the body. The biotransformation process is to alter the metabolized compound so that it is:

i) No longer biologically active within the body and

ii) More polar and water-soluble and consequently can be entered from the body.

For most instances the liver acts as a detoxification organ.

3.3 Excretion by lungs:

The lungs primarily excrete volatile organic compounds. The process is one of passive diffusion, governed by the difference between plasma and alveolar vapor pressure. Volatiles that are highly fat-soluble tend to persist in body reservoirs and take some time to migrate from adipose tissue to plasma to alveolar air. Less fat-soluble volatiles are exhaled fairly promptly until the plasma level has decreased to that of ambient air. Pulmonary excretions are the reverse of the uptake process in that compounds with low solubility in the blood and perfusion-limited in their rate of excretion, whereas those with high solubility are ventilation-limited.

4 Detoxification

Detoxification of the body refers to cleansing of the bowels, kidneys, lungs, liver and the blood. Essentially anything that supports elimination in the body can be said to help detoxification. Even simple things as drinking extra water per day or eating more fruit and vegetables can help eliminate more toxins.

Inner cleansing to eliminate the toxins we inhale and ingest everyday is an essential component of any healing program as well as preventing diseases. Removing chemicals, carcinogenic materials and other byproducts are absolutely critical in creating and maintaining a healthy life style.

Benefits of detoxification:

- Cleansing the digestive tract of accumulated waste and fermenting bacteria.
- Purification of the liver, kidneys and blood.
- Enhanced mental clarity as chemical overload is reduced.

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