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CHEMICAL HAZARDS IN PHARMACEUTICALS: IMPACT AND IMPLICATIONS FOR INDUSTRY SAFETY

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ABSTRACT

Chemical hazards pose significant risks in pharmaceutical industries and laboratories. This topic examines the types, sources, routes of exposure, and effects of chemical hazards commonly encountered in these settings. Major categories discussed include irritants, sensitizers, carcinogens, corrosives, mutagens, teratogens, reactive chemicals, and flammables. Common hazardous chemicals like methanol, ethylene glycol, and heavy metals are explored in detail, along with their toxicities and treatment approaches. This topic outlines key preventive measures, including engineering controls, administrative practices, and personal protective equipment. Proper handling, storage, labeling, and disposal procedures are emphasized. A systematic approach to hazard identification, risk assessment, and implementation of control measures is recommended to minimize chemical exposures and protect worker health and safety. This content provides practical guidelines for managing chemical hazards through a combination of technical, organizational, and personal protective strategies in pharmaceutical and laboratory environments.

Keywords: Chemical hazards, Occupational health, Risk assessment, Personal protective equipment.

INTRODUCTION

Chemical hazards are produced by chemical synthesis, manufacturing, processing, transportation, and their effect on human and environmental conditions. A chemical hazard is a type of occupational hazard caused by exposure to chemicals in the workplace. Hazardous materials encompass a wide range of substances, including industrial and agricultural chemicals, pesticides, pharmaceuticals, cosmetics, and food additives. These materials can pose risks to workers through direct contact or exposure in the workplace. To ensure the safe handling of these substances, it's crucial to have comprehensive knowledge about their characteristics, potential health and environmental impacts, and appropriate control measures. This information should be readily available, cost-effective to access, and, despite its inherent complexity, presented in a clear, concise manner. The goal is to enable users to easily identify and understand key risks and necessary protective actions associated with these hazardous materials.

There are many types of hazardous chemicals, including neurotoxins, immune agents, dermatologic agents, carcinogens, reproductive toxins, systemic toxins, asthma genes, and sensitizers. [1]

- Many chemicals can cause severe burns if they come into contact with living tissues or through other routes, like inhalation.
- Living tissues may be destroyed by chemical reactions such as dehydration, digestion, oxidation, etc.
- The eye and mucous membranes of the throat are particularly susceptible to the effects of corrosive dust, mist, and gases.
- Chloroform, benzene, chlorinated hydrocarbons, and low-boiling-point fractions of petroleum are some of the common organic solvents used in the pharmaceutical industry.

TYPES OF CHEMICAL HAZARDS

- Irritant chemicals
- Sensitizers
- Carcinogens
- Corrosives
- Mutagens
- Teratogens
- Reactive chemicals
- Flammables
- Asphyxiants

Irritants

Chemical hazards that are classified as irritants cause harm to the eyes, skin, or respiratory tract of a person. Irritants are either highly, moderately, or slightly

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water-soluble. The hazards can manifest as redness, rashes, inflammation, coughing, or haemorrhaging. Irritants are mostly short-term, severe illnesses but can also have long-lasting side effects in some people. People can also have an allergic reaction to some of these chemical materials, which can have long-lasting health impacts or even be fatal.

Some examples of irritant chemicals are nickel chloride and chromic acid.

Sensitizers

Sensitizers are also known as allergens, meaning they cause an allergic reaction in people who face repeated exposure over time to certain chemicals. Reactions to chemicals deemed sensitizers vary from person to person and can be either acute or chronic. Chemical exposure can manifest as swelling of the airway or develop into dangerous illnesses such as lung disease. Some diseases, such as asthma and contact dermatitis, become common among people due to overexposure to chemicals.
Some examples of allergens are chlorine and alkalis.

Carcinogens

Carcinogens are cancer-causing chemical substances, and a small amount of such a chemical is enough to severely harm human health. The hazards of such chemical substances will only appear many years after exposure. There are over 200 known human carcinogens.
Some examples of carcinogens are benzene, cadmium, formaldehyde, and vinyl chloride.

Corrosives

Chemical corrosives cause visible and/or irreversible changes to the composition of a material due to direct contact. Similarly, these can also cause a localized reaction in the human body at the point of contact. However, corrosive chemicals also have the potential to produce systemic chemical exposure away from the point of contact when mixed with other substances.
Some examples of corrosives include sulfuric acid and sodium hydroxide.

Mutagens

Chemicals classified as mutagens cause genetic changes to a cell's DNA and RNA. Genetic changes can cause cancer, prevent normal biological functions, or result in the malfunction of a particular organ.
Some examples of mutagens include benzene, ionizing radiation, and hydrogen peroxide.

Teratogens

Chemical teratogens can disrupt the normal development of a foetus, causing birth defects and even the healthy advancement of pregnancy.
Some examples of teratogens include thalidomide, ionizing radiation, and organic mercury compounds.

Reactive Chemicals

Chemical substances that cause a chemical hazard, such as an explosion, when mixed or combined with other chemical or non-chemical substances, such as water or air.
Some examples of reactive chemicals include nitric acid, benzoyl peroxide, and silane.

Flammables

Many chemicals are characterized as flammable because they can easily burn or ignite when exposed to oxygen.
Some examples of flammable chemicals are methanol, acetone, propane, and butane.

Asphyxiants

Chemical asphyxiants deprive the body of oxygen; interrupting the transfer and use of oxygen by the bloodstream.
Some examples of asphyxiants are carbon monoxide and cyanide. [2-3]

Sources of Chemical Hazards

Chemical hazards are toxic, corrosive, irritant, carcinogenic, flammable and mutagenic. According to the workplace hazardous material information, chemical hazards can be classified as:

Class A:

- Compressed gas
- Dissolved gas or liquified gas

Class B:

- Flammable gases
- Flammable and combustible liquids
- Flammable solids
- Flammable aerosols
- Reactive flammable material

Class C:

- Oxidizing material- oxidizer and organic peroxide.
- Oxidizer-chlorates, nitric oxide, peroxides, nitriles.
- Organic peroxide -tetrahydrofuran, diethyl ether, dioxane and methyl isobutyl ether.

Class D:

- Poisonous and infectious materials
  eg: cyanides, tea salts and asbestos.

Sources of Hazards in Pharmaceutical Industries

- Handling and storage of huge quantity of hazardous chemicals.
- Transferring, loading and unloading of solvents and chemicals to reaction vessels.
- Emission of hazardous air pollutants from reaction vessels due to overloading or under designed reaction vessels.
- Volatile organic compounds (VOCs) release from uncontained vessels.

- Reaction vessels and most common VOCs include methanol, dichloromethane, toluene, ethylene glycol, n-dimethyl formamide and acetonitrile.
- Leaks of effluents from waste water treatment plants or from effluent collection sumps from process areas.

Routes of Chemical Exposure

While the use of chemicals in processes, production, and goods has benefited people in many ways, these chemical substances are also the cause of chemical hazards. There are several routes of chemical exposure, they are described below: [4-5]

- **Inhalation** – that is breathing in toxic vapors or small chemical particles.
- **Absorption** – such as direct exposure to the skin by touching a chemical substance without any protection such as wearing gloves.
- **Injection** – that is when a sharp contaminated object or needle accidentally penetrates a worker's body (such as hand or foot).
- **Ingestion** – that is when toxins are accidentally swallowed.

Effects of Chemicals on Exposure

- Skin burn
- Ache
- Ulcer in hand, nose etc.
- Cancer

  Many chemicals can cause severe burns when they come in contact with living tissues.
- Living tissues may be destroyed by following chemical reactions:
  - ❖ Dehydration by strong dehydrating agents
  - ❖ Digestion by strong acids and bases
  - ❖ Oxidation by strong oxidizing agents [6]

Common Chemical Exposures and Their Treatment

Heavy metals

- Metals comprise three –fourths of the element in periodic table.
- Most of the known metals are quite toxic to living organisms when present in excess.

Treatment Strategies

- Removal of the subject from the sources of exposure.
- Treatment with chelating agents, such as EDTA, cysteine and N –acetyl cysteine.
- Hemodialysis or chelating agents.
- Administration of some antioxidants, vitamin C, E.

Methanol

- Methyl alcohol is used as a pharmaceutical and industrial solvent.
- It is also used as wood naphtha to denature ethanol in the preparation of industrial methylated spirits.
- Methyl alcohol is also used as an extraction solvent in food processing.
- Methyl alcohol is readily absorbed from the gastro intestinal tracts and distributed throughout the body fluids.

Methanol Toxicity

- Characteristic symptoms of methyl alcohol poisoning are caused by toxic metabolites and develop after a latent period of about 12 to 24 hours.
- Metabolic acidosis with rapid shallow breathing.
- Severe abdominal pain, gastrointestinal disturbances, pain in the back and extremities.
- Coma which is severe cases may terminate in death due to respiratory failure or rarely to circulatory collapse.

Treatment of Methanol Toxicities

- Gastric lavage may be considered if the patient presents within 1 hour of ingesting methyl alcohol.
- Activated charcoal is probably of little use as it does not absorb significant amounts of methyl alcohol.
- Hemodialysis may be indicated to increase the removal of methyl alcohol and its toxic metabolites.

Ethylene Glycol

- Ethylene glycol is commonly encountered in antifreeze solutions and has been used illicitly to sweeten some wines.
- Ethylene glycol is absorbed from the gastrointestinal tract and is metabolized, chiefly in the liver, by alcohol dehydrogenase.

Ethylene Glycol Toxicities

- Toxic effects arising from the ingestion of ethylene glycol results from its major metabolites: aldehydes, glycolates, lactate.
- Clinical features may be divided into 3 stages depending on the time lapses since ingestion:

❖ 0-12 hours - the patient may show signs of the drunkenness, nausea, vomiting.

❖ 12-24 hours - tachycardia, mild hypertension and heart failures.

❖ 24-72 hours - protein urea, renal failure, respiratory failure, cardiovascular collapse and sometimes coma and death.

Treatment of Ethylene Glycol Toxicities

- The stomach should be emptied by lavage if ingestion of ethylene glycol was within the preceding hours.
- Metabolic acidosis should be corrected with sodium bicarbonate intravenously and hypocalcemia corrected with calcium gluconate.
- Hemodialysis or peritoneal dialysis may be of value.

Some other chemicals that show hazardous effect on exposure include benzene, formaldehyde, vinyl chloride etc. [7-8]

Preventive Measures

- Solvent used in extraction, purification of synthetic drugs and chemical analysis should be handled with care.
- Flammable and explosive chemicals should be kept at proper distance.
- Tolerance level for toxic chemicals set by federal regulation have to be followed.
- Suitable label to the chemicals for proper handling.
- Personal protective cloth
- Application of cream before commencement of work.
- Use of goggles

Management to Over Exposure to Chemicals

- Removal from exposure

Prompt removal of the person from the exposure site is the first step and air respirators and lifelines are also mandatory first aids.

- Resuscitation

Resuscitation means restoration of life of one who is apparently dead. Further supportive care should be provided as with any other medical emergency.

- Decontamination

A victim whose skin or clothing has been contaminated requires immediate removal of garments and shoes, it is advised.

- Symptomatic treatment

Acute over-exposure may result in a variety of signs and symptoms that require general supportive medical management regardless of the specific agent. Examples include the control of convulsive seizures, treatment of bronchospasm etc. [9]

Controlling Chemicals Hazards in the Workplace

There are three general methods for controlling one's exposure to hazardous substances:

- Engineering Controls
- Work Practices and Administrative Controls
- Personal Protective Equipment

In the laboratory, these methods or a combination of them can be used to keep exposure below permissible exposure limits.

Engineering Controls

Engineering Controls include the following:

- Substitution of a less toxic material.
- Change in process to minimize contact with hazardous chemicals.
- Isolation or enclosure of a process or operation.
- Use of wet methods to reduce generation of dusts or other particulates.
- General dilution ventilation
- Local exhaust, including the use of fume hoods.

Work Practices and Administrative Controls

Work practice changes can include rotation in assignments and also by adjusting work schedules so that workers are not overexposed to a hazardous chemical. Administrative controls are changes in work procedures with the goal of reducing the duration, frequency, and severity of exposure. Examples of administrative controls are:

- Elimination – Eliminate the hazard whenever possible to eliminate the risk.
- Substitution – Use less dangerous, more stable chemicals when possible.
- Modification –Before conducting the actual procedure, always perform a dry run to identify and resolve possible safety hazards. Modify the process to reduce risk.
- Work practices – Follow standard operating procedures established for the materials and processes used in your lab. Never work alone.
- Segregation – Establish a designated, restricted access work area.

Personal Protective Equipment

When engineering controls are not sufficient to minimize exposure, personal protective equipment, including gloves, eye protection, respirators and other protective clothing should be used.

Some of the important steps used to controlling chemical hazards in the workplace are:

- Reduce or eliminate the use of hazardous chemicals whenever possible.
- Maintain adequate ventilation systems to reduce concentrations of airborne chemicals.
- Practicing good personal hygiene (e.g., washing hands) and maintaining regular workplace cleaning routines.
- Lean how to avoid carrying hazardous substances home.
- Introduce administrative controls to minimize exposure to chemicals (e.g., rotate workers through different jobs or locations).
- Perform maintenance work in off hours so that accidental release of toxic substances will affect fewer workers.
- Use personal protective equipment and devices.
- Maintain equipment in good order to prevent leaks and breakdowns that may release toxic substances. [10-11]

Chemical Safety: What to do and What to Avoid

- **Know the hazard before using the chemicals**

Before using the chemicals, the hazardous properties of all chemicals involved and the possible hazards at every stage of the process should be fully understood. Appropriate safety measures can then be taken.

- **Use appropriate control measures and personal protective equipment**

Appropriate control measures (such as engineering control) should be used to reduce the exposure to the hazard to the lowest level. Personal protective equipment should only be a supplement to, and not in lieu of, control measures,and should be selected appropriate to the hazards to be encountered.

- **Keep the work area well-ventilated, or even work under local exhaust ventilation**

Always keep the work area well-ventilated to avoid accumulation of hazardous gas/vapour. Increase the ventilation by mechanical means if necessary. In case where more hazardous chemicals or processes are encountered, work under local exhaust ventilation.

- **Keep away from any ignition source when handling flammable substances**

Ignition source may ignite the vapour of the flammable substance, and even lead to explosion.

- **Don't eat, drink and smoke**

Dangerous substances can easily enter the body while eating, drinking or smoking during use of chemicals, and would be injurious to health.

- **Don't touch chemicals with bare hands. Wear protective gloves**

Dangerous substances can easily enter the body through the skin while touching chemicals with bare hands, and would be injurious to health. If the chemical is corrosive, the hands will suffer from chemical burn. Appropriate protective gloves should be worn.

- **Don't suck chemicals with your mouth. Use appropriate liquid delivery tools**

Dangerous substances can easily enter the body during sucking chemicals with mouth, and would be injurious to health. If the chemical is corrosive, the mouth will suffer from chemical burn. Appropriate liquid delivery tools such as hand pumps should be used.

- **Don't use containers with narrow openings for a process that evolves heat and/or gases**

As the opening of the container is narrow, the releasing gas bubble may carry along hot liquid out of the container. At the same time, the heat and gas generated may tremendously increase the pressure inside the container which consequently burst. It will be more hazardous if dangerous substances are involved.

- **Don't mix oxidizing agents with flammable / combustible substances**

When oxidizing agent such as potassium permanganate is in contact with flammable / combustible substance, including sulphur powder, carbon powder, zinc dust, wood dust, etc., vigorous oxidation reaction may occur spontaneously evolving large amount of heat and possibly gases. This may also lead to fire and explosion.

- **Don't mix acids with bleaching solutions**

When bleaching solution is mixed with acid, reaction occurs spontaneously liberating toxic gases. [6]

Table 1: Clinical symptoms and hazard causing chemicals

Organ	Symptoms	Chemicals
Eyes	Corneal and conjunctival disturbances	Sulphur dioxide, hydrogen sulphide
Nervous system	Drowsiness	CNS depressants
Mouth	Green tongue	Vanadium
Throat	Salivation	Mercury
Lungs	Shortness of breath, chest tightness or pain	Asbestos, Bauxite dust

Figure 1: Hierarchy of controls

Hazard symbol	Meaning	Typical hazard
	Moderate health hazard	Causes skin irritation
	Serious health hazard	Causes breathing difficulties
	Toxic	Could cause death if swallowed or inhaled
	Corrosive	Damages skin and clothing
	Flammable	Catches fire easily
	Oxidising	Makes flammable substances burn more fiercely
	Harmful to the environment	Could cause damage to animal and plant life

Figure 2: Different symbols used to denote chemical hazards

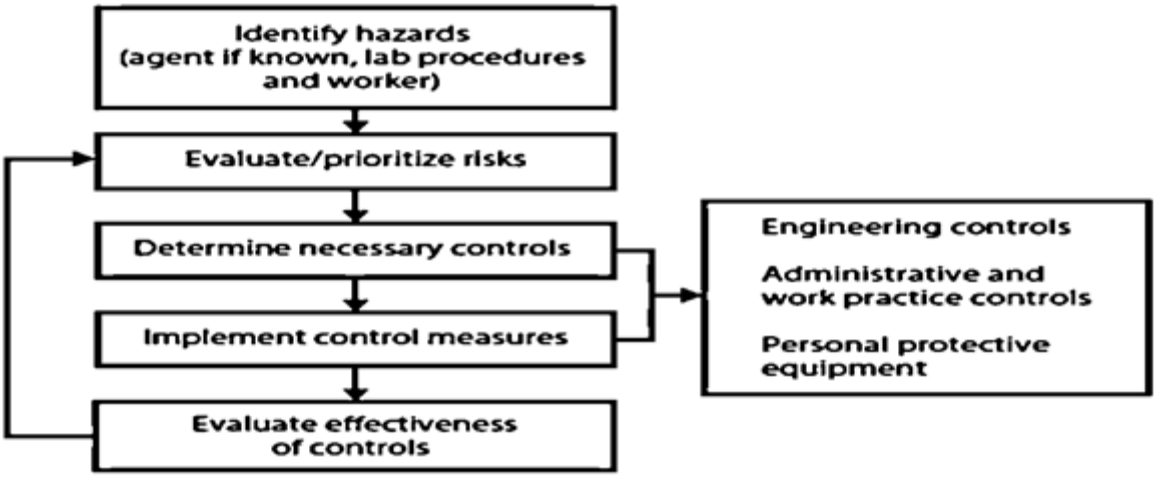

Figure 3: Diagnosis and control of chemical hazards

SAFETY ASPECTS

- Disposable gowns made of fabric that has low permeability to the agents in use, with closed fonts and cuffs, intended for single use.
- Powder free gloves, labelled and tested for drugs used with chemotherapy, made of latex, nitrile, neoprene.
- Face and eye protection when splashing is possible.
- Approved respirator when there is a risk of inhaling drug aerosols. The labelling of solvents to indicate their properties and health and fire hazards, is an extremely important method for controlling the hazards.
- Substitution of more harmful material by one that is less dangerous to health.
- To prevent or reduce dangerous exposure to toxic materials. [8-12]

CONCLUSION

The prevalence of chemical hazards in the pharmaceutical industry necessitates stringent measures to protect workers and the environment. This topic underscores the diversity and severity of chemical hazards, highlighting their sources, exposure routes and health effects. The study reveals the main causes of these risks, particularly in pharmaceutical environments where significant volumes of dangerous compounds are handled, processed, and stored on a daily basis. OSHA emphasizes a hierarchy of controls to manage workplace hazards, particularly those posed by chemical substances. The primary approach begins with engineering and work practice controls, which aim to physically alter the workplace or procedures to reduce exposure. These measures should be implemented as extensively as possible. Respiratory protection becomes necessary when engineering controls are impractical or still in progress. Personal protective equipment (PPE), while less preferable due to its reliance on consistent use and potential limitations in fully eliminating risks, remains a viable measure when other controls are insufficient.

Effective diagnosis and control of chemical hazards are critical to preventing harm to people, the environment, and the workplace. By identifying potential hazards, assessing risks, and implementing controls such as substitution, isolation, ventilation, and personal protective equipment, industries can minimize exposure and prevent accidents. Regular monitoring, training, and maintenance are also essential for ensuring the continued effectiveness of control measures. A proactive approach to diagnosing and controlling chemical hazards is essential for creating a safe and healthy work environment, and for promoting a culture of safety and responsibility.

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REFERENCES

1. Pharmaceutical production and management by C.V.S Subrahmanyam.
2. Hazard analysis by HACCP in safety management systems Q.A volume-2
3. Agarwal, Princy & Goyal, Anju & Vaishnav, Rajat. *et al*, Chemical hazards in pharmaceutical industry: An overview. *Asian Journal of Pharmaceutical and Clinical Research*. 11(27), 2018, 10.22159
4. Bhusnure, Dr. Omprakash. Chemical hazards and safety management in pharmaceutical industry. *Journal of Pharmacy Research.* 2018, 12.
5. Section 6A: Controlling Chemical Exposures | Office of Environmental Health and Safety [Internet]. ehs.princeton.edu. Available from: https://ehs.princeton.edu/laboratory-research/laboratory-safety/laboratory-safety-manual/sec6a

6. Occupational Safety and Health Administration. Chemical Hazards and Toxic Substances - Controlling Exposure | Occupational Safety and Health Administration [Internet].
7. Hazardous substance fact sheet; new jersey; 2000
8. Chemical Hygiene Plan [Internet]. blink.ucsd.edu.cited 2024.
9. Reyes J. Chemical Hazards: Definition & Types [Internet]. *SafetyCulture*. 2024.
10. Khan, I., Shah, S.M. *et al*, Hazards in Pharmaceutical Industry. In: Khan, S.A. (eds) Essentials of Industrial Pharmacy. AAPS Advances in the Pharmaceutical Sciences Series, 46. Springer, Cham. 2022
11. Chemicals in the Workplace [Internet].
12. Types of Chemical Hazards and How to Manage Them [Internet]. OSHA 8, 24 and 40 Hour Hazwoper, Hazmat, DOT, RCRA Courses.