World Journal of Pharmaceutical Science and Research
www.wjpsronline.com
Review Article
ISSN: 2583-6579
SJIF Impact Factor: 5.111
Year - 2025
Volume: 4; Issue: 2
Page: 57-63

A REVIEW ARTICLE ON AN OVERVIEW ABOUT THE STUDIES IN TOXICOLOGY

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Article Received: 21 January 2025 | | ***Article Revised: 10 February 2025*** | | ***Article Accepted: 03 March 2025***

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How to cite this Article: Sarmatha V., Ponnarasan T., Palanivel S., Sangameswaran B. (2025). A REVIEW ARTICLE ON AN OVERVIEW ABOUT THE STUDIES IN TOXICOLOGY. World Journal of Pharmaceutical Science and Research, 4(2), 57-63. https://doi.org/10.5281/zenodo.15109102

ABSTRACT

Toxicology is “the science of poisons”; more specifically the chemical and physical properties of poisons, their physiological or behavioral effects on living organisms, qualitative, and quantitative methods for their analysis and the development of procedures for the treatment of poisoning. Although the history of poisons dates to the earliest times, the study and the science of toxicology can be traced to Paracelsus (1493–1541) and Orfila (1757–1853). This paper will review the historical progress of clinical and forensic toxicology by exploring analytical techniques in drug analysis, differing biological matrices, clinical toxicology, therapeutic drug management, workplace drug testing, and pharmacodynamic monitoring.[1]

KEYWORDS: Pharmacodynamic, Toxicology, drug analysis.

INTRODUCTION

Metals and inorganic chemicals to large complex organic molecules, yet all possess the potential to induce toxicity. Thus, the challenge in this field refers to the application of basic chemistry, biochemistry, physiology, and pathology, along with experimental observation, to gain an understanding of how and why substances cause disruption in biological systems, which lead to toxic effects. In recent years, the problem of human and animal exposure to potentially toxic chemicals in the environment was brought to the attention of the public through the publication of *Silent Spring* (Rachel Carson, 1962). The book describes the devastating effects of **pesticides** on the flora and fauna of the North American environment.[2]

HISTORICAL ASPECTS

In the public arena, toxicology has been referred to as 'the study of poisons', Poisons span a wide range of sources and chemical forms, from naturally occurring plant alkaloids to synthetic nerve gases. Recently the study of poisons has become a justifiable scientific pursuit. Poisons have also played an important part in human history as subtle and silent military weapons. Prehistoric humans were aware that liquids extracted from animals and plants contained natural poisons which were used on their weapons.[3]

SCOPE AND IMPORTANCE OF TOXICOLOGY

Nevertheless, certain toxicants are even deleterious for the stems and the ova. The study of toxicology may be system-wise and also agent- wise. In this way, we may have systemic toxicology involving toxicology of central nervous system, hepatic system, respiratory system, ophthalmic system, etc. The study would include defenses of each of these systems against assault from foreign chemicals, responses and reactions as also injuries caused through excesses. An agent-wise study would take up drugs, pesticides, food additives, chemicals, heavy metals, trace elements, polymers, radiation, chemical carcinogens, teratogens.[4]

IMPACT OF TOXICOLOGY

Impact of Toxicology on General Medicine

The last few decades have brought tremendous advancement toward materials used in medicine and drugs production. Many medical devices (being produced from materials called 'bio') from dental restorations to cardiovascular stents are applied to the human organism.

Dentistry

In dentistry, a wide range of materials are used: dental amalgams, resin-based composites, polymethylmethacrylate resins, cements, ceramics, root canal filling materials and dental metal alloys, materials for short-term application in the oral cavity.

Impact of Toxicology on Forensic Sciences

Forensic toxicology uses the tools of analytical chemistry and testimonies as well as expertise to investigate the source of exposure to chemical, in the viewpoint of obligatory law.

Impact of Toxicology on Environmental Sciences

Since the 1960s, toxicology has entered a phase of rapid development and had an important influence in initiating the modern era of environmental science, known as environmental toxicology or ecotoxicology. It is defined as the study of the effects of industrial and agricultural toxins on human health and the environment.

Impact of Toxicology on Agriculture

The excessive use of many classes of pesticides like fumigants, fungicides, herbicides, insecticides, and fertilizers as an integral part of intensive agriculture caused environmental hazard because of low biodegradability.

Impact of Toxicology on Biotechnology

Toxicology serves society in many ways, not only to protect humans and the environment from the deleterious effects of toxicants but it also had an impact on biotechnology to develop more selective and safe toxicants such as biopesticides.[5]

TOXICITY STUDIES

Definition

Toxicity studies investigate the safety profile of the candidate compound. They also provide important information about the absorption, distribution, metabolism, and excretion (ADME) of the compound in the body.

Types of Toxicology Studies

The following kinds of toxicology studies must be performed during non-clinical testing:

- Systemic toxicology studies
- Single-dose studies
- Repeated-dose studies
- Reproductive toxicology studies
- Local toxicology studies
- Hypersensitivity studies
- Genotoxicity studies
- Carcinogenicity studies

Systemic toxicity studies

Systemic toxicology studies investigate the toxicity profile of the candidate compound in all of the animal's tissues and organs. Systemic toxicology studies can be either single-dose or repeated-dose studies.

Reproductive toxicity studies

Reproduction toxicity studies investigate the effect of the candidate compound on the ability to reproduce and develop normally.

Local tolerance studies

Local tolerance studies investigate the effect of the compound on the skin or eyes. These local toxicity studies are usually part of the general toxicity studies.

Genotoxicity studies

Genotoxicity studies investigate the effect of the candidate compound on the chromosomes and genes, and are generally needed to support human safety.

Carcinogenicity studies

Carcinogenicity studies assess the effect that the candidate compound has on cancer generation. Carcinogenicity studies are generally conducted to support the marketing application of a new medicine..

Sub-chronic Studies

Most of the chemicals, especially drug and food additives, are taken in repeated doses and it is essential to know what would happen on long-term use.

Mutagenicity Tests

A number of simpler tests that are less time- and animal-consuming have been developed for prediction of carcinogenicity.[6]

CLASSIFICATION OF TOXIC SUBSTANCE

Pharmaceutical and Therapeutic Agents

As pharmacologically active agents, ‘drugs and chemicals are our friends’. Their benefit to society has enabled humans to improve their quality of life as well as their lifespan..

Food Additives

Many different additives are combined with food-processing systems to alter the flavor or color, prevent spoilage, or chemically change the nature of the foodstuff.

Industrial chemicals

In general, industrial exposure includes exposure to chemical solvents used as a basis for chemical reactions.

Environmental Pollutants

There are several chemical sources of environmental pollution including industrial processes, Environmental pollutants are released into the atmosphere, waterways, oceans, or discarded on land.

Naturally Occurring Toxins

Naturally occurring toxins of animal, plant, and microbiological origins comprise a wide variety of chemical types, result in a variety of toxic effects, and are a significant cause of human poisonings.

Household Poisons

Household poisons include some of the substances in the previous categories such as pesticides, drugs, and solvents. Exposure to these types of compounds is usually acute rather than chronic.[7]

SYMPTOMS AND SIGNS

- Seek immediate medical advice if you think someone has swallowed. Signs of a medicine or drug overdose Medicine overdoses are the most common type of poisoning in the UK.
- **Gastrointestinal**: Nausea, vomiting, diarrhea, stomach pain.
- **Neurological**: Headache, dizziness, weakness, confusion.
- **Cardiovascular**: Sinus tachycardia, dysrhythmias, asystole.
- **Respiratory**: Tachypnea, breathing difficulties.
- **Skin**: Skin rash, redness, pain, burning, or stinging.
- **Eye**: Eye pain, redness, swelling, or tearing.
- **Other**: High temperature, chills, loss of appetite, irritability.[8]

TREATMENT OF TOXICOLOGY

Paracetamol

Paracetamol is a widely used over-the-counter painkiller.

Aspirin

Aspirin is an anti-platelet medicine that thins the blood and reduces the risk of blood clots forming (arterial thrombosis).

Tricyclic antidepressants

Tricyclic antidepressants are used to treat clinical depression, as well as a number of other mental health conditions, such as panic disorder and obsessive compulsive disorder (OCD).

Selective serotonin reuptake inhibitors (SSRIs)

SSRIs are a newer type of antidepressant that is also used to treat mental health conditions such as OCD and anxiety disorder.

Beta blockers

Beta blockers are used to treat a number of conditions that affect the heart or blood, such as high blood pressure (hypertension), angina and heart failure.

Calcium-channel blockers

Calcium-channel blockers are used for the treatment of high BP.

Benzodiazepines

Benzodiazepines are a type of tranquilizer, often used on a short-term basis to treat anxiety and sleeping problems (insomnia).

Opioids

Opioids are a type of stronger painkiller used to treat moderate to severe pain. They include codeine and morphine, as well as the illegal drug heroin.[9]

TARGET ORGAN TOXICITY

LIVER TOXICITY

Definition

One of the most important causes of liver dysfunction is drug-induced liver injury (DILI) which can lead to a wide spectrum of symptoms ranging from mild non-specific symptoms like asymptomatic transaminitis, acute hepatitis, chronic hepatitis, cholestasis to liver failure.

Objectives

- Review the drugs that can cause liver toxicity.
- Describe the pathophysiology of drug induced liver damage.

Etiology

There are many classes of drugs causing drug-induced liver injury including nonsteroidal anti-inflammatory drugs (NSAIDs), anti-infective drugs (anti-tubercular drugs), anti-cancer drugs, hormonal drugs, immunosuppressive agents, sedative, and neuropsychiatric drugs.

Epidemiology

Drug-induced liver injury is the most common cause of acute liver failure (ALF) in the United States and Europe and accounts for 20% to 40% of all instances of fulminant hepatic failure.

Pathophysiology

Liver damage can be hepatocellular, cholestatic, or mixed (includes features of both). Cholestatic damage commonly occurs due to the drug or the drug metabolite.

Evaluation

In most cases, drug-induced liver injury may cause mild to moderate elevation of liver tests, but in rare cases, it can lead to fatal outcomes. It can cause elevation of liver enzymes including alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), and total bilirubin.

Treatment / Management

Discontinuing the suspected drug is the first step in the management of drug- induced liver injury. N-acetylcysteine is the antidote for acetaminophen poisoning. However, intravenous N- acetylcysteine has been shown to improve survival with non-acetaminophen-related acute liver failure.

Complications

- Acute Respiratory failure
- Acute liver failure
- Acute renal failure[10]

CONCLUSION

Far more chemicals are in the human environment than can be evaluated for potential toxicity with available methods and resources. Therefore, some chemicals have to be selected for testing for their potential impact on public health, and that requires a priority- setting process. Much of the information needed to set priorities for testing is fragmentary or lacking; little if any toxicity information is available on most chemicals, and the information on human exposure to or potential toxicity of only a few is more than minimal.[11]

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