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Selective Toxicity

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Abstract

Various toxicants differ in their chemical constitutions, as they may possess various functional groups (chemical diversity) that are largely responsible for their different modes of action. On the other hand, there is a great difference in different forms of life (biological diversity). These variations may be due to differences in morphological, anatomical, histological, cytological and biochemical features of organisms. Owing to great variations in the structure and function of organisms, it is very difficult to predict the toxic effects of a chemical to human-beings on the basis of experiments performed on the laboratory animals. The biological diversity, on the other hand, is advantageous in developing specific drugs or toxicants (e.g. pesticides, etc.), which are effective against a certain group of organisms or certain individuals.

Keywords: Selective Toxicity; Species Differences; Susceptibility Genes

Introduction

Selective toxicity

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

The living matter that is injured is termed the uneconomic form (or undesirable), and the matter protected is called the economic form (or desirable). They may be related to each other as parasite and host or may be two tissues in one organism. By taking advantage of the biological diversity, it is possible to develop chemicals that are lethal for an undesired species and harmless for other species [1].

In agriculture, for example, there are fungi, insects, and even competitive plants that injure the crop, and thus selective pesticides are needed. Similarly, animal husbandry and human medicine require chemicals, such as antibiotics, that are selectively toxic to the undesirable form but do not produce damage to the desirable form.

Drugs and other chemicals used for selective toxic purposes are selective for one of two reasons.

(1) The chemical is equally toxic to both economic and uneconomic cells but is accumulated mainly by uneconomic cells.

(2) It reacts fairly specifically with a cytological or a biochemical feature that is absent from or does not play an important role in the economic form.

Methodology

Accumulation

The selective toxicity of an insecticide spray may be partly due to a larger surface area per unit weight that causes the insect to absorb a proportionally larger dose than does the mammal being sprayed. The effectiveness of radioactive iodine in the treatment of hyperthyroidism (as well as its thyroid carcinogenicity) is due to the selective ability of the thyroid gland to accumulate iodine. A major reason why chemicals are toxic to one, but not to another, type of tissue is that there are differences in accumulation of the ultimate toxic compound in various tissues. Selectivity resulting from differences in distribution usually is caused by differences in the absorption, biotransformation, or excretion of the toxicant. This, in turn, may be due to differences in the ability of various tissues to transport or bio-transform the chemical into the ultimate toxic product [2].

Selective toxicity caused by differences in comparative cytology is exemplified by a comparison of plant and animal cells. Plants differ from animals in many ways—for example, absence of a nervous system, an efficient circulatory system, and muscles as well as the presence of a photosynthetic mechanism and cell walls. The fact that bacteria contain cell walls and humans do not has been utilized in developing selective toxic chemotherapeutic agents, such as penicillin and cephalosporins, that kill bacteria but are relatively nontoxic to mammalian cells [3].

Species Differences

As discussed above, there are many reasons for selective toxicity among different species. It is important to recognize that both quantitative and qualitative differences in response to toxic substances may occur among different species. For example, the LD50 for the highly toxic dioxin, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), differs by more than 1000-fold between guinea pigs and hamsters. Not only does the lethal dose for TCDD vary widely among species, so do the particular target organs affected [4].

Large differences in carcinogenic response between experimental animal species are not unusual. For example, mice are highly resistant to the hepatocarcinogenic effects of the fungal toxin aflatoxin B1. Dietary doses as high as 10,000 parts per billion (ppb) failed to produce liver cancer in mice, whereas in rat›s dietary doses as low as 15 ppb produced a significant increase in liver tumors. The mechanistic basis for this dramatic difference in response appears to be entirely related to species differences in the expression of a particular form of glutathione Stransferase (mGSTA3-3) that has unusually high catalytic activity toward the carcinogenic epoxide of aflatoxin. Mice express this enzyme constitutively, whereas rats normally express a closely related form with much less detoxifying activity toward aflatoxin epoxide [5].

Examples

- ✓ **Demylination** as a toxic effect to diorthocresyl phosphate DOCP is recorded in **poultry** not in other species.
- ✓ **B-naphthalamine** induce cancer bladder in **dog** but not in **rat or rabbit**.
- ✓ Special enzymes as **atropinase** found in **rabbit.**
- ✓ The **PH of the stomach** affects the action of zinc phosphide, urea and ammonium compounds.
- ✓ **Anatomical variations of GIT** also affect the absorption of poisons e.g ruminants take long time in absorption of poison so it dilutes and excrete it.
- ✓ **Microbial activity in the rumen** can increase or decrease the toxicity e.g conversion the nitrate to nitrite.

Results and Discussion

Individual Differences in Response

Even within a species, large inter-individual differences in response to a chemical can occur because of subtle genetic differences. Hereditary differences in a single gene that occur in more than %1of the population are referred to as genetic polymorphism and may be responsible for idiosyncratic reactions to chemicals [6].

Susceptibility genes

As our understanding of the human genome increases, more "susceptibility genes" will be discovered, and it is likely that the etiology of many chronic diseases will be shown to be related to a combination of genetics and environment. The study of "gene-environment" interactions, or "Ecogenetics" is a rapidly developing field of substantial relevance to toxicology.

It is likely that the majority of chronic diseases develop as a result of the complex interplay between multiple genes and the myriad of environmental factors, including diet, lifestyle, and occupational and/or environmental exposures to toxic substances. For example, it is recognized that approximately %50 of the Caucasian population has a gene deletion for the enzyme glutathione S-transferase M1. This enzyme has no apparent significant physiologic function, and people missed it, are functionally and physiologically normal. However, epidemiologic studies have indicated that smokers who missed this gene be at slightly increased risk of developing lung cancer compared with smokers who have one or both copies of the normal gene [7,8].

Age

Age may be important in determining the response to toxicants. Some chemicals are more toxic to infants or the elderly than to young adults. Due to the undeveloped biotransformation and elimination mechanisms in young and low vitality and resistance in elder ones [10 ,9].

For example:

Parathion is more toxic to young animals.

Nitrosamines are more carcinogenic to newborn or young animals.

Sex

Toxic responses can vary depending on sex [11].

Examples

Male rats are 10 times more sensitive than females to liver damage from DDT, dimefox and sharadan.

Female rats are twice as sensitive to parathion as male rats. Zeralenone more effective in female which has estrogenic effect.

Hexabarbital more effective in female due to influenced biotransformation by sex hormone.

Steroid hormone in male increase the biotransformation of chemicals related to MFO.

In pregnancy and lactation, the marked increase in some organs as liver, adrenals, ovaries and uterus this followed increase in microsomal protein which enhance detoxification of toxicants [12].

State of health

Diseased animals are more affected by toxicants.

Liver disease may reduce the activity of MFOs. Also, it can reduce synthesis of protective macromolecules as glutathione and metallothionein allowing increased effect of poisons.

Lung disease increase the effect and the absorption of volatile toxicant.

Kidney the main organ of elimination, if diseased, slow elimination time of poison so increase its effect.

GIT disease lead to constipation and ulcers lead to increase absorption and increase toxicity of poisons [13].

Environmental factors [14].

Environmental Temperature

In low temperature, metabolic activities increased to keep the warmness. This leads to increase biotransformation of toxicants.

In high temperature, pushing more blood to skin for cooling, making skin rapid absorption to some chemicals as insecticides (Brent, 2004).

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Tannins and proteins precipitate some poisons in GIT and prevent absorption.

Phytic acid in plants chelates some metallic toxicants.

Calcium and zinc inhibit absorption of lead.

Protein deficiency impairs enzyme synthesis, MFO and hepatic glutathione which essential for biotransformation and detoxification.

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