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〈シンポジウム："General Toxicology"〉

一般毒性，特に慢性毒性を中心として

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General Toxicity – Special Reference to Chronic Toxicity

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Abstract

Since all drugs, which possess biological activity, are potentially dangerous, knowledge of the toxicity of a compound is an essential prerequisite to the initiation of clinical trials.

General toxicity studies are divided into acute and chronic toxicity categories based upon the duration of drug administration.

Acute toxicity refers to the toxic effects produced by a single dose of a chemical agent. This is usually quantified in terms of the medium lethal dose of the chemical agent. Acute toxicity data are required as part of a new drug application. An observation period of at least 72 hours using at least two species of animal and oral, subcutaneous, and intravenous (or intraperitoneal) routes of administration is necessary. The LD_{50} value is a convenient way to compare the toxicity of chemical agents, with a drug having a lower LD_{50} being more toxic than one having a higher LD_{50}. The LD_{50} values are influenced by various factors, such as animal species, strain, sex, age, feeding conditions – isolated or aggregated, and other environmental conditions, therefore for a comparison of LD_{50}'s to be meaningful, the measurements should be made under identical conditions.

Contrary to acute toxicity studies in which lethal doses are used, both toxic and nontoxic dose levels are employed in a chronic study. Because chronic toxicity studies examine a relatively large number of parameters over a wide range of doses, this type of study usually provides the most useful information relative to the potential toxic effect of a compound during clinical usage. The development of various toxic effects over time is one of the important features of chronic toxicity studies, and therefore we have to consider studies so as to gain maximum data possible.