A second type of computer model uses information concerning a chemical's three-dimensional structure instead of its physical properties. An example of this is the production of synthetic vaccines by the computer-aided modeling of a virus' protein structure in three dimensions.

The purpose of mathematical modeling is to define the relationship between a chemical's structure and its biological activity – (the QSAR equation). This equation can be used in two ways to limit the use of animals:

- It can suggest methods of changing or extending a chemical family in a specific manner, in terms of structure or activity.
- It can predict the biological response in an animal to an available, but as yet untested, chemical.

Consequently, computers can reduce animal use in drug screening by predicting the biological reactions caused by untested drugs, and their therapeutic effectiveness, based on knowledge of their 3-dimensional structure.

Work on such a "predictive" equation using a computer is described by Kurt Enslein of Health Designs, Inc., Rochester, NY. In a monograph issued by Princeton Scientific Publishers, Enslein discusses efforts to estimate oral LD-50 in rats and mice by analyzing statistical structure/activity models of chemicals used in this drastic animal bioassay. The LD-50 is a method used to estimate a chemical's acute toxicity by determining the concentration necessary to kill half of a test group of animals. Enslein and his colleagues randomly selected 2,000 chemicals from 4,500 already tested by the LD-50 method.

The computer-estimated LD-50 values of the selected chemicals compared favorably with the values obtained from the animal bioassays. Hence Enslein's research group concluded that these estimates were reasonable in many applications of the LD-50:

- Dose ranging: Finding the range of doses for acute or chronic detailed bioassays.
- Selection of least toxic compounds from a structurally-related series.
- Environmental evaluation. Effluents can be sampled to determine which chemicals need priority.
- Any applications for acute toxicity information.

In addition to reducing animal use, other advantages of the estimated oral LD-50 include lower cost, greater repeatability and faster response.

Computers can be utilized also to process, organize and make accessible international literature, and analyze experimental design to aid in eliminating duplicative or inconsequential experiments. Eventually, computers may be able to mimic a complete biological system.

Bacterial Cultures/Protozoan Studies

Many single-cell organisms react to chemicals in the same manner as humans, and many have parallel nutritional needs. Thus, bacteria and protozoa have been used extensively in a number of research areas, with wider applicability as biochemical laboratory techniques and analytical methods are developed and refined.

Single-cell organisms can be used to assay vitamin levels in pharmacological and toxicological studies and in the screening of antibiotics. In recent years, these organisms have been used as screening systems to detect carcinogens (cancer-causing agents), since they are very sensitive to mutagens (genetics-altering agents). The Ames Test, which utilizes a strain of Salmonella bacteria, has exhibited an excellent correlation (98% predictive success) between mutagenicity (genetics-altering ability) and carcinogenicity (cancer-causing potential). It provides an effective and economic alternative to animal tests in the pre-screening stages of carcinogenicity testing.

What are the advantages of using single-cell organisms in research and testing? They reproduce rapidly at body temperature, dividing every 20-30 minutes, which permits short-term monitoring, through many generations, under easily standardized and experimentally controlled conditions. Also, they are inexpensive in terms of storage, upkeep and maintenance, and are less likely to spread disease through a laboratory.

Human Studies

Since a major portion of biomedical research and testing is devoted to investigations of diseases afflicting humans and human reaction to chemical substances, we are the preferred experimental subjects whenever possible. This is especially true because of the problems encountered when animal test results are extrapolated to human beings. Although researchers may argue that the use of animals is essential in human studies based on anatomical and physiological similarities between mammalian species, the differences are significant. While human tissue cultures may alleviate some of the problem, *in vitro* (outside the whole animal) techniques still cannot mimic the responses of complex system interactions. However, whole body metabolism, systemic (through the body) drug response, and disease patterns *can* be investigated using human volunteers in carefully controlled studies that will provide data more relevant than that obtained from animal testing. Of course, it is necessary to obtain informed consent by the human volunteers, and to