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A Review on Oral Toxicity Study

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ABSTRACT : -

Introduction: Acute oral toxicity refers to those adverse effects that occur after oral administration of a single dose of a substance or multiple doses given within 24 hours. Delayed death means that the animal does not die or does not appear to be dying within 48 hours, but dies later in the 14-day observation period.

Background: The Organization for Economic Co-operation and Development (OECD) is an international organization that works to build good policies for a better life. Many studies are being done; However, the current focus is on investigating oral toxicity.

Main Body: Oral poisoning refers to the adverse effects caused by taking a substance into the body through the mouth. That study is called an oral toxicity study. The experimental principle in this study is based on a stepwise procedure using a small number of animals in each step.

Conclusion: Assessing the safety of potential drug candidates is a major goal of oral toxicology studies in the drug development process. To achieve this, validated methodologies and appropriate animal models are used. From that review, we consider that all information about the OECD guidelines for oral toxicity studies is presented here in simple terms, so that it is now easily accessible to readers.

Keywords: OECD, Acute, Sub-acute, Sub-chronic, Rodents, Non-Rodents, Fixed Dose, Up & Down.

OECD GUIDELINES

Introduction

The OECD Guidelines are a specialized tool for assessing the potential adverse effects of chemicals on human health and the environment. Procedures for safety testing are widely known as standards. Professionals in business, academia, and government use this resource when testing and evaluating chemicals (industrial chemicals, pesticides, personal care products, etc.). Thousands of national experts from OECD member countries contribute to the frequent updating of these guidelines.

Oral toxicity studies

Adverse effects from chemical ingestion are known as oral poisoning. Oral toxicology is the term for its study. The test in this audit is based on a step-by-step approach and uses a small number of animals at each stage, according to the guiding principle of the test.

TYPES OF ORAL TOXICITY STUDY

1) ACUTE ORAL TOXICITY

a) ACUTE TOXIC CLASS METHOD (423)

b) FIXED DOSE PROCEDURE (420)

c) UP AND DOWN PROCEDURE (425)

2)SUB ACUTE ORAL TOXICITY (407)

3) SUB-CHRONIC ORAL TOXICITY

a. NON-RODENTS (409)

b. RODENTS (408)

1. ACUTE ORAL TOXICITY

A) ACUTE TOXIC CLASS METHOD (423)

INTRODUCTION

Based on new scientific findings or development of assessment methods, the OECD Guidelines for the Testing of Chemicals are frequently revised. The standard acute toxicity test of Test Guideline 401 was replaced by Guideline 423, established in March 1996. Based on the recommendations of several experts, the revision is considered necessary because: i) international agreement has been reached on the LD50 cut-off standard for the classification of chemicals that are different from the cut-off -offs proposed in the 1996 version of the Guide; and ii) testing in one gender (usually female) is considered sufficient.

PRINCIPLE

The main idea of the test is to collect sufficient data on the acute toxicity of the test phase in the steps used to allow the classification of the smallest animal in each phase. One of the prescribed doses of the drug was administered orally to a group of laboratory animals. A stepwise approach to chemical testing is used, with each step using three animals of the same sex (usually male).

METHODOLOGY

Selection of animal species

Rats are the recommended rodent species, but other rodents can be used. Usually women work (9). This is because a literature review of standard LD50 tests showed little difference in sensitivity between the sexes, and where differences were found, females were generally less sensitive (11).

Housing and feeding conditions

The room where the experimental animals are located must be kept at a temperature of 22°C (+3°C). When cleaning the room, aim for a relative humidity between 50% and 60%, with a minimum of 30% and ideally no more than 70%. Artificial lighting should follow a 12-hour light-dark cycle.

Preparation of animals

Before dosing, the animals were kept in their cages for at least 5 days to allow them to acclimatize to the laboratory environment. They are then randomly selected, marked for personal identification and kept in their cages. **Preparation of doses**

By adjusting the concentration of the dose preparation, the test chemical must usually be provided in a constant amount over the dose range to be tested. However, when testing liquid end products or mixtures, using anhydrous test material, i.e. at constant concentration, may be more suitable for further risk assessment of the substance, and some regulatory agencies require it. The maximum dose for administration should not be exceeded under any circumstances.

Depending on the size of the test animal, the maximum amount of fluid can be given at one time.

RESULT

− tabulation of response data and dose level for each animal (i.e. animals showing signs of toxicity including mortality; nature, severity, and duration of effects);

− tabulation of body weight and body weight changes;

− individual weights of animals at the day of dosing, in weekly intervals thereafter, and at the time of death or sacrifice;

− date and time of death if prior to scheduled sacrifice;

2. FIXED DOSE METHOD (420)

INTRODUCTION

In light of new scientific findings or evolving assessment techniques, the OECD Guidelines for the Testing of Chemicals are frequently reviewed. As the first substitute for the typical acute toxicity test, as defined in Test Guideline 401, the original Guideline 420 was adopted in July 1992. According to the recommendations of several expert meetings, the revision was deemed necessary because: i) a global agreement had been reached on standardised LD50 cut-off values for the classification of chemical substances, which differ from the cut-offs suggested in the 1992 version of the Guideline; and ii) testing in one sex (typically females) is now regarded as sufficient.

PRINCIPLE

With the fixed doses of 5, 50, 300, and 2000 mg/kg (exceptionally, an additional fixed dose of 5000 mg/kg may be considered; see paragraph 19), groups of animals of a single sex are dosed in a stepwise approach. Based on a sighting study, the first dosage level is chosen as the dose anticipated to result in some toxicity symptoms without having a significant toxic effect or having a fatal outcome. A further OECD Guidance Document (8) provides a detailed description of the clinical indicators and symptoms connected to pain, suffering, and impending mortality.

METHODOLOGY

Selection of animal species

Rats are the recommended rodent species, but other rodents can be used. Women usually work (7). This is because a review of the literature on conventional LD50 tests shows that women are generally more sensitive, although gender differences in sensitivity are sometimes observed (10).

Housing and feeding conditions

The temperature in the space used to house experimental animals should be 22°C (+ 3°C). Aim for 50–60% relative humidity, except while cleaning a room, even though it should be at least 30% and should not exceed 70%. Artificial lighting should be used, with 12 hours of light followed by 12 hours of darkness.

Preparation of animals

Prior to the commencement of dosing, the animals are randomly chosen, marked to allow for individual identification, and housed in their cages for at least 5 days to allow for acclimatisation to the lab environment.

Preparation of doses

In general, test chemicals need to be given in a consistent volume over the range of doses that need to be evaluated by changing the concentration of the dosing preparation. However, where a liquid end product or mixture is to be tested, the use of the undiluted test material, i.e. at a constant concentration, may be more pertinent to the ensuing risk assessment of that chemical, and is a mandate of some regulatory agencies.

RESULT

- tabulation of response data and dose level for each animal (i.e. animals showing signs of toxicity including mortality, nature, severity and duration of effects);

- tabulation of body weight and body weight changes;

- individual weights of animals at the day of dosing, in weekly intervals thereafter, and at time of death or sacrifice;

- date and time of death if prior to scheduled sacrifice;

3) UP AND DOWN METHOD (425)

INTRODUCTION

In light of new scientific findings or evolving assessment techniques, the OECD guidelines for the Testing of Chemicals are routinely reviewed. Dixon and Mood (1)(2)(3)(4) were the first to introduce the idea of the up-and-down testing approach. For the purpose of determining the acute toxicity of chemicals, Bruce proposed the use of an up-and-down approach (UDP) in 1985 (5). The up-and-down experimental design, which is used to calculate an LD50, comes in a variety of forms.

PRINCIPLE

A maximum of 5 animals may be used in the Limit Test, which is a sequential test. 2000 mg/kg or, more atypically, 5000 mg/kg may be utilised as the test dose. The procedures for testing at 2000 mg/kg and 5000 mg/kg differ slightly from one another (for limit tests at 2000 mg/kg and 5000 mg/kg, respectively, see paragraphs 23–25 and 26–30).

METHODOLOGY

Selection of Animal Species

Each animal must be between 8 and 12 weeks old at the time of dosing and weigh within 20% of the mean initial weight of any animals that have already received a dosage.

Housing and Feeding Conditions

The chamber housing the experimental animals should be 22°C (plus or minus 3°C). The target relative humidity should be between 50 and 60 percent, even though it should be at least 30% and should not go beyond 70% other than while cleaning a room. Artificial lighting should be used, with 12 hours of light and 12 hours of darkness. Each animal is kept in its own enclosure.

Preparation of Animals

Prior to dosing, the animals are maintained in their cages for at least 5 days to give them time to acclimatise to the laboratory environment. They are then randomly chosen, marked to allow for individual identification, and kept in their cages. Care must be taken to guarantee that animals in the proper size and age range are accessible for the duration of the trial, much like with other sequential test designs.

Preparation of Doses

The maximum dose volume for administration must not be exceeded in any situation. Depending on the size of the test animal, a maximum amount of liquid can be given at once. The volume in rodents should typically not be greater than 1 ml per 100 g of body weight; however, in the case of aqueous solutions, 2 ml per 100 g body weight can be taken into consideration.

RESULT

− body weight/body weight changes;

− tabulation of response data and dose level for each animal

− individual weights of animals at the day of dosing, in weekly intervals thereafter, and at the time of death or sacrifice ;

− time course of onset of signs of toxicity and whether these were reversible for each animal;

− necropsy findings and any histopathological findings for each animal, if available;

− LD50 data;

− statistical treatment of results

Discussion and interpretation of results.

SUB-ACUTE ORAL TOXICITY (407)

INTRODUCTION

In light of advancements in science, the OECD Guidelines for the Testing of Chemicals are routinely reviewed. In 1981, the initial Test Guideline 407 was approved. A revised version was adopted in 1995 in order to gather more data from the study animal, particularly on neurotoxicity and immunotoxicity. 2 To update current Test Guidelines and create new Test Guidelines for the screening and testing of suspected endocrine disruptors, the OECD launched a high-priority initiative in 1998 (8). The effort included updating the OECD recommendation for "repeated dose 28-day oral toxicity study in rodents" (TG 407) with criteria that could identify the endocrine activity of test chemicals.

PRINCIPLE

For a total of 28 days, the test drug is given daily in progressive doses—one dose level per group—to various experimental animal groups. The animals are rigorously monitored every day for signs of toxicity during the administration period. A 28-day research can help determine the necessity for further, longer-term studies by revealing information on the effects of repeated oral exposure. Information on choosing concentrations for longer-term experiments can also be found there.

METHODOLOGY

Selection of animal species

The rat was the only animal employed in the global validation programme for the detection of endocrine disruptors. Employing young, healthy adults from regularly used laboratory strains is recommended. Women should not be fertile or pregnant.

Housing and feeding

Every action should follow regional guidelines for the care of laboratory animals. It should be 22°C (plus or minus 3°C) in the room used for testing animals. With the exception of while cleaning a room, the relative humidity should be at least 30% and ideally not exceed 70%, but the target should be between 50% and 60%. Artificial lighting with a photoperiod of 12 hours of light and 12 hours of darkness is preferred. Conventional laboratory meals may be utilised for feeding along with an endless supply of drinking water.

Preparation of animals

The control and treatment groups are randomly allocated to healthy young adult animals. The placement of cages should be done in a way that minimises any potential negative impacts. Prior to the start of the treatment trial, the animals are individually identified and maintained in their cages for at least five days to give them time to get used to the laboratory environment.

Preparation of doses

The test substance is given orally, through the meal, or through drinking water. The oral administration technique depends on the goal of the study and the physical, chemical, and toxico-kinetic characteristics of the test substance. 16 The test material is suspended or dissolved in a suitable vehicle as

needed. The use of an aqueous solution or suspension is advised whenever practical, followed by consideration of a solution or suspension in oil (such as corn oil) and finally feasible solutions in other vehicles. The hazardous properties of the vehicle must be known for all types of vehicles besides watercraft. It is important to assess the test substance's stability inside the car.

RESULT

- body weight/body weight changes;

- food consumption, and water consumption, if applicable;

- toxic response data by sex and dose level, including signs of toxicity;

- sensory activity, grip strength and motor activity assessments;

- haematological tests with relevant base-line values;

- clinical biochemistry tests with relevant base-line values;

- necropsy findings;

- a detailed description of all histopathological findings;

- absorption data if available;

- statistical treatment of results, where appropriate. Discussion of results.

3) SUB-CHRONIC ORAL TOXICITY

A) RODENTS (408)

INTRODUCTION

The OECD Guidelines for Chemical Testing are routinely reviewed in light of new scientific findings. Adopted in 1981, the first version of directive 408. Based on the conclusions of an OECD Consultation Meeting of Experts on Sub-chronic and Chronic Toxicity Testing conducted in Rome in 1995, a revised version was adopted in 1998 in order to collect additional data from the study's animals (1).

PRINCIPLE

For a period of 90 days, the test material is orally administered daily to various groups of experimental animals, one dose level per group. Animals are constantly monitored for signs of toxicity during the administration time. During the test, any animals that pass away or are killed are necropsied, and any remaining animals are likewise killed and examined when the test is over.

METHODOLOGY

Selection of animal species

Even while it makes biological sense that other species will react to toxins in a similar way to the rat, using smaller species could lead to greater endpoint measurement uncertainty since smaller organs are more difficult to dissect. It is best to use common laboratory strains of young, healthy adult animals.

Housing and feeding conditions

It should be 22°C (plus or minus 3°C) in the room used for testing animals. Although it is recommended that the relative humidity not exceed 70% unless when cleaning a room, the target should be between 50% and 60%. Artificial lighting should follow a 12-hour cycle of light and darkness.

Preparation of animals

Characteristics of the test animals should include species, strain, source, sex, weight, and/or age. The control and treatment groups should be distributed at random among the animals. Cages should be set up such that any negative impacts from cage location are reduced. A special identifying number ought to be given to each animal.

Preparation of doses

The test substance is given orally, through food, or through water. The oral administration technique depends on the goal of the investigation and the physical/chemical characteristics of the test substance. The test material is suspended or dissolved as necessary in an appropriate vehicle.

RESULT

Body weight and body weight changes;

- food consumption, and water consumption, if applicable;

- toxic response data by sex and dose level, including signs of toxicity;

- nature, severity and duration of clinical observations (whether reversible or not);

- results of ophthalmological examination; sensory activity, grip strength and motor activity assessments (when available);- clinical biochemistry tests with relevant base-line values;-

- necropsy findings;- absorption data if available

B) NON RODENTS (409)

INTRODUCTION

In light of advancements in science, the OECD Guidelines for the Testing of Chemicals are routinely reviewed. In 1981, the first version of Directive 409 was adopted. The goal of the alterations made in this upgraded version was to gather more data from the study's animal subjects. The results of an OECD Consultation Meeting of Experts on Sub-chronic and Chronic Toxicity Testing conducted in Rome on November 2-3, 1995, served as the foundation for this revised version of Guideline 409 (1).

PRINCIPLE

For a period of 90 days, the test material is orally administered daily to various groups of experimental animals, one dose level per group. Animals are constantly monitored for signs of toxicity during the administration time. During the test, any animals that pass away or are killed are necropsied, and any remaining animals are also killed and necropsied after its completion.

METHODOLOGY

Selection of animal species

Dogs should be of a specific breed; the beagle is usually utilised. Dogs are a common non-rodent animal. Mini-pigs and other species, such as swine, may also be employed. Primates should only be used under specific circumstances. Young, healthy animals should be used, and in the case of dogs, dosage should start no later than 9 months of age and preferably no earlier than 4-6 months..

Housing and feeding conditions

Regular laboratory diets and an endless supply of drinking water may be employed for feeding. The need to guarantee a correct mixing of the test chemical when administered by this method may impact the diet choice. The species-appropriateness of the cage is important. Artificial lighting is preferred, with 12 hours of light and 12 hours of darkness.

Preparation of animals

The test species that are chosen and their source will determine how long acclimatisation takes. For dogs or specially bred pigs from a local colony, it is advised to wait at least 5 days; if the animals came from outside sources, it is advised to wait at least 2 weeks. Characteristics of the test animals should include species, strain, source, sex, weight, and/or age..

Preparation of doses

The test substance might be given intravenously, orally, orally in pill form, or in the meal or water. The goal of the study and the physical-chemical characteristics of the test substance determine the oral delivery route. The test material is suspended or dissolved in a suitable vehicle as needed.

RESULT

- body weight/body weight changes;

- food consumption, and water consumption, if applicable;

- toxic response data by sex and dose level, including signs of toxicity;

- nature, severity and duration of clinical observations (whether reversible or not); - ophthalmological examination;

- haematological tests with relevant base-line values

CONCLUSION

OECD assists countries in harmonising Guidelines for the Testing of Chemicals and Good Laboratory Practice, in order to ensure high quality and reliable data and for countries and industry to fully benefit from the OECD agreement on Mutual Acceptance of Data (MAD) and avoid duplicative testing. Saving Costs in Chemicals Management.

Tabulation of response data and dose level for each animal are noted. BW, time of sacrifice and time and date of death. Histopathology and necropsy finding. Evaluation of the safety of possible medication candidates is the main goal of oral toxicology studies in the drug development process. Validated methodologies and pertinent animals model are used to achieve this. From that review, we presume that all data of oral toxicity study of OECD guidelines has been given here in simple clause form. Consequently, readers now find it simple.

DISCUSSION

Among OECD guidelines we have focused on oral toxicity study here. The purpose of this study is to obtain information on the biological activity of a chemical and gain insights into its mechanism of action. At first the medication is tested on animals to avoid adverse effects on human.

The goal of toxicity testing is to identify possible adverse effects of exposure to environmental agents to develop those response relationships that can elucidate the severity of effects associated with known exposures, and ultimately to predict the effects of exposure of human population.

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