8.00 TOXICOLOGICAL STUDIES

Acute Oral Toxicity – Acute Toxic Class Method (OECD Guidelines - 423)

The acute toxic class method is performed with the help of 3 animals of a single sex per step. Depending on the mortality and moribund status of the animals, on the average 2 - 4 steps may be necessary to allow judgment on the acute toxicity of the test substance. This procedure results in the use of a minimal number of animals while allowing for acceptable data based on scientific conclusions. The acute toxic class method is based on biometric evaluations.

Based on a stepwise procedure with the use of a minimum number of animals per step, sufficient information is obtained on acute toxicity of the test substance to enable the classification according to the other schemes for acute oral toxicity. The substance is administered orally to a group of experimental animals at one of the defined doses. Absence or presence of compound related mortality of the animals dosed at one step will determine the next step about further testing as well as dosing of three animals with same dose or next higher or lower dose level.

Method

Preparation of animals

The animals are randomly selected, marked to permit individual identification and kept in their cages for at least 5 days prior to the start of the test to allow for acclimatization to the laboratory conditions.

Procedure

Three animals are used for each step and the dose level is used from the starting dose level viz 5, 50, 300 and 2000 mg / kg body weight. Treatment of animals at the next dose should be delayed until one is confident of survival of
the previously dosed animals. The test substance is administered in a single dose to the animals by gavages using a stomach tube in the form of aqueous solution 2ml/ 100mg body weight.

Results

LD$_{50}$ was done as per the OECD guidelines (revised Draft 423) for fixing the dose for the pharmacological evaluation. The LD$_{50}$ of both the extracts and formulations, as per OECD falls under Class 4 values with no signs of acute toxicity (LD$_{50} > 2000$ mg. / kg). The pharmacological evaluation was carried out at 200 mg / kg and 300 mg / kg dose levels.