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Research Models and Services
Teklad Custom Diets

Cuprizone diets: A trusted tool for neuroscience research

Bis(cyclohexanone)oxaldihydrazone, commonly referred to as cuprizone, causes demyelination of the central nervous system in rodents, most notably, the corpus callosum of mice. Cuprizone is a copper chelator; however, the exact mechanism of cuprizone-induced damage to the central nervous system remains unclear. Despite an unknown mechanism of action, dietary cuprizone administration is a well-characterized and reliable method used to study de- and remyelination processes involved in diseases of myelin dysfunction such as multiple sclerosis and certain psychiatric disorders.

CUPRIZONE AND CONTROL DIETS

CUPRIZONE %	BASE DIET: 2016	BASE DIET: 2018
0% or control	TD.00217	TD.00588
0.2%	TD.140800	TD.140803
0.2% with Red food dye	TD.140801	TD.140804
0.3%	TD.140802	TD.140805

If you require an alternate concentration, base diet, or color not shown in this table, please contact a nutritionist at askanutritionist@inotivco.com to assist you in setting up a new product code prior to your next diet order.

We encourage you to use our stocked supply, but if you prefer to send the cuprizone, we are happy to accommodate you. If you choose this option, please consult a nutritionist before sending your cuprizone.

KEY PLANNING INFORMATION

Ordering

- Minimum order quantity is 3 kg, sufficient for feeding ~20 mice or four-six rats for one month.
- We make your diet fresh to order in pellet or powder form, and typical lead-time is two weeks (four weeks if irradiated).
- Irradiation (20 - 50 kGy) is optional, and must be requested at time of order. Effects of irradiation on cuprizone are unknown. However, several research groups are successfully producing demyelination with irradiated cuprizone diets.

Packaging and labeling

- We recommend vacuum packaging in 500 g, 1 kg, or 2 kg packs.
- Box and package labels indicate the diet code, description, batch specific lot number, and manufacture date.

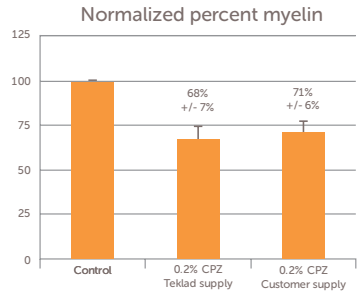
Shelf life and storage

- Store diet refrigerated, away from light, and plan to use within six months.

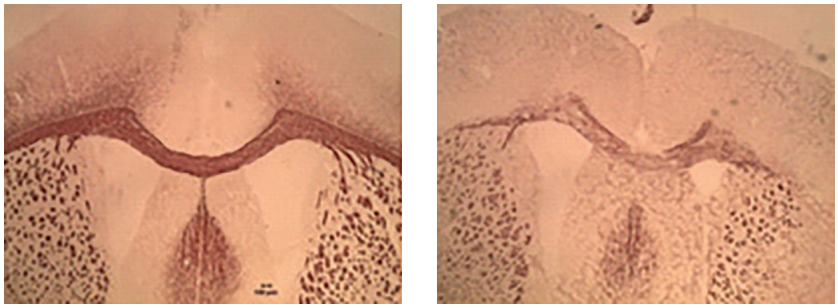
Plan to change out feed on cage tops at least once per week. Due to cuprizone stability concerns, some researchers report changing food as frequently as every two days.

EIGHT WEEK OLD C57BL/6 MICE FED 2016 WITH 0.2% CUPRIZONE (CPZ) DIET FOR SIX WEEKS (N=5 CPZ GROUPS, N=2 CONTROL)

Data provided by NYU Researchers
JL Salzer, EM Grund, and J Samanta



Percent myelin in area of corpus callosum and external capsule normalized to control.



Representative image from control (left) and 0.2% CPZ- Teklad supply (right). Notice the greater amount and more organized structure of the myelin in the control vs. cuprizone treated mouse.

KEY POINTS FROM LITERATURE

Induction method

- In acute studies, cuprizone containing diets are fed for 4-6 weeks (1-13). Substantial remyelination occurs within 4-6 weeks after cuprizone withdrawal.
- In chronic studies, cuprizone is administered for 12 weeks or longer (3, 7, 10, 12). In contrast to acute treatment, remyelination is incomplete and may require 12 weeks to reach maximal levels.
- The typical dietary inclusion of cuprizone is 0.2% (1-7, 9-13). A slightly higher inclusion of 0.3% is also common (1, 4, 8, 13) and could result in more complete demyelination or shorten the treatment time. The higher level may be preferable in some mouse strains, but is not as well tolerated in others.

Model characteristics

- C57Bl/6 is the most common mouse strain utilized (1-12) although BALB/c, CD-1, Swiss and mice with mixed background may also experience demyelination through cuprizone administration (2, 10, 13).
- Mice are usually eight weeks, but occasionally treatment is started in mice that are several months of age (9). Younger mice tend to have variable response and poor tolerance of cuprizone treatment (7).
- Male mice are predominantly used since estrogen and progesterone can influence myelination, however some researchers utilize both sexes and report that sex does not matter when using C57Bl/6 mice (5, 7, 12).

Additional considerations

- Expect weight loss during the first week of cuprizone administration. Weight recovery typically occurs by the end of treatment or within a week of cuprizone removal (2, 5, 8, 11).
- Signs of spontaneous remyelination have been observed transiently during cuprizone administration (4, 6, 7).

Material safety

- Cuprizone is not hazardous according to OSHA criteria. Accidental exposure can be minimized by using typical lab precautions of lab coat, gloves and mask when handling the diet.
- Your chemical safety department should be contacted for additional institution specific guidelines for handling and disposal of cuprizone-containing diets.

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