Adding Compounds to Purified Diets: A simple way to optimize compound delivery in animal studies

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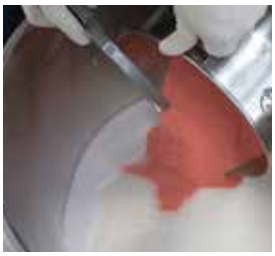


In preclinical research, the precise and consistent administration of test compounds, whether pharmaceuticals, nutraceuticals, whole foods, or investigational agents, is paramount for accurate and reproducible study outcomes. While traditional methods such as oral gavage or injection are common, it is typically possible to dose test compounds via diet.

Why Dose via Diet?

Reduced Stress & Improved Welfare
Relative to traditional dosing (e.g., gavage or injection), which can be invasive and stressful, requiring restraint, anesthesia, or sedation, dietary dosing offers a gentle, consistent delivery method that reduces variability and improves reproducibility.

Controlled Exposure, Natural Uptake
Animals consume compounds voluntarily, simulating real-world administration with minimal handling stress—ideal for behavior, CNS, and endocrine studies.

Labor & Time Efficient
Dietary administration simplifies workflow and minimizes handling.

Compatible with Genetic & Disease Models
Our diets can be tailored to generate knockout or inducible models, allowing precise compound dosing without confounding interventions.

Flexible, Low-Dose Capabilities
We routinely dose compounds at ppm (or lower) levels, which is critical for studies that determine safe exposure levels, identify the lowest dose at which adverse effects occur, and establish the maximum dose that can be administered without unacceptable toxicity.

Flexible and Scalable
We can produce pelleted micro batches as small as 500 grams, with precise incorporation and quick turnaround (5–7 business days). We can also make large batches upon request as high as 1500 kg.

Applications

Subacute & chronic toxicity
Reproductive & developmental toxicity
Carcinogenicity & genotoxicity studies
CNS modulation
Pharmacokinetics (PK), Pharmacodynamics (PD) and dose-response experiments
Dose range-finding studies
Safety pharmacology
Target validation & mechanism-of-action studies
Metabolic, cardiovascular, and endocrine models
Inducible systems

Common Compounds We Incorporate

Gene expression tools:	CNS modulators:	Disease inducers:
Doxycycline, Tamoxifen	PLX5622, PLX3397	Adenine, Cuprizone

Therapeutics:	Supplements:	Flavoring agents:
NSAIDs, Chemotherapeutics, Anti-Retrovirals, Statins	Carbonyl Iron, Antioxidants, Nutraceuticals	Peanut flavor Fruit flavors

Whole food ingredients:
Freeze-dried ingredients including fruits, vegetables, meats and other food ingredients

Designing Your Custom Compound Diet

Research Diets, Inc. specializes in incorporating your compounds into any experimental diet homogeneously and our production group and facility are well equipped for this purpose. When formulating a test compound diet, our scientific team consults with you on several key factors:

1. Compound Information

- Compound name
- Safety profile and MSDS
- Physical form *(free-flowing powder, crystalline, liquid, solution)*
- Purity *(percent active compound or drug)*
- Storage and handling conditions

This ensures optimal handling, dosing, and integration during production.

2. Diet Type (Background Matrix)

- Grain-based diets *(also known as chows)*
- Purified OpenSource Diets® *(recommended for reproducibility)*
  Purified diets minimize batch variability and eliminate background interferences *(e.g., phytoestrogens, heavy metals)*, providing a clean base.

The appropriate background diet depends on the research goal and animal model (and in some cases the ingredient or compound of interest) and our scientific team can assist with a suitable diet selection.

3. Target Dose & Homogeneity

We can blend compounds homogeneously in powder or liquid form at precise concentrations including ppm or lower levels. When concentrations are low *(below 10 ppm)*, we recommend solubilizing the compound in a solvent *(e.g., water, ethanol)* prior to distributing it in the diet.

4. Compound Stability

Some compounds may be sensitive to moisture or heat that could be generated during production. We use cold extrusion pelleting to create pellets. The dietary ingredients are forced through a die to form a specific shape *(often cylindrical)* and then cut into pellets. Our team can advise if:

- Powdered diets are preferable
- Irradiation may affect stability
- Alternative handling procedures are required

How to Calculate the Diet Dose of your Compound

STEP 1: VARIABLES NEEDED

Variables		Units
Single Daily Dose	SD =	Cmpd/kg BW/day
Body Weight	BW =	BW/animal
Daily Food Intake	FI =	Diet/day
Diet Dose	DD=	Cmpd/kg Diet

STEP 2: PLUG FIGURES INTO FORMULA

Formula: DD= (SD X BW)/FI

Typical body weight and food intake estimates allow for optimal dosing and adjustments can be implemented over time to account for growth-related changes.

5. Dietary Caloric Density

Rodents typically regulate their food intake based on caloric content rather than weight, adjusting consumption to meet their energy needs. Because different diets can vary in caloric density—particularly high-fat diets, which are more energy-dense—rodents often eat less quantity by weight *(grams)* when consuming them relative to lower fat diets. We formulate our high-fat and control low fat diets based on calories to ensure similar nutrient concentrations per calorie of the diet consumed. For compound dosing, we also recommend adding them to diets varying in fat contents on a calorie basis rather than by weight, ensuring uniform exposure between diet groups that differ in calorie density.

6. Palatability & Toxicity Considerations

Concerns often arise regarding whether the administered ingredient can impact palatability of the diet. If the added ingredient alters food intake, either due to a more or less favorable flavor profile or toxicity, the actual dose the animals receive will likely be affected. Generally, unless the compound is overtly toxic, animals will typically consume the diet as it is their only food source. Furthermore, most compounds have minimal effect on palatability at low doses. For compounds with strong taste or toxicity, we can:

- Adjust sucrose content *(for e.g. tamoxifen diets)*
- Add masking flavors *(peanut flavor, fruit flavors, etc.)*
- Monitor for visceral illness *(see kaolin pellets below)*

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Test Compounds

Assessing Visceral Illness: Kaolin Pellets

Visceral illness is an undesirable side effect of some pharmaceutical treatments and experimental paradigms, and confounds the study of appetite regulation. Visceral illness describes a range of nausea and concomitant anorexia caused by many factors, including ingestion of toxins, infections, presence of cancer, etc. Consumption of non-nutritive substances (pica behavior) such as kaolin has been documented to reflect feelings of visceral illness in rats and mice. We can also formulate kaolin pellets mixed with carmine, a dye not absorbed in the gastrointestinal tract to estimate kaolin consumption by determination of carmine fecal excretion.

Kaolin Use in Research

Cost Effective Indicator

Research Diets, Inc. offers, a non-nutritive kaolin pellet for use in your research. It is a cost effective, easy to use, early indicator of visceral illness in your experimental animals. Early identification of this adverse experience profile of a compound saves money and streamlines the rational drug design process. Researchers studying metabolic disorders rely on food intake measures as a primary endpoint in evaluating the efficacy of experimental treatments. However, anorectic effects can reflect primary efficacy or secondary effects due to visceral illness. Consumption of kaolin offers early insight into the mechanisms operating in your in vivo studies.

Tools & Resources

- Diet Dose Calculator: Online tool to calculate dietary inclusion levels: https://researchdiets.com/opensource-diets/custom-diets
- Nair AB, Jacob S. 2016. A simple practice guide for dose conversion between animals and human. J Basic Clin Pharm. 7(2):27–31.
- Vasanthi SS, Massey N, Nair SN, Mochel JP, Showman L, Thippeswamy T. 2023. Exploring the benefits of in-diet versus repeated oral dosing of saracatinib (AZD0530) in chronic studies: insights into pharmacokinetics and animal welfare. Front Vet Sci. 10:1297221.

Ready to Start?

Our scientific team is here to help design your custom diet solution-from compound evaluation to final formulation.
Contact us today to streamline your compound dosing with confidence and scientific precision.

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