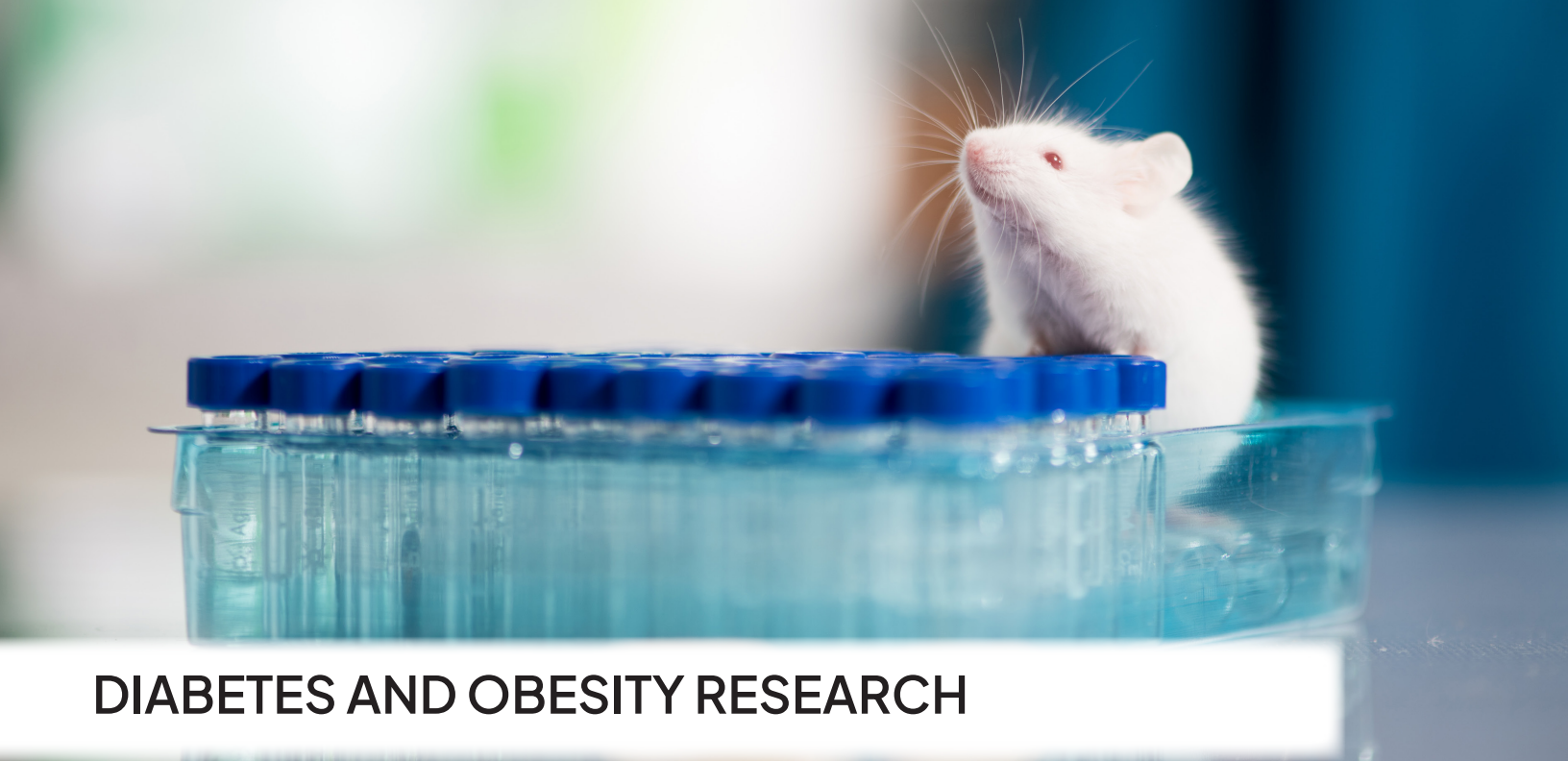




DIABETES AND OBESITY RESEARCH

According to the World Health Organization, approximately 830 million people worldwide live with diabetes, with the majority residing in low- and middle-income countries. Mortality rates associated with diabetes have also increased since the 2000s. Since diabetes can cause or contribute to complications affecting multiple physiological systems, including the cardiovascular, nervous, and renal systems, the growing global burden of diabetes underscores the need for research aimed at understanding the underlying disease mechanisms and developing effective therapeutic strategies.

ALZET® Osmotic Pumps have been used extensively in biomedical research since the 1970's and have become increasingly utilized in metabolism research, including studies of diabetes and obesity, a major risk factor for diabetes. Researchers have relied on ALZET Pumps to provide continuous, controlled delivery of a wide range of agents over extended periods. This approach enables the investigation of disease mechanisms and the evaluation of potential therapeutic strategies in diabetes, obesity, and related comorbidities.



BENEFITS OF ALZET PUMPS IN DIABETES & OBESITY RESEARCH

- Small size for implantation in mice and larger lab animals
- Continuous and controlled delivery of peptides and proteins agents
- Improved bioavailability of compounds with short half-lives
- Reliable technology with over 24,000 publications
- Simple design and easy to use
- Convenient and cost-effective dosing method
- Reduced animal handling and stress
- Automatic nighttime and week-end dosing

Diabetes/Obesity Research Applications

Energy Homeostasis

ALZET Pumps can be used for continuous administration of peptide hormones and neuropeptides involved in hunger regulation, including neuropeptide Y, insulin, leptin, and ghrelin. This allows researchers to investigate the relationships between energy intake, energy expenditure, and weight regulation. The pumps have also been used in animal models of insulin and leptin resistance to study the mechanisms contributing to diabetes and obesity.

Neuroscience

ALZET Pumps can be connected to a cannula to deliver compounds directly into the brain. Since the hypothalamus plays a central role in hunger regulation, researchers can use this approach to deliver agents that modulate signaling pathways directly within this region. This method bypasses the blood-brain barrier enabling investigation of the potential anti-obesity effects of these agents.

Researchers are also investigating the molecular pathways underlying diabetic neuropathy, including mechanisms associated with myelin damage, nerve regeneration, and nerve pain. In models of diabetic neuropathy, ALZET Pumps have been used to continuously deliver test agents, including intrathecal administration of β -nerve growth factor, to investigate potential therapeutic targets and pain-management strategies.

Diabetes is associated with an increased risk of neurodegenerative diseases, including Alzheimer's disease. ALZET Pumps are often used in studies of cognitive decline and memory deficits, providing a means of investigating how diabetes may contribute to the progression of neurodegenerative diseases.

Cardiovascular Diseases

According to the Journal of the American Heart Association, obesity contributes to multiple cardiovascular risk factors, including type 2 diabetes. Individuals with obesity and type 2 diabetes are also more likely to develop and die from cardiovascular diseases.

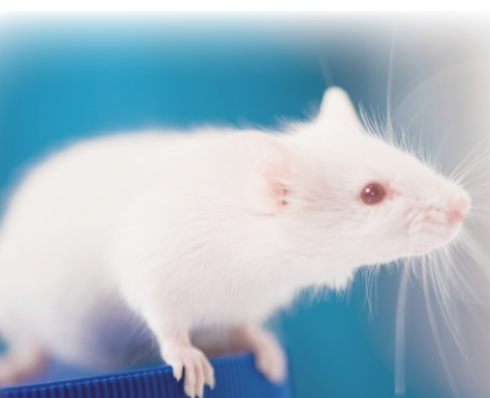
ALZET Pumps are used to investigate mechanisms linking diabetes and obesity with cardiovascular diseases. A common application involves using an ALZET Pump to continuously deliver angiotensin II, thereby inducing models of hypertension or abdominal aortic aneurysms (AAA) in diabetic mice. These models enable researchers to investigate the vascular and molecular mechanisms that contribute to the pathogenesis and progression of hypertension, AAA, stroke, atherosclerosis, and heart failure in the context of diabetes and obesity.

Renal Diseases

Hypertension is a major contributor to kidney damage and hypertensive nephropathy, while prolonged hyperglycemia can lead to diabetic nephropathy. To model advanced diabetic nephropathy, researchers are using ALZET Pumps to induce hypertension into diabetic animals.

ALZET Pumps are also used to study the mechanisms behind hyperglycemia. Recent studies have identified pathways involving cGMP inhibition and thioredoxin interacting protein upregulation, both of which are associated to kidney damage.

ALZET Pumps have also been instrumental in investigating renal hemodynamics and the mechanisms contributing to diabetic and obesity-associated kidney disease. They have helped reveal potential therapeutic targets including, apelin/apelin receptor-mediated blood flow to improve glomerular endothelial cell function, inhibition of activin signaling to reduce macrophage-associated inflammation, and ATRAP (angiotensin II type 1 receptor-associated protein) deletion in conjunction with overactivation of the RAS (renin-angiotensin system).



GLP-1 Administration

GLP-1's have been used to treat type 2 diabetes by helping to lower blood sugar levels. More recently, there has been an uptick in GLP-1 usage to treat obesity since they are highly effective for maintaining weight loss. Within the last few decades, ALZET Pumps have been used to continuously deliver GLP-1's to investigate effects of weight loss on the body and potential combination therapeutic strategies. Below are a few GLP-1's recently delivered with the pumps.

- Exendin-4 (peptide found in venom of Gila monster)
- Exenatide (synthetic version of exendin-4, marketed as Byetta®)
- Semaglutide (marketed as Ozempic®, Rybelsus®, Wegovy®)
- Liraglutide (marketed as Saxenda®, Victoza®)



Pump use in Published Studies

ALZET Pumps have been used to successfully deliver agents in over 1680 diabetes and obesity publications to date. Popular compounds include peptide/steroid hormones, enzyme inhibitors, and in recent years, GLP-1's. Below is a list of agents used in publications recently added to the ALZET Bibliography. If you would like a list of citations specific to your research interest, please contact us.

Agent	Description
Aldosterone	Steroid hormone
Leptin	Peptide hormone
Dexamethasone	Corticosteroid
CXCL14	Protumorigenic chemokine
MOTS-c, human	Peptide
S961	Selective insulin receptor antagonist
WRW4	Synthetic peptide, FPRL1 antagonist
Proline	Amino acid
Fibroblast growth factor - 21	Protein, FGF21 agonist
Lipopolysaccharide	Endotoxin glycolipid
Compound 15	NaPi2b inhibitor
Letrozole	Aromatase inhibitor

Technical Tip: Weight Change during Pump Implantation

When formulating a test solution, researchers should adjust the solution concentration so that, when loaded into a pump, the animal will receive the desired daily dose. As with many metabolic studies, body weight fluctuates over time which can affect the dose delivered. Listed below are different options to consider when using ALZET Osmotic Pumps in studies where weight changes are expected.

Option 1: Calculate the drug dose based on the starting weight of each animal.

Option 2: Calculate the drug dose based on the estimated average body weight of the animal during the infusion period. *Note: Animals will receive a higher dose at the beginning of study and a lower dose towards end of the study.*

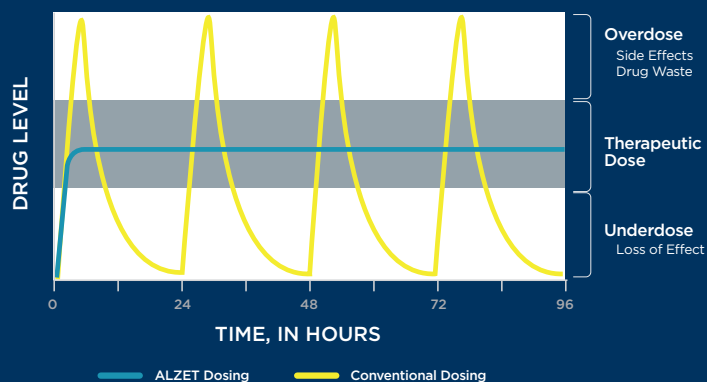
Option 3: Replace pumps during the course of a long-term study to adjust dosing. For example, a 4-week dosing study could use two 2-week ALZET Pumps. The first pump would contain a dose based on the estimated animal weight for the first 2 weeks of the study. After 2 weeks of infusion, the pump would be replaced with a second 2-week pump containing a dose adjusted for the estimated animal weight during weeks 3-4.

Why researchers use ALZET Pumps in diabetes/obesity studies

Chronic treatment Create disease model Improve efficacy	“Metabolic endotoxemia and its associated inflammatory profile were modeled using an indwelling mini osmotic pump to continuously dispense LPS solution. Our results reveal that low-dose LPS treatment over the course of 6 weeks is sufficient to significantly increase microglial recruitment in the amygdala (Amyg) and hippocampus (HPC; in both dorsal and ventral subregions), reduce serum corticosterone and melatonin, and decrease anxiety-like and impulsive behaviors.” <i>ME Klug et al. Comprehensive Physiology. 2025; 15(5):e70044</i>
Chronic delivery Stable plasma concentrations	“Additionally, a comparison group received synthetic Exe4 peptide via a subcutaneously implanted osmotic pump (Peptide), releasing Exe4 peptide into the host circulatory system and then removed at 8 weeks after initial implantation to simulate treatment interruption. Plasma Exe4 concentration sustained in Donor+-Cas9-treated mice over 24 weeks, while Exe4 was undetectable in Donor-treated mice from 4 weeks post-injection (Fig. 4b). The Peptide group maintained sustained Exe4 concentration for 8 weeks, but it became undetectable after pump removal.” <i>J Hirose et al. Communications Medicine (London). 2025; 5(1):269</i>
Targeted delivery Chronic treatment	“To specifically explore the role of brain estrogen synthesis, an osmotic pump was surgically implanted to continuously infuse the aromatase inhibitor Letrozole into the lateral ventricle..” <i>Maric et al. Molecular Metabolism. 2025;99:102202</i>
Improve efficacy	“To address the possibility that BHB is too rapidly cleared from the bloodstream to elicit durable metabolic effects, we next tested a continuous BHB administration paradigm using subcutaneous (sc) osmotic minipumps with 4-wk infusion periods.” <i>C Astudillo-Guerrero et al. American Journal of Physiology-Cell Physiology. 2025;329(3):C834-C847</i>
No stress Targeted delivery	“Therefore, we implant the osmotic minipump allowing the substances to enter the lateral ventricle slowly, to reduce the hypothalamic damage caused by syringe insertion or acute inflammation caused by a high dose of CF. Avoiding hypothalamic damage is critical for confirming the independent obesogenic role of CF and CXCL1 in CP. Thus, we implanted an osmotic minipump allowing CF into the lateral ventricle slowly and chose the lateral ventricle rather than the hypothalamus as the insertion site.” <i>Y Xiao et al. FASEB Journal. 2024;38(23):e70242</i>

The power of continuous delivery

Injections can result in great variations in serum and tissue concentrations. Immediately after injection, compound concentrations commonly exceed effective levels, resulting in overdosing and toxicity. Rapid clearance causes periods between injections wherein the compound is absent from serum and tissues, resulting in underdosing and lack of drug effect. ALZET pumps deliver compound solutions at controlled and predictable rates, ensuring that constant and optimum levels of test agents are maintained throughout the study duration.



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