Study Title: Effect of novel compounds on a diet-induced obese mouse model

Study Objectives

The goal of the study was to assess the effect of a peptide on diet-induced obesity and obesity related parameters.

INTRODUCTION

Obesity is a growing problem in the West, affecting 30% of the American population. Diseases associated with obesity continue to rise as major causes of premature death, with obesity now believed to be the second only to cancer and the leading cause of death in the United States. Treatments to reduce the incidence of obesity will improve the health of treated individuals as well as reducing the health care costs associated with palliative treatment of associated diseases.

METHODS AND RECORDS

Following a 2 week acclimation period, fifty mice were selected for continuation on study, based on body weight and weight gain over acclimation.

Mice were dosed daily SQ for 6 weeks. Body weights were measured daily, and food intake and clinical observations were recorded weekly.

In the final week of dosing, body composition was measured by EchoMRI NMR and underwent a Glucose Tolerance Test as described below:

Glucose Tolerance Test (GTT)

Mice were fasted overnight (no more than 16 hours) prior to glucose administration, mice were bled from tail tip for blood glucose assessment followed by 50uL blood draw by RO. Mice was then administered 2 g/kg glucose by oral gavage. Blood glucose was measured by tail tip at 15, 30, 60, 90, and 120 minutes post administration. A second 50uL blood draw was taken following the 30 minute time point.

At the end of study, mice were euthanized by CO_2 inhalation.

Blood Processing Details:

Blood Collected: Blood was processed for serum by collection into non-heparinized hematocrit tubes into serum microtainer tubes, spun for 12 minutes at 12,000 RPMs in a 4°C centrifuge, and then transferred to 0.5 mL microcentrifuge tubes for storage at -80°C until sent for analysis.

Treatment Protocol

| Gp	n	Treatment	Dose (mg/kg)	Dose Regimen
1	10	Control	n/a	SC, daily for 6 weeks
2	10	Rosiglitazone	25	

Body Weight:

Body weights (g) were averaged by treatment group. Error bars represent standard error of the mean (SEM).
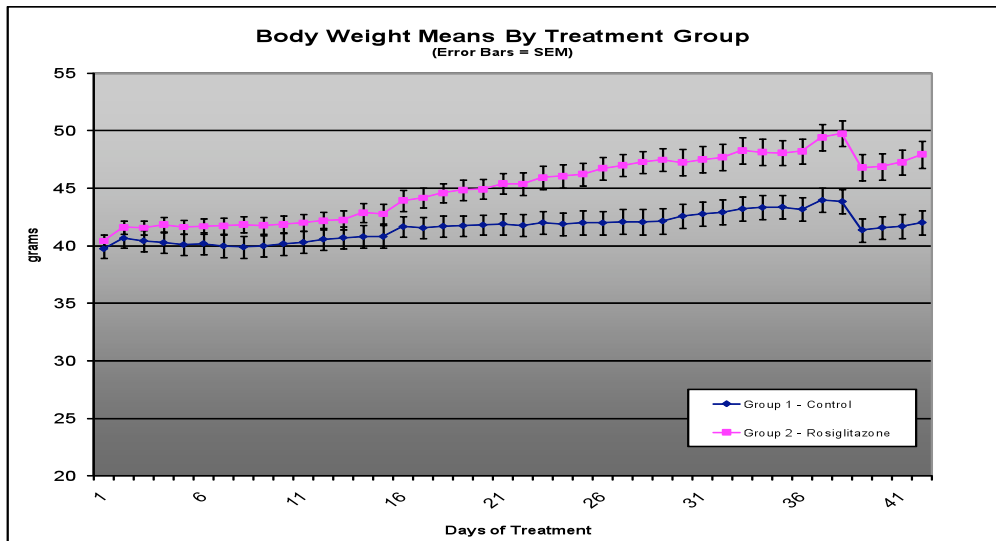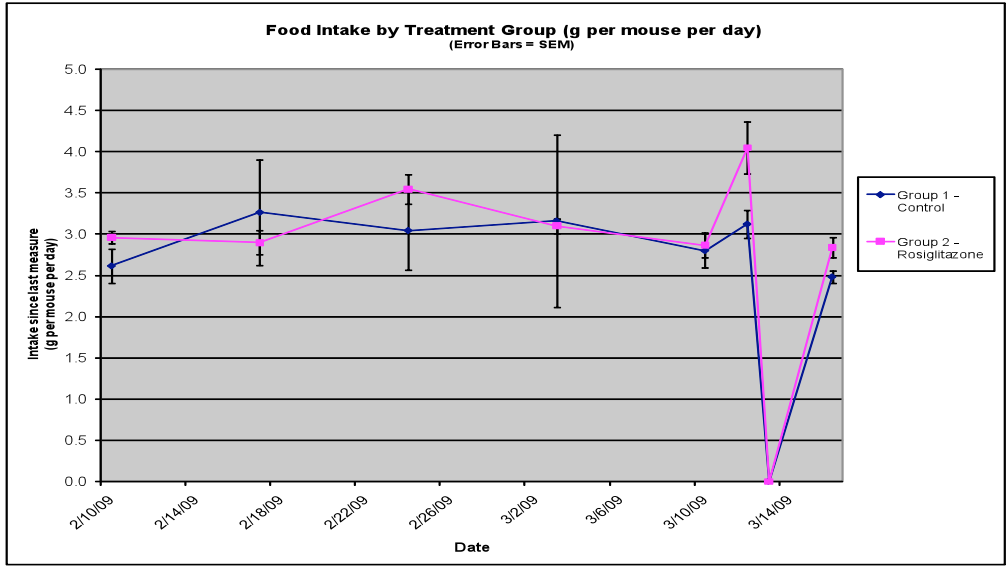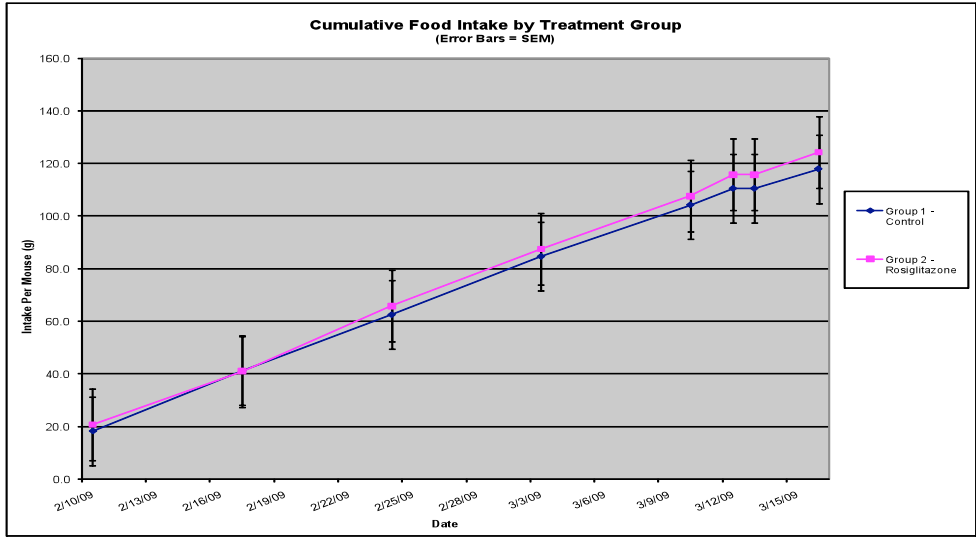

Change in Body Weight:

Body weight change was calculated for each mouse by subtracting the body weight on the first day of dosing (baseline) from the body weight on the last day of dosing (final) and calculating the percent change from baseline body weight: $[=100*(FinalWeight – BaselineWeight)/BaselineWeight]$. Average percent body weight change was then calculated by treatment group. Error bars represent standard error of the mean (SEM).
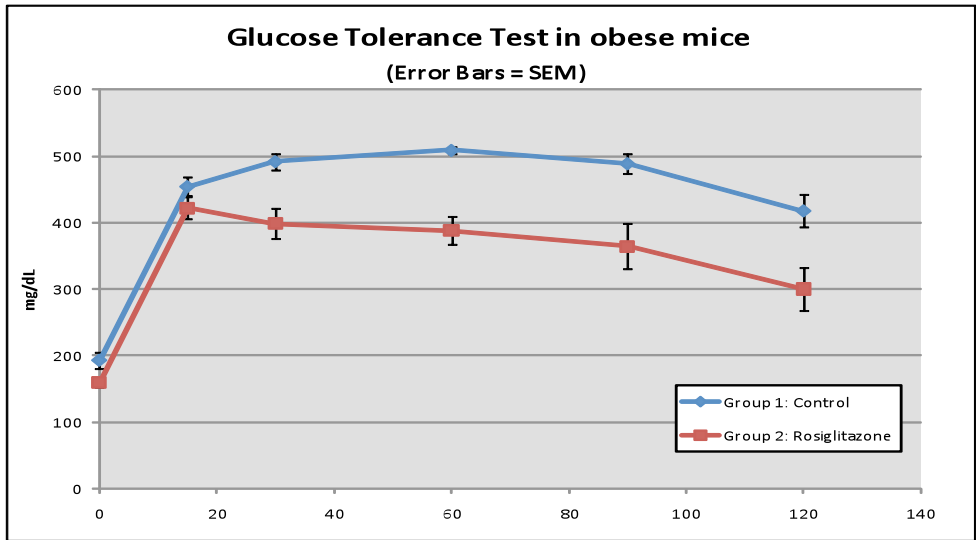
Percent of Baseline Body Weight By Treatment Group
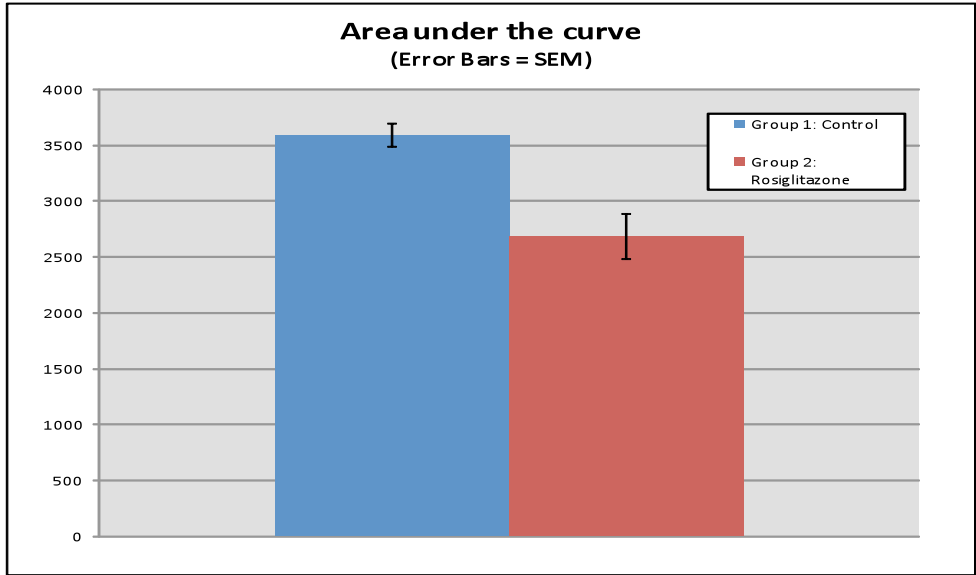(Error Bars = SEM)
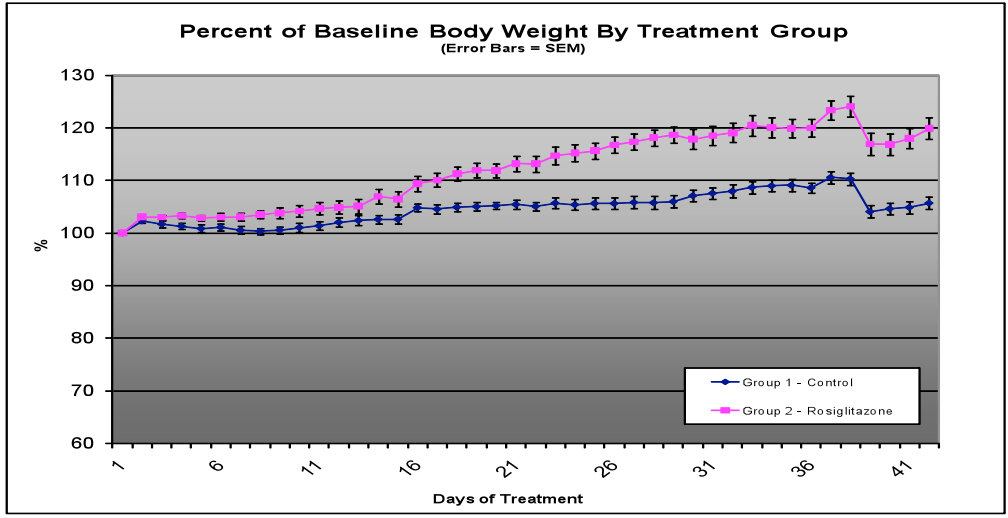
Food Intake:

Intake per mouse per day was calculated based on food intake per cage. Mean intake by treatment group was then calculated weighted by number of mice per cage. Therefore, measurements from cages with 5 mice per cage receive 5/8 of weighting and cages with 3 mice per cage receive 3/8 weighting when 8 mice per treatment group, etc. Error bars represent standard error of the mean (SEM).
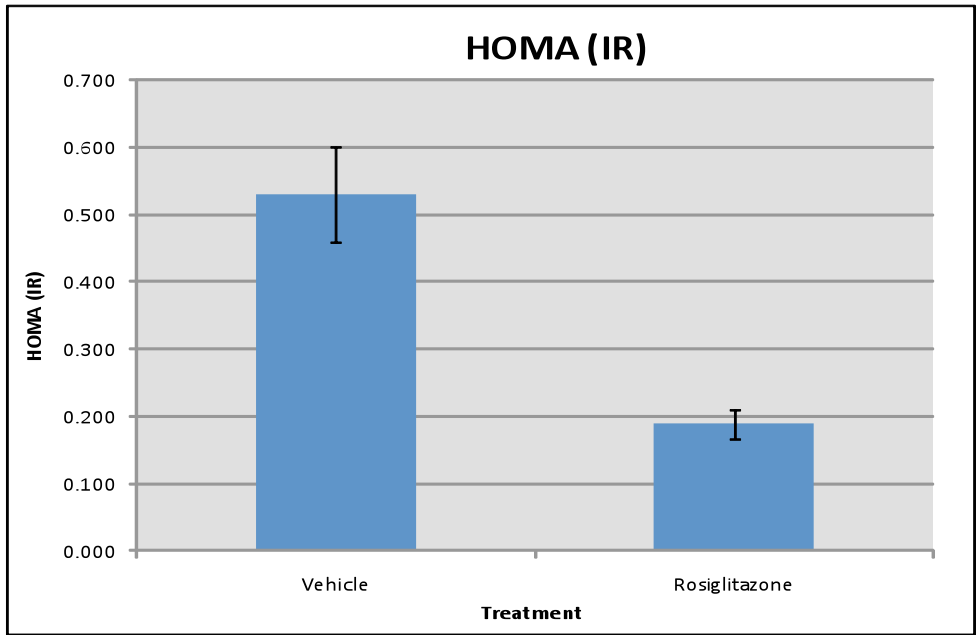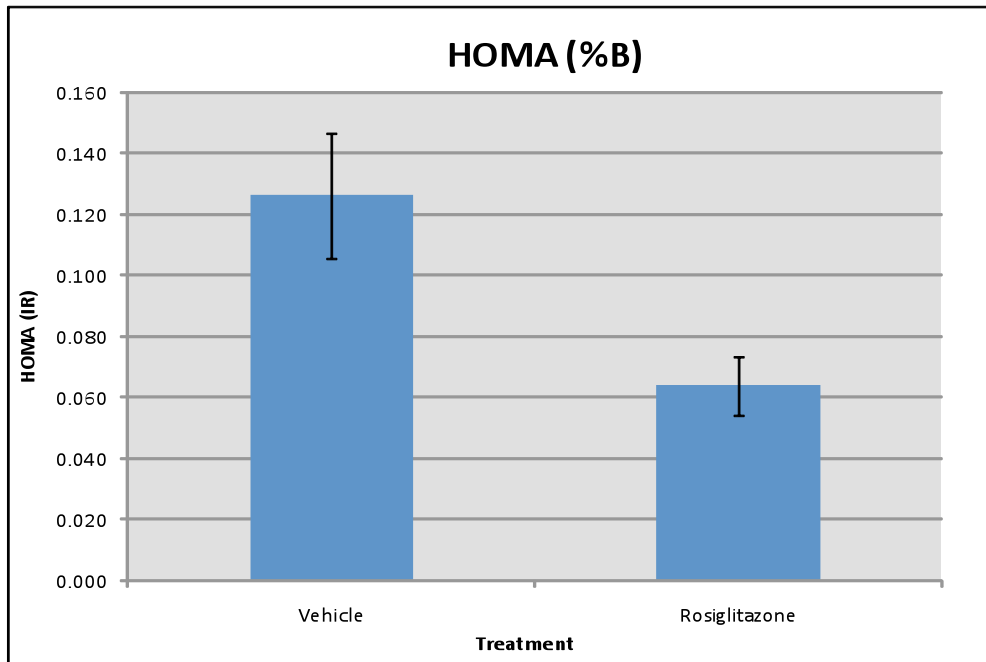

Food Intake by Treatment Group (g per mouse per day)
(Error Bars = SEM)

Cumulative Food Intake by Treatment Group
(Error Bars = SEM)

Glucose Tolerance Test (GTT):

Glucose Tolerance Test in obese mice
(Error Bars = SEM)

Area under the curve
(Error Bars = SEM)

Group 1: Control
Group 2: Rosiglitazone

HOMA

HOMA (IR)

APPENDICES

The following sections contain confidential data and results pertaining to the study.

Appendix 1: Data