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Simultaneous LC-MS/MS Quantitation of Semaglutide and Cagrilintide Enables Pharmacokinetic Evaluation of a Novel Nanoparticle Oral Co-Delivery Platform

PRECLINICAL STUDY | BEAGLE DOG MODEL

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PURPOSE

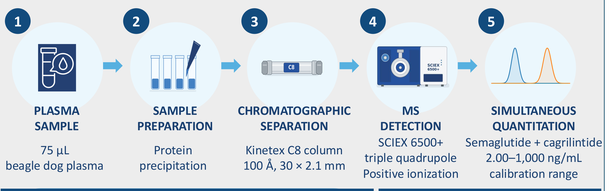
Combination therapies pairing GLP-1 receptor agonists with amylin analogs have demonstrated improved clinical outcomes for obesity, but oral co-delivery remains limited by poor peptide bioavailability and formulation challenges.

This preclinical study evaluated a novel oral delivery platform using polymerized ursodeoxycholic acid (pUDCA) nanoparticles to independently encapsulate semaglutide and cagrilintide before combining both nanoparticle populations into a single oral tablet, enabling oral co-delivery of two distinct therapeutic peptides, a GLP-1 receptor agonist and an amylin agonist, in a beagle dog model.

OBJECTIVE(S)

Develop a sensitive, high-throughput LC-MS/MS assay for simultaneous quantitation of semaglutide and cagrilintide in beagle dog plasma to support preclinical pharmacokinetic evaluation of the novel pUDCA oral co-delivery platform.

METHOD(S)

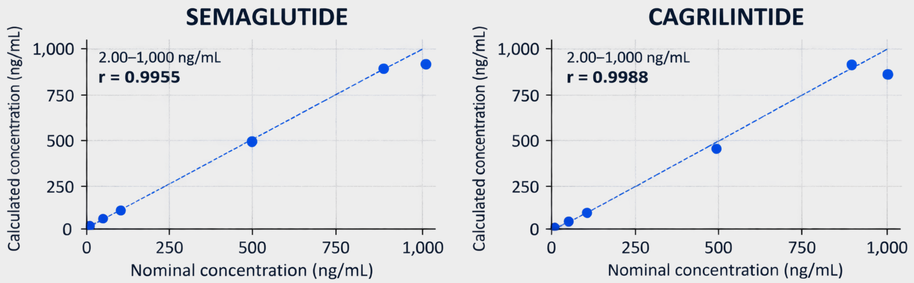


METHOD PARAMETERS	
Matrix	Beagle dog plasma
Sample volume	75 µL
Sample preparation	Protein precipitation
UPLC	Shimadzu Nexera XR LC-30AD
Column	Kinetex C8, 100 Å, 30 × 2.1 mm
Mobile phase A	0.1% formic acid in water
Mobile phase B	0.1% formic acid in acetonitrile
Flow rate	0.7 mL/min
Mass spectrometer	SCIEX 6500+
Ionization mode	Positive
Calibration range	2.00–1,000 ng/mL
Regression	Linear, $1/x^2$ weighting

MRM TRANSITIONS	
Semaglutide	1029.400 → 1238.400
Cagrilintide	1103.00 → 1142.00
Internal standard (both analytes) **Heavy semaglutide**	1039.100 → 1246.200

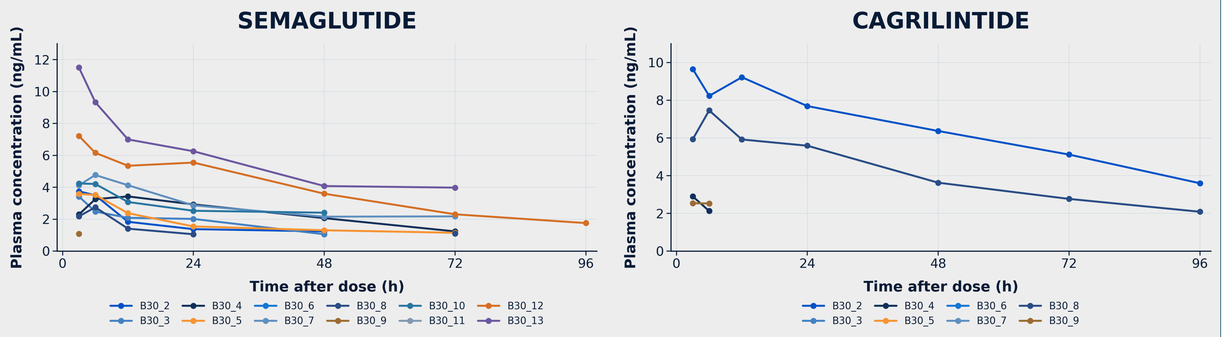
RESULT(S)

Simultaneous quantitation across a 500-fold calibration range



Preclinical dosing: Beagle dogs received a single oral tablet containing pUDCA nanoparticles with 0.33 mg of encapsulated semaglutide and 0.33 mg of encapsulated cagrilintide.

Simultaneous bioanalysis enabled direct PK evaluation



Plasma concentration–time profiles for semaglutide and cagrilintide following oral administration of a single pUDCA nanoparticle co-delivery tablet in beagle dogs. Individual quantifiable concentrations are shown.

Oral co-delivery demonstrated systemic exposure of both peptides

BOTH PEPTIDES QUANTIFIED

Quantifiable semaglutide and cagrilintide concentrations were observed in beagle dog plasma following oral administration of the pUDCA nanoparticle co-delivery formulation.

FOUNDATION FOR FURTHER OPTIMIZATION

These initial pharmacokinetic findings support proof of concept for the pUDCA nanoparticle co-delivery platform and provide a foundation for continued formulation development and evaluation of systemic exposure.

CONCLUSION(S)

ONE METHOD. TWO PEPTIDES.

A sensitive, efficient LC-MS/MS method enabled simultaneous quantitation of semaglutide and cagrilintide across a 2.00–1,000 ng/mL calibration range.

BIOANALYSIS ENABLED DIRECT PK EVALUATION.

Simultaneous quantitation supported preclinical pharmacokinetic evaluation of both peptides following oral administration of the single-tablet pUDCA nanoparticle co-delivery platform.

ORAL CO-DELIVERY DEMONSTRATED SYSTEMIC EXPOSURE.

Preclinical results demonstrated measurable systemic exposure of semaglutide and cagrilintide following oral administration of the pUDCA nanoparticle co-delivery formulation in beagle dogs. These initial findings support proof of concept for the platform and provide a foundation for continued formulation optimization and pharmacokinetic evaluation.

FUNDING/GRANT/ENCORE/ REFERENCE OR OTHER USE

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References: N/A

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