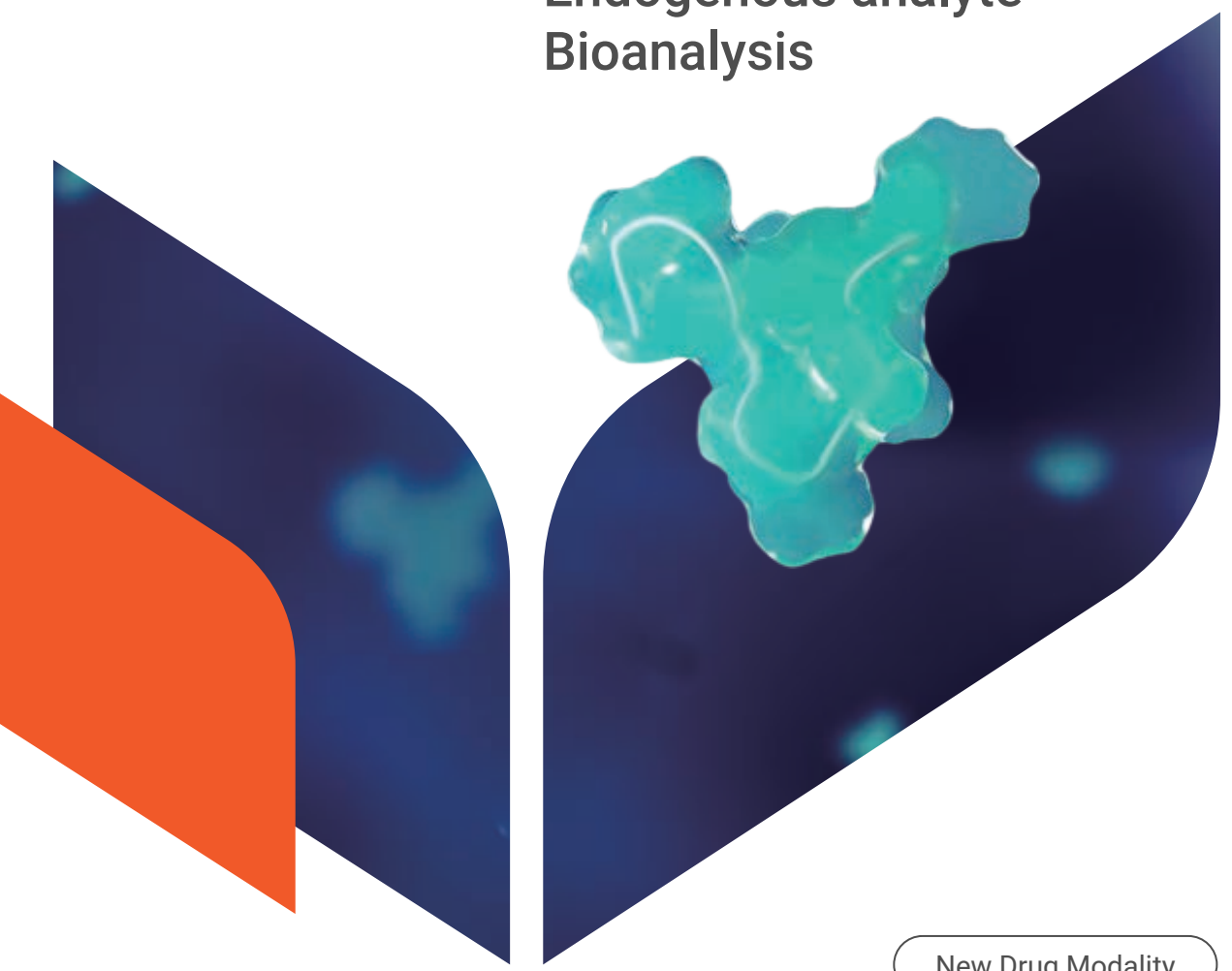
Laboratory Testing Division
Bioanalytical Services

WuXi AppTec

GLP-1

Analogs/ Multifunctional peptides/ Endogenous analyte Bioanalysis



New Drug Modality

Bioanalytical Services

Global Integrated Bioanalytical Platform

WuXi AppTec Bioanalytical Services operates globally and has leading integrated laboratories in China and the U.S. We adhere to GLP and GCP principles and strictly follow high industry regulatory standards. Our comprehensive platform, equipped with advanced instruments and staffed by experienced experts, provides professional one-stop services in preclinical/clinical mass spectrometry, immunochemistry, molecular/cellular, and central laboratory services to global clients.

Shanghai, China
Headquarters
Bioanalytical Services (Clinical)
Central Lab

Suzhou, China
Bioanalytical Services (Preclinical)
Antibody Service

New Jersey, USA
Bioanalytical Services (Preclinical/Clinical)
Central Lab

Chengdu, China
Bioanalytical Services (Preclinical)

Nantong, China
Bioanalytical Services (Preclinical)

18+ Years lab operations in China and the U.S.
24,300 m² lab space

5,000+ small molecule validated methods
2,800+ large molecule validated methods
2M+ samples analyzed per year

Global Regulatory Standards

Successfully passed global regulatory inspections, comply with GLP, GCP, CAP quality standards
200+ China NMPA
30+ International regulatory agencies (U.S. FDA, OECD, EMA, PDMA, CAP)

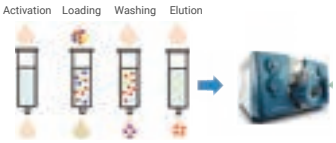
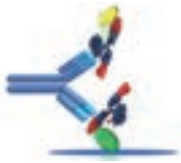
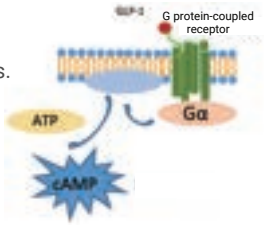
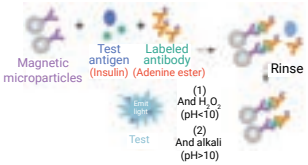
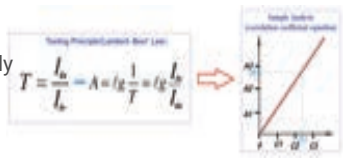
GLP-1 analogs are modified versions of human GLP-1 designed to mimic its natural physiological effects while avoiding rapid enzymatic degradation. These structural modifications extend the half-life of the analogs, making them highly effective in glycemic control.

Endogenous drugs are medications with the same chemical structure as substances naturally found in the human body, such as ions, hormones, vitamins, amino acids, and glucose.

Multifunctional peptides consist of two or more peptides linked together, designed to target multiple receptors and exhibit various pharmacological activities. They demonstrate synergistic effects through different mechanisms, enhancing safety and efficacy. Several GLP-1 peptide drugs, for example, offer multiple physiological benefits, including glucose-lowering, blood pressure reduction, weight loss, and vascular protection.

WuXi AppTec's Bioanalytical Services (BAS) has successfully supported over 100 preclinical and 30 clinical projects involving GLP-1 analogs. With extensive expertise in bioanalytical method development, we are dedicated to accelerating R&D projects and addressing analytical challenges. We offer comprehensive bioanalytical assay services for GLP-1 analogs across all stages of preclinical and clinical development, with the goal of assisting our sponsors in expediting global IND, NDA, and BLA submissions.

Bioanalytical Solutions for GLP-1 Analogs

Research Content		Analyte	Analytical Platform	Study Design
Pharmacokinetics/ Toxicokinetics	PK/ TK	GLP-1 analogs	ELISA/MSD/ AlphaLISA	**Key reagents:** ▪ Biotinylated anti-GLP-1 specific antibody A ▪ Ruthenium-labeled anti-GLP-1 specific antibody B 
			LC-MS	**Sample preparation:** ▪ Protein precipitation ▪ Solid-phase extraction 
Immunogenicity	ADA	Anti-drug antibodies	MSD	**Key reagents:** ▪ Anti-drug antibodies (positive control) ▪ Biotinylated drugs ▪ Ruthenium-labeled drugs 
			Radioimmunoassay (RIA)	**Key reagents:** ▪ Anti-drug antibodies (positive control) ▪ Isotope-labeled drugs 
	NAb	Neutralizing antibodies	Cell-based assay (recommended) or non-cell-based assay	After binding with GLP-1 analogs, G protein-coupled receptors can upregulate intracellular cAMP levels. Neutralizing antibodies block the binding of GLP-1 to the receptors, thereby downregulating cAMP. The level of intracellular cAMP can be measured using a cAMP assay kit. 
Pharmacodynamics	PD/Biomarker	Insulin and blood glucose	Chemiluminescence assay (immunological method)	▪ Using aminoenone (AE) as a chemiluminescent label for insulin detection 
			Blood glucose testing (biochemical testing)	▪ Lambert-Beer's Law ▪ Absorbance is directly proportional to the concentration of the analyte 

Bioanalytical Challenges and Experience with GLP-1 Analogs

Challenges	
TK/PK	▪ Sensitivity ▪ Stability ▪ Specificity ▪ Endogenous
LC-MS/MS	▪ Low recovery, prone to binding with plasma proteins ▪ Low sensitivity ▪ Non-specific binding ▪ Severe chromatographic carryover ▪ Matrix effect
Anti-drug antibodies	▪ Drug tolerance ▪ Low sensitivity
Neutralizing antibodies	▪ Drug tolerance ▪ Method robustness ▪ Sensitivity

Endogenous Drugs	
▪ GLP-1	▪ Total T3/T4
▪ PEG-GH	▪ DHA & EPA
▪ IL-2	▪ EPO
▪ IL-15	▪ GH
▪ FSH	▪ G-CSF
▪ rHCG	▪ PTH
▪ rIFN	▪ Insulin
▪ Rpsh	▪ rHNGF
▪ NGF	▪ ANG-PTL3
▪ Dopamine	▪ PVCP
▪ TSH	

GLP-1 Analogs
▪ Liraglutide
▪ Exenatide
▪ Dulaglutide
▪ Semaglutide
▪ Tirzepatide

The LC-MS/MS platform offers significant advantages in developing highly sensitive analytical methods for GLP-1 analogs, particularly those with molecular weights below 10 kDa. Its high selectivity and specificity make it an ideal choice for accurate and precise analysis in this context.

Platform	Size of Analyte	Sensitivity	Specificity	Method Requirements
LC-MS/MS	<10 kDa	>1ng/mL	High	Internal standard Solid-phase extraction plate (optional)
LBA	≥10 kDa	>10 pg/mL	High	Providing specific antibodies

Considerations for bioanalysis of biosimilar drugs

Biosimilar drugs must demonstrate similarity to their reference drugs in pharmacokinetics, safety (including immunogenicity), and other key parameters. A critical consideration in bioanalysis is whether to use the one-assay method, which focuses solely on the biosimilar, or the two-assay method, which includes both the biosimilar and the reference drug, for comparative evaluation. Drawing from our extensive project experience, we offer the following recommendations.

	One-Assay or Two-Assay Method	Consideration Points
LC-MS/MS	One-assay method	No additional assessment is required
LBA	One-assay method (recommended)	Comparisons will be made in terms of precision and accuracy, and other aspects
Anti-drug Antibodies	One-assay method (recommended)	Comparisons will be made in terms of sensitivity, drug tolerance, and other aspects
Neutralizing Antibodies	One-assay method (recommended)	Comparisons will be made in terms of sensitivity, drug tolerance, and other aspects

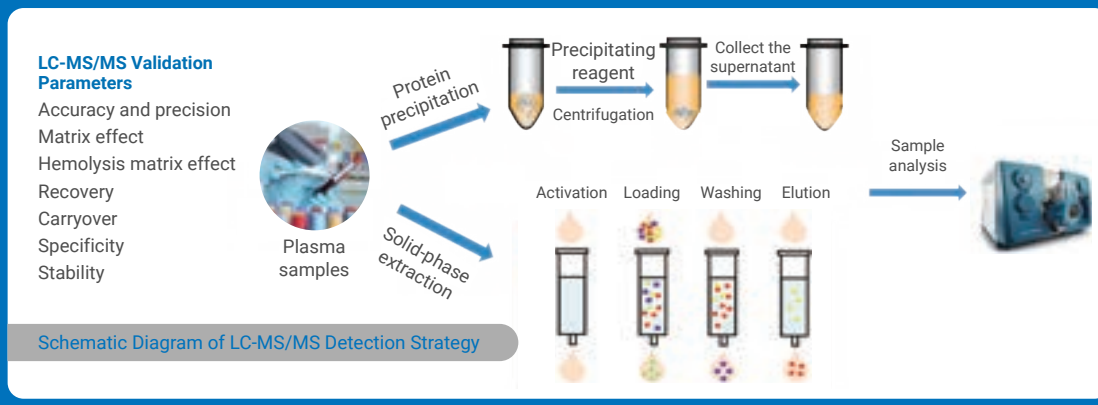
GLP-1 Analogs Case Study

Background:

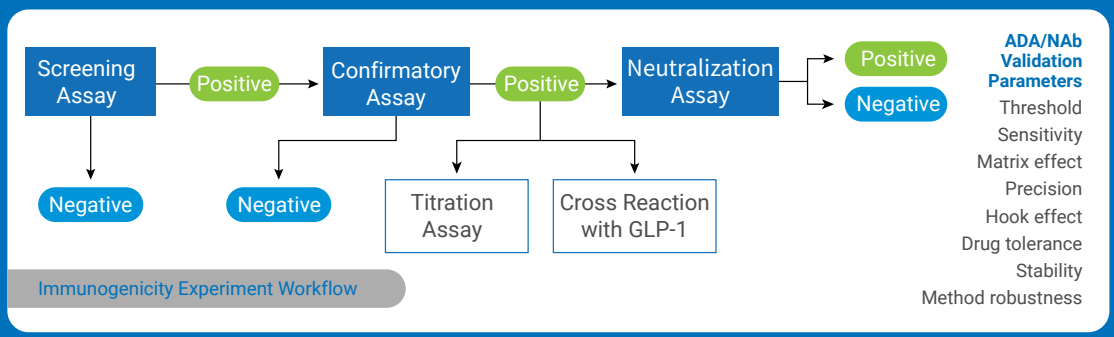
Liraglutide, a marketed drug, works by binding to and activating GLP-1 receptors. It enhances insulin secretion in response to elevated blood glucose levels and reduces excessive glucagon secretion in a similar glucose-dependent manner. This dual action helps to regulate blood sugar levels by increasing insulin when glucose levels are high and decreasing glucagon. Liraglutide has been demonstrated to be highly effective in managing blood glucose levels in adults with type 2 diabetes.

Study Design:

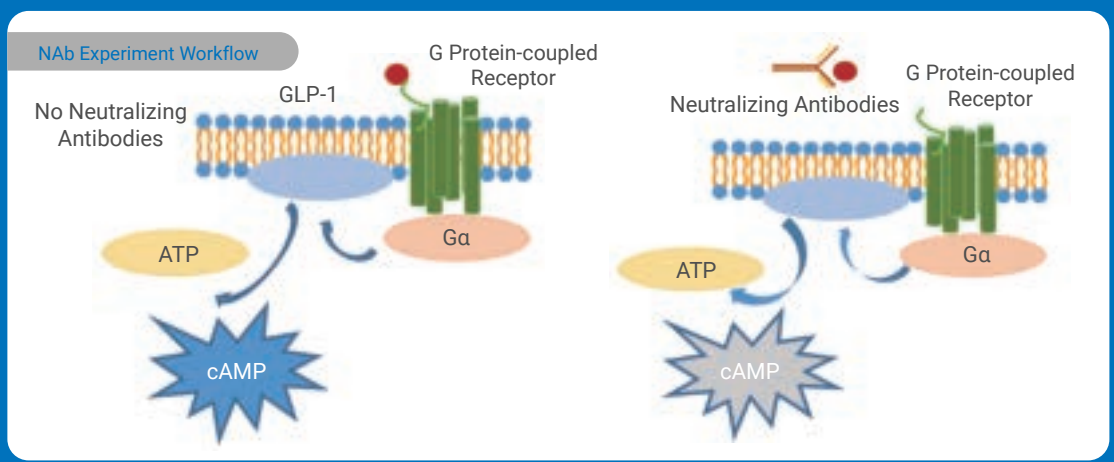
We provide customized services according to global regulatory guidance, in support of IND submissions.
PK: LC-MS method for determining GLP-1 analogs concentration in human/animal plasma
ADA: Electrochemiluminescence method for detecting anti-drug antibodies in human/animal serum
NAb: Cell-based assay for detecting neutralizing antibodies in human/animal serum



Schematic Diagram of LC-MS/MS Detection Strategy



Immunogenicity Experiment Workflow



Our Advantages

Global Integrated Platform: We provide one-stop services to global sponsors, from preclinical to clinical stages, supported by multiple BAS sites worldwide.

Customized Services: Our sponsor-centric professional project management team delivers tailored services to meet your specific needs.

Experienced Team: Our core technical team members boast over 10 years of experience, with our management team having more than 20 years.

Statistical Services: Our immunogenicity cut-point determination offers expedited data delivery, ensuring you quickly get accurate, reliable results. Our services are grounded in scientific rigor, providing enhanced accuracy and dependable outcomes.

We offer extensive experience with more than 100 projects covering endogenous drug targets including GLP-1, PEG-GH, IL-2, FSH, EPO, GH, TSH, and more

Common Industry References

1. Guiding Principles for Validation of Quantitative Analysis Methods for Biological Samples, Chinese Pharmacopoeia 2020 Edition
2. Bioanalytical Method Validation and Study Sample Analysis M10, International Council for Harmonization
3. Bioanalytical Method Validation, U.S. Food and Drug Administration
4. Clinical Pharmacology Considerations for Antibody-Drug Conjugates, U.S. Food and Drug Administration
5. Immunogenicity Testing of Therapeutic Protein Products—Developing and Validating Assays for Anti-Drug Antibody Detection, US Food and Drug Administration

LEARN MORE
LABTESTING.WUXIAPPTEC.COM/BIOANALYTICAL-SERVICES

TALK TO AN EXPERT
LABTESTING.WUXIAPPTEC.COM/TALK-TO-AN-EXPERT

WuXi AppTec
Laboratory Testing Division
Bioanalytical Services

Info@wuxiapptec.com