

1. HPLC analysis conditions for the six drugs are as follows

Table 1 The HPLC analysis conditions for the six drugs

DRUG NAME	COLUMN SPECIFICATION OF CHROMATOGRAPHY	COLUMN TEMPERATURE	MOBILE PHASE COMPOSITION	CHECK WAVELENGTH	FLOW VELOCITY	INJECTION VOLUME
Metformin hydrochloride	Agilent ZORBAX Bio-SCX Cation Exchange Column	30°C	1.7% hydrogen phosphate solution (adjusted to pH 3.0 with phosphoric acid (PA))	218 nm	1 mL/min	10 µL
Glibenclamide	Agilent 5 HC-C18 (2)	30°C	Methanol: 0.1% sodium dihydrogen phosphate (70:30, v/v; pH adjusted to 3.0 ± 0.05 with PA)	233 nm	1 mL/min	10 µL
Fenofibrate	Agilent 5 HC-C18 (2)	30°C	Acetonitrile: water adjusted to pH 2.5 with PA (75:25, v/v)	286 nm	1 mL/min	10 µL

1. HPLC analysis conditions for the six drugs are as follows

Table 1 The HPLC analysis conditions for the six drugs (Continued)

DRUG NAME	COLUMN SPECIFICATION OF CHROMATOGRAPHY	COLUMN TEMPERATURE	MOBILE PHASE COMPOSITION	CHECK WAVELEN GTH	FLOW VELOCITY	INJECTIO N VOLUME
Lovastatin	Agilent 5 HC-C18 (2)	30°C	Acetonitrile with 0.1% orthophosphoric acid (OA): water with 0.1% OA (80:20, v/v)	238 nm	1.5 mL/min	10 µL
Duloxetine hydrochloride	Agilent 5 HC-C18 (2)	30°C	0.025 mol/L potassium dihydrogen phosphate (PDP) solution: acetonitrile: methanol (3:2:2, v/v/v)	290 nm	1.0 mL/min	20 µL
Entecavir	Agilent 5 HC-C18 (2)	30°C	0.1% formic acid (FA): methanol (90:10, v/v)	254 nm	1 mL/min	10 µL

2.Main Reagents

Table 2 Main Reagents

REAGENT OR RESOURCE	SOURCE	IDENTIFIER
Glibenclamide	Sigma-Aldrich (Shanghai) Trading Co., Ltd.	10238-21-8
Metformin hydrochloride	Sigma-Aldrich (Shanghai) Trading Co., Ltd	1115-70-4
Fenofibrate	Sigma-Aldrich (Shanghai) Trading Co., Ltd	49562-28-9
Lovastatin	Sigma-Aldrich (Shanghai) Trading Co., Ltd.	75330-75-5
Duloxetine hydrochloride	Sigma-Aldrich (Shanghai) Trading Co., Ltd.	136434-34-9
Entecavir	Sigma-Aldrich (Shanghai) Trading Co., Ltd.	142217-69-4
DMSO	Sigma-Aldrich (Shanghai) Trading Co., Ltd	67-68-5
Fetal Bovine Serum (FBS)	Gibco	A5256701

2. Main Reagents

Table 2 Main Reagents(Continued)

REAGENT OR RESOURCE	SOURCE	IDENTIFIER
Sodium Chloride	Xilong Scientific	7647-14-5
Penicillin-Streptomycin	Sigma-Aldrich (Shanghai) Trading Co., Ltd.	P0781
DMEM Medium	Gibco	11960044
Glucose	Sigma-Aldrich (Shanghai) Trading Co., Ltd	50-99-7
Recombinant Human Insulin Injection	Sigma-Aldrich (Shanghai) Trading Co., Ltd	11061-68-0
CCK-8 Assay Kit	Suzhou New Sai Mei Biotechnology Co., Ltd.	C6005
Glucose Oxidase (GOD-POD) Assay Kit	Nanjing Jiancheng Bioengineering Institute	A154-1-1
Interleukin-6 (IL-6) ELISA Kit	Shanghai Xinyu Bio	-

2.Main Reagents

Table 2 Main Reagents (Continued)

REAGENT OR RESOURCE	SOURCE	IDENTIFIER
LDL-C Assay Kit	Nanjing Jiancheng Bioengineering Institute	A113-1-1
0.1% Triton X-100/PBS Solution	Shanghai Yuanye Biology	R32835
Sulfuric Acid	Xilong Scientific	7664-93-9
Diethyl Ether	Xilong Scientific	60-29-7
AST Assay Kit	Nanjing Jiancheng Bioengineering Institute	C010-2-1
ALT Assay Kit	Nanjing Jiancheng Bioengineering Institute	C009-2-1
Total Cholesterol (T-CHO) Assay Kit	Nanjing Jiancheng Bioengineering Institute	A111-1-1
Tumor Necrosis Factor- α (TNF- α) Kit	Shanghai Xinyu Biology	-

2.Main Reagents

Table 2 Main Reagents (Continued)

REAGENT OR RESOURCE	SOURCE	IDENTIFIER
Triglycerides (TG) Assay Kit	Nanjing Jiancheng Bioengineering Institute	A110-1-1
Liver Glycogen	Shanghai Xinyu Bio	-
HDL-C Assay Kit	Nanjing Jiancheng Bioengineering Institute	A112-1-1
Insulin (INS) ELISA Kit	Shanghai Xinyu Bio	-
GSP ELISA Kit	Shanghai Xinyu Bio	-
Blood Glucose (GLU) Assay Kit	Shanghai Xinyu Bio	-
GLP-1 ELISA Kit	Shanghai Xinyu Bio	-
Human C-Peptide ELISA Kit	Shanghai Xinyu Biology	-

2.Main Reagents

Table 2 Main Reagents (Continued)

REAGENT OR RESOURCE	SOURCE	IDENTIFIER
IRS ELISA Kit	Shanghai Xinyu Bio	-
P-IRS ELISA Kit	Shanghai Xinyu Bio	-
PI3K ELISA Kit	Shanghai Xinyu Bio	-
P-PI3K ELISA Kit	Shanghai Xinyu Bio	-
P-AKT ELISA Kit	Shanghai Xinyu Bio	-
GLUT4 ELISA Kit	Shanghai Xinyu Bio	-
AKT ELISA Kit	Shanghai Xinyu Bio	-

2.Main Reagents

Table 2 Main Reagents (Continued)

REAGENT OR RESOURCE	SOURCE	IDENTIFIER
Bovine Serum Albumin (BSA)	Wuhan Servicebio Technology Co., Ltd.	GC305010
PBS Buffer	Wuhan Servicebio Technology Co., Ltd.	G0002
Anhydrous Ethanol	Sinopharm Chemical Reagent Co., Ltd.	64-17-5
Dimethyl benzene	Sinopharm Chemical Reagent Co., Ltd.	1330-20-7
EDTA Antigen Retrieval Solution (pH 8.0)	Wuhan Servicebio Technology Co., Ltd.	G1206
Adherent slides (cryosections)	Servicebio Technology Co., Ltd.	G6012-2

2.Main Reagents

Table 2 Main Reagents (Continued)

REAGENT OR RESOURCE	SOURCE	IDENTIFIER
EDTA Antigen Retrieval Solution (pH 9.0)	Wuhan Servicebio Technology Co., Ltd.	G1203
n-Butanol	Sinopharm Chemical Reagent Co., Ltd.	71-36-3
Neutral Balsam	Sinopharm Chemical Reagent Co., Ltd.	96949-21-2
Lactic Acid Antigen Retrieval Solution (pH 6.0)	Wuhan Servicebio Technology Co., Ltd.	G1202
Organic Self-Quenching Fluorescent Agents	Wuhan Servicebio Technology Co., Ltd.	G1221
Adherent slides (paraffin sections)	Servicebio Technology Co., Ltd.	G6012-1

2.Main Reagents

Table 2 Main Reagents (Continued)

REAGENT OR RESOURCE	SOURCE	IDENTIFIER
CY3-Labeled Goat Anti-Rabbit IgG	Wuhan Servicebio Technology Co., Ltd.	GB15336
Universal Tissue Fixative	Wuhan Servicebio Technology Co., Ltd.	G1101
Alexa Fluor 488 Labeled Goat Anti-Mouse IgG	Wuhan Servicebio Technology Co., Ltd.	GB123493
Anti-Fluorescence Quenching Mounting Medium (containing DAPI)	Biyun Tian Biotechnology Co., Ltd.	P0131
Eastep® Super Total RNA Extraction Kit	Promega Bioproducts Co., Ltd. (Shanghai, China)	LS1040
Calenduloside E	Shanghai Yuanye Biology	26020-14-4
Environmentally Friendly Degreasing Agent	Wuhan Servicebio Technology Co., Ltd.	G1128
Methotrexate	Sigma-Aldrich (Shanghai) Trading Co., Ltd.	59-05-2

2.Main Reagents

Table 2 Main Reagents (Continued)

REAGENT OR RESOURCE	SOURCE	IDENTIFIER
Hematoxylin-Eosin (H&E) High-Resolution Permanent Staining Kit	Wuhan Servicebio Technology Co., Ltd.	G1076
Insulin	Wuhan Servicebio Technology Co., Ltd.	GB1533
Glucagon	Wuhan Servicebio Technology Co., Ltd.	GB123493
Epidermal Growth Factor	Gibco	62253-63-8
Glutamine	Gibco	25030081
0.25% Trypsin-EDTA (1X) Phenol Red	Gibco	25200-056
MCDB131 Medium	Gibco	10372019

3. Main Instruments

Table 3 Main Instruments

Instrument Name	Manufacturer	Model
Microplate Reader	Tecan Trading (Shanghai) Co., Ltd.	Infinite M200 PRO
Blood Glucose Meter	Roche Diagnostics GmbH	ACCU-CHEK
Tissue Dehydrator	DIAPATH S.p.A., Italy	Donatello
Embedding Machine	Wuhan Junjie Electronics Co., Ltd.	JB-P5
Pathological Microtome	Leica Instruments (Shanghai) Co., Ltd.	RM2016
Freezing Stage	Wuhan Junjie Electronics Co., Ltd.	JB-L5
Tissue Flatteners	Jinhua Kedi Instrument Equipment Co., Ltd.	KD-P
Oven	Tianjin Laiborui Instrument Co., Ltd.	GFL-230
Cryostat Microtome	Thermo Fisher Scientific (China) Co., Ltd.	CRYOSTAR NX50

3. Main Instruments

Table 3 Main Instruments (Continued)

Instrument Name	Manufacturer	Model
Upright Optical Microscope	Nikon Corporation, Japan	ECLIPSE E100
Imaging System	Nikon Corporation, Japan	Eclipse Ti2
NanoDrop 2000 Spectrophotometer	Thermo Fisher Scientific Shanghai Co., Ltd.	NanoDrop 2000
RevertAid RT Reverse Transcription Kit	Thermo Fisher Scientific Shanghai Co., Ltd.	K1622
Real-Time Fluorescent Quantitative PCR System	Thermo Fisher Scientific	QuantStudio 5
Ultra-High Performance Liquid Chromatography-Tandem Mass Spectrometry	Waters Corporation	Waters UPLC Acquity I-Class PLUS; Waters Xevo G2-XS QTof
Programmable Peristaltic Pump	Jiangsu Aiweide Biotechnology Co., Ltd.	-
Organ-on-Chip Flow Controller	Jiangsu Aiweide Biotechnology Co., Ltd.	-
Confocal Microscope	Nikon Corporation, Japan	AX R Confocal Microscope

3.Main Instruments

Table 3 Main Instruments (Continued)

Instrument Name	Manufacturer	Model
Analytical Balance	Mettler Toledo Technology (China) Co., Ltd.	MA204/A
Clean Bench	Likang Precision Technology (Shanghai) Co., Ltd.	OptiClean 1300
Ultrapure Water Machine	Likang Precision Technology (Shanghai) Co., Ltd.	Smart-ROB
Biochemical Incubator	Shanghai Yiheng Scientific Instruments Co., Ltd.	Blue pard
CO ₂ Incubator	Likang Precision Technology (Shanghai) Co., Ltd.	HF90
Inverted Optical Microscope	Motic Industrial Group Co., Ltd.	AE31E-100W
Ice Maker	Changshu Xueke Electric Appliance Co., Ltd.	IMS-70
Pipettes (Various Specifications)	Eppendorf AG	Eppendorf Research plus
Fully Automatic Autoclave	Tianmei Yituo Laboratory Equipment (Shanghai) Co., Ltd.	FLS-1000

3.Main Instruments

Table 3 Main Instruments (Continued)

Instrument Name	Manufacturer	Model
Electric Constant Temperature Water Bath	Shanghai Yiheng Scientific Instruments Co., Ltd.	HWS-26
Palm Centrifuge	Hefei Lanjieke Technology Co., Ltd.	LX-200B
Benchtop Low-Speed Centrifuge	Sigma-Aldrich (Shanghai) Trading Co., Ltd.	3-18ks
Low-Temperature Grinder	Xiwei Biotechnology Co., Ltd.	SWE-P
Refrigerator	Qingdao Haier Co., Ltd.	BCD-192TGN
Microwave Oven	Galanz Microwave Appliance Co., Ltd.	P70D20TL-P4
Decolorizing Shaker	Wuhan Saierwei Biotechnology Co., Ltd.	DS-2S100
Vortex Mixer	Wuhan Saierwei Biotechnology Co., Ltd.	MV-100
Scanner	3DHISTECH Kft.	Pannoramic MIDI

3.Main Instruments

Table 3 Main Instruments (Continued)

Instrument Name	Manufacturer	Model
Anaerobic Workstation	Munro Instruments Ltd., UK	AW400TG
Electric Blast Drying Oven	Shanghai Yiheng Scientific Instruments Co., Ltd.	BPG-9240A
Ultrasonic Cleaner	Ningbo Xinzhi Biotechnology Co., Ltd.	SB25-12DTD
Gas Chromatograph	Agilent Technologies, Inc.	8890 GC System

4. Primers for qRT-PCR assay

Table 4 Primers for qRT-PCR assay

Gene name	Forward primer (5'-3')	Reverse primer (5'-3')
<i>Gapdh</i>	AGGTCGGTGTGAACGGATTTG	TGTAGACCATGTAGTTGAGGTCA
<i>Irs1</i>	TCCCAAACAGAAGGAGGATG	CATTCCGAGGAGAGCTTTTG
<i>Pik3r1</i>	TATTGCGAGGGAAGCGAGAC	ACTTCGCCGTCTACCACTAC
<i>Akt1</i>	AAGAAGGAGGTCATCGTCGC	CTTGAGGGCCGTAAGGAAGG
<i>Slc2a4</i>	CTGTCGCTGGTTTCTCCAAC	CGGCAAATAGAAGGAAGACG
<i>Foxo1</i>	CGGGCTGGAAGAATTCAATTC	AGTTCCTTCATTCTGCACTCGAA
<i>Gsk3b</i>	TTGGAGCCACTGATTACACG	CCAACCTGATCCACACCACTG
<i>Pck1</i>	GGAAGAACAAGGAGTGGAGAC	CAGGCAGGGTCAATAATGGG
<i>G6pc</i>	TGCAAGGGAGAACTCAGCAA	GGACCAAGGAAGCCACAATG