Faculty of Women for Arts, Science & Education
Biochemistry and Nutrition Department

Metabolomic Response of Feeding Functional Foods and Exercise on Obesity Risk in Rats

Thesis
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"وقالوا الحمد لله الذى هدانا لهذا وماكنا
لنهتدى لولا أن هدانا الله"

صدق الله العظيم

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Abstract

Obesity is one of the independent risk factors for serious health problems associated with many ailments and its incidence has increased in recent years as a major health problem worldwide. Obesity induces perturbation in metabolism which demand a corresponding shift in research more focus towards large scale unbiased analytical approaches "metabolomics" by which we can monitor changes in metabolome. Therefore, metabolomics is used in this research to monitor the outcome of treatment with some functional foods and exercises, by observing whether the metabolic phenotypes of treated, diseased rats shifts in the cluster of healthy controls.

Study had been carried out by inducing obesity in the rats through administration of high fat diet (HFD). Obese rats were subsequently treated with functional foods used for obesity management including grapefruit, pomegranate, red cabbage and/or swimming exercise. Histopathological studies and conventional biochemical biomarkers were measured in obese rats. In parallel, serum and urine samples were analyzed using gas chromatography-mass spectrometry (GC-MS) followed by multivariate data analysis to classify samples and determine if such treatments can help revert obesity related metabolic changes back to normal status. Further and to pinpoint active agents in these functional food juices, ultra performance liquid chromatography coupled to high resolution TOF MS was used for profiling of secondary metabolites.

Results from this study led to the identification of key metabolites markers for obesity and changes in their levels upon which were further used to assess the role of functional foods in obesity management. The results showed that obesity is related to lipids, amino acids and central tricarboxylic acid (TCA) pathways. Distinct variations in certain metabolites were recorded in obese rats including L-aspartic, L-alanine, L-glutamine, L-glycine, phenylethanolamine, α-aminobutyric acid, β-hydroxybutyric acid, lactate, phosphate and oxalate. Functional food treatments and exercise were both found to be quite effective in restoring obesity-related metabolic disruptions in obese rats and back to normal status as revealed from orthogonal partial least squares-discriminating analysis (OPLS-DA). Thus, Metabolomics approaches provide essential insights into obese metabolic disturbances and functional foods and/or exercise stratification for obesity management.

List of Abbreviations

AMPK	Activated protein kinase
α - AB	Alpha- aminobutyric acid
AIN-93	American institute of nutrition (1993)
AMDIS	Automated mass spectral deconvolution and identification system
B.P.	Base Peak
BMI	Body mass index
BWG	Body weight gain
BCAAs	Branched chain amino acids
CV	Central vein
DNA	Deoxyribonucleic acid
ESI	Electro Spray Ionization
GPR	G- protein-coupled receptors
GC	Gas chromatography
GC/MS	Gas chromatography coupled with Mass Spectroscopy
GSH	Reduced glutathione
GK	Goto-Kakizaki
H&E	Haematoxylin and Eosin
Hz	Hertz
HCA	Hierarchical clustering analysis
HFD	High fat diet
h.	Hour(s)
HMDB	Human Metabolome Database
IS	Internal standard
LDH	Lactate dehydrogenase
LSD	Least significant difference

LC	Liquid chromatography
LC-MS	liquid chromatography mass spectrometry
LDL-C	Low density lipoprotein- Cholesterol
MS	Mass spectroscopy
m/z	Mass-to-Charge Ratio
MeOH	Methanol
[M]+	Molecular ion
M.W	Molecular weight
MVA	Multivariate analysis
NIST	National Institute of Standards & Technology
NIH	National Institutes of Health
MSTFA	N-methyl-N-(trimethylsilyl)-trifluoroacetamide
OPLS-DA	Orthogonal Projections to Latent Structures Discriminant Analysis
PLS-DA	Partial least squares discriminant analysis
ppm	Part Per Million
PDA	Photodiode array (detector)
PCA	Principle component analysis
^{1}H NMR	Proton nuclear magnetic resonance
PDC	Pyruvate dehydrogenase complex
qTOF	Quadrupole-time-of-flight
ROS	Reactive oxygen species
RI	Retention index
Rt	Retention time
r.p.m	Revolutions per minute
RNA	Ribonucleic acid
ROC	Receiver operating characteristic
SOMs	self-organizing maps

SCFAs	short chained fatty acids
SD	Standard diet
SEM	Standard error of mean
TC	Total cholesterol
TAGs	Triacylglycerols
TCA	Tricarboxylic acid cycle
TMS	Trimethyl silyl
T_2DM	type 2 diabetes mellitus
UPLC	Ultra Performance Liquid Chromatography
UV	Ultraviolet
v/v	Volume per Volume
WAT	White adipose tissue
WHO	World Health Organization

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