

THE EFFECT OF AN AQUEOUS EXTRACT OF  
TURERMIC AND A COMBINATION OF CHINESE  
HERBS ON GLUCOSE HOMEOSTASIS.

By

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# Declaration

I certify that the substance of this thesis does not contain any work that has been previously published or written, except where due reference is made in the text. This thesis has not already been submitted for any degree and is not currently being submitted for any other degree.

I certify, to the best of my knowledge, any help received in preparing this project and any sources, have been acknowledged in this report.



Mechele Collins

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# ANNOTATIONS

ADP	Adenosine Diphosphate
Akt	protein kinase B
ALT	alanine aminotransferase
AMP	Adenosine Monophosphate
AMPK	AMP-activated protein kinase
AS160	a substrate of Akt
ASP	Acylation Stimulating Protein
ATP	Adenosine Triphosphate
BGL	Blood Glucose Levels
BMI	Body Mass Index (Body mass/Height <sup>2</sup> )
Ca <sup>2+</sup>	Calcium
cAMP	Cyclic Adenosine Monophosphate
CRP	C-Reactive Protein
ER	Endoplasmic Reticulum
ES	Endoplasmic stress
FBGL	Fasting Blood Glucose Level
FFA	Free Fatty Acids
G6Pase	glucose-6-phosphatase
GGT	$\gamma$ -glutamyltransferase
GIP	Gastric Inhibitory Polypeptide
GK	Glucokinase
GLP-1	Glucagon-like-peptide-1
GS	Glycogen Synthase
HbA <sub>1c</sub>	glycosylated haemoglobin
HK	Hexokinase
HKI	Hexokinase I
HKII	Hexokinase II
IGF-1	Insulin-like growth factor-1
IKK	inhibitor of nuclear factor- $\kappa$ B Kinase
IL-6	Interleukin-6
IL-7	Interleukin - 7
IL-18	Interleukin-18
IRS1	insulin receptor substrate 1
IRS-1 and -2	tyrosine phosphorylation of insulin receptors
JNK	c-Jun NH <sub>2</sub> -terminal kinase
K <sup>+</sup>	Potassium
K <sup>+</sup> ATP	Potassium Adenosine Triphosphate
NF $\kappa$ B	Nuclear-factor- $\kappa$ B
NO	Nitrous Oxide
MODY	Maturity Onset Diabetes of the Young

PI3K	phosphatidylinositol-3-kinase
PC-1	A membrane protein
PEPCK	phosphoenolpyruvate carboxykinase
PKA	Protein Kinase A
PKC	Protein Kinase C
PPAR's	peroxisome proliferators-activated receptors
PPAR- $\gamma$	Peroxisome proliferator-activated receptor – gamma
PTEN	a lipid/protein phosphatase
RBP4	Retinol binding protein 4
SGLT1	Sodium/glucose co-transporter
TNF- $\alpha$	Tumour Necrosis Factor - $\alpha$
TZDs	Thiazolidinediones

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## ABSTRACT

Type 2 Diabetes is currently in epidemic proportions throughout the world and the prevalence is increasing rapidly worldwide, costing several billion dollars to the world economy every year. If new treatments are found that would be economically viable for third world countries to produce there may be a way of controlling this epidemic. Although the effects of current hypoglycaemic drugs appear to be sufficient and blood glucose levels are normalised initially, they still tend not to stop the micro-vascular effects of the disease and their effectiveness appears to diminish overtime. There has been a recent trend for people to turn to alternative therapies for treatment of their diabetes and also there is a search for new and more effective treatments. Many herbs have been used by various cultures, however, little if any; scientific research has been carried out to show their efficacy and effectiveness. Therefore the aim of this study was to determine which of several culinary herbs, Australian plants and a combination of Traditional Chinese Medicines (Glucostat) might be beneficial in the treatment of Type 2 diabetes.

An in-house developed *in-vitro* bio-assay method was employed in this study to screen the effects of treatments of an aqueous extract of the culinary herbs, Australian plants and Glucostat on glucose uptake in mice heart tissue under different glucose concentrations. These results indicated that some of the extracts increased the uptake of glucose in the mice heart tissues, some had no

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effect and others appeared to be toxic. From these results it was decided to examine Turmeric and Glucostat further.

The aqueous extract of Turmeric resulted in a dose dependent effect on the uptake of glucose in mice the heart tissue culture and also a decrease in glucose output mice liver tissue culture at hyperglycaemic conditions but not at normoglycemic conditions. The greatest effect in increasing glucose and decreasing gluconeogenesis was when 10 µg/ml of the Turmeric extract was used with a glucose concentration of 6 mM. Dry roasting or boiling of the Turmeric decreases its effectiveness, suggesting the active constituent/s is a protein, which is supported by the fact that diethyl ether did not extract the active constituents. The addition of insulin and Wortmannin to heart and liver tissue culture indicated that the Turmeric is acting via the insulin pathway with an additive effect to insulin at all concentrations of Turmeric extract. There was an antagonistic reaction when Turmeric and Metformin were used in conjunction.

An aqueous extract of Glucostat increased the uptake of glucose in mice heart tissue culture and decreased gluconeogenesis from the mice liver tissue, in a dose dependent manner at hyperglycaemic conditions but not at normoglycemic conditions. The greatest effect in increasing glucose and decreasing gluconeogenesis was when 10 µg/ml of the Turmeric extract was used with a glucose concentration of 8 mM. Boiling of the Glucostat decreased its ability to increase the uptake of glucose or decrease the glucose output at lower concentrations, however, at higher concentrations (20 µg/ml) it increased the

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uptake and output, suggesting more than one active ingredient; the diethyl ether solvent extract supporting this. The addition of insulin and Wortmannin indicated that the Glucostat was acting via the insulin pathway with some of its active constituents entering below the PI3K level, while some of its active constituents entered above this level as they were blocked by Wortmannin. There is a synergistic reaction when Glucostat and Boiled Glucostat was added with Metformin to the heart and liver tissue cultures, therefore they could possibly be used in conjunction with each other.

A single sheep experiment showed that Glucostat taken orally did not have any effect on glucose clearance when compared to those treated with saline; however, Glucostat given intravenously exhibited a greater clearance rate, than those treated with saline.

A small scale clinical trial suggested that Turmeric can aid in decreasing the fasting blood glucose levels (FBGL), of individuals who have a moderately high FBGL without having any effect on those with a low to normal level, and in particular, in the case of those who have an arthritic condition. Whether this is due to increasing the ability to exercise or a direct effect needs to be investigated further. The small scale clinical trial suggested that Glucostat can lower FBGL in the majority of individuals who have moderately high FBGL, including those already on antidiabetic medications, without having any effect on those with low to normal levels.

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The results from these studies suggest that Turmeric and Glucostat will increase glucose uptake in mice heart tissue and also decrease gluconeogenesis in the liver tissue. The clinical trials suggested that both the Turmeric and the Glucostat may assist in decreasing the FBGL of people with slightly elevated FBGL. Further studies will need to be carried out to determine the mechanism/s of action/s of the herbs and also the optimal dosage and routes of administration.