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Antidiabetic and Anti-inflammatory Properties of Some Selected Plant Leaves: A Transcriptomic Approach

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Author for Correspondence*: afadipe@unimed.edu.ng <https://dx.doi.org/10.4314/sokjmls.v9i4.5>**Abstract**

Transcriptomics is regarded as a high throughput technology that is concerned with determining how the transcriptome changes, based on various factors, at a certain time point and at a given biological state. This study investigated the expression levels of critical genes of interest in selected tissues of the pancreas, small intestine, kidney, and liver. In this study, male albino rats were placed on four different herbs-supplemented diets containing 30% and 70% respectively on each plant for seven days after which they were sacrificed by cervical dislocation. Tissues were collected and various gene expression assays were carried out including RNA extraction, conversion to cDNA, gene amplification, and gel electrophoresis. The results showed the genes expressed in the pancreas as Glut4, Insulin, CACNA1a and KCJN5. In the pancreas, *Mangifera indica*, *Peperomia pellucida* and *Momordica foetida* expressed insulin and KCJN5 genes in significant measures, (upregulated). In the small intestine, GLP-1 and GLUT-2 were expressed in all groups however at higher concentrations, except for *P. pellucida* which was expressed at low concentration (30%). In the kidney, the TNF-alpha gene was downregulated by all the extracts, while interleukin (IL1-alpha) was upregulated. In the liver, PFK1 and G6pD genes were expressed by all the extracts. It was observed that there is modulation of gene and transcriptomic alterations when normal rats were exposed to these selected herbs, with *M. indica*, *P. pellucida* and *M. foetida* showing to be less toxic, more promising, and effective in genes expressed in diabetic management. This study therefore might offer a key to unlocking new therapeutic targets for the treatment of diabetes and inflammation.

Keywords: Transcriptomic, Inflammation, Upregulated, Downregulated.**Introduction**

Transcriptomic is an unbiased, sensitive, and personalized approach with the potential to reveal new predictive biomarkers of disease and ultimately improve the decision-making process in the assessment of biological activities of medicinal herbs or drug (Sandvik *et al.*, 2006). When performed in a dose response format, the observed transcriptional changes can provide both quantitative and qualitative information on the dose of the administered agent at which cellular processes are affected. Transcriptomic approaches have transformed the way in which physicians approach diagnosis, prognosis, and treatment, and in which regulators approach risk assessment (Heidecker *et al.*, 2008).

The transcriptome includes the total complement of messenger RNA (mRNA) molecules (also called transcripts) produced in a specific cell or the population of cells comprising a tissue (Heidecker *et al.*, 2008). A number of essential biological processes, including development, differentiation, and Transcriptomic is regarded as a high throughput technology concerned with determining how the transcriptome changes with respect to various factors at a certain time point and at a given biological state. Disease pathogenesis are governed by the very complicated regulation of gene expression. This regulation exhibits enormous heterogeneity in various tissues and in response to stimuli (Sandvik *et al.*, 2006). Transcriptomic and global gene expression are powerful tools used in the field of

toxicology and, as in most cases; toxicity is not expected to occur without alterations at the transcriptional level (Gibbs *et al.*, 2011). A common application of transcriptomic in toxicology is to compare gene expression after a chemical exposure from a diseased and non-diseased tissue to provide a list of genes that show altered expression in the diseased group. These discoveries not only improve our understanding of disease pathophysiology, but they also identify transcripts that may serve as novel biomarkers that may be evaluated qualitatively or quantitatively (Gibbs *et al.*, 2011).

Glucose uptake and storage in peripheral tissues such as skeletal muscles and adipose tissue is a major regulatory process in the homeostatic control of blood glucose levels. Glucose uptake is mediated through the translocation of the Glut4 receptor from the interior to the cell surface which is stimulated by the insulin signaling pathway initiated by activation of the insulin receptor. Any defect in this pathway triggers the development of hyperglycaemia in type II diabetes. Thus, measurement of glucose uptake into peripheral tissues is an important mechanism to assess insulin sensitivity (Turban *et al.*, 2005). GLUT4 is stored in the cell in transport vesicles, and is quickly incorporated into the plasma membrane of the cell when insulin binds to membrane receptors. According to Ilyin *et al.* (2004), a biomarker is an attribute that may be objectively tested and assessed as an indicator of typical biologic processes, pathologic processes, or pharmacologic reactions to a therapeutic intervention. Although it is simple to understand a single biomarker, transcriptome studies have demonstrated that aggregate measures made up of numerous genes are equally useful as biomarkers of complicated disease. *GLUT4*, also known as solute carrier family 2, is a protein encoded, in humans, by the *SLC2A4* gene. As glucose levels increase, insulin is released from the pancreas and into the blood stream. Increased insulin levels cause the uptake of glucose into the cells (Gogte, 2000). In addition to being engaged in a number of calcium-dependent processes, such as muscular contraction, hormone or neurotransmitter release, and gene expression, calcium voltage-gated channel subunit alpha1 A (CACNA1-) mediates the entry of calcium ions into excitable cells.

It was reported that, although not as high as the expression by the brain, stomach or testis, the pancreas produced a significant level of CACNA1- α . Potassium channels are the most prevalent type of ion channel and are present in almost all living things (Littleton and Ganetzky, 2000). They form potassium-selective pores that span cell membranes, are present in most cell types, and control a wide range of cell functions. Potassium channels may also be involved in maintaining vascular tone. They also regulate cellular processes like the secretion of hormones (e.g. insulin) and other chemical reactions.

Glucagon like peptide (GLP) is a 30 amino acid long peptide hormone derived from the tissue-specific posttranslational processing of the proglucagon gene expressed in several organs including the gut (intestinal enteroendocrine L-cells), GLP-1 is the only known incretin describing its ability to decrease blood sugar levels in a glucose-dependent manner by enhancing the secretion of insulin. The ability of GLP-1 to stimulate insulin secretion in a glucose-dependent manner is by far the substance's most notable effect (Kristine and Catherine, 2003).

TNF-alpha is one of the cytokines that make up the acute phase reaction and is a cell signaling protein (cytokine) implicated in systemic inflammation.

This cytokine has been implicated in a variety of diseases, including autoimmune diseases, insulin resistance, and cancer (Vassali, 1992; Pfeffer, 2003). Reduced production of TNF-alpha may limit the release of acute phase mediators and thereby facilitate autoimmunity (Paul and Carroll, 1999). This suggests that mangiferin may play a role in cancer combination therapy. Mangiferin mediates the downregulation of necrosis factor kappa B (NF-B), suppresses of NF-B activation induced by inflammatory agents, including tumor necrosis factor (TNF), increases the intracellular glutathione (GSH) levels, and potentiates chemotherapeutic agent-mediated cell death. Increased intracellular (GSH) levels are known to suppress the TNF-induced activation of NF-B (Vassali, 1992; Paul and Carroll, 1999; Pfeffer,

2003). A member of the interleukin 1 family of cytokines is interleukin 1 alpha. According to Nicklin *et al.* (1994), interleukin 1 is in charge of causing inflammation and promoting fever and sepsis. To stop those processes and treat disorders, IL-1 inhibitors are being created. Only when stimulated, a wide range of different cells can be made to transcribe IL-1 genes and create IL-1 precursors (Fieldmann and Saklatvala, 2001). Although IL-alpha interacts with other cytokines in a variety of ways, its synergism with TNF is the most reliable and clinically significant (Dinarelo, 2001). One of the most crucial glycolysis regulating enzymes is phosphofructokinase-1 (PFK-1), which catalyzes the conversion of fructose 6-phosphate and ATP to fructose 1, 6-bisphosphate and ADP. According to a paper by Usenik (2010), the liver expresses the PFK-1 L isoform. Glycolysis and gluconeogenesis cannot occur simultaneously due to the tight regulation of PFK1 (Usenik, 2010). The enzyme responsible for catalyzing the last stage of glycolysis is called pyruvate kinase. The liver contains one of this enzyme's isozymes (Gupta and Bamezai, 2010). As a regulatory enzyme, pyruvate kinase controls the biochemical process known as gluconeogenesis, in which the liver produces glucose from pyruvate and other substrates (Berg *et al.*, 2002)

Omics, such as functional genomics, transcriptomics and proteomics, can be applied to study the gene/protein functions of medicinal herbs and to evaluate the herb/host interactions.

Materials and Methods

Collection and Identification of plant materials:

Fresh leaves of the following four selected plants were used for this study: Mango (*Mangifera indica*), mistletoe (*Tapinanthus bangwensi*) from cocoa plant, giant bitter lemon cucumber (*Momordica foetida*) and Sliver bush (*Peperomia pellucida*). They were harvested from different locations in Akure and Akungba-Akoko, Ondo State, Nigeria as reported by Fadipe and Saliu, 2021.

Sample Preparation

The leaves of *M. indica*, *T. bangwensi* and *M. foetida* were thoroughly washed and air dried for

two months, the dried leaves were blended into fine powder using an electric blending machine (Marlex CM/L7371373) as done by Fadipe and Saliu (2021). While that of *Peperomia pellucida* were freeze dried (Lyophilized) using a Lyophilizer. 30%weight/weight (30g leaf extract and 70g growers mash) and 70%weight/weight (70g leaf extract and 30g growers mash) weight ratios were used to measure the ground plant components. Grower's mash made up the entire control group. Using a graduated cylinder, 100ml of honey was added to 100g of grower's mash and weighed powdered extract. The honey and powdered leaf extracts were well combined. This is done to make it easier for the rats to consume the extracts, especially the bitter ones like those from *M. foetida*, or bitter gourd.

Ethical approval:

All procedures were examined and approved by the ethics committee (I R B) of Faculty of Science of Adekunle Ajasin University, Akungba-Akoko.

Animal Treatment:

Twenty albino rats in all were employed, divided into five groups of four each. The control group is in the fifth group. The animals were weighed before the experiment and stabilized for seven days by being given water and grower's mash made by Guinea Feed Nigeria Limited. Rats were fed various weights of the produced extract for six days, after which they underwent a 12-hour overnight fast. The control group was given clean water and just growers' mash as food. Vital organs such as the liver, kidney, small intestine, and pancreas were taken out of the rats on the seventh day and processed for genetic expression.

Gene expression

Prior to the polymerization reaction, the maps of the organs were prepared and placed in the PCR machine (Multigene Optimax) developed by Labnet International Inc.

RNA isolation

Each animal's tissue was homogenized after being removed and placed in Eppendorf tubes with 50 μ l of Trizol reagent. The homogenates were mixed with 100 μ l of gradient separation media (chloroform), vortexed for 30 min at 1500

rpm, and the supernatant, which contains the RNA, was aspirated into fresh, labeled tubes. The supernatant was combined with 100µl of the precipitating medium (isoamyl alcohol) and vortexed for 30 min at 1500 rpm to recover the RNA as pellets. The supernatant was then decanted. 50 micro liters of 70 percent ethanol were added, centrifuged at 15,000 rpm for 5 minutes, and the supernatant was then decanted with the top left off to let the ethanol escape. To the total RNA extracted from tissues, 50µl of nuclease-free water were added. All samples were diluted to the same quantity before being used, and the concentration of total RNA was quantified using UV absorbance spectrophotometry (JENWAY 6305) for RNA (mRNA) quantification.

Reverse transcription:

The random oligo primer, dNTPs, reverse transcriptase, reverse transcriptase buffer, and nuclease-free water were added to a cocktail of 2µl of reverse transcriptase to start the reverse transcription process.

Twenty microliters (20µl) of total RNA from all the samples were mixed with 2µl of reverse transcriptase to create complementary DNA (cDNA). The sample is then incubated for 4 hours at 65 degrees Celsius in a total reaction volume of 22 µl for the conversion in the thermocycler.

Polymerase Chain Reaction (PCR):

Five microliters (5µl) of the synthesized cDNA was aliquoted into a primer-specific PCR cocktail after being diluted in nuclease-free water. A total of 5.0 microliters of PCR reaction mixture made up of 2 microliters of PCR master mix, 2micro liters of forward and reverse primers (Inqaba Biotech, South Africa), and 5 microliters of cDNA template. Each example animal's basal gene expression was monitored using a -actin-specific primer. Utilizing a Multigen Optimax PCR machine, the PCR was conducted. Each cycle of the PCR amplification process involved denaturation, annealing, and extension. Amplification conditions were: 94°C pre-denaturation for 5mins, 94°C for 30sec, Annealing 55°C (T_m) for 30 seconds and Extension 72°C for 30 secs and then 5 min at 72°C by 30 cycles.

Agarose Gel Electrophoresis:

PCR amplicons were submitted for densitometric run in agarose gel electrophoresis. Briefly, 0.5X agarose was prepared in 50ml TBE-buffer. Under buffered conditions, gel was allowed to solidify at room temperature. 5µL PCR amplicons together with 5µL DNA loading buffer was loaded into pre-formed wells. Snapshots revealing the relative density of DNA bands were taken under UV-gel documentation. The metrics of average band density after 15 minutes of buffered run were analyzed with ImageJ (NIH).

Statistical Analysis: The band densities of the gene expression were quantified and subjected to analysis of variance, using ordinary one-way ANOVA at 95% level of significance using GraphPad Prism 7.

Results

Transcriptomic alterations that occurred on culinary exposure of normal albino rats to leaves of mistletoe (*Tapinanthus bangwensi*), mango plant (*Mangifera indica*), silver bush (*Peperomia pellucida*) and large bitter melon (*Momordica foetida*).

GLUT4 was not expressed in the pancreas by any of the extract compared to the control. Insulin was significantly expressed by 70% *M. indica*, 70% *P. pellucida* and 70% *M. foetida* compared to the control, (p>0.05). CACNA1-alpha was significantly expressed by 30% *P. pellucida* compared to the control. KCJN5 was expressed by 70% *T. bangwensi* compared to the control. In the pancreas of the normal rats GLUT-4 was down regulated by all the extract, KCJN5 was up regulated by 70% extract of *T. bangwensi* only (Figures 1, 2, and 3).

The insulin gene was up regulated by a higher dose of *M. indica*, *M. foetida*, and a lower dose of *P. pellucida* (Figure 4).

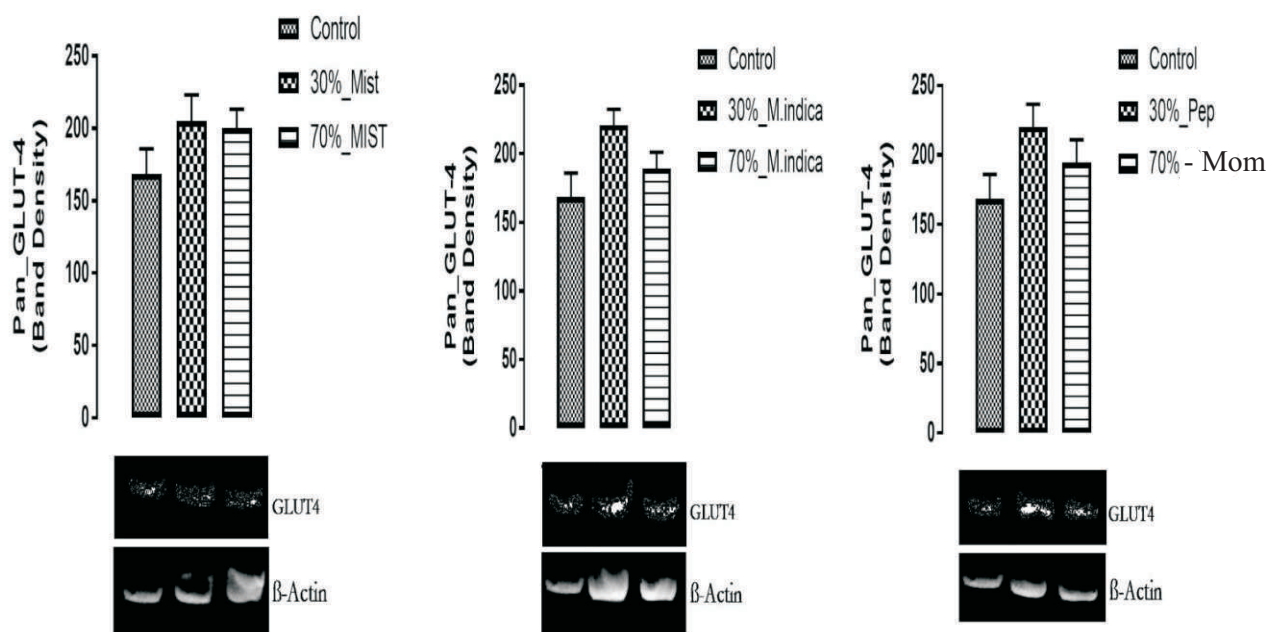
GLP-1 was expressed in the small intestine by 70% *T. bangwensi*, 70% *M. indica*, 30% *P. pellucida*, and 70% *M. foetida* compared to control, (p>0.05). GLUT-2 was expressed significantly by 70% *T. bangwensi*, 30% and 70% *M. indica*, 30% *P. pellucida* and 70% *M. foetida* compared to the control. In the small

intestine GLP-1 and GLUT-2 genes were up regulated by *T. bangwensi*, *M. indica*, *M. foetida*, and *P. pellucida* (Figure 5 and 6).

TNF- α was down regulated in the kidney by all the extracts. IL-1-alpha was significantly expressed by all the extract compared to the control, ($p > 0.05$). PFK-1 was expressed significantly by 70% *T. bangwensi*, 30% and 70% *M. indica*, 30% *P. pellucida* and 70% *M. foetida* compared to the control (Figures 7, 8, and 9).

G6PD was significantly expressed in the liver by 30% and 70% *T. bangwensi*, 30% and 70% *M.*

indica, 30% *P. pellucida* and 70% *M. foetida* compared to the control, ($p > 0.05$). GLUT-4 was significantly expressed in the liver by 30% and 70% mistletoe, 70% *M. indica* and 30% *P. pellucida* compared to the control. Pyr-kinase was significantly expressed by 30% and 70% *T. bangwensi*, *M. indica*, *P. pellucida* and *M. foetida* respectively compared to control ($p > 0.05$). In the liver, glucose-6-phosphate dehydrogenase (G6PD), glucose transporter-4 (GLUT-4) and pyruvate kinase were upregulated by *T. bangwensi*, *M. indica*, *P. pellucida* and *M. foetida*. (Figures 10, 11 and 12).



Key: Mist= Mistletoe (*Tapinanthus bangwensi*), **M. indica**= Mango (*Mangifera indica*), **Pep**= *Peperomia pellucida*, **Mom**= *Momordica foetida*. (NB: Applies to Figures.1 -12)

Figure 1: The effects of plant extracts on the expression of Glucose transporter-4 (GLUT-4) gene on the pancreas of rats.

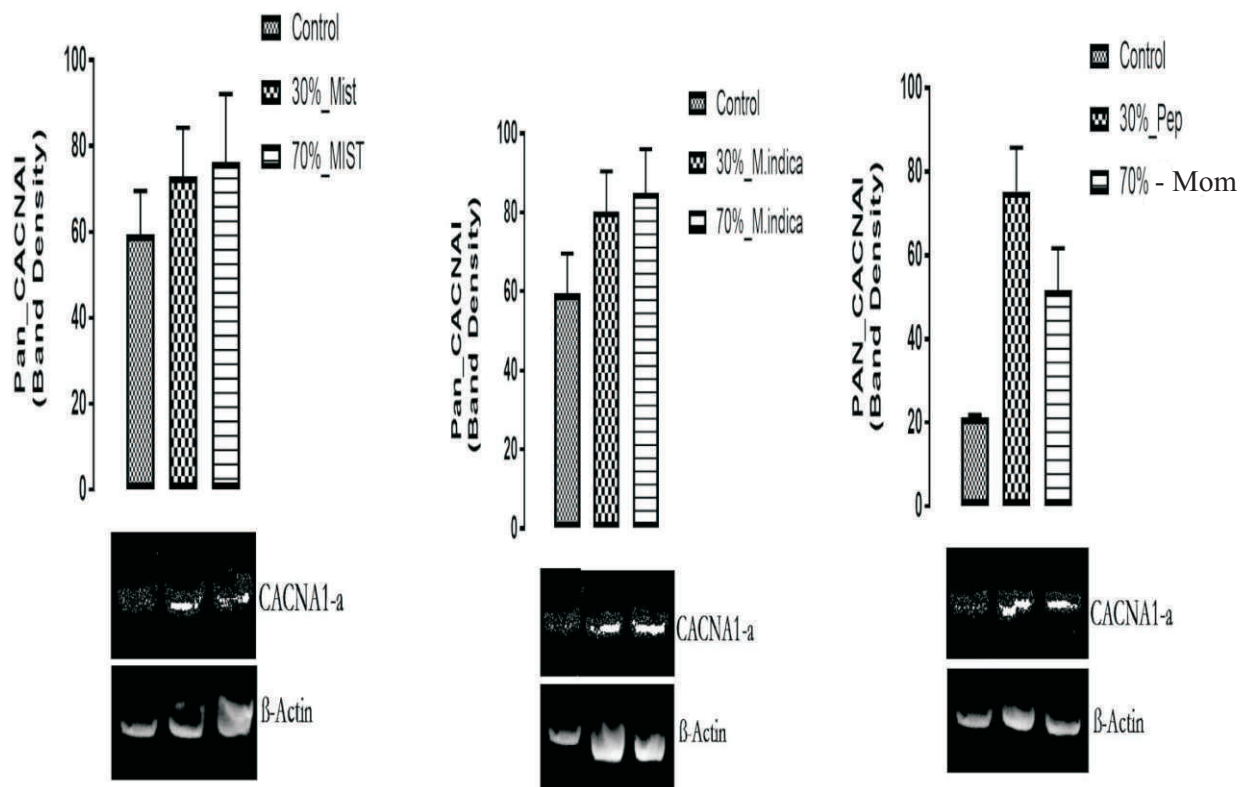


Figure 2: The effects of plant extracts on the expression of calcium channel voltage-gated 1alpha (CACNA1-a) gene on the pancreas of rats.

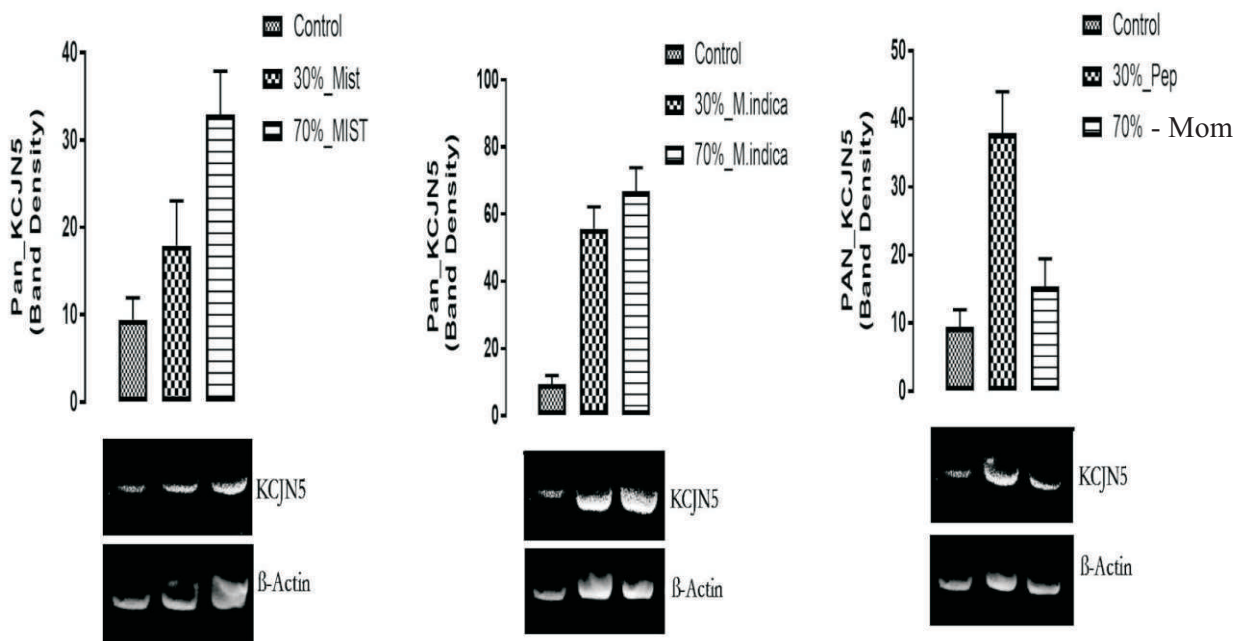


Figure 3: The effects of plant extracts on the expression of potassium channel on the pancreas of albino rats.

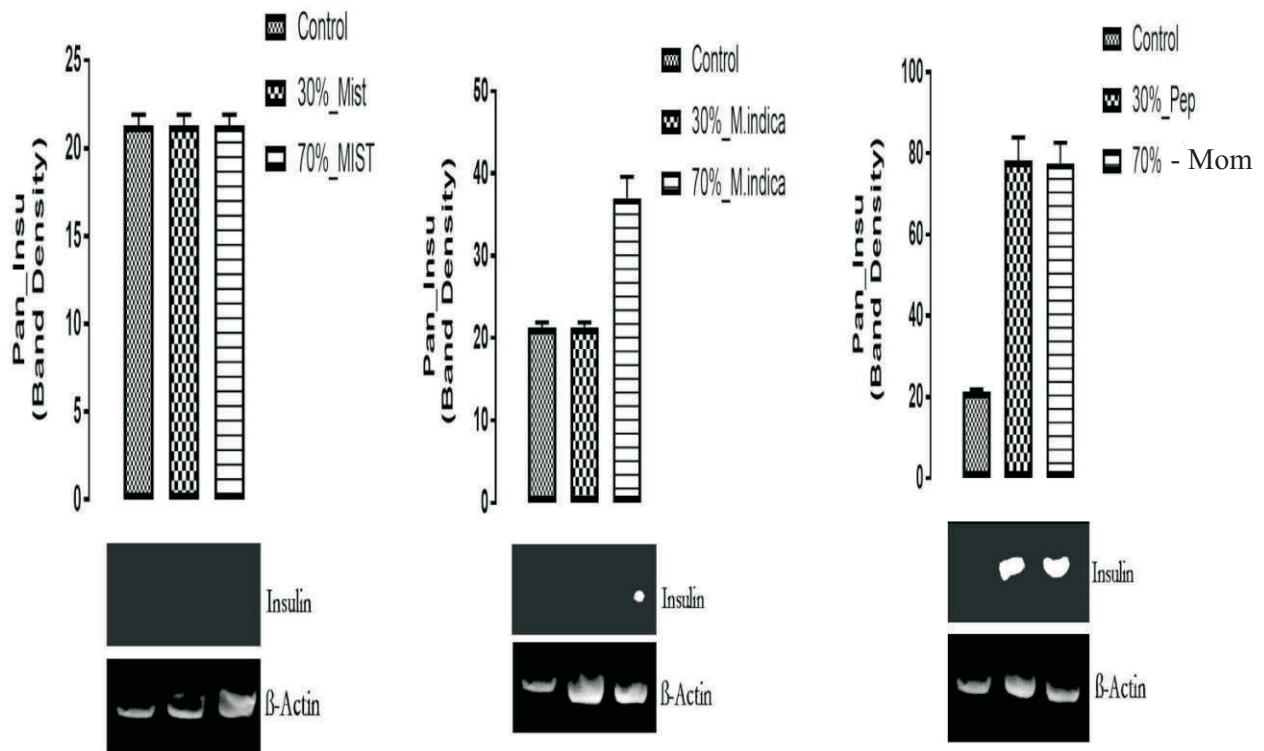


Figure 4: The effects of plant extracts on the expression of Insulin gene on the pancreas of albino rats.

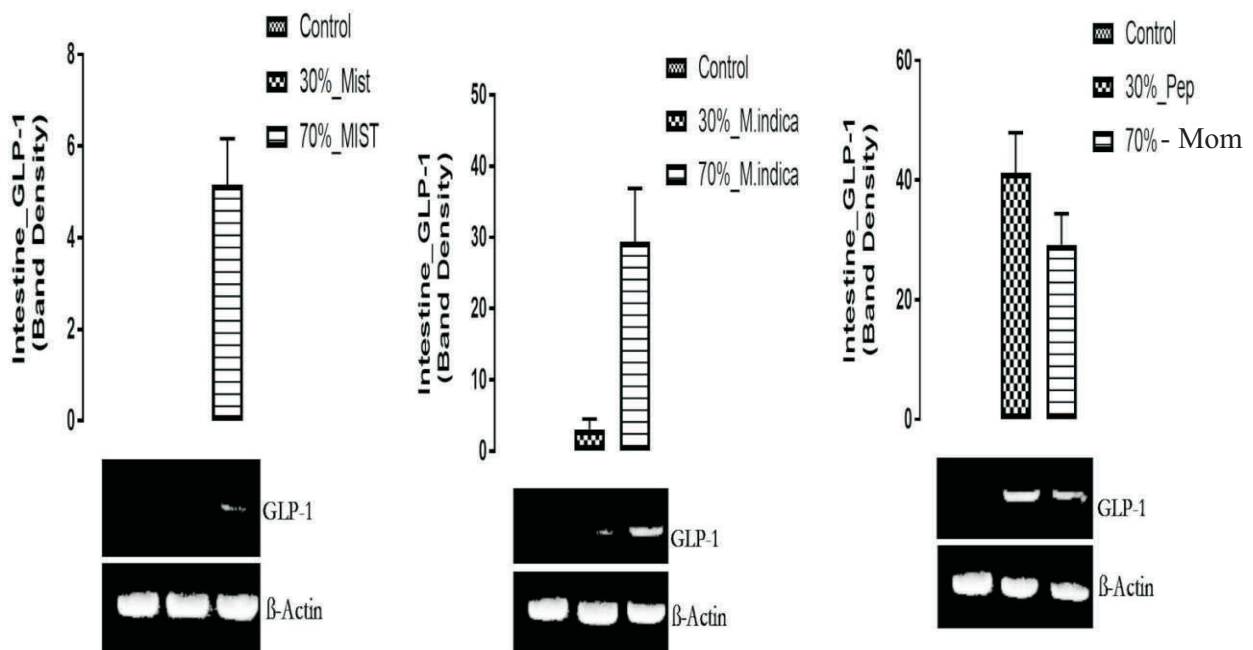


Figure 5: The effects of plant extracts on glucagon-like peptide (GLP) gene on the small intestine of albino rats.

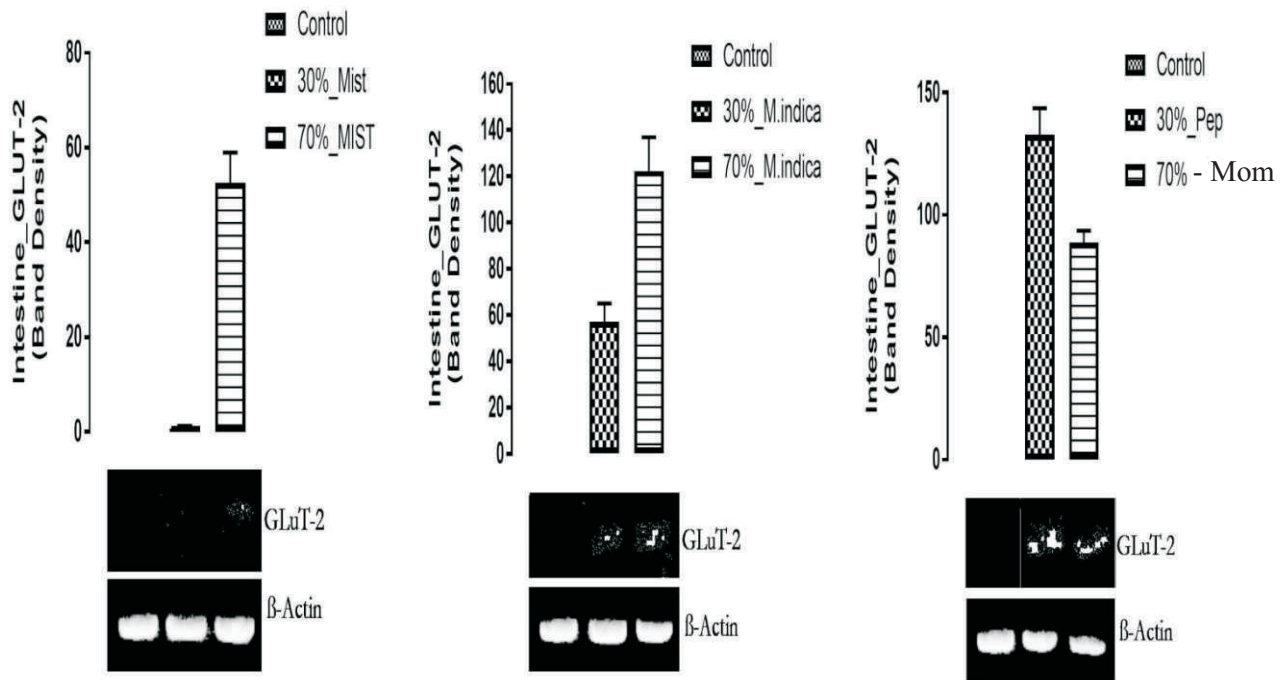


Figure 6: The effect of plant extracts on the expression of glucose transporter 2(GLUT-2) gene in the small intestine of albino rats.

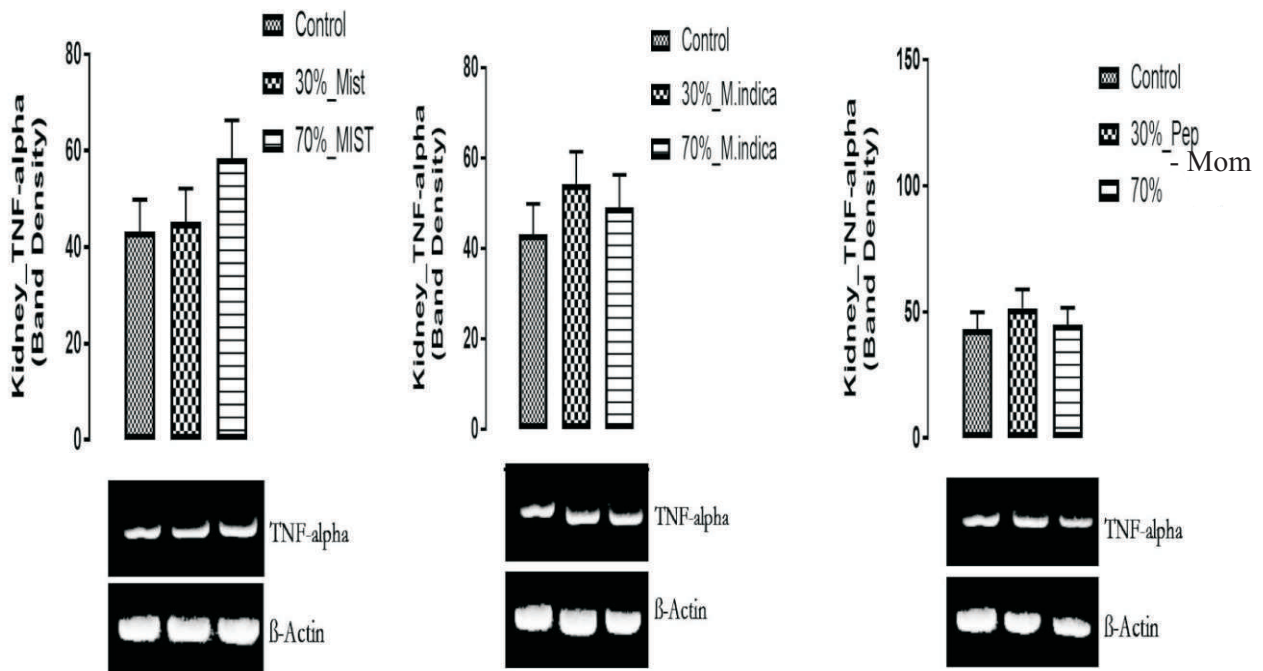


Figure 7: The effects of plant extracts on the expression of tumour necrosis factor- α (TNF- α) gene in the kidney of albino rats.

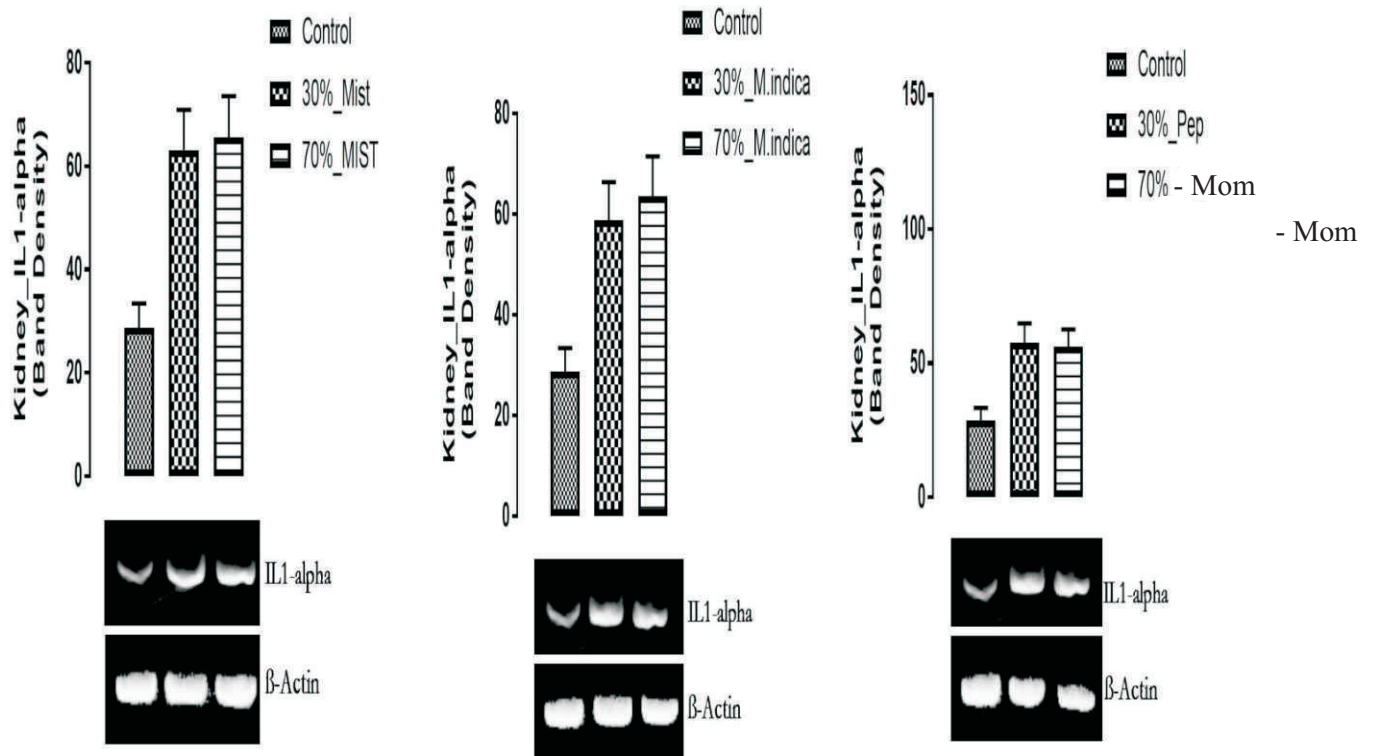


Figure 8: The effects of plant extracts on the expression of interleukin-1α (IL-1α) gene on the kidney of albino rats.

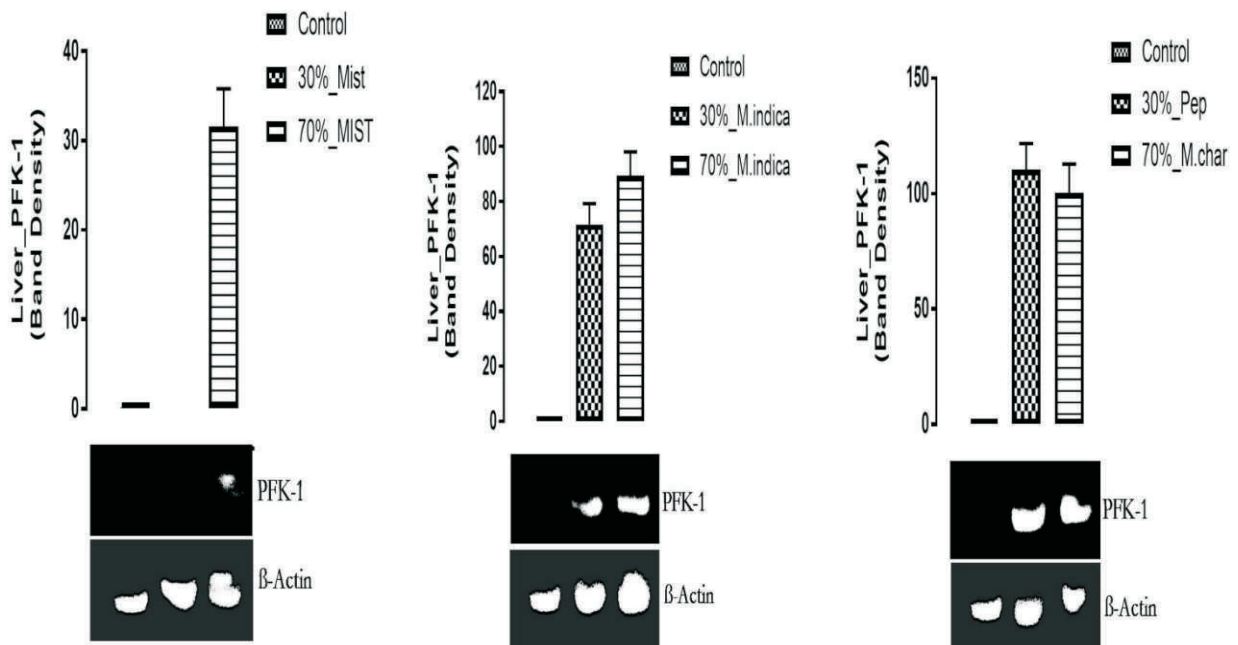


Figure 9: The effects of plant extract on the expression of phosphor-fructo-kinase gene on the liver of albino rats.

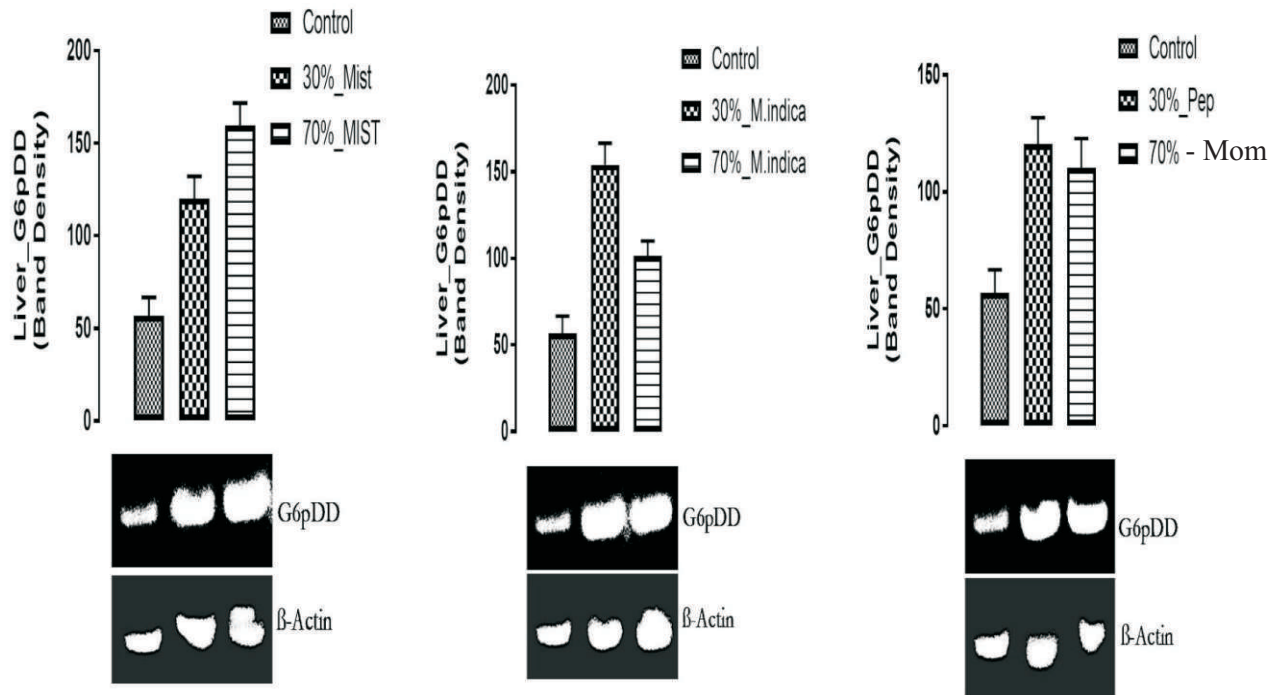


Figure 10: The effects of plant extracts on the expression of Glucose-6-phosphate dehydrogenase gene on the liver of albino rats.

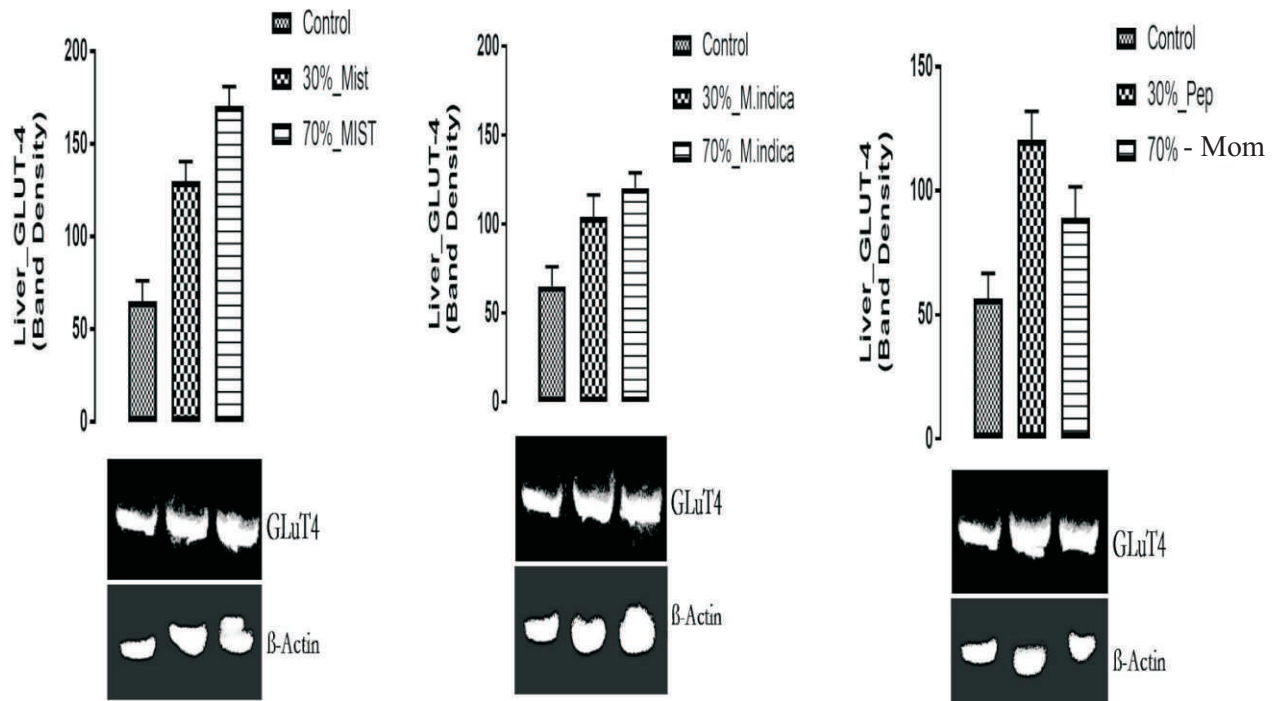


Figure 11: The effects of plant extracts on the expression of glucose transporter- 4- (GLUT-4) gene on the liver of albino rats.

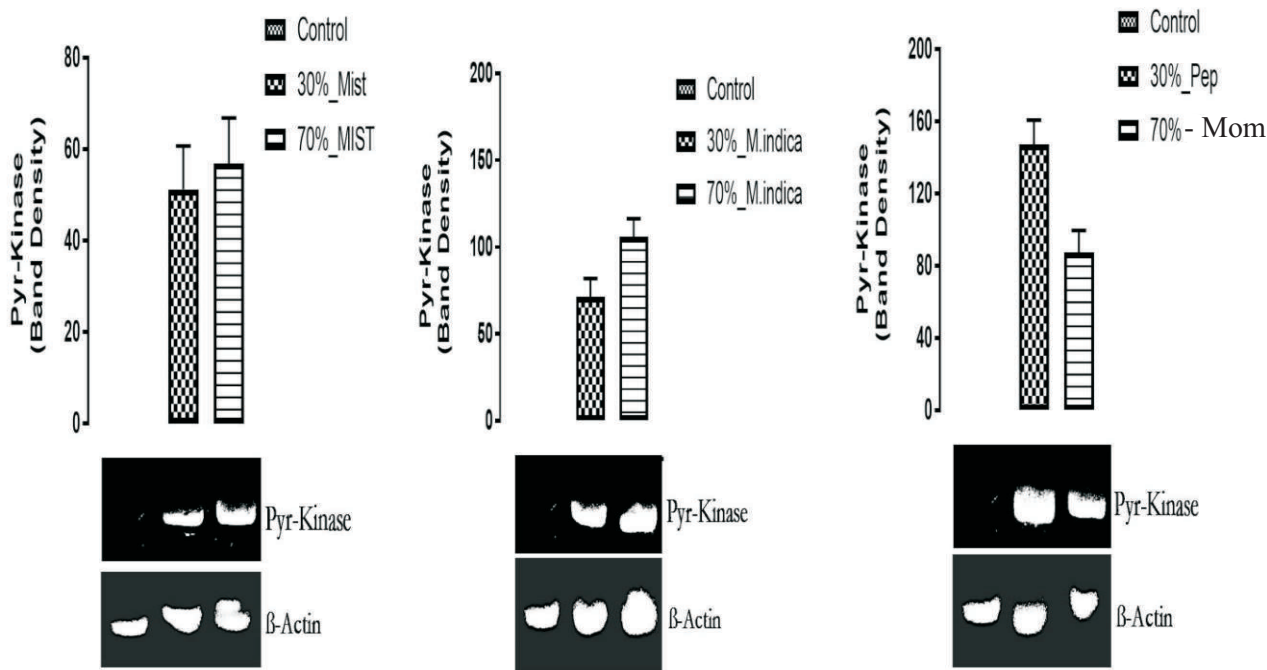


Figure 12: The effects plant extracts on the expression of pyruvate kinase gene in the liver of albino rats.

Discussion

Insulin is produced by the β -cells of the pancreatic islets which are sensitive to glucose concentrations such that when there is rise in the blood glucose, the beta cells secrete insulin into the blood and activate several glucose uptake routes to mop up excessive glucose from the blood to their target tissues as metabolic fuel; when glucose levels is low at the normal threshold, secretion of insulin is inhibited. In this study insulin production was upregulated by *M. indica*, *P. pellucida* and *M. foetida*. This may be as a result of the normal insulin production from the islets of Langerhans for the sake of glucose homeostasis. This is in line with the work done by Gray and Flatt (1999) that *T. bangwensi* had no effect on insulin levels or even on glucose levels to trigger the expression of insulin. *M. indica* at a higher dose of 70% was able to trigger an increase. Up regulation of insulin by *M. indica* extract may be due to the hypothesis that *M. indica* has hypoglycemic effect at sufficient doses resulting from the stimulation of beta cells to release insulin (Sharma *et al.*, 1997; Aderibigbe *et al.*, 2001). The dose at 30% can be said to have been insufficient to help alleviate hyperglycaemia if there was any. The increased production of

insulin from the beta cells of the pancreatic islets in response to both doses of *P. pellucida* and *M. foetida* may be as a result of the anti-diabetic effects of these herbs which may be due to the stimulation of β -cells to release insulin (Sharma *et al.*, 1997), it may also be due to an intestinal reduction of the absorption of glucose (Aderibigbe *et al.*, 2001). But majorly the different chemical constituents of the plant, especially the saponin, flavonoids alkaloids and other chemical compounds present in the plant may be involved in the observed hypoglycemic effects of the plants extract (Sheik *et al.*, 2013).

In addition to mediating the entry of calcium ions into excitable cells, calcium voltage-gated channel subunit alpha1-a (CACNA1-a) is also engaged in a number of calcium-dependent processes, such as muscle contraction, hormone or neurotransmitter release, and gene expression.

It was reported that, although not as high as the expression by the brain, stomach or testis, the pancreas produced a significant level of CACNA1-a (Mojiminiyi *et al.*, 2008). An increase in the concentration of free intracellular Ca^{2+} turns on the contractile mechanism in smooth muscle. The source of calcium (Ca^{2+}) is the extracellular fluid or release from internal pools. Thus, vascular smooth muscle relaxant

agents may produce their effects by inhibiting either or both sources of Ca^{2+} (Mojiminiyi *et al.*, 2008). In this study there was a down regulation of CACNA-1 in all experimental groups except *P. pellucida* compared to the control group. This is an indication that these extracts except *P. pellucida* had possible calcium antagonist activity which is in line with Ekpenyong, (1999) who concluded that *T. bangwensi* exhibits a nonspecific relaxant and possible calcium antagonist activity and suggested that it might also act directly on the vascular smooth muscle via calcium dependent mechanism.

There were slight and statistically significant up regulation in the expression of the gene KCJN5, a potassium inwardly rectifying channel. It was up regulated by *T. bangwensi* at 70%, *M. indica* at both 30% and 70%, and 30 % *P. pellucida* compared to the control.

Internal rectifier with G protein activation is a kind of G protein-gated ion channel, potassium channel 4 is a protein that is encoded by the KCNJ5 gene in humans. Most mammalian cells include potassium channels, which are involved in a variety of physiologic reactions. Since their dysfunction can result in diseases (like diabetes), they also govern cellular processes including the release of hormones (for example, insulin release from beta-cells in the pancreas) (Rang 2003). It suggests that having the KCNJ5 gene may prevent insulin from being produced too much or too little, hence preventing hyperglycemia and hypoglycemia.

There was a significant expression of GLP-1 in the small intestine of the animals fed with *T. bangwensi*, *M. indica*, *P. pellucida*, and *M. foetida* compared to the control. It has been reported that GLP-1 is a 30 amino acid long peptide hormone derived from the tissue-specific posttranslational processing of the proglucagon gene expressed in several organs including the gut (intestinal entero-endocrine L-cells) (Kristine and Catherine, 2003). Along with GIP, GLP-1 is the only known incretin that has been shown to lower blood sugar levels in a glucose-dependent way by increasing insulin production (Kristine and Catherine, 2003).

P. pellucida, which up-regulated insulin levels in

the pancreas as seen in this study, also upregulated GLP-1 levels. It can be inferred that the plant may be a potent incretin-mimetic in the enhancement of insulin secretion.

This study also revealed the expression of glucose transporter-2 (GLUT-2), there was a significant expression of GLUT-2 in the small intestine of the animals fed with higher concentration of the extracts compared to the control group, disagreeing therefore with past works done by Thorens, (2015).

TNF-alpha was down regulated in all the groups compared to the control. TNF-alpha is one of the cytokines that make up the acute phase reaction and is a cell signaling protein (cytokine) implicated in systemic inflammation. This cytokine has been implicated in a variety of diseases, including autoimmune diseases, insulin resistance, and cancer (Pfeffer, 2003). Mangiferin, a phytochemical present in *M. indica*, mediates the downregulation of $\text{NF-}\kappa\text{B}$, suppresses $\text{NF-}\kappa\text{B}$ activation induced by inflammatory agents, including tumor nuclear factor (TNF), increases the intracellular glutathione (GSH) levels and potentiates chemotherapeutic agent-mediated cell death; this suggests a possible role in combination therapy for cancer. It is likely that these effects are mediated through mangiferin ROS quenching and GSH rising; increased intracellular (GSH) levels are indeed known to inhibit the TNF-induced activation of $\text{NF-}\kappa\text{B}$. This result suggests that these selected herbs may have anti-inflammatory and anti-toxicity properties (Vassali, 1992; Paul and Carroll, 1999; Pfeffer, 2003).

Interleukin1- α (IL-1 α), was expressed significantly in this present work. Interleukin 1 alpha is a cytokine of the interleukin 1 family. In general, interleukin 1 is responsible for the production of inflammation, as well as the promotion of fever and sepsis. To stop those processes and treat disorders, IL-1 inhibitors are being created. Thus IL-1 α appears to be expressed at low levels in some organs under steady state conditions, while some may express IL-1 α during stress (Moshe *et al.*, 2002).

PFK in the liver was upregulated by *T. bangwensi*, *M. indica*, *P. pellucida* and *M. foetida*. Since PFK-1 is one of the most important regulatory enzymes of glycolysis, its up-regulation is not far-fetched from the facts that *T. bangwensi*, *M. indica*, *P. pellucida* and *M. foetida* expressed insulin gene and therefore may be needed for the conversion of glucose to pyruvate to prevent hypoglycaemia (Usenik *et al.*, 2010).

This study showed that G6pD was significantly expressed in all the experimental groups compared to the control. The result of this study may be because of the presence of some phytochemicals in these extracts that have antioxidant properties. This is in contrast to the work done by Agbafor, (2015) on leaf extract of *Sennahirsuta* that lowered the production of this enzyme in the rats used. The insulin-regulated glucose transporter known as glucose transporter type 4 (GLUT-4) is typically present in adipose tissues and striated muscle (skeletal and cardiac muscle).

Although it has been reported that Glut-4 is not expressed in liver cells, there was a significant expression of Glut-4 in the liver cells of the rats fed with *T. bangwensi*, *M. indica* and *P. pellucida* this agrees with result from a study on expression of GLUT-4 mRNA, (Aschenbach *et al.*, 2009)

Conclusion

It can be concluded from this research work that these selected herbs (*M. indica*, *P. pellucida*, *T. bangwensi* and *M. foetida*), were observed to cause some transcriptomics alterations when administered orally to laboratory rats.

- Extracts of *M. indica*, *P. pellucida* and *M. foetida* up regulated the expression of insulin gene, glucose transporter-4- and glucagon-like peptides gene which are involved in glucose metabolism. It can therefore be said that these extracts have anti diabetic agents.
- All the extracts *M. indica*, *P. pellucida*, *T. bangwensi* and *M. foetida* have the ability to alleviate inflammation due to the down regulation of tumour necrosis factor which is one of the cytokines responsible for acute phase reaction i.e. anti-inflammatory ability.
- All the extracts are observed to be non-toxic by the down-regulation of TNF- α gene, except for *T. bangwensi* that is known to be cytotoxic on

cancerous cells. Some of these observations have justified the traditional claims or use of these herbs for medicinal purposes.

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