Effect of Sulphonylurea Derivatives and Short Chain Fatty Acids on Expression of Incretins Hormone in living Animal Cells

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ABSTRACT

Dietary fibres are a type of carbohydrates that are found in plant-based foods. They are not absorbed or digested by the body but play an important role in maintaining good health. Short-chain fatty acids (SCFAs), primarily acetate, propionate, and butyrate, are metabolites formed by gut microbiota from these complex dietary carbohydrates. The formed acids have a role in the secretion of hormones such as glucagon-like peptide-1 (GLP-1) and glucose-dependent insulin tropic polypeptide (GIP) that help the body to control diabetes. Diabetes mellitus is a chronic disease that occurs when the pancreas fails to produce enough insulin, or when the body cannot use it effectively. The hormones GLP-1 and GIP, which secreted after a meal, like other enteroendocrine hormones help to orchestrate the body's response to the availability of newly absorbable nutrients and are noteworthy, stimulate postprandial insulin secretion. This study clarifies the effects and the roles of organic compounds such as Short Chain Fatty Acids (SCFAs) and sulphonylurea derivatives on body glucose homeostasis and clarifies the effects of both SCFAs and sulphonylurea on incretin expression by investigating the expression of GLP-1 and GIP hormones in tissues and blood samples.

Keywords: Microbiota, Enteroendocrine hormones, Sulphonylurea derivatives, glucagon-like peptide-1 (GLP-1).

INTRODUCTION

Diabetes Mellitus is becoming the fast prevalence disease, approaching epidemic ratio, all over the world. The International Diabetes Federation (IDF) listed Egypt among the world top 10 countries in the number of patients with diabetes. It is expected that the number of patients with diabetes in the Middle East and North Africa (MENA) region to grow by 96% from year 2013 to 2035 or from 34.6 million to 67.9 million. In Egypt, the prevalence of diabetes is around 15.56% among adults between 20 and 79 years of age, with an annual death of 86,478 related to diabetes. In 2013, the IDF estimated that 7.5 million individuals have diabetes and around 2.2 million have pre-diabetes in Egypt. Furthermore, reports indicate that 43% of patients with diabetes and most patients with pre-diabetes in Egypt are likely undiagnosed. It is alarming that diabetes prevalence in Egypt has increased rapidly within a relatively short period from approximately 4.4 million in 2007 to 7.5 million in 2013. It is expected this number will jump up to 13.1 million by 2035 (IDF, 2013). By micro biota in the colon and the distal small intestine Short Chain Fatty Acids (SCFAs) are produced from dietary fiber, resistant starch and other low-digestible polysaccharides in a fermentation process (Kaual et al., 2011).

There are very important role of SCFAs in regulation of gut hormones. Endocrine cells in the gastrointestinal tract (named enteroendocrine cells) secrete a range of hormones that regulate glucose homeostasis, gut motility, epithelial proliferation, appetite and adiposity. Two gut peptides, glucagon dependent insulin tropic polypeptide (GIP, formerly known as gastric inhibitory polypeptide) and glucagon like peptide 1 (GLP-1), are widely recognized for their role as incretions, and under lie the augmentation of insulin secretion that is observed when glucose is administered orally rather effect has been estimated to account for 50–70% of total postprandial insulin secretion (Holst, 2007). Although it primarily considered as a response to oral glucose, it may also play a physiological role following lipid ingestion (Lindgren et al., 2011).

Sulphonylureas derivatives are used for the treatment of type 2 diabetes. Glimepiride is one of the third generation sulphonylurea drug having a poor aqueous solubility, slow dissolution rate and low elimination half-life (2-3hrs) (Davis, 2004). Glimepiride has a number of advantages over other members of sulph-onylurea, currently used as lower dosages, fast onset of action and lower C-peptide level of insulin, this is because of less secretion of insulin and more prony-ounced extra pancreatic effects (Ammar et al., 2006). The acting mechanism of glimepiride is binding to the specific site on pancreatic β-cells and blocks the ATP-Dependent potassium channels to stimulate the insulin release. Due to the short elimination half-life, frequent dosing is required which leads to the adverse effects such as headache and gastrointestinal disorders (Mrillerg et al., 1994). Therefore, this study was carried out to investigate the effect of sulphonylurea derive-atives and SCFAs on the expression of incretions hormone.

MATERIALS AND METHOD

This study was carried out in Chemistry Department, Faculty of Science Suez Canal University and Scientific & medical Research Center (Molecular Biology Unit), Zagazig University. This study was done from November 2017 until March 2018.

Experimental animals

Fifty young adult healthy male albino rats, weighed between 150 and 200 g, were used in this study. The rats obtained from the El-Nile pharmaceutical and Chemical Industries Company, Cairo, Egypt. They
were maintained on standard pellet diet and tap water. The animals were housed in suitable cages in conditioned atmosphere (22-25°C). The experiment was accomplished in accordance to the internationally accepted standard ethical guidelines for laboratory animal use.

Dosages for treatment

Four different treatments were carried out in which two different concentrations of either SCFAs or glimepiride were prepared. For SCFAs, a mixture of 500 ml of propionic acid (35mmol/l) and 500ml of butyric acid (20mmol/l) was used and named A. However, the second concentration, B, of SCFAs was a mixture of 500 ml of propionic acid and 500 ml of butyric acid with concentration of 50mmol and 30mmol/l, respectively. For glimepiride, two different solutions were prepared in which 0.150 and 0.075 mg of glimepiride were separately dissolved in 10 ml sterile distilled water and left overnight. The preparation of glimepiride was carried out by melting the desired amount of glimepiride (mg) in 10 ml distill water and left overnight. Dosage was prepared for 21 days by melting 15.75 mg of glimepiride in 210 ml of distill water.

The Experimental design

Rats were randomly divided into 5 groups with 10 rats each. The groups were as follow: Group1, no dose was given (control group). Group2, in this group 3ml (1.5ml every 12hours) were injected daily, for each rat, with stock solution A that prepared from a mixture of 500ml of propionic acid (35mmol/l) and 500 ml of butyric acid (20mmol/l). Group3, the rats were separately injected daily with 3ml (1.5ml every 12 hours) of higher concentration of SCFAs. The injected solution contained propionic (50mmol/l) and butyric acids (30mmol/l). Group 4, in this group each rat was injected with 1 ml per day with stock solution prepared from 0.150 mg of glimepiride. Group5, each rat in this group was injected separately with 1 ml, per day, of stock solution contained 0.075 mg of glimepiride.

All groups were given their own dose for three weeks and kept under healthy housed mentioned conditions. The rats were slaughtered at the end of the examined period. The whole experiment was carried out in animal house at Faculty of Medicine, Zagazig University.

GLP-1and GIP gene expression detection protocol

All members of this study were subjected to relative quantitative expression of GLP-1and GIP in peripheral blood and intestinal tissues by Real-time RT-PCR technique. The Analyzes were performed using Strata gene MX 3005p Real Time .This method involved extraction of mRNA, reverse transcription to cDNA then selective amplification via Real-time PCR system using DNA fluorescent dyes.

Sampling technique

(A) Blood sample

Before scarifying the treated rats, about 30μl of blood was collected from eye (veins orbital plexus), for each rat per treatment, in one sterile EDTA vacuHOLDER's tube and directly sent for analyses.

(B) Tissue sample

The rats were slaughtered and the dissected. The intestines were taken (all intestine), washed by saline solution then after placed in phosphate buffer saline (pbs). The intestines were collected for each group in sterile Falcon tube.

RNA extraction (for blood and tissue)

RNA was purified from anticoagulated peripheral blood and animal tissue samples using Easy-RED Total RNA Extraction Kit.

Total RNA isolation from blood sample

A volume of 250μl of sample was prepared in 1.5 ml microcentrifuge tube and 750 μl of easy-REDTM Total RNA Extraction Kit. For SCFAs, a mixture of 500 ml of propionic acid (35mmol/l) and 500ml of butyric acid (20mmol/l) was used and named A. However, the second concentration, B, of SCFAs was a mixture of 500 ml of propionic acid and 500 ml of butyric acid with concentration of 50mmol and 30mmol/l, respectively. For glimepiride, two different solutions were prepared in which 0.150 and 0.075 mg of glimepiride were separately dissolved in 10 ml sterile distilled water and left overnight. The preparation of glimepiride was carried out by melting the desired amount of glimepiride (mg) in 10 ml distill water and left overnight. Dosage was prepared for 21 days by melting 15.75 mg of glimepiride in 210 ml of distill water.

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Total RNA isolation from blood sample

A volume of 250μl of sample was prepared in 1.5 ml microcentrifuge tube and 750 μl of easy-REDTM Solution was added. The samples were mixed in room temperature for 15 sec by vigorously vortex and the tube was incubated at room temperature (15 ~ 30°C) for 5 min. After then, 200μl of Chloroform was added and the sample was mixed in room temperature for 15 sec by vigorously vortex. Then the tube was incubated at room temperature for 5 min. After centrifuged the tube at 13,000 rpm at (4°C) for15min, 400μl of the upper fluid was transferred to a new 1.5 ml centrifuge tube. (400μl) of isopropanol (2-propanol) was added and mixed it well by inverting the tube 4 ~ 5 times. The tube was incubated for 10 min at room temperature. After centrifuged the tube at 13,000 rpm (4°C) for10 min, supernatant was removed without disturbing the pellet. 70% ethanol was added and mixed the solution well by inverting the tube 4 ~ 5 times. The mixture was centrifuged for 5 min at 13,000 rpm (4°C). The supernantant was discarded without disturbing the pellet. The pellet retained the RNA was dried and kept at -80°C till use. After then, RNA was dissolved by using 20-50μl of RNase free water.

Total RNA isolation from tissue sample

(A) Homogenization

Tissue samples (100 mg) were taken in Falcon tubes7.5ml of 0.9 %saline was added. Homogenization of the sample was done by vortexing.

(B) Phase separation

A volume of 250μl from homogenized tissue was prepared in 1.5ml micro-centrifuge tube and 750μl of easy-REDTM Solution was added. The sample was mixed for 15 sec vigorously vortex and the tube was incubated at room temperature for 5 min. After then, 200μl of chloroform was added and the sample was mixed vigorously for 15 sec. Then, the tube was incubated at room temperature for5min. After centrifugation of the tube at 13000 rpm (4°C) for15 min, 400 μl of the supernatant was transferred to a new 1.5 ml centrifuge tube. (400μl) of isopropanol (2-propanol) was added and mixed well by inverting the tube 4~5 times. The tube was incubated for 10 min at room temperature. After centrifuged the tube at 13,000 rpm (4°C) for 10 min, carefully the supernatant was removed without disturbing the pellet. 70% ethanol was added and the solution was mixed well by inverting the tube 4~5 times. The mixture was centr-
thufuged for 5 min at 13000 rpm (4°C). The pellet
retained the RNA was dried and kept at -80°C till use.
After then, RNA was dissolved by using 20-50μL of
RNase free water.

Reverse transcription

The reverse transcription reaction was performed by
High Capacity cDNA Reverse Transcription Kits, that
transcription Kits contain all the reagents needed for
reverse transcription (RT) of total RNA to single
stranded cDNA using a reaction size of 20μL.

The cDNA Reverse Transcription Reactions

Volume of 10μL of 2X RT master mix was pipetted
into each well. 10μL of RNA sample was pipetted into
each well, pipetting up and down two times to mix.
The wells were centrifuged to spin down the contents and to
eliminate any air bubbles. The wells were placed on ice
until the thermal cycler was ready.

Real time PCR amplification

The cDNA was amplified with Thermo Scientific
Maxima SYBR Green/ROX qPCR Master Mix (2X), in
which The fluorescent dye in the master mix intercalates’
into the amplification product during the PCR
process and enables the rapid analysis of target DNA.
The Master Mix contains all reagents required for
qPCR (except template and primer) in a premixed 2×
centred ready-to-use solution. Primer design for
qPCR is one of the most important factors to obtain
efficient amplification and the primers design has been
known through (Naresh et al., 2015), (Table 1).

PCR conditions

An initial denaturation step at 95°C for 15 min was
performed. Then 50 cycles of denaturation 95°C (30s),
annealing: 55°C (30s) and elongation: 72°C (30s).
Reading was taken at annealing; 55°C followed by one
cycle for dissociation curve at 95°C for 1min, 55°C for
30sec and 95°C for 30sec.

RESULTS

Expression of GLP-1 and GIP hormone in blood

GLP-1 and GIP genes expression in blood samples
were detected which reveals the positive effect of both
SCFAs used in this trial. GLP-1 expression was
slightly increased compared to control blood sample.
Increasing the dose of SCFAs displayed an increase in
gene expression and recorded higher expression of
0.61more than the control sample. (Figure 1, A). However,
for level GIP gene expression in blood, highly up
regulation was recorded in compared to control sample
and recorded two times higher the control (2.29/
GIP/GAPDH as arbitrary units). Meanwhile, increase
concentration dose of SCFAs (propionic acid, 50
mmol/l and butyric acid, 30 mmol/l) enhance and up
regulate the expression by 2.8 times higher than control
and more pronounced to the first concentration used
(propionic acid, 35 mmol/l and butyric acid, 20
mmol/l). Also, we investigated the effects of glime-
piride on GIP-R and GLP-1R mRNA in the blood
samples. Similar results were obtained when glime-
piride was used (Group 4 and 5). Meanwhile, higher
dose of glimepiride showed an inhibitory effect for
GLP-1 gene expression in blood serum (Figure 1, A).
Nevertheless, GIP expression reported adverse effect,
contrary to GLP-1, and recorded high expression level.
GIP-gene expression was up regulated by 2.46 and 2.7
(GIP/GAPDH as arbitrary units) times more than
control sample for Group 4 and 5.

Expression of GLP-1 and GIP hormone in Tissue

Intestinal tissue of the treated rats showed GLP-1
and GIP genes expression in which relative increase of
GLP-1 mRNA level was recorded (Figure 1 B). GIP
expression level was also upregulated with low dose of
SCFAs (Group 2) and dropped down with higher con-
centration (Group 3).

Treatment with glimepiride, which belongs to the
class of drugs known as sulfonylureas, recorded down-
regulation of GLP-1 mRNA level (Fig. 1B). Increasing
the dose lead to more inhibitory effect and GLP-1 level
was decreased. In parallel, GIP level expressed was
highly affected by glimepiride doses used and recorded
lower level of expression. More inhibitory effect on
gene expression was recoded with higher dose (0.150
mg of glimepiride).

Real time polymerase chain reaction depends up on
the exponential amplification of a specific DNA
fragment, used as a template to make millions of
copies. There are different between Real time PCR and
conventional PCR because it allows the continuous
monitoring of the DNA produced in each cycle by
using fluorophore dyes. Fluorescence is released every
time after that a new DNA copy is synthesized, the
quantity of DNA produced depend up on the amount of
fluorescence Furthermore, real time PCR systems
provide higher sensitivity and robustness, with the
additional possibility to quantify the initial amount of
target DNA present in a sample. The results of Real
time PCR are visualized in an amplification plot (S1,
plateau).

The number of PCR cycles is plotted in the X axis,
while fluorescence is represented on the Y axis. The
amplification curve consists of three phases, the first
called an initial phase where the produced
fluorescence is below the detection level of the thermo
cycler, a second phase in which the fluorescence
increases (being this increment exponential at the
beginning of the phase), and a third phase where the
reaction ends and the fluorescence is stabilized. Within
the second phase, it is possible to set a threshold value,
which indicates the area of exponential increase.

Threshold Cycle (CT) is the intersection point
between the amplification curve and the threshold line.
At this point we can find the cycle in which the fluo-
rescence reaches the threshold value. The higher the
initial DNA amount, the lesser number of cycles are
needed (low Ct values) to reach the threshold the initial
DNA amount, the lesser number of cycles are needed
(low Ct values) to reach the threshold (Table 2).
According to the results from real time PCR we get the
value of CT for all groups for of blood and tissue
samples..
Effect of Sulphonylurea Derivatives

Table (1): List of the Target gene primer names and their nucleotide sequences.

<table>
<thead>
<tr>
<th>Target gene</th>
<th>Forward</th>
<th>Reverse</th>
</tr>
</thead>
<tbody>
<tr>
<td>glucagon-like peptide-1</td>
<td>5′-AATCTTGCCACCGGGACTT-3′</td>
<td>5′-AGTGACTGGCAGAGATGTG-3′</td>
</tr>
<tr>
<td>glucose-dependent insulin tropic</td>
<td>5′-AACAAACGGCCACAGGAGGC-3′</td>
<td>5′-AGCAAGCCAAAGCTAGGTCA-3′</td>
</tr>
<tr>
<td>Reference primer</td>
<td>5′-ACTGCCACTCTTCACCTTCG-3′</td>
<td>5′-CACCCGTGTGCTAGCCGTA-3′</td>
</tr>
</tbody>
</table>

Table (2): The ∆CT for tissue and blood samples for all groups in case of GLP-1 and GIP.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>T.GLP-1</th>
<th>T.GLP-1</th>
<th>B.GLP</th>
<th>B.GIP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>4</td>
<td>4</td>
<td>15.8</td>
<td>4.8</td>
</tr>
<tr>
<td>Group 2</td>
<td>4.2</td>
<td>4.69</td>
<td>15.89</td>
<td>7.09</td>
</tr>
<tr>
<td>Group 3</td>
<td>4.1</td>
<td>3.44</td>
<td>16.41</td>
<td>7.6</td>
</tr>
<tr>
<td>Group 4</td>
<td>3.7</td>
<td>3.69</td>
<td>15.69</td>
<td>7.26</td>
</tr>
<tr>
<td>Group 5</td>
<td>3</td>
<td>2.9</td>
<td>14.59</td>
<td>7.5</td>
</tr>
</tbody>
</table>

From the tables and figures we noted that there are up regulation for the mRNA expression (GLP-1) and (GLP) for all groups in blood samples under effect of different doses of Propionic acid, Butyric acid and Glimepiride.

DISCUSSION

Diabetes mellitus is becoming the fast growing epidemic all over the world. In Egypt, diabetes mellitus
is a major emerging clinical and public health problem (Hegazi et al., 2015). Diabetes type 2 management guidelines include dietary and exercise modifications and medications such as metformin sulphonyl urea insulin, Sodium-glucose cotranspor-ter type 2 (SGLT2) inhibitors (Paresh et al., 2017). Both of GIP and GLP-1 together are responsible for the incretion effect in healthy sub-jects, it is possible to analyze the incretion defect in patients with type 2 diabetes. Theoretically, the defect could be due to impaired secretion or accelerated metabolism of the incretion hormones; alternatively, the effect of the hormones could be compromised. There are many publications on the secretion of GIP in type 2 diabetes, and both increased, normal, and decreased secretion have been reported (Krarrup, 1988) Incrections hormones became an important therapeutic target for treatment of diabetes type2 by developing DPP-4 resistant GLP-1 analogue and by inhibiting the degrading enzyme DPP-4 (AyseNur et al., 2015) . These drugs are considered to be a medication option in diabetes management according to the 2016 American Diabetes Association. Both are well tolerated option that improves glycemic control with a low incidence of hypoglycemia and weight gain (Zappas et al., 2017). Incrections hormones affect glucose homeostasis through several mechanisms; decrease in appetite, reduction of body weight, improvement in insulin secretion and delay in gastric emptying (Prashant et al., 2014) .This study was designed to investigate the effects of SCFAs (butyrate and propionate) on expression of GIP and GLP-1 in experimental animals aiming to explore another way for taking benefits of both SCFAs and incretions. The results of the present study showed that the expression of GIP and GLP-1 in blood and tissues were up regulated by butyrate and propionate indicating the positive effects of these SCFAs. As regard to tissues , the expression of GIP was markedly increased more than GLP-1, this may be attributed to the presence of k-cells in both proximal duodenal mucosa and throughout the entire intestinal mucosa ( Mortensen et al., 2003), while L-cells which synthesizer GLP-1 is present in the distal intestinal mucosa (Mojsov et al., 1986 )As for blood, the expression of GIP and GLP-1 was up-regulated by butyrate and propionate , the effects on expression of both GIP and GLP-1 were nearly the same. So, the results of the present study confirm the previous findings of (Yadav et al., 2013). Also (Freeland et al., 2010), reported that rectal but not intravenous infusion of SCFAs was effective in up regulation of GLP-1 expression .The effect of SCFAs on expression of incretions is mediated by FFAR2 and FFAR3 (Herr et al., 2012). (Tolhurst et al., 2012) found that butyrate have a slower potency than acetate and propionate in stimulating GLP-1 secretion. However, acetate was not used in this study because it induces ulcers in GIT mucosa (Aguilar et al., 1999). Also the study showed that the expression of the Incretions hormone was up regulated in control group and this is due to the food provided to the rats. Since the food contains of fibre such as corn, beans and others material. These fibres were fermented by intestinal bacteria releasing the short chain fatty acids. Thus, the intestinal cells absorbed these acids and incretions unregulated. Dietary fibres have raised much interest, as they exert beneficial effects on body weight, food intake, glucose homeostasis, and insulin sensitivity this due to Short chain fatty acids (SCFAs), the end products of fermentation of dietary fibres by the anaerobic intestinal micro biota, have been shown to exert multiple beneficial effects on mammalian energy metabolism (Gijis et al., 2013). Several studies revealed the hypoglycaemic effects of SCFAs via multiple mechanisms including decr-eased expression of glycogenic enzymes glucose phosphatase and phosphoeno-lypyruvate carboxyl kinase (Sakakibara et al., 2006), increasing gut hormones PYY (satiety hormone) and by increasing glucose handling by muscle and adipose tissues (Boey et al., 2006). So, this study extends the hypoglycaemic effects of SCFAs by another mec-hanism through up regulation of incretions expression providing a special attention for the benefits of SCFAs on glucose homeostasis.

Sulphonylurea is still being as the second line recom-mended choice of oral glucose-lowering treatment after metformin (Kharbenda et al., 2013). It can be also used either alone or in combination with another diabetes medication (NICE clinical guideline 66, 2008). Glimepiride is one of the third generations of sulphonylurea. Glimepiride have a number of advan-tages over other members of sulphonylurea, curre-ntly in the market such as lower dosages, fast onset of action and lower C-peptide level of insulin, this is because of less secretion of insulin and more pronounced extra pancreatic effects .Glimepiride has the highest activity to increase the glucose transport in all sulphonylurea drugs. Glimepiride also has blood platelet aggregation inhibiting property (Huibin et al., 2015) .The most surprising finding in this study was the up regulating effect of sulph-onylurea on expression of both GIP and GLP-1. As regard to tissues, the effects of sulphonylurea on GIP were more pronounced than on GLP-1. But, the effects on expression of both GIP and GLP-1 were the same in blood .The hypoglycemic effects of sulphonylurea is mediating by increasing insulin secretion through inhibition of K+ efflux from panc-reatic β-cells via sulphonylurea receptors which may be closely linked to an ATP sensitive K⁺ Chanel. Also, sulphonylurea...
reduces serum glucagon level. The finding of our study provides unexpected mechanism for the hypoglycemic effects sulphonylurea and its derivatives by up regulation of incretions expression. Incretions in turns have different hypoglycemic effects.

CONCLUSION

The present study revealed that both SCFAs and sulphonylurea have up regulating effects on expression of incretions leading to augmentation of their hypoglycemic effects.

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تأثير مشتقين السلفونيل بوريا والأحماض الدهنية قصيرة السلسلة على تكوين هرمون الأكرازتين في خلايا الحيوانات الحية

عماد جاد، طاهي جودة، محمد عبد الغني، نرمين رافت

التعليم العربي

تهدف هذه الدراسة إلى توضيح دور الأحماض الدهنية قصيرة السلسلة وكذلك مشتقين السلفونيل بورية في إفراز هرمون الأكرازتين من الخلايا المعمية وبالتالي حث التكزيز على مواد الأكرازتين. أجريت هذه الدراسة على 50 فأر وزن 200-150 جرام تقريباً تم تقسيمهم ورعايتهم في مركز بيت الحيوان بكلية الطب جامعة الرقاص. تم تحضير تركيزات مختارة من أحماض الديوكسين والبيروبوبين والبيروبينك، ثم تم تحضير تركيزات مختلفة من مركز الجمل البعيد لإعلانها كجرعات للفأر. تم تقسيم الفأر إلى خمس مجموعات فحصية، وتعتبر جرعات المجموعة الأولى موضعية ضاربتين (GLP) و35 مل مول من حمض اليسوبينك، 15 مل مول من حمض الديوكسين (GIP) و5 مل مول من حمض بوريون، 30 مل مول من حمض الديوكسين.凶

المجموعة الثانية اشتملت على 10 الفأر، المجموعة الثالثة اشتملت على 15 الفأر (مجموعة 4) وتم تعاطف جرعات يومية من محلول تحضير 150 مل مول من كل الفأر، المجموعة الخامسة اشتملت على 10 فأر (مجموعة 5) وتم تعاطيف جرعات يومية من محلول تحضير Glimepiride تركيز 0.75 مل مريء من كل فأر.

في الخاتمة، تمت تمديد سلسلة الدراسة ورفع تطبيق GLP-1 في جذع الحياة، على الشعيرات في المجموعة اللبية، والبيروبين وGIP، بالإضافة إلى الأخرى، وتم تقييم البناء والنمذجة في المجموعة الخالية. في تلك الصورة، تمت تأثير مريح عن GLP-1 وGIP، ولكن في المجموعة الثانية، كانت هناك جرعة توزع في المجموعة الثانية بناءً على تأثير الأحماض الدهنية القصيرة السلسلة.

الملخص العربي

- تأثير مشتقين السلفونيل بوريا والأحماض الدهنية قصيرة السلسلة على تكوين هرمون الأكرازتين في خلايا الحيوانات الحية

- تهدف هذه الدراسة إلى توضيح دور الأحماض الدهنية قصيرة السلسلة وكذلك مشتقين السلفونيل بورية في إفراز هرمون الأكرازتين من الخلايا المعمية وبالتالي حث التكزيز على مواد الأكرازتين. أجريت هذه الدراسة على 50 فأر وزن 200-150 جرام تقريباً تم تقسيمهم ورعايتهم في مركز بيت الحيوان بكلية الطب جامعة الرقاص. تم تحضير تركيزات مختارة من أحماض الديوكسين والبيروبينك، ثم تم تحضير تركيزات مختلفة من مركز الجمل البعيد لإعلانها كجرعات للفأر. تم تقسيم الفأر إلى خمس مجموعات فحصية، وتعتبر جرعات المجموعة الأولى موضعية ضاربتين (GLP) و35 مل مول من حمض اليسوبينك، 15 مل مول من حمض الديوكسين (GIP) و5 مل مول من حمض بوريون، 30 مل مول من حمض الديوكسين. تأثير فعالة عن GLP-1 وGIP، ولكن في المجموعة الثانية، كانت هناك جرعة توزع في المجموعة الثانية بناءً على تأثير الأحماض الدهنية القصيرة السلسلة.

- في الختام، تمت تمديد سلسلة الدراسة ورفع تطبيق GLP-1 في جذع الحياة، على الشعيرات في المجموعة اللبية، والبيروبين وGIP، بالإضافة إلى الأخرى، وتم تقييم البناء والنمذجة في المجموعة الخالية. في تلك الصورة، تمت تأثير مريح عن GLP-1 وGIP، ولكن في المجموعة الثانية، كانت هناك جرعة توزع في المجموعة الثانية بناءً على تأثير الأحماض الدهنية القصيرة السلسلة. ي الحديد على وجود تأثير قوي على مشتقين السلفونيل بورية (GIP) في إطار هرمون الأكرازتين، وهذا قد تكون قد تحدث بشكل رئيسي يكون تأثير بعض هذه المركبات على التمثيل الغذائي للسكر. ويبدو أن هذه الدراسة قد أثارت اهتمامات من حيث التأثير على مستقبلات الأكرازتين في خلايا الحيوانات الحية، وتعتبر تأثير مريح عن GLP-1 وGIP، ولكن في المجموعة الثانية، كانت هناك جرعة توزع في المجموعة الثانية بناءً على تأثير الأحماض الدهنية القصيرة السلسلة.

- ومنهجية متعلقة للتعرف على علاجات جديدة لمرضى السكري.

- تأثير مشتقين السلفونيل بوريا والأحماض الدهنية قصيرة السلسلة على تكوين هرمон الأكرازتين في خلايا الحيوانات الحية

- تهدف هذه الدراسة إلى توضيح دور الأحماض الدهنية قصيرة السلسلة وكذلك مشتقين السلفونيل بورية في إفراز هرمون الأكرازتين من الخلايا المعمية وبالتالي حث التكزيز على مواد الأكرازتين. أجريت هذه الدراسة على 50 فأر وزن 200-150 جرام تقريباً تم تقسيمهم ورعايةهم في مركز بيت الحيوان بكلية الطب جامع...