INVESTIGATION OFTHE ROLE OFQUERCETIN AND RUTIN ON DIABETES ASSOCIATED BEHAVIORAL DYSFUNCTION IN SWISS ALBINO MICE

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CONTENT

CERTIFICATE

This is to certify that the project entitled "Investigation Of The Role Of Quercetin And Rutin On Diabetes Associated Behavioral Dysfunction In Swiss Albino Mice." which is being submitted by **SohailSankhyan** in partial fulfillment for the award of degree of M.Tech in Biotechnology from Jaypee University of Information Technology is the record of candidate's own work carried out under my supervision. This work has not been submitted partially or wholly to any other University or Institute for the award of this or any degree or diploma.

Dr.Udayabanu M

Associate Professor

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Sohail Sankhyan

ABSTRACT

The study was designed to investigate the effect of antidiabetic drugs and antioxidants on STZ induced diabetic mice on the basis of anxiety testing. Animals were divided into groups (Control, Control+Rosiglitazone, Control+Quercetin, Control+Rutin ,induced with Diabetes (STZ induced, STZ+Rosiglitazone, STZ+Quercetin, STZ+Rutin)) and were orally administered with the drug i.e Rosiglitazone(both control, STZ induced) , antioxidant i.e Quercetin, Rutin for 21days. Anxiety and Stress behaviour was assessed from day 22-27 in which the anxiety and stress was checked through Anxiety testing method Elevated Plus Maze (EPM). Results revealed that animals induced with STZ were having high anxiety and stress compared to those of control, Diabetic animals which were subjected to Rosiglitazone showed freezing, slow locomotion effect and those subjected to quercetin showed reduced anxiety, attenuated depression, reduced freezing and normalized locomotion activity. Results revealed that time taken by the control animals was equal to that taken by the STZ+ Quercetin.

CHAPTER 1

INTRODUCTION

Diabetes mellitus is a pathologic state which help in ensuing severe imbalances of the metabolism and also lead to non-physiologic altrations in many of the tissues, markers with oxidative strain in rats having diabetes in pancreatic islets and found to have an increased reactive oxygen species (ROS). Diabetics and trial animal fashions show off excessive oxidative stress because of chronic and continual hyperglycemia, thus reduce the interest of the antioxidative resistance machine and consequently elevate free radical generation.

Streptozocin is a chemical that is mainly poisonous to the beta cells producing insulin in the pancreas in the mammals. This is also used in medication for curing the Langerhans cancers and is utilized for the clinical studies to supply a version in animal with hyperglycemia in a massive dosage as well as type 2diabetes or Type1 Diabetes with multiple low doses.

Streptozotocin is the compound having glucosamine-nitrosourea, with distinct agents of alkylation inside the nitrosourea elegance, which is harmful to cells via manner of causing breakage to the DNA, although other methods can moreover make contributions. poly ADP-ribosylation is activated due to DNA damage, which might be essential in diabetes induction than damaging of DNA on its own.

Streptozotocin is comparable enough with glucose which can be transported into the basic unit through the glucose shipping protein GLUT2, however isn't identified by using the opposite glucose transporters. This explains its relative toxicity to beta cells, for the reason that those cells have mainly excessive ranges of GLUT2.

Streptozotocin is authorized with the aid of theUnited States Food and Drug Administration (FDA) for treating metastatic most cancers in the islet cells of the pancreas. It consists of a huge chance of toxicity and infrequently help in curing many cancers, It is typically confined to patients having cancers which is difficult to be eliminated with the aid of surgery. Streptozotocin in patients can lessen the size of the tumor and decrease signs.

The excessive toxic nature of the beta cells, researches in medical, streptozotocin has additionally used from long time for inducing diabetes in the swiss albino mice. It is a synthetic antineoplastic agent this is an anti-tumor antibiotic and is linked to different nitrosureas which are used in most cancers chemotherapy.

This leads to the development of stress and anxiety as there is a poor management of the glucose levels in the body. The conditions which usually develops is of either hyperglycemia or hypoglycemia thus leads to development of anxiety and stress. Food products which are natural have been used for fighting against human illnesses from past years. Flavonoids that are occurring naturally in flavones , isoflavones and anthocyanidins had been planned as an useful nutritional source of the control and in preventing diabetes and its complications which are long term .

Flavonoids originated from food tend to get better metabolism of glucose, profile of lipid, hormones regulations and human frame enzymes, in addition protection of person from illnesses like obesity, diabetes and their complications.Flavonoids signify the usual and extensively distributed group of phenolics present in plant and are plentiful in ingredients. The most common native flavonoids is quercetin ,especially in glycosidic forms inclusive of rutin. Quercetin and rutin are the flavonoids most abundantly consumed in meals. Rutin is abundantly found in onions, apples, tea and red wine etc

Flavonoids constitute a massive class of as a minimum 6000 phenolic compounds observed such as greens, cocoa, chocolate, tea, soy, red wine, herbs and beverage merchandise.Flavonoids encompass rings (aromatic) also known as A and B rings which are linked by way of a 3-carbon chain that joins an heterocyclic ring which is oxygenated. Flavonoids thus play an important role in stz induced diabetes as it prevents the anxiety and stress occurrence in a diabetic patient thus overcoming the the limitations of the anti diabetic drugs e.grosiglitazone , reducing the chances of heart attack. An antidiabetic drug, rosiglitazone within the thiazolidinedione class. It act as an sensitizer of insulin, by means of attachment to the PPAR present in the fat cells and creating the cells greater attentive for the insulin.

CHAPTER 2

LITERATURE REVIEW

(2.1)Streptozotocin:

Streptozotocin is the compound having glucosamine-nitrosourea, with distinct agents of alkylation inside the nitrosourea elegance, which is harmful to cells via manner of causing breakage to the DNA, although other methods can moreover make contributions. poly ADP-ribosylation is activated due to DNA damage, which might be essential in diabetes induction than damaging of DNA on its own.

Streptozotocin is comparable enough with glucose which can be transported into the basic unit through the glucose shipping protein GLUT2, however isn't identified by using the opposite glucose transporters. This explains its relative toxicity to beta cells, for the reason that those cells have mainly excessive ranges of GLUT2.

Streptomyces achromogenes help in producing antibiotic Streptozotocin,which has been extensively applied for inducing diabetes in the mice. It helps in stimulating the certainly happening metabolic ailment DM by using causing pancreatic β cells degradation. The β cellular STZ toxicity is linked to the moiety of the glucose in its structure, allowing STZ to enter the cell thru the lower similarity of the Glut 2 present in the plasma membrane.

Streptozotocin is determined to be poisonous to the pancreatic beta cells, the cells that commonly adjust glucose of the blood tiers by generating the insulin hormone. This advised the usage of the drug as a model(animal) of diabetes, and as a treatment for beta cells in case of cancer. The National Cancer Institute found usage of STZ in most chemotherapy for cancers. Approval from FDA for streptozotocin as a remedy for islets cells of pancreas and approval become granted in July 1982. This drug turned into finally advertised as Zanosar

(2.2) Flavonoids(Quercetin &Rutin)

Flavonoids arise usually, in the nation of the plant. They feature as pigments of the plant, which are accountable in the colors of the plants. Plant polyphenolics, flavonoids is as pigments found in leaves of plant, barks,seeds, culmination and flora. They are associated with C nutrition, to which help in offering synergistic effects. The pharmacological outcomes that a lot of conventional herbal tablets can be approved to their flavonoid elements, which blocks the

positive enzymes and own activities associated with antioxidants. 3,3′,4′,five-7-pentahydroxyflavone, quercetin is a chemically associated flavonol with kaemferol. As a part of the flavonoid circle of relatives, quercetin is extensively distributed among the plants, and might be the maximum abundant of the flavonoid molecules inside the plant.

Quercetin sources consist of brassica inexperienced greens, berries,onions, parsley, apple, legumes, inexperienced tea, citrus fruits, pink grape wines, and so on. Quercetin helps in prevening the oxidative damage and the cell dying by numerous methodologies, together with oxygen radical scavenger ,xanthine oxidase inhibitor , peroxidation of lipid, and steel ions chelators. Quercetin possesses a catalogue of pharmacological moves, consisting of aerobic-protection, cataract prevention, anti-cancer interest, effects of anti-ulcer , anti-inflammatory, anti-allergic, antiviral and antibacterial activities.

Rosiglitazone is an drug for anti diabetic within the class of thiazolidinedione. It is advertised via the pharmaceutical corporation GlaxoSmithKline (GSK) as a stand-on my own use for the drug in aggregate of metformin or glimepiride. Despite its effectiveness at lowering sugar level in blood for type 2 diabetes as its use caused dangers of heart attacks and demise. This was due to the increased anxiety and stress.

Quercetin on the hand was able to reduce the problems of anxiety and stress thus preventing of the occurrence of heart attack and death in case of diabetic patients.The mixture of rosiglitazone with insulin led to an increased rate of congestive heart failure.

Diabetes is a collection of different,hormonal and problems of metabolism characterized by using hyperglycemia and glucosurea, due to errors in secretion of insulin,motion of insulin, or each. The persistent hyperglycemia of diabetes is related to long-time period harm, disorder, and failure of diverse organs within the body. Reserve of pancreatic insulin is an essential part of islet characteristic, with strong coupling among secretion of insulin and producing which is important for proper working of pancreatic beta cells.

Storage size for insulin is decided by means of the compatability between the charges of biosynthesis of insulin and its secretion, in addition to by way of the range and quantity of the beta cells, i.e., the beta-cellular mass. In grownup mammals, beta-cellular mass is different to

evolve secretion of insulin to lengthy-term changes in insulin call for. This has been established again and again below physiological in addition to pathological conditions of insulin resistance. Although specifically proven in rodents. The decline of metabolic kingdom in type2 of the diabetes consequences specially from revolutionary beta-cellular failure

Thus, it is significantly vital to decide whether or not practical beta-cellular reduction of mass in kind 2 of diabetics. Type 1 animal model with diabetic is to assess the variations in the reserve of pancreatic insulin through beta-cell mass, and affect of set off induction of normoglycaemia on pancreatic beta-cells, because hyperglycemia is also related to speedy decrease of stores of pancreatic insulin, worthy adjustments in beta cells proliferation, and also in loss of life that culminates in morphology of islets.

(2.3)Anti diabetic drugs and antioxidants

RUTIN:-

It can be widely extracted from herbal resources along with buckwheat,oranges, grapes, lemons, limes peaches and berries .Mice with diabetic fed on the rutin at a hundred mg/kg weight loss program showed lowering glucose of plasma and growth in levels of insulin have been found alongside the healing of glycogen content and the activities of carbohydrate metabolic enzymes. Rutin could enhance the metabolic status of rats experimentally-brought to diabetes.

QUERCETIN:-

Quercetin to broaden it as antidiabetic drug which help in preventing and managing the DM. It is one of the widely used flavonols in nutritional for humans. Which is broadly spreaded in distinctive varieties of fruits, tea,pepper, coriander,fennel, radish, berries, onions,apples and wine. Several research have mentioned mechanism of action of quercetin in diabetes, like decreases in lipid level per oxidation, will increase in antioxidant enzymes activity, insulin-based activation of PI3K inhibition, and discount in intestinal absorption of glucose by using inhibiting the GLUT2

ROSIGLITAZONE:-

It is a member of the class thiazolidinedione of medication. Which act as sensitizers of insulin. They lessen glucose level, fatty acid level,and insulin blood concentrations. They function by means of attachment to the peroxisome proliferator-activated receptor. PPARs are the elements of transcription which are living inside the nucleus and end up activated by using ligands which includes thiazolidinediones class.

Antidiabetic drugs and antioxidants play an important role in STZ induced diabetes. Rosiglitazone is an antidiabetic drug which is helpful in reducing the blood sugar in the case of type 2 diabetes. Though helpful but is not used so often as it increases stress and anxiety in the diabetic organism. Increased stress and anxiety increases the risk of heart attack thus leading to the death of the organism. Due to this limitation the drug not widely used but is used in some cases.

Rutin and Quercetin on the other hand are antioxidants flavonoids which is derived from various natural sources such as apple,legumes,etc . These play an important role in diabetes especially quercetin, it overcomes the rosiglitazone limitations by reducing the anxiety and stress conditions for the patients significantly having an antidepressant effect on the diabetic organism.nutritional supplementation with antioxidants inclusive of vitamins, and flavonoids has been used in tries to save from the incidence of many continual diseases.

Basically flavonoids are evidently going on phenolic compounds which might be allotted in plants. They include huge range of organic activity and lot of research has been carried out on their capacity feature in treating diabetes and different diseases. Most importantly the flavonoids and their related herbal compounds are regarded to encompass antidiabetic capacity, proven in severa animal fashions. Such useful flavonoids are less carried out resulting from its poor solubility, bioavailability reduction; metabolism which is first pass and degradation in intestine.Thus, flavonoids are able to improve, stabilize and prolonged maintaining the secretion of insulin,in the human islets and the cells of pancreas respectively.

The activity of the flavonoids and the antidiabetic drugs is checked and the results are compared, Anxiety testing is involved in the comparison which includes various methods for testing.

CHAPTER-3

MATERIALS AND METHODS

(3.1)Animals:

Swiss albino mice weighing 20–25 g were housed within the facility for animals with12 hours of light-darkish cycle, having 23 ±1 °C temperature and humidity to be 60-65%. All the experiments was completed after approval from Institute Animal Ethics Committee according with the pointers of CPCSEA,India. All the essential efforts had been made to limit the suffering for the animals(mice). They have been lived in macrolon cages beneath widespread conditions of laboratory (light from 9.00 A.M. To 7.00 P.M., 25 ± 2 ºC, humidity fifty five%) .Animals had been given widespread rat pellets for eating and water thus animals were housed under normal conditions. (4 weeks).

(3.2) Experimental design:-

A total of 37 mice were used in the experiment and were grouped into six parts with marking on their body equating to the drug induced.Grouping was done accordingly and the animals were grouped into :-

1. Control.(No mark)

2. Control + Rosiglitazone.(Head)

3. Control + Quercetin.(Body)

4. Control +Rutin.(Tail)

5. Streptozotocin(STZ)(Abdomen).

6. STZ+ Rosiglitazone(Abdomen+Head)

7. STZ+Quercetin(Abdomen+body)

8. STZ+Rutin.(Abdomen+tail)

- Drug was orally injected in the mice.Wistar strain mice weighting (25-30 g) were housed under normal contiditions.
- 40 mice were used and were grouped-(control[normal], control+Rosi, control+Querceten, control+Rutin)&(STZ, STZ+Rosi,STZ+Querceten,STZ+Rutin).
- The mice were then provided with oral dosage of each drug/anti-oxidant every day for 21 days.
- Initially weight of each mice is noted and then it is again noted at the end of 2^{nd} ,4^{th}& 6^{th} week after the dosage started.
- Behavioral tests were performed from(22-27) day. This involved the elevated plus maze for anxiety testing and memory dysfunction test

(3.3) Elevated Plus Maze Anxiety testing:

EPM is used to assess anxiety conduct in rodents .We used this version to evaluate the effect of quercetin treatment on STZ brought on tension in mice on day 22 B/W 4 and 7 pm. The equipment consisted of significant platform (10 × 10 cm) from which two opposing open palms (50 × 50 cm) and two opposing closed hands (50 × 50 × 25 cm) originated. Arms of the EPM had been extended to the peak of 50 cm from the ground. Entire experiment became finished underneath low intensity mild inside a darkish room.The elevated plus maze is a generally used for the behavioral assay in the rodents and it has been validated to review the anti-anxiety effects of pharmacological agents and hormones(steroid), and it helps to define brain regions and mechanisms essential for the anxiety-related behavior. Rats or mice are usually located at the junction of the four arms of the maze, in frount of an open arm, and entries/duration in each arm are recorded by a video-tracking system and observer for 3 minutes. Other ethological parameters (i.e., rears, head dips and stretched-attend postures) can also be observed by the help of this test. An increase in open arm activity shows anti-anxiety behavior of the mice. In our laboratory, rats or mice are exposed to the plus maze on one occasion.

A Y-fashioned apparatus that included an increased open alley and an enclosed alley, which did not, changed into first described through Montgomery. This task become changed into an improved maze with 4 fingers (open and two enclosed) which can be arranged to form a plus shape and become defined via Handley+ and Mithani3. These authors defined the assessment of anxiety conduct of rodents by means of the usage of the ratio of time spent on the open hands to the time spent on the closed hands. Unlike other behavioral assays used to assess anxiety responses that depend on the presentation of noxious stimuli (i.e electric powered shock, food/water deprivation, loud noises, exposure to predator smell, and many others.) that generally produce a conditioned reaction, the elevated plus maze relies upon rodents' proclivity toward darkish, enclosed areas (method) and an unconditioned worry of heights/open spaces.

Responses of behavioral within the extended plus maze are without problems assessed and quantified by way of an observer. Briefly, rodents are located in the intersection of the four arms of the multiplied plus maze and their behavior is normally recorded for 3 min. This become based totally upon the early studies by means of Montgomery that discovered that mice validated the maximum sturdy avoidance responses inside the first 3 min after placement inside the improved open alleys. The behaviors which might be normally recorded while rodents are inside the increased plus maze are the time spent and entries made at the open and closed hands. Behavior on this challenge (i.e., interest in the open arms) displays a battle among the rodent's choice for covered areas (e.g., closed hands) and their innate motivation to discover novel environments.

Anti-tension conduct may be determined simultaneously with a degree of spontaneous motor activity albeit the arm entries made in the maze may not be an highest quality measure of motor hobby. The expanded plus maze has face validity, this is the capability of a challenge is meant to diploma. As an example, within the improved plus maze, the anxiety or worry of open areas/heights of rodents seems to be measured. In this example, the open fingers are averted and rodents spend most of the people of the time on this venture inside the closed arms of the maze. Different anxiety-associated behaviors of rodents, consisting of freezing/immobility and defecation, are accelerated at the open palms of the maze as compared to the closed fingers.

(3.4) PROTOCOL FOR ANXIETY TESTING

The rotodents were first provided with the pre-exposure of the Pluz Maze model(Instrument demonstration)

Mice was placed on the centre of the maze facing the open arm

Mice was allowed to move on the maze and at the same time was recorded through video camera.

Total time for one mice was observation was 3 mins and time for each arm is noted separately.

The amount of time spent in the closed / open arm then tells about the anxiety and stress in the mice.

Anxiety reduction is indicated in the plus maze by an increase in the portion of the time spent in the open arms

i.e = TIME SPENT IN OPEN ARM /TOTAL TIME SPENT IN BOTH ARMS

Chapter 4

Result and Discussion

Table 1: Weights of Swiss albino mice

Group	Weight (22 jan 2017)	Weight (6 feb 2017)	Weight (19 feb 2017)
Control (Male)			
1) FR	34.3	33.8	23.9
2) FL	32.2	33.9	30.0
3) FRL	32.0	33.1	32.6
(Female)			
1) BR	32.8	29.6	29.6
2) BL	22.6	22.5	23.5
Control + Rosi (Male)			
1) FR	27.1	28.5	32.2
2) FL	31.9	31.2	31.2
3) FRL	30.9	25.7	27.2
(Female)			
1) BR	21.4	Dead	Dead
2) BL	27.4	22.6	23.4
Control + Rutin			
(Male)	31.0	30.9	29.7
1) FR	31.4	28.2	27.1
2) FL	29.0	30.0	29.4
3) FRL	32.0	32.1	32.5
4) BL			
(Female)	27.7	29.6	27.6
1) BR			
Control + Quercetin			
(Male)	28.0	28.1	25.0
1) FR	33.5	33.1	31.9
2) FL			
STZ (Male)			
1) FR	26.5	26.9	28.5
2) FL	26.1	24.7	26.3
3) FRL	26.8	26.1	27.5
4) BR	27.8	28.1	28.4
(Female)			
1) BL	23.8	25.7	26.2

2) BRL	24.8	24.9	25.3
STZ (Rosi- Male) 1) FR (Female) 1) FL 2) FRL 3) BR	 27.4 25.3 24.0 21.2	 24.7 26.2 20.8 Dead	 21.1 27.5 Dead Dead
STZ (quercetin- Male) 1) FR 2) FL (Female) 1) FRL 2) BR	 27.9 27.5 19.6 21.6	 24.3 25.7 Dead 20.7	 Dead 26.8 Dead 22.0
STZ (Rutin- Male) 1) FR 2) FL 3) FRL 4) BR 5) BL 6) BRL	 26.7 26.9 27.4 28.4 24.9 25.7	 23.0 26.5 24.6 28.6 21.8 24.5	 22.5 25.9 25.6 Dead 23.3 24.2

The above table represents the weights of swiss albino mice from the starting of the study till the end of the fourth week.

FR = FRONT RIGHT

FL= FRONT LEFT

FRL= FRONT RIGHT LEFT

BR= BACK RIGHT

BL= BACK LEFT

BRL= BACK RIGHT LEFT

Table 2: Anxiety test for Swiss albino mice

Group	IN TIME (3 min)	OUT TIME (3 min)
Control (Male) 1) FR 2) FL 3) FRL (Female) 1) BR 2) BL	 131 133 130 136 140	 40 38 42 39 36
Control + Rosi (Male) 1) FR 2) FL 3) FRL (Female) 1) BL	 147 143 141 148	 27 30 32 29
Control + Rutin (Male) 1) FR 2) FL 3) FRL 4) BL (Female) 1) BR	 145 140 143 139 141	 30 35 32 35 34
Control + Quercetin (Male) 1) FR 2) FL	 143 139	 32 37
STZ (Male) 1) FR 2) FL 3) FRL 4) BR (Female) 1) BL 2) BRL	 150 147 143 148 145 142	 24 27 30 26 28 31
STZ (Rosi- Male) 1) FR	 144	 30

(Female) 1) FL	146	27
STZ (quercetin- Male) 1) FL (Female) 1) BR	131 133	39 37
STZ (Rutin- Male) 1) FR 2) FL 3) FRL 4) BL 5) BRL	144 140 145 142 144	31 34 29 32 30

The above table represents the time taken by the swiss albino mice for each arm in elevated maze test. Total time for the mice on the maze was 3 min. The in time represents the total time the mice stayed on the closed arm of the maze and the out time represents the total time the mice stayed on the open arm of the maze.

Thus from the above observation we see that the anxiety test of the quercetin falls in the same range that of the control.

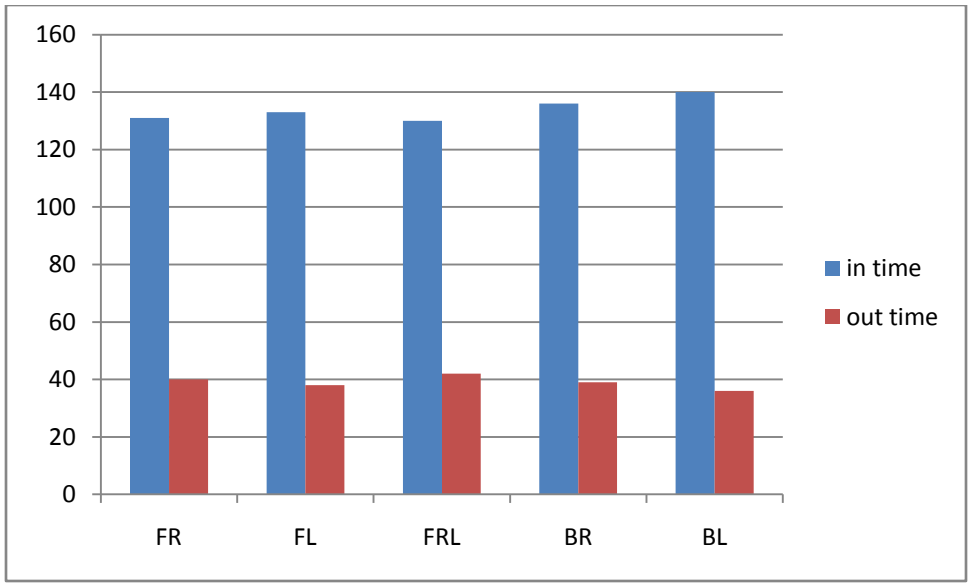

Fig 1:Graph for Control in anxiety test

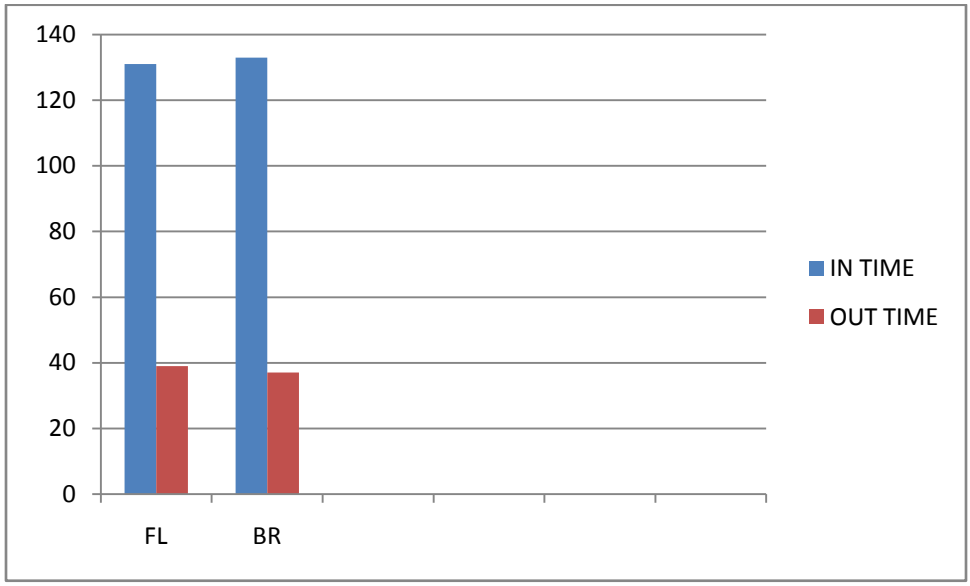

Fig 2:Graph for STZ + QUERCITIN in anxiety test

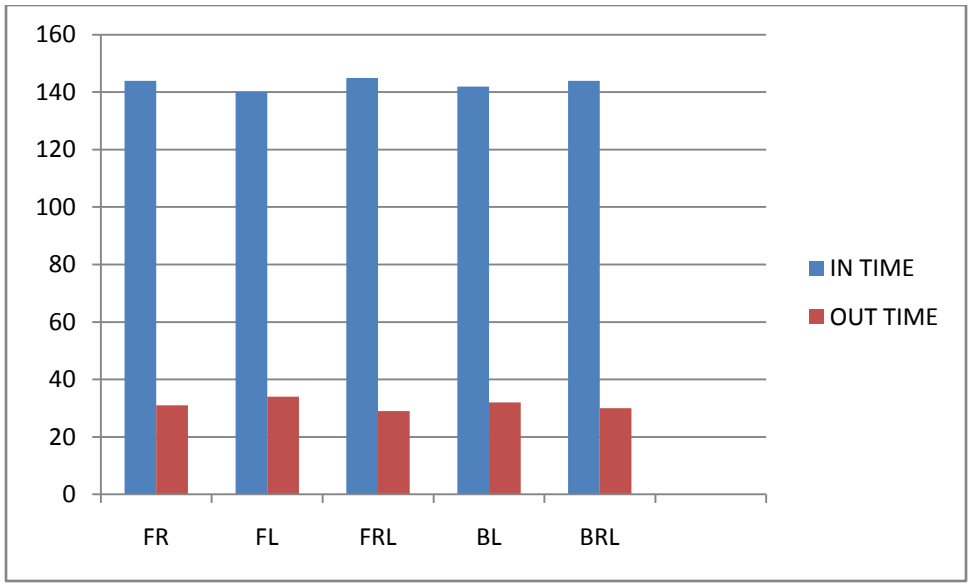

Fig 3: Graph for STZ in anxiety test

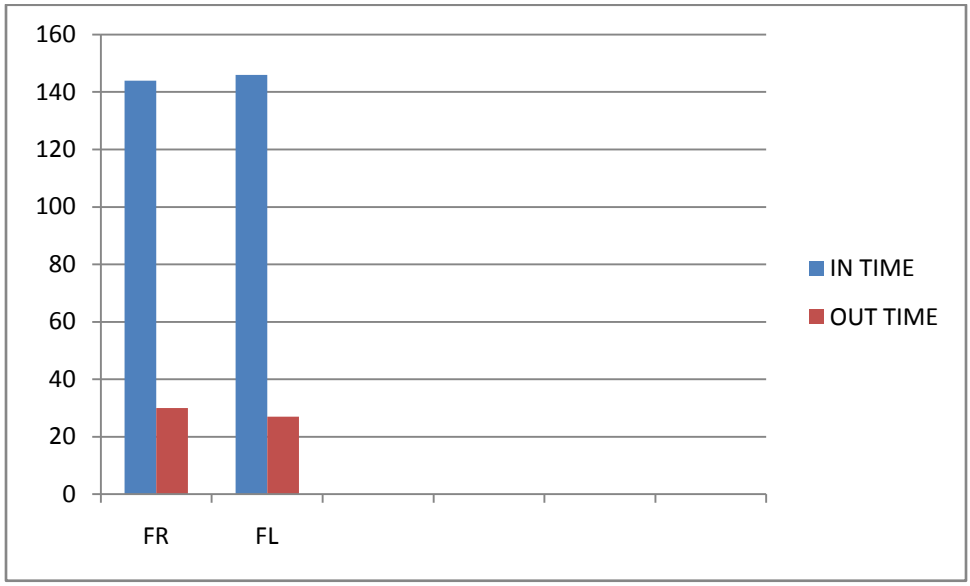

Fig 4: Graph for STZ ROSI in anxiety test

From the above graphs (Fig 1, 2) it can be seen that the time range for the control falls in the same range that of STZ induced, treated by quercetin thus showing reduced anxiety in the STZ + quercetin induced mice. Fig 3,4 shows no reduced effects on anxiety in antidiabetic drug induced STZ mice.

Table 3: Memory test of Swiss albino mice

Group	Day 0 TIME(SEC)	DAY 7 TIME(SEC)
Control (Male) 1) FR 2) FL 3) FRL (Female) 1) BR 2) BL	 1:09 1:07 1:10 1:14 1:20	 48 54 47 56 52
Control + Rosi (Male) 1) FR 2) FL 3) FRL (Female) 1) BL Control + Rutin (Male) 1) FR 2) FL 3) FRL 4) BL (Female) 1) BR	 1:24 1:30 1:22 1:34 1:20 1:25 1:30 1:28 1:31	 59 1:11 1:04 1:12 57 59 1:00 1:07 1:10
Control + Quercetin (Male) 1) FR 2) FL	 1:19 1:22	 56 1:00
STZ (Male) 1) FR 2) FL 3) FRL 4) BR (Female) 1) BL	 1:35 1:32 1:37 1:40 1:34	 1:19 1:17 1:15 1:25 1:16

2) BRL	1:31	1:18
STZ (Rosi- Male) 1) FR (Female) 1) FL	 1:30 1:45	 1:06 1:15
STZ (quercetin- Male) 1) FL (Female) 1) BR	 1:11 1:14	 47 51
STZ (Rutin- Male) 1) FR 2) FL 3) FRL 4) BL 5) BRL	 1:25 1:31 1:27 1:35 1:22	 1:00 1:07 1:10 1:17 1:14

The above table shows the time taken by of mice from the edge of the open arm to the closed arm. On day 0 the mice was exposed to the apparatus of the maze test, then the time was noted again on day 7 which shows that mice showed faster movement as compared to the day 0, In case of quercetin the movement of mice was faster on day 7 as compared to day 0.

CONCLUSION

It was concluded from this study that antioxidants showed anti diabetic effects based on the anxiety testing, which clearly shows that the anxiety in case of the STZ induced + quercetin was similar to the control (non diabetic). Average time spend inside the maze for the control (non diabetic mice) was 134 seconds and average out time was 38 seconds while average time spend inside the maze of quercetin treated mice was 132 seconds and out time was estimated to be 37 seconds.

It clearly shows that quercetin helped in improving the stress and anxiety/depression with improved locomotive activity with reduced freezing of the swiss albino mice.

It was also noted that the mice whose tail was touching the surface of the maze moved slow and had freezing rather than to those whose tail was not touching the surface.

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