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Potential Capacities for the Release and Storage of Hepatic Glucose by the Medicinal Recipe Composed of *Parquetina nigrescens* and *Erythrina senegalensis* in Healthy Rats and Rats Made Diabetic

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Abstract | **Original Research Article**

The medicinal recipe, composed of an aqueous extract of *Parquetina nigrescens* (Periplocaceae) and *Erytrina senegalensis* (Fabaceae) (RPNES) leaves, is used in traditional medicine in Ivory Coast to treat diabetes. This work aims to evaluate the antidiabetic potential of this drug recipe (RPNES) by studying its effects on the release of hepatic glucose in healthy rats and the storage of hepatic glucose in rats made diabetic by Streptozotocin. After 28 days of treatment of healthy rats with RPNES at doses of 400, 600 and 800 mg/kg BW, the dosage of glucose released by the liver, isolated and incubated at 37°C for 60 min in glucose-lactam Mac Ewen, shows that this recipe acts on liver function by reducing, in a dose-dependent manner, the release of hepatic glucose (glycogenolysis). In rats made diabetic by injection of streptozotocin, after 90 days of treatment with RPNES at a dose of 800 mg/kg BW, it appears that the drug formula promotes hepatic glucose storage (glycogenogenesis). The effects of RPNES at a dose of 800 mg/kg BW on hepatic glucose in rats are essentially identical to those obtained in rats treated with glibenclamide (10 mg/kg BW), the reference hypoglycemic and antidiabetic substance. This study also shows that in healthy rats, RPNES, administered for 28 days, does not cause changes in transaminase levels (ALAT and ASAT). Thus, it does not cause any damage to the liver of healthy rats. In rats made diabetic, then treated with RPNES for 28 days, the serum concentrations of these liver enzymes (ALAT and ASAT) decrease over time and return to normal. RPNES therefore corrects the liver damage caused by Streptozotocin. These results demonstrate that the medicinal formula composed of *Parquetina nigrescens* and *Erytrina senegalensis* has antidiabetic properties, justifying its use in traditional medicine for the treatment of diabetes.

Keywords: Diabetes, Parquetina nigrescens, Erytrina senegalensis, glycogenolysis, glycogenogenesis, streptozotocin.

INTRODUCTION

The liver is an organ that stores glucose in the form of glycogen. This mechanism is mediated by insulin produced by the islets of Langerhans in the pancreas. As a result, metabolic imbalances caused by low or absent insulin secretion can occur, leading to diabetes.

This condition is the fourth leading cause of hospitalization and death worldwide each year (Whiting *et al.,* 2011). Thus, the search for natural alternative solutions has become a scientific and medical priority. The WHO therefore encourages the integration of medicinal plants into modern healthcare systems, but also emphasizes the importance of conducting scientific studies on plant species used for therapeutic purposes to ensure their safety and efficacy (WHO, 2013).

In Ivory Coast, several plants are used alone or in combination as a medicinal recipe in traditional medicine in the treatment of diabetes. This is the case of *Parquetina nigrescens* (Periplocaceae) and *Erythrina senegalensis* (Fabaceae) which are used, combined as a

medicinal recipe, against diabetes. The aim of this work is to study the therapeutic potential of a medicinal recipe composed of *Parquetina nigrescens* (Periplocaceae) and *Erythrina senegalensis* (Fabaceae) on diabetes by evaluating its capacity to release and store hepatic glucose in healthy rats and rats made diabetic by the administration of Streptozotocin.

I. MATERIALS AND METHODS

1. MATERIALS

1.1 Plant Material

The plant material consisted of dried leaves of *Parquetina nigrescens* (Periplocaceae) and *Erythrina senegalensis* (Fabaceae). The leaves of these plants were collected in Dimbokro (Ivory Coast) in October 2018. They were identified and authenticated at the National Floristic Center (CNF) of the Félix Houphouët-Boigny University (Abidjan, Ivory Coast), where herbarium number 15031 of *Parquetina nigrescens* (Periplocaceae) and number 14625 of *Erythrina senegalensis* (Fabaceae) are located.

1.2 Animal Material

Male albino white rats, *Rattus norvegicus* (Muridae), of the Wistar strain, were used for pharmacological studies on hepatic glucose storage and release and for the determination of liver parameters, particularly transaminases. They weighed between 150 and 200 g. These rats were bred in the animal facility of the UFR Biosciences at the UFHB.

All experimental protocols on these animals are conducted in accordance with Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes and under Commission Recommendation 2007/526/EC concerning guidelines for the housing and care of animals used for experimental and other scientific purposes (Anonymous, 2010).

2. METHODS

2.1- Diabetes Induction Method

Diabetes was induced in rats by subcutaneous injection of Streptozotocin (Sigma Aldrich, Germany) dissolved in a citrate buffer solution (pH = 4.5) at a dose of 65 mg/kg BW. Fifteen minutes (15 min) later, they received a nicotinamide solution at a dose of 230 mg/kg BW also subcutaneously.

Two weeks after the Streptozotocin injection, rats with a fasting blood glucose level greater than or equal to 2 g/L were considered diabetic and selected for the study (Ekissi *et al.,* 2021).

2.2- Preparation of a medicinal recipe (RPNES) composed of an aqueous extract of *Parquetina nigrescens* (Periplocaceae) and *Erythrina senegalensis* (Fabaceae)

As is customary among traditional practitioners, 70 g of dried *Parquetina nigrescens* leaf powder and 30 g of dried *Erythrina senegalensis* leaf powder are combined (7/3 w/w) in 1 L of distilled water. The mixture is boiled at 100°C for 20 minutes. The resulting decoction is allowed to cool to room temperature (25-30°C) and filtered three times through absorbent cotton before being filtered through Whatman No. 2 filter paper, then dried in an oven (Vacutherm Vacuum Oven, France) at 50°C. The dry extract obtained is the aqueous extract of the medicinal recipe (RPNES).

2.3- Method for studying the effects of the drug recipe (RPNES) on glucose released by the liver of healthy rats

2.3.1- Experimental protocol

This study was conducted on 50 normoglycemic rats (healthy rats), with a body weight between 150 and 200 g, divided into 5 groups of 10 rats.

- Rats in group 1 (control) received 2 ml of distilled water by gavage for 28 days (duration of the experiment).
- Rats in groups 2, 3, and 4 received RPNES at doses of 400, 600, and 800 mg/kg BW, respectively.
- Rats in group 5 received 10 mg/kg BW of glibenclamide.

After 28 days of treatment, 5 animals from each group were sacrificed, and a liver fragment weighing 2 g was removed from each rat in each group. The liver fragments collected from groups 1, 2, 3, 4, and 5 were immersed in solutions S1, S2, S3, S4, and S5, respectively, containing 4 ml of glucose-lactam Mac Ewen, and then incubated at 37°C for 60 minutes. The supernatant of each solution is taken to measure the quantity of glucose, in the presence of the reagents: glucose oxidase (GOD) and peroxidase (POD).

2.3.2- Determination of Glucose Released by the Liver

The principle of this assay is that in the presence of GOD, glucose is oxidized to gluconic acid. The hydrogen peroxide released during the reaction reacts under the action of GOD with phenol and 4-aminophenazole to form a pink complex. The intensity of the color is proportional to the concentration of glucose released.

The determination of glucose released by the liver is performed using an AKEMIA MAX spectrophotometer (BIOLABO Diagnostics, France), at 500 nm, at 0 min (before the organs were dissolved), then 10, 20, 30, 40, 50, and 60 min after immersing the organs in the glucose-lacquered MacEwen solution.

2.4- Method for Studying the Effects of Drug Regimen (RPNES) on Glucose Stored by the Liver of Diabetic Rats

2.4.1 Experimental Protocol

This study was conducted on 40 Wistar rats divided into four groups of 10 rats. Their weight ranged from 150 to 200 g.

- Group 1 consisted of normoglycemic control rats (healthy rats) receiving 2 ml of distilled water orally.
- Group 2 consisted of diabetic control rats also receiving 2 ml of distilled water orally.
- Group 3 consisted of diabetic rats receiving 800 mg/kg BW of RPNES daily.
- Group 4 is the group of diabetic rats receiving glibenclamide daily at a dose of 10 mg/kg BW.

The animals are treated for 90 days.

2.4.2 Determination of Glucose Stored by the Liver

After 90 days of treatment, the animals are sacrificed and a liver fragment weighing 5 g is removed from each rat in each group, cut into small pieces, and then ground in 30 ml of 4% trichloroacetic acid. The resulting ground material is placed in a test tube and centrifuged at 4500 rpm for 5 minutes, then the supernatant is collected. 95% ethanol is then added to the supernatant (ethanol/supernatant, 2/1 v/v), then the mixture is stirred and heated slowly in a water bath until boiling.

The glycogen precipitates and the resulting suspension is cooled before being centrifuged at 4500 rpm for 10 min. 2 ml of 2.5 N sulfuric acid (H_2SO_4) are added to the pellet (precipitated glycogen) and the tube is heated for 30 min. This step allows the glycogen to hydrolyze into glucose. After hydrolysis, the tube is cooled and 1 drop of Dinitro-Phenolphthalein is added, followed by 2.5 N sodium hydroxide until a pinkish-red color is obtained. This step neutralizes the acidity of the hydrolyzate.

For each sample, the glucose thus formed is measured in the presence of GOD and POD reagents (Trinder, 1969) according to the colorimetric method of Beer (1852) and Kahou *et al.,* (2016).

The principle of the assay is that in the presence of glucose oxidase (GOD), glucose is oxidized to gluconic acid. The hydrogen peroxide released during the reaction reacts under the action of peroxidase (POD) with phenol and 4-aminophenazole to form a pink complex. The intensity of the color is proportional to the glucose concentration in the sample. The level of glucose stored by the liver is determined using the AKEMIA MAX spectrophotometer (BIOLABO Diagnostics, France) at a wavelength of 500 nm.

2.5. TRANSAMINASE DETERMINATION

2.5.1. Glutamic-oxaloacetic transaminase assay

Principle

Aspartate aminotransferase (AST) or glutamic-oxaloacetic transaminase (GOT) catalyzes the reversible transfer of the amine group from aspartate to α-ketoglutarate, with the formation of glutamate and oxalacetate. The oxalacetate produced is reduced to malate by malate dehydrogenase (MDH). During this reaction, an equivalent amount of nicotinamide adenine dinucleotide hydrogen (NADH) is oxidized to NAD+.

$$\text{Aspartate} + \alpha\text{-ketoglutarate} \xrightarrow{\text{Aspartate aminotransferase}} \text{Glutamate} + \text{Oxalacetate}$$

$$\text{Oxalacetate} + \text{NADH} + H^+ \xrightarrow{\text{Malate dehydrogenase}} \text{Malate} + NAD^+$$

The rate of NADH consumption, determined photometrically at 340 nm, is directly proportional to the activity of AST in the sample (Gella *et al.,* 1985).

✓ Reagent Composition

- Reagent 1: Tris buffer (pH 7.8) and aspartate
- Reagent 2: NADH, MDH, and α-ketoglutarate

✓ Procedure

To prepare the working solution, one tablet of Reagent 2 is dissolved in 15 mL of the buffer solution (Reagent 1), then 100 µL of serum or the standard (AST) is added to 1 mL of the working solution. One minute (1 min) after mixing, the absorbance is read every minute for 3 min at 340 nm using an AKEMIA MAX spectrophotometer (BIOLABO Diagnostics, France). The AST content is expressed in IU/L.

2.5.2. Glutamic-pyruvic transaminase assay

✓ **Principle**

Alanine aminotransferase (ALAT) or glutamic-pyruvic transaminase (GPT) catalyzes the reversible transfer of the amino group from alanine to α-ketoglutarate, forming glutamate and pyruvate. The resulting pyruvate is reduced to lactate by lactate dehydrogenase (LDH). During this reaction, an equivalent amount of NADH is oxidized to NAD+.

$$\text{Alanine} + \alpha\text{-ketoglutarate} \xrightarrow{\text{Alanine aminotransferase}} \text{Glutamate} + \text{Pyruvate}$$

$$\text{Pyruvate} + \text{NADH} + H^+ \xrightarrow{\text{Lactate dehydrogenase}} \text{Lactate} + NAD^+$$

The rate of NADH consumption, determined photometrically at 340 nm, is directly proportional to the ALT activity in the sample (Gella *et al.,* 1985).

✓ **Reagent Composition**

- Reagent 1: Tris buffer (pH 7.8) and L-alanine
- Reagent 2: NADH, LDH, and α-ketoglutarate

✓ **Procedure**

To prepare the working solution, one tablet of Reagent 2 is dissolved in 15 mL of the buffer solution (Reagent 1), then 100 µL of serum or the standard (ALT) is added to 1 mL of the working solution. One minute (1 min) after mixing, the absorbance is read every minute for 3 min at 340 nm using an AKEMIA MAX spectrophotometer (BIOLABO Diagnostics, France). The ALAT content is expressed in IU/L.

2.6. Statistical Analysis and Graphing Methods

Data analysis was performed using GraphPad Instat software (San Diego, CA, USA). Results were presented as the mean, followed by the standard error of the mean (M ± SEM). The difference between two values was determined using the Turkey-Kramer comparison test and was considered insignificant for $p > 0.05$, marginally significant for $p < 0.05$ (*), significant for $p < 0.01$ (**), and highly significant for $p < 0.001$ (***).

GraphPad Prism 8 software (San Diego, CA, USA) was used to plot the graphs.

II- RESULTS

1. Effects of the drug recipe (RPNES) and glibenclamide on glucose release from the liver of normoglycemic rats

The glucose concentration of each of the glucose-lactam Mac Ewen solutions before the experiment was 2 g/L. The concentration of the control solution (S1), containing the liver of control rats that received distilled water after 60 minutes, increased from 2 g/L at the beginning of the experiment to 2.69 g/L at the end of the experiment (after 60 minutes); a 34.5% increase in glucose levels. The glucose concentrations of solutions S2, S3 and S4, which received the liver of rats treated with RPNES at the respective doses of 400, 600 and 800 mg/kg BW, are 2.64 g/L, 2.49 g/L and 2.34 g/L respectively, 60 minutes after the organs have been in these solutions. In these solutions, the glucose level therefore increases by 32% (S2), 24.5% (S3) and 17% (S4) compared to Initial glucose concentration. In solution S5, which contains the livers of rats treated with glibenclamide at a dose of 10 mg/kg BW, the glucose concentration at the end of the experiment was 2.31 g/L; a 15.5% increase compared to the initial glucose concentration (2 g/L).

Figure 1 shows the hepatic glucose concentration of rats that received or did not receive RPNES or glibenclamide. It appears that the hepatic glucose level of rats treated with RPNES at 400 mg/kg BW decreased, but not significantly ($p > 0.05$), compared to the liver glucose level of control rats. However, compared with the liver glucose level of control rats, the liver glucose concentrations of rats treated with RPNES at doses of 600 and 800 mg/kg BW decreased in a dose-dependent manner, with decreases of 8.18% ($p < 0.05$) and 12.27% ($p < 0.01$), respectively, compared with the liver glucose level of control rats. Compared with the liver glucose level of control rats, the decrease in liver glucose concentrations of rats treated with Glibenclamide at 10 mg/kg BW (12.64%) was similar ($p > 0.05$) to that of rats treated with RPNES at a dose of 800 mg/kg BW.

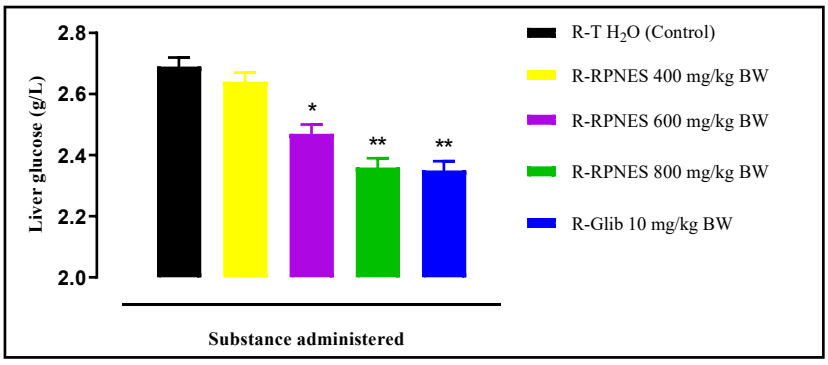

Figure 1: Dose-response effects of drug recipe (RPNES) and Glibenclamide on hepatic glucose release of normoglycemic rats, after 60 min of liver incubation

*n = 5; * p < 0.05; ** p < 0.01* compared to control rats

R-T H_2O: Control rats receiving only distilled water

R-RPNES: Rats treated with RPNES at doses of 400, 600 and 800 mg/kg BW

R-Glib: Rats treated with Glibenclamide at a dose of 10 mg/kg BW

2. Effects of the drug recipe (RPNES) and glibenclamide on glucose stored in the liver of diabetic rats

At the end of the 90-day experiment, in healthy (untreated) control rats, the level of stored hepatic glucose was 0.56 ± 0.04 g/L (Figure 2). In contrast, in diabetic control rats, this level was 0.25 ± 0.03 g/L; a highly significant decrease ($p < 0.001$) in the level of stored hepatic glucose of 50% compared to that of healthy controls. When diabetic rats were treated for 90

days with RPNES at a dose of 800 mg/kg BW or Glibenclamide at a dose of 10 mg/kg BW, the levels of stored hepatic glucose measured were 0.49 ± 0.03 g/L and 0.52 ± 0.07 g/L, respectively; i.e., increases in stored hepatic glucose levels of 77.41 % and 87.09 % respectively ($p < 0.001$). Thus, when diabetic rats were treated with RPNES or Glibenclamide, the levels of stored hepatic glucose measured after 90 days became substantially identical ($p > 0.05$) to those of healthy control rats.

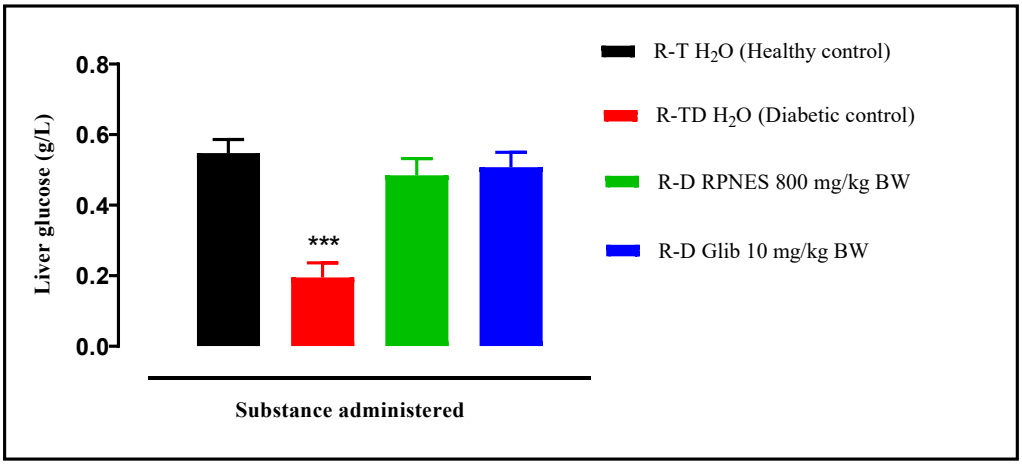

Figure 2: Effects of the drug recipe (RPNES) and glibenclamide (Glib) on hepatic glucose storage in diabetic rats, after 90 days of treatment

*n = 10; * p < 0.05; *** p < 0.001 compared to healthy control rats*
R-T H_2O: Normoglycemic control rats receiving only distilled water
R-TD H_2O: Diabetic control rats receiving only distilled water
R-D RPNES: Diabetic rats treated with RPNES at 800 mg/kg BW
R-D Glib: Diabetic rats treated with glibenclamide (10 mg/kg BW)

3. Effects of the drug recipe (RPNES) on serum aspartate aminotransferase (AST) concentrations in healthy and diabetic rats

During the 28 days of experiments, serum aspartate aminotransferase (AST) concentrations in healthy control rats and healthy rats treated with RPNES at a dose of 800 mg/kg BW did not vary significantly ($p < 0.05$) and were statistically identical. They were approximately 48.5 ± 3 IU/L (Figure 3).

When rats were made diabetic by streptozotocin, serum AST concentrations increased significantly over time. From 48.5 ± 3 IU/L in healthy rats, it increased to 80 ± 4.1 IU/L after diabetes induction; or 64.94% increase ($p < 0.001$), then it stabilizes ($p > 0.05$) until the end of the experiment. In diabetic rats, after 7 days of treatment of diabetic rats with RPNES at a dose of 800 mg/kg BW, there is a decrease in the serum concentration of AST which becomes significant ($p < 0.05$) on the 14th day, then continues until the 28th day of treatment. Thus, on the 28th day, the serum concentration of AST becomes statistically identical ($p > 0.05$) to that of healthy control rats.

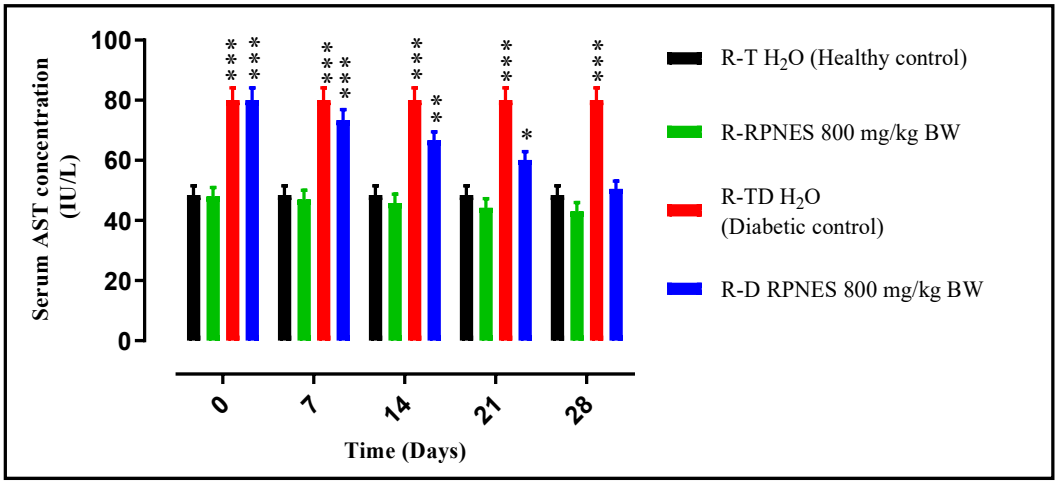

Figure 3: Effects of the drug recipe (RPNES) on serum aspartate aminotransferase (AST) levels in healthy and diabetic rats

4. Effects of the drug recipe (RPNES) on serum alanine aminotransferase (ALT) levels in healthy and diabetic rats

The serum alanine aminotransferase (ALT) levels in healthy control rats did not vary significantly over the 28 days of experimentation and were statistically identical ($p > 0.05$) to that of healthy rats treated with 800 mg/kg BW of RPNES. It is thus of the order of 38.5 ± 4.5 IU/L (Figure 4).

When rats are made diabetic by Streptozotocin, the serum ALT concentration increases significantly ($p < 0.001$), going from 38.5 ± 4.5 IU/L to 62.25 ± 3.6 IU/L; i.e., a 61.69 % increase. This ALAT level stabilizes ($p > 0.05$) thereafter until the end of the experiment. From the 7th day of treatment of diabetic rats with RPNES at a dose of 800 mg/kg BW, there appears a progressive decrease, as a function of time, of the serum concentration of ALT which becomes insignificant ($p < 0.05$) from the 14th day of treatment. Thus, on the 28th day of treatment, the serum concentration of ALT returns to normal, statistically identical ($p > 0.05$) to that of healthy control rats.

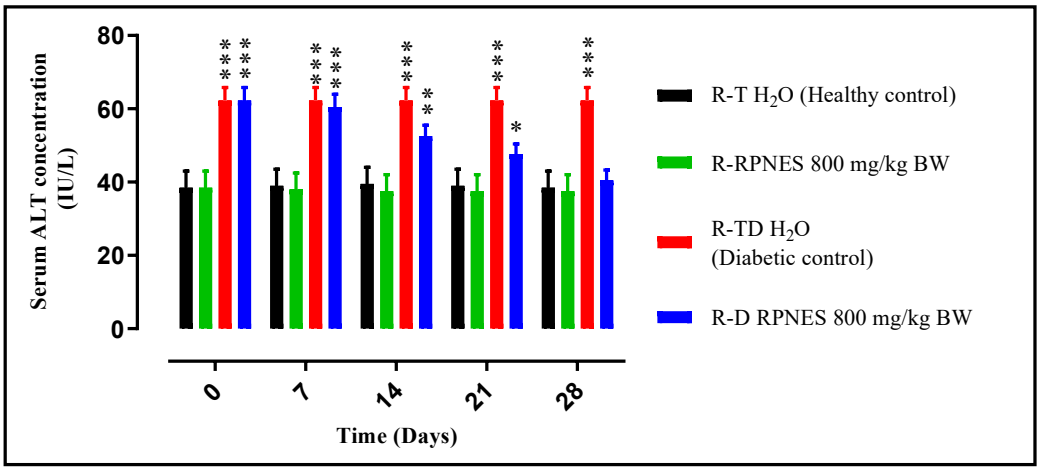

Figure 4: Effects of drug recipe (RPNES) on serum alanine aminotransferase (ALT) levels in healthy and diabetic rats ***n = 10***

** $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ compared to healthy control rats*
R-T H_2O: Normoglycemic control rats receiving only distilled water
R RPNES: Normoglycemic rats treated with RPNES at 800 mg/kg BW
R-TD H_2O: Diabetic control rats receiving only distilled water
R-D RPNES: Diabetic rats treated with RPNES at 800 mg/kg BW

III. DISCUSSION

The level of glucose released from the liver of normoglycemic control rats increases progressively over time. It therefore appears that the liver normally releases glucose (Claude, 1953). This has been demonstrated by Claude Bernard since 1853. He showed that under physiological conditions, the liver releases glucose to meet the body's physiological needs (Claude, 1953). The production of hepatic glucose and its release into the bloodstream are thought to be due to the hydrolysis of glycogen into glucose by the enzyme glycogen phosphorylase (Madsen, 1991).

Compared to normoglycemic control rats, treatment of normoglycemic rats with the drug recipe (RPNES) at doses of 400, 600, and 800 mg/kg BW resulted in a dose-dependent decrease in the level of glucose released from the liver. These results are similar to those of Méa *et al.,* (2017) who showed that the aqueous extract of *Justicia secunda* (Acanthaceae) reduces the release of hepatic glucose. This effect of RPNES would support the ability of this medicinal recipe to maintain glucose stored in the liver, and therefore its hypoglycemic and antihyperglycemic potential (Ekissi *et al.,* 2021).

Glucose release from the liver of rats treated with RPNES at a dose of 800 mg/kg BW was substantially identical to that of rats treated with glibenclamide at a dose of 10 mg/kg BW. Thus, the reduction in hepatic glucose release in the presence of RPNES could be explained by an inhibition of the enzyme glycogen phosphorylase, the mechanism by which glibenclamide, the reference hypoglycemic substance, acts (Kahou *et al.,* 2016).

Injection of Streptozotocin (diabetogenic compound) into rats results in an increase in blood sugar which remains high (14 days after injection), reflecting the onset of experimental diabetes following necrosis of pancreatic β cells. Indeed, Streptozotocin (STZ) is an antibiotic isolated from a strain of bacteria; notably *Streptomyces achromogenes* (Vavra *et al.,* 1959), which causes massive destruction of β cells in the islets of Langerhans, thus leading to diabetes. Streptozotocin is taken up by the pancreatic β cell via the GLUT2 glucose transporter. STZ impairs glucose oxidation and causes insulitis and a decrease in the sensitivity of the β cell to glucose (Szkudelski, 2001). It also induces the formation of free radicals which contribute to the destruction of

pancreatic β cells. After their formation, these molecules act in synergy with STZ to generate damage at the DNA level, thus leading to the diabetic state (Pavana *et al.,* 2007).

In rats made diabetic by Streptozotocin, the level of stored hepatic glucose is reduced by 50%, compared to that of healthy control rats (non-diabetic). The decrease in hepatic glucose storage observed in diabetic rats is explained by an alteration in insulin secretion after administration of Streptozotocin. Indeed, Aughsteen (2000) and Szkudelski (2001) showed that Streptozotocin decreases insulin secretion because Streptozotocin causes a release of nitric oxide (NO) inside the hepatic cell with alkylation of DNA, leading to the depletion of ATP in the β cells of the islets of Langerhans. These effects result in a reduced storage of glycogen in the liver of rats made diabetic (Kebièche *et al.,* 2011). Streptozotocin injection causes a reduction in insulin secretion. This insulinopenia could be the cause of glycogen degradation, because insulin acts on the liver by inhibiting glycogenolysis (Girard, 2008).

When diabetic rats were treated with RPNES for 90 days, the level of stored hepatic glucose increased significantly and became almost identical to that of healthy control rats. These results show that RPNES promotes glucose storage in the liver. The effect of RPNES on hepatic glucose storage is similar to that of Glibenclamide. It can therefore be suggested that, like Glibenclamide, the mechanism of action of RPNES is through its direct action on GLUT2 receptors (glucose transporter in the cell) or through the stimulation of residual β cells of the pancreas to allow glucose storage. Similar results were reported by Kebièche (2009) and Ladouari (2013) who respectively showed that flavonoid extracts of *Ranunculus repens* (Ranunculaceae) and the aqueous extract of *Zygophyllum album* (Zygophylaceae) promote glucose storage in the liver of diabetic rats.

To examine the effects of RPNES aqueous extract on liver function, healthy and diabetic rats were treated with this extract for 28 days, and serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels were then measured.

RPNES, at a dose of 800 mg/kg BW, appeared to have no significant effect on ALT and AST levels in healthy rats. Similar effects were obtained by N'guessan *et al.,* (2020) with the aqueous extract of *Solanum torvum* (Solanaceae) administered for 28 days to healthy rats at a dose of 250 mg/kg BW. The fact that RPNES at 800 mg/kg BW does not cause changes in the levels of these transaminases (ALT and AST) in treated healthy rats indicates that this extract, at this dose, does not cause liver damage (Mikolo *et al.,*2020).

In rats made diabetic by Streptozotocin, a significant increase in liver enzymes ALT and AST was noted, which is an indicator of hepatotoxicity. These results are consistent with those of Al-Ghaithi *et al.,* (2004) who observed an increase in plasma liver enzymes following the injection of Streptozotocin. On the other hand, administered to diabetic rats, RPNES at a dose of 800 mg/kg BW decreased liver levels of ALT and AST, which returned to normal after 28 days of treatment. RPNES therefore cancels the hepatotoxic effects of Streptozotocin. It can be concluded that the aqueous extract of the drug recipe has hepatoprotective effects.

Similar results were obtained with extracts of *Tetracera potatoria* (Dilleniaceae) and *Solanum torvum* (Solanaceae) administered to rats at doses of 2000 mg/kg BW and 250 mg/kg BW by Mikolo *et al.,* (2020) and N'guessan *et al.,* (2020), respectively. Al-Ghaithi *et al.,* (2004) also showed that oral administration of the aqueous extract of colocynth seeds "*Citrullus colocynthis*" in rats made diabetic by streptozotocin significantly reduced AST levels and caused a significant decrease in alkaline phosphate levels.

These effects of RPNES on transaminases could be due to the presence of antioxidant compounds in this extract. Indeed, it was reported by Guenzet *et al.,* (2014) that *Zygophyllum gaetulum* (Zygophyllaceae) would oppose the damage caused by Streptozotocin, at the liver level thanks to its richness in antioxidants.

IV. CONCLUSION

This study shows that the aqueous extract of the medicinal recipe, composed of *Parquetina nigrescens* and *Erythrina senegalensis* (RPNES), has effects on liver function. Indeed, RPNES has antidiabetic properties and appears to act by inhibiting the release of glucose from the liver (glycogenolysis) and promoting hepatic glucose storage (glycogenogenesis) in diabetic rats. Furthermore, this medicinal recipe does not cause liver damage in healthy rats and, in diabetic rats, corrects streptozotocin-induced hepatotoxicity.

These results justify the use of the medicinal recipe, composed of *Parquetina nigrescens* and *Erythrina senegalensis*, in traditional medicine to treat diabetes.

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