Vol. 17(6), pp. 110-117, July 2023
DOI: 10.5897/AJPP2023.5356
Article Number: 3645DBB70915
ISSN 1996-0816

http://www.academicjournals.org/AJPP

ACADEMIC JOURNALS
expand your knowledge

African Journal of Pharmacy and Pharmacology

Full Length Research Paper

Effects of traditional remedy *Sarenta* and glibenclamide combination on hyperglycemia orally induced in rats

Kouakou Sylvain*, Yapo Guy, Djadji Ayoman, Adehouni Yacouba, Kouakou-Siransy G. and Irié-N'Guessan G.

Laboratory of Pharmacology, UFR Pharmaceutical and Biological Sciences, Félix Houphouët Boigny University, 01 BP V34 Abidjan, Ivory Coast.

Received 4 April, 2023; Accepted 2 June, 2023

Herbal preparations are commonly used by low-income populations to treat diabetes. The objective of this work was to evaluate interaction between *Sarenta* remedy with antidiabetic drug such as glibenclamide. Experimental study was carried out according to protocol described by Kambouche. Before giving different solutions on study, baseline blood glucose was taken using "One call plus" glucometer, then glycaemia measure was determined every hour (T1h, T2h, T3h, T4h and T5h). *Sarenta* (3.33 mg b.w.) + glibenclamide (10 mg b.w.) significant decreased sugar blood at 1st to 2nd hour followed by hypoglycemia from 3rd to 5th hour. Glycemia reduction was respectively 24.83% (T2h); 37.66% (T3h); 46.50% (T4h) and 55.33% (T5h). *Sarenta* (6.66 mg b.w.) + glibenclamide (10 mg b.w.), also decreased glycaemia from 1st to 2nd hour around 15.41% (T2h), then reached normal value from 2nd to 5th hour. The last combination *Sarenta* (13.33 mg b.w.) + Glibenclamide (10 mg b.w.) had same effects as previously with normal glycaemia value close to 12.25% (T2h). *Sarenta* (6.66 and 13.33 mg b.w.) + glibenclamide 10 mg b.w. interaction lowered hyperglycemia without induced hypoglycemia. This euglycemic effect makes this remedy a potential phytomedicine candidate that could be combined with conventional drugs for diabetes treatment.

Key words: Blood sugar, conventional drugs, diabetes, interactivity.

INTRODUCTION

Diabetes is a metabolic disease characterized by chronic hyperglycemia linked either to insufficient production of insulin, or absence of its action, or both (Grimaldi, 2009). The number of people living with diabetes constitute a global public health problem (WHO, 2016), which complications can cause blindness, kidney failure, lower limb amputation and many other long-term consequences that seriously affect quality of life (Collins et al., 2015; Moxey et al., 2011). In Ivory Coast, the prevalence of diabetes was 5.6% in men and 4.4% in women (Agbre-Yace et al., 2016; WHO, 2016). Many molecules used for diabetes treatment have significant side effects which push low-income populations chose natural remedies to take care because of their effectiveness and their low

*Corresponding author. E-mail: lsk_land@yahoo.fr. Tel: +225 0707886877.

Figure 1. *Sarenta* remedy in 500 ml bottle.
Source: Photographed by Kouakou S. Landry October 8, 2020

cost. *Sarenta* is remedy registered with National Program for Promotion of Traditional Medicine (PNPMT) of Ministry in charge of Health in Côte d'Ivoire. This preparation composed with 14 plants, is commonly used traditionally against high blood pressure, inflammation, immunodeficiency, malaria, viral diseases, pains and fever. Several studies published by our team on *Sarenta* remedy have proved its analgesic and anti-inflammatory properties without ulcerogenic risk (Kouakou et al., 2017; Effo et al., 2018), antihyperglycemic (Fattoh, 2017; N'guessan-Irié et al., 2019) and antioxidant potential.

However, the interaction between the remedy *Sarenta* and a conventional anti-diabetic drug has not yet studied, and the objective of this study was to evaluate interaction between *Sarenta* remedy and glibenclamide, the reference antidiabetic molecule.

MATERIAL

Animal material

Animals used for this study provided from Training and Research Unit in Pharmaceutical and Biological Sciences-Abidjan were *wistar* rats (*Rattus norvegicus)* male and female sex (Festing, 1979) with weight around 170 ± 22 g.

Rats were acclimatized (temperature at 22 ± 3° C and humidity at 50-60% with a cycle of 12 h of light and 12 h of darkness) in plastic cages containing sawdust and bottles which allowed them to have free access to drink water.

Animals' litter was renewed every 2 days and the diet consisted of pellets enriched with fish-based products, minerals, oil, lysine, methionine and vitamin additives (A, B, D3, E).

Presentation of *Sarenta* remedy

Sarenta is a traditional health remedy based on several plants, including *Ageratum conyzoides*, *Cassia occidentalis*, *Eucalyptus globulus*, *Ocimum gratissimum*, *Moringa oleifera, Tamarindus indica*, *Newbouldia leavis*, *Mikania cordata, Olax subscorpioideae* and more others. This product is an Ivorian traditional healer property, registered in the database of the Ministry in charge of health in Côte d'Ivoire. *Sarenta* is a brownish aqueous suspension, with characteristic odor and bitter taste, marketed in a plastic bottle of 500 mL (Figure 1). According to author and promoter of this remedy, *Sarenta* has been sold for more than twenty years and is indicated for treatment of various pathologies such as diabetes, malaria, viral diseases, pains, fever and immunodeficiency.

Chemicals products and solvents

1) Glucose powder (D glucose, Prolabo ®, Cambodia);
2) Sodium chloride (NaCl) 0.9% (Pharmivoire®, Ivory Coast)
3) Distilled water (Pharmivoire®, Ivory Coast);
4) Glibenclamide 5 mg (Daonil ®, Sanofi Aventis-France)

METHODS

Sarenta dry extract mass estimation

Sarenta remedy were introduced into an oven for 1 h drying at 60° C. ± 5° C. Mass of dry residue was obtained by difference between mass of beaker after drying and that of empty beaker. *Sarenta* 10mL contains 0.067 g or 67 mg dry extract.

Sarenta remedy concentration range preparation

From dose prescribed by the promoter of *Sarenta* remedy, we estimated experiment dose according to Shin et al. (2010) and this dose was 13.33 mg b.w. in rats. A concentration range at 13.33; 6.66 and 3.33 mg b.w. was prepared for the test by homogenized 39.90 mg dry *Sarenta* remedy in 30 mL of physiological water to obtain a solution at 13.33 mg/kg (1.33 mg/mL). From this stock solution a half (½) dilution was done to obtain two daughter solutions at 6.66 mg b.w. (0.66 mg/mL) and 3.3 mg b.w. (0.33 mg/mL).

Glibenclamide 10 mg b.w. preparation (reference solution)

Glibenclamide used was in scored tablet dosed at 5 mg. Twelve tablets were introduce in 60 mL of physiological water to prepare glibenclamide solution at 10 mg b.w. (1 mg/mL).

Glucose 5 g b.w. solution preparation (0.5 g/mL or 500 mg/mL)

Thirty grams of glucose anhydrous powder were mixed with 60 mL of physiological water to obtain glucose solution at 5 g/kg (0.5 g/ml). This solution was used to induce hyperglycemia in animals.

Evaluation of interaction between *Sarenta* and glibenclamide in hyperglycemic rats

Method used was described by Kambouche et al. (2011) and the test consisted on oral glucose overload at rate of 5 g/kg b.w. One hour later, animals were treated with various substances under study (0.9% NaCl, *Sarenta* extracts, glibenclamide) and glycaemia was evaluated during five hours (T1h, T2h, T3h, T4h, T5h).

Operating procedure

The baseline glycaemia of rats, fasted 6 h before experiment, was

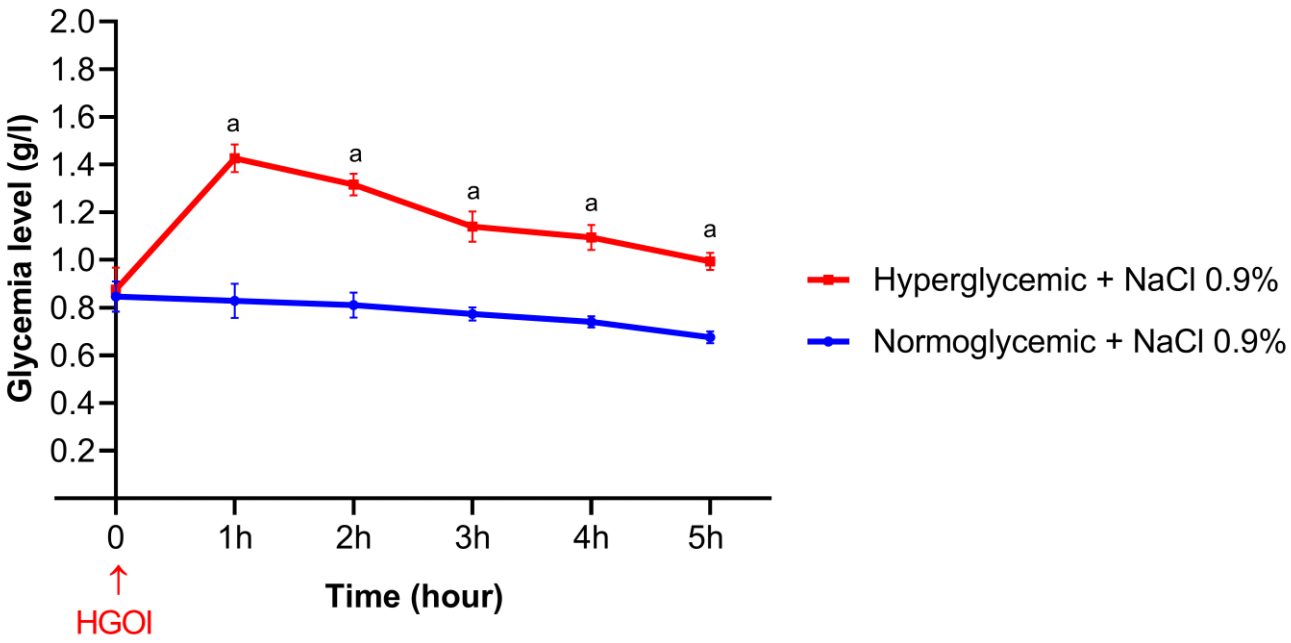

Figure 2. Glucose overloads effect on baseline glucose level. (a) Glibenclamide group compared to Normoglycemic control group: T1h (p = 0.001); T2h (p = 0.4912); T3h (p = 0.0342); T4h (p = 0.001); T5h (p = 0.001). (b) Glibenclamide group compared to Hyperglycemic control group: T1h (p = 0.001); T2h (p = 0.001); T3h (p = 0.001); T4h (p = 0.001); T5h (p = 0.001)
Source: Graph Pad Prism software (version 8.0.2)

measured by taking blood from the tail vein. Glucose level was twice reading on glucometer "One Call Plus". Then all rats were overload of glucose and one hour later blood sugar was measured again, and only hyperglycemic rats (blood sugar increase at least 0.7 g/l) were retained for the test. These animals were reparteed in five groups of six rats (to which we added a normoglycemic control group) have received by gavage at rate of 1 mL/100 g various solutions under study as follows:

1) Group 1 (Normoglycemic control group): normoglycemic rats received 0.9% NaCl physiological water
2) Group 2 (Hyperglycemic control group): hyperglycemic rats received 0.9% NaCl physiological water
3) Group 3 (Reference): hyperglycemic rats received Glibenclamide 10 mg/kg
4) Group 4 (Test 1): hyperglycemic rats simultaneously received *Sarenta* + Glibenclamide respectively at doses of 3.3 mg b.w. and 10 mg b.w.
5) Group 5 (Test 2): hyperglycemic rats simultaneously received *Sarenta* + Glibenclamide respectively at doses of 6.7 mg b.w. and 10 mg b.w.
6) Group 6 (Test 3): hyperglycemic rats simultaneously received *Sarenta* + Glibenclamide respectively at doses of 13.7 mg b.w. and 10 mg/kg

After substances (0.9% NaCl, *Sarenta* extracts, Glibenclamide) administration, glycemia was again measured every hour for 5 h, at T1h, T2h, T3h, T4h and T5h. Blood glucose change percentage was determined following formula (Kambouche et al., 2011):

$$VG = \frac{Gt - G0}{G0} \times 100$$

G0: Blood sugar at time T0 (Baseline blood sugar in rats fasted for 6 h); Gt: Glycemia at a time t after administration of different substances

Data analysis

Data were entered with Microsoft Office Excel 2013 spreadsheet and analyzed using Graph Pad Prism software (version 8.0.2). Groups' results given as mean ± standard deviation (SD) were compared by variance analysis (ANOVA) at risk α 5% with Tukey's statistic test. From T1h to T5h, blood glucose values were compared to normoglycemic control group and hyperglycemic control group.

Ethical considerations

Experimental procedures carried out complied with guidelines recommendations for care and use of laboratory animals, including declarations of European Union concerning animals' manipulations (OECD 407, 2008; Louhimies, 2002).

RESULTS

Hyperglycaemia orally induced

Figure 2 shows evolution of glycemia after administration of 5 g b.w. glucose solution.

One hour after glucose administration, blood glucose initially at 0.87 g/dl ± 0.093 went up to 1.42 g/dl ± 0.058 (T1h), then gradually decreased to 1.31 g/dl ± 0.046 (T2h); 1.14g/dl ± 0.063 (T3h); 1.09g/dl ± 0.053 (T4h) and

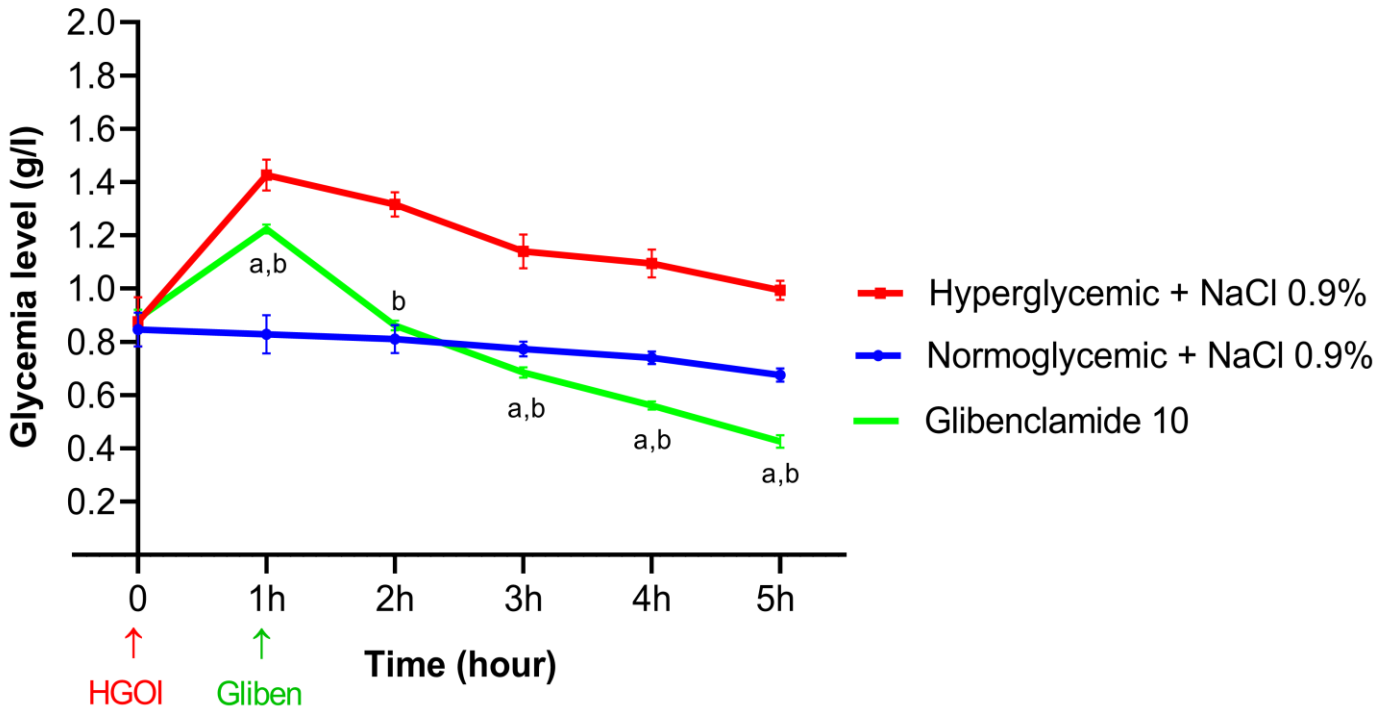

Figure 3. Hyperglycemia evolution after glibenclamide administration. (a): Glibenclamide group compared to Normoglycemic control group: T1h (p = 0.001); T2h (p = 0.4912); T3h (p = 0.0342); T4h (p = 0.001); T5h (p = 0.001). (b): Glibenclamide group compared to Hyperglycemic control group: T1h (p = 0.001); T2h (p = 0.001); T3h (p = 0.001); T4h (p = 0.001); T5h (p = 0.001).
Source: Graph Pad Prism software (version 8.0.2)

0.99 g/dl ± 0.036 (T5h) representing respectively 42.66% (T1h); 31.66% (T2h); 14% (T3h); 9.41% (T4h) and less than 0.66% (T5h) of its initial value. Compared to normoglycemic control group, blood glucose level at T1h increase around 41.93% and at following hours (T2h to T5h), hyperglycemia had gradually decreased but still remained high respectively at 38.48; 32.16; 32.36 and 32.04%.

Glibenclamide effect on hyperglycaemia orally induced

Figure 3 shows hyperglycemia evolution after administration of glibenclamide 10 mg b.w.

One hour after glucose administration, blood glucose initially at 0.88 g/dl ± 0.033 went up to 1.22 g/dl ± 0.017 (T1h), then quickly decreased to 0.86 g/dl ± 0.018 (T2h); 0.68 g/dl ± 0.019 (T3h); 0.56 g/dl ± 0.016 (T4h) and 0.42g/dl ± 0.023 (T5h) representing respectively 22.33% (T1h); and less than 13.83% (T2h); 31.50% (T3h); 43.91% (T4h) and 57.33% (T5h) of its initial value. Compared to normoglycemic control group, blood glucose level at T1h increase around 32.28% then decreased to reach normal value at T2h followed by hypoglycemia start representing 12;89% (T3h); 31.94% (T4h) and 58.20% (T5h).

Effect of *Sarenta* and glibenclamide combination on hyperglycaemia orally induced

Figure 4 describes hyperglycemia evolution after treatment with combination of *Sarenta* 3.33 mg b.w. and glibenclamide 10 b.w.

One hour after glucose administration, blood glucose initially at 0.88 g/dl ± 0.033 went up to 1.22 g/dl ± 0.084 (T1h), then decreased to 0.75 g/dl ± 0.065 (T2h); 0.62 g/dl ± 0.013 (T3h); 0.53 g/dl ± 0.055 (T4h) and 0.44g/dl ± 0.030 (T5h) representing respectively 22.50% (T1h); and less than 24.83% (T2h); 37.66% (T3h); 46.50% (T4h) and 55.33% (T5h) of its initial value. Compared to normoglycemic control group, blood glucose level at T1h increase around 32.38% then decreased to reach normal value close to 7.76% at T2h; followed by hypoglycemia start representing 24;06% at T3h; 38.31% at T4h and 51.11% at T5h.

Figure 5 describes hyperglycemia evolution after treatment with combination of *Sarenta* 6.66 mg b.w. and glibenclamide 10 mg b.w. One hour after glucose administration, blood glucose initially at 0.83 g/dl ± 0.114 went up to 1.23 g/dl ± 0.053 (T1h), then decreased to 0.84 g/dl ± 0.082 (T2h); 0.73 g/dl ± 0.022 (T3h); 0.67 g/dl ± 0.020 (T4h) and 0.60g/dl ± 0.007 (T5h) representing respectively 23.83% (T1h); and less than 15.41% (T2h); 27.00% (T3h); 32.50% (T4h) and 39.16% (T5h) of its

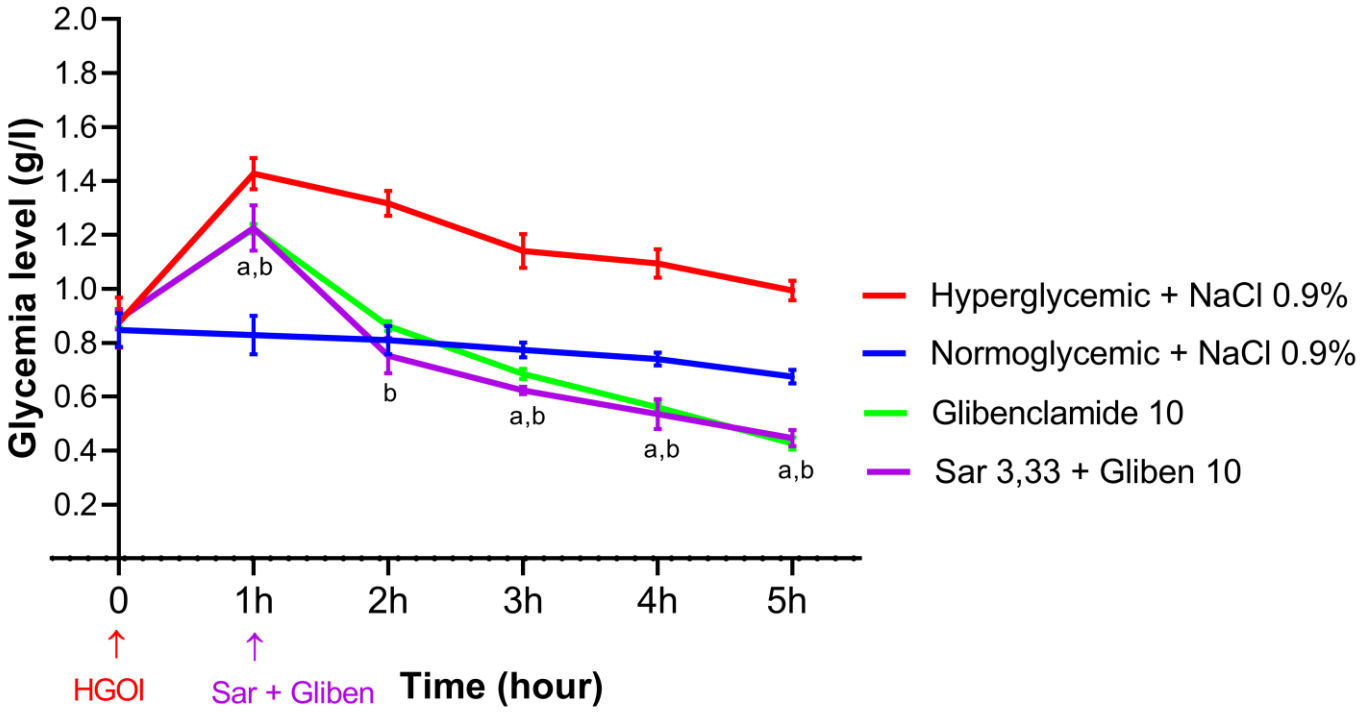

Figure 4. Hyperglycemia evolution after *Sarenta* 3.33 and glibenclamide 10 administration. (a): Sarenta 3.33 + gliben 10 group compared to Normoglycemic control group: T1h (p = 0.001); T2h (p = 0.3508); T3h (p = 0.001); T4h (p = 0.001); T5h (p = 0.001). (b): Sarenta 3.33 + gliben 10 group compared to Hyperglycemic control group: T1h (p = 0.001); T2h (p = 0.001); T3h (p = 0.001); T4h (p = 0.001); T5h (p = 0.001).
Source: Graph Pad Prism software (version 8.0.2)

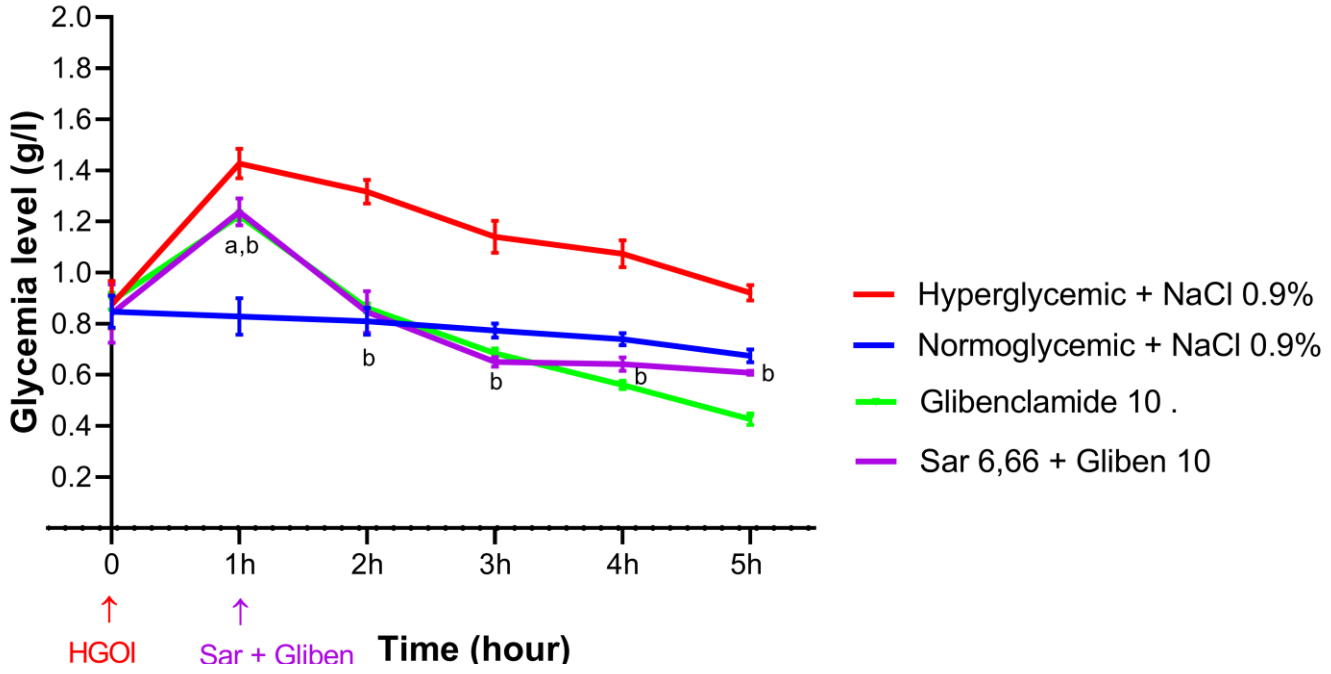

Figure 5. Hyperglycemia evolution after *Sarenta* 6.66 and glibenclamide 10 administration. (a): Sarenta 13.33 + gliben 10 group compared to Normoglycemic control group: T1h (p = 0.001); T2h (p = 0.1973); T3h (p = 0.9929); T4h (p = 0.1050); T5h (p = 0.9982). (b): Sarenta 13.33 + gliben 10 group compared to Hyperglycemic control group: T1h (p = 0.021); T2h (p = 0.001); T3h (p = 0.001); T4h (p = 0.001); T5h (p = 0.001)
Source: Graph Pad Prism software (version 8.0.2)

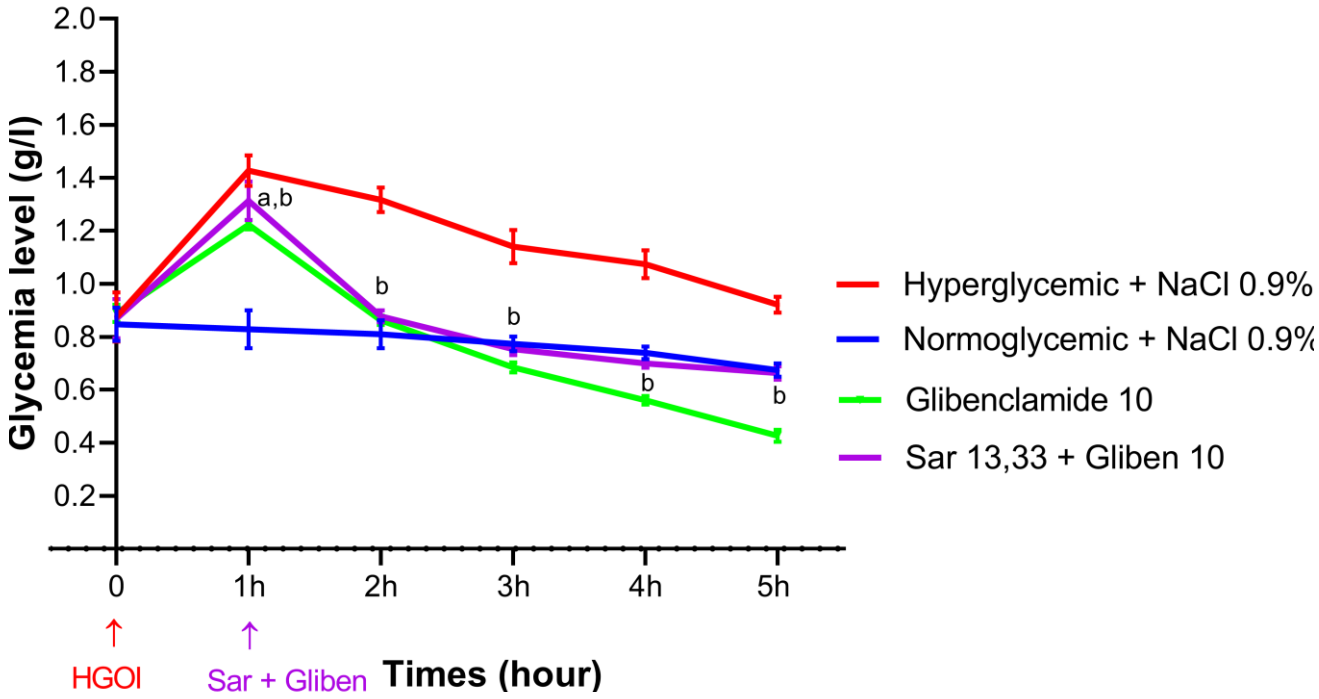

Figure 6. Hyperglycemia evolution after *Sarenta* 13.33 and glibenclamide 10 administration. (a): Sarenta 13.33 + gliben 10 group compared to Normoglycemic control group: T1h (p = 0.001); T2h (p = 0.1973); T3h (p = 0.9929); T4h (p = 0.1050); T5h (p = 0.9982). (b): Sarenta 13.33 + gliben 10 group compared to Hyperglycemic control group: T1h (p = 0.021); T2h (p = 0.001); T3h (p = 0.001); T4h (p = 0.001); T5h (p = 0.001).
Source: Graph Pad Prism software (version 8.0.2)

initial value. Compared to normoglycemic control group, blood glucose level at T1h increase around 33.10% then decreased to reach normal value from T2h to T5h representing 4;23% (T2h); 5;93% (T3h); 9.62% (T4h) and 10.95% (T5h).

Figure 6 describes hyperglycemia evolution after treatment with combination of *Sarenta* 13.33 mg b.w. and glibenclamide 10 mg b.w.

One hour after glucose administration, blood glucose initially at 0.86 g/dl ± 0.074 went up to 1.31 g/dl ± 0.072 (T1h), then decreased to 0.87 g/dl ± 0.022 (T2h); 0.75 g/dl ± 0.024 (T3h); 0.66 g/dl ± 0.015 (T4h) and 0.66g/dl ± 0.025 (T5h) representing respectively 31.33% (T1h); and less than 12.25% (T2h); 24.33% (T3h); 33.58% (T4h) and 33.75% (T5h) of its initial value. Compared to normoglycemic control group, blood glucose level at T1h increase around 36.92% then decreased to reach normal value from T2h to T5h representing 7.69% (T2h); 2;20% (T3h); 11.41% (T4h) and 1.88% (T5h).

DISCUSSION

General study objective was to evaluate interaction between *Sarenta* remedy and glibenclamide, the reference antidiabetic molecule. Experiment on rats which consisted to administrate orally glucose overload at 5g b.w., followed by administration of different substances on study, enabled us to make following observations:

Oral glucose overload

Oral administration of 5 g b.w. of the glucose solution in fasting animals caused hyperglycaemia from 1st hour followed by a gradual fall during 5 h without reaching normal values during the experiment. Physiologically, in face of hyperglycemia, Langerhans β cells islets are stimulated and produce insulin (Magnan and Ktorza, 2005), a hormone that facilitates the entry of glucose into muscle cells, adipocytes and hepatocytes (Sherwood et al., 2013; Tremblay et al., 2009), allowing blood sugar to normalize over time.

Our results are similar to those of N'guessan -Irié et al. (2019) who showed in their work focus on antihyperglycemic activity and hypoglycemic risk of *Sarenta* that orally glucose solution at 5 g b.w. administration in rats led to hyperglycemic peak at 1st hour followed by its decline from 2nd hour. Rasolofoson et al. (2017) work also brought out same findings that we observed because these researchers, using an extract codified No. 4 in experimental hyperglycemic model on mice, revealed that glucose solution administration by oral route increases blood glucose level until a peak at

1st hour, followed by drop of this value from 2nd hour until 5th hour.

Glibenclamide effect on hyperglycemia orally induced

Glibenclamide at 10 mg b.w. lowered hyperglycemia orally induced in animals. The drop in blood sugar with this molecule appeared from 2nd hour and continued to reach hypoglycaemia values from 3rd to 5th hour. The hypoglycaemia observed in animals is well known and is an adverse effect of glibenclamide, which is a second-generation secretagogue sulfonylurea with a short half-life (ANSM, 2009), inducing exocytosis of insulin granules (Thulé and Umpierrez, 2014; Gribble and Reimann, 2003), at origin of hypoglycaemia outside meals.

Sarenta with glibenclamide interaction effect in hyperglycemic rats

Sarenta 3.33 mg b.w., and glibenclamide 10 mg b.w. induced animals' glycemia decrease at 2nd hour around normal value, followed by appearance of hypoglycaemia at 3rd hour until 5th hour, with kinetics progression similar to that of Glibenclamide 10 mg b.w. Interaction of solutions does not seem to be beneficial because at these doses, which was the lowest evaluated in our study, *Sarenta* remedy would be in too small quantity to correct hypoglycaemia induced by glibenclamide. When *Sarenta* dose was doubled to 6.66 mg b.w., hyperglycaemia was normalized from 2nd hour until end of the experiment without onset hypoglycaemia. Interaction of solutions seems to be beneficial because at this median dose evaluated in our study, *Sarenta* remedy corrected glibenclamide hypoglycaemic effect. Keep going on test using *Sarenta* at 13.33 mg b.w., we observed same kinetics progression effect like previous dose. Presence of various plants in *Sarenta* remedy as *Ageratum conyzoides* (Nyunaï, 2015), *Cassia occidentalis* (Arya et al., 2013), *Eucalyptus globulus* (Goetz, 2007), *Ocimum gratissimum* (Aguiyi et al., 2000), *Moringa oleifera* (Jaiswal et al., 2009) and *Tamarindus indica* (Maiti et al., 2004; Zohrameena et al., 2017) could explain these effects observed in our study, because these plants can decrease blood sugar after hyperglycaemia orally induced. According to Shrayyef et al. (2010), any extract or any molecule able to reduce hyperglycaemia would act not only by inhibit glucose intestinal absorption, but also activate glucose use by muscle and adipose tissue, or stimulate insulin secretion from pancreas.

However, our results are different from those obtained by N'guessan-Irié et al. (2019) who work on antihyperglycemic activity and hypoglycemic risk of same *Sarenta* remedy. These researchers showed hypoglycemic effect at 209.5 mg b.w. in rats. Indeed, doses evaluated by N'guessan-Irié team (209.5 mg b.w.) was sixty-three, thirty-one and fifteen higher than those evaluated in present study which were 3.33; 6.66 and 13.33 mg b.w. Hypoglycemic effect observed with N'guessan-Irié team could be linked to *Sarenta* remedy toxicity at doses much higher than those admitted by *Sarenta* remedy promoter.

Conclusion

Herbal *Sarenta* remedy is preparation produce by an Ivorian traditional medicine practitioner and used in treatment of various diseases like diabetes, high blood pressure, inflammation, immunodeficiency, malaria, viral diseases, pains, and fever. Our results showed that glibenclamide alone decreased hyperglycaemia and induced hypoglycaemia over time. In combination with *Sarenta*, at sufficient doses, in particular at 6.66 mg b.w., and 13.33 mg b.w., euglycemic effect appeared allows us to propose *Sarenta* as potential phytomedicine candidate that could be combined with conventional drugs for diabetes treatment.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

REFERENCES

Agbre-Yace M, Oyenusi E, Oduwole A, Ake M, Abodo J (2016). Prevalence of diabetes mellitus among children and adolescents in the district of Abidjan in Cote d'Ivoire: a population-based study. Journal of Diabetes and Metabolic Disorders 15:1-9.

Aguiyi J, Obi C, Gang S, Igweh A (2000). Hypoglycaemic activity of *Ocimum gratissimum* in rats. Fitoterapia 71(4):444-46.

Arya S, Jogender S, Singh S (2013). Antidiabetic activities of Cassia occidentalis. Recent Research in Science and Technology 5(1):51-53.

Collins A, Foley R, Gilbertson D et Chen S (2015). United States Renal Data System public health surveillance of chronic kidney disease and end-stage renal disease. Kidney International Supplements 5(1):2-7.

Effo K, Djadji A, N'Guessan B, Kouakou S, Anzoua E, Fatto N and Kouakou-Siransy N (2018). Evaluation anti-inflammatory activity and ulcerogenic Risk of "*Sarenta*", an Ivorian Herbal Preparation. Journal of Pharmaceutical Research Science and Technology 2(3):1-7. ISSN: 2581-3080

Fattoh N (2017). Analgesic, morphine, antioxidant, anti-inflammatory activity and quality of " *Sarenta* ": a traditional herbal remedy. Pharmacy thesis: Abidjan. Felix Houphouët University Boigny. Faculty of Pharmacy 166 p.

Festing M (1979). Suitability rat for fifferent investigations. In: Inbred and genetically defined strains of laboratory animals, Part I, Mouse and Rat (PL Altman, DD Katz, Eds.). Federation American Society Experimental Biology. Bethesda, MD, pp. 237-238.

Gribble F, Reimann F (2003). Sulphonylurea action revisited: post-cloning era. Diabetology 46(7):875-91.

Grimaldi A (2009). Treatise on Diabetology, 2nd Edition. Medicine Sciences, Flammarion.

Goetz P (2007). Phytotherapy of diabetes, Phytotherapy 5:212-17.

Kambouche N, Merah B, Derdour A, Bellahouel S, Younos C, Soulimani R (2011). Antihyperglycemic activity of a β- sitoglucoside sterol isolated from Anabasis plant articulated (Forssk) Moq. Phytotherapy 9:2-6.

Kouakou-Siransy G, Effo K, Irie-Nguessan G, Koua E (2017). Analgesic efficacy, quality and safety of "*Sarenta*": An Herbal Preparation from Ivorian Traditional Medicine. International Journal of Pharmacology 13(3):257-265.

Louhimies S (2002). Directive 86/609/EEC on the protection of animals used for experimental and other scientific purposes. Alternate Laboratory Animals 30(2):217-219.

Magnan C, Ktorza A (2005). Production and secretion of insulin by pancreatic β cell. EMC-Endocrinologie 2(4):241-264.

Maiti R, Jana D, Das U, Ghosh D (2004). Antidiabetic effect of aqueous extract of seed of Tamarindus indica in streptozotocin-induced diabetic rats. Journal of Ethnopharmacology 92(1):85-91.

Moxey PW, Gogalniceanu P, Hinchliffe RJ, Loftus IM, Jones KJ, Thompson MM, Holt PJ (2011). Lower extremity amputations- A review of global variability in incidence. Diabetic Medicine 28(10):1144-1153.

N'guessan-Irié G, Tako A, Effo E, Kouakou L, Kouakou G (2019). Hyperglycaemia lowering activity and hypoglycaemic risk assessment of *Sarenta*, an Ivorian traditional herbal. International Journal of Basic and Clinical Pharmacology 141:8-9

Organisation for Economic Co-operation and Development (OECD) (2008). Test No. 407: repeated dose 28-day oral toxicity study in rodents. OECD Publishing.

Rasolofoson M (2017). Study activity of codified extract No. 4 in mice hyperglycemia. Pharmacy thesis: Madagascar. Antananarivo University 21 p.

Shin JW, Seol IC, Son CG (2010). Interpretation of animal dose and human equivalent dose for drug development. *The* Journal of Korean Medicine 31(3):1-7.

Sherwood L, Berthet J, Amar-Costesec A (2013). Human physiology. 2nd edition ch. XVII. Paris (France): Ed. New Horizons, P. 562-572.

Shrayyef M, Gerich J (2010). Normal glucose homeostasis. Principle of Diabetes pp. 19-35.

Thulé P, Umpierrez G (2014). Sulfonylureas: a new look at old therapy. Current Diabetes Reports 14:1-8.

Tremblay L, Faucher J, Bergeron A (2009). Taming your diabetes. Outpatient program of HCLM Diabetes Education Center, 3rd edition, Charles LeMoyne Hospital pp. 4-48.

World Health Organization (WHO) (2016). Genève. Profils des pays pour le diabète. OMS.