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Blood Glucose Measurement in Diabetic Patients Undergoing Comparative Treatment with a Medicinal Plant

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ABSTRACT

The management of non-communicable chronic diseases such as diabetes and hypertension remains a concern in developing countries. In Guinea, whether by choice or necessity, traditional medicine and herbal remedies are the primary recourse for the population, both in rural and urban areas. Previous investigations led to the development of two phytomedicines designed for managing essential hypertension (HTN) and type 2 diabetes (DT2), named "Guinex-HTN®" and "Sattagas." An evaluation of their therapeutic benefits was conducted during a prevalence survey carried out in Dubréka. This survey revealed a prevalence of 73.52% (211/287) for HTN, 36.58% (105/287) for DT2, and 33.45% (96/287) for combined DT2/HTN. The therapeutic potential of Sattagas and the combination of Sattagas with Guinex-HTN were assessed in diabetic and hypertensive diabetic patients, respectively. Comparisons were made between Sattagas, Metformin, Sattagas plus Metformin, and Sattagas plus Guinex-HTN regarding their impact on blood glucose levels and/or blood pressure values. After 6 months of treatment with 2 x 2 capsules per day, the anti-diabetic potential of Sattagas was confirmed by a significant reduction in blood glucose levels (from 2.59 ± 0.43 to 1.22 ± 0.43) in 80.95% (85/105) of patients, as well as a significant decrease in blood pressure values (from 177 ± 20.77/98 ± 10.70 to 149 ± 29.02/85 ± 13.64) in 90.16% (55/61) of hypertensive diabetics. The anti-diabetic effect of Sattagas (from 2.19 ± 0.29 to 1.22 ± 0.31 g/l) was similar to that of Metformin (from 2.14 ± 0.23 to 1.28 ± 0.41 g/l), and a synergistic effect was observed when Sattagas

was combined with Metformin (from 2.21 ± 0.49 to 1.10 ± 0.20 g/l). In hypertensive diabetics, the combination of Sattagas and Guinex-HTN demonstrated a beneficial effect on blood pressure values. Except for some symptoms (epigastric pain, nausea, diarrhea, drowsiness, fatigue) reported in 17 out of 103 patients that did not interfere with the continuation of treatment, both phytomedicines were well tolerated. Sattagas and Guinex-HTN, two products derived from Guinean pharmacopoeia, represent interesting and accessible alternatives for managing type 2 diabetes and hypertension, particularly among underprivileged populations in rural and urban areas of Guinea.

1. INTRODUCTION

According to WHO statistics, non-communicable chronic diseases cause over 41 million deaths worldwide each year (including 29 million in low- and middle-income countries). Among non-communicable diseases, metabolic diseases account for the highest mortality rate, with over 20% of annual deaths [1]. The global burden of metabolic diseases continues to rise, becoming a major issue for human health, public finances, and the budgets of patients and their families. Reducing this burden is one of the significant challenges for development in the 21st century [2]. A major concern in the management of metabolic diseases is the onset of complications such as retinopathy, nephropathy, neuropathy, renal failure, and strokes, many of which are irreversible [3, 4]. The morbidity and mortality associated with metabolic diseases are largely preventable through education, risk factor modification, and adherence to treatment regimens. However, implementing these interventions can be challenging and requires their integration into primary care systems to make them affordable, effective, and accessible to all patients [5-8].

In Africa, for various reasons, populations often turn to medicinal plants to address hypertension and diabetes. In Guinea, ethnobotanical studies conducted at IRDPMAG have identified *Englerina lecardii*, a plant from the Loranthaceae family used in traditional Guinean medicine for diabetes treatment, along with *Hymenocardia acida*, a plant from the Hymocardiaceae family used for hypertension treatment. Formulations of the extracts from *Englerina lecardii* and *Hymenocardia acida* have led to the development of two phytomedicines named "Sattagas" and "Guinex-HTN®." Preliminary ethnotherapeutic evaluations carried out by IRDPMAG demonstrated promising hypoglycemic and antihypertensive activities of these phytomedicines in diabetic and hypertensive patients, respectively. Considering these results, further investigations were warranted.

Thus, this study aims to explore the therapeutic potential of local resources, represented by medicinal plants, to enrich the array of safe and accessible antidiabetic and antihypertensive medications for Guinean populations.

2. STUDY FRAMEWORK, MATERIALS AND METHODS

2.1. Study Framework

Two sites served as the study framework: the urban commune of Dubréka [9] and the commune of Matoto (ENTA Health Center). The Institute for Research and Development of Medicinal and Food Plants of Guinea was established in March 2000 with the mission of contributing to the improvement of public health through the rational use of local resources. In Guinea, the management of non-communicable diseases such as hypertension (HTN) and diabetes remain very modest. It is limited to measuring blood pressure and glucose levels and the low availability of antihypertensive medications (Amlodipine 10: 30 tablets: 30,000 Fg; Injectable Furosemide: 1 ampoule at 2,000 Fg; Captopril: 20 tablets at 10,000 Fg; Nifedipine: 20 tablets at 20,000 Fg; Injectable Hydralazine and methyldopa are free for pregnant women) and antidiabetic medications (Actrapid (incretin): 50,000 Fg; Mixtard (incretin): 50,000 Fg; Metformin (Biguanides) 500 mg: 20 tablets at 10,000 Fg; Metformin 850 mg (Biguanides): 20 tablets at 15,000 Fg in hospitals). The sources of

pharmaceutical supplies are varied (SOGUIPREM, PCG, SOGUIMAP, and others). The inaccessibility of antidiabetic and antihypertensive treatments for a significant portion of the population is noted in all communes. This situation encourages the population to turn to traditional medicine. Conventional management of type 2 diabetes (DT2) is still in its early stages. Indeed, until 2018, there was no unit of diabetology in the Prefecture of Dubréka; once hyperglycemia was detected, patients were generally referred to the diabetology service at Donka National Hospital. In 2019, the non-communicable diseases program established a diabetology unit. Furthermore, this program is now considered in all prefectures. Currently, a diabetologist is responsible for patient management. However, this care still has limitations, particularly due to the lack of biological tests such as HbA1C measurement, for example. The ant attraction test or urine testing to detect sweetness are the most commonly used methods. The most commonly used plants among patients include: *Afzelia africana* Smith ex Pers. (Fabaceae); *Allium sativum* L. (Alliaceae); *Anacardium occidentale* L. (Anacardiaceae); *Carica papaya* L. (Caricaceae); *Cassia sieberiana* DC (Fabaceae); *Jatropha curcas* L. (Euphorbiaceae); *Lannea acida* A. Rich. (Anacardiaceae); *Moringa oleifera* Lam. (Moringaceae); *Nauclea pobeguinii* (Pobéguin ex Pellegr.) Petit (Rubiaceae); *Persea americana* Mill. (Moraceae); *Tamarindus indica* L. (Fabaceae); *Tamarindus indica* L. (Loranthaceae).

2.2. Materials

- **Phytomedicines**

They are represented by Sattagas and Guinex-HTN. They are the result of research conducted by IRDPMAG and by the company AMB-Pharma (Guinea) in collaboration with the Michel Iderne Group (France).

- **Plant material**

The plant was identified by the botany department of IRDPMAG-Dubréka and a herbarium sample was deposited at the center. The leaves were dried in the shade at room temperature in the laboratory for 6 weeks, then pulverized in the mill, and the powder was used for extraction. The following activities were carried out at the University of Angers in France in cooperation with IRVPMAG.

Dosage: 2 × 2 capsules per day.

- **Reference drug**

It is represented by Metformin. It is an oral antidiabetic from the biguanide family, originally extracted from lilac (*Galega officinalis*). It remains among the drugs used as first-line treatment in diabetic patients. The drug is contraindicated in the presence of renal insufficiency (clearance < 30 ml/min) [10].

Dosage: 1 capsule per day of treatment.

2.3. Methods

2.3.1. Variables Submitted to the Study

- **Biological Variables:** Blood glucose, creatinine, total cholesterol, triglycerides, HDL, LDL, HbA1C, hypertension (HTN).
- **Epidemiological Variables:** Age, sex, marital status.
- **Other Variables (lifestyle habits):** Smoking, alcohol consumption, cola nut, Maggi Cube, Soumbara, salt, family medical history (hypertension or diabetes), anthropometric variables: weight, height.
- **Biomaterial:** Blood pressure.

The approach consisted of a prevalence survey on hypertension, which allowed for the selection of patients who participated in the clinical evaluation. Given the close proximity of elders to the population and their knowledge of sociocultural habits, initial contacts were made with them to consider collaboration. To reduce the workload, their involvement was limited to the recruitment phase. Data collection focused on sociodemographic information (age, sex), lifestyle habits such as smoking, alcohol consumption, cola nut, Maggi Cube, Soumbara, salt, family medical history (hypertension or diabetes), anthropometric parameters (weight, height), blood pressure, and blood glucose levels. A total of 287 volunteers aged 20 years and older were selected. Blood glucose levels (g/l) were measured using a One Touch Ultra Mini glucometer. Blood

pressure was measured on the left arm three times, at 5-minute intervals, using an electronic blood pressure monitor, Tensioval Comfort Classic IP20, in each subject at rest for at least ten minutes after removing shoes and any heavy clothing. The standards for physical measurements (blood pressure and anthropometric parameters) are expressed in international units: blood pressure in mm Hg; weight in kg; height in m; hypertension is defined as a blood pressure ≥ 140/90 mm Hg. Weight measurement was taken using an electronic weighing scale (accuracy within 0.1 kg). The subject stood lightly dressed and without shoes. Height was measured using a stadiometer (accuracy within 1 centimeter) in a standing position without shoes. The body mass index (BMI) was calculated by dividing weight (kg) by height (m^2). Overweight was defined as 25 ≤ BMI < 30, obesity as BMI ≥ 30, and underweight as a BMI of less than 18.5. Thus, 63 diabetic subjects without hypertension, after two weeks of monitoring and one week of hygienic-dietary measures, were included in the study.

All reagents used were provided by the LGA laboratory (Guineo-German) located in Landreah in Conakry in the commune of dixinn. Control plasmas were integrated into the series as internal quality control, and the samples were kept subject to possible external quality control, particularly for the most stable parameters: biochemistry. If a patient's HbA1C is greater than or equal to 6.5% and blood sugar ≥ 1.26 g/l, the patient is therefore included in the study versus Metformin.

For the other stages, we only took into account blood sugar. Third, in addition to blood sugar, the patient's blood pressure is also affected.

Patients received one week of treatment. The study design provides a visit every seven days for a clinical and biological assessment. The monitoring team made rounds twice a week to count the phytomedicines. The treatment for each patient lasted for 6 months.

2.3.2. Study Type

This is a longitudinal, open, descriptive, and analytical observational study conducted from April 22, 2015, to June 20, 2018, involving patients aged 20 years and older with type 2 diabetes, whether hypertensive or not. The studies focused on the therapeutic evaluation of Sattagas and Sattagas versus Metformin in the treatment of diabetes.

2.3.3. Data Collection, Processing, and Analysis

- **Data collection**

Ethnobotanical data were collected from hypertensive patients using herbal remedies. Interviews focused mainly on the local names of the plants, the parts of the plants used, the method of preparation, the purchase of the plants, and the concomitant use of conventional antihypertensive drugs.

- **Data processing and analysis**

The data were entered into Excel and analyzed using Tanagra. The descriptive component involved calculating proportions and averages (or medians) based on the nature of the variable being described. The confidence level used was 95%. The data analysis consisted of describing the study populations according to sex, age, stage of hypertension and diabetes, duration of diabetes, family history of hypertension and diabetes, and the duration of diabetes, as well as comparing the parameters of included patients "before and after" according to the endpoints. For the statistical comparisons, we used the following tests:

- Mann & Whitney test
- Friedman test and multiple comparisons
- Wilcoxon test

2.3.4. Ethical Considerations

The authorization to conduct the trial was obtained from the National Ethics Committee. Informed consent was systematically sought and obtained from each individual selected for the study. Participants with abnormalities were provided with referrals for appropriate care and advice, as well as free medical assistance for the most part (consultations, medications, laboratory tests). Patients are free to discontinue treatment due to severe adverse effects.

2.3.5. Limitations and Difficulties

- Criteria for non-inclusion

The non-inclusion criteria included: type 1 diabetes (or treated with insulin); pregnant or breastfeeding women; hypertension associated with diabetes; the presence of another major pathology or any other complications of diabetes based on the anamnesis and clinical examination.

- Exclusion criteria during the study

The exclusion criteria included: selected subjects not attending the second follow-up; worsening of diabetes (Blood glucose ≥ 4 g/L and/or appearance of ketonuria with two crosses); intolerance to the phytomedicine (significant diarrhea and/or vomiting); personal decision of the patient; signs of lactic acidosis; severe allergic manifestations; major deterioration of general health.

- Endpoints

The primary endpoint for assessing efficacy in the study is the average reduction in fasting blood glucose and/or HbA1c. The tolerance endpoints for the phytomedicine are clinical parameters (proportion of reported side effects and their intensity or severity) and biochemical parameters systematically monitored before inclusion, and then at 3 months and 6 months of treatment (creatinine, triglycerides, cholesterol levels).

3. RESULTS

A total of 287 individuals, including 174 women, were randomly selected during the study period. The female-to-male ratio was 1.54. With 73.52% (211/287), the prevalence of hypertension is significantly high in Dubréka and affects all age groups starting from 20 years old: 13.04% (3/23); 53.12% (17/32); 64.10% (25/39); 84.12% (53/63); 93.24% (69/74); and 86.27% (44/51) respectively for the age groups 20 - 29 years, 30 - 39 years, 40 - 49 years, 50 - 59 years, 60 - 69 years, and over 70 years. This prevalence is significant in both women at 75.29% (131/174) and men at 70.79% (80/113). The older age groups are the most affected.

The overall prevalence of diabetes is 36.59% (105/287), with 38.05% (43/113) among men and 35.63% (62/174) among women. By age group, the prevalence is as follows: 40.63% (13/32); 25.64% (10/39); 47.62% (30/63); 45.95% (34/74); and 41.46% (17/41) starting from the age group 30 - 39 years.

Out of 105 diabetic and hypertensive patients, consent was obtained for participation in a clinical trial, of which two dropped out of the study.

Table 1 presents the sociodemographic and clinical characteristics of the study population.

Table 1. Sociodemographic and clinical characteristics of the total study population.

Initial Characteristics	Women	Men
Age (years)	52.69 ± 16.85	56.65 ± 14.05
Weight (kg)	71.90 ± 16.10	70.81 ± 13.79
Height (m)	1.60 ± 0.08	1.68 ± 0.07
BMI (kg/m^2)	28.26 ± 6.05	24.88 ± 5.16

Clinical trial

3.1. First Trial

Forty-two naïve patients who were unaware of their diabetic status were selected to participate in a clinical trial after one week of monitoring.

Initial Characteristics of 42 Patients Treated with Sattagas

Table 2 provides information on the parameters of naïve patients at inclusion. The average age is over

40 years for both men and women (46 ± 12.89 versus 54 ± 14.78). The average BMI is less than 30 kg/m^2. The average duration of diabetes is over 4 years for both men and women. The blood glucose level is over 2 g/L.

Table 2. Presentation of variables at inclusion. Presentation of the variables of the 42 patients at inclusion.

Parameters	Phytomed	Groups	Mean	CI (95)	Median
Age	Sattagas	Women (23)	46 ± 12.89	51 - 41	50
		Men (19)	54 ± 14.78	61 - 47	55
+BMI (kg/m^2)		Women	26.59 ± 4.88	29 - 25	25
		Men	25.84 ± 4.04	27.49 - 24	21
Duration of diabetes (years)		Women	4 ± 4.43	6 - 2	2
		Men	4 ± 4.43	6 - 2	2
Blood glucose (g/l)		Women	2.49 ± 0.39	2.65 - 2.33	2,40
		Men	2.71 ± 0.55	2.96 - 2.46	2,63
SBP (mm Hg)		Women	121 ± 12.38	126 - 115	120
		Men	118 ± 12.79	124 - 112	119
DBP (mm Hg)		Women	80 ± 8.38	83 - 80	85
		Men	75 ± 8.67	79 - 71	75
HR (bpm)		Women	85 ± 15.64	91 - 79	80
		Men	85 ± 11.19	90 - 80	83

Table 3 provides information on the evolution of blood glucose levels and blood pressure values of 42 naive diabetic patients.

Table 3. Evolution of blood glucose and blood pressure values in diabetic patients treated with Sattagas (n = 42). During this treatment, a slight increase in blood pressure was observed. The heart rate remained the same.

Parameters/Days	Diabetics (n = 42)	
	Day 0	Day 180
Blood glucose (g/l)	2.59 ± 0.48	1.22 ± 0.43
SBP (mmHg)	120 ± 12.51	139 ± 27.05
DBP (mmHg)	78 ± 8.71	84 ± 13.62
HR (bpm)	85 ± 13.65	84 ± 19.77

Figure 1 shows the evolution of glycemia in naïve diabetic patients treated with Sattagas.

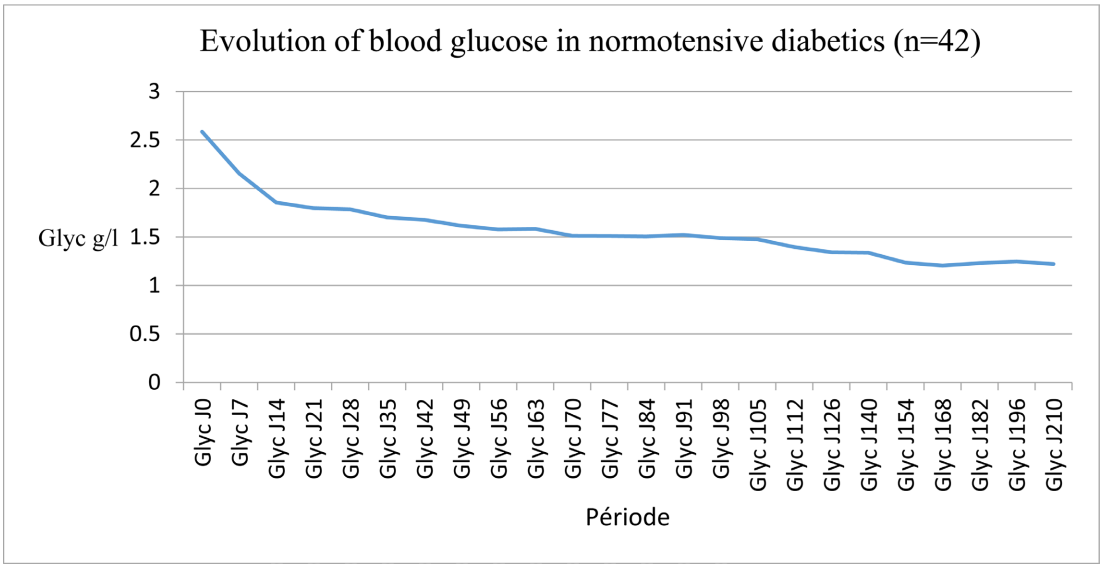

Figure 1. Evolution of blood sugar in naïve diabetic patients treated with Sattagas.

In patients treated with Sattagas, a very significant decrease in blood glucose was observed, dropping from 2.59 ± 0.48 g/l to 1.22 ± 0.43 g/l (Friedman test, P = 0.000). However, we tend to observe a slight increase in blood pressure.

3.2. Second Trial

Sixty-three patients with both an HbA1c greater than 6.5% and a fasting blood glucose ≥ 1.26% were included in a second clinical trial comparing treatment with Metformin.

Table 4 provides information on the number of patients included for each treatment.

Twenty-one patients were included in each treatment group (3-arm treatment). The first arm included patients who received only Metformin. The second arm combined Metformin and Sattagas. The third arm received only Sattagas.

Table 4. Distribution by treatments.

Test Medications	Frequency	Percentage
Metformin	21	33.3
Metformin + Sattagas	21	33.3
Sattagas	21	33.3
Total	63	100

In Table 5, distribution of treatments by gender.

Twenty-one patients were included in each treatment group, representing a percentage of 33.33% (21/63). Men and women are approximately proportionate in each treatment group, with 35% (14/40) being women and 34.78% (8/23) being men. In all three groups, we noted a higher number of women than men, with 63.49% (40/63) being women compared to 36.50% (23/63) being men.

Table 5. Distribution of treatments by sex.

Sex/Medications		Treatment			Total
		Metformin	Metformin + Sattagas	Sattagas	
Sex	Women	13	13	14	40
	Men	8	8	7	23
Total		21	21	21	63

Comparative studies of biological parameters at inclusion

In Table 6, the blood glucose values of the patients were compared at the beginning of the treatment.

Table 6. Blood glucose values of patients at inclusion.

Attribute_Y	Attribute_X	Description					Statistical Test		
		Value	Examples	Average	Rank sum	Rank mean	Statistics	Value	Probability
Glyc0	Treatment	Met + Satt	21	2.2148	653.5	31.119	Kruskal-Wallis	0.291029	0.864577
		Satt	21	2.1886	709	33.7619	KW (corr.ties)	0.299054	0.861115
		Met	21	2.14	653.5	31.119			
		All	63	2,1811	2016	32			

There was no significant difference between baseline blood glucose levels (before patient inclusion). Patients included in the 3 groups were homogeneous at the start of treatment from a glycemic point of view ($p = 0.86$).

In Table 7, the total cholesterol levels of the patients were compared.

At baseline, there was no significant difference in total cholesterol levels among the three groups ($P = 0.624635$). The means and standard deviations are the same for the three treatment groups.

Table 7. Total cholesterol levels of patients at baseline.

Attribute_Y	Attribute_X	Description					Statistical test		
		Value	Examples	Average	Rank sum	Rank mean	Statistics	Value	Probability
Chol T0	Treatment	Met + Satt	21	2.03	664.5	31.6429	Kruskal-Wallis	0.940972	0.624699
		Satt	21	1.9948	618.5	29.4524	KW (corr.ties)	0.941176	0.624635
		Met	21	2.1743	733	34.9048			
		All	63	2.0663	2016	32			

In Table 8, HDL cholesterol values were compared at the start of treatment.

A significant difference was noted between the baseline HDL levels (P = 0.02436). The mean is higher in patients treated with Sattagas and Metformin compared to those treated with the combination of both.

Table 8. HDL cholesterol levels at inclusion.

Attribute_Y	Attribute_X	Description					Statistical test		
		Value	Examples	Average	Rank sum	Rank mean	Statistics	Value	Probability
HDL0	Treatment	Met + Satt	21	1.7281	509	24.2381	Kruskal-Wallis	7.417163	0,024512
		Satt	21	0.5043	674.5	32.119	KW (corr.ties)	7.428931	0,024368
		Met	21	0.5757	832.5	39.6429			
		All	63	0.936	2016	32			

LDL cholesterol of all patients was compared at baseline in Table 9.

Table 9. Comparative study of baseline LDL cholesterol.

Attribute_Y	Attribute_X	Description					Statistical test		
		Value	Examples	Average	Rank sum	Rank mean	Statistics	Value	Probability
LDL0	Treatment	Met + Satt	21	1.4067	735	35	Kruskal-Wallis	0.935587	0.626383
		Satt	21	1.2595	622.5	29.6429	KW (corr.ties)	0.935811	0.626313
		Met	21	1.3248	658.5	31.3571			
		All	63	1.3303	2016	32			

There was no significant difference between the three treatment groups in baseline LDL cholesterol levels. They are all comparable.

In Table 10, triglycerides were compared at baseline.

We did not note any significant difference between baseline triglycerides. They are therefore all comparable in the three groups at the start of treatment.

Table 10. Comparative study of starting triglycerides.

Attribute_Y	Attribute_X	Description					Statistical test		
		Value	Examples	Average	Rank sum	Rank mean	Statistics	Value	Probability
Triglyc0	Treatment	Met + Satt	21	1.3238	696	33.1429	Kruskal-Wallis	0.995536	0.607886
		Satt	21	1.3714	604.5	28.7857	KW (corr.ties)	1.005698	0.604805
		Met	21	1.3429	715.5	34.0714			
		All	63	1.346	2016	32			

In Table 11, creatinines were compared at the start of treatment.

There is no significant difference between the creatinines of the different treatment groups at inclusion (P = 0.4186).

Table 11. Comparative study of starting creatinine levels.

Attribute_Y	Attribute_X	Description					Statistical test		
		Value	Examples	Average	Rank sum	Rank mean	Statistics	Value	Probability
Creat0	Treatment	Met + Satt	21	86.9524	762.5	36.3095	Kruskal-Wallis	1.741567	0.418623
		Satt	21	81.2381	625.5	29.7857	KW (corr.ties)	1.77163	0.412378
		Met	21	82.381	628	29.9048			
		All	63	83.5238	2016	32			

Table 12 provides information on the baseline HbA1C levels of patients.

No statistically significant difference was noted between the baseline HbA1C levels of the different treatment groups.

Table 12. Comparative study of baseline HbA1C levels.

Attribute_Y	Attribute_X	Description					Statistical Test		
		Value	Examples	Average	Rank sum	Rank mean	Statistics	Value	Probability
HbA1C0	Treatment	Met + satt	21	11.2095	763.5	36.3571	Kruskal-Wallis	1.998087	0.368232
		Satt	21	10.0286	598.5	28.5	KW (corr.ties)	1.999046	0.368055
		Met	21	10.1571	654	31.1429			
		All	63	10.4651	2016	32			

Effect of medications on blood sugar

- Effects of the Metformin + Sattagas Combination on Blood Glucose

Blood glucose levels decreased very significantly (P = 0.000) from 2.21 ± 0.49 g/l to 1.10 ± 0.20 g/l (Friedman test: P = 0.0000) during treatment with the combination of Metformin and Sattagas. Sattagas, when combined with Metformin, contributes to a very significant reduction in blood glucose levels.

- Effects of Sattagas on Blood Glucose

Blood glucose levels decreased very significantly (P = 0.000) from 2.19 ± 0.29 g/l to 1.22 ± 0.31 g/l (Friedman test: P = 0.0000). The phytomedicine significantly reduced blood glucose levels.

- Effects of Metformin on Blood Glucose

Blood glucose levels decreased very significantly (Friedman test: P = 0.0000) from 2.14 ± 0.23 g/l to 1.28 ± 0.41 g/l during treatment with Metformin.

Tolerance

- Effect on total cholesterol

In Table 13, the action of the different drugs on the total cholesterol level was evaluated.

A significant decrease in total cholesterol was noted during treatment with the combination of Metformin plus Sattagas. On the other hand, this decrease is not significant with Sattagas and Metformin alone.

Table 13. Effect on total cholesterol.

Products	Total Cholesterol	Mean	Friedman Test
Metformin + Sattagas	Cholest0	2.03 ± 0.58	P = 0.03375
	Cholest3	1.82 ± 0.60	
	Cholest6	1.98 ± 0.56	
Sattagas	Cholest0	1.99 ± 0.41	P = 0.07791
	Cholest3	1.69 ± 0.35	
	Cholest6	1.88 ± 0.43	
Metformin	Cholest0	2.17 ± 0.59	P = 0.27253
	Cholest3	1.96 ± 0.42	
	Cholest6	2.02 ± 0.43	

-Effect on LDL

In Table 14, the effect of the different treatments on LDL was evaluated.

A very significant decrease in LDL reduction was noted in the combined treatment and the treatment with Metformin.

Table 14. Effect on LDL.

Products	LDL	Moyenne	Friedman Test
Metformin + Sattagas	LDL0	1.41 ± 0.57	P = 0.00177
	LDL3	0.99 ± 0.44	
	LDL6	1.10 ± 0.40	
Sattagas	LDL0	1.26 ± 0.60	P = 0.08351
	LDL3	1.01 ± 0.65	
	LDL6	1.20 ± 0.56	
Metformin	LDL0	1.32 ± 0.62	P = 0.00993
	LDL3	0.96 ± 0.41	
	LDL6	1.19 ± 0.52	

-Effect on Triglycerides

Table 15 provides information on the effect of different treatments on triglyceride levels.

Only treatment with Metformin significantly reduced triglycerides.

Table 15. Effect on triglycerides.

Products	Triglycerides	Moyenne	Friedman Test
Metformin + Sattagas	Triglycerides0	1.32 ± 0.51	P = 0.74985
	Triglycerides3	1.42 ± 0.68	
	Triglycerides6	1.43 ± 0.76	
Sattagas	Triglycerides0	1.37 ± 0.81	P = 0.20993
	Triglycerides3	1.44 ± 0.97	
	Triglycerides6	1.26 ± 0.76	
Metformin	Triglycerides0	1.35 ± 0.43	P = 0.00480
	Triglycerides3	1.66 ± 0.54	
	Triglycerides6	1.28 ± 0.35	

-Effect on creatinine

The effect on creatinine of the different treatment groups was evaluated in Table 16.

The combination of the phytomedicine with Metformin and Metformin alone significantly reduced the creatinine level.

Table 16. Effect on creatinine.

Products	Creatinine	Moyenne	Friedman Test
Metformin + Sattagas	Creatinine0	86.85 ± 15.11	P = 0.02926
	Creatinine3	80.40 ± 20.47	
	Creatinine6	78.26 ± 13.02	
Sattagas	Creatinine0	81.20 ± 15.60	P = 0.22979
	Creatinine3	78.67 ± 12.85	
	Creatinine6	76.33 ± 17.27	
Metformin	Creatinine0	82.35 ± 15.20	P = 0.01442
	Creatinine3	85.28 ± 18.71	
	Creatinine6	74.56 ± 18.92	

- Effect on HbA1C

The effect of the different treatments on HbA1C has been described in Table 17.

A non-significant decrease in HbA1C reduction is noted by all three types of treatment.

Effectiveness of Medications over Time

A significant difference in blood glucose reduction was observed during treatment with the combination of the reference medication and phytomedicine, as well as with phytomedicine alone. Indeed, these two medications do not reduce blood glucose in the same manner throughout the treatment. The reduction is

greater at the beginning of the treatment than at the end. In contrast, Metformin reduces blood glucose in a consistent manner throughout the treatment.

Table 17. Effect on glycated hemoglobin.

Products	HbA1C	Moyenne	Friedman Test
Metformin + Sattagas	HbA1C0	11.21 ± 3.82	P = 0.0736
	HbA1C3	9.95 ± 2.35	
	HbA1C6	9.82 ± 2.13	
Sattagas	HbA1C0	10.03 ± 3.59	P = 0.20190
	HbA1C3	8.41 ± 1.66	
	HbA1C6	8.87 ± 2.69	
Metformin	HbA1C0	10.16 ± 3.26	P = 0.17009
	HbA1C3	9.60 ± 2.12	
	HbA1C6	9.33 ± 2.31	

3.3. Third Trial

Twenty-six patients with both hypertension and diabetes were subjected to a third clinical trial.
Therapeutic evaluation of Sattagas versus Sattagas-Guinex-HTN
Characteristics of the initial parameters
In Table 18, the variations of the different treatment groups were evaluated.

Table 18. Variation of the initial parameters.

Parameter	Treatment	Group	Mean	95 CI	Median
Age	Sattagas	Women (18)	56 ± 11.53	61.33 - 50.67	55
		Men (8)	61 ± 6.25	65.33 - 56.67	60
	Sattagas + Guinex-HTN	Women (21)	55 ± 10.63	59.55 - 50.45	55
		Men (14)	58 ± 7.43	61.92 - 54.08	59
IMC (kg/m^2)	Sattagas	Women (21)	27.83 ± 5.34	30.30 - 25.36	27
		Men (14)	28.06 ± 5.22	31.68 - 24.44	26
	Sattagas + Guinex-HTN	Women (21)	28.23 ± 5.09	30.41 - 26.05	28
		Men (14)	25.55 ± 3.97	27.63 - 23.47	24
Diabetes duration (year)	Sattagas	Women (21	3 ± 2.07	4 - 2	3
		Men (14)	4 ± 3.96	7 - 1	3
	Sattagas + Guinex-HTN	Women (21	4 ± 4.44	6 - 2	2

Continued

		Men (14)	5 ± 3.73	7 - 3	4
blood sugar (g/l)	Sattagas	Women (21	2.72 ± 0.50	2.95	3
		Men (14)	2.34 ± 0.56	2.72 - 1.95	2.27
	Sattagas + Guinex-HTN	Women (21)	2.43 ± 0.40	2.60 - 2.26	2.44
		Men (14)	2.42 ± 0.45	2.66 - 2.18	2.37
PAS (mmm Hg)	Sattagas	Women (21	148 ± 18.69	157 - 139	147
		Men (14)	151 ± 20.37	165 - 136	146
	Sattagas + Guinex-HTN	Women (21	178 ± 22.69	188 - 168	175
		Men (14)	176 ± 17.4	185 - 167	175
PAD (mmm Hg)	Sattagas	Women (21)	91 ± 8.79	95 - 87	92
		Men (14)	85 ± 13.98	95 - 75	96
	Sattagas + Guinex-HTN	Women (21)	97 ± 10.79	102 - 92	98
		Men (14)	101 ± 10.58	107 - 95	100
FC (mmm Hg)	Sattagas	Women (21)	87 ± 12.28	93 - 81	91
		Men (14)	82 ± 20.49	96 - 68	84
	Sattagas + Guinex-HTN	Women (21)	88 ± 15.41	95 - 81	85
		Men (14)	81 ± 12.31	87 - 75	80

In Table 19, a comparative study of the reduction of blood sugar and blood pressure values of different patients was determined.

We note a significant decrease in the reduction of blood sugar and blood pressure values of diabetic hypertensive patients treated with Sattagas and Sattagas + Guinex-HTN.

Table 19. Comparison of baseline and end-of-treatment blood sugar levels.

Status Days	DT2/HTN (n = 26) Sattagas		DT2/HTN (n = 35) Sattagas + Guinex-HTN	
	D0	D180	D0	D180
Glycemia	2.61 ± 0.54	1.10 ± 0.33	2.43 ± 0.41	1.16 ± 0.33
PAS	149 ± 18.87	142 ± 23.14	177 ± 20.77	149 ± 29.02
PAD	89 ± 10.74	86 ± 10.58	98 ± 10.70	85 ± 13.64
HR	86 ± 15.03	80 ± 11.28	85 ± 14.41	84 ± 13.37

Figure 2 shows the change in blood glucose levels in patients treated with Sattagas.

Overall, there was a significant decrease in blood glucose reduction (Friedman test P = 0.000) in patients

treated with Sattagas.

Figure 3 shows the variation in blood glucose in patients treated with Sattagas plus Guinex-HTN.

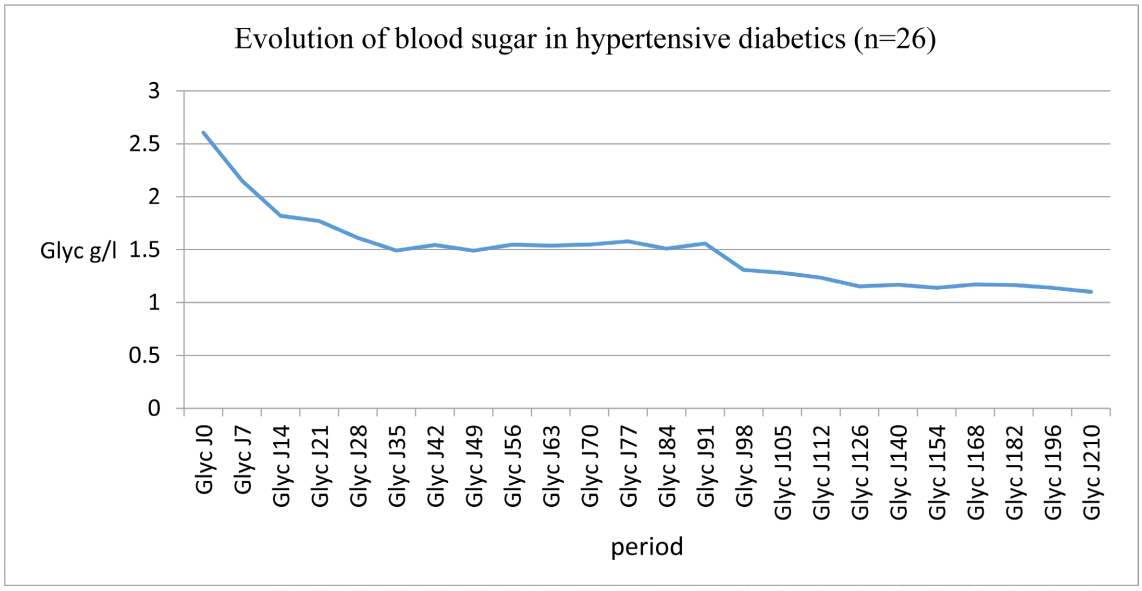

Figure 2. Change in blood glucose levels in patients treated with Sattagas.

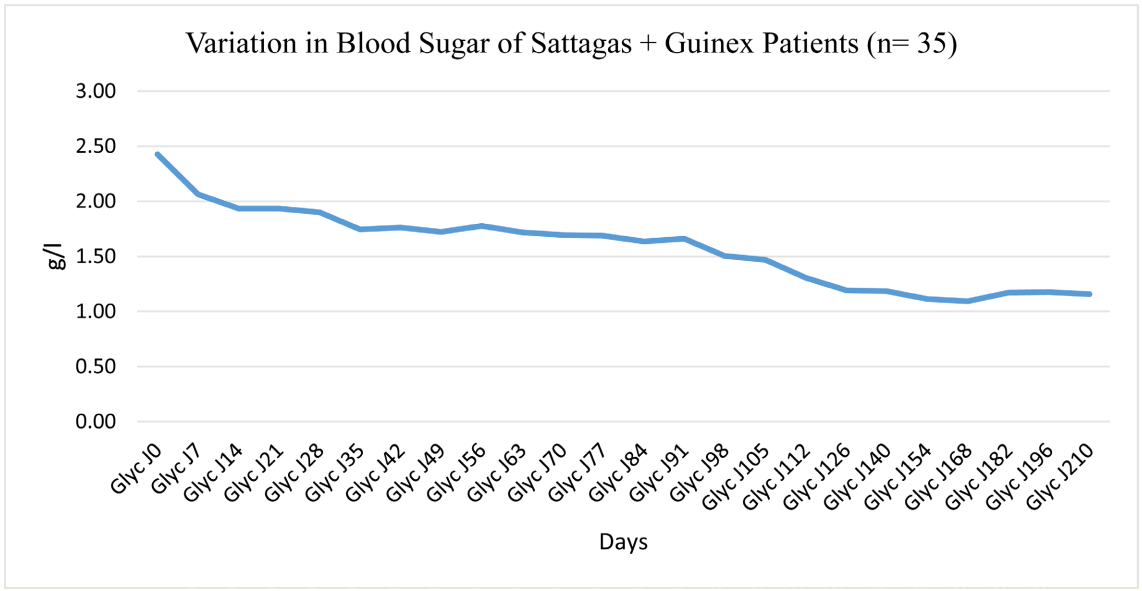

Figure 3. Blood sugar variation of patients treated with Sattagas plus Guinex-HTN.

There is a significant decrease in blood sugar reduction in patients treated with Sattagas plus Guinex-HTN (P = 0.000) Friedman Statistic.

Table 20 compares diabetic hypertensive patients and diabetics treated with Sattagas.

The difference in blood sugar reduction between diabetic hypertensive patients and diabetics treated with Sattagas is significant at the end of the treatment. At this time, the reduction is greater in diabetic hypertensive patients than in diabetics alone.

In diabetic patients without hypertension who received only Sattagas, there was a reduction in blood

glucose from 2.59 ± 0.48 to 1.22 ± 0.43 g/L. In contrast, in hypertensive diabetic patients treated with Sattagas, a greater reduction in blood glucose was observed, decreasing from 2.61 ± 0.54 to 1.10 ± 0.33 g/L, along with a reduction in blood pressure readings from 149 ± 18.87 to 142 ± 23.14 for systolic pressure, and from 89 ± 10.74 to 86 ± 10.58 for diastolic pressure. The same pattern was observed in hypertensive diabetic patients in group 2, where blood glucose decreased from 2.43 ± 0.41 to 1.16 ± 0.33, along with a significant reduction in blood pressure values from 177 ± 20.77 to 149 ± 29.02 for systolic pressure and from 98 ± 10.70 to 85 ± 13.64 for diastolic pressure. A significant decrease in blood glucose was noted in all three treatment groups (P = 0.000).

Side Effects and Clinical Signs during Treatment

The various side effects reported by 17 patients out of the 103 who received Sattagas are summarized in Table 21. In summary, no major adverse effects were reported. The majority of clinical side effects noted were of a digestive nature: diarrhea at 4.85% (5/103); nausea at 0.97% (1/103); and epigastric pain at 3.88% (4/103). Symptoms of polyuria (29.13%), polyphagia (7.77%), and polydipsia (4.85%) may be related to hyperglycemia itself. One subject reported drowsiness, which could not be explained, particularly as it could not be attributed to hypoglycemia. No subject reached a creatinine level that could cause renal toxicity (men: >53 - 97 µmol/l; women: 44 - 80 µmol/l). Good therapeutic adherence was observed in all patients.

The majority of the reported clinical side effects were of a digestive nature: diarrhea at 4.85% (5/103); nausea at 0.97% (1/103); and epigastric pain at 3.88% (4/103).

The various clinical signs detailed in Table 22 may be related to the pathology itself.

Table 20. Comparative study of patients treated with Sattagas.

		Value	Examples	Average	Rank sum	Rank mean	Mann-Whitney U	383,50000
Value	Group	HTN/DiabRed%_98-105	26	2.2526	1059.5	40.7500	E (U)	546.00000
		DiabRed%_98-105	42	0.6206	1286.5	30.6310	V (U)	6234.89816
		All	68	1.2446	2346.0	34.5000	|Z|	2.05797

Table 21. Side effects observed during treatment with medications.

Side Effects	Sattagas (DT2/HTN) (26)	Sattagas + Guinex-HTN (DT2/HTN) (35)	Sattagas (DT2) (42)
Epigastric Pain	1	2	1
Nausea	0	1	0
Diarrhea	2	2	1
Drowsiness	1	0	0
Fatigue	1	2	3

Table 22. Clinical signs observed during treatment with medications.

Side Effects	Sattagas/HTN (26)	Sattagas + Guinex-HTN (35)	Sattagas (42)
Polyurie	8	12	10
Polyphagie	1	2	5
Polydipsie	2	1	2

The symptoms of polyuria (29.13%), polyphasia (7.77%), polydipsia (4.85%) reported in this study may be related to the pathology itself.

4. DISCUSSIONS

Given that all treatment groups are homogeneous at baseline for glycemic values, the observed significant differences are associated with the effects of the tested products: Sattagas, Sattagas plus Metformin, and Metformin. With Sattagas plus Metformin, there is a decrease in blood glucose from 2.21 ± 0.49 g/L to 1.10 ± 0.20 g/L (P = 0.000); with Sattagas from 2.19 ± 0.29 g/L to 1.22 ± 0.31 g/L (P = 0.000); and with Metformin from 2.14 ± 0.23 g/L to 1.28 ± 0.41 g/L (P = 0.000). These results confirm the reduction in blood glucose attributed to Sattagas as described in the ethnobotanical assessments conducted by IRDPMAG [11]. Evidently, the combination of Metformin with Sattagas showed a better reduction effect compared to Metformin alone and Sattagas alone.

Regarding the biological parameters evaluated during the Sattagas versus Metformin trial, it should be noted that the combination of Sattagas plus Metformin had a more significant reduction impact compared to Metformin alone, significantly lowering total cholesterol, LDL cholesterol, and creatinine levels. With Sattagas, a non-significant decrease in these biological parameters was observed. To determine the true relationship between Sattagas and the observed biological variations, it will be necessary to consider this in future clinical trials of Sattagas and to include a sufficient number of patients. The non-significance of these parameters could be explained by the small number of patients included in the study. Metformin has been shown to reduce LDL [12], triglycerides [13], and creatinine [14, 15]. In our study, Metformin did not significantly reduce total cholesterol, despite literature reporting a reduction in cholesterol levels due to Metformin [16-18].

A non-significant reduction in HbA1C was observed across all three treatment groups, but it was sufficient to result in a 1.1% reduction in cardiovascular risk compared to the results of the ACCORD trial [19], [20]. Some authors highlight an additional reduction in HbA1C with the combination of Metformin and oral antidiabetic agents (OADs) [21], estimated at around 1.0%. While some studies did not observe any significant difference in HbA1C reduction with Metformin [22], other authors mention a reduction in HbA1C of 1.12% [23].

Numerous other clinical trials have been conducted measuring HbA1C levels. Some of these highlight that a reduction in HbA1C does not lead to any benefits; the ADVANCE trial indicated that a small difference in HbA1C logically does not lead to a reduction in cardiovascular risk, even after 10 years of follow-up [24]. The VADT trial concluded that reducing HbA1C in patients does not provide any clinical microvascular or macrovascular benefit. However, an increase in severe hypoglycemia was noted [25]. Other studies report the opposite; the UKPDS 33 trial emphasized that the reduction in HbA1C levels in patients from the Metformin group resulted in a 32% decrease (95% CI = 13 - 47; P = 0.002) in the relative risk of all diabetes-related complications (a very composite criterion) [26, 27]. Ray's meta-analysis indicates that intensive glycemic control reduced non-fatal myocardial infarctions by 17% (OR = 0.83; 95% CI = 0.75 - 0.93). This reduction corresponds to approximately one avoided heart attack for every 100 patients treated intensively over 5 years. There was no significant effect on strokes or total mortality (OR = 1.02; 95% CI = 0.87 - 1.19) [28]. The Currie trial observed that adjusted total mortality increased when HbA1C exceeded 8% but also when it was below 7.4%. This study advises that for young patients, at the onset of diabetes, in primary prevention, with a low cardiovascular risk and low hypoglycemia risk, it is reasonable to maintain HbA1C < 7%, preferably with Metformin. Moreover, for older patients, after 8 to 10 years of diabetes, in secondary prevention or with high cardiovascular risk, an HbA1C between 7.5% and 8% is an acceptable position [29].

For all three treatment groups, it appears that the mean glycemia at the 1st, 3rd, and 6th months differs from the corresponding HbA1C levels. It is not surprising that the HbA1C level is not correlated with the mean glycemia over a period of three months [30]. The HbA1C level can be misleading in individuals with various hemoglobinopathies, iron deficiency, hemolytic anemia, or severe liver or kidney disease [31, 32]. Studies conducted among ethnic groups indicate that at similar glycemic values, African Americans, Native

Americans, Hispanic Americans, and Asians have higher HbA1C levels than white individuals [33].

Although a target blood pressure of <140/85 mmHg was not achieved, as recommended by the ESC and certain authors [34, 35], it is noteworthy that the combination of Sattagas plus Guinex-HTN had a significant impact on reducing blood pressure values in hypertensive diabetics. Some studies have highlighted the severity of diabetes associated with hypertension, such as the MRFIT trial, which indicated the exacerbating role of diabetes in the risk related to hypertension compared to the non-diabetic population, as well as the continuous increase in risk for diabetics with rising blood pressure [36]. Similarly, the HOT trial aimed at optimizing diastolic blood pressure (DBP) indicated that the risk of serious cardiovascular events was multiplied by 2.06 (95% CI = 1.24 - 3.44, P = 0.005) in the group with a target DBP of 90 mmHg compared to the group with a target DBP of 80 mmHg [37].

Others have indicated the importance of treatment, such as the ESCAPE trial, which, after a mean follow-up of 8.4 years, showed a significant reduction of 24% (95% CI = 8 - 38, P = 0.005) in all diabetes-related events, a 32% reduction (95% CI = 6 - 51, P = 0.02) in diabetes-related deaths, and a 44% reduction (95% CI = 1165, P = 0.01) in strokes. These results confirm the necessity of lowering blood pressure in patients with type 2 diabetes [38].

Finally, according to the ACCORD BP trial, reducing the systolic blood pressure of high-risk type 2 diabetes patients to below 120 mmHg does not confer any benefit compared to a systolic blood pressure < 140 mmHg (1.87% vs. 2.09% HR = 0.88, 95% CI = 0.73 - 1.06, P = 0.20), alongside an increase in adverse effects (3.3% vs. 1.3%, P < 0.001) [39]. The non-randomized INVEST-BP study concluded that, in practice, there is no clinical benefit to lowering the systolic blood pressure of type 2 diabetes patients below 130/80 mmHg. In terms of the benefit/risk ratio, maintaining a systolic blood pressure between 130 and 140 mmHg is an acceptable compromise [40].

There is a consistent reduction in blood glucose through the reference product during the treatment duration, whereas the effect of the tested phytomedicine tends to diminish by the end of the treatment. Although side effects (polyuria, polyphagia, polydipsia) have been reported by some patients, this relationship remains to be confirmed, considering that diabetes-related side effects could justify such a condition. Patients treated with Guinex-HTN and Sattagas (2 capsules twice daily) found this dosage quite burdensome and consequently expressed a desire for a reduction in dosage (1-2 capsules per day, similar to other conventional antihypertensives).

5. CONCLUSION

The study of the antidiabetic effect of Sattagas versus Metformin in three treatment groups, each comprising 21 patients, shows that all the following biological parameters—glycemia, LDL cholesterol, total cholesterol, triglycerides, creatinine, and glycosylated hemoglobin—are homogeneous. The combination of Sattagas and Metformin contributes to a highly significant decrease in glycemia, total cholesterol, and creatinine levels. No significant reduction in glycosylated hemoglobin was observed in the treatment groups, and Sattagas did not significantly reduce triglycerides either.

6. GENERAL CONCLUSION

The prevalence study of diabetes associated with hypertension conducted in the urban community of Dubréka in Lower Guinea, which was cross-sectional in nature, found a prevalence of hypertension at 73.52% (211/287), diabetes at 36.58% (105/287), and that of hypertensive diabetics at 33.45% (96/287). The discovery of hypertension was incidental in 15.17% (32/211) of the surveyed subjects. Women are more affected than men, with rates of 75.29% (131/174) compared to 70.80% (80/113). The prevalence of hypertension is higher among overweight individuals at 40.76% (86/211) than among the obese at 26.54% (56/211). The relative risk of developing hypertension is higher in patients with two risk factors at 51.66% (109/211), followed by those with three risk factors at 28.91% (61/211).

The discovery of diabetes was incidental in 77.09% (82/105) of the surveyed subjects. Women are more affected by diabetes than men, with rates of 59.05% (62/105) compared to 40.95% (43/105). The prevalence

of diabetes is higher among overweight individuals at 44.76% (47/105) than among the obese at 26.66% (28/105) and the non-obese at 25.71% (27/105). The risk of developing diabetes is higher in patients with three risk factors at 58.10% (61/105) and two risk factors at 38.10% (40/105).

In our study, 91.43% (96/105) had hypertension associated with diabetes, including 90.70% (39/43) of men and 91.93% (57/62) of women. Only 30.43% (7/23) of known diabetics and 7.30% (13/179) of known hypertensive patients were under treatment. The management of cardiovascular risk factors must be comprehensive, as the presence of multiple risk factors exponentially increases the likelihood of cardiovascular risk.

Sattagas and the combination of Sattagas/Guinex-HTN have significantly reduced glycemia and blood pressure values (< 1.26 g/L and systolic/diastolic blood pressure < 140/90 mm Hg) in diabetic and hypertensive diabetic patients. Glycemia decreased significantly (P = 0.000) from 2.21 ± 0.49 to 1.10 ± 0.20 g/L (Friedman Test: P = 0.0000) with Metformin plus Sattagas; with the phytomedicine (P = 0.000) from 2.19 ± 0.29 to 1.22 ± 0.31 g/L (Friedman Test: P = 0.0000); with Metformin (Friedman Test: P = 0.0000) from 2.14 ± 0.23 to 1.28 ± 0.41 g/L.

Increased heart rates (>80 beats per minute at rest) were recorded in all diabetic participants of the study. This means persisted at the end of the treatment.

Tolerability was better with the combination of Metformin/Sattagas and Metformin. A significant decrease was noted in total cholesterol (Friedman Test P = 0.03375); LDL (Friedman Test P = 0.00177); triglycerides (Friedman Test P = 0.00480); and creatinine (Friedman Test P = 0.02926) with this combination (Metformin plus Sattagas), alongside reductions in LDL, triglycerides, and creatinine by Metformin with values (P = 0.00993; P = 0.00480; P = 0.01442). However, the reduction in total cholesterol was not significant in the case of Metformin. Despite the values of P being non-significant with Metformin plus Sattagas (P = 0.0736); Sattagas (P = 0.20190); Metformin (P = 0.17009) with HbA1C, it is noteworthy that a reduction of 1% in HbA1C was observed in all groups, which is likely to reduce cardiovascular risk.

Sattagas associated with Guinex-HTN appears to have a much more significant impact on reducing blood pressure values compared to Sattagas alone in hypertensive diabetics (177 ± 20.77/98 ± 10.70 to 149 ± 29.02/85 ± 13.64) for the combination and (149 ± 18.87/89 ± 10.74 to 142 ± 23.14/86 ± 10.58) for Sattagas. In this case, the development of this phytomedicine should be encouraged.

No subjects experienced adverse effects that would necessitate stopping the treatment. Good therapeutic adherence was noted in all patients.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest regarding the publication of this paper.

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