Original Paper   http://ajol.info/index.php/ijbcs   http://indexmedicus.afro.who.int

Complementary and alternative medicines among diabetic patients attending the clinical laboratory of Centre MURAZ, Burkina Faso

Sami E. KAM[1,2*], Roland N.T. MEDA[2], Adama SANOU[1,3], Abdoulaye SEGDA[2], Isaac S. BONI[2], Chériléila THIOMBIANO[1], Amariane KONE[1], Donald S.B DA[1], Michel MOUKORO[1], Rakiéta SAWADOGO[1], Benjamin K. KOAMA[2] and Abdoul-Salam OUEDRAOGO[1]

[1]*Laboratoire de Recherche en Biochimie, INSP/Centre MURAZ, 01 BP 390 Bobo-Dioulasso 01, Burkina Faso.*
[2]*Laboratoire de Recherche et d'Enseignement en Santé et Biotechnologies Animales, Université Nazi Boni, 01 BP 1091 Bobo-Dioulasso 01, Burkina Faso.*
[3]*Departement de Biochimie-Microbiologie, UFR/SVT, Université Nazi Boni, 01 BP 1091 Bobo-Dioulasso 01, Burkina Faso.*
Corresponding author; E-mail: kamsamieric@yahoo.fr; Phone: 00 226 76 64 49 73.

ABSTRACT

The use of complementary and alternative medicine in the management of diabetes is of growing health and economic importance in Africa. This study aimed to determine medicinal practices among diabetic patients attending the clinical laboratory of Centre MURAZ, Burkina Faso. A semi-structured survey was carried out from April to August 2022 among patients. The glycaemia and glycated hemoglobin levels in patients were evaluated respectively by enzymatic colorimetric and turbidimetric immunoassay methods. Fifty diabetic subjects were enrolled. They were mainly illiterate and in 40 to 60 age group. The most pathologies were type II, with common risk factors such as family history (64%) and hypertension (51.06%). The conventional treatment was dominant (68%), followed by the combination of conventional and traditional medicine based on medicinal plants (30%). *Sclerocarya birrea* (38.46%) and *Euphorbia hirta* (30.76%) were the most used species. A glycemic imbalance was noted in most of patients, and was significant in patients using a combination of conventional and traditional medicine (P = 0.0134), followed by patients with traditional treatment only (P = 0.0247). Almost all of glycemic balances were not significantly influenced by medicinal practices. This study highlighted various therapies used among diabetic patients attending the clinical laboratory of Centre MURAZ. © 2024 International Formulae Group. All rights reserved.

Keywords: Diabetes, medicinal practices, glycemic balance, Centre MURAZ, Burkina Faso.

INTRODUCTION

Nowadays diabetes mellitus (DM) is one of the most prevalent metabolic disorder worldwide. Indeed, 422 million people were affected globally in 2014; and this is projected to reach 693 million in 2045 (Asharani et al., 2020). This pathology causes higher rates of morbidity and mortality. As an example, in 2017, 5 million of deaths in the world were attributable to diabetes or related complications such as nephropathy, retinopathy, cardiovascular and cerebrovascular diseases (Cho et al., 2017). In the same year, 15.9 million Africans were living with diabetes and 42.9 million people aged 18 to 99 were pre-diabetes (Kouassi et al., 2020). In sub-Saharan Africa than elsewhere, DM remains a public health concern. Its prevalence varies from 0.2% to 12%, with many undiagnosed cases and predictions of around 90% by 2030 (Yaméogo et al., 2016). This prevalence in Burkina Faso was 4.9% among population aged 25 to 64 in 2013; and was more significant in urban areas (5.8%) than in rural ones (4.6%) (Ministry of Health, 2014).

Diabetes management is essential for life quality and expectancy improvement. It includes generally lifestyle changes, oral hypoglycemic agents use, and insulin injection (Deeg, 2005). However, because patients in sub-Saharan Africa face challenges in accessing the health care in addition to medicines high cost and customary beliefs, the majority resort exclusively or partially to traditional medicines (Gning, 2007). Studies also showed that a great diversity of plants are using in DM management in this area. Indeed, a cross-sectional survey conducted in Dakar (Senegal) among diabetes patients showed that forty-one medicinal plants were used with mostly satisfactory results (65%) (Dièye et al., 2008). In Togo, 132 plant recipes are used by traditional healers as antidiabetics (Gbekley et al., 2015).

Another study carried out in Burkina Faso showed that 28 medicinal plants are used for diabetes management in Bobo-Dioulasso region (Segda et al., 2023). In addition, several studies have proven the antidiabetic properties of medicinal plants in cells and animals (Matalqah and Al-Tawalbeh, 2019; Paul et al., 2024; Upadhyay et al., 2024). However, so far, few clinical trials have been carried out to prove the efficacy and the innocuousness of these plants in human beings. This study aimed to determine complementary and alternative medicinal practices among diabetic patients in order to enlighten future research on diabetes management.

MATERIALS AND METHODS

Study site

This study was performed at Centre MURAZ, a research institute of the Ministry of Health and Public Hygiene located in Bobo-Dioulasso, west region of Burkina Faso. This center created in 1939 is part of National Institute of Public Health (INSP). Its mission is to contribute to the prevention, diagnosis and control of communicable and non-communicable diseases. The Clinical Laboratory of Centre MURAZ has a great reputation, and receives patients of Bobo-Dioulasso and beyond.

Study population

All patients seen in the clinical laboratory of Centre MURAZ and respecting the following conditions:

- ✓ be confirmed diabetic;
- ✓ have the medical prescription for glycaemia and glycated hemoglobin;
- ✓ be fasting for 8 to 12 hours.

Patients whose antidiabetic treatment was unknown and serum was icteric or hemolyzed were excluded from the study.

Ethical considerations

All protocols followed were in accordance with the ethical requirements of Centre MURAZ qualified in the conduct of clinical trials (N° 2024/042/MSHP/MESRI/CERS). Each study participant gave his free and informed consent.

The anonymity and the information obtained from participants are kept strictly confidential.

Study design

A semi-structured survey was carried out from April to August 2022 among diabetic patients attending the clinical laboratory of Centre MURAZ. Data collected were: sociodemographic characteristics, clinical status and therapeutic approach of the interviewees. The glycemic balance in diabetic patients was assessed through the measurement of glycaemia and glycated hemoglobin levels respectively by enzymatic colorimetric (INDIKO, Thermoscientific) and turbidimetric immunoassay (HumaMeterA1c, Human) methods. Medicinal plants used were botanically identified through the "catalogue des plantes vasculaires du Burkina Faso"; and authenticated by a botanist from University Nazi BONI, Burkina Faso.

Data analysis

The R (4.2.1) and GraphPad (8.0.2.263) softwares were used respectively for statistical analysis and graphical representations. Statistical analysis was performed using ANOVA test. The significance threshold of the statistical tests was 5%.

RESULTS

Sociodemographic characteristics

This study involved 50 diabetics with 43.14% of male and 56.86% of female. Their average age was 56.02 ± 11.19 years with a minimum of 26 years and a maximum of 83 years. Around 36% of respondents were illiterate and 32% had reached secondary school and the other interviewees had primary and university levels (16% each). Figure 1 shows patients' distribution according age groups and sex. The majority of diabetics was females in the 40 to 60 age group followed by 60 to 80.

Clinical status of diabetes

Figure 2 presents the clinical status of the diabetics surveyed. More than 70% of them did not know their diabetic type; and 30% had type II (Figure 2a). For 52% of the patients, the disease duration was less than 5 years (Figure 2b); and were diagnosed mainly in the 40 and 50 age group, followed by the 50 to 60 years group (Figure 2c).

Main risk factors and associated diseases

A family history of diabetes was recorded in most of the respondents (64%). In addition to this pathology, 66% of patients suffered from other types of disease, such as hypertension (51.06%), heart disease (17.02%), asthma and obesity (8.51% each) followed by Gout (6.38%). Hemorrhoid, Sinusitis, Ulcer and Nerve disease were the least cited (Table 1).

Therapeutic approach

Figure 3 summarizes the medicinal practices of diabetics. Around 92% of patients used conventional treatment as monotherapy (68%), or in association with traditional medicine (24%). Metformin (28.30%), glucophage (18.86%) and insulin (13.20%) followed by Glyferon and Glimepiride (8.51% each) were the most cited conventional drugs (Table 2). Pure traditional medicine based on medicinal plants was used by 6% of respondents.

Medicinal plants used

The results showed that 30% of interviews have used a traditional herbal for diabetes treatment. The species used and their frequency of use are shown in Table 3. Eight (8) medicinal plants belonging to 6 families were used for DM management. The Anacardiaceae (3 species) was the most represented family. *Sclerocarya birrea* (A.Rich.) Hochst. (38.46%) and *Euphorbia hirta* L. (30.76%) were the most used plant species, followed by *Mangnifera indica* L.

[cult.] (23.07%) and *Ziziphus mauritiana* Lam. (15.38%).

Preparation and administration methods

Leaves (71.43%) followed by stem bark (21.42%) were the most used plant organs (Figure 4); and the decoction (60%) was the main method of preparing recipes (Figure 5). The preparations were taken orally.

Glycemic balance in patients

The glycemic balance of the patients was assessed by measuring blood sugar and glycated hemoglobin levels (HbA1c). The results were analyzed according to the reference values used in clinical laboratory (Centre MURAZ) for glycaemia (3.5-6.11 mmol/L) and the recommendations of International Diabetes Federation (IDF) and American Diabetes Association (ADA) for glycated hemoglobin levels ($\leq$ 7%). A glycemic imbalance was noted in most patients who had hyperglycemia (80%) and high levels of glycated hemoglobin (64%) (Table 4).

Effect of treatments on glycemic balance

The patients were divided into four groups based on their medicinal practice. The epidemiological-clinical characteristics of the patients groups are summarized in the Table 5. The average age was higher in patients receiving traditional (67.66 years) and modern (56.38 years) treatment only. The disease duration was higher in patients receiving conventional treatment. Significant differences were found in the patients' mean blood glucose levels (P = 0.024). These values were higher in diabetics who used traditional medicine (P = 0.0247) and those who combined traditional and conventional medicines (P = 0.0134). Almost all (98%) of the mean HbA1C levels were out of balance and were not significantly influenced by medicinal practices (P = 0.32).
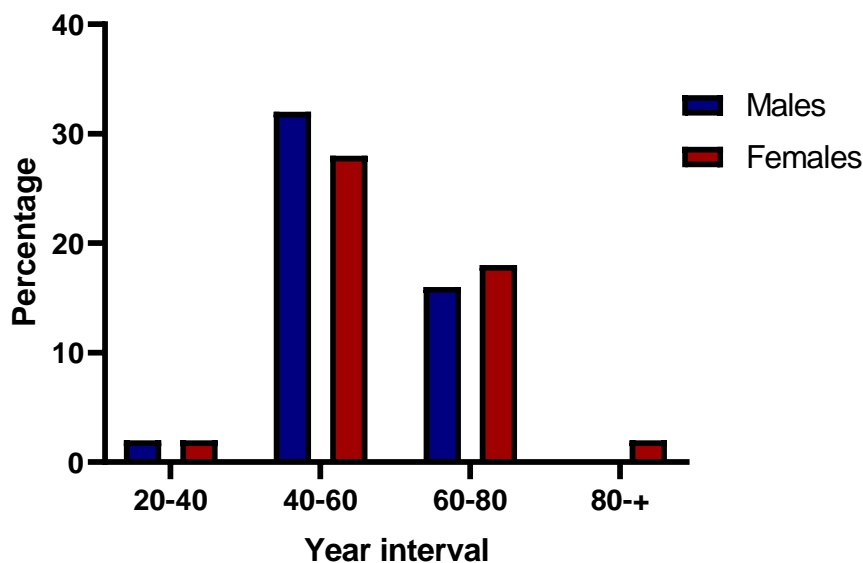

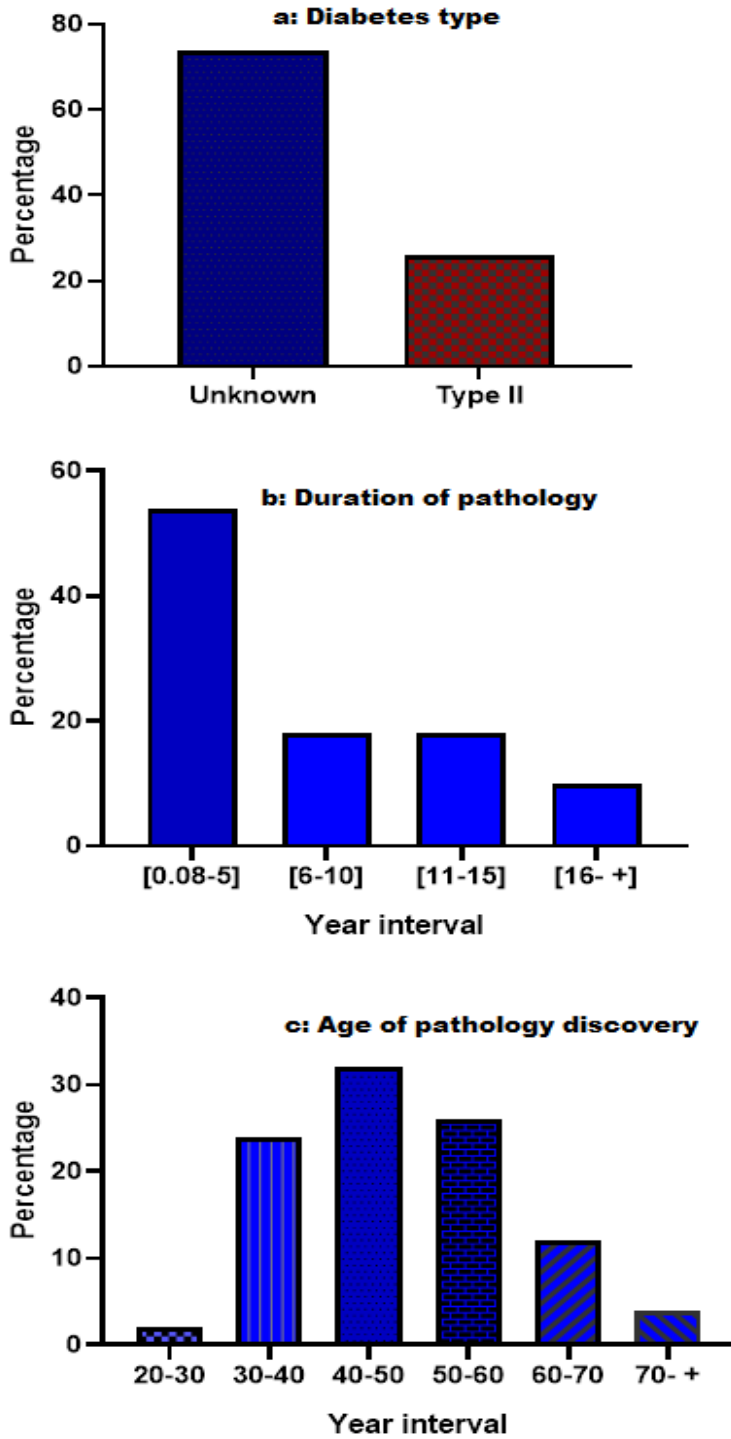**Figure 1:** Distribution of patients according to age groups and sex.

Figure 2: Clinical status of diabetes.

Table 1: Diseases associated to diabetes in patients.

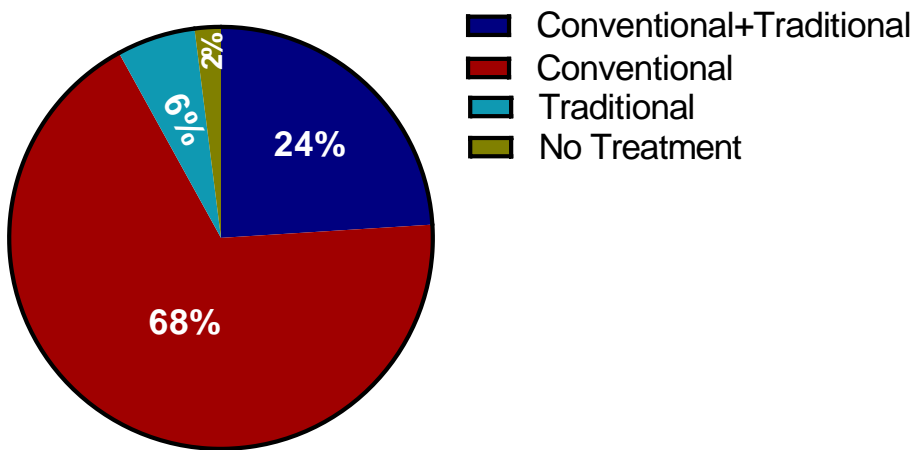| Disease	Citation Score	Citation frequency (%)
Hypertension	24	51.06
Heart disease	8	17.02
Asthma	4	8.51
Obesity	4	8.51
Gout disease	3	6.38
Hemorrhoid	1	2.12
Sinusitis	1	2.12
Ulcer	1	2.12
Nerve disease	1	2.12

Figure 3: Patients' therapeutic approach.

Table 2: Conventional drug used by patients.

Drug	Citation Score	Citation frequency (%)
Metformin	15	28.30
Glucophage	10	18.86
Insulin	7	13.20
Glyferon	3	8.51
Glimepiride	3	8.51
Gluforte	2	5.66
Metforal	2	5.66
Ranophage	1	1.88
Geminor	1	1.88

Melmet	1	1.88
Diamicron	1	1.88
Glusinet	1	1.88
Stagid	1	1.88
Fairmet	1	1.88
Clibenclamide	1	1.88
Meforan Myl	1	1.88
Amarel	1	1.88
Glibomet	1	1.88

Table 3: Medicinal plants used.

| Plant name	Local name	Families	RFC (%)	Part used	Mode of preparation
Sclerocarya birrea (A.Rich.) Hochst.	Nogosigawaba	Anacardiaceae	38.46	Leaves, Stem barks	Powder, Maceration, Decoction
Euphorbia hirta L.	Tougani sindji	Euphorbiaceae	30.76	Leaves	Decoction
Mangifera indica L. [cult.]	Mangoro yiri	Anacardiaceae	23.07	Leaves	Decoction
Ziziphus mauritiana Lam.	Tomono yiri	Rhamnaceae	15.38	Leaves	Decoction
Detarium microcarpum Guill. & Perr.	Tama Koumba	Fabaceae	7.69	Leaves	Powder, Maceration
Combretum micranthum G.Don	N'golobgè	Combretaceae	7.69	Leaves	Decoction
Anacardium occidentale L. [cult.]	Finssan yiri	Anacardiaceae	7.39	Leaves	Decoction
Nauclea latifolia Sm.	Bati yiri	Rubiaceae	7.69	Stem roots	Maceration

RFC Relative Frequency of Citation
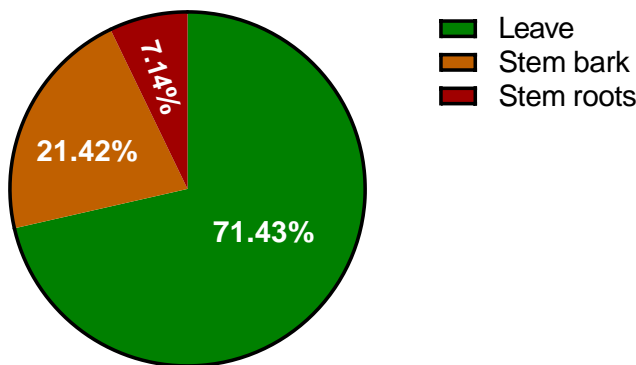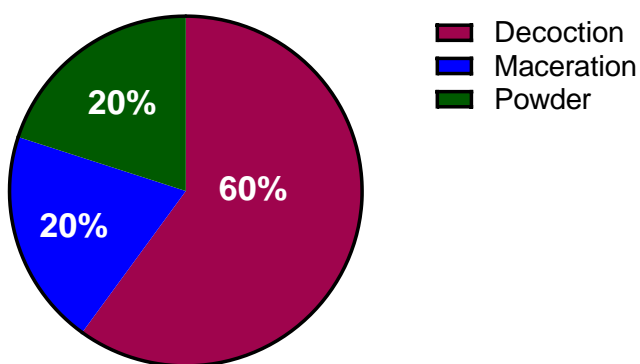

Figure 4: Plant parts used.

Figure 5: Drug preparation methods.

Table 4: Glycemic balance of patients.

	Patients number	(%)
Biological marker		
Glycemia (mmol/L)		
<3,5	0	0
3,5 à 6,11	10	20
> 6,11	40	80
HbA1c (%)		
<6%	9	18
6 à 7%	9	18
> 7%	22	64

Tableau 5: Epidemiological-clinical characteristics.

	Conventional + traditional	Conventional	traditional	No treatment	P value
Patients number	12	34	3	1	0.001
Average age (years)	52±8.36	56.38±11.08	67.66±10.15	52±0.00	0.45
Age of pathology (years)	6.13±8.87	7.53±6.76	3.03±2.96	4±0.00	0.017
Glycemia (mmol/L)	10.7±0.94	8.22 ±0.56	12.2±2.65	7.3±0.00	**0.024**
HbA1C (%)	9.2±1.13	7.66±0.35	9.26±0.96	6.3±0.00	**0.32**

Significance threshold = 5%.

DISCUSSION

This study aimed to determine complementary and alternative medicinal practices among diabetic patients attending the clinical laboratory of Centre MURAZ, Burkina Faso. Fifty (50) diabetics were involved and 30% had diabetes type II. The majority of diabetics was females and was in the 40 to 60 age group followed by the 60 to 80 group. A survey carried out in 2013 by Ministry of Health had shown that diabetes prevalence in Burkina Faso generally increases with age and the female gender represents an important risk factor. This female predominance would be linked to factors such as obesity considered as beauty criterion; longer life expectancy and menopause (Diouf et al., 2013). Another study conducted in 2014 in three health centers of Bobo-Dioulasso also showed that the group of patients over 40 years was extremely affected by diabetes (Koevi et al., 2014). This could be explained by a change in carbohydrate metabolism favored by aging (Fattorusso and Ritter, 2004; Haslett-E, 2004). The main risk factors and associated diseases were respectively family history of diabetes and hypertension. Hypertension is known to be a major factor associated with diabetes as previously reported by Sagna et al., 2014. This predominance could also be linked to the high frequency of this pathology in Burkina Faso in general (Soubeiga et al., 2017). Concerning therapeutic approach, four types of medicinal practices have been identified with a dominance of conventional treatment as monotherapy, or in association with plant-based traditional medicine. Eight (Gbekley et al., 2015) medicinal plants belonging to 6 families were used for DM management. *Sclerocarya birrea*, *Euphorbia hirta*, *Mangnifera indica*, *Ziziphus mauritiana*, were the most used plant species. Previous studies have also demonstrated the frequent use of some of these plants as antidiabetics by traditional healers, patients, nurses and other local actors (Gbekley et al., 2015; Diop et al., 2022). Other works have documented the presence of normoglycaemic substances in extracts of *S. birrea*, and *M. indica* and *E. hirta* (Afolayan and Sunmonu, 2010; Patil et al., 2011; Fofie et al., 2013). Decoction was the main method of preparing recipes and traditional drugs were taken orally. The glycemic balance of the patients was assessed by measuring blood sugar and glycated hemoglobin levels. According to the "Revue francophone des laboratoires" (2018), HbA1c is the reference parameter allowing an overview of glycemic balance over 2 to 3 months preceding the dosage (Hay-Lombardie and Bigot, 2018). HbA1c is a glycation-related product of blood proteins whose accumulation causes complications microvascular: nephropathy, retinopathy, neuropathy; and macrovascular: cardiovascular diseases, stroke (Anago et al., 2022). HbA1c was abnormal in the majority of patients. A glycemic imbalance was noted in most patients and was not significantly influenced by medicinal practices. A monitoring of epidemiological-clinical characteristics could contribute to a better evaluation of treatments effects on glycemic balance.

Conclusion

This study summarizes various medicinal practices and diverse epidemiological-clinical characteristics among 50 diabetics attending the clinical laboratory of Centre MURAZ. Four types of medicinal practices have been identified with a dominance of conventional treatment as monotherapy, or in association with traditional medicine plant-based. Almost all of patients had a glycemic imbalance. This study highlighted the reality of DM management in the present study, and could contribute to improving the diabetics care.

COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHORS' CONTRIBUTIONS

The authors confirm contribution to the paper as follows: study conception and design: SEK, RNTM, AS and A-SO; data collection analysis and interpretation of results: ISB, RS, DSBD and MM; draft manuscript preparation: AS, CT, AK and BKK. All authors reviewed

the results and approved the final version of the manuscript.

ACKNOWLEDGMENTS

REFERENCES

Afolayan AJ, Sunmonu TO. 2010. *In vivo* studies on antidiabetic plants used in South African herbal medicine. *Journal of Clinical Biochemistry and Nutrition*, **47**(2): 98–106. DOI: https://doi.org/10.3164/jcbn.09-126R.

Anago E, Djogbede G, Fiogbe EMS, Segbo GAJ, Akpovi DC. 2022. Rôle de la glycation des protéines dans les complications et la thérapie du diabète: revue bibliographique. *Int. J. Biol. Chem. Sci.*, **16**(6): 2930-2944. DOI: https://dx.doi.org/10.4314/ijbcs.v16i6.37.

Asharani PV, Abdin E, Kumarasan R, Devi F, Kumar S, Shafie S, Jeyagurunathan A, Chua BY, Vaingankar JA, Fang SC, Lee ES, Dam RV, Chong SA, Subramaniam M. 2020. Study protocol for a nationwide Knowledge , Attitudes and Practices (KAP) survey on diabetes in Singapore's general population. *BMJ Open*, **10**: e037125, 1–8. DOI: https://doi.org/10.1136/bmjopen-2020-037125.

Cho NH, Shaw JE, Karuranga S, Huang Y, da Rocha Fernandes JD, Ohlrogge AW, Malanda B. 2018. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. *Diabetes Research and Clinical Practice*, **138**: 271-281. DOI: https://doi.org/10.1016/j.diabres.2018.02.023.

Deeg M. 2005. Basic approach to managing hyperglycemia for the nonendocrinologist. A*m J Cardiol*, **22**: 37–40.

Dièye AM, Sarr A, Diop SN, Ndiaye M, Sy G, Diarra M, Rajraji/Gaffary I, Ndiaye/Sy A, Ndiaye B, Faye B. 2008. Medicinal plants and the treatment of diabetes in Senegal : survey with patients. *Fundamental & Clinical Pharmacology*, **22**: 211–216. DOI: https://doi.org/10.1111/j.1472-8206.2007.00563.x.

Diop M, Niang-Diop F, Dieng SD, Samb A, Manga GED, Sané AP, Sène MB, Sambou B, Goudiaby A, Diatta EA. 2022. Ethnobotanical study of medicinal plants for treatment of diabetes and hypertension used in communities near Fathala Forest, Senegal. *Ethnobotany Research and Applications*, **23**(7): 1–15. DOI: https://doi.org/10.32859/era.23.7.1-15.

Diouf NN, Boye O, Soumboundou M, Guèye MW, Sawaré EM. 2013. Evaluation de l'équilibre glycémique chez les sujets âgés présentant un diabète de type 2. *Revue Médicale de Madagascar*, **3**(2): 269–272.

Fattorusso V, Ritter O. 2004. Maladies du métabolisme et de la nutrition. In *Vadémécum Clinique : du Diagnostic au Traitement* (17th edn). MASSON : Paris ; 802-821.

Fofie YNG, Sanogo R, Diarra B, Kanadjigui F, Kone-Bamba D. 2013. Antioxidant and anti-hyperglycaemic activity of *Euphorbia hirta* L. on Wistar rats. *Int. J. Biol. Chem. Sci*, **7**(6): 2558-2567. DOI: http://dx.doi.org/10.4314/ijbcs.v7i6.30.

Gbekley EH, Karou DS, Gnoula CAK, Anani K, Tchacondo TA, Amegnona BK, Simpore J. 2015. Étude ethnobotanique des plantes utilisées dans le traitement du diabète dans la médecine traditionnelle de la région Maritime du Togo. *PAMJ*, **20**(437). DOI: https://doi.org/10.11604/pamj.2015.20.437.5660.

Gning SB, Thiam M, Fall F, Ba-Fall K, Mbaye PS, Fourcade L. 2007. Le diabète sucré en Afrique subSaharienne aspects épidémiologiques, difficultés de prise en charge. *Medecine Tropicale*, **67**(6): 607–611.

Haslett-E C. 2004. *Médecine Interne Principes et Pratiques* (19th edn). Maloine : Paris.

Hay-Lombardie A, Bigot-Corbel E. 2018. Biomarqueurs permettant le suivi de

l'équilibre glycémique du patient diabétique. *Revue Francophone des Laboratoires*, **502**: 33-43.

Koevi KA, Millogo V, Ouedraogo M, Ouedraogo GA. 2014. Diagnostic des causes de complication du diabète et des méthodes de prévention à Bobo-Dioulasso , au Burkina *Faso. Int. J. Biol. Chem. Sci.*, **8**(6): 2709–2720. DOI: http://dx.doi.org/10.4314/ijbcs.v8i6.30

Kouassi KC, Fétéké L, Etassoli S, Gbekley EH, Karou DS. 2020. Prévalence du pré-diabète et du diabète avec profil lipidique évalué, en milieu hospitalier urbain: étude rétrospective sur 3538 patients reçus au CHU Campus de Lomé. *Int. J. Biol. Chem. Sci*, **14**(7): 2415-2422. DOI: https://dx.doi.org/10.4314/ijbcs.v14i7.4.

Matalqah SM, Al-Tawalbeh DM. 2019. Medicinal plants potential against diabetes mellitus: review article. *IJP*, **6**(2): 39–53. DOI: https://doi.org/10.13040/IJPSR.0975-8232.IJP.6(2).39-53.

Ministry of Health. 2014. Rapport de l'enquete nationale sur la prevalence des principaux facteurs de risques communs aux maladies non transmissibles au Burkina Faso enquete STEPS 2013. p 81.

Patil R, Patil R, Ahirwar B, Ahirwar D. 2011. Current status of Indian medicinal plants with antidiabetic potential: A review. *Asian Pacific Journal of Tropical Biomedicine*, SUPPL. 2, s292-298. DOI: https://doi.org/10.1016/S2221-1691(11)60175-5.

Paul T, Pathak K, Saikia R, Gogoi U, Jyoti SJ, Das, A. 2024. The Role of Medicinal Plants in the Treatment and Management of Type 2 Diabetes. *Current Traditional Medicine*, **10**(2): 83–96. DOI: https://doi.org/10.2174/22150838096662 30223164613.

Sagna Y, Tieno H, Guira O, Yanogo DAR, Benon LE, Zida S, Nikiema P, Kabore PR, Tonde AP, Traore R, Ouedraogo DD, Drabo, YJ. 2014. Prevalence and associated risk factors of diabetes and impaired fasting glucose in urban population ; a study from Burkina Faso. *Journal of Diabetology*, **2**(4): 2–10.

Segda A, Meda RN, Bangou MJ, Koama BK, Ouoba HY, Kagambega W, Kam SE, Ouedraogo GA. 2023. Ethnobotany of Medicinal Plants for Diabetes and Antioxidant Activity of Selected *Phyllanthus amarus* Schum and *Thonn ., Chrysanthellum americanum* (L .) Vatke. and *Striga hermonthica* (Delile) Benth. of Burkina Faso. *Natural Products Chemistry and Research*, **11**(03): 1–7. DOI: https://doi.org/10.35248/2329-6836.23.11.3.1-7.

Soubeiga JK, Millogo T, Bicaba BW, Doulougou B, Kouanda S. 2017. Prevalence and factors associated with hypertension in Burkina Faso: A countrywide cross-sectional study. *BMC Public Health*, **17**(1): 1–8. DOI: https://doi.org/10.1186/s12889-016-3926-8.

Upadhyay TK, Das S, Mathur M, Alam M, Bhardwaj R, Joshi N, Sharangi AB. 2024. Medicinal plants and their bioactive components with antidiabetic potentials. *Antidiabetic Medicinal Plants*, **2024**: 327–364. DOI: https://doi.org/10.1016/B978-0-323-95719-9.00017-3.

Yaméogo T, Rouamba N, Sombié I, Djingri L, Kyelem C, Ouédraogo M, Guira O, Sawadogo A, Drabo Y. 2016. Facteurs d'adhésion des diabétiques à leur suivi dans un contexte de ressources limitées : cas du Burkina Faso. *RAFMI*, **3**(2): 17–22.