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Nigerian medicinal plants with *in vivo* anti diabetic activity: A systematic review and Meta-analysis

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Abstract
The aim of this study was to systematically review the literature for scientific information on Nigerian medicinal plants with antidiabetic activity providing researchers with valuable information on the most common plants species and methods used. A search was carried out for studies investigating the antidiabetic activity of Nigerian medicinal plants using the following scientific data bases; science direct, Google scholar, PubMed and Directory of open access journals (DOAJ). The search included articles from January 2014-2019. To assess the quality of the Studies, the Jadad scale was used. The information recorded included; plant name, family, diabetic model used, Intervention, duration of study and Outcome. Randomized controlled trials which evaluated the hypoglycemic effects of plants with significant outcome of decrease in fasting blood glucose (FBG) were included. Most of the plants in this study showed significant glycemic control. There is need for further studies to identify the phytochemicals responsible for the activity.

Keywords: medicinal plants, antidiabetic, systematic review, meta-analysis

1. Introduction

Worldwide, approximately 422 million people suffer from Diabetes mellitus [1] and by the year 2040, the number of people with Diabetes mellitus is estimated to rise to 642 million globally [2]. Diabetes Mellitus (DM) is a chronic metabolic disorder characterized by inadequate secretion of insulin or development of insulin resistance. The disorder is characterized by hyperglycemia, polyuria, polydipsia and polyphagia. Diabetes mellitus is classified into two main types namely; type 1 and type 2 diabetes mellitus. Type 1 which is also called as insulin dependent diabetes is an autoimmune disorder leading to destruction of pancreatic β-cells which leads to decrease in the secretion of insulin [3].The increase in prevalence of diabetes and the side-effects of current drugs used in management of diabetes mellitus necessitates the need to search for alternatives [4,5]. About 80% of the populations in developing countries rely on medicinal plants as the main source of treatment of diseases [6, 7, 8].

The catalogue of antidiabetic medicinal plants is growing at a high rate especially in Africa. This may be due to the high cost of managing diabetes which forces patients to source for alternative and cheaper options. This overreliance on antidiabetic medicinal plants has probably invoked scientists to bioassay these plants in an effort to identify more hypoglycemic medicinal plants. The antidiabetic potential of some medicinal plants extracts has been demonstrated in human and animal models of type II diabetes [9]. There is an increase in the number of scientific publications on medicinal plants and diabetes [10]. Therefore the aim of this study is to systematically review the literature for scientific information on Nigerian medicinal plants with antidiabetic activity providing researchers with valuable information on the most common plants species and methods used.

2. Materials and Method

2.1 Sources of information and eligibility criteria

The present meta-analysis was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [11]. A search was carried out for studies investigating the antidiabetic activity of Nigerian medicinal plants using the following scientific data bases; science direct, Google scholar, Science direct, PubMed, Hindawi and Directory of open access journals (DOAJ). The search included articles from January 2014-2019. The Jadad scale was used to evaluate the quality of the studies [12]. The search terms were antidiabetic activity, medicinal plants. The search was limited to Nigerian authors. The information recorded include; name of plant, family, local name(s), diabetic model used, dose used, part of plant used, duration of study and Outcome.

2.2 Inclusion Criteria

Randomized controlled trials which evaluated the antidiabetic effects of plants with significant outcome of decrease in blood glucose were included. The search was limited to articles in English language and authors with Nigerian affiliation.

2.3 Exclusion Criteria

Articles with Jadad score less than three (3), studies targeting specific mechanism of action, *in vitro studies* and studies on diabetic complications were excluded.

3. Results

A total of 15,283 records were identified through database search; 3,830 entries for PubMed, 9591 from science direct, 121 from

Table 1: Animal studies on Nigerian Medicinal Plants

S/N	Plants	Target	Groups	Intervention	Duration	Drug standard	Author(s)
1	*Tamarindus Indica*	Alloxan	Diabetic rats	1000mg/kg 90%methanol stem-bark extract	24hours	Metformin	Yerima, 2018 [13]
2	*Clerodendrum volubile*	Streptozocin	normal and diabetic rats	400mg/kg n-butanol, ethyl acetate, methanol leaf extracts	21days	glibenclamide	Erukainure *et al*., 2018 [14]
3	*Dennettia tripetala*	Streptozocin	normal and diabetic rats	50mg/kg seed methanol extract	10days	glibenclamide	Innocent *et al*.,2017 [15]
4	*Ocimum canum*	Streptozocin	diabetic rats	100mg/kg methanol leaf extract	15days	glibenclamide	Ononamadu *et al*., 2019 [16]
5	*Gouania longipetala*	Alloxan	diabetic rats	150mg/kg methanol leaf extract	21days	glibenclamide	Maxwell *et al*., 2014 [17]
6	*Thaumatococcus danielli*	Streptozocin	Normal and diabetic rats	500mg/kg ethanol leaf extract	14days	Glibenclamide	Folorunsho *et al*., 2019 [18]
7	*Balanites aegyptiaca*	Streptozocin	Normal and diabetic	200mg/kg70% ethanol stem-bark extract	120minutes	metformin	Mhya *et al*., 2016 [19]
8	*Cucumis sativus*	Alloxan	Diabetic rats	400mg/kgAqueous stem-bark extract	15days	metformin	Ibitoye *et al*., 2017 [20]
9	*Morinda lucida*	Alloxan	Normal and diabetic rats	500mg/kg stem-bark aqueous extract	8days	glibenclamide	Adeneye *et al*., 2017[21]
10	*Ocimum gratissimum*	Streptozocin	Normal and diabetic rats	250mg/kg 80% methanol leaf extract	28days	metformin	Stanley *et al*., 2017[22]]
11	*Sapium ellipticum*	Streptozocin	Normal and diabetic rats	800mg/kg ethanol	21days	metformin	Osasaneng 2017[23]
12	*Citrus aurantifolia*	Alloxan	normal and diabetic rats	100mg/kg Aqueous	14 days	Metformin	Ibrahim *et al*., 2018 [24]
13	*Ricinus comminus*	alloxan	normal and diabetic rats	400mg/kgSeed methanol extract	21days	metformin	Nwodo *et al*., 2016 [25]
14	*Salacia lehmbachii*	alloxan	normal and diabetic rats	400mg/kg 96% methanol Stem bark	21 days	glibenclamide	Joseph *et al*., 2018 [26]
15	*Uvaria chamae*	Alloxan		400 mg/kg Root ethanol	15days	glibenclamide and pioglitazone	Jonathan *et al*., 2018 [27]
16	*Aristolochia ringens*	streptozotocin	diabetic rats	150mg/kg Methanol leaf and stem bark	7days	metformin	Sulayman *et al*., 2019 [28]
17	*Jatropha curcas*	Alloxan	normal and diabetic rats	Methanol leaf	7days	metformin	Aina *et al*., 2016 [29]
18	*Massularia acuminata*	alloxan	diabetic rats	89.44 mg/kg 70% ethanol Stem	5days	glibenclamide	Emmanuel *et al*., 2018 [30]
19	*Strophanthus hispidus*	Alloxan	normal and diabetic rats	200mg/kg Aqueous Root	28 days	Glibenclamide	Fageyinbo *et al*., 2019 [31]
20	*Moringa oleifera*	Alloxan	diabetic rats	Ethanol 800mg/kg seeds,leaves, stem, roots	6hours	acarbose	Idakwoji *et al*., 2016 [32]
21	*Vernonia amygdalina*	streptozotocin	diabetic rats	200mg/kg Chloroform Leaves	28days	metformin	Stanley *et al*., 2019 [33]
22	*Anogeissus leiocarpus*	alloxan	diabetic rats	200mg/kg Ethanol roots	24hours	glibenclamide	Omeje *et al*., 2016 [34]
23	*Mitracarpus Scabrum*	Alloxan	normal and diabetic rats	300mg/kg leaves	14days	glibenclamide	Abubakar *et al*., 2016 [35]
24	*Hoslundia opposita*	alloxan	normal and diabetic rats	220 mg/kg Seed oil	96hours	metformin	Jubril, *et al*., 2014 [36]
25	*Senna singueana*	Streptozotocin	normal and diabetic rats	300mg/kg Acetone Stem-bark	28days	metformin	Mohammed and Shahidul 2014 [37]
26	*Parkia biglobosa*	streptozotocin	normal and diabetic rats	300mg/kg n-butanol leaves	5days	Metformin	Mohammed *et al*., 2016 [38]
27	*Blighia sapida*	Alloxan	normal and diabetic rats	400mg/kg methanol leaves	28days	glibenclamide	Oloyede *et al*., 2014[39]
28	*Chrysophyllum albidum*	alloxan	normal and diabetic rats	200 mg/kg ethanol Seeds	7days	metformin	Engwa *et al*., 2016[40]
29	*Anthocleista vogelii*	alloxan	normal and diabetic rats	200mg/kg Root bark Chloroform	21days	glibenclamide	Anyanwu *et al*., 2018[41]
30	*Synsepalum dulcificum*	streptozotocin	normal and diabetic rats	60 mg/kg 80% methanol Leaves	21days	glibenclamide	Obafemi, *et al*., 2019[42]
31	*Cola nitida*	fructose and streptozotocin	normal and diabetic rats	300 mg/kg aqueous seeds	42days	Metformin	Ochuko *et al* 2019 [43]
32	*Curculigo pilosa*	streptozotocin	normal and diabetic rats	methanol, n-butanol Rhizomes	28days	glibenclamide	Kayode and Charles, 2019 [44]
33	*Phyllanthus fraternus*	streptozotocin	normal and diabetic rats	200-300mg/kg leaves	28days	metformin	Nadro and Elkanah 2017[45]
34	*Phoenix Dactylifera*	Alloxan	normal and diabetic rats	400mg/kg ethanol seeds	14days	glibenclamide	Abiola *et al*., 2018[46]
35	*Acacia ataxacantha*	streptozotocin	normal and diabetic rats	125-500mg/kg 95% ethanol Roots	7days	metformin	Arise *et al*., 2016[47]
36	*Borassus aethiopum*	Alloxan	normal and diabetic rats	100-500mg/kg aqeous fruit	28days	glibenclamide	Issaka *et al*., 2016[48]
37	*Cnidoscolus aconitifolius*	streptozotocin	normal and diabetic rats	500 mg/kg	28days	glibenclamide	Achi *et al*., 2016[49]
38	*Adansonia digitata*	Alloxan	normal and diabetic rats	200mg/kg fruit aqueous	14days	Chlorpropamide	Muhammad *et al*., 2016[50]
39	*Newbouldia laevis*	alloxan	normal and diabetic rats	250-1000mg/kg Hydro alcohol leaves	24hours	glibenclamide	Osigwe *et al*., 2015[51]
40	*Ceiba pentandra*	Alloxan	normal and diabetic rats	200-800mg/kg stem-bark methanol	14days	glibenclamide	Odoh *et al*., 2016[52]
41	*Tabernaemontana pachysiphon*	alloxan	normal and diabetic rats	125-1000mg/kg methanolstem bark	14days	glibenclamide	Osamuyi *et al*., 2017[53]
42	*Ageratum conyzoides*	streptozotocin	normal and diabetic rats	200-800mg/kg ethyl acetate, leaves	14days	metformin	Agbafor *et al*., 2015 [54]
43	*Myrianthus arboreus*	streptozotocin	normal and diabetic rats	100-400mg/kg Ethanol stem bark	28days	glibenclamide	Dickson *et al*., 2016 [55]
44	*Dioscoreophyllum cumminsii*	alloxan	diabetic rats	50-300mg/kg leaves	21days	glibenclamide	Oloyede *et al*., 2015[56]

Directory of open access journals (DOAJ), 1051 from Hindawi and 690 from Google scholar. After duplicate papers were discarded and filters applied a selection of 5,986 studies remain. 5, 714 studies were screened out by reading the title paper, abstract and full paper for the following reasons; 5,535 did not meet the inclusion criteria, 123 studies had a Jadad Scale less than three (3), 35 studies were *in vitro* studies and 33 studies were on diabetic complications. A total of 44 articles were included in this study.

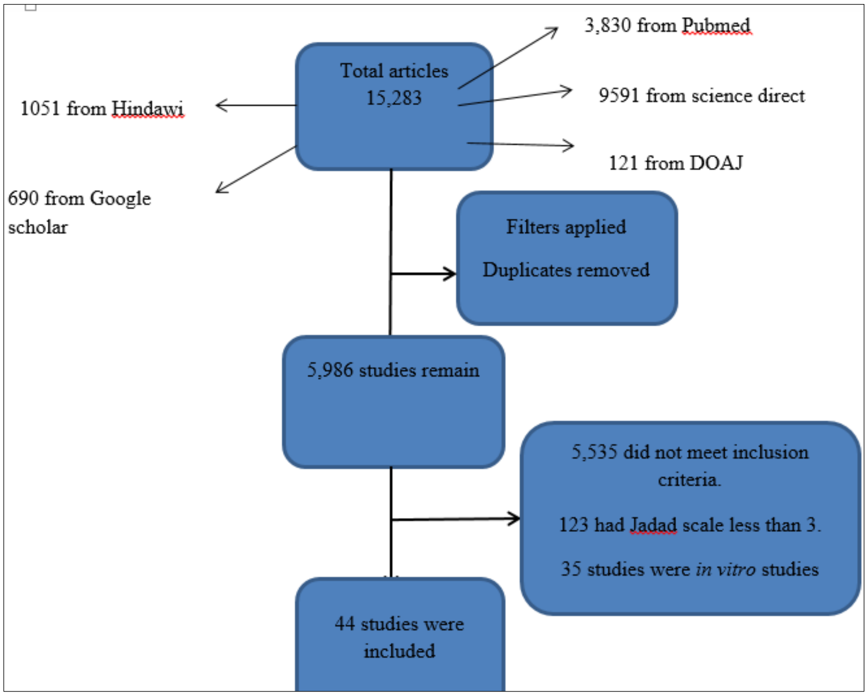

Fig 1: Flowchart of the selection of the articles

Plant parts used as material for the extraction and biological activity should be based on the ethnopharmacological use of the plants. This will direct researchers interested in isolation and characterization of active phytochemicals as well as researchers interested in clinical studies [57]. In the present study, 35.56% used leaves, 17.78% used stem bark, 11.11% seeds, 4.44% rhizomes, 11.11% fruit, 13.33% roots and 6.67% used mixed plant parts. Among the plants, 60% were trees, 31.11% shrubs and 8.89% herbs.

Chemical methods for the induction of diabetes provide a simple and cost effective model of diabetes in animals [58]. In the articles reviewed, 55.56% used alloxan to induce diabetes, 42.22% used Streptozocin while 2.22% used combination of Streptozocin and fructose. 88.89% of studies chose the oral route to administer plant extracts, while 11.11% chose the intraperitoneal route.

Conclusion

The systematic review and meta-analysis on Nigerian medicinal plants with antidiabetic activity will provide researchers with valuable information on the most common plants species and methods used.

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