Journal of Stress Physiology & Biochemistry, Vol. 20, No. 1, 2024, pp. 79-91 ISSN 1997-0838

ORIGINAL ARTICLE

OPEN ACCESS

Effects of Catechol containing fraction and other fractions of *Nauclea latifolia* aqueous root-bark extract on blood glucose, lipid profile and serum liver enzymes in streptozotocin – induced diabetic Wistar albino rats

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Received September 25, 2023

Background. Diabetes mellitus has been a menace to healthy human condition from antiquity. There has been continuous search for plant medicinal substances for drug development with an aim to managing this ailment with minimal drug side effects.

In this research work, effects of fractions of aqueous root-bark extract of *Nauclea latifolia* on blood glucose, lipid profile and serum liver enzymes in diabetic rats were investigated. Thirty –five Wistar albino rats weighing 164.1 – 171.6 grammes were used for this study involving aqueous root-bark extract fractions A, B, C and D. The rats were divided into 7 groups of 5 rats each. Group 1 was normal non-diabetic control, group 2 was diabetic control and groups 3, 4, 5 and 6 were rats treated with 250 mg/kg body weight of varying root-bark fractions while group 7 was diabetic rats treated with 5mg/kg. body weight of glibenclamide, the standard anti-diabetic drug. Fasting blood glucose levels were determined using digital glucometer (Acuu-chek, Mannheim, Germany). Lipid profile was determined using standard procedures. Serum liver enzymes were determined using assay kits. Fraction A was analyzed using gas chromatography- mass spectroscopy and nuclear magnetic resonance spectroscopy.

Results. Fraction A demonstrated the most effective anti-diabetic property compared to fractions B, C and D. It caused significant reduction in blood glucose levels. It also brought about significant decrease in the levels of triacylglycerol, very low density lipoprotein cholesterol and low density lipoprotein cholesterol. Aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase levels were also significantly reduced by it. Fraction A was found to contain catechol as the most abundant active principle.

Conclusion. Previous works on catechol show that catechol moiety either exists as a free molecule or a substituent of flavonoids and that it confers on them their anti-diabetic property. Since the catechol containing fraction A caused significant reduction in glucose levels, lipid profile and serum liver enzymes, it therefore has the potential for the management of diabetes mellitus and ameliorating its complications in clinical medicine.

Key words: Diabetes mellitus, Nauclea latifolia, Aqueous Extract, Catechol

Diabetes mellitus has been a threat to humanity from ancient times (Jonathan *et al.*, 2018). This disease has continued to inflict havoc globally (Tabish, 2007). It is a non-communicable disease characterized by metabolic disorder of various aetiologies described by sustained hyperglycaemia with disorders of carbohydrate, protein and fat metabolism due to abnormality in insulin secretion, its action or both (Alberti and Zimmet, 1998; Lowell *et al.*, 2021). Diabetes mellitus has been recognized as one of the significant killer diseases and a major cause of death in low- and middle income countries, WHO (2014). The disease, with time, affects adversely vital organs like the kidney, eye, heart, liver and the brain (Deshpande *et al* 2008; Al-Lawati, 2017). It is described as a global fatal trouble (Al-Lawati, 2017).

These complications increase the suffering of these patients as well as causing financial burden on them (Scully, 2012). The complications have been linked with short life expectancy in the diabetic patients (Sean *et al.,* 2017). Whereas majority of diabetic patients need oral hypoglycaemic drugs and or insulin, some of these patients can be managed on diet alone (Aguora *et al.*, 2015; Forouhi *et al.*, 2018). Presently, there are many natural or synthetic anti-diabetic drugs in pharmaceutical market. However, these drugs are not readily affordable in addition to their adverse side effects (Akomas *et al.*, 2014; Ayinla *et al.,* 2014; Aguora *et al.,* 2015). These disadvantages have led to the increased interests in researching towards the discovery of affordable and safer products for the management of diabetes mellitus in recent times (Remigio *et al.,* 2022; Dasofunjo *et al.,* 2013; Thomson *et al.,* 2007). The World Health Organization has also encouraged research into plant hypoglycaemic agents (Aguora *et al.,* 2015).

The use of plant agents for the management of diseases like diabetes mellitus is not a recent phenomenon. Since ancient times, humanity has looked for solutions for their disease conditions from the plant kingdom (Stojanoski, 1999; Biljana, 2012). The first recorded proof of medicinal plant utilization dates back to as far as 5000 years ago (Kelly, 2009). For instance, the Chinese book on roots and grasses referred to as 'Pen T'Sao" which was written by Emperor Shen Nung Circa 2500 BC described 365 drugs (dried parts of medicinal plants) many of which are still in use today and include *Rhei rhisoma*, *Camphor*, *Theae folium*, *Podophyllum*, the great yellow *Gentian, Ginseng*, *Jimson* weed, *Cinnamon* bark and *Ephedra* (Biljana, 2012). In this study, fractions of aqueous root-bark extract of *Nauclea latifolia* plant were investigated for their effects on blood glucose level, lipid profile and serum liver enzymes in streptozotocin - induced diabetic Wistar albino rats as well as the identification of the bioactive principle in the *Nauclea latifolia* root-bark fraction A.

Nauclea latifolia (African peach) is a herbal medicinal plant commonly used by the Idoma natives of North Central Nigeria for the management of diabetes mellitus (Ochalefu et al, 2018). It is an evergreen multi-stemmed tree and grows to a height of between 10 – 30 metres. The plant is mainly found in the humid tropical rain forest zone and the savannah wood lands of West and Central Africa (Okwori *et al.*, 2008).

MATERIALS AND METHODS

Sample collection and preparation

The root bark of *Nauclea latifolia* was harvested from the wild around the Federal University of Agriculture Makurdi, Benue State, Nigeria. The plant material was identified at the Federal School of Forestry, Jos, Plateau State, Nigeria where it was assigned voucher number FHJ 279 and deposited at the school's herbarium. The root bark was air-dried to a constant weight under shade and then pulverized into powder and stored in air-tight container until its usage.

Extraction

One hundred grammes of the pulverized root-bark was macerated in 1000 ml distilled water at a ratio of 1:10 (powder / solvent) (Das, Tiwari and Shrivastava, 2010). This was stirred intermittently at room temperature for 48 hours, followed by its filtration using muscilin cloth and Whatman No 1 filter paper size 110 mm. The filtrate was concentrated to dryness using water bath at 45^{o}C. This extract was stored in the refrigerator at 4^{o}C.

Fractionation of the Aqueous Root-bark Extract using Column Chromatography

Twenty grammes of the extract was completely mixed with forty grammes of silica gel (silica gel 60-120 mesh) and then dissolved in 100 ml of methanol to form slurry. This was allowed to dry forming a powder. The column was blocked at the stop cock lower down the column. The powder was then carefully poured into the column and mixtures of solvents (methanol, n-hexane and ethyl acetate) were used to run the column. After the column has been loaded, the stop cock was opened to enable the solvent level to drop to the top of the bed (packing). Necessary precaution was taken to ensure that the solvent layer did not go below this point as allowing the solvent level going below the stationary phase will result in air bubbles and channel formation leading to poor separation. The solvent was allowed to elute through the column one drop at a time. Eighteen fractions were collected. The fractions were pooled together to form four major fractions (fractions A, B, C and D) based on their polarity using thin layer chromatography. The fractions were put in water bath at 45^{o}C to enable evaporation of their solvent.

Administration of *Nauclea latifolia* aqueous root-bark extract fractions to streptozotocin-induced diabetic rats

Thirty- five male Wistar albino rats weighing 164.1-171.6 grammes were used for the study involving aqueous root-bark extract fractions A, B, C and D. The rats were divided into 7 groups of 5 rats each. Group 1 was normal, non-diabetic control, group 2 was diabetic control and groups 3, 4, 5 and 6 were diabetic rats treated with 250 mg/kg. body weight of *Nauclea latifolia* root-bark fractions A, B, C and D respectively while group 7 was diabetic rats treated with 5 mg/kg. body weight of glibenclamide, the standard anti-diabetic drug.

Evaluation of effects of fractions of aqueous root-bark extract of *Nauclea latifolia* on blood glucose level.

The fractions of aqueous root-bark of *Nauclea latifolia* were administered orally via intra-pharyngeal feeding canula to the diabetic rats at a dose of 250mg/kg. body weight following the determination of their initial blood glucose levels. The *Nauclea latifolia* fractions and the standard anti-diabetic drug, glibenclamide (5mg/ kg. body weight) were administered daily for 10 days.

The blood of the experimental rats was collected for fasting blood glucose determination on days 3, 7 and 10 by tail tipping method. The sample of blood was taken through a tiny incision on the tail tip. The blood sample was dropped on the dextrostix reagent pad that was inserted into the digital glucometer (Accu-chek, Mannheim, Germany) and the readings were recorded.

Determination of lipid profile and serum liver enzymes

Total cholesterol (TC), high density lipoprotein cholesterol (HDL-C) and triacylglycerol were determined using assay kits from Agape Diagnostic Switzerland. Very low density lipoprotein cholesterol (VLDL-C) was calculated according to the method of Burstein and Samaile (1960) by dividing the concentration of triacylglycerol by a factor of 5. The estimation of low density lipoprotein cholesterol (LDL-C) was done using the method of Friedwald, Levy and Fredrickson (1972) that entails the differential subtraction of the sum of the cholesterol fractions from total cholesterol

LDL = TC - HDL – VLDL

Assays of serum alanine aminotransferase and aspartate aminotransferase (Reitman and Frankel, 1957) were done according to procedures outlined in the manuals of Randox Laboratories, Antrim, United Kingdom. Serum alkaline phosphatase was analyzed using kits from Teco Diagnostic Anaheim, United States of America.

Further purification of root-bark fraction A using column chromatography

Fraction A having been found to have more positive effects on the biochemical parameters was subjected to further column chromatographic analysis to enhance its purity (This procedure was carried out after the Gas Chromatography – Mass Spectroscopy analysis of the fraction). Similar thin layer chromatographic procedure was performed for all the sub- fractions collected from the column chromatography of fraction A. Sub-fractions with similar polarity were also combined. Evaporation of the solvent left behind dried whitish crystal substance

which was subjected to Nuclear Magnetic Resonance Spectroscopy (NMR- Spectroscopy) analysis for characterization and structural elucidation (Figure 1).

Gas Chromatography-Mass Spectroscopy (GC-MS) analysis of *Nauclea latifolia* Root- bark Fraction A

The root-bark fraction A was analyzed using Gas Chromatography-Mass Spectroscopy at the Multi-user Signs Research Laboratory, Ahmadu Bello University, Zaria, Nigeria.

The conditions were set thus:

i In-port temperature 230°C
ii Initial temperature 105°C
iii Ramp rate 5° per 5 minutes till 300°C
iv Eluates were detected using a Mass Spectrum Detector (MSD).

Peaks were identified using comparison of their Kovat's indices, literature reports and National Institute for Standards (NIST) – 14 Libraries of compounds.

Determination of the purified sample using Nuclear Magnetic Resonance (NMR) Spectroscopy

The proton NMR spectrum of the purified sample was acquired on a Bruker AV III 400MHZ spectrophotometer at the Strathclyde Institute of Pharmacy and Biological Sciences, University of Strathclyde, Glasgow, Scotland. Deuterated Chloroform, $CDCl_3$, was used as solvent.

Statistical Analysis

The statistical analysis was done using statistical package for social sciences (SPSS version 24) software package programme. The results were expressed as Mean ± SEM (standard error of mean), where n = 5, analyzed by one – way Analysis of Variance (ANOVA) and the level of significance determined by least significant difference (LSD). The p values of 0.05 and less were taken to imply statistical significance between the means.

RESULTS

Effects of fractions of aqueous root- bark extract of *Nauclea latifolia* on blood glucose levels in diabetic Wistar albino rats.

Table 1 shows the effects of fractions of root-bark extract of *Nauclea latifolia* and glibenclamide on blood glucose levels of the diabetic rats. Root-bark fraction A reduced the blood glucose level significantly ($p < 0.05$) on days 3, 7 and 10 when compared with the diabetic control rats. Blood glucose level was decreased significantly ($p<0.05$) by fraction B on day 10 while both fractions C and D led to significant reduction ($p< 0.05$) of the blood glucose level on day 7 only.

Effects of fractions of aqueous root-bark extract of *Nauclea latifolia* on serum lipid profile of diabetic Wistar albino rats

Table 2 shows a significant increase ($p < 0.05$) in the levels of total cholesterol, triacylglycerol, very low density lipoprotein and low density lipoprotein cholesterol in the diabetic control rats compared with the normal control rats whereas the high density lipoprotein cholesterol level was significantly lowered ($p < 0.05$) in the diabetic control rats compared with the normal control rats. *Nauclea latifolia* root-bark fractions A, B, C and glibenclamide significantly reduced ($p < 0.05$) the total cholesterol in the diabetic treated rats compared with the diabetic control rats. The decrease in total cholesterol in the diabetic rats treated with root-bark fraction D was non-statistically significant ($p > 0.05$) compared with the diabetic control. Fractions A, B and D increased non-statistically significant ($p > 0.05$) high density lipoprotein cholesterol level in the diabetic treated rats compared with the diabetic control. Treatment of the diabetic rats with fraction C led to non-significant decrease in high density lipoprotein cholesterol when compared with the diabetic control.

Fractions A and B brought about a significant decrease ($p <0.05$) in triacylglycerol in the diabetic treated rats compared with the diabetic control. Fractions C and D reduced triacylglycerol insignificantly ($p > 0.05$). Very low density lipoprotein cholesterol levels were reduced significantly ($p > 0.05$) in the diabetic treated rats with fractions A, B, D and glibenclamide when compared with the diabetic control. There was non-significant reduction ($p > 0.05$) in very low density lipoprotein cholesterol by fraction C. Fractions A, C and glibenclamide decrease significantly low density lipoprotein cholesterol in the diabetic treated rats compared with the diabetic control. There was non-significant reduction ($p > 0.05$) of low density lipoprotein

cholesterol by fractions B and D in the diabetic treated rats compared with the diabetic control rats (Table 2).

Effects of fractions of aqueous root-bark extract of *Nauclea latifolia* on serum liver enzymes in streptozotocin –induced diabetic Wistar albino rats.

Serum aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase levels were significantly increased ($p < 0.05$) in the diabetic control rats when compared with the normal control. Fraction A and glibenclamide reduced significantly ($p < 0.05$) the level of aspartate aminotransferase in the treated rats compared with the diabetic control rats. Fractions B, C and D did not impact significantly ($P > 0.05$) on aspartate aminotransferase level.

Alanine aminotransferase level was significantly reduced ($p < 0.05$) by fractions A, B, C and glibenclamide. Fraction D did not affect its level significantly. Fraction A and glibenclamide caused significant reduction ($p < 0.05$) in alkaline phosphatase level in the diabetic treated rats whereas fractions B, C and D have no significant effects on them ($p > 0.05$) (Table 3).

Gas Chromatography-Mass Spectroscopy (GC-MS) result of aqueous root-bark extract fraction A

The result of the GC-MS analysis showed catechol to be the most abundant bioactive principle in fraction A. Other compounds were found in trace amounts only. Catechol has a high match value of 97 (Table 4).

Result of Nuclear Magnetic Resonance (NMR) Spectroscopy confirming that the bioactive principle in *Nauclea latifolia* aqueous root-bark extract fraction A to be catechol

The following signals at δ 6.90, 6.89, 6.88, 6.87, 6.87, 6.86, 6.84, 6.83, 6.82, 6.81, 6.80 and 6.79 ppm were typical for a disubstituted aromatic system and were consistent with literature reports for catechol (Guadalupe *et al*, 2010; Lambert *et al.,* 1975; Urara *et al.*, 2015). Hence the purified substance in fraction A, DO3, (NMR sample number) was identified as catechol (Figure 2 and 3).

Table 1: Effects of Fractions of Aqueous Root- bark Extract of *Nauclea latifolia* (*NL*) 250mg/kg.body weight and Glibenclamide (5mg/kg.body weight) on Fasting Blood Glucose levels (mg/dl) in Diabetic Wistar Albino Rats.

Treatment/Group	Day 0	Day3	Day7	Day 10
Normal control (Group A)	99.40±2.98	101.40±4.05	99.60±3.61	99.20±2.18
Diabetic control (Group B)	328.40±10.50	357.20±9.68**	362.60±11.50**	365.00±7.65**
NL-root fraction A (Group C)	299.80±26.40	252.20±34.35*	235.20±28.86*	198.00±27.59*
NL-root fraction B (Group D)	302.80±5.72	342.60±6.61	354.00±6.15	265.60±3.37*
NL-root fraction C (Group E)	352.00±33.38	341.20±34.40	293.80±27.99*	334.00±32.36
NL-root fraction D (Group F)	368.80±26.21	350.60±26.54	299.80±24.12*	347.00±23.14
Glibenclamide (Group G)	330.20±12.54	270.60±14.18 *	250.00±17.96*	169.40±10.70*

Values are Mean ± SEM of 5 determinations
*= Statistically significant when compared to diabetic control at ($p < 0.05$)
**= Statistically significant when compared to normal control at ($p < 0.05$)

Table 2: Effects of fractions of aqueous root- bark extract of *Nauclea latifolia* (*NL*) (250mg/kg. body weight) and glibenclamide (5mg/kg.body weight) on serum lipid profile of streptozotocin-induced diabetic Wistar albino rats.

Treatment /Group	Total cholesterol (Mmol/L)	HDL-C (Mmol/L)	Triacylglycerol (Mmol/L)	VLDL-C (Mmol/L)	LDL-C (Mmol/L)
Normal control (Group 1)	1.88±0.05	0.61±0.03	0.80±0.09	0.16±0.02	1.11±0.05
Diabetic control (Group 2)	2.32±0.09**	0.43±0.03**	1.39±1.27**	0.28±0.03**	1.61±0.08**
NL-root fraction A (Group 3)	1.69±0.05*	0.53±0.05	1.10±0.06*	0.22±0.01*	0.94±0.07*
NL-root fraction B (Group 4)	2.06±0.13*	0.45±0.05	1.13±0.04*	0.23±0.01*	1.38±0.13
NL-root fraction C (Group 5)	1.98±0.07*	0.41±0.03	1.25±0.04	0.25±0.01	1.32±0.09*
NL-root fraction D (Group 6)	2.14±0.09	0.50±0.22	1.16±0.10	0.23±0.02*	1.41±0.08
Glibenclamide (Group 7)	1.72±0.90*	0.59±0.08*	0.84±0.09*	0.17±0.02*	0.97±0.09*

HDL-C = High density lipoprotein cholesterol
VLDL-C = Very low density lipoprotein cholesterol
LDL-C = Low density lipoprotein cholesterol
Values are Mean±SEM of 5 determinants
* = Statistically significant when compared to diabetic control at ($p < 0.05$)
** = Statistically significant when compared to normal control at ($p < 0.05$)

Table 3: Effects of fractions of aqueous root- bark extract of *Nauclea latifolia* (*NL*) 250mg/kg.body weight and glibenclamide (5mg/kg. body weight) on serum liver enzymes of streptozotocin- induced diabetic Wistar albino rats.

Treatment	AST (IU/L)	ALT (IU/L)	ALP (IU/L)
Normal control (Group 1)	48.40± 4.86	18.40± 0.81	21.64± 1.48
Diabetic control (Group 2)	74.40± 3.96**	39.00±3.16**	33.16± 2.52**
NL- root fraction A (Group 3)	65.80± 8.29*	23.60± 1.44*	26.32± 2.40*
NL-root fraction B (Group 4)	73.00± 2.78	31.40± 1.60*	33.64± 4.26
NL- root fraction C (Group 5)	74.80± 4.50	25.80± 2.50*	29.40± 1.24
NL- root fraction D (Group 6)	68.00± 8.31	37.80± 2.52	32.74± 2.97
Glibenclamide (Group 7)	63.00±5.00*	20.40± 1.44*	26.22± 1.78*

AST= Aspartate aminotransferase
ALT= Alanine aminotransferase
ALP= Alkaline aminotransferase
Values are Mean± SEM of 5 determinations.
* = Statistically significant when compared to diabetic control at ($p < 0.05$)
**= Statistically significant when compared to normal control at ($p < 0.05$).

Table 4: Gas chromatography-mass spectroscopy (GC-MS) result of aqueous root-bark fraction A

Peak number	Retention time	Library ID	Reference number	CAS number	Quality of Match
5	15.879	catechol	5860	000120-80-9	97

Figure 1: The purified whitish crystal substance subjected to Nuclear Magnetic Resonance (NMR) Spectroscopy analysis for characterization and structural elucidation (Picture snapped by the researcher).

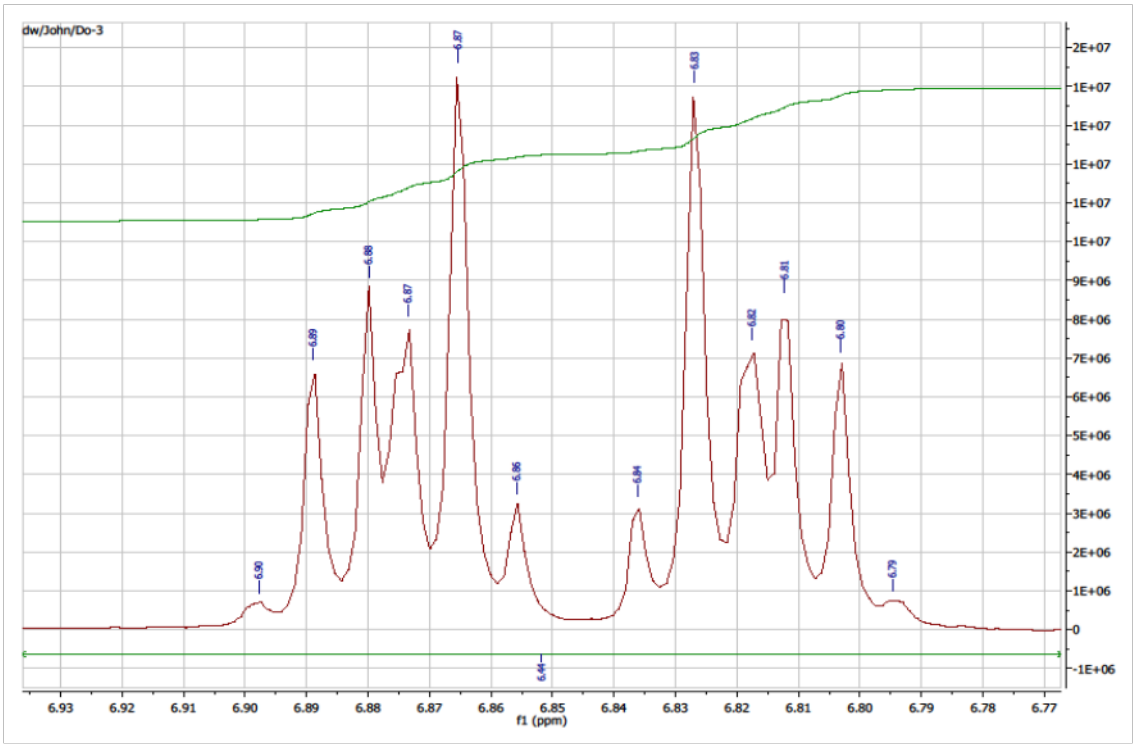

Figure 2. Nuclear Magnetic Resonance (NMR) Spectroscopy Spectrum of catechol, the active principle in *Nauclea latifolia* aqueous extract of root-bark fraction A.

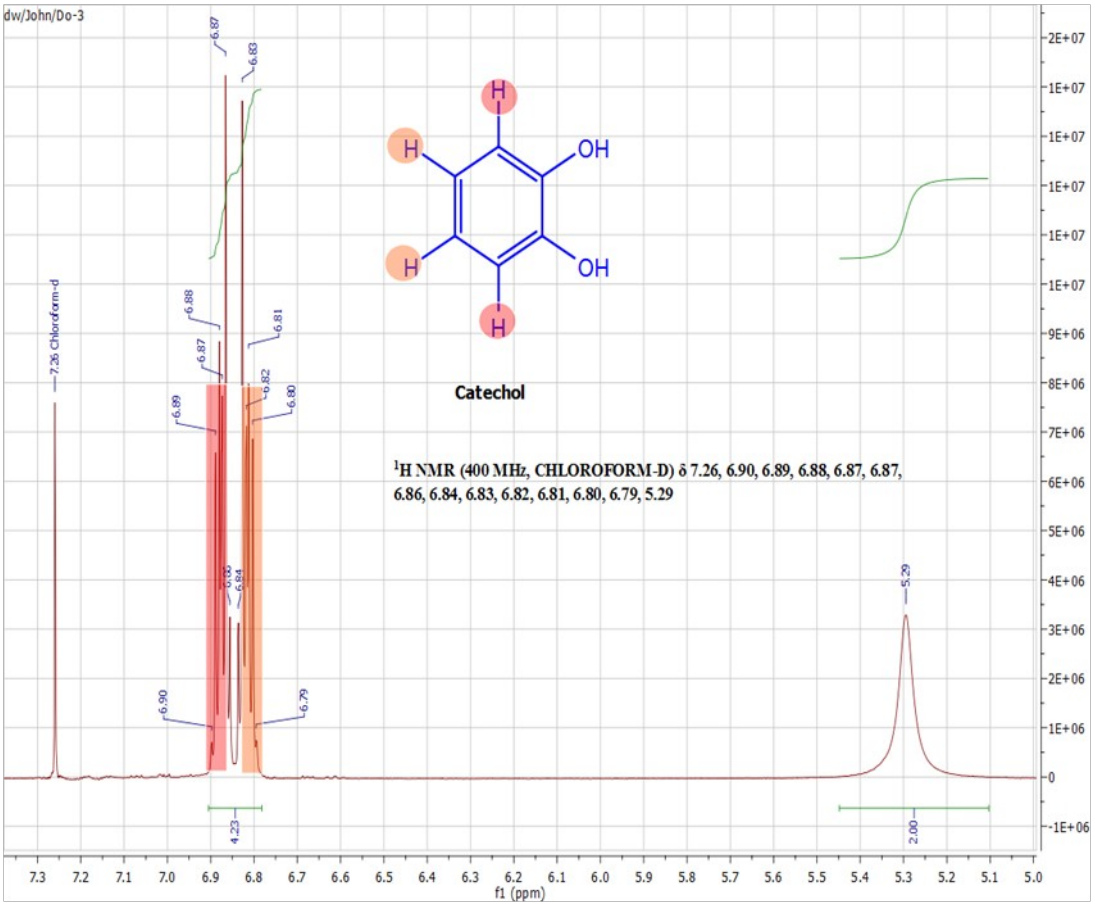

Figure 3. The structure of catechol the bioactive principle in *Nauclea latifolia* aqueous extract of root-bark fraction A

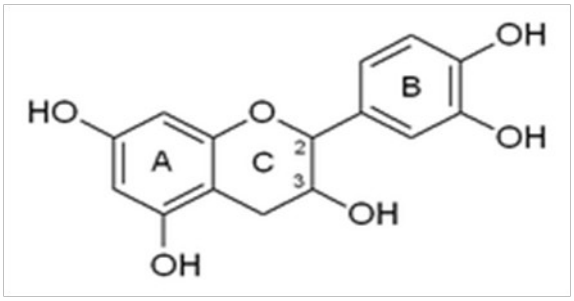

Figure 4. Chemical structure of catechin (a flavonoid) containing catechol (Courtesy of Royal Society of Chemistry, 2015).

DISCUSSION

In this study fraction A of the aqueous root-bark extract of *Nauclea latifolia* was found to demonstrate the most effective anti-diabetic property in terms of lowering blood glucose level and causing favourable effects on both blood lipid and serum enzyme levels when compared with fractions B, C and D. This fraction was found to contain the bioactive compound, catechol. Catechol which is also known as Pyrocatechol or 1, 2 – dihydrobenzene is an organic compound with molecular formular, C_6H_4 (OH) $_2$. The compound occurs as a feathery white crystal that is very rapidly soluble in water. It exists either as a free molecule or a substituent of flavonoids like catechin, quercetin, fisetin and eriodictyol where it represents a 1, 2 dihydrobenzene group (Fitzgerald, 2011; Kapiszewska *et al.,* 2003). Flavonoids are made up of two aromatic rings (A and B rings) connected by a 3 – carbon chain that forms an oxygenated heterocyclic ring (C ring). The B ring is the orthohydroxyl (catechol) structure of flavonoids. (Figure 4).

This B ring hydroxyl configuration in flavonoids is

said to be the most important determinant of reactive oxygen species scavenging activity of flavonoids. This is because it donates hydrogen and an electron to hydroxyl, hydroperoxyl and peroxynitrite radicals (Spencer *et al.,* 2012). The catechol structure of the B ring confers anti-oxidative potential to flavonoids (Krych and Gebieka, 2013). This enhances their ability to improve the release of insulin through their anti-oxidative effects on pancreatic β- cells which protect them against further hyperglycemia – induced destruction particularly in type 1 diabetes mellitus (Shi *et al.,* 2019). Many studies support blood glucose lowering activity of flavonoids with catechol moiety (Yeon *et al.,* 2015; Zhang *et al*, 2015).

Catechin, a flavonoid containing catechol moiety have been found to have hypoglycaemic activity (Cremonini *et al.*, 2019; Roghani and Baluchnejadmojarad, 2010; Zhang *et al.,* 2011). Earlier researches have reported the inhibiting effects of catechol containing flavonoids on alpha – glucosidase (Zhenhua *et al.*, 2014). This membrane bond enzyme is located in the brush border of the small intestine. It catalyses the final step in the digestive process of carbohydrates to release monosaccharides that are absorbable thereby causing increased blood glucose level (Bras *et al.,* 2014). Alpha-glucosidase inhibitors are used to control blood sugar levels in diabetes mellitus (Zhenhua *et al.*, 2014). The presence of catechol system in the B ring of flavonoids contributes to the distribution of electron cloud that then becomes accessible to give hydrogen atoms to form hydrogen bonds with active site residues of alpha- glucosidase. This plays a critical role in inhibiting its action (Vaya *et al.,* 2003; Carina *et al.,* 2017).

The reduction in blood glucose levels with the administration of catechol moiety containing flavonoids is also attributed to the stimulation of insulin secretion from the remaining portion of beta cells of the pancreas (Chung *et al.,* 2012). Other mechanisms of action of these flavonoids in lowering blood glucose is that they might carry out insulin like effect on peripheral tissues by either enhancing glucose uptake or inhibiting hepatic gluconeogenesis (Chen *et al.,* 2020). The flavonoid, quercetin which contains catechol moiety has been investigated to raise the activity of glycogen synthase, the rate limiting enzyme in glycogen synthesis. This enhances the conversion of excess glucose to its storage form, glycogen. It increases glycolysis while decreasing gluconeogenesis (Yeon *et al.,* 2015).

Catechol containing flavonoids ameliorate lipid profile by inhibiting the major enzymes involved in lipid synthesis in addition to reducing intestinal lipid absorption. They lead to significant decrease in serum levels of triacylglycerol, very low density lipoprotein cholesterol, low density lipoprotein cholesterol (Babu and Liu, 2008; Zheng *et al.,* 2011; Courtney *et al.,* 2017). These results observed in the lipid profile might be due to a reduction in the activity of 3 – hydroxyl - 3-methyl glutaryl coenzyme A (HMG- CoA reductase) and an increase in the activities of plasma lipoprotein lipase and lecithin cholesterol acyltransferase (LCAT) (Zheng *et al.,* 2011; You *et al.*, 2008; Prince and Kannan, 2006). LCAT plays a key role in the maturation of high density lipoprotein composition, structure, intravascular metabolism and plasma concentration (Chen *et al.,* 2008; Zheng *et al.,* 2011).

The mechanism of the hypolipidaemic effects of flavonoids containing catechol also includes improvement of insulin / glucagon ratio which entails low fatty acid biosynthesis in the liver via the reduction of the expression of sterol regulation element binding protein (SREBP – 1). SREBP – 1 is a transcription factor which controls de novo lipogenesis through induction of lipogenic enzymes (Hwang *et al.,* 2011; Liu *et al.,* 2011; Sharma *et al.,* 2011). The ameliorating effect of catechol containing flavonoids on lipid profile confers on them health benefits in the management of cardiovascular diseases (Babu and Liu, 2008; Ciumărnean *et al.,* 2020). They slow the progression of atherosclerotic cardiovascular disease. Their consumption has been associated with a decrease in endothelium -1 (a molecule involved in blood pressure regulation) and a reduction in myocardial ischaemic perfusion injury (Jun-Ying *et al.*, 2021; Peregrin, 2005).

There are previous reports on the hepatoprotective effects of catechol containing flavonoids (Tapas *et al.,* 2008; Wu *et al.,* 2006). The administration of catechin which contains catechol to alloxan- induced diabetic

mice led to a significant reduction in the serum liver enzymes, aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase (Kadhim, 2013).

CONCLUSION

Fraction A of the aqueous root-bark extract showed the most effective anti-diabetic potential compared to fractions B, C and D of the extract. This fraction was found to contain the bioactive compound, catechol using both Gas chromatography- Mass spectroscopy and Nuclear magnetic resonance spectroscopy. Previous reports on catechol show that it either exists as a free molecule or a substituent of flavonoids and that it confers on them their anti-diabetic property. From the findings it can be deduced that catechol containing fraction of *Nauclea latifolia* plant has the potential for use in the management of diabetes mellitus and its complications in clinical medicine.

ETHICAL APPROVAL

The ethical guidelines for the care and use of research animals were closely followed.

ACKNOWLEDGEMENTS

The authors express their gratitude to Dr. John Vershima Anyam for allowing the use of his laboratory for part of the initial work. We also appreciate every other persons who assisted us in one way or the other at various stages of this research work.

CONFLICTS OF INTEREST

The authors declare that they have no potential conflicts of interest.

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