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REPRODUCTIVE FUNCTION AND LIPID PROFILE EVALUATION OF ETHANOLIC LEAF EXTRACTS OF *BREYNIA NIVOSA* ('OGWU EZE') IN FEMALE WISTAR RATS

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ABSTRACT
The reproductive functions as well as the effect on lipid profile of female albino rats fed with ethanolic extract of *Breynia nivosa* leaf were assessed. The extraction was carried out with 70% ethanol after the leaves were air dried for 2 weeks and ground. Gas chromatographic study, as well as the qualitative and quantitative phytochemical screenings of the leaf extract were evaluated using standard methods. The extract was orally administered to albino rats weighing between 160g to 180g which were randomly grouped into five (5) groups with five wistar rats per group. Groups 1-3 received 300mg/kg, 200mg/kg and 100mg/kg respectively of the ethanol extracts while group 4 received 10mg of atorvastatin and group 5 served as control received water and rat chow *ad libitum*. After a period of 21 days of the extract administration the rats were sacrificed under ketamine anaesthetic and the serum level of follicle stimulating hormone (FSH), luteinizing hormone (LH), progesterone, and oestrogen and lipid profile were analysed. The gas chromatogram showed that the extract contains ninety one (91) compounds with Hexadecanoic acid ethyl ester (5.54) as the highest percentage followed by Linoleic acid ethyl ester (4.05) and 2,4-Di-tert-butylphenol (4.04) while Heptadecane, 2,6,10,14-tetramethyl is the least percentage. The result of the phytochemical analysis showed that the leaf contains abundant cyanogenic glycosides, moderate alkaloids and tannins, and traces of phenols, flavonoids, saponins and steroids. The quantities of the parameters showed phenols (0.22±0.01), alkaloid (3.31±0.01), flavonoid (1.65±0.00), saponins (0.84±0.00), steroids (0.18±0.10), cyanogenic glycosides (4.54±0.02) and tannins (1.9±0.02). While result of the hormone assay showed that the leaf extract significantly decreased progesterone level in group 1 and 2 ($p<0.05$) and also group 3 but statistically not significant ($p>0.05$). The extract also significantly decreased oestrogen ($p<0.05$) in group 1 with non-significant increase in groups 2 and 3 ($p>0.05$). The Leaf extract also significantly decreased the level of FSH group 1 ($P<0.05$) as well as groups 2 and 3 but statistically not significant ($p>0.05$). The leaf extract significantly decreased the level of LH in group 3 ($P<0.05$). The *B. nivosa* significantly increased the levels of LD ($p<0.05$), total cholesterol ($p<0.05$) and triglyceride ($p<0.05$) when compared with both the positive control and control but significantly decreased HDL ($p<0.05$). From the above findings, the use of *Breynia nivosa* leaf should be done with caution as it possesses a hyperlipidemic effect and the tendency to decrease fertility in female as shown by a decrease in female sex hormones.

KEYWORDS: Breynia nivosa, female wistar rats, hypolipidemic activities, reproductive function.

INTRODUCTION
Patronage of herbal remedy and concoctions has been dated back to antiquity and still gaining substantial grounds in the present day medical practices. However, despite the numerous numbers of herbs the earth as well as our dear nation is blessed with, not so many of these herbs have undergone scientific investigations for their medicinal or toxic effects on man. In the world at large,

herbal/plant derived medicinal substances are now starting to be used in addition to scientifically proven therapies.[1]

Breynia nivosa (B. nivosa) is a shrub commonly found or grown in tropical Africa and in public areas and gardens usually for beautification commonly called "ice plant or snow bush" In South-East Nigeria, the plant is locally called "ogwu eze" in Igbo language. In traditional medicine B. nivosa is used to soot headaches, toothaches and tooth infections whereas the stem is commonly used as chewing sticks.[2] The flowery leaf has been found to be among the many used herbal medicinal substances believed to be used prophylactically or therapeutically in treating many diseases such as malaria.[3] The stem of *B. nivosa* is used as chewing stick in South-East Nigeria.[4,5] It is also used for its attractive foliage, and is found in gardens and public places.[6] Ethno-medically, it is used for the treatment of headache, toothache and tooth infections.[6]

Breynia nivosa is also found to possess boosting effect on the male reproductive function hence, can be patronised in the management of male infertility as well as sexual disorders.[7]

Having been found to possess significant male fertility function it is logical to also determine if the fertility boosting ability may be extended to the female Wistar rats, Hence this research.

Serum lipid profile test entails the test done to evaluate the serum level of the important body lipids of which their alteration may constitute significant physiologic derangement. They include the serum total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL) and triglycerides. In this research the various levels of these parameters were ascertained from both the test and control of the Wistar rats that were used for the research.

Infertility is said to be the inability of becoming pregnant by the females or unable to induce pregnancy by the males despite adequate copulation within a period of one year. Infertility presently has gained for itself a significant stance as one of the major problems experienced in some marriages in Africa.[8] About 15% to 17% of the world's couples are facing the challenge of infertility and about 50% of them are as a result of female infertility factors.[9]

Given that *Breynia nivosa* has been found to significantly elevate the male sex hormones as well as some haematological parameters in Wistar rats,[7] the result of this research will shed more light on its effect in female wistar rats. This research was undertaken to evaluate the effect of ethanol leaf extract of *Breynia nivosa* on reproductive function and lipid profile of female Wistar rats.

MATERIALS AND METHODS

Procurement of Experimental Animals

Twenty five (25) female adult Wistar rats (150g – 200g) were obtained from animal farm of Physiology department located at the Department of Human Physiology, Abia State University Uturu , Abia State. The animals were bred in the experimental house of Department of Human Physiology, Faculty of Basic Medical Science, Abia State University under standard conditions. They were acclimatized for two weeks, having free access to water and food.

The animal feed was bought from a local market dealer in Amamptu Uli, in Anambra State, Nigeria.

Plant and Drug Collection

Fresh leaves of *Breynia nivosa* were collected from Mary the Queen Catholic Parish, Azia. Anambra State. Nigeria. Atorvastatin 10mg was purchased from Juhel Pharmaceuticals Awka. Anambra State.

Identification of the Plant

The plant was identified and authenticated by a botanist at the Department of Botany, Nnamdi Azikiwe University, Awka with the herbarium number NAUH – 227A.

Preparation of the Extract

Breynia nivosa leaves were shade-dried at room temperature for two weeks. The leaves were then ground to powdered form using electric blender. 200g of the dried powdered form was then soaked in 70% ethanol for 48 hours. The mixture was then filtered and evaporated to dryness at 40^{o}C. The extract (0.02g, 0.04g and 0.06g respectively) was then diluted with appropriate millilitre of distilled water to obtain 100mg/kg, 200mg/kg and 300mg/kg using the formula below.

Dose (ml) = (required dose (mg/kg) × weight of animal (kg)) / stock (mg).[10]

The prepared extract was stored in a refrigerator at 4^{o}C until time for use.

Qualitative and Quantitative Determination of Phytochemical Screening of the Leaves of *B. Novisa* was done according to[11,12,13]

Acute Toxicity Study of Ethanol Leaf Extract of *Breynia Nivosa*

The median lethal dose (LD50) of ethanol leaf extract of *Breynia Nivosa* was done by[3] according to Lorke's method.[14]

Experimental Design and Protocol

The rats were divided into five (5) groups (1, 2, 3, 4 and control) of five animals each. The last group served as the control and were given food and water *ad libitum* throughout the period of the research and group 4 rats were given tabs atorvastatin 10mg p.o., while groups 1, 2 and 3 were the experimental groups and were administered with 300mg/kg, 200mg/kg and 100mg/kg

of ethanolic leaf extract of *Breynia nivosa* respectively for 21days through oral administration using orogastric cannula. The dosages were however dependent on the outcome of the toxicity test (LD50) of the extract according to.[3]

Collection of Blood Samples

Twenty four (24) hours after the administration of the last treatment, the animals were transported to the Human Biochemistry Lab Nnamdi Azikiwe University for collection of blood samples for serum analysis of follicle stimulating hormone (FSH), luteinizing hormone (LH), progesterone, oestrogen and lipid profile. The rats were anaesthetised with ketamine 0.3ml intraperitonially. Blood samples were collected through cardiac puncture.

Determination of Serum Progesterone

Serum progesterone was determined according to the method described by.[15]

Determination of Serum Lipid Profile

Serum total cholesterol (TCHOL)

This was done by using UV-VIS spectrophotometer (Model 752G, China) as recommended by.[16]

Determination of serum high density lipoprotein (HDL)

This was done using a known standard method as recommended by,[16] using UV-VIS spectrophotometer (Model 525G, China).

Determination of serum triglycerides (TRIGS)

This was done using a known standard method as recommended by, [16] using UV-VIS spectrophotometer (Model 752G, China).

Determination of low density lipoprotein cholesterol (LDL)

Low density lipoprotein was calculated from total cholesterol, triglycerides and HDL cholesterol following formula provided by.[17]

Statistical Analysis

The results were subjected to statistical analysis using SPSS (version 17.0) and P values less than 0.05 ($P<0.05$) were regarded as significant.

RESULTS

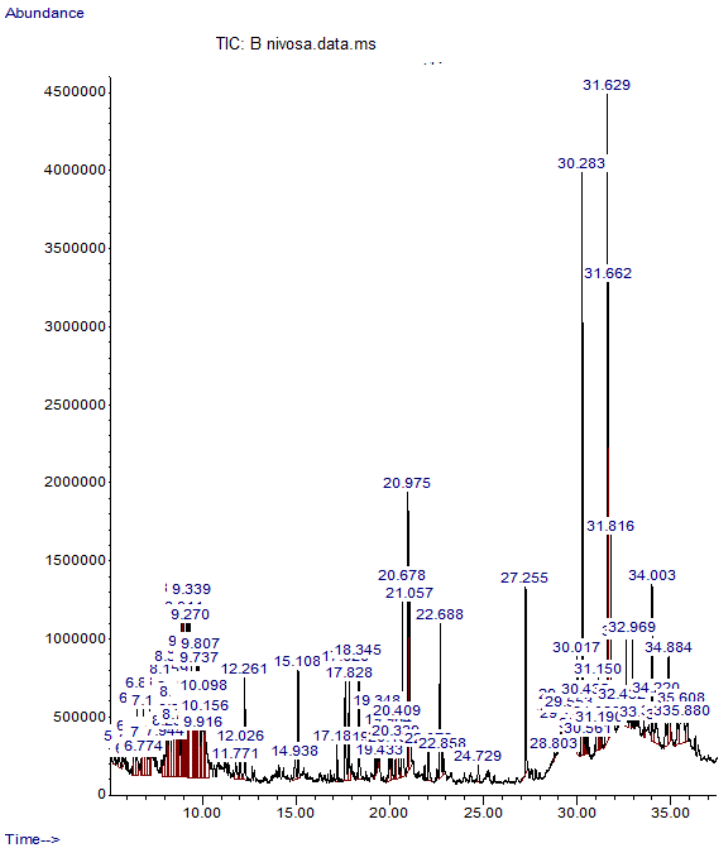

Fig. 1: Gas chromatogram of *breynia nivosa* leaf extract.

The chromatogram above showed that *Breynia nivosa* contains ninety one (91) compounds with Hexadecanoic acid, ethyl ester (5.54) as the highest percentage followed by Linoleic acid ethyl ester (4.05) and 2,4-Di-tert-butylphenol (4.04) while Heptadecane, 2,6,10,14-tetramethyl is the least.

Table 1: Qualitative phytochemical composition of ethanolic leaf extract of *breynia nivosa.*

Phytochemical Parameters	Phenols	Alkaloids	Flavonoids	Saponins	Steroids	Cyanogenic glycosides	Tannins
Ethanolic Extract	+	++	+	+	+	+++	++

Key: + = Mild, ++ = moderate, +++ = Abundant

The result of phytochemical analysis of *Breynia nivosa* in Table 1 above showed abundance of Cyanogenic glycosides and moderate level of alkaloids and tannins with traces of saponins, phenols, flavonoids and steroids.

Table 2: quantitative phytochemical composition of ethanolic leaf extract of *breynia nivosa.*

Phytochemical composition	**Quantity (mg/100g)**
Phenols	0.22± 0.01
Alkaloids	3.31± 0.01
Flavonoids	1.65± 0.00
Saponins	0.84± 0.00
Steroids	0.18± 0.10
Cyanogenic glycosides	4.54± 0.02
Tannins	1.9± 0.02

The result of quantitative phytochemical composition of ethanolic extract of breynia nivosa, as shown in table 2 above revealed the following: phenols (0.22±0.01 mg/100g), alkaloids (3.31±0.01mg/100g), flavonoids (1.65±0.00mg/100g), saponons (0.84±0.00mg/100g), steroids (0.18±0.10mg/100g), cyanogenic glycosides (4.54±0.02mg/100g), tannins (1.9±0.02mg/100g).

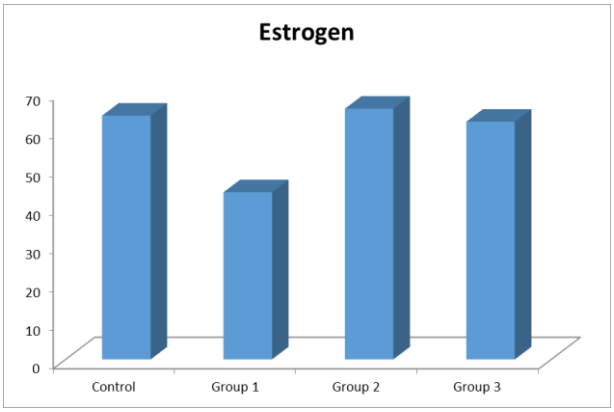

Fig. 2: Effects of ethanolic extract of *breynia nivosa* on estrogen.

Figure 2 above showed a statistically significant decrease in estrogen ($p<0.05$) in group 1 and statistically non-significant increase in estrogen in groups 2 and 3 ($p>0.05$).

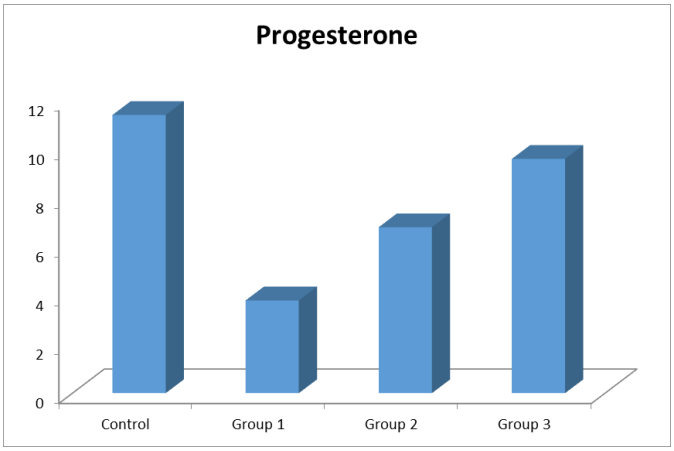

Fig. 3: Effects of ethanolic extract of *breynia nivosa* on progesterone in female albino rats.

The above results in figure 3 showed that the ethanolic leaf extract significantly decreased progesterone level in group 1 and 2 ($p<0.05$) and also decreased progesterone level in group 3 but was statistically not significant ($p>0.05$).

Table 3: Effects of ethanolic extract of *breynia nivosa* on luteinizing hormone (lh) in female albino wistar rats.

Hormones	Control (mIU/ml)	Group 1 (mIU/ml)	Group 2 (mIU/ml)	Group 3 (mIU/ml)
Luteinizing Hormone	0.84±0.23	0.44±0.03	0.85±0.19	1.18±0.21

Data expressed as mean ± standard error of mean.

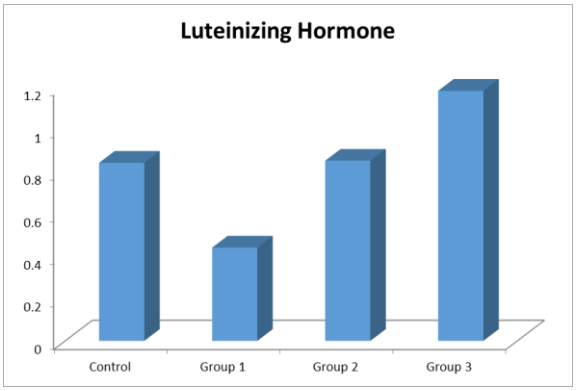

Fig. 4: Effects of ethanolic extract of *breynia nivosa* on luteinizing hormone in female albino rats.

The result in in figure 4 showed that the leaf extract significantly increased the level of LH in group 3 ($P<0.05$) with also an increase in group 1 though statistically not significant ($p>0.05$). It also showed a decrease in group 1 which is statistically not significant ($p>0.05$) when compared with control.

Table 4. Effects of Ethanolic Extract of *Breynia Nivosa* on Follicle Stimulating Hormone (FSH) In Female Albino Rats.

Hormones	Control (mIU/ml)	Group 1 (mIU/ml)	Group 2 (mIU/ml)	Group 3 (mIU/ml)
Follicle Stimulating Hormone	2.10±.33	0.60±0.07	1.5±0.15	1.86±0.26

Data expressed as mean ± standard error of mean.

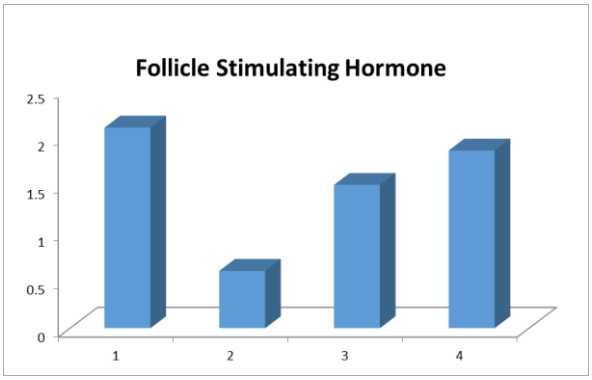

Fig. 5: Effects of ethanolic extract of *breynia nivosa* on follicle stimulating hormone (fsh) in female albino rats.

The result above in figure 5 showed that the leaf extract significantly decreased the level of FSH group 1 ($P<0.05$) and also decreased the level of FSH in groups 2 and 3 but statistically not significant ($p>0.05$).

Table 5. Effects of ethanol extract of *breynia nivosa* leaf on total cholesterol in female albino wistar rats.

Hormones	Group 1 (mg/dl)	Group 2 (mg/dl)	Group 3 (mg/dl)	Group 4 (positive control) (mg/dl)	Control (mg/dl)
Total cholesterol	235.90±0.41	235.08±0.81	261.60±0.55	192.99±1.27	191.50±2.60

Data expressed as mean ± standard error of mean.

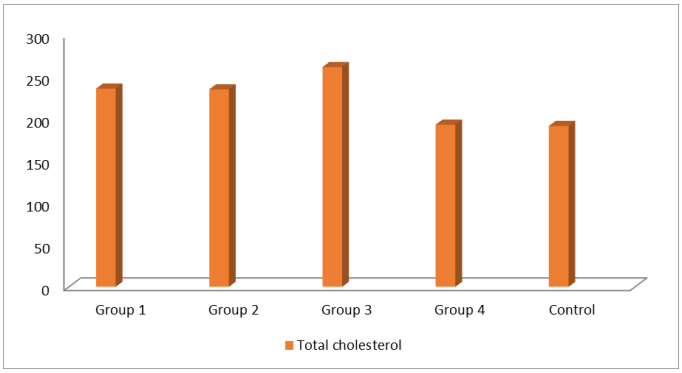

Fig. 6: Effects of ethanol extract of *breynia nivosa* leaf on total cholesterol in female albino wistar rats.

Figure 6 above *Breynia nivosa* ethanolic leaf extract significantly increased the level of total cholesterol ($p<0.05$) in all the groups when compared with both the positive control and control.

Table 6: Effects of ethanol extract of *breynia nivosa* leaf on high density lipoprotien in female albino rats.

Hormones	Group 1 (mg/dl)	Group 2 (mg/dl)	Group 3 (mg/dl)	Group 4 (positive control) (mg/dl)	Control (mg/dl)
HDL	118.83±0.77	119.21±0.57	60.33±0.44	147.86±0.36	144.02±1.71

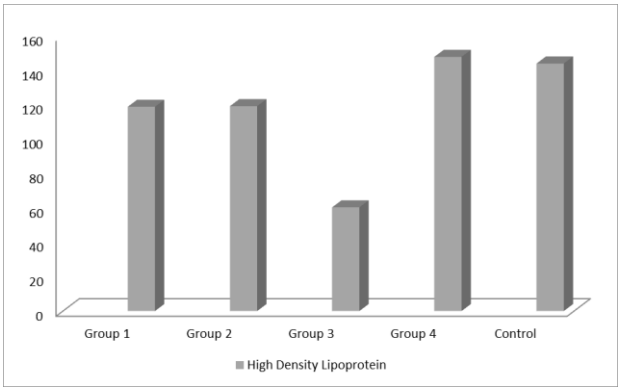

Fig. 7: Effects of ethanol extract of *breynia nivosa* leaf on high density lipoprotien in female albino wistar rats.

The result in figure 7 above showed that *Breynia nivosa* ethanolic leaf extract significantly decreased the level of total cholesterol ($p<0.05$) in all the groups when compared with both the positive control and control.

Table 7: Effects of ethanol extract of *breynia nivosa* leaf on triglyceride in female albino wistar rats.

Hormones	Group 1 (mg/dl)	Group 2 (mg/dl)	Group 3 (mg/dl)	Group 4 (positive control) (mg/dl)	Control (mg/dl)
Triglyceride	152.42±1.10	161.52±8.59	185.17±10.33	134.88±6.39	142.90±0.27

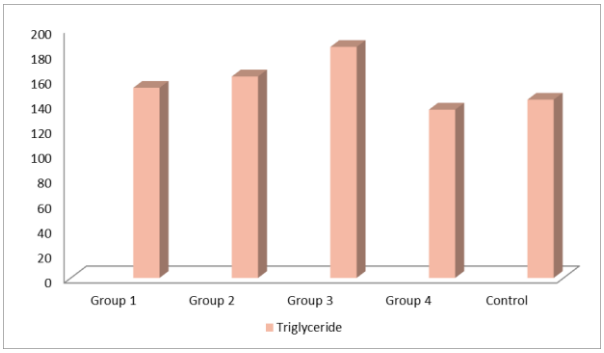

Fig. 8: Effects of ethanol extract of *breynia nivosa* leaf on triglyceride in female albino wistar rats.

The above result in figure 8 showed that *Breynia nivosa* ethanolic leaf extract significantly increased the level of triglyceride ($p<0.05$) in all the groups when compared with both the positive control and control.

Table 8: Effects of ethanol extract of *breynia nivosa* leaf on low density lipoprotein (ldl) in female albino wistar rats.

Hormones	Group 1 (mg/dl)	Group 2 (mg/dl)	Group 3 (mg/dl)	Group 4 (positive control) (mg/dl)	Control (mg/dl)
LDL	86.59±0.35	83.57±1.70	164.22±1.88	18.16±0.1.76	18.90±2.54

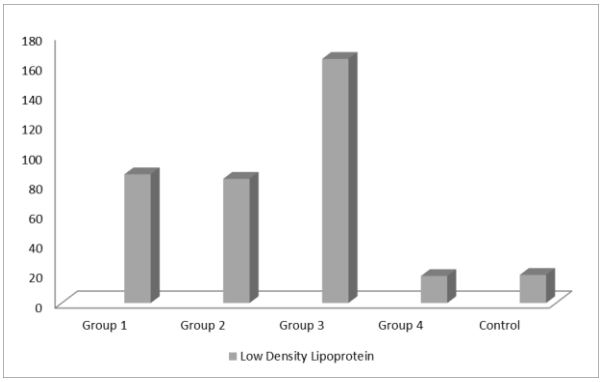

Fig. 9: Effects of ethanol extract of *breynia nivosa* leaf on low density lipoprotein in female albino wistar rats.

The result above in figure 9 showed that *Breynia nivosa* ethanolic leaf extract significantly increased the level of low density lipoprotein ($p<0.05$) in all the groups when compared with both the positive control and control

DISCUSSION

This research was on the reproductive function evaluation of female albino rats administered with ethanol leaf extract of *Breynia nivosa* focusing on the changes in the following hormones: luteinizing hormone, follicle stimulating hormone, progesterone and oestrogen. Also evaluated were the effects of this extract on lipid profile of female albino rats treated with ethanol extract of *Breynia nivosa* looking at the changes in the serum level of total cholesterol, low density lipoprotein, high density lipoprotein and triglycerides.

Prior to this research many researchers have found *Breynia nivosa* to possess medicinal properties. One of which was that done by[7] stating that the leaf possesses male sex function boosting capacity. However, *Breynia nivosa* leaf extract could be hepatotoxic despite its medicinal properties.[18]

The chromatogram in fig. 1 showed that *Breynia nivosa* is rich in multiple compounds of which are of physiologic merits and demerits. The gas chromatographic study revealed that the leaf extract contains Hexadecanoic acid, ethyl ester (5.54) in highest percentage relative to the other components and studies showed that this compound possesses the ability to raise the serum LDL. Hence, this maybe the reason for the various effects of *Breynia nivosa* extract on the reproductive hormones and the lipid function parameters.

The phytochemical analysis of leaf extract of *Breynia nivosa* showed that the leaf of *Breynia nivosa* contained phenols, alkaloids, flavonoids, saponin, steroids, cyanogenic glycosides, and tannin with cyanogenic glycosides being the most abundant followed by alkaloids. This phytochemical finding agrees with that found by.[19,20]

The result of the progesterone analysis (figure 3) showed that the ethanol leaf extract caused a statistically significant decrease in the level of progesterone in groups 1 and 2 ($P<0.05$). There was also a decrease in that of group 3 though statistically not significant. This decreasing effect of the leaf extract on the test groups may be due to the high level of the phytochemical cyanogenic glycoside component of *Breynia nivosa* which possesses the ability of decreasing fertility in adult female rats fed with cyanogenic glycoside containing meals.[21]

This present study showed that *Breynia nivosa* though very medicinal and as well may possess male sexual function boosting capability with significant level of cyanogenic glycoside may be unsafe for females in need of offspring as it decreases the progesterone level which is a very crucial hormone in the sustainability of the foetus in the uterus after fertilization and implantation has occurred.[7] Hence, the shrub, while being patronized for other medicinal properties, care should be taken by females in their reproductive age still in want of children. If it must be patronised, it should be at a low dose.

The result in figure 2 showed that group 1 orally administered with high dose of the leaf extract alone significantly decreased the level of oestrogen ($P<0.05$). However, there is non-significant increase in the

oestrogen level in the lower dose groups (groups 2 and 3) which may be due to chance or idiopathic cause and this further buttresses the need for caution by females of reproductive age that consume the *Breynia nivosa* for different purposes.

Table 4 showed that high dose (group 1) of the leaf extract significantly decreased the level of FSH ($P<0.05$). This decrease in the FSH may be attributed to the phytochemicals in the *Breynia nivosa* especially that of the glycosides which possesses the ability of decreasing serum FSH. This agrees with the work by[22] which revealed that ethanol leaf extract of *Telfairie occidentalis* (which contains some similar phytochemicals as *Breynia nivosa* such as glycosides and flavonoid) on male reproductive activity revealed that there was significant decrease in FSH when treated with the leaf extract. However when compared to the findings of [7] the aqueous leaf extract possesses elevating effect on FSH. This present study in females treated with the ethanolic leaf extract of *Breynia nivosa* revealed contrary finding of decrease in FSH levels. These discrepancies may be attributed to the difference extracting medium – aqueous and ethanol – which may have altering effect on some of the phytochemical components of the leaf. Also to be considered maybe that *Breynia nivosa* does not have the same effect in male FSH as in female FSH.

The above result in figure 4 showed that low dose (group 3) of the leaf extract significantly increased the level of LH ($P<0.05$). This effect may be as result of physiologic regulatory mechanism to try to maintain a homeostatic hormonal state as luteinizing hormone of the pituitary gland normally induces the secretion of progesterone by the ovary. Meanwhile, according to [23] there was decrease in the LH/FSH ratio in the animal models treated with flavonoid which is an active component of the phytochemical component of *Breynia nivosa*. This result of [23] may be said to support the current finding of this research and also that the increase seen may be attributed to flavonoid content of *Breynia nivosa*.

Breynia nivosa prior to this study has not been analysed for its effect on the serum lipid profile. Therefore, the finding of this research which portrayed that leaf extract of *Breynia nivosa* elevated the bad serum cholesterols (LDL) may be the reason for the decrease in the female reproductive hormone in the animals administered with the leaf extract.

Table 5 showed that the leaf extract of *Breynia nivosa* statistically increased the serum level of total cholesterol ($P<0.05$) at all doses. This may be attributed to hexadecanoic acid, ethyl ester and cyanogenic glycoside phytochemical component of *Breynia nivosa*. Cyanogenic glycoside has been implicated to enhance conversion of the rate limiting enzyme – hydroxyl methyl glutaryl coenzyme A (HMG-CoA) into mevalonate which causes increased synthesis of cholesterol. Also, hexadecanoic acid also known as palmitic acid which is of highest percentage composition of the *Breynia nivosa* extract according to the gas chromatogram is implicated in elevation of total cholesterol. Hence, the significant increase seen in the group of rats administered with the leaf extract may as well be attributed to the chromatographically phytochemical component.

When compared with a known hyperlipidaemia drug – atorvastatin. The result showed that the leaf extract of *Breynia nivosa* statistically increased the serum level of serum total cholesterol more at all doses than atorvastatin ($P<0.05$).

This further buttresses the fact that *Breynia nivosa* has an active substance that possesses the ability to enhance the rate limiting enzyme HMG-CoA in the synthesis of cholesterol, a luxury not possessed by the statins already scientifically established to confer inhibitory action to the enzyme.[24] Thus, *Breynia nivosa* according to this research may not be used as an alternative to the statins for reduction of cholesterol synthesis.

It was found that the leaf extract of *Breynia nivosa* significantly decreased serum level of high density lipoprotein at all doses ($P<0.05$). This may be attributed to the abundant level of the phytochemical, cyanogenic glycoside and hexadecanoic acid, which according to,[25] these prominent compounds have been found to decrease the serum level of high density lipoprotein.[25]

This finding showed that *Breynia nivosa* leaf has hyperlipidemic effect hence, may not be used in alleviating female infertility, having been found to possess diminishing effect on serum HDL.

When compared with atorvastatin the result showed that leaf extract significantly reduced the level of serum HDL more than atorvastatin at all doses ($P<0.05$).

This present study may suggest that *Breynia nivosa* having the capacity of increasing cholesterol synthesis generally with relative decrease in serum HDL, should be avoided by females with infertility secondary to hormonal imbalance or dyslipidemia. Result of Table 7 above showed that there was statistically significant increase in the serum triglyceride of wistar rats administered with the leaf extract at ($P<0.05$). Palmitic acid serves as a substrate for synthesis of saturated and unsaturated long chain fatty acid and in turn also serves as substrate for the synthesis of triglyceride which may be the reason for the increase seen in the wistar rats giving the high content in the leaf extract.

When compared with atorvastatin *Breynia nivosa* showed a statistically significant increase in serum triglyceride in all doses ($p<0.05$) which showed further that *Breynia nivosa* does possess a substance that favours cholesterol or lipid synthesis and cannot be used as a hypolipidemic agent. The above result showed that there

were statistically significant increase in the serum LDL at all doses of the leaf extract (P<0.05).

The phytochemical findings of *Breynia nivosa* leaf extract showed that it contains an abundant cyanogenic glycoside which when metabolised, is converted to hydrogen cyanide which is a potent causative agent of iodine deficiency that gives rise to hypothyroidism and eventual dyslipidemia (high LDL). Also, hexadecanoic acid ethyl ester has the capability of elevating LDL and this compound was also found to be the one with the highest percentage in the chromatographic studies. Hence, *Breynia nivosa* leaf extract may not be used as a remedy for infertility secondary to dyslipidaemia, as the leaf elevates LDL.

When compared with atorvastatin, it was found that the drug atorvastatin was more potent in reduction of LDL (P<0.05) than *Breynia nivosa* which may also be attributed to the cyanogenic glycosides phytochemical component of the leaf extract.

CONCLUSION

In conclusion, ethanolic extract of *Breynia nivosa* leaf may not be a very good choice to patronise in infertility cases in female wistar rats as well as humans as opposed to that carried out in male counterparts by.[7] The leaf extract also expressed ability to possess the potential of elevating the lipid profile markers total cholesterol, LDL and TG while decreasing serum HDL. Therefore, should be used with caution, especially among females of reproductive age and those with high risk of development of hyperlipidemic ailments.

REFERENCES

1. Oyedemi S., Oyedemi B., Ijeh I., Ohanyerem P., Coopoosamy R. *and* Aiyegoro O. Alpha-amylase inhibition and antioxidative capacity of some antidiabetic plants used by the traditional healers in Southeastern Nigeria. *The Scientific World Journal*, 2017; 11.
2. Amadi E.S., Oveka C.A., Onveagba R.A., Ugbogu O.C., Okoli, I. Antimicrobial screening of Breynia nivosusand Ageratum conzynoides against dental caries organisms. Journal of Biological Sciences., 2007; 7(2): 354-358.
3. Okokon J.E., Davis K., Azare B.A., Antimalarial activities of Breynia nivosa. *Journal of Herbal Drugs*, 2015; 5(4): 168-172.
4. Sofowora, E.A. Medicinal Plants and Traditional Medicine in Africa. John Wiley and Sons Ltd., Hoboken, 1982; 64-79.
5. NNMDA. Medicinal Plants of Nigeria: South-East Nigeria, Nigeria Natural Medicine Development Agency. Federal Ministry of Science and Technology, 2008; 1: 90.
6. Onyegbule, F.A., Ilouno, I.O., Ikeh, C., Umeokoli, B.O., Eze, P.M. Evaluation of phytochemical constituents, analgesic, anti-inflammatory, antimicrobial and antioxidant activities of extracts of Breynia nivosa leaves. Planta Med., 2014; 80: LP18. DOI: 10. 1055/s-0034-1395078.
7. Ukwubile C.,. Ikpefan E., Samagoro C., Abdulrahaman A., Nuhu A., Tam L. Evaluation of Sperm and Haematological Parameters Boosting Potential of *Breynia Nivosa* (W.Bull) Sm. (Euphorbiaceae) Leaf Extract In Male Albino Rats. *Nig. J. Pharm. Res.*, 2018; *14(1): 103-110.*
8. Bodenner, C. Infertility Is Brutal on Marriage or Not?, 2016. https://www.theatlantic.com/international/archive/2016/10/indonesia/623046/
9. Borght, V., and Wyns, C. Fertility and infertility: Definition and epidemiology. *Clinical Biochemistry*, 2018; 62: 2–10.
10. Oghenesuvwe E. E. Guidelines on Dosage Calculation and Stock Solution Preparation in Experimental Animals' Studies. *Journal of Natural Sciences Research*, 2014; *4: 18.*
11. Harborne, J. Phytochemical Methods. Chapman and Hall Limited. London, 1973; 49-188.
12. Trease, G.E. and Evans, W.C. Pharmacognosy. 11th Edition, Bailliere Tindall, London, 1989; 45-50.
13. Sofowora, A. Medicinal Plants and Traditional Medicine in Africa. Spectrum Books Limited. Ibadan, 1993; 191-289.
14. Lorke D. A new approach to practical acute toxicity testing. Archives of Toxicology, 1983; 54(4): 275–287.
15. 15 Abraham, G.E. The application of natural steroid radioimmunoassay to gynaecology endocrinology. In: Abraham G.E, editor. Radio assay systems in Clinical Endocrinology, Basel. *Marcel Dekker*, 1981; 475-529.
16. WHO, (2004). Recommendations for the preparation, characterization and establishment of international and other biological reference stardards. WHO Experimental Committee on biological standardization. Fifty-fifth report. WHO Technical Report Series No., 932. http://www.whoint/blood products/norms/en/
17. Martin, A.C. Clinical Chemistry and Metabolic Medicine in: Lipoprotein. Hodler, A. and Edward, A . (eds). 7th ed; Bookpower, London, UK., 2006; 201.
18. Enwelum, H.O., Nwankwo, A.A. and Nwozor, C.M. Hepatotoxic Effects of Ethanolic leaf Extract of *Breynia nivosa* (Snow bush) in Wistar rats. *Tropical Journal of Applied Natural Sciences*, 2021; 3(2): 1-8.
19. Ezeigbo R., Nwachukwu I., Ike-Amadi C. and Suleiman J. Evaluation of the Phytochemical, Proximate and Mineral Constituents of Breynia nivosa Leaf. *International Journal of Biochemistry Research & Review*, 2017; 20(2): 1-8. Article no. IJBCRR. 37965.
20. Ezekwesili C. and Ogbunugafor H. Blood glucose lowering activity of five Nigerian medicinal plants in alloxan-induced diabetic wistar albino rats; *Animal Research International*, 2015; 12(2): 2150–2158.

21. Olusi S. Oke O. Odusote A. Effects of Cyanogenic Agents on Reproduction and Neonatal Development in Rats; *Biologia Neonatorum*, 1979; 36(5-6): 233–243.
22. Grace, E., Grace, S., Nse, U., Edikan, N.., and Emmanuel, O. Effect of ethanol leaf extract of Telfairia occidentalis on male reproductive activities. *GSC Advanced Research and Reviews*, 2020; *5*(3): 074–084.
23. Zhang J, Zhang H, Xin X, Zhu Y, Ye Y, Li D. Efficacy of Flavonoids on Animal Models of Polycystic Ovary Syndrome: A Systematic Review and Meta-Analysis. *Nutrients*, 2022; 14(19): 4128.
24. Zhou Q. and Liao J. Statins and cardiovascular diseases: from cholesterol lowering to pleiotropy. Current pharmaceutical design, 2009; 15(5): 467-78.
25. French M., Sundram K and Clandinin M. Cholesterolaemic effect of palmitic acid in relation to other dietary fatty acids. *Asia Pacific Journal of Clinical Nutrition*, 2002; *11(7): S401-7.*