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Biometric Analysis of *Hunteria umbellata* (K.Schum.) Hallier f and Metformin in the treatment of diabetes

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ABSTRACT: Diabetes is a disease of genetic and environmental origin. It affects the glucose-insulin endocrine metabolic regulatory system due to the malfunction of the insulin producing cells of the pancreas. The purpose of this study is to carry out a comparative analysis of the potencies of hunteria umbellata and metformin on Type 1 diabetes mellitus using bio-statistical analysis. The period of attaining normal blood glucose level across times was taken into consideration as a basis for comparing the efficacy of the oral antidiabetic herbal drug to that of the orthodox antidiabetic drug. The biometric analysis of data from five diabetic patients that were placed on herbal treatment were taken daily for a period of 3 weeks during which they attained normal fasting blood glucose level of between 70mg and 100mg as compared with a recovery period of 8 weeks for the 15 patients treated with metformin 500mg. These results showed that hunteria umbellata is more efficacious in the treatment of diabetes mellitus than metformin 500mg.

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Diabetes mellitus (DM) is a group of metabolic conditions characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both, Ezeja *et al*., (2015). It is a disease in the glucose-insulin endocrine metabolic regulatory system, in which the pancreas either does not release insulin or does not properly use insulin to uptake glucose in the plasma. This disease is referred to as hyperglycaemia (Karamanou *et al*., 2016; American Diabetes Association, 2009). The Hindu scholars in 1500 BC described DM as a mysterious disease causing thirst, enormous urine output, and wasting away of the body with additional effect that flies and ants are attracted to the urine of the sufferers (Das and Shah, 2011). In 250 BC, Appollonius of Memphis coined diabetes meaning 'siphon', because the disease drains more fluid from the body than what a person could consume (Verma, 2016). During the 17th century, Thomas Willis added the term 'mellitus' to diabetes because of the extreme sweet taste of the urine.

The pioneers in the treatment of DM were Sushruta, Arataeus, and Thomas Willis, Karamanou *et al*., (2016). The prevalence of diabetes is increasing rapidly worldwide and the World Health Organization in 2003 predicted that by 2030 the number of adults with diabetes would have doubled worldwide, from 177 million in 2000 to 370 million. The worldwide estimated prevalence of diabetes among adults in 2010 was 285 million and this value is predicted to rise to 439 million by 2030, Ozougwu *et al*., 2013). Diabetes does not manifest as a single disease, but as many presentations. It is therefore referred to as 'starvation in the midst of plenty' (Dean and McEntyre, 2004). According to Janaka and Luigi (2016), major manifestations of diabetes includes: dehydration in the body, passing of excessive urine, and body weakness at all times.

There exist three types of diabetes mellitus, namely: Type 1 diabetes mellitus, Type 2 diabetes mellitus and Gestational diabetes mellitus. According to literature, glucose utilization and anti-oxidative mechanisms of the aqueous *hunteria umbellata* (HU) seed extract have been used in the management of diabetes.

Both orthodox antidiabetic drugs and herbal antidiabetic formulas have performed excellently well in the treatment of mild cases of DM. In the work of Ezeja *et al*., (2015), rats were injected with freshly prepared 150 mg/kg body weight of alloxan monohydrates dissolved in sterile cold normal saline, given via the intraperitoneal route.

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Dry seeds of the plant, *Hunteria umbellata* K. Schum (family: Apocynaceae), are highly valued in African traditional medicine (ATM) in the treatment of various human diseases, including diabetes mellitus and obesity. Huntaria umbellata plant is known to the Yoruba race as 'Abeere' (Adeneye, 2011). In ATM, HU plant has wide therapeutic applications spanning the local treatment of pains, gastric ulcers, liver diseases, obesity, diabetes mellitus to mention but a few. Metformin is an oral antidiabetic orthodox drug commonly used for the treatment of Type II diabetes mellitus (Kaku, 2010; Rojas, 2013). However, its effects on patients are derived usually from clinical experiments. In their study, a dynamic model of Type II diabetes mellitus with the treatment of metformin was proposed (Fabietti, 2007). The Type II diabetic model is a modification of an existing compartmental diabetic model (Al-Akwaa, 2006). **T**he purpose of this study is to carry out a comparative analysis of the potencies of *hunteria umbellata* and metformin on Type 1 diabetes mellitus using bio-statistical analysis.

MATERIALS AND METHODS

Materials used to carry out the biometric analysis include: huntaria umbellata seed, metformin 500mg, blender, graduated cylinders, coconuts, beakers, cups, spoons, water, 1 oz shot glasses, Accu-chek active pack comprising of a blood glucose meter, a test strip and a lancing device used for taking blood sugar test; MatlabR2013a composing of high-level technical computing language with interactive environment for algorithm development, and data analysis; and Microsoft Excel, a Microsoft office tool used to collate and manipulate huge volume of data with variants of computational features of the data collected. The study entails empirical analysis of data collected from a population of twenty type II DM patients partitioned into two: fifteen were treated with metformin 500mg while five were treated with huntaria umbellata.

The huntaria umbellata seeds which has been blended to powder form was mixed with coconut water in ratio 1:5 for 20 minutes. The mixture is then shaken vigorously before it is administered on patients in a dose of one 1 oz. shot glass taken twice a day within eight hours' time interval (Akinmegha, 2016). While the dosage of huntaria umbellata was consistent, that of metformin varied with severity of DM commencing with one tablet taken religiously twice within an interval of eight hours per patient per day (Rojas, 2013). The empirical data obtained were drawn from the monitoring of the blood glucose levels for one month and sixteen weeks respectively for the patients that were treated with *hunteria umbellata* and those that were place on metformin 500mg. The algorithm involved in the monitoring is as follows:

1). Wash and dry the patients' hands with warm water to help the blood flow; 2). Turn on the meter and prepare a test strip as outlined in users' manual: many Accu-Chek meters turn on automatically when a strip is inserted. 3). Choose a suitable spot on the finger but don't check from the same finger all the time: the side of the fingertip may be less painful than the pads. 4. Prepare the lancing device according to the user guide provided, then lance your fingertip to get a drop of blood. 5). Touch and hold the test strip opening to the drop until it has absorbed enough blood to begin the test. 6). View the test result. 7). Record the results in a logbook, and 8). Discard the used lancet properly.

After tabulating the results derived from the aforementioned procedure, the clinical data for both partitions of the population were normalized using Microsoft excel to an initial normal fasting blood glucose of 180mg/dl. Data from patients treated with *hunteria umbellata* were as summarized in Table 1, and Table 2 contains the corresponding normalized data.

Table 1: *hunteria umbellata* Data

Week	P1	P2	P3	P4	P5
0	196	194	201	173	187
1	172	175	186	169	183
2	125	128	141	127	143
3	98	88	98	76	97

Table 2: Normalised Data for Patients treated with *hunteria umbellata*

Week	P1	P2	P3	P4	P5	AVG
0	180	180	180	180	180	180
1	172	162	167	176	176	171
2	115	119	126	132	138	126
3	93	82	91	79	93	88

Bio-statistical models were used for results analyses. The one-way analysis of variance (ANOVA) and the Multi-comparison ('post hoc') test were used to determine the significance of the drugs and the difference between the estimated mean values of drugs used by the two treatment groups. In the one-way ANOVA, the following parameters were taken into consideration

The significance level ($\propto = 0.05$)

The null hypothesis: $H_0 : \mu_1 = \mu_2$; where

μ_1 = mean period of treatment 1 (Metformin 500mg),

μ_2 = mean period of treatment 2 (*hunteria umbellata*)

If the P-value is less than the significance level, it rejects the null hypothesis.

Alternative hypothesis.

$H_1: \mu_1 \neq \mu_2$

In the post hoc test, the Turkey-Kramer honest significant difference (HSD) procedure was implemented as default, based on standard studentized range distribution. Its implementation is based on

optimal results for a balanced one way ANOVA and according to Ostertagová (2013), the HSD test is conservative when there are unequal sample sizes. However, HSD test yields no result for two samples comparison since two-group case can be adequately addressed by a t-test (Zabell, 2008). And the t-test and the F-test are equivalent when statistical analysis involves only two means to be compared, $F = t^2$.

RESULTS AND DISCUSSION

The results of the study for both treatments were encouraging. The graphical details of the patients' responses to treatments in the both cases for hunteria umbellata and metformin 500mg is as contained in Figure 1. According to the figure, there exists great disparity in the behavior of the two graphs. The graph of *hunteria umbellata* is almost a decreasing section of a parabola while the graph of metformin 500mg can be likened unto a steadily declining plane surface with low angle of declination. .The translation of the two analogies is that the potency of *hunteria umbellata* is more than twice of that of metformin 500mg in the treatment of diabetes mellitus. The literary interpretation of the Figure 1 is clear. Metformin cures DM in eight weeks while *hunteria umbellata* achieves a more effective result in just three weeks. The outcomes of the one way ANOVA affirm the aforementioned assertion. Table 3 contains the results of the one way ANOVA as produced by MATLAB. However, for the purpose of clarity, we have presented the results in the traditional format for easy interpretation.

Figure 2 is the block diagram for the multi-comparison (post hoc) test to establish the validity of the result of the one-way ANOVA. The Figure indicated that after three weeks the patients treated with hunteria umbellata had recovered fully from diabetes mellitus while the group being treated with metformin 500mg is still in the process of recovery.

Table 3: Result of the One-Way ANOVA

Variance source	Sum of squares (SS)	Degrees of Freedom (DF)	Mean square (MS)	F-Statistic	P-value
Treatments	21493.6	1	21493.6	6.11	0.025
Error	56256.4	16	3516	-	-
Total	77750	17	-	-	-

Of concern in Table 3 is the p-value of the distribution. The comparison of the p-value to the significance level α of the distributions enables us to assess the null hypothesis; we therefore determine whether the difference between the means are statistically significant. In this work, the null hypothesis states that the means of the length of treatment for both drugs are equal. Usually, a significance level denoted as α or alpha of 0.05 is adequate. A significance level of 0.05 indicates a 5% risk of concluding that a difference exists when there is no actual difference. Since the p-value of 0.025 is less than the significance level of$\propto =$ 0.05, we reject the null hypothesis and conclude that the periods of treatment of diabetes mellitus based on huntaria umbellata and that of metformin 500mg indeed have different means.

Table 3 revealed that statistically, there is a significant difference in the mean fasting blood glucose (FBG) of patients using the two drugs. The effect of the oral antidiabetic herbal drug has a high significance obtained from the result of the p-value.

In Figure 2, the blue horizontal line indicates metformin (clinical data) treatment with estimated mean of 131.8889, while the red horizontal line shows the huntaria umbellata (Abeere) treatment with estimated Mean of 62.7778.

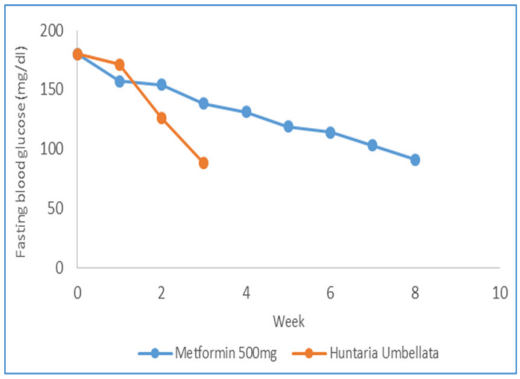

Fig 1: Normalized data from patients placed on *hunteria umbellate*

Huntaria umbellata (Abeere) takes 3 weeks to attain normal FBG. From this study, it can be inferred that huntaria umbellata takes an average of 3 weeks to attain normal FBG compared to metformin which takes an average of 8 weeks, providing a better understanding of the herbal formula (Huntaria Umbellata) for Diabetes treatment.

The results showed that huntaria umbellata has greater efficiency in reducing blood glucose level than that of metformin 500mg by a factor of 2.67.

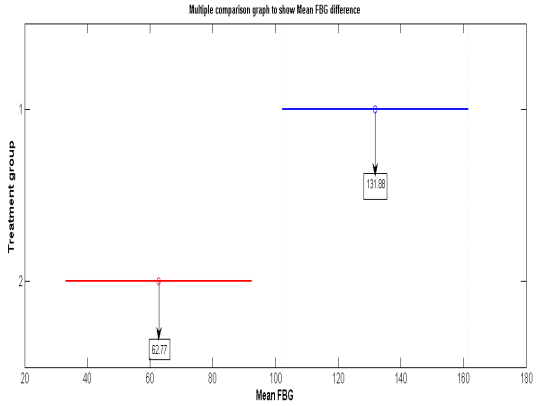

Fig 2: Multi-comparison (Post Hoc) Test of Mean FBG difference after week 3

The results of the study agree with existing literature. Kaku (2010) and Rojas (2013) both attested to the efficacy of metformin in the treatment of type II DM affirming the period of treatment of between two and three months. In the work of Verma, (2016), the potency of various plants as viable options to orthodox medicines like metformin was established. Another advantage of huntaria umbellata over and above metformin was the absence of most side effects associated with metformin. For instance, patients placed on metformin exhibited such symptoms as abdominal pains, belching, chest pain, diarrhea, headache, nausea and vomiting, runny nose and weakness. The only complaint recorded with patients treated with *hunteria umbellata* was extreme bitterness which caused one of the patients to vomit seldomly.

Conclusion: In this work, we have exploited the healing properties of *hunteria umbellata* (abeere) with the possibility of exploring same as possible prescription for DM patients in hospitals in Africa. The study showed the efficacy of the plant in reducing blood sugar based on the p-value obtained from the one way ANOVA of the mean lengths of treatments of patients with DM using huntaria umbellate on one group and metformin 500mg on the second group.

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