

1 **COMPARATIVE EFFECT OF TWO ANTI-DIABETIC PLANTS:**  
2 ***Cataranthus roseus* and *Nauclea latifolium* ON SOME BIOCHEMICAL**  
3 **INDICES OF STREPTOZOTOCIN**  
4 **INDUCED DIABETIC ALBINO WISTAR RATS**  
5  
6  
7

8 **ABSTRACT**

9 The study was carried out to investigate the comparative effects of two anti-diabetic plants  
10 *Cataranthus roseus* (C.R) and *Nauclea latifolium* (N.L) on some biochemical indices of  
11 streptozotocin induced diabetic albino wistar rats. **Methods:** Ethanolic leaf extracts of C.R. and  
12 N.L. were given at daily doses of 500mg/kg body weight in two divided doses each for 14 days.  
13 Thirty albino wistar rats were divided into five (5) groups, consisting of 6 rats each viz: Group  
14 1(normal control), Group 2(diabetic control), Group 3(insulin treated), Group 4(received N.L)  
15 and Group 5 (received C.R.). **Results:** Fasting blood glucose levels showed significant decrease  
16 ( $P<0.05$ ) in all the test groups compared to diabetic control and closely related to the insulin  
17 treated groups. A significant increase ( $P<0.05$ ) was observed in triglycerides (TG) and total  
18 cholesterol (TC) concentration of all treated groups compared to the diabetic control group. The  
19 concentration of VLDL-cholesterol was significantly increased ( $P<0.05$ ) in the diabetic control  
20 group and insulin group when compared to the normal control group. LDL-cholesterol concentration  
21 (mg/dl) was significantly increased ( $P<0.05$ ) in all the treated groups when compared to the  
22 normal control group except for C.R treated group that shows a significant decrease compared  
23 with the diabetic control group. AST activity was increased in insulin and diabetic groups. A  
24 significant reduction ( $P<0.05$ ) was observed with the treated group of C.R. and N.L compared to  
25 the normal control group. Significant increase in ALT activity was observed in diabetic and  
26 insulin groups compared to the treated groups and the normal control groups. Also observed was  
27 a decrease in albumin level in groups treated with the extracts. Marked reduction in total protein  
28 level was observed in groups treated with extracts and insulin, compared to the normal control  
29 group. Serum concentrations of  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Cl}^-$  in diabetic control groups showed a significant  
30 increase ( $P<0.05$ ) compared to the normal control group.  $\text{K}^+$  concentration was observed to be  
31 significantly decreased ( $P<0.05$ ) in all groups treated with extract and insulin compared to the  
32 normal control group. A significant increase ( $P<0.05$ ) in concentration of  $\text{Cl}^-$  was observed in all

33 groups treated with the extracts and insulin compared with normal control groups. **Conclusions:**  
34 The results demonstrated that *C.roseus* and *N.latifolium* have anti-diabetic and hypolipidaemic  
35 properties and could be potential herbal remedy in treating and managing diabetic conditions.  
36 **Key:** *Cataranthus roseus*, *Nuclea Latifolium*, triglycerides (TG) and total cholesterol (TC)  
37 concentration.

38

39

## 40 **1. Introduction**

41 Herbal medicines are popular remedies for disease used by a vast majority of the world's  
42 population. Formulation from herbs, have attained widespread acceptability as therapeutic agent  
43 [1]. Report by World Health Organization (WHO), [2], estimates that more than 80% of the  
44 world population relies on traditional medicine for their primary health care needs. People living  
45 in small isolated villages and natural communities use folk medicine from treatment of common  
46 infectious diseases [3]. Medicinal plants have acquired increasing significance in development  
47 co-operation over the last few years ([http://www.traffic.org/about/priority medicinal trade html](http://www.traffic.org/about/priority_medicinal_trade.html)).  
48 Their use and conservation are cross-sectorial concerns that embrace not only health-care but  
49 also natural conservation, biodiversity, economic assistance, trade and legal aspects, including  
50 intellectual property. Even today, the majority of the world's population is dependent upon  
51 traditional medicine and also on the use of plants and plant extracts. This is particularly true of  
52 poorer sections of the population in developing countries, because natural remedies are not only  
53 cheaper than modern medicines but are often the only medicines available in various rural  
54 regions. Beside serving medical and cultural functions, medicinal plants in developing countries  
55 have important economic role. The gathering of wild medicinal herbs provides economically  
56 disadvantaged groups such as small holders and handless herd's people with their only form of  
57 cash income.

58 Worldwide, a total of at least 35,000 plant species are used for medicinal purposes. The most  
59 important industrial medicines nowadays are based on not more than about 90 species, whilst  
60 traditional remedies in developing countries are usually based on mixtures of herbs collected in  
61 the wild. In Indonesia, for example up to three quarters of all instance of sickness are treated  
62 with mixture of teas – known as Jamu – which contain plant extracts from up to 30 different  
63 kinds of dried plant species. Plants are not just the main component of traditional medicines,  
64 according to estimates by the World Health Organisation, they also form up to about 70 percent  
65 of the basis of modern pharmaceutical products. One example is acetylsalicylic acid, the main  
66 ingredient, in painkillers (headache tablets) which was first extracted from domestic willow as  
67 long as 150years ago [4]. According to World Health Organization estimates of about 346  
68 million people worldwide have diabetes. In 2004, an estimated 3.4 million died from  
69 consequences of high blood sugar and more than 80% of diabetic related death occurring in low  
70 – and middle income countries. WHO projects that diabetic death will double in 2030? A report  
71 estimated that 25.8 million people in United State are affected with diabetes, 8.3% of the U.S  
72 population, (18.8 million people) are diagnosed while 7.0 million are undiagnosed. In Nigeria,  
73 WHO estimated diabetes mellitus prevalence to be 3.4% which may be under represented as  
74 more than half a million people in Lagos State alone are living with diabetes mellitus [4,4].  
75 *Vernonia amygdalina*, *Gongronema latifolium* and *Cataranthus roseus* are three known plants  
76 used in traditional medicine for the treatment or management of disease conditions. *Nauclea*  
77 *latifolium* and *Cataranthus roseus* will be used in this research. *Cataranthus roseus*, common  
78 name Madagascar periwinkle, or rosy periwinkle is an attractive small shrub with graceful pink  
79 or white salveer form flowers. Native to South eastern and eastern Madagascar [5].*Nauclea*  
80 *latifolium* commonly known as pin cushion tree, is a straggling shrub or small tree of about 10ft  
81 high and is a native of the tropic, Africa and Asia. The leaves are broadly elliptic to round ovate.  
82 It is found in areas like Abuja, Enugu, Akwa Ibom, Cross River, Kontangora, Shaki and some

83 other parts of Nigeria [6]. However, this plants have been over time used in the management of  
84 some other metabolic diseases in Nigeria. Progressive metabolic disorder characterized by  
85 hyperglycaemia mainly due to absolute (Type1DM) or relative (Type2 DM) deficiency of insulin  
86 hormone. DM virtually affects every system of the body mainly due to metabolic disturbances  
87 caused by hyperglycaemia, especially if diabetes control over a period of time proves to be  
88 suboptimal. Until recently it was believed to be a disease occurring mainly in developing  
89 countries, but recent findings reveal a rise in number of new cases of type 2 DM with onset and  
90 associated complications in developing countries [7]. Diabetes is associated with complications  
91 such as cardiovascular diseases, nephropathy, retinopathy and neuropathy, which can lead to  
92 chronic morbidities and mortality. World Health Organization [7,7]. estimates that more than  
93 346 million people worldwide have DM. This number is likely to be more than double by 2030  
94 without any intervention. Almost 80% of diabetes deaths occur in low and middle –income  
95 countries. Recent report, India today heads the world with over 32million diabetes patients and  
96 this number is projected to increase to 79.4 million by the year 2030.

97  
98  
99

## 2. MATERIALS AND METHODS

100  
101  
102

### 2.1 Chemicals and reagents

103 Ethanol (90%) was obtained from James Burrogh Limited, 60 Montford place London  
104 99.9%v/v min, one touch plus blood glucometer strips which were purchased from Globus  
105 Chemical, 55 Mayne Avenue, Calabar, Cross River State, Nigeria. A7413-106 Streptozotocin  
106 was obtained from sigma –Aldrich, Inc, St Louis, Mo63103, USA. All routine assay kits were  
107 from Agape Diagnostic Switzerland GmbH. Langackerstress 29-6330-Switzerland were  
108 obtained from spectrum Egyptian Company for Biotechnology (S.A.E) ObourCity industrial

109 area. Block 20009 8 pieces 19A Cairo, Egypt, human insulin injection was obtained from  
110 Atrapid Novo Nordisk A/s, DK-2880 Bagsvaerd, Denmark, Needles and other syringes used  
111 were purchased from Peace Land Pharmacy Limited, 476 Ndidem Isang Iso road, opposite  
112 Calabar Municipal Council Calabar.

113

## 114 **2.2 Methods**

### 115 **Collection of plant materials**

116 Fresh and matured leaves of *Nauclea latifolium* was harvested from the Endocrine  
117 Research Farm while *Cataranthus roseus* were harvested from the staff village environment,  
118 University of Calabar, in August 2018. They were authenticated by a botanist Dr Mike Eko,  
119 Department of Botany, University of Calabar, Calabar and voucher specimens deposited in an  
120 herbarium in the Department of Botany. The leaves were rinsed severally with clean tap water to  
121 remove dust particles and debris followed with distilled water thereafter allowed to completely  
122 drain. The dry *Nauclea latifolium* and *Cataranthus roseus* leaves were blended with the use of  
123 Cornono (EL legitima) VC.I.A. S.A manual hand blended, (Medellin-Colombia) into powder and  
124 3kg of the *Nauclea latifolium*, was weighed out and soaked in 2000ml of 80% ethanol while 800g  
125 of *Cataranthus roseus* was weighed out and soaked in 1000ml of 80% ethanol. The mixture was  
126 allowed for 48 hours in the refrigerator at 40 oc for thorough extraction of the plant's active  
127 components. These were then filtered with a cheese cloth and later with Whatman No.1 filter  
128 paper to obtain a homogenous filtrate. These filtrates were then concentrated in vacuo at low  
129 temperature (37 – 40°C) to about one tenth the original volume using a rotary evaporator. The  
130 concentrates were allowed open in a water bath (40°C) for complete dryness yielding 34.9g

131 (3.49%) and 29g (3.62%) respectively. The extracts were then refrigerated at 2 – 80C until when  
132 used.

133

### 134 2.3 **Animals**

135 Thirty albino rats (males only) of Wistar strain weighing about 140-180g were obtained  
136 from the animal house of the Department of Biochemistry, University of Calabar, Calabar. The  
137 animals were allowed to acclimatize for three weeks in the animals' house of the Department of  
138 Biochemistry. The animals were housed in well ventilated cages (wooden bottom and wire mesh  
139 top) and kept under controlled environmental conditions of temperature (25±500C), relative  
140 humidity (29±2%) and 12 hours' light/dark cycle.

141

### 142 2.4 **Experimental design**

143 The design consisted of 30 rats divided into five (5) groups consisting of 6 animals each  
144 (table 1). The doses used were based on the predetermined LD50 value obtained from  
145 preliminary studies.

146

### 147 2.5 **Method of Acute toxicity test LD50**

148 The acute toxicity study of *Cataranthus roseus* and *Nauclea latifolium* was carried out  
149 using the [8]. The LD50 value was determined, Confirmatory test was carried out and the LD50  
150 was calculated from the graph of percentage (%) of mortality (converted to probit) against Log-  
151 dose of the extract.

152

153

154 2.6 **Induction of experimental diabetes**

155 Principle:

156 Streptozotocin is approved by the U.S. Food and Drug Administration (FDA) for treating  
157 metastatic cancer of the pancreatic islets cells. Since it carries a substantial risk of toxicity and  
158 rarely cure the cancer, its use is generally limited to patients whose cancer cannot be removed by  
159 surgery. In these patients streptozotocin can reduce the tumour size and reduce symptoms  
160 (especially hypoglycaemia due to excessive insulin secretion by insulinomas).

161

162 2.7 **Anti-diabetic activity**

163 Fasting blood glucose was determined after deprivation of food for 16 hours with free  
164 access of drinking water. Hyperglycaemia was induced by a single intraperitoneal injection of  
165 100mg/kg body weight streptozotocin (STZ), a-Aldrich, Inc, St. Louis, Mo63103, U.S.A) in  
166 sterile saline. After 5 days of streptozotocin (STZ) injection, the hyperglycaemic rats (glucose  
167 level >8.3mmol/dl) were separated and divided into different groups comprising of 6 rats each  
168 for the anti-diabetic study.

169

170 **2.8 Extract and drug administration**

171 Before administration, the extracts were reconstituted in normal saline (vehicle) and  
172 administered orally twice daily at a dose of 500mg/kg body weight for the single dose of  
173 250mg/kg of the extracts of C. R and N. L, Insulin was administered at 5IU/kg b.wt, And the  
174 control animal received 0.2mlq of normal saline (Placebo) Respectively.

175

176 **2.9 Experimental design**

177 Diabetic animals were grouped as shown in table 1 below.

178

179

TABLE 1

180

Animal grouping and treatment scheme

<b>Diabetic rats Groups</b>	<b>No of animals</b>	<b>Treatment</b>	<b>Dosage</b>
1	6	Normal control	0.2ml of normal saline
2	6	Diabetic control	Placebo
3.	6	Insulin	51 $\mu$ /kg
4.	6	<i>Nauclea latifolium</i>	500mg/kg body weight/day
5.	6	<i>Cataranthus roseus</i>	500mg/kg body weight/day

181

182

183

184

185

186

187

188

189

190

191

192

193

194

### **3.0 Collection of samples for analysis**

195

196

At the end of the 14 days' food was withdrawn from the rats and they were fasted overnight but had free access to water. They were then euthanized under chloroform vapour and



197 sacrificed. Whole blood was collected via cardiac puncture using sterile syringes and needles.  
198 The blood was transferred into plain tubes and allowed to clot for about two hours. The clotted  
199 blood was thereafter centrifuged at 3,000rpm for 10 minutes to recover serum from clotted cells.  
200 Serum was separated with sterile syringes and needles and stored frozen until used for  
201 biochemical analysis.

202

### 203 3.1 Data and statistical analysis

204 Blood glucose levels were expressed in mg/dl as mean + SEM. The data were statistically  
205 analyzed using ANOVA with multiple comparisons versus control group by Punnett's method  
206 using SPSS software version 17. The value of  $P < 0.05$  were taken as significant.

207

208

209

### 210 3.2 RESULTS

211

212

TABLE 2

213 Phytochemical components of Ethanolic extracts of *Cataranthus roseus* and  
214 *Nauclea latifolium*

215

Components	<i>Cataranthus roseus</i>	<i>Nauclea latifolium</i>
1. Flavonoids	++	+
2. Saponins	+	+++
3. Polyphenols	+++	+
4. Alkaloids	++	+
5. Tannins	+	N.D
6. Hydrocyanide (HCH)	N.D	+++

216

217 Key

218 + = Present

219 ++ = Highly present

220 +++ = Very highly present

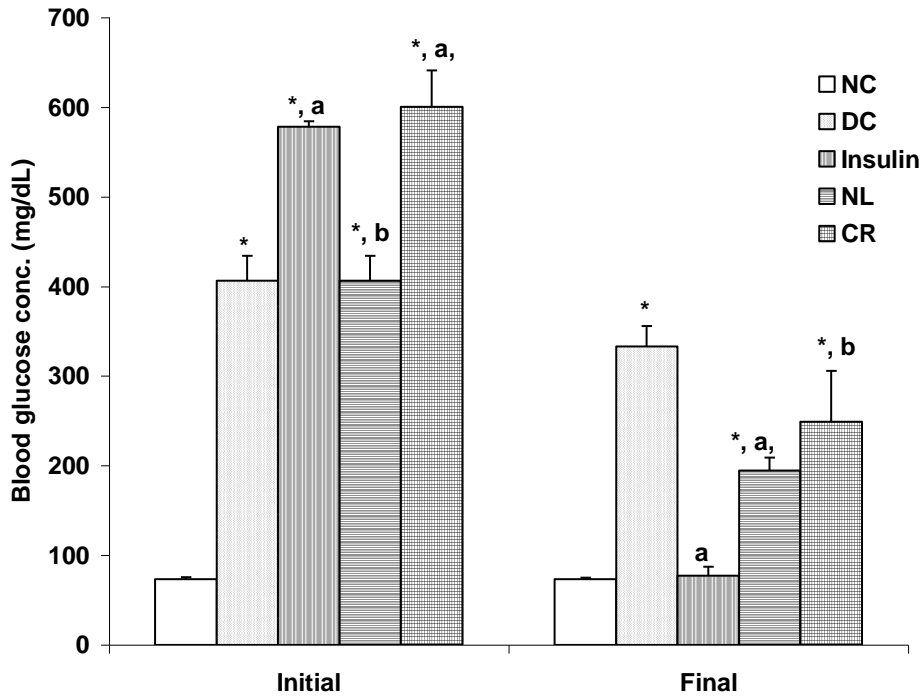
221 N.D = Not Detected

222

223

224           The result in table 1 shows that the phytochemicals present in *Cataranthus roseus* and  
225 *Nauclea latifolium*. Contains flavonoids, polyphenols and Alkaloids were found to be present in  
226 appreciable amount in *Cataranthus roseus* with saponins, tannins are found to be in traceable  
227 concentration. Also, saponins and hydrocyanide were detected at higher levels in *Nauclea*  
228 *latifolium* with flavonoids, polyphenols all in traceable amount.  
229

230  
231  
232  
233  
234  
235  
236  
237  
238  
239  
240  
241  
242  
243  
244  
245  
246  
247  
248  
249  
250  
251  
252  
253  
254  
255



256 **FIGURE 1:** Initial and final blood glucose level of diabetic rats.

257 Values are expressed as mean + SEM, n = 6.

258 \*Significantly different from NC at  $p < 0.05$ .

259 a =  $p < 0.05$  vs DC.

260 b =  $p < 0.05$  vs Insulin.

261 c =  $p < 0.05$  vs NL

262 **Change in fasting blood glucose (FBG) level of experimental rat model**

263 The results in figure 1 illustrate the initial and final blood glucose level of diabetic rats.  
264 The results showed that at the initial period of treatment there was a significant increase ( $P < 0.05$ )  
265 in fasting blood glucose of the insulin group. However, treatment with the extract of N.L and  
266 C.R, resulted in a significant ( $P < 0.05$ ) reduction in Fasting Blood Glucose (FBG) relative to

267 diabetic control and insulin treated group. The reduction in serum glucose may be due to the  
268 regeneration of beta cells of the pancreas, which were destroyed by STZ [9]. Fig.1 shows a  
269 presentation of the result of FBG that was observed in experimental period compared to the  
270 normal control. Upon treatment with both extracts and insulin respectively, a marked reduction  
271 in FBG was observed at the final day of the experimental period, which was significant ( $P<0.05$ )  
272 compared with the diabetic control and normal control. Therefore, this research reflected the  
273 beneficial effect of plant extracts on the glucose level of diabetes albino wistar rats. The  
274 reduction in glucose level in extract treated group may be due to the insulin-like effects of the  
275 extracts, as insulin increase glucose uptake by the cells. Reduction in glucose level of diabetic  
276 extract-treated group may also be due to the renewal of cell following extract administration. The  
277 renewal of cells in diabetics has been studied in several animal models. It has been suggested  
278 that regeneration of islet cells after the use of extract may be the primary cause of the recovery of  
279 stz induced albino wistar rat.

280

281

282

283

284

285

286

287

288

289

290

291

292

293

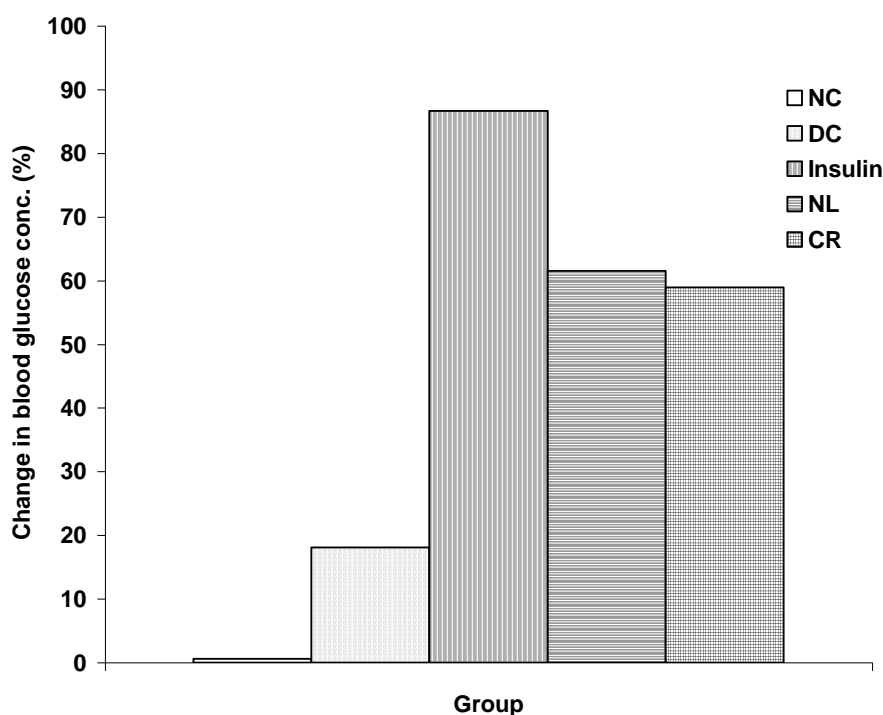
294

295

296

297

298

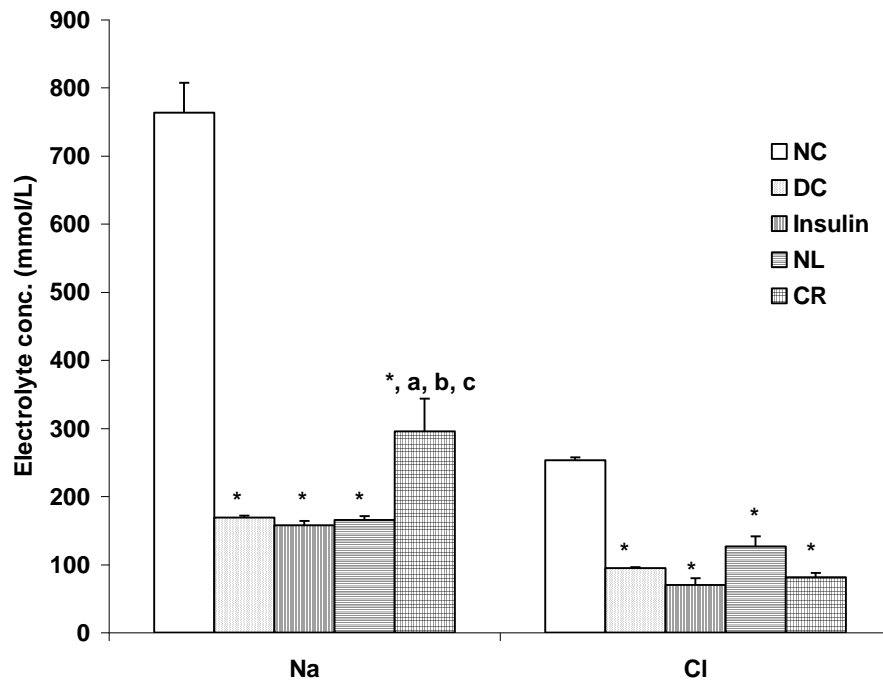


299  
300  
301  
302  
303  
304  
305  
306  
307  
308  
309  
310  
311  
312  
313  
314  
315  
316  
317  
318  
319  
320  
321  
322  
323  
324  
325  
326  
327  
328  
329  
330  
331  
332  
333  
334  
335  
336  
337  
338  
339

**FIGURE 2:** Percentage change in blood glucose level of diabetic rats.

Values are expressed as mean + SEM, n = 6.

Also from Fig.2, percentage (%) change in the blood glucose showed a relative decrease in all the experimental groups.



**FIGURE 3:** Sodium and chloride ion concentrations of experimental rats.

340 Values are expressed as mean + SEM, n = 6.

341 \*significantly different from NC at p<0.05.

342 a = p<0.05 vs DC.

343 b = p<0.05 vs Insulin.

344 c = p<0.05 vs NL

345

346

347

348

349 .

350

351

352

353

354

355

356

357

358

359

360

361

362

363

364

365

366

367

368

369

370

371

372

373

374

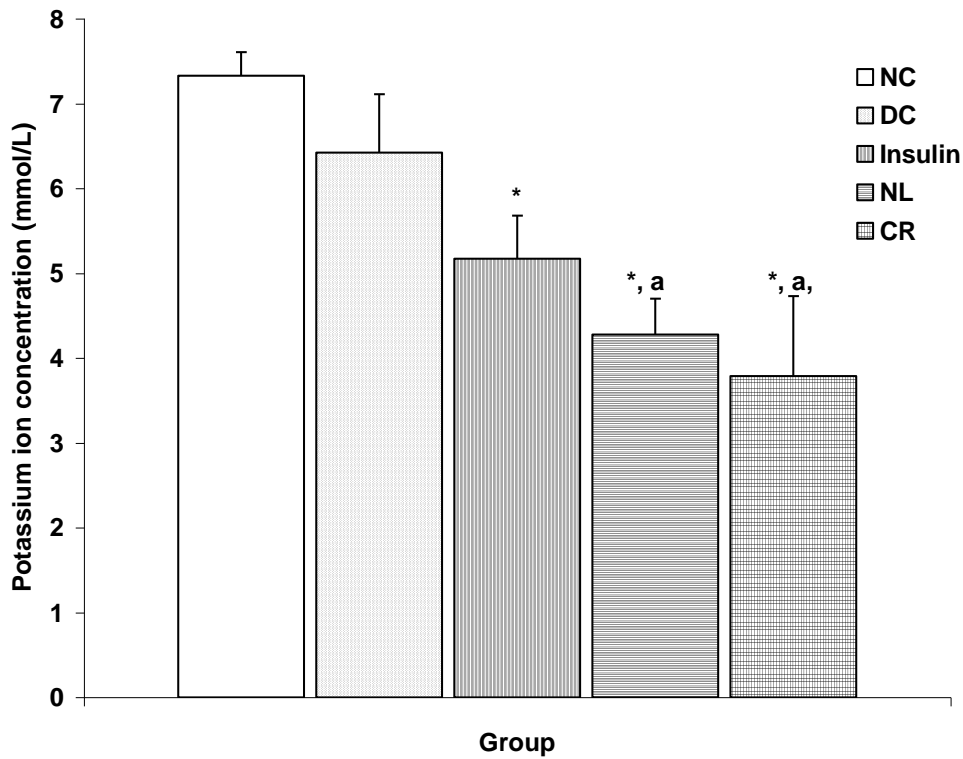
375

376

377

378

379



380 **FIGURE 4:** Potassium ion concentration of experimental rats. Values are expressed as mean +  
381 SEM, n = 6.

382 \*significantly different from NC at  $p < 0.05$ .

383 a =  $p < 0.05$  vs DC.

384 b =  $p < 0.05$  vs Insulin

385

386

387

388

389

390

391

392

393

394

395

### 396 **3.3 Effect on electrolyte concentration**

397 The effect of the two anti-diabetic plants *N. latifolium* and *C. roseus* indicated in fig.3 and  
398 fig.4, showed a representation of sodium, chloride and potassium ion concentration in diabetic  
399 rats. From the result, a significant decrease in sodium and chloride was observed in all treated  
400 groups with the extract and insulin at ( $P < 0.05$ ) compared to the normal control and related to the  
401 diabetic control. Also observed from fig.4 was a significant decrease in potassium concentration  
402 in all treated groups compared to both diabetic and normal control groups.

403

404

405

406

407

408

409

410

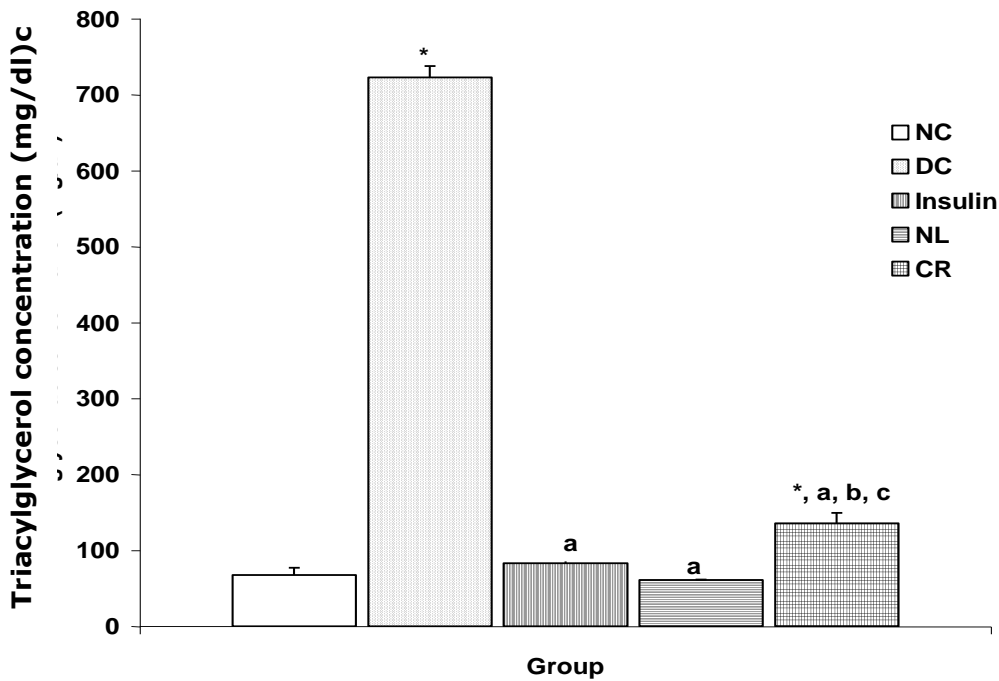
411

412

413



414  
415  
416  
417  
418  
419  
420  
421  
422  
423  
424  
425  
426  
427  
428  
429  
430  
431  
432  
433  
434  
435  
436  
437  
438  
439  
440  
441  
442  
443  
444  
445  
446  
447



448 **FIGURE 5:** Triglyceride concentration of experimental rats. Values are expressed as mean +  
449 SEM, n = 6.

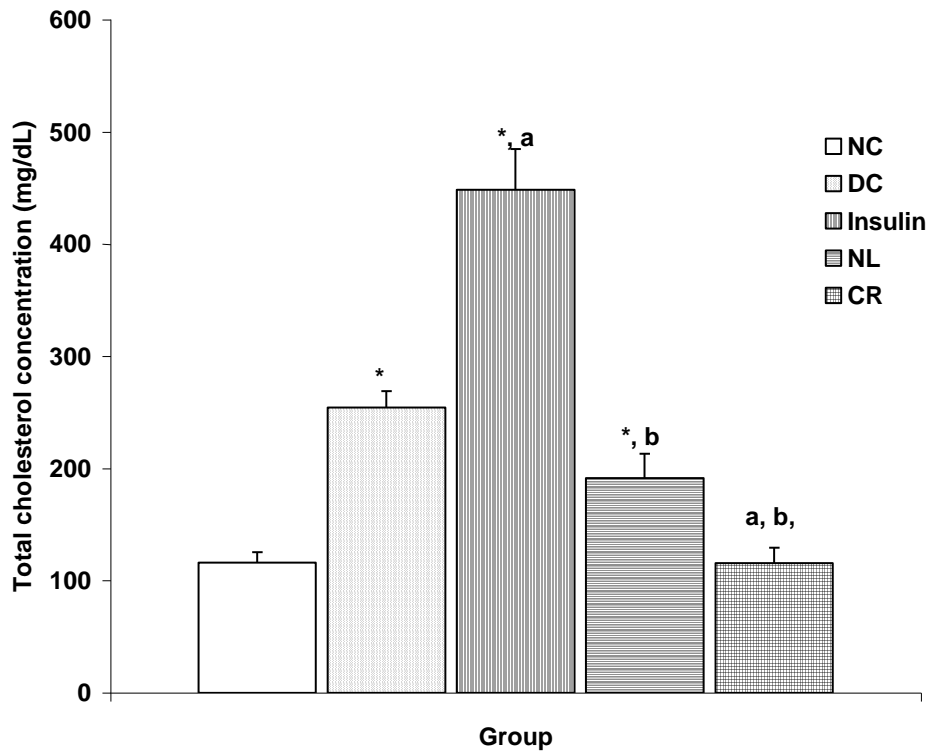
450 \*significantly different from NC at  $p < 0.05$ .

451 a =  $p < 0.05$  vs DC.

452 b =  $p < 0.05$  vs Insulin.

453 c =  $p < 0.05$  vs NL

454  
455  
456  
457  
458  
459  
460  
461  
462  
463  
464  
465  
466  
467  
468  
469  
470  
471  
472  
473  
474  
475  
476  
477  
478  
479  
480  
481  
482  
483  
484  
485  
486  
487  
488  
489  
490  
491  
492



**FIGURE 6:** Total cholesterol concentration of experimental rats.

Values are expressed as mean + SEM, n = 6.

\*significantly different from NC at  $p < 0.05$ .

a =  $p < 0.05$  vs DC.

b =  $p < 0.05$  vs Insulin.

c =  $p < 0.05$  vs NL

493

494

495

496

497

498

499

500

501

502

503

504

505

506

507

508

509

510

511

512

513

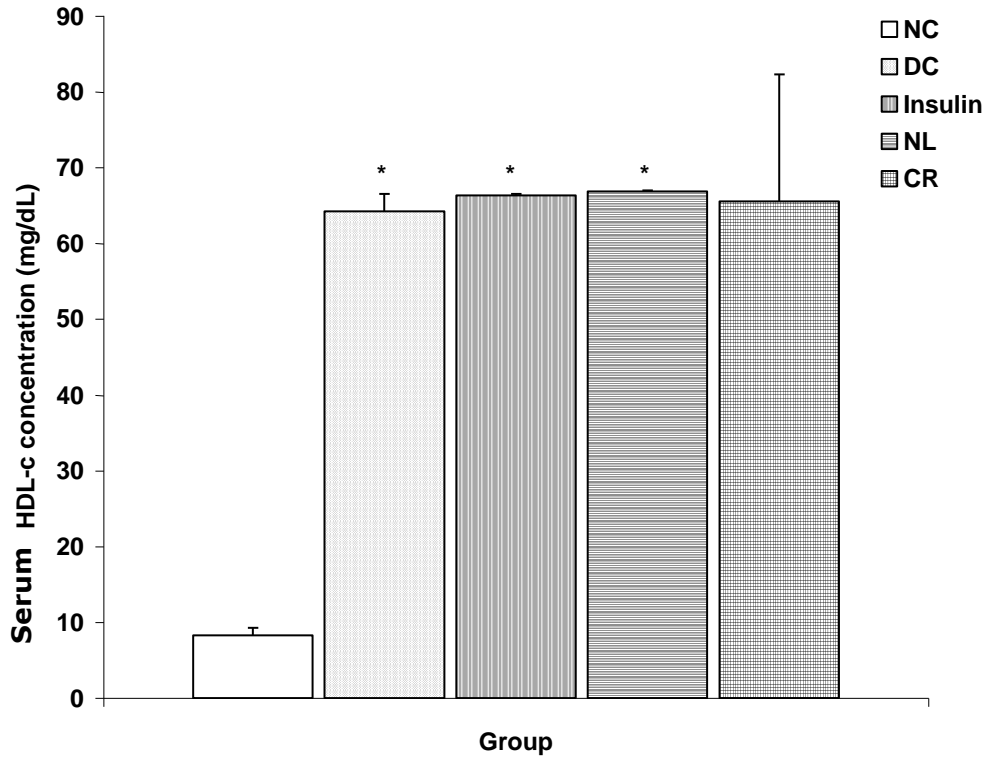
514

515

516

517

518



514

515

516

517

518

**FIGURE 7:** High density lipoprotein concentration of experimental rats.

519

Values are expressed as mean + SEM, n = 6.

520

\*significantly different from NC at  $p < 0.05$ .

521

522

523

524

525

526

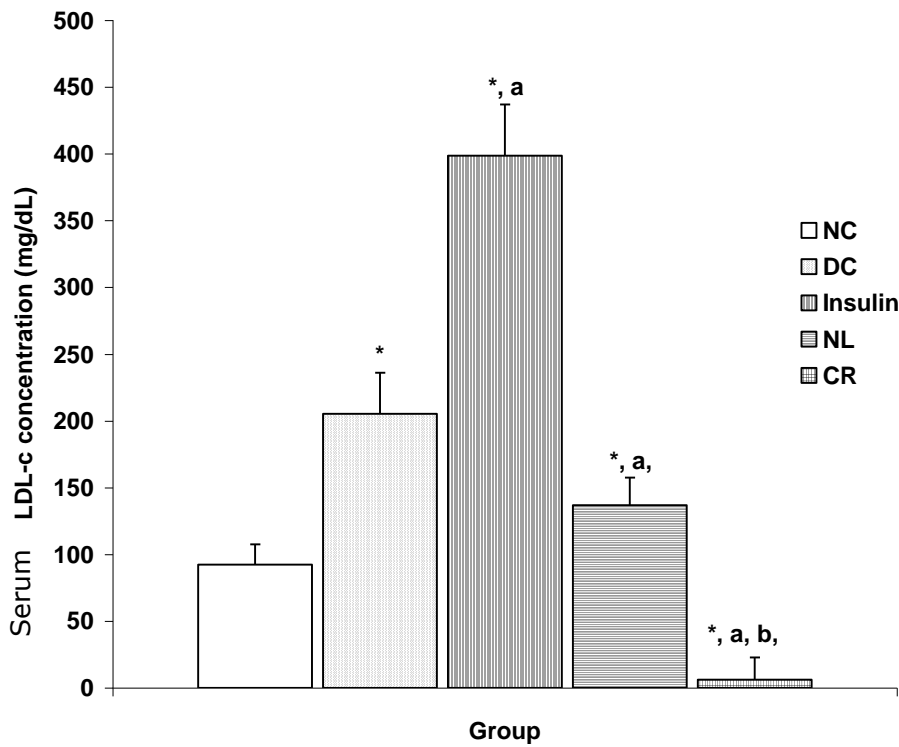
527

528

529

530

531  
532  
533  
534  
535  
536  
537  
538  
539  
540  
541  
542  
543  
544  
545  
546  
547  
548  
549  
550  
551  
552  
553  
554  
555  
556  
557  
558  
559  
560  
561  
562  
563  
564  
565  
566  
567  
568  
569



**FIGURE 8:** Low density lipoprotein concentration of experimental rats.

Values are expressed as mean + SEM, n = 6.

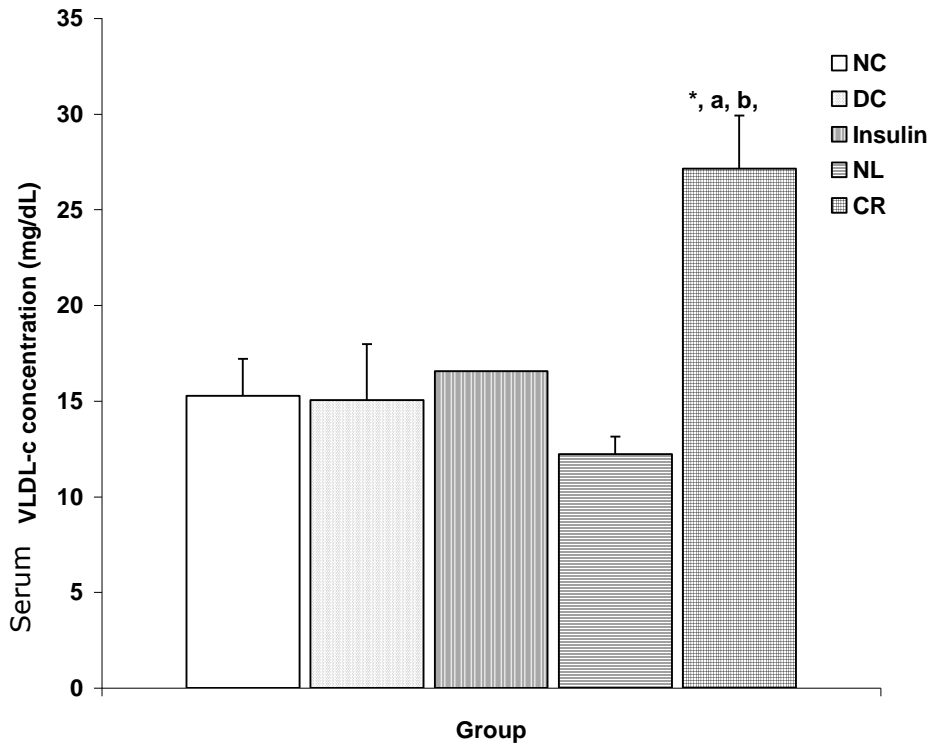
\*significantly different from NC at  $p < 0.05$ .

a =  $p < 0.05$  vs DC.

b =  $p < 0.05$  vs Insulin.

c =  $p < 0.05$  vs NL.

570  
571  
572  
573  
574  
575  
576  
577  
578  
579  
580  
581  
582  
583  
584  
585  
586  
587  
588  
589  
590  
591  
592  
593  
594  
595  
596  
597  
598  
599  
600  
601  
602  
603  
604  
605  
606  
607  
608  
609



**FIGURE 9:** Very low density lipoprotein concentration of experimental rats. Values are expressed as mean + SEM, n = 6.

\*significantly different from NC at  $p < 0.05$ .

a =  $p < 0.05$  vs DC.

b =  $p < 0.05$  vs Insulin.

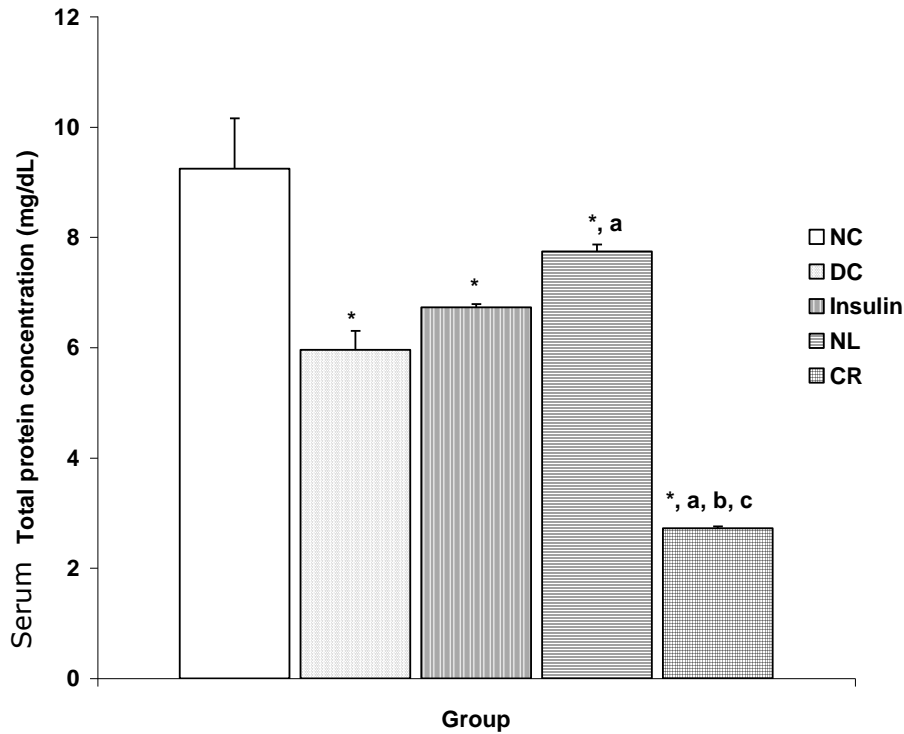
c =  $p < 0.05$  vs NL

610  
611  
612  
613  
614  
615  
616  
617  
618  
619  
620  
621  
622  
623  
624  
625  
626  
627  
628  
629  
630  
631  
632  
633  
634  
635  
636  
637  
638  
639  
640

### 3.4 Effect of treatment on serum lipid profile of experimental rats triacylglycerol

The effect of the two anti-diabetic plants *N. latifolium* and *C. roseus* indicated in figure 5, triacylglycerol concentration shows a significant ( $P<0.05$ ) decrease in all the treated groups compared to the diabetic control groups. Also the result in figure 6, total cholesterol concentration shows a significant decrease ( $P<0.05$ ) in the treated groups compared to the diabetic control groups and normal control groups. However, from the figure 7 there is a significant increase ( $P<0.05$ ) was observed in the HDL-C level in all the treated groups when compared to the diabetic control and the normal control groups. In figure 8, it was observed that there was a significant increase in LDL concentration ( $P<0.05$ ) in the insulin group compared to the diabetic control group and a significant decrease in all the extract treated groups compared to the normal control. The result for VLDL shown a significant ( $<0.05$ ) increase in the extracts treated groups compared to the insulin group and the diabetic control group respectively in (fig.9). The presence of these substances may be responsible for their antihyperglycaemic action. [10]. had earlier in his report indicated that plants endowed with flavonoids, glycosides and polyphenoles are likely to possess both hypoglycaemic and anti-hyperglycaemic properties.

641  
642  
643  
644  
645  
646  
647  
648  
649  
650  
651  
652  
653  
654  
655  
656  
657  
658  
659  
660  
661  
662  
663  
664  
665  
666  
667  
668  
669  
670  
671  
672  
673  
674  
675  
676  
677  
678  
679  
680



**FIGURE 10:** Total protein concentration of experimental rats. Values are expressed as mean +

SEM, n = 6.

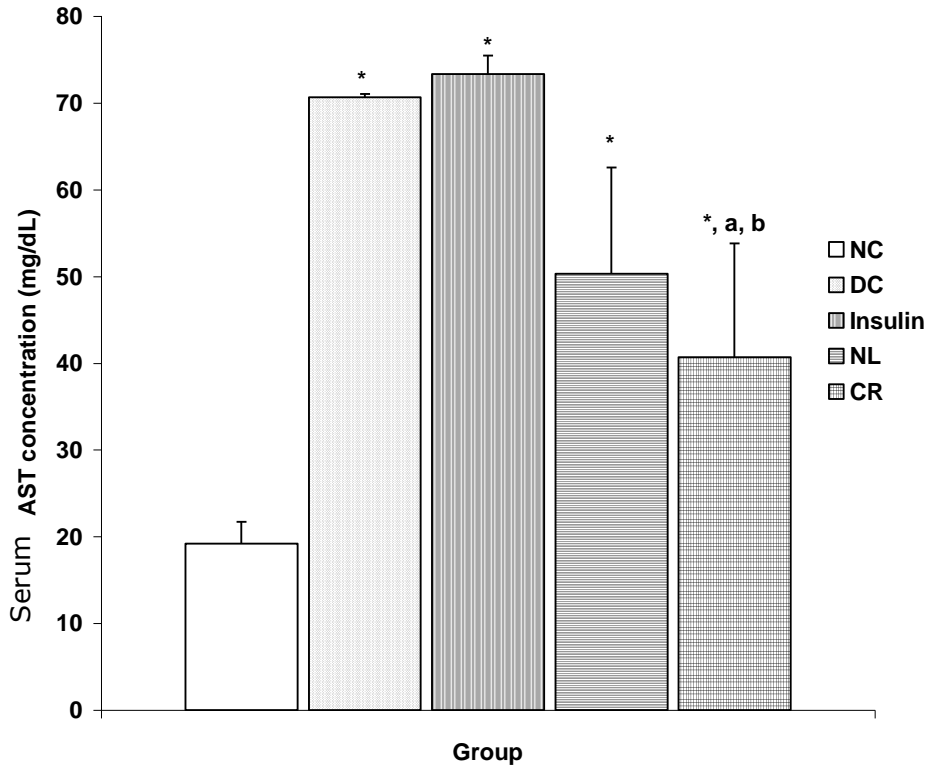
\*significantly different from NC at  $p < 0.05$ .

a = significantly different from DC at  $p < 0.05$ .

b =  $p < 0.05$  vs Insulin.

c =  $p < 0.05$  vs NL.

681  
682  
683  
684  
685  
686  
687  
688  
689  
690  
691  
692  
693  
694  
695  
696  
697  
698  
699  
700  
701  
702  
703  
704  
705  
706  
707  
708  
709  
710  
711  
712  
713  
714  
715  
716  
717  
718  
719  
720  
721



**FIGURE 11:** Aspartate aminotransferase concentration of experimental rats.

Values are expressed as mean + SEM, n = 6

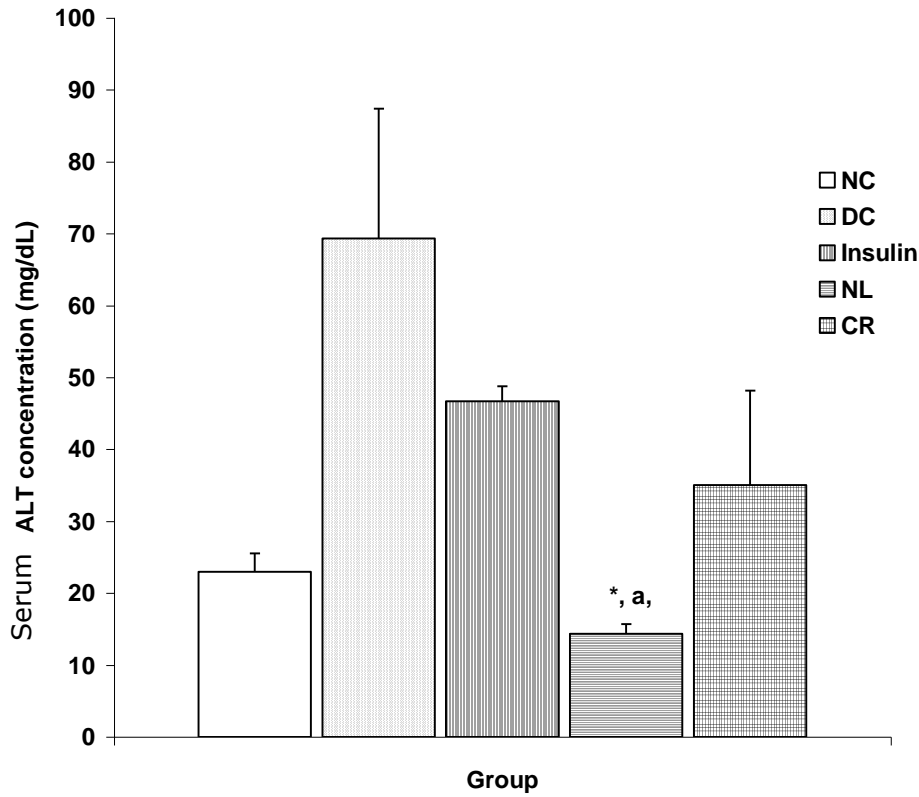
\*significantly different from NC at  $p < 0.05$ .

a = significantly different from DC at  $p < 0.05$ .

b =  $p < 0.05$  vs Insulin.



722  
723  
724  
725  
726  
727  
728  
729  
730  
731  
732  
733  
734  
735  
736  
737  
738  
739  
740  
741  
742  
743  
744  
745  
746  
747  
748  
749  
750  
751  
752  
753  
754  
755  
756  
757  
758  
759  
760  
761



**FIGURE 12:** Alanine aminotransferase concentration of experimental rats.

Values are expressed as mean + SEM, n= 6

\*Significantly different from NC at p<0.05.

a = significantly different from DC at p<0.05.

b = p<0.05 vs Insulin.

762        **4. DISCUSSION**

763            Diabetes mellitus (DM) is an endocrine disorder characterized by chronic  
764 hyperglycaemia with many disturbances of carbohydrate, fat, and protein metabolism due to  
765 decrease in insulin secretion. The result of this research reflected the beneficial effect of plant  
766 extracts on the glucose level of diabetes albino wistar rats. The reduction in glucose level in  
767 extract treated group may be due to the insulin-like effects of the extracts, as insulin increase  
768 glucose uptake by the cells. Reduction in glucose level of diabetic extract-treated group may also  
769 be due to the renewal of cell following extract administration. The renewal of cells in diabetics  
770 has been studied in several animal models. It has been suggested that regeneration of islet cells  
771 after the use of extract may be the primary cause of the recovery of stz induced albino wistar rat.  
772 The presence of these substances may be responsible for their antihyperglycaemic action. [10-  
773 10]. had earlier in his report indicated that plants endowed with flavonoids, glycosides and  
774 polyphenols are likely to possess both hypoglycaemic and anti-hyperglycaemic properties.  
775 However, it is not known how the ethanolic extract of the leaves of *N. latifolium* exert its  
776 hypoglycaemic effect. Moreover, the hypoglycaemic activity of the leaves of the plant may be  
777 due to this secondary metabolite involved in the stimulation of the  $\beta$ -cells and subsequent  
778 secretion of insulin [11]. The significant decrease in electrolyte in the extracts treated groups  
779 may be attributed to the actions of the bioactive components, and suggests that these extracts  
780 may be nephrotoxic. Diabetes mellitus is associated with disturbance in electrolytes metabolism.  
781 Electrolytes are dissolved mineral used by the body to conduct electricity. Potassium, sodium  
782 and calcium are all important for proper electrolyte balance. Electrolytes are vital for proper  
783 electric signals in the heart. Electrolytes are salts that conduct electricity and are found in the  
784 body fluid, tissues and blood. Examples are chloride (C), calcium, Magnesium, sodium and

785 potassium. Sodium ( $\text{Na}^+$ ) is concentrated in the (ICF) proper balance is essential for muscles co-  
786 ordination heart fluid absorption and excretion, nerve function and concentration [12]. The  
787 kidney regulates fluid absorption and excretion and maintain a narrow range of electrolyte  
788 function. Sodium and potassium are filtered and its secretion into the bile by the liver [13]. Too  
789 much or too little sodium (hyponatraemia) or potassium hyper or hyperkalaemia) caused by  
790 poor diet, hydration, medication and disease, results in an imbalance. Hyponatraemia is the most  
791 common electrolytes imbalance [14]. It is associated with kidney disease such as nephrotic  
792 syndrome and acute renal failure (ARF). Sodium is the major positive ion (cation) in fluid  
793 outside of cells too much or too little sodium therefore can cause cells to malfunction, and  
794 extremes of it in the blood can be fatal. Potassium is the major positive ion (cation) found inside  
795 of cells. The proper level of potassium is essential for normal cell function. An abnormal  
796 increase in potassium or decrease in potassium (hyperkalemia) can profoundly affect the nervous  
797 system and increase the chance of irregular heart beat (arrhythmias), which when extreme can be  
798 fatal. An abnormally low level of potassium ( $\text{K}^+$ ) is called hypokalemia. The adrenal gland  
799 makes a hormone (aldosterone) that signals the kidneys to excrete or conserve potassium based  
800 on the body needs. Electrolytes play a vital role in maintaining homeostasis within the body.  
801 They help to regulate myocardial and neurological function, fluid balance, oxygen delivery, acid-  
802 base balance and much more, the most serious electrolyte disturbance involved abnormalities in  
803 the level of sodium and potassium. The result of the lipid profile from the study shows a  
804 significant decrease in TG, TC, LDL with a significant increase in HDL and VLDL. These  
805 increase shows that HDL serve as acceptor of cholesterol from various tissues [15]. They  
806 promote the removal of cholesterol from cells and its secretion into the bile by the liver [16].  
807 This result further confirmed the use of these two traditionally used medicinal plants for the

808 management of diabetic and related cardiovascular implications. The best single indicator of the  
809 likelihood of developing atherosclerotic heart disease is not total plasma cholesterol but rather  
810 the ratio of plasma LDL cholesterol to plasma HDL-cholesterol. High levels of HDL are  
811 negatively associated with the risk of coronary heart disease, high level of TG, which in the  
812 fasting condition are found mainly in VLDL, are positively related to the risk for coronary heart  
813 disease [17]. As LDL carries most of the plasma cholesterol, the total plasma cholesterol may  
814 also be a good index for the risk of coronary heart disease, when the high cholesterol level is not  
815 due to a high HDL level. However, the total cholesterol of HDL ratio may be the most potent or  
816 efficient predictor for the risk of coronary heart disease [18]. The extract may cause increase in  
817 HDL level by inducing APOA-1 production [19]. Suggested that increase in HDL levels after  
818 treated may be due to the induction of APOA-1 production. In the present study the  
819 comparative effect of the extracts *Cataranthus roseus* and *Nauclea latifolium* indicates that they  
820 were an increase in AST and ALT levels thus suggesting that these extracts are hepatoprotective  
821 on the liver where these enzymes are synthesized [20]. However, the result of Albumin and total  
822 protein shows a remarkable decrease when compared to the normal control treated with the  
823 extracts of *Nauclea latifolium* and *Cataranthus roseus*. The findings suggest that the extracts  
824 may have the potentials to reverse the potential risk of hepatotoxicity but probably requires long  
825 durations for total restoration of the liver synthetic function. The results are consistent with the  
826 report by [21]. on the effect of *Nauclea latifolium* leaves aqueous extracts on blood glucose  
827 levels of normal alloxan induced diabetic rats. Our finding on *Cataranthus roseus* and *Nauclea*  
828 *latifolium* was inconsistent with earlier reports.

829

830

831 **5. Conclusion**

832 The findings of the present research were concluded that the ethanolic extracts of *N.*  
833 *latifolium* and *C. roseus* has a beneficial effect on serum level of glucose, lipid profile, serum  
834 enzymes and electrolyte. This study also exposes the therapeutic value of this medicinal plants  
835 and its efficacy in the management of diabetes and it related complication.

836  
837  
838 **Conflict of interest**

839 The authors declare that they have no competing interests.

840  
841  
842  
843  
844 **References**

- 845  
846  
847 [1] Karuvilla, A. (2002). Herbal formulation as pharmacotherapeutic agent. *India Journal of*  
848 *Experimental Biology*, 40:7-11.  
849  
850 [2] World Health Organisation (WHO). (2008). *Traditional medicine*. Retrieved June 09,  
851 2008 from [www.who.int/mediacentre/fact-sheet/fs/134/en](http://www.who.int/mediacentre/fact-sheet/fs/134/en).  
852  
853  
854 [3] Lagnika, E. Anago, and Sanni, A. (2004). Screening for antibacterial, antioxidant activity  
855 and toxicity of some medicinal plant used in Benin folkloric medicinal. *Journal of*  
856 *Medicinal Plants*. 5(5), 773-777.  
857  
858 [4] Keem, S. and Read, M. M. (1994). Cite guide to plant in trade [http://www.traffic-](http://www.traffic-org/disatches/archives/june2000/samerica3org/disatches/archives/june2000/samerica3)  
859 [org/disatches/archives/june2000/samerica3](http://www.traffic-org/disatches/archives/june2000/samerica3org/disatches/archives/june2000/samerica3).  
860  
861  
862  
863 [5] Candolle, K. E. (1901). *Plantae madagascariensess ab alberto mocquersio lectae*. Bull  
864 Boissier. (6): 549-587. <http://www.tropicos.org/reference/1950>  
865  
866 [6] Okiemy-Andissa N, M. L., Miguel, A. W., Etou, J. M., Ouamba, M., Gbeassor and A. A.  
867 Aben (2004). Adalgesic effect of aqueous and hydroalcoholic extracts of three Congolese  
868 medicinal plants: *Hyptis svavolens*, *Nauclea latifolium* and *Ocimum gratissimum*.  
869 *Parkistan Journal Biological Science*, 7, 1613-1615  
870

- 871 [7] World Health Organisation (WHO). (2011). Diabetes in the world health organisation  
872 country and regional data. Retrieved January 19 2012 from  
873 www.who.int/diabetes/fact/world figures/en/index.html.  
874  
875
- 876 [8] Lorke, D. (1983). A new approach to practical acute toxicity testing. *Archives of toxicology*,  
877 53, 275 – 287  
878
- 879 [9] Robertson, J. and Harmon, S. (2006). Diabetes, Glucose toxicity and oxidative stress: A  
880 case of double jeopardy for the pancreatic islet of beta cell. *Journal of Free Radical and*  
881 *Biological Medicine*, 41, 177-184.  
882
- 883 [10] Burrows, G. E. and Tyrl, R. J. (2001). Toxic plants of North America. Iowa State  
884 University Press. 1002-1004.  
885
- 886 [11] Tende J. A., Ezekiel I., Dikko, A. A. U. and Goji, A. D. T. (2011). Effect of ethanolic  
887 extract of *Moringa oliefera* on blood glucose levels of streptozotocin-induced diabetic  
888 and normglycemic rats. *British Journal of Pharmacology and Toxicology*, 2 (1), 1-4.  
889
- 890 [12] Perez, G. O., Lespier, L., Knowles, R., Oster, R. and Vamonde, C. A. (1977). Potassium  
891 homeostasis in chronic diabetes mellitus. *Annal Journal of Internal Medicine*, 137(8),  
892 1018-1022.  
893
- 894 [13] Vander, A., Sherman, J. and Lucian, D. (1998). Human physiology: The mechanism of  
895 body function. 7<sup>th</sup> Ed. New Jersey: McGraw-Hill.  
896
- 897 [14] Feldt-Rasmussen, B., Hegedus, L., Mathiesen, E. R. and Deckert, T. (1996). Kidney  
898 volume in type 1 (insulin-dependent) diabetic patients with normal or increased urinary  
899 albumin excretion: Effect of long-term improved metabolic control. *Metabolism*, 51, 31 –  
900 36.
- 901 [15] Akpanabiantu, M. I., Umoh, I. B., Udosen, E. O., Udo, A. E. and Edet, E. E. (2005). Rat  
902 serum electrolyte lipid profile and cardiovascular activity of *Nauclea latifolium* leaf  
903 extract administration. *Indian Journal of Clinical Biotechnology*, 20, 29 – 34  
904  
905  
906
- 907 [16] Vander, A., Sherman, J. and Lucian, D. (1998). Human physiology: The mechanism of  
908 body function. 7<sup>th</sup> Ed. New Jersey: McGraw-Hill  
909  
910
- 911 [17] Hokanson, J. E. and Austen, M.A. (1996). Plasma triglyceride level is a risk factor for  
912 cardiovascular disease independent of high density lipoprotein cholesterol levels, a meta-  
913 analysis of population based prospective studies. *Journal of Cardiovascular Risk*, 3, 213.  
914
- 915 [18] Ohlesen, S. and Rogers, D. (2004). Herbal formation as pharmacotherapeutic agent.  
916 *Indian journal of Experimental Biology*, 40: 7-11.

917  
918  
919  
920  
921  
922  
923  
924  
925  
926  
927  
928  
929  
930  
931  
932  
933  
934  
935

- [19] Lahoz, R., Rena, J. and Mostaza, M. (2003). APOA-1 promoters, atherosclerosis. *Journal of Indian Academy of Clinical Science*, 168(2), 289-295
- [20] Bergmeyer, H. U., Horder, M. and Rej, R. (1986). Approved recommendation on IFCC methods for the measurement of catalytic concentration of enzymes part 2 IFCC method for Aspartate Amino transferase. *Journal of Clinical Chemistry Clinical Biochemistry*. 24, 497 – 510.
- [21] Gidado, A. D., Ameh, A. and Atawodi, S. E. (2005). Effects of *Nauclea latifolia* Leaves aqueous extracts on blood glucose levels of normal and alloxan-induced diabetic rats. *African Journal of Biotechnology*, 4, 91-93.