

Full Length Research Paper

Preliminary study into the long term effects of a hypoglycaemic polyherbal formula (Yem-Kem) on some biochemical parameters in normal rabbits

Ojekale, A. B.^{1*}, Kappo, M. A.¹, Agbasoro, S.² and Kazeem, A.²

¹Department of Biotechnology, University of the Western Cape, Bellville, Cape Town, South Africa.

²Department of Biochemistry, Lagos State University, Ojo, P.M.B.001, Apapa, Lagos, Nigeria.

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The blood glucose lowering capacity of the polyherbal formula (Yem-Kem) was investigated in this study in an *in vivo* clinical trial using normal Sprague-Dawley rabbits orally administered with the formula over a 60 day period. The results showed that continuous exposure to the extract resulted in an overall lowered blood glucose level, lowered body weight and serum triglycerides, an increased alkaline phosphatase level, and fairly stable bilirubin levels. The formula is efficient as a hypoglycemic formulation, but its toxicity or otherwise cannot be established by this study.

Key words: Hypoglycaemia, serum analytes, enzymes, herbal formula, Yem-Kem.

INTRODUCTION

Medicinal plants and herbal therapy are integral part of the lifestyle/health delivery system of Nigerians, as in most parts of the world. A large number of people revert back to nature for treatment to their different ailments, with believe and conviction that medications composed of natural products such as plant parts are not harmful (toxic). The use of medicinal plants as treatment for physiological conditions is supported by the United Nations, as highlighted in the report on the 3rd United Nations Conference on the Least Developed Countries (2001), amongst others. This hyped up trend has thrown up a lot of alternate (complementary) health practitioners, and subsequently, herbal products.

Diabetes is a very common condition that is not tribe, gender or age discriminating. High blood glucose levels characterize it, with a myriad of secondary complications emanating from this, resulting in significant levels of morbidity and mortality (Covington, 2001). There is no permanent cure to it; instead it is maintained with drugs, diet, and lifestyle adjustment. Quite a number of medicinal plants/compounds (over 1200) have been established to possess hypoglycaemic potentials (O'Connell, 2006).

A number of plants on the Nigeria scene have also yielded positive results as hypoglycemic agents e.g. *Mangifera indica* (Okochi et al., 1997), *Ceiba pentandra* (Ladeji et al., 2003) and *Loranthus micranthus* (Osadebe et al., 2004).

Diabetes mellitus is managed almost always throughout the lifetime of the individual concerned, though this is type and aetiology dependent. Management can be through drugs (orthodox or complementary), adjustment in nutritional life style, or a combination of both. In the case of management using herbal products, the issue of toxicity comes into play, and has to be considered

Most results emanating from these plants/products are from tests conducted using animal models, with emphasis on the glucose lowering capacity (hypoglycaemia) of the plant (Okochi et al, 1997). There is a dearth of literature on the medium/long term toxicity potentials of these medicaments, and of the scientific literature scoured on hypoglycaemic plants/products. As at the time of this study, there was no mention of long term toxicity effects of the herbal product being evaluated in this study. This study was undertaken to evaluate the long term effects of one of the numerous brands of polyherbal formulations (YEM-KEM) in the Nigeria market, and thus contribute to the growing body of scientific literature on (commercial) herbal products, their benefits, toxicities and long term effects.

*Corresponding author. E-mail: aojekale@uwc.ac.za.

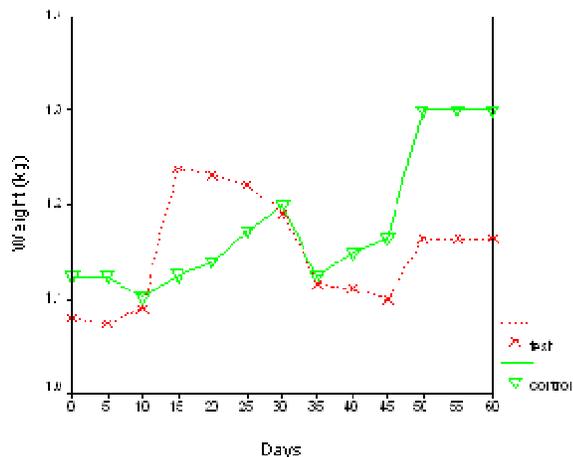


Figure 1. Graph showing weight changes in rabbits after long-term exposure to Yem-Kem hypoglycaemic herbal extract.

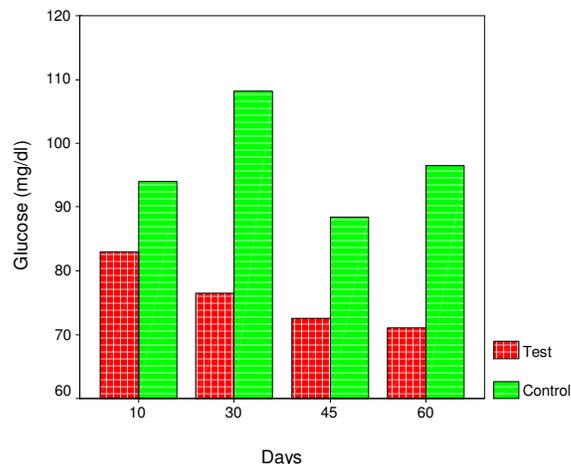


Figure 2. Bar chart showing glucose levels in rabbits after long term exposure to Yem-Kem hypoglycaemic herbal extract.

MATERIALS AND METHODS

Sample collection and reconstitution

The herbal product (Yem-Kem) was purchased from an accredited dealer of the manufacturer. The gelatin casing enclosing the product was carefully removed aseptically, and the contents therein mixed with sterile distilled water.

Study design

Sprague-Dawley rabbits weighing between 1.2 ± 0.4 kg were obtained from the animal house of the College of Medicine of the University of Lagos. They were housed in plastic cages in a 12 h light/dark cycle. Access to food (commercial rabbit feed), and water was *ad libitum*. The *ad libitum* access to feed is to simulate real life situation, where most diabetics resist/revolt against the notion of restricted/structured dietary regime. The animals were placed into two groups as follows. IN group I (test), the extract was administered twice daily, according to the manufacturer's regimen for the duration of the study, while in group II (control) water was administered throughout the study. Group I animals were orally administered with the extract daily using an oesophageal catheter for the duration of the study (60 days).

The individual weights of the rabbits in each group were monitored every five (5) days, and rabbits were made to fast overnight prior to days on which they were sacrificed (days 10, 30, 45, and 60). Sacrifice was achieved via anaesthesia, and according to the laid down ethics of the Institution (Internationally acceptable) regarding animal experiments.

Biochemical analyses

Bilirubin was determined using the modified method by Henry (1974). Triglyceride and proteins were determined according to Tietz (1990). Glucose and alkaline phosphatase were determined using Randox® Kits.

Data analyses

Data values used for plotting graphs are means, with $n = 6$ for all groups, while graphs were plotted using MS Excel for Windows (XP

version). SPSS (version 14) was used in the determination of the levels of significance of the treatment regime to the parameters measured (ANOVA). All data used in plotting graphs are mean values ($\bar{x} \pm \text{SEM}$).

RESULTS AND DISCUSSION

The results from this study has shown that the herbal formulation is effective in the reduction of blood glucose as seen in Figure 2, where a drop of $\approx 20\%$ drop is noticed in the blood glucose concentration of the test group between days 10 and 60, when compared to the group of control animals, considering that all animals used in this study were normoglycaemic. This pattern is similar to the report of Chang et al. (2005), where a Korean herbal formulation (containing *Trichosanthis radix*, *Puerariae radix*, *Rehmanniae radix*, *Schizandrae fructus*, *Glycyrrhizae radix*, *Coicis semen* and *Oryzae semen*) was studied, and Weil (2007), where *Salacia oblonga* (Indian plant) reduced post prandial blood glucose levels by $\approx 25\%$, after some days of administration.

The efficacy of the formulation is further heightened by the overall body weight reduction (Figure 1), which is recommended for diabetic patients, especially the obese ones (Covington, 2001), accompanied by concomitant reduced levels of serum triglycerides (Figure 3), of which high levels are associated with cardiovascular problems (Ojekale et al., 2007). These results are similar to reports of Mutalik et al. (2005), where Dianex, a polyherbal formula was tested in mice. The total serum protein levels (Figure 4) which give a rough idea of the working efficiency of the kidney and liver, declined from day 10 -- 60 in the test group showing physiological adjustment to the presence of the herb. Like all other medicines, Yem-Kem presence in the body initially alters the working efficiencies of the system, and depending on its toxicity, it could

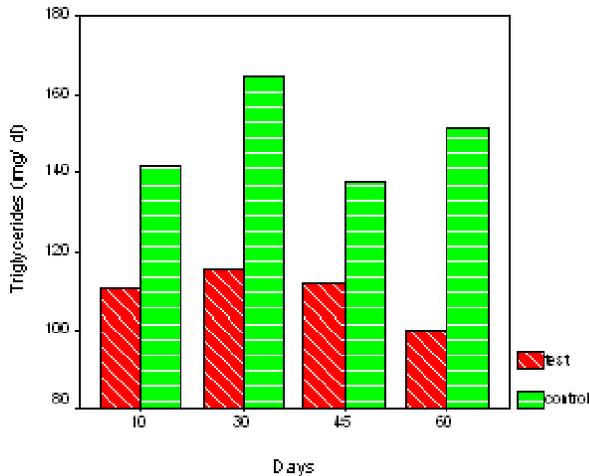


Figure 3. Bar chart showing serum triglycerides levels in rabbits after long term exposure to Yem-Kem hypoglycaemic herbal extract.

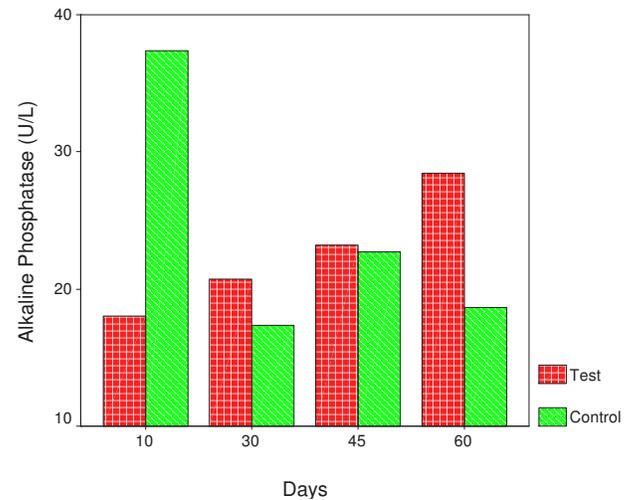


Figure 5. Bar chart showing alkaline phosphatase levels in rabbits after long-term exposure to Yem-Kem hypoglycaemic herbal extract.

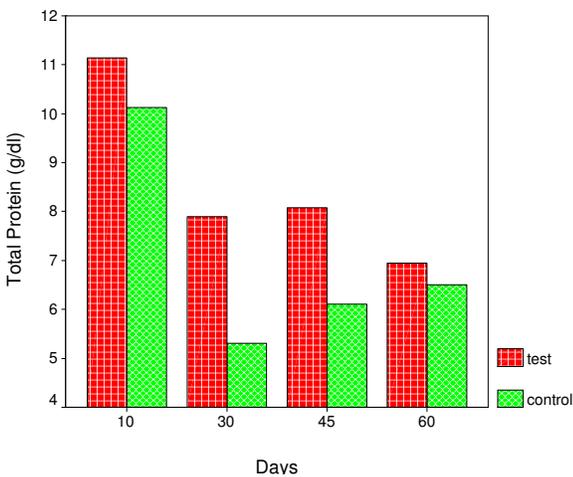


Figure 4. Bar chart showing total protein levels in rabbits after long-term exposure to Yem-Kem hypoglycaemic herbal extract.

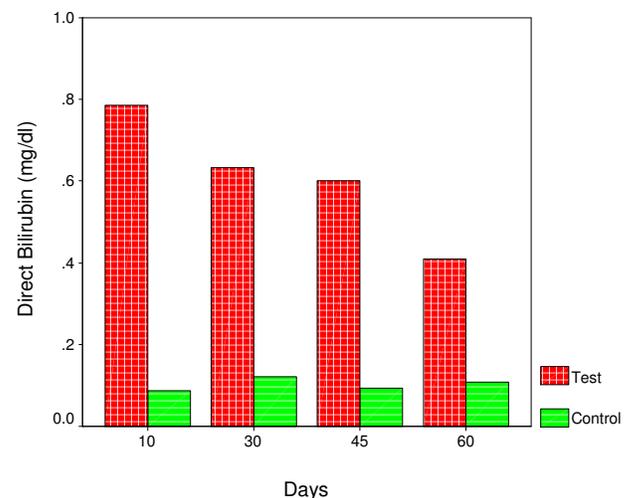


Figure 6 . Bar chart showing direct bilirubin levels in rabbits after long term exposure to Yem-Kem hypoglycaemic herbal extract.

return to normal range. Bilirubin levels consequent upon the administration of this formula (Figures 6 and 7) portend many possibilities, such as possible obstruction of biliary ducts. Further tests need be carried out though.

A progressive increase in serum alkaline phosphate levels was noticed as the days progressed in the study, with about a 30% increase noticed on day 60 compared to day 10 (Figure 5). increases in the levels of these enzymes are normally associated with a variety of diseases, but a less than three fold increase is normally considered insignificant (Wiwaniitkit, 2001), as the presence of drugs, such as this herbal formula alters the levels of the enzyme.

There is limited knowledge about the ingredients in herbal medicines, and their effects in humans (Chan,

1997). According to the label on the package, the herbal formula comprises the following plants; *Eugenia caryophyllata*, *Pyrenacantha pipernegrum* and *Cinchoma succirubora*. None of these plants, from the very scanty literature available on them, have been shown to possess hypoglycaemic properties. This product taken at this level shows the kind of synergism that is common in herbal medications, where their individual components lack any activity. But once together as a polyherbal product, activities unknown to the individual components are very well expressed. It can be safely concluded here that within the scope of this study, the maufacturer’s claims about the drug had been affirmed, while the level of its

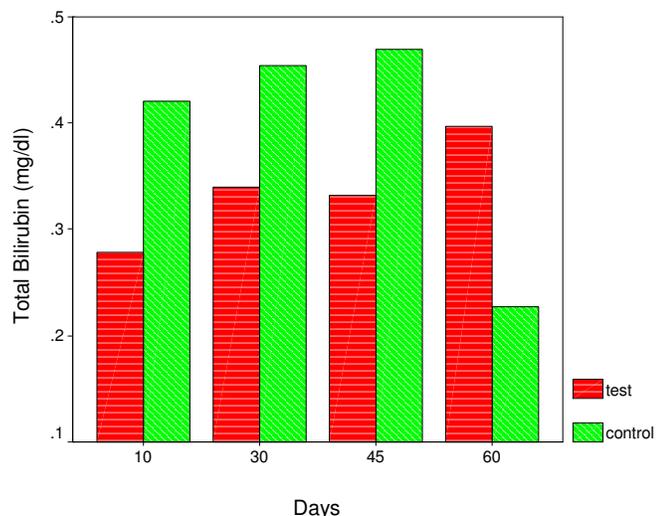


Figure 7. Bar chart showing total bilirubin levels in rabbits after long term exposure to Yem-Kem hypoglycaemic herbal extract.

toxicity, though inconclusive in this study, needs to be comprehensively investigated.

REFERENCES

- Chan TY (1997). Monitoring and Safety of Herbal medicines. *Drug Saf.* 17(4): 209-215.
- Chang MS, Oh MS, Kim DR, Jung KJ, Choi SB, Ko BS, Park SK (2005). Effects of Okchun-San, a herbal formulation, on blood glucose levels and body weight in a model of type 2 diabetes. *J. Ethnopharmacol.* (Epub ahead of print).
- Covington MB (2001). Traditional Chinese medicine in the treatment of Diabetes. *Diabetes Spectr.* 14(3): 154-159.
- Ladeji O, Omekarah I, Solomon M (2003). Hypoglycaemic properties of aqueous bark extract of *Ceiba pentandra* in streptozotocin-induced diabetic rats. *J. Ethnopharmacology.* 84(2-3): 139-142.
- Mutalik S, Chetana M, Sulochana B, Devi PU, Udupa N (2005). Effect of Dianex on experimentally induced diabetes mellitus. *Phytother. Res.* 19(5): 408-415.
- O'Connell B (2006). Herbal supplements in Diabetes Management. <http://www.diabetesselfmanagement.com/article.cfm?SID=2&TID=17&SSL=n&AID=410&STID=38&page=6>.
- Ojekale AB, Ojiako OA, Saibu GM, Lala A, Olodude OA (2007). Long term effects of aqueous stem bark extract of *Cissus populnea* (Guill and Per.) on some biochemical parameters in normal rabbits. *Afr. J. Biotechnol.* 6(3): 247-251.
- Okochi VI, Ojekale AB, Obolo O, Arukwe U (1997). The effect of *Mangifera indica* leaf and bark extracts on blood glucose level of rabbits. *Niger. Qtr. J. Hosp. Med.* 7(2): 154-157.
- Osadebe PO, Okide GB, Akabogu IC (2004). Study on anti-diabetic activities of crude methanolic extracts of *Loranthus micranthus* (Linn) sourced from five different host trees. *Ethnopharmacology*, 95(2-3): 133 – 138.
- Third United Nations Conference on the Least Developed Countries. (Discussion document) (2001). <http://www.intracen.org/bsrt/ppmedplants2.pdf>.
- Tietz NW (1990). Clinical guide to laboratory test. In fundamentals of Clinical Chemistry (ed N.W.Tietz), WB Saunders, Philadelphia.
- Wiwanitkit V (2001). High serum alkaline phosphatase levels, a study in 181 Thai adults. *BMC Family Practice*, 2:2 (<http://www.biomedcentral.com/1471-2296/2/2>).