A REVIEW ON GONGRONEMA LATIFOLIUM, AN EXTREMELY USEFUL PLANT WITH GREAT PROSPECTS

Olugbenga Morebise

Correspondence:
Olugbenga Morebise, Ph.D
Faculty of Basic Medical Sciences,
Roseau, Commonwealth of Dominica, West Indies
All Saints University School of Medicine, Roseau, Commonwealth of Dominica, West Indies.
e-mail: olugbengamorebise@gmail.com

ABSTRACT

Gongronema latifolium is a plant that has a wide range of nutritional and ethnomedical uses in different tropical African communities. Scientific reports on the chemical composition and bioactivity (anti-inflammatory, antimicrobial, antidiabetic, antioxidant, anticancer and allelopathic properties) of the plant material by different authors were discussed in this review. Future prospects of the plant extracts in the areas of herbal formulations, food preservation, alcoholic fermentation and beer production, drug discovery and allelopathy were also highlighted.

*Keywords*: Gongronema latifolium, diabetes mellitus, anti-inflammatory, antidiabetic, antimicrobial, antioxidant, anticancer, allelopathy, Olugbenga Morebise

1. INTRODUCTION
*Gongronema latifolium* Benth belongs to the family Asclepiadaceae. It is an edible nutritional/medicinal plant mostly found in the rain forest zones in Nigeria and other tropical African countries [1, 2]. The plant produces white latex and yellow flowers [1] and can be propagated by seed or stem cuttings [3]. *G. latifolium* is known by the Ikales of Ondo State of Nigeria as Iteji [4, 5]. The Ibos call the plant Utazi, the Efik/Ibibio call it Utasi while the Yorubas call it Arokeke [3]. To the Akan-Asantes of Ghana, *G. latifolium* is known as Kurutu Nsurogya; the Serers of Senegal call it Gasub while to the Kissis of Sierra Leone it is known as Ndodo-Polole [3].

![Gongronema latifolium plant](image)

Figure 1: The *Gongronema latifolium* plant

### 2. NUTRITIONAL USES OF *GONGRONEMA LATIFOLIUM*

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The leaves of *G. latifolium* are used as vegetables in preparation of soups to which they add a bitter-sweet flavor [4, 6]. The leaves are also sometimes used to spice locally brewed beer [3]. The soft stem is used as chewing stick in Sierra Leone [7].

3. **ETHNOMEDICAL USES OF GONGRONEMA LATIFOLIUM**

There have been reports of various uses of *Gongronema latifolium* in folklore medicine by different ethnic groups. Morebise and Fafunso [4] and Morebise et al. [5] reported that the leaves of this plant are used by the Ikales of Ondo State of Nigeria to treat malaria, nausea and anorexia. Edet et al. [8] also reported that the leaf extract of *G. latifolium* is commonly used by the Efik and Quas tribes of Cross River state of Nigeria to treat malaria, diabetes, hypertension and constipation.

Mosango [7] reported that *G. latifolium* is used in some West African communities to treat cough, intestinal worms, dysentery, dyspepsia and malaria. He reported that in Sierra Leone, an infusion or decoction of the stems with lime juice is taken to treat colic and stomach aches, while in Senegal and Ghana, *G. latifolium* leaves are rubbed on joints of children to help them walk while the boiled fruits of this plant are eaten as a laxative [7]. Essien et al. [9] reported that *G. latifolium* is used to treat cough in Nigeria. Asthmatic patients can chew the fresh leaves of *G. latifolium* to relieve wheezing while a cold maceration of the roots of the plant can be consumed as treatment for asthma [7, 9]. Mosango [7] also reported the use of this plant in some communities to treat viral hepatitis, bilharzia and other microbial infections.

Iwu [6] and Oliver-Bever [10] reported that the leaves of *G. latifolium* are used in some local communities as a vermifuge and stomachic. Owu et al. [11] reported that the leaves are also
used to treat dyspepsia in some local communities. Essien et al. [9] reported that the leaves of *G. latifolium* are used to treat fowl cough in Nigeria.

4. PHYTOCHEMICAL AND NUTRITIONAL COMPOSITION

Iwu [6] reported flavones and sterols as active constituents of *G. latifolium*. Morebise and Fafunso [4] reported the presence of saponins and flavonoids in the methanolic extract of *G. latifolium leaves*. Eze and Nwanguma [12] reported the occurrence of tannins in the leaves of the plant. B-Sitosterol, lupenyl esters, pregnane ester and essential oils have also been reported to be present in the body parts [13, 14].

Saponins are bioactive glycosides of steroids or triterpenes [15, 16]. The triterpene or steroidal rings are usually referred to as sapogenins or aglycones [15, 17]. The saponins are known to have a bitter taste, form stable foams in aqueous solutions, interact with cholesterol, bile acids and other 3-β-hydroxy steroids to form mixed micelles, and to exhibit some cytotoxicity [15, 16, 18]. Apart from *G. latifolium*, many other medicinal plants are also known to be rich in the saponins. Examples are *Panax ginseng*, Liquorice, *Bupleurum falcatum* and *Vernonia amygdalina* [19, 20].

![Saponin Diagram](image-url)
Flavonoids are widely distributed and form major colouring components of plants. They are a large group of phenolic compounds and are responsible for a variety of pharmacological activities [21-23]. They exist as aglycones, glycosides and methylated derivatives and can be further divided into different groups like the flavones, flavonols and flavanones [21]. Some plant flavonoids have been shown to exhibit protective effects against infectious, cardiovascular, carcinogenic and age-related diseases [22, 23].

Figure 2: Basic sapogenin structure

Tannins are large polyphenolic compounds that contain many hydroxyl and other groups, such as carboxyls, which usually form strong complexes with various macromolecules. Tannins possess astringent and medicinal properties [24]. The structure of tannic acid, a tannin, is shown below.

Figure 3. Flavone backbone (2-phenyl-1,4-benzopyrone)
B-Sitosterol is a plant sterol (phytosterol). Phytosterols are known to have beneficial effects in helping to reduce cholesterol absorption in the intestines [25].

Eleyinmi [26] did nutritional analysis of the *G. latifolium* leaves and reported that the crude protein content was 27.2%, dry weight, while the lipid extract, ash, crude fibre and nitrogen free extractives were 6.07%, 11.6%, 10.8%, and 443.3% dry matter, respectively. He reported that leucine, valine, phenylalanine, aspartic acid, glutamic acid and glycine were abundant in the plant material, with aspartic acid, glutamic acid and glycine having 13.8%, 11.9%, and 10.3%, respectively of the total amino acid composition. Likewise, saturated and unsaturated
fatty acids were 50.2% and 39.4% of the oil, respectively. He also reported occurrence of minerals in the plant material [26].

5. **SCIENTIFIC REPORTS ON G. LATIFOLIUM PLANT EXTRACTS**

i. **Anti-inflammatory activity**

Morebise *et al.* [5, 27-29] reported the anti-inflammatory activity of the leaf extracts of *G. latifolium*. Both aqueous and methanolic extracts of the leaf significantly (P=0.05) inhibited the carrageenan-induced rat paw oedema in a dose-related manner [27]. The extracts also significantly inhibited the acetic acid-induced vascular permeability and the leukocyte migration assay conducted on experimental mice. The carrageenan-induced rat paw oedema test is an established protocol to test for acute inflammation [30, 31] while the leucocyte migration assay and acetic acid-induced vascular permeability experiments are additional established anti-inflammatory tests [32, 33]. Morebise *et al* [28] also reported that the methanolic extract of the plant leaf material significantly inhibited the nystatin-induced rat paw oedema and also significantly stabilized erythrocyte membrane subjected to heat- and hypotonic solution-induced lyses.

To test for possible anti-inflammatory property of the plant in chronic inflammatory conditions, arthritis was induced in experimental rats and *G. latifolium* extracts were found to significantly and dose-dependently inhibit the arthritis formation and to lower the serum levels of Gamma-glutamyl transferase, alanine aminotransferase and aspartate aminotransferase [29]. The total serum protein and the globulin fraction were significantly (P=0.05) raised while the albumin fraction and the serum glucose were significantly reduced [29].
ii. **Antimicrobial activity**

Morebise and Fafunso [4] reported the antimicrobial action of the saponin fraction obtained from the methanolic extract of *G. latifolium* leaves. The fraction strongly inhibited the human pathogenic microbes that were tested, including *Bacillus cereus, Staphylococcus aureus, Candida albicans* and *Aspergillus niger*. Eleyinmi [26] reported that the methanolic extract of the plant leaves showed inhibitory activity against *Salmonella enteritidis, Salmonella cholerasius ser typhimurium, Pseudomonas aeruginosa* and *Listeria monocytogenes* while the aqueous extract showed inhibitory activity against *E. coli* and *P. aeruginosa*. Edim *et al.* [3] gave a review of reports on inhibitory effects of *G. latifolium* plant extracts on *Staphylococcus aureus*.

Adeleye *et al.* [34] reported that the aqueous and ethanolic extracts together with the essential oil from *G. latifolium* leaves were evaluated for inhibitory activity against bacteria isolated from HIV patients in Lagos, Nigeria. They found out that the essential oil and the extracts showed moderate inhibitory activity against *Staphylococcus sp., Escherichia coli, Shigella sp., Salmonella sp., Klebsiella pneumonia, Pseudomonas aeruginosa, Onchrobactrum anthropi, and Candida albicans*. The inhibitory effects were comparable to those of Ampicillin but less than those of Ciprofloxacin and Chloramphenicol in the study [34]. Enyi-Idor *et al.* [35] also reported the antibacterial activity of the leaf extracts of *G. latifolium* on *Staph. aureus and E. coli*. Essient *et al.* [9] reported the antioxidant and antitussive effect of *G. latifolium* leaf extracts on Hubbard broilers and concluded that their findings confirmed the antitussive use of *G. latifolium* leaves to treat fowl cough in Nigeria.

iii. **Antidiabetic activity.**
There have been several reports on the antidiabetic activity of the leave extracts of *G. latifolium*. In the study conducted by Sylvester *et al.* [36], experimental rats were subjected to Streptozotocin-induced diabetes mellitus and then treated with *G. latifolium* leaf extracts. They reported that the extracts significantly (*P*=0.05) lowered the blood glucose of the diabetic rats by 66.34%. They also reported that diabetic induction caused significant (*P*=0.05) increases in total cholesterol (TC) and LDL cholesterol (54.42% and 55.0%, respectively), compared with the normal control (NC). Treatments with the extracts significantly decreased these by 58.70% (TC) and 71.70% (LDL), respectively. The levels of AST and ALT enzymes were significantly lowered in the extract-treated animals compared with the diabetic control [36].

Edet *et al.* [8, 37] also reported their findings on allozan-induced diabetic rats treated with *G. latifolium* leaf extracts. In their 2009 report [37], the extracts lowered the serum activities of the following enzymes: creatine kinase (CK), CKMB isoform, lactate dehydrogenase, alanine aminotransferase (ALT) and aspartate aminotransferase (AST), compared with control. They concluded that the *G. latifolium* extracts may have protective effects on both heart and skeletal muscles during cardiac and skeletal muscle diseases. In their 2011 report [8], *G. latifolium* leaf extracts reversed the alterations in haematological indices (WBC counts, haemoglobin count, packed cell volume) and weight loss caused by alloxan-induced diabetes in male Wistar rats. Owu *et al.* [11] also reported the antidiabetic and antiulcerogenic effects of *G. latifolium* leaf extracts on Streptozotocin-induced diabetic rats. They also reported that the extract significantly reduced the blood glucose of the diabetic animals to levels similar to the nondiabetic control [11].
iv. **Antioxidant activity.**

Numerous reports have shown that *G. latifolium* leaf extracts exhibit antioxidant property.

Ugochukwu and Babady [38] reported that oral administration of aqueous and ethanolic extracts of *G. latifolium* leaf to Streptozotocin-induced diabetic rats significantly raised the activity of superoxide dismutase, glutathione reductase, glutathione peroxidase and glucose-6-phosphate dehydrogenase (G6PD). The level of reduced glutathione was increased while lipid peroxidation was decreased. They concluded that *G. latifolium* leaves could exert their antidiabetic activity through their antioxidant properties [38].

Nwanjo *et al.* [39] reported the anti-lipid peroxidative property of the aqueous extract of *G. latifolium* leaves in experimental rats subjected to Streptozotocin-induced diabetes. They found out that the extract significantly increased the activity of superoxide dismutase and lowered the level of the plasma lipid peroxidation product, malondialdehyde.

Eze and Nwanguma [12] reported the antioxidant activity of the tannin extract from *G. latifolium* leaves on partially purified lipoxygenase from *Cucumeropsis manii* seeds. The inhibitory effects of the tannin extract and of two known antioxidants: ascorbic acid and propyl gallate, on the partially purified lipoxigenase was investigated. The extract significantly inhibited the lipoxigenase and this inhibitory activity compared well with those of ascorbic acid and propyl gallate. They suggested that the extract could be included in food processing to hinder the deteriorative effects of lipoxigenase [12].

v. **Anticancer activity.**

*G. latifolium* leaf extracts were reported by Iweala *et al.* [40] to exhibit strong inhibitory activity against human lung carcinoma and human breast adenocarcinoma *in vitro*. The extracts also
exhibited free scavenger scavenging activity against 1,1-Diphenyl-2-picrylhydrazyl (DPPH) in vitro. Previous reports have indicated that phytochemicals could prevent cancer and other chronic diseases by their antioxidant activity as free radical scavengers [41-43].

vi. **Allelopathic activity.**

Morebise and Fafunso [4] reported the phytotoxic activity of saponin extracts from *G. latifolium* leaves. The saponin extract showed strong inhibitory activity against the germination of bean and maize seeds, and against the growth of their seedlings. Inhibition of root and shoot lengths was concentration-dependent and the roots were more sensitive than the shoots to the effect of the extract [4].

vii. **Beer production**

Adenuga *et al.* [44] conducted an experiment in which sorghum beer was brewed with the extracts of *G. latifolium, Vernonia amygdalina* and *Garcinia kola* to impart bitter taste and flavor as substitutes for hops used for beer production. Sensory evaluation of the beer samples was done by trained panelists. The panelists adjudged the *G. latifolium* flavoured beer as better than the other samples and that it compared favourably with hopped beer in terms of flavor and taste.

viii. **Toxicological study**

Interestingly, Sylvester *et al.* [36] reported that acute toxicity of the ethanolic extract of the plant on mice showed 0% lethality when administered intraperitoneally at 1000mg/kg body weight, but 100% mortality when administered at 2000mg/kg. This clearly suggests that the
plant material is not toxic at the safe doses being consumed. More research is needed in this area.

6. GENERAL DISCUSSION

The reports by the different authors highlighted in this review have justified the ethnomedical uses of *G. latifolium* plant material. The antihyperglycemic and antihyperlipidemic activity of the leaf extracts together with their raise of antioxidant enzymes and lowering of lipid peroxidation products in diabetic rats, as shown in the bioactivity reports, suggest possible mechanisms of action of the plant material in alleviating diabetic condition; this confirms the traditional use of the plant to treat diabetes mellitus. The anti-inflammatory, antioxidant and antimicrobial properties of this plant also support its use to treat various ailments including malaria, pains, nausea, intestinal discomforts, cough and other disorders. Inflammation and oxidative stress have been implicated in a host of disorders [45-47]. The *Gongronema latifolium* plant has been described as a reservoir of many natural antioxidants [48].

7. FUTURE PROSPECTS

i. **Isolation and characterization of active products**

In view of the vast array of bioactivity reports on *G. latifolium*, there is the need to focus research on the isolation and characterization of some of the individual active compounds and their use in the pure form for bioactivity studies. Hopefully, therapeutic drugs could be derived from the plant just as other plants have yielded some important drugs. For example, Quinine is obtained from the Cinchona plant, Artemisinin from *Artemisia anua* and Vincristine from *Catharanthus roseus* [49, 50]. A large percentage of Orthodox drugs in clinical management of
cancer have their roots in plants and other natural products [51] while more than 60% of cancer patients still resort to use of herbs to manage the disease [52].

ii. **Herbal Supplements/ Formulations**

Researchers should look into the possibility of using *G. latifolium* leaf extracts as approved medicinal formulations or supplements, especially for diseases like diabetes mellitus, sickle cell disease, malaria and other disorders for which the plant is being used ethnomedically. During the past decades, the World Health Organization (WHO) and several Governments in the developing countries have campaigned for the promotion and integration of herbal remedies in healthcare delivery as supplementary contributions to modern medical facilities [53].

iii. **Food Production and Preservation**

Based on the research findings highlighted in this review, commercial application of *G. latifolium* extracts as alternative to hops in beer production should be looked into. Also, commercial use of the extracts as food supplements or for food preservation is an interesting area which researchers can focus on.

iv. **Allelopathy**

Allelopathy is an emerging approach to agricultural issues like inter-cropping, pest management, crop rotation and growth enhancement [54]. A lot of research has been done to explore the inhibitory potential of different allelopathic crops and trees for weed management [55-58]. The inhibitory property of allelochemicals has been attributed to the blockage or cessation of important physiological and metabolic processes of plants [54]. Since allelochemicals do not have residual toxic effects, they are better alternatives to synthetic herbicides [59].
Allelopathic property of *G. latifolium*, if properly utilized, could effectively be used in weed control, plant selection, herbicidal application and crop rotation. This should be another area of research focus.

v. **Novel Research in Fermentations.**

*G. latifolium* leaf extracts were reported to increase the levels of reduced glutathione, glucose-6-phosphate dehydrogenase and the antioxidant enzymes in both experimental animals and *in vitro* studies (see notes on antioxidant activity). Can *G. latifolium* extracts do same in fermentations? Since alcohol is toxic because of its generation of free radicals that cause oxidative stress thereby destroying cells and tissues [60], increase in reduced glutathione, glucose-6-phosphate dehydrogenase (G6PD) and the antioxidant enzymes by *G. latifolium* extracts would boost the performances of the microorganisms being used for the fermentation process. Most yeast cells can tolerate between 10 and 15% alcohol in the fermenter depending on the yeast strain and environmental conditions [61]. Rossi *et al.* [62] suggested that the use of genetically modified *Saccharomyces cerevisiae* that produces high quantities of G6PD in ethanol production would have a positive effect on distillery profits. This is because G6PD would produce NADPH that would increase the amount of reduced glutathione. In the same vein, if *G. latifolium* can increase the levels of G6PD, reduced glutathione and superoxide dismutase in fermentation (just like it did in the animal and *in vitro* studies mentioned in this review) that would lead to more profits for brewery and other fermentation industries. Novel experiments are needed to be designed and conducted in this direction.

vi. **Mechanisms of action of isolated and characterized compounds.**

Several possible mechanisms of action of the extracts have been suggested by the authors of the articles that were reviewed. However, as active compounds are isolated from the plant and are
characterized, researchers should do studies on the molecular mechanisms of action of the characterized compounds. For instance, what is the action of the compound on cyclooxygenase (COX)? Is there any inhibitory preference for COX-1 or COX-2? How does the compound interact with G6PD, superoxide dismutase, lipoxygenase or any other enzyme? What are the molecular mechanisms of the anticancer, antimicrobial and phytotoxic properties of the drugs? These are further areas of research to look into.

CONCLUSION

The research reports highlighted in this review have tremendously justified the ethnomedical use of *Gongronema latifolium* plant. The plant material also has great prospects as highlighted in the review.

COMPETING INTERESTS

The author hereby declares that no competing interest exists.

REFERENCES

1. Hutchinson J, Dalziel J.M. *Flora of West Tropical Africa*. P. 60. The Crown Agents for the Colonies. 4, Milbank, Westminster; 1931.

2. Chattopadhyah RR. A comparative evaluation of some blood sugar lowering agents of plant origin. J Ethnopharmacol. 1999; 67: 367-372.

3. Edim EH, Egomi UG, Ekpo UF, Archibong EU. A review on *Gongronema latifolium* (Utasi): A novel antibiotic against *Staphylococcus aureus* related infections. International Journal of Biochemistry and Biotechnology. 2012; 1(8): 204-208.
4. Morebise O, Fafunso MA. Antimicrobial and phytotoxic activities of saponin extracts from two Nigerian edible medicinal plants. Biokemistri. 1998; 8(2): 69-77

5. Morebise O, Fafunso MA, Makinde JM, Olajide OA. Evaluation of the bioactivity of *Gongronema latifolium* leaf extract in rodents. Science Focus. 2006; 11(1): 27-30.

6. Iwu MM. Dietary plants and masticatories as sources of biologically active substances. In, 4th OAU/ STRC INTER-AFRICAN symposium on traditional pharmacopoeia and African medicinal plants. Abuja-Nigeria. 1988; p 70 & 379

7. Mosango DM. *Gongronema latifolium* Benth. Record from PROTA4U. Schmelzer GH, Gurib-Fakim A (eds.). Plant Resources of Tropical Africa (PROTA); available at http://www.prota4u.org/search.asp accessed 18 June 2015

8. Edet EE, Akpanabiatu MI, Uboh Fe, Edet TE, Eno AE, Itam EH et al. *Gongronema latifolium* crude leaf extract reverses alterations in haematological indices and weight-loss in diabetic rats. J Pharmacol Toxicol. 2011; 6(2): 174-181.

9. Essien JP, Ebong GA, Akpan EJ. Antioxidant and antitussive properties of *Gongronema latifolium* leaves used locally for the treatment of fowl cough in Nigeria. J Appl Sci Environ Manage. 2007; 11(4): 47-50

10. Oliver-Bever B. Medicinal plants in tropical West Africa. Cambridge University Press, London. 1986; p 89-90.

11. Owu DU, Nwokocha CR, Obembe AO, Essien AD, Ikpi DE, Osim EE. Effect of *Gongronema latifolium* ethanol leaf extract on gastric acid secretion and cytoprotection in Streptozotocin-induced diabetic rats. West Indian Med J. 2012; 61(9).
12. Eze SO, Nwanguma BC. Effects of tannin extract from Gongronema latifolium leaves on lipoxygenase Cucumeropsis manii seeds. Journal of Chemistry. 2013; 2013: 1-7.

13. Ekundayo O. Constituents of Gongronema latifolium Benth Hook (Asclepiadaceae). Quart J Crude Drug Res. 1980; 3: 127-129

14. Schneider C, Rotscheidt K, Breitmaier E. Four new pregnane glycosides from Gongronema latifolium (Asclepiadaceae). J Prak Chemie. 1993; 335(6): 532-536.

15. Cheeke PR. Nutritional and physiological implications of saponins—A review. Canadian J Animal Science. 1971; 51: 621-632.

16. Das MC, Mahato SB. Triterpenoids—A review. Phytochemistry. 1983; 22: 5 & 1071

17. Price KR, Johnson TI, Fenwick GR. The chemistry and biological significance of saponins in foods and feeding stuffs. CRC Critical Reviews in Foods Science and Nutrition. 1987; 26 (2): 22-135

18. Oakenfull D. Aggregation of saponins and bile acids in aqueous solutions. Australian J Chemistry. 1986; 39: 1671

19. Campbell JB. Saponins—Adjuvants: Theory and practical applications. Edited by DES Stewart-Tull. Chap 4. Butterworth-Heinemann Inc. Toronto, London, New York. 1993.

20. Ohigashi H, Tisaka M, Takagaki T, Mozaki H et al. Bitter principle and a related steroid glucoside from Vernonia amygdalina, a possible medicinal plant for wild chimpanzees. Agric Biol Chem. 1991. 55(4): 1201

21. Kumar S, Pandey AK. Chemistry and biological activities of flavonoids: An overview. The Scientific World Journal. 2013; vol 2013.

22. Cook NC, Samman S. Review: Flavonoids—Chemistry, metabolism, cardioprotective effects and dietary sources. Journal of Nutritional Biochemistry. 1996; 7(2): 66-76
23. Pandey AK. Anti-Staphylococcal activity of a pan-tropical aggressive and obnoxious weed *Parihenium histerophorus*: an in vitro study. National Academy Science Letters. 2007; 30(11-12): 383-386.

24. Mole S. The Systematic Distribution of Tannins in the Leaves of Angiosperms: A Tool for Ecological Studies. Biochemical Systematics and Ecology. 1993; 21 (8): 833–846

25. Rudkowska I, AbuMweis SS, Nicolle C, Jones PJ. Cholesterol-lowering efficacy of plant sterols in low-fat yogurt consumed as a snack or with a meal. J Am Coll Nutr. 2008; 27 (5): 588–95

26. Eleyinmi AF. Chemical composition and antibacterial activity of *Gongronema latifolium*. Journal of Zhejiang University Science B. 2007; 8(5):352-358.

27. Morebise O, Fafunso MA, Makinde JM, Olajide OA, Awe EO. Antiinflammatory property of the leaves of *Gongronema latifolium*. Phytotherapy Research. 2002; 16: 75-77.

28. Morebise O, Fafunso MA, Makinde JM. Membrane stabilizing activity: A possible mechanism of action for the anti-inflammatory property of *Gongronema latifolium* leaves. Int J Biomed Hlth Sci. 2005; 1(1): 15-19.

29. Morebise O, Fafunso MA, Makinde JM, Ajani RA. Biochemical studies on the activity of *Gongronema latifolium* leaves in experimental arthritis. Int J Biomed Health Sci. 2005; 1(2): 71-76.

30. Winter CA, Risley EA, Nuss CW. Carageenan-induced oedema in hind paw of the rat as an assay for anti-inflammatory drugs. Proceedings of the Society for Experimental Biology and Medicine. 1962; 111: 544-547.

31. Mossa JS, Rafatullah S, Galal AM, Al-Yahya MA. Pharmacological studies of Rhus retinorrhoea. International Journal of Pharmacognosy. 1995; 33: 242-246.
32. Whittle BA. The use of changes in capillary permeability in mice to distinguish between narcotic and non-narcotic analgesic. British Journal of Pharmacology and Chemotherapy. 1964; 22: 246-253.

33. Ribeiro RA, Frores CA, Cunha FQ, Ferreira SH. IL-8 causes in vivo neutrophil migration by a cell-dependent mechanism. Immunology. 1991; 73: 473-477.

34. Adeleye IA, Omadime ME, Daniels FV. Antimicrobial activity of essential oil and extracts of Gongronema latifolium on bacterial isolates from bloodstream of HIV infected patients. J Pharmacol Toxicol. 2011; 6(3): 312-320.

35. Enyi-Idoh K, Utsalo S, Arikpo G, Eja M. time-dependent evaluation of the antibacterial and phytochemical properties of Vernonia amygdalina and Gongronema latifolium. The Internet Journal of Herbal and Plant Medicine. 2012; 1(2).

36. Sylvester EG, Israel EU, Olajumoke AD. The effect of Gongronema latifolium leaf extract on blood biochemical assay in diabetic rats. Journal of Scientific Research & Reports. 2015; 6(7): 514-522.

37. Edet EE, Akpanabiatu MI, Eno AE, Umoh IB, Itam EH. Effects of Gongronema latifolium crude leaf extract on some cardiac enzymes of alloxan-induced diabetic rats. African Journal of Biochemistry Research. 2009; 3(11): 366-369.

38. Ugochukwu NH, Babady NE. Antioxidant effects of Gongronema latifolium in hepatocytes or rat models of non-insulin dependent diabetes mellitus. Fitoterapia. 2002; 73(7-8): 612-618.

39. Nwanjo HU, Okafor MC, Oze GO. Anti-lipid peroxidative activity of Gongronema latifolium in Streptozotocin-induced diabetic rats. Nigerian Journal of Physiological Sciences. 2006; 21(1-2): 61-65.
40. Iweala EEJ, Liu F, Cheng R, Li Y. Anti-cancer and free radical scavenging activity of some Nigerian food plants in vitro. Int J Cancer Res. 2015; 11(1): 41-51.

41. Sun J, Chu YF, Wu X, Liu RH. Antioxidant and antiproliferative activities of common fruits. J Agric Food Chem. 2002; 50: 7449-7454.

42. Liu RH. Health benefits of fruits and vegetables are from additive and synergistic combinations of phytochemicals. Am J Clin Nutr. 2003; 78: 517S-520S.

43. Liu RH. Potential synergy of phytochemicals in cancer prevention: Mechanism of action. J Nutr. 2004; 3479S-3485S.

44. Adenuga W, Olaleye ON, Adepoju PA. Utilization of bitter vegetables (Gongronema latifolium, Vernonia amygdalina) and Garcinia kola extracts as substitutes for hops in Sorghum beer production. African Journal of Biotechnology. 2010; 9(51): 8819-8823.

45. Yesilada E, Ustun O, Sezik E, Takaishis Y, Ono Y, Honda G. Effects of Turkish fold remedies on inflammatory cytokines. J Ethnopharmacol. 1997; 58: 59-73.

46. Vane JR, Bakhle YS, Botting RM. Cyclooxygenase 1 and 2. Annu Rev Pharmacol Toxicol. 1998; 38: 97-120.

47. Chan FKL, Hung LCT, Suen BY, Wu JCY, Lee KC, Leung VKS et. al. Celecoxib versus diclofenac and omeprazole in reducing the risk of recurrent ulcer bleeding in patients with arthritis. N Engl J Med. 2002; 347: 2104-2110.

48. Atangwho IJ, Ebong PE, Eyong EU, Williams IO, Eteng MU, Egbung GE. Comparative chemical composition of leaves of some antidiabetic medicinal plants. Afr J Biotechnol. 2009; 8: 4685-4689.
49. Gulati AS, Bharel S, Srivastava PS, Abdin MZ, Jain SK. Experimental studies on Artemisia, a herbal remedy to malaria. Fitoterapia. 1996; 67(5): 403-410.

50. Rajaonarivony IM. The implementation of a governmental policy in natural products research and development in Madagascar. In, Science in Africa, A symposium at the 1996 annual meeting of the American Association for the Advancement of Science. Baltimore, Maryland. 1996; P83.

51. Cragg GM. Paclitaxel (Taxol): A success story with valuable lessons for natural product drug discovery and development. Med Res Rev. 1998; 18: 315-331.

52. Madhuri S, Pandey G. Some dietary agricultural plants with anticancer properties. Plant Arch. 2008; 8: 13-16.

53. Nkunya MHH. Natural products research and development, the Tanzanian experience. In, Science in Africa, A symposium at the 1996 annual meeting of the American Association for the Advancement of Science. Baltimore, Maryland. 1996; P35-49.

54. Farooq M, Bajwa AA, Cheema SA, Cheema ZA. Application of allelopathy in crop production. Int J Agric Biol. 2013; 15: 1367-1378.

55. Cheena ZA, Khaliq A, Saeed S. Weed control in maize (Zea mays L.) through sorghum allelopathy. J Sustain Agric. 2004; 23: 73-86.

56. Iqbal J, Cheena ZA, An M. Intercropping of field crops in cotton for the management of purple nutsedge. Plant Soil. 2007; 300: 163-171.

57. Jamil M, Cheena ZA, Mushtaq MN, Farooq M, Cheena MA. Alternative control of wild oat and canary grass in wheat fields by allelopathic plant water extracts. Agron Sustain Dev. 2009; 29: 475-482.
58. Farooq M, Habib M, Rehman A, Wahid A, Munir R. employing aqueous allelopathic extracts of sunflower in improving salinity tolerance in rice. J Agric Soc Sci. 2011; 7: 75-80.

59. Bhadoria PBS. Allelopathy. A natural way towards weed management. Amer J Exp Agric. 2011; 1: 7-20.

60. Wu D, Zhai Q, Shi X. alcohol-induced oxidative stress and cell responses. Journal of Gastroenterology and Hepatology. 2006; 3:S26-S29.

61. Alba-Lois L, Segal-Kischinevzky C. Beer and wine makers. Nature education. 2010; 3(9): 17.

62. Rossi FG, Silva DP, Almeida e Silva JB, Taqueda ME, Vitolo M, Pessora-Jr A. Effect of cultivation conditions on Glucose-6-phosphate dehydrogenase production by genetically modified Saccharomyces cerevisiae. Braz J Chem Eng. 2009; 26(1)