THE PROSPECT OF USING LOCAL VEGETABLES TO CONTROL DIABETIC MENACE

11TH
School of Health Technology Lecture Series

BY
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The prospect of using local vegetables to control diabetic menace by Iwuji, S. C. is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.
Synopsis

- What is diabetic menace?
- How much is the menace?
- Any existing solution(s)?
- Are there some antidiabetic local vegetables?
- Any prospect and challenge(s) in their use?
- What next?

What do you think..........?
Summary
Diabetes is a fast growing menace to health, economy and development, especially in the poorer countries. Its current pharmaceutical therapy is confronted by high costs, side effects, inadequacy of trained manpower and relevant facilities. Phytomedicine has been in existence but with uncertain prospect in the control diabetic menace. Safe phytotherapy of diabetes is being investigated and is highly encouraged. Some local vegetables were found / shown to have antidiabetic properties / potentials, depending on dose, extraction method and solvent used. The prospect of using local vegetables to control diabetic menace is good but depends on further modern researches and local drug development efforts of Government, Universities and Pharmaceutical companies.
Glossary

- **Vegetables** are those herbaceous plants whose part or parts are eaten as supporting food or main dishes and they may be aromatic, bitter or tasteless (Edema, 1987).
- **Diabetes** is a metabolic disorder that causes persistent high level of blood glucose (hyperglycaemia).
- **Diabetic menace** include diabetes and its complications
- **Local** means Nigerian
1.0 INTRODUCTION
1.1 Background of the lecture
Vegetables are the cheapest and most available sources of important nutrients and some have medicinal properties (Okafor, 1983). Diabetes mellitus (DM) or simply diabetes was one of the first diseases described (1500 BC) as ‘great emptying of urine’ (Poretsky, 2009). Diabetes is of global concern (CDC, 2000).

WHO Expert Committee on diabetes (DM) recommended that traditional herbs be investigated further (Halberstein, 2005) since much is not known about their specific mechanisms of action (Patel et al., 2012) and their prospect in diabetes control in Nigeria.

The lecture briefly reviewed the menace of diabetes, examined its current control measures / strategies and the vision of using local vegetables to minimize diabetes and its complications in Nigeria.

1.2 What is diabetes mellitus (DM)?

The United Nations (UN) defines diabetes as a chronic, debilitating, and costly disease associated with severe complications which pose severe risks for families, member states, and the entire world; and serious challenges to the achievement of the internationally agreed developmental goals, including the Millennium Development Goals (MDGs) (IDF, 2011).

1.3 Patho-physiology of DM

1.3.1 Physiology of glucose metabolism:
A number of human glucose homeostatic mechanisms contribute to the maintenance of normal Fasting Blood Glucose (FBG) of 4-6mMol/L or 80-110mg/dL (Sacher and McPherson, 2001). Insulin plays vital roles in the utilization of glucose in the blood. It facilitates the normal metabolism of glucose by the human cells.

1.3.2 Pathology of the DM
Abnormal, inadequate or insensitivity to insulin may result in failed glucose homeostasis. Consequently, the FBG becomes persistently equal to or greater than 7.0 mMol/L (126 mg/dL) (WHO, 2006).

1.3.3 Main types of diabetes
4 main causes of diabetes result in 4 main types of DM thus:
   1. Insulin dependent diabetes mellitus (IDDM)
2. Non-insulin dependent diabetes mellitus (NIDDM) (>90%) (IDF, 2011)
3. Multiple other specific causes (e.g. drug)

1.3.4 Manifestations of diabetes
Figure 1 shows the common signs and symptoms of diabetes.

![Figure 1: Overview of the most significant symptoms of diabetes](http://en.wikipedia.org/wiki/file:main_symptoms_of_diabetes.png)

1.4 Epidemiology of diabetes
Globally, about 437 million people are diabetic (WHO, 2013). Global prevalence is more than 8.5% (IDF, 2011). Diabetic incidence is doubling (Wild et al., 2004). In 2010, diabetes took 12% of total global health care costs (Shaw *et al.*, 2010). In Africa, 4.5% are diabetic; 80% are undiagnosed (IDF, 2011). In certain parts of Nigeria, the prevalence can be as high as 40.5% (Maori *et al.*, 2012) or as low as 2.5% (WHO, 2009). In Port Harcourt, the prevalence of diabetes was 16 - 23.4% (Nwafor and Owhoji, 2001). In Owerri, 15.5% were pre-diabetic (Ogbru *et al.*, 2012)

1.5 Co-morbidities/ complications of DM
Long-term diabetes is associated with other illness or complications like:
- Erectile dysfunction,
• Blindness,
• Poor wound healing,
• Kidney failure,
• Heart disease, etc (Nathan et al., 2009).
These are mainly due microangiopathy and neuropathy associated with the disease (Boussageon et al., 2011).

1.6 Preventable risk/causative factors of DM
These major factors include:

Pathologic states
• Over weight / obesity
• Hypertension
• Dyslipidaemia

Lifestyles
• Poor diet,
• Physical inactivity, and
• Lack of regular exercise.

2.0 Current Control of Diabetes
2.1 Pharmacotherapy of Diabetes
 Insulin Preparations (Injectibles or Inhalants) e.g. insulin lispro; Humulin; NPH (isophane)
 Oral Antidiabetic Agents
  a. Insulin Secretagogues (sulfonylureas, etc.)
     ▪ 1st sulfonylureas: e.g. Tolbutamide (orinase); Chlorpropamide (Diabinese);
     ▪ 2nd sulfonylureas e.g. glyburide or glibenclamide; glipizide or glydiazinamide (glucotrol)
  b. Biguanides (metformin, phenformin)
  c. Others

2.2 Challenges of current diabetic pharmacotherapy
 a. Inability to control all the pathological aspects of the diabetes,
 b. Enormous cost, and
 c. Poor availability for many rural populations in developing countries (WHO, 2002)
 d. Insufficient to prevent diabetic complications (Vuksan et al., 2001).
e. Dangerous side effects like rapid hypoglycaemia, cholestasis, etc. (Saxena and Kishore, 2004).
f. Questionable safety (Monami et al., 2006).
g. Hence, the need for prospecting safer drugs (Noor et al., 2008), perhaps from local vegetables.

2.3 Diabetes Phytomedicine

Since time immemorial, before the advent of insulin, plant extracts have been used to treat DM (Osunwole, 1999; Bnouham et al., 2006; Aissaoui et al., 2011).

About 400-800 plants have antidiabetic potentials (Alarcon-Aguilara et al., 1998; Onoagbe and Esekheigbe, 1999). Most of these plants had been confirmed to have hypoglycaemic effects in animal models (Gupta et al., 2005; Kesari et al., 2006, Iwuji et al., 2010; Iwuji et al., 2014). Some have also been evaluated in human beings (Herrera-Arellano et al., 2004; Jayawardena et al., 2005).

2.3.1 Reported Diabetes Phytomedicine

a. Extract from bitter leaf mixed with pure honey: 2 table spoons twice daily before food.
b. Unripe paw paw peeled and soaked in water for three days: One glass of the liquid is taken thrice daily for three days.
c. Guava and scent leaves concocted: sip slowly

Each treatment should be repeated intermittently (Aiyeloja and Bello, 2006).

Table 1 shows some local vegetables that deserve further studies to prospect their use in the control of diabetic menace.
<table>
<thead>
<tr>
<th>English Name</th>
<th>Botanical Name</th>
<th>Local Names</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chaya leaf</td>
<td><em>Cnidoscolus aconitifolius</em> (CA)</td>
<td>‘Hospital is too far’; ‘ogwu obara’, <em>efo iyana ipaja</em></td>
<td>Oladeinde et al., 2007; Iwuji et al., 2014a</td>
</tr>
<tr>
<td>Bitter leaf</td>
<td><em>Vernonia amygdalina</em></td>
<td>‘Olugbu; Ewuro; Shiwaka’</td>
<td>Iwuji et al., 2013c</td>
</tr>
<tr>
<td>Scent leaf</td>
<td><em>Ocimum gratissimum</em></td>
<td>‘Nchuanwu’; Efinrin nla; Dadoya</td>
<td>Iwuji et al., 2010; Iwuji et al., 2013c</td>
</tr>
<tr>
<td>Amaranth</td>
<td><em>Amaranthus cruentus</em> L.</td>
<td></td>
<td>Velarde-Salcedo et al., 2012; Jalalpure et al., 2004</td>
</tr>
<tr>
<td>Water leaf</td>
<td><em>Talinum triangulare</em> (Jacq.)Wild.</td>
<td>Nte-oka/inene</td>
<td>Xu et al., 2014</td>
</tr>
<tr>
<td>Bush buck</td>
<td><em>Gongronema latifolium</em> L.</td>
<td>Ayo-ishi; Aayu; Tafarunua</td>
<td>Itelima., 2014</td>
</tr>
<tr>
<td>Garlic</td>
<td><em>Viscum album</em></td>
<td></td>
<td>Itelima., 2014</td>
</tr>
<tr>
<td></td>
<td><em>Allium sativum</em></td>
<td></td>
<td>Jeloder et al., 2009</td>
</tr>
<tr>
<td>Plant Name</td>
<td>Scientific Name</td>
<td>Indigenous Name</td>
<td>Reference(s)</td>
</tr>
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<td>--------------------</td>
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</tr>
<tr>
<td>Jute mallow</td>
<td><em>Cochorus olitorius L.</em></td>
<td>Og-wu akom;</td>
<td>Kim et al., 2000;</td>
</tr>
<tr>
<td>Neem tree</td>
<td><em>Azadirachta indica</em></td>
<td>Dongoyaro; Maina</td>
<td>Kumar et al., 2011</td>
</tr>
<tr>
<td>Indian spinach</td>
<td><em>Basella rubra L.</em></td>
<td></td>
<td>Nirmala et al., 2009</td>
</tr>
<tr>
<td></td>
<td><em>Murraya koenjii</em></td>
<td></td>
<td>Kim et al., 2000; Kumar et al., 2011</td>
</tr>
<tr>
<td></td>
<td><em>Rauvolfia vomitoria</em></td>
<td></td>
<td>(Aiyeloja and Bello, 2006)</td>
</tr>
<tr>
<td>Guava</td>
<td><em>Psidium guajava</em></td>
<td>Ugova/ugwoba, Gurofa, Gwaabaa</td>
<td>(Aiyeloja and Bello, 2006)</td>
</tr>
<tr>
<td>Onion bulb</td>
<td><em>Allium cepa</em></td>
<td>Yabasi, Alubosa, Alabasa</td>
<td>(Aiyeloja and Bello, 2006)</td>
</tr>
<tr>
<td>Beletic Myrobalan</td>
<td><em>Terminila bellirica</em></td>
<td></td>
<td>Manila et al., 2012</td>
</tr>
</tbody>
</table>
Figure 1: Chaya leaf

Figure 2: Water leaf
2.3.2 Challenges of Phytomedicine
a. Some herbs only have mild or placebo antidiabetic effect and their usage should depend on proven safety and effectiveness (Gori and Campbell, 1998).
b. Some potential antidiabetic vegetables may contain harmful phytochemicals (Radominska-Pandya, 2010).
c. Poor preparation of some vegetables before consumption could be dangerous (e.g. Fresh Chaya leaves contain cyanide)

Therefore, preparations require further studies and strict monitoring.

2.3.3 Safety limit of antidiabetic vegetables

- Possible adverse potential of vegetables (e.g. chaya):
  - Pyrrolizidine alkaloids in chaya could be carcinogenic and hepatotoxic (Fu et al., 2002; Xia et al., 2006).
  - Poorly prepared chaya vegetable could be toxic (Ross-Ibarra and Molino-Crux, 2002).

- Lethality of antidiabetic vegetables:
  - The mean lethal dose (LD50) of *Cnidoscolus aconitifolius (CA)* is 7.348g/Kg in animal model (Adebiyi et al., 2012).
  - LD50 of 5.0g/Kg is relatively safe (Lorke, 1983).

3.0 Prospecting an antidiabetic extract

3.1 Evaluating the antidiabetic potential of local vegetables

  a. Phytochemistry
     - Bio-flavonoids are phenolic secondary plant metabolites.
     - Bio-flavonoids are well-known for their multi-directional biological activities including anti-diabetic efficacy (Brahmachari, 2009; Qi et al., 2010)

  b. Pre-clinical antidiabetic screening
     - Experimental assessments *in vivo* and *in vitro*.

  c. Clinical trials
     - Human studies

3.2 Advantages of Pharmaceuticals derived from Phytomedicine
Metformin came from the traditional approach of using *Galega officinalis*. It is safer than Phenformin (not derived from plant) because Metformin is known to be euglycaemic agent and it rarely causes acute hypoglycemia and lactic acidosis.

Typical antidiabetic phytomedicine does not depend on functioning pancreatic β-cells.

### Table 2: Major Antidiabetic Phytochemicals in local vegetables (*Cnidoscolus* leaves)

<table>
<thead>
<tr>
<th>S/N</th>
<th>Antidiabetic constituent</th>
<th>Hydro-methanol extract (1:4, v/v) %</th>
<th>Aqueous extract (%)</th>
<th>Hydro-ethanol extract (1:4, v/v) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Saponins</td>
<td>33.3</td>
<td>33.3</td>
<td>33.3</td>
</tr>
<tr>
<td>2</td>
<td>Flavonoids</td>
<td>66.7</td>
<td>66.7</td>
<td>66.7</td>
</tr>
</tbody>
</table>

(Key: - = relatively absent; 33.3% = weakly present; 66.7% = moderately present; 100% = strongly present) (Iwuji et al., 2013a; Iwuji and Nwafor, 2015)

### 3.3 Prospect of Bio-flavonoids in controlling diabetic menace

Numerous studies have been carried out to explore their potential role of flavonoids in the treatment of diabetes (Jung et al., 2006; Matsui et al., 2006; Qi et al., 2010)

Iwuji and Nwafor (2015) had reported some bio-flavonoids in a local leaf that deserve further investigations.
Flavonoids were formerly referred to as Vitamin P (Benthsath et al., 1937) (probably because of the effect they had on the permeability of vascular capillaries). Probable, flavonoids favourably alter the transport of glucose and or insulin across the cell membranes.
The isolation and identification of these phyto-flavonoids from any local vegetable indicates that the extract could be useful in the control of diabetic menace. For instance, Figure 7 shows a local vegetable studied to prospect its antidiabetic use. As shown in Table 1, this *Cnidoscolus aconitifolius* is locally known as ‘*hospital is too far*’ in the south southern Nigeria and ‘*ogwu obara*’ in the south eastern Nigeria.

![Image](image1)

**Figure 7**: Leaves of *Cnidoscolus aconitifolius (CA)* investigated (Iwuji, 2014)
Following the reported nutritional (Iwuji et al., 2013), phytochemical (Iwuji et al., 2014) and nuclear magnetic resonance (NMR) (Iwuji and Nwafor, 2015) analyses of the hydro-methanol extract of CA, this local vegetable was subjected to some vigorous *in vivo* investigations. Figure 8 shows one of the results depicting a dose–response relationship of its glucose lowering potential (Iwuji, 2014; Iwuji et al., 2014).

![Figure 8: Histogram showing the dose-blood glucose lowering relationship of Cnidoscolus aconitifolius (CA) extract in alloxan-induced diabetic albino rats. (*significant p ≤0.05; Each bar represents change ± SEM; n=5.*)](image)

In this Figure 8, as the dosage of CA is increasing (blue bars), the blood glucose lowering effect also increased. Figure 9 showed that the glucose lowering potential of a vegetable could also depend on the solvent used during fractionation of the extract.
In Figure 9, chloroform fraction of hydro-methanol extract had greatest glucose lowering potential when compared with ethanol and butanol fractions.
4.0 Conclusion
Diabetes with its complications is now a growing menace in Nigeria. Prospect of using vegetables in the control of this menace was reviewed and validated. This prospect could be enhanced by best choice of phytochemical extraction, separation and analytical techniques and solvents. Local vegetables containing flavonoid compounds could have antidiabetic activity. Antidiabetic vegetables were reportedly safer but could have dose – and solvent- dependent adverse effects. Preparation of the medicines from leaves should be regulated to avert possible toxicity.

5.0 Recommendations
a. Local vegetables with antidiabetic potential should be fully investigated.

b. Antidiabetic compounds in local vegetables should be isolated, identified and characterized.

c. Strict regulation of herbal preparations and consumption to ensure safety and effectiveness.

d. Adequate provision of modern drug research equipment/ facilities/ materials in Nigerian Universities to develop safer drugs.

e. The public should increase the consumption of certified antidiabetic vegetables or phytomedicines.

References


Dr. S. C. Iwuji is a lecturer in the Department of Biomedical Technology, Federal University of Technology Owerri (FUTO) since 2012. He had studied in various programmes of health science and technology with core researches in Human Physiology and Safety. He had his tertiary education from all the southern zones of Nigeria with distinguished higher academic degrees in Human Physiology and Pharmacology. He obtained final professional diplomas in Public Health, Science Laboratory Technology, Biomedical Engineering, Environmental Health, etc. Consequently, Sam is a biomedical scientist, a technologist, a health officer and a Fellow of the College of Biomedical Engineering and Technology (CBET), Nigerian Institute of Biomedical Engineering (NIBE).

As a Human Physiologist and Safety Pharmacologist, he tries to understand and explain the functional characteristics and mechanisms of the living human body or structure, and further investigates the potential undesirable pharmacodynamic effects of substances on physiological functions in relation to normal or abnormal exposures. His works were guided by the fact that the Sub-Saharan Africa is currently bedeviled with health problems mostly associated with poverty (ignorance), poor environmental sanitation and life-styles. Current devastating problems under his study include diabetes, drug misuse, malarial and pollution effects on biologic functions.

With his knowledge so far, he had proffered and published some indigenous, cost effective and multi-dimensioned solutions to some health challenges. So he had published 3 relevant scientific books; over 22 journal papers & 10 abstracts/short notes. He also published over 10 health articles in Newspapers/Magazines and had written several news-talks, despite his myriad of activities: Dr. Iwuji is the National General Secretary (elect) of the National Association of Biomedical Engineering and Technology (NABET); an Associate of Nigerian Environmental Society (NES) & Nigerian Institute for Science Technology (NIST) and was the old Imo State Students’ President of the National Association of Environmental Health Officers of Nigeria (NAEHON). He is a member of the Physiological Society of Nigeria (PSN), with International affiliations. He is the current Chairman of his Town Union in Owerri zone; General Secretary of his
home, church & neighbourhood Communities, etc. He is also the Coordinator, Editor and so on in so many other notable organizations.

Since 2005, he had actively participated in the evolution of all the novel SOHT programmes, particularly the Nigerian foremost Biomedical Technology programme. He had actively participated in most academic/administrative duties, including coordination of some school and departmental courses; coordination of lectures/examinations, SIWES, admissions, elections, ethics, welfare, departmental management, continuing/linkage and post graduate programmes. These exposures were due to his membership to several committees at various levels in the University. He was appointed as a member of SOHT Lecture Series Committee, SOHT SIWES and SOHT library BMT Coordinator by our excellence-thirsty and articulate Dean, former Dean of Deans, Professor INS Dozie.

Perhaps, these academic and service strides motivated the Biomedical students’ Association that offered Dr. Iwuji an Award of Excellence in 2009; in 2014, the Mbano students’ Association from Federal Polytechnic Nekede gave him an Award of Honour; an Award of Recognition came from his home Catholic Church, amidst other local and international nominations for awards.

Dr Iwuji has been a resource person for National Open University of Nigeria (NOUN) Abuja; College of Biomedical Engineering and Technology of Nigeria (CBET), Owerri; Environmental Health Officers Registration Council of Nigeria (EHORECON) Abuja; Centre for Continuing Education (CCE), FUTO, etc. He was a pioneer staff of Choba-Uiport Community Bank, Port Harcourt; a JONGRES Wood Industry, Owerri & JONGRES Environmental Health & Safety Consult, etc. in Lagos & Owerri. His diverse work experience had earned him some entrepreneurial skills. Also his flair in writing, research and farming (especially aquaculture) are enterprising.

Dr. Iwuji hails from Umuakama Ezumoha in Isiala Mbano LGA of Imo State, Nigeria. He is gracefully married and with children.

To GOD is all the Glory, Amen!!

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