ORIGINAL ARTICLE

THE USE OF '*GARCINIA KOLA*' IN THE TREATMENT OF ORAL CANDIDA INFECTION IN HIV PATIENTS

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ABSTRACT

BACKGROUND: The antifungal effect of chlorhexidine has been demonstrated for the treatment of oral candidiasis in Human Immunodeficiency virus positive patients. However, it is associated with teeth and mucosal staining, bitter taste and it is not readily available in an average Nigerian pharmacy shop. *Garcinia kola* is affordable, widely available antifungal agent with no reported side effects. This study aims to determine the effect of *Garcinia kola* extract on oral *Candida* infection in HIV patients; to compare its efficacy with chlorhexidine mouthwash and to assess the side effects of *Garcinia kola.*

MATERIALS AND METHODS: A double blinded clinical trial was carried out on newly diagnosed HIV patients with clinically diagnosed *Candida* infection at Aids Preventive Initiative of Nigeria clinic of Lagos University Teaching Hospital, Nigeria. They were also screened for other medical conditions. *Garcinia kola* extract and chlorhexidine mouthwash were administered for 3 weeks to the patients randomly selected into the two treatment groups of 33 patients each.

RESULTS: Sixty one patients completed the study, with 33 patients on G. kola and 28 patients on chlorhexidine. Oral Candidiasis was cleared with *Garcinia kola* in 27 (81.8%) patients, while 20(71.4%) patients had it cleared with chlorhexidine at the end of the 3rd week. There was no statistical significant difference between patients' response to *Garcinia kola* and chlorhexidine.

CONCLUSION: This study has shown that *Garcinia kola* is effective against candida infection. For cost-effective treatment of oral candida infection in resource limited countries, *Garcinia kola* may be considered a preferred alternative to chlorhexidine.

Keywords: Candida infection, HIV patient, *Garcinia kola,* Chlorhexidine.

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INTRODUCTION

Candida infections, otherwise known as candidiasis, moniliasis, commonly occur in patients who are immunocompromised in conditions such as in leukemia, diabetes and Human Immunodeficiency Virus or Acquired immunodeficiency syndrome (HIV/AIDS). However, without treatment in HIV/AIDS, oral candidiasis may spread to the oesophagus causing invasive oesophageal candidiasis and disseminated candidiasis, which is categorized as an AIDS defining illness. Human Immunodeficiency virus (HIV) infection is a global pandemic and a critical public health problem. HIV is a retrovirus that belongs to the family of lentiviruses. It is a highly variable virus which mutates very readily within the body of an infected person. There are two types of HIV patients: HIV-1 and HIV-2. HIV/AIDS patients which are prone to candida infection and other opportunistic infections.

Oral Candida infection can be treated with antifungal drugs such as nystatin, miconazole, fluconazole, voriconazole, and caspofungin. Many of them are associated with side effects which include nausea, vomiting, diarrhoea, headache, hepatitis, dyspepsia, skin rashes, and fever. Drug resistance is also a common feature with them [1,2,3] All these resulted in the drive for alternate medications. Alternate to the commonly used oral antifungal suspension is chlorhexidine. This is also known to have side effects which include staining of teeth and tongue and change in taste. These also discourage drug compliance, which prompted us to the quest for another alternative drug, *Garcinia kola*.

Garcinia kola (G. Kola) Heckel (family *Guttiferea*) is known in commerce as 'bitter kola', 'false kola' or 'male kola'; it is also called 'akiilu' in Igbo, 'orogbo' in Yoruba, and 'namiji goro' in Hausa.[4, 5] *Garcinia kola* is a medium-sized evergreen tree, mostly about 12m high but sometimes up to 28m in height, and 1 to 5m width. [6] It is a food and of high socio-economic importance. Some proprietary dietary supplements containing *G. kola* extracts already exist in U.S.A. and some African markets.[7] It is widely used in traditional medicine and with great promises for modern clinical uses. *Garcinia kola* has many chemical components, but GB-1a (hydroxybiflavanonol) is the main component exhibiting significant ($p<0.05$) bacteriocidal activity against Gram positive and Gram negative bacteria, and fungistatic against *Candida albican* and *Aspergillus flavus*. Ongoing researches have shown *G. kola* to have effect on some common micro-organisms.[8]

Therefore, the objectives of the study were to determine the effect of *Garcinia kola* extract on oral *Candida* infection in HIV patients; to compare its efficacy with chlorhexidine mouthwash and to assess the side effects of *Garcinia kola*.

MATERIALS AND METHODS

A double blinded clinical trial was carried out on newly diagnosed HIV patients with clinically diagnosed *Candida* infection at Aids Preventive Initiative of Nigeria (APIN) clinic of Lagos University Teaching Hospital (LUTH), Lagos, Nigeria. Every consecutive HIV positive patient presenting with oral candidiasis were recruited among the patients seen in the APIN clinic, LUTH.

The patients were also screened for other medical conditions to rule out any other underlying medical problems. Written informed consent was obtained from all the patients before enrollment in the study. Ethical approval for the study was obtained from the Health Research and Ethics committee of Lagos University Teaching Hospital (LUTH.

The concentration of chlorhexidine used was 0.2%. A concentration of 30% (30g in 100ml) of *G.kola* was obtained by cold extraction process which was like ordinarily chewing the nut under hygienic condition. Preparation of the *G. kola* extract was performed using *G.kola* nuts of about 2000g by weight. The seed coats on the nuts were removed to expose the white inner parts, before the nuts were washed, cut into pieces and blended. The water extraction mixture obtained was poured into a beaker and allowed to stand on the bench for 15 hours.[9] It was filtered and the extract (supernatant) was preserved in the refrigerator for the clinical trial.

The patients were randomly allocated by a trained assistant to two different treatment groups (*Garcinia kola* extract and Chlorhexidine). There were 33 patients in *Garcinia kola* group and 33 in chlorhexidine group. The mouth rinses were dispensed in identical containers, labeled A and B. The assistant thereafter dispensed the different mouthwashes to the patients according to the group they have been randomly assigned to. Each patients was told to use the mouthwash 3 times daily and 30minutes before using any fluoride containing toothpastes (this is to prevent inactivation of chlorhexidine). They were also told to swish the solution around the mouth and leave for 1min before spitting out.

At the end of the 3rd week, the treatment was stopped. The assistant kept a record of the treatment received by each patient. The investigator was not aware of the patients' treatment groups until after the final treatment outcome was determined. Administration of questionnaire and clinical examination were used to collect the patients' data.

The patients were reviewed weekly and the treatment outcome was recorded. All the patients had 3 recall visits. The clinical effectiveness of *Garcinia kola* extract and chlorhexidine was determined using these criteria:

1. Totally cleared (the lesion completely cleared in the oral cavity)
2. Partially cleared (the lesion partially cleared in the oral mucosa)
3. Not cleared (the lesion remained the same).

During the period of this study, no observable side effect(s) of *G.kola* and chlorhexidine was noticed. The patients whose Candida infection did not clear at the end of the third week were placed on fluconazole.

RESULTS

A total of 66 patients were selected but 61 (92.4%) patients completed this study and were analyzed. There were 43(70.5%) females and 18 (29.5%) males, with female to male ratio of 2.4:1. Most of the patients were in the 30 to 39 years (37.7%) age group, with a mean age of 37.2 ± 11 years and a median age of 35 years (Table 1).

The pattern of distribution of the disease was: 28(45.9%) patients with erythematous candidiasis, 22 (36.1%) patients with pseudomembranous candidiasis, 6(9.8%) patients with angular cheilitis and 5(8.2%) patients combination of pseudomembranous and erythematous candidiasis. Erythematous candidiasis was the most common variant seen.

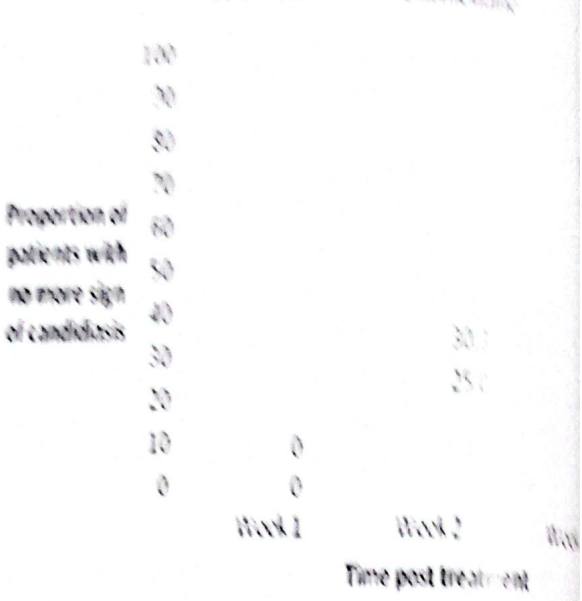
In the *G. kola* group with 33 patients who completed the study, 27 (81.8%) of the patients had their oral candidiasis completely cleared at the end of the 3rd week. The rate at which the lesion cleared was higher between week 2 and 3 than during the first week. In the chlorhexidine group with 28 patients, with a higher rate of

clearing between week 2 and 3 than during week 1, but at a consistently lower rate than with *G. kola*. At the end of the 3rd week, 20(71.4%) patients had their lesion completely cleared. Observation showed that more patients had their lesions cleared during the follow up period with *G. kola* than with chlorhexidine (Figure 1).

Table 1: Age distribution of patients

Age (year)	HIV positive (n = 61)	
	Frequency	Percent
< 20	3	4.9
20 – 29	11	18.0
30 – 39	23	37.7
40 – 49	15	24.6
50 – 59	7	11.5
= 60	2	3.3
Total	61	100

Figure 1: Proportion of HIV positive patients with no more sign of candidiasis



DISCUSSION

Previous study by Kantheti LP et al, [10] reported female preponderance where the prevalence of *Candida* colonization was determined in HIV positive patients naive to highly active anti-retroviral therapy (HAART). Similarly, there was female predilection for HIV positive patients with oral candidiasis in this study. Furthermore, the infection has been reported to be more prevalent in individuals within the 30 to 39 years age group who are usually more sexually active. [11] This is consistent the findings in this study.

Erythematous candidiasis (45.9%) and pseudomembranous candidiasis (36.1%) were the most common types of candida infections in this study. Report by Bodhade et. al, [12] have shown that erythematous candidiasis is dominant in patients infected with HIV virus. This is contrary to the findings of Agbelusi et al., [13] Arotiba et al., [14] and Taiwo et al., [15] who observed pseudomembranous candidiasis to be the dominant variant. Vanderwaal et al., [16] also observed pseudomembranous candidiasis to be a dominant variant in AIDS patients.

In the HIV positive patients studied, the success rate of *Garcinia kola* was 81.8% while the success rate was 71.4% for chlorhexidine. Chlorhexidine has fungistatic and fungicidal action[17,18, 19]. The antifungal effects which have been demonstrated both in' vivo and in vitro include its effects on *Candida*. [20,21,22] Chlorhexidine (0.2%) is widely prescribed due to its broad spectrum activity on bacteria and *C.albicans*. [23,24] Studies have shown that exposure of *C. albicans* isolates or the buccal epithelial cells to 0.2% chlorhexidine gluconate profoundly suppressed the ability of

Candida to adhere to buccal cells, both in healthy [28,29] and diseased individuals [27]. This evidence reveals it as an appropriate alternative to conventional antifungals in the management of oral candidiasis.[21,23] Ehigiola and Samaranayake [30] showed its importance as an adjunct in the treatment of *candidal* infection with conventional antifungal drug, which has a short duration of action (chlorhexidine has a long duration of action) supporting its use as an alternate oral antifungal therapy. However, this study also showed *Garcinia kola* to be more effective against Candida than Chlorhexidine.

Interest in plant extracts demonstrating antimicrobial and pharmacological ability is on the increase recently.[28,29] Medicinal plants are important sources of new chemical substances with potential therapeutic benefits.[30] Phytochemicals derived from plants have shown great promise in the treatment of intractable infectious diseases including opportunistic AIDS infections. Plants containing *Garcinia* biflavonones have been found to be active against a wide variety of micro-organisms. *G. kola* has been shown to have anti-fungal effect from its crude extracts demonstrated by the study carried out at the Guiness Eye centre, LUTH, where fungal samples cultured from swabs obtained from conjunctiva discharges of the patients exhibited significant sensitivity and growth inhibition. These organisms were *Candida albicans*, *Bacillus subtilis*, *Staphylococcusaureus*, *Streptococcus pneumonia*, *Enterococcus faecalis*, *Escherichia coli*, and *Klebsiella pyocyannae* amongst others.[31] Similar work done by Akerele et al.,[9] also showed clinical significant inhibitory activities against these micro-organisms. It has also been shown reported by Sote and Wilson[32] to be effective against Fusobacterium nucleatum, Prevotella intermedia and Campylobacteria gingivalis.

Other in vitro studies carried out on *Garcinia kola* were control of trypanosome proliferation in mice, [33] fertility enhancer in cat fish,[34] reduction of intraocular pressure and miosis (as antiglaucoma),[35] thus further supporting the benefits of *Garcinia kola*. It was also used to reduce pain and sub-chondral pressure in knee osteo-arthritis in an in-vivo study.[36] In the present study, no observable side effect was noticed with *Garcinia kola*, similar to previous report by Dada and Ikuerowo.[37] Those whose candidal infection did not clear were given fluconazole at APIN clinic.

In conclusion, this study has shown that *Garcinia kola* is effective against candida infection. For cost-effective treatment of oral candida infection in resource limited countries, *Garcinia kola* may be considered a preferred alternative to chlorhexidine.

Recommendation: The effect of *Garcinia kola* on oral candida infection on HIV in this study is encouraging, though the lesion did not clear totally in some patients at the end of the 3rd week. Further studies may reveal better ways of utilizing *Garcinia kola* for a more effective treatment of oral candidiasis.

Conflict of interest: none declared

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