

MEDICINAL PROPERTIES OF FRACTIONATED ACETONE/WATER NEEM (*AZADIRACHTA INDICA*) LEAF EXTRACT FROM NIGERIA: A REVIEW

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Summary: The global scenario is now supporting the development of modern drugs from less toxic plant products with proven medicinal properties. Each part of neem plant (*Azadirachta indica* A. Juss) reportedly has various medicinal properties and has been in use in many continents for centuries. Recently, a fractionated neem-leaf extract known as IRAB with reported activities against Malaria, HIV/AIDS and cancer has been developed into a drug and currently marketed in Nigeria as IRACAP®. This paper reviews the medicinal properties, clinical studies and safety concerns of this fractionated acetone-water neem leaves extract as a footstep to further studies both on the extract and/or its chemical constituents.

Key words: IRAB, *dogonyaro*, Malaria, Nigeria

Introduction

Extracts from neem tree (*Azadirachta indica* A. Juss) also called “*dogonyaro*” in Nigeria are most consistently recommended in ancient medical texts for gastrointestinal upsets, diarrhea and intestinal infections, skin ulcers and infections, and malaria (Schmutterer, 1995). India encouraged scientific investigations of neem tree as part of his program to revitalize Indian tradition and also increase commercial interest on neem (Stix, 1992) and presently some authors believe that no other plant or tree in the world has been so extensively researched or used, in all possible capacities so far. In Africa extracts from Neem leaves have provided various medicinal preparations (Ekanem, 1971 and Udeinya, 1993). A fractionated acetone-water extract also known as IRAB has been showing safer medicinal properties (Mbah et al, 2007). In-vitro studies with malaria-infected erythrocytes and metastatic cancer cells had earlier shown that IRAB has broad-spectrum anti-cytoadhesion activity which has been beneficial in HIV/AIDS (Udeinya et al, 2004). Mbah et al (2007) reports IRAB as safe and able to increase CD4+ cell levels in HIV/AIDS patients.

Extraction, fractionation, Chemical components of Nigerian neem leaf extract (IRAB)

Fractionated neem leaves extract with registered U.S. Pat. No. 5,370,873 issued Dec. 6, 1994 (also known as IRAB) is registered and marketed in Nigeria in 250mg capsules as IRACARP® (NAFDAC Registration number A7-0319L). Extraction is done using neem leaves collected in Nigeria in a mixture of acetone and water (1:1, by vol.) as described by Udeinya (1993). Residue from the bottom layer of the crude extracts is then fractionated by standard, high-performance liquid chromatography (HPLC) (Udeinya et al, 2006). The end product (IRAB) is a complex molecule (202 Daltons) with functional groups that include sodium salts of carboxylic acid and a non-aromatic dialcohol (Mbah et al, 2007).

Reported medicinal actions of IRAB:

In-vitro and in-vivo studies on IRAB have revealed the following activities:

Anti-malaria:

Extracts from Nigerian neem leaves (*Azadirachta indica*) have been earlier reported to have anti-malarial activities (Ekanem, 1971), but Udeinya (1993) demonstrated that acetone/water mixture is a more efficient solvent than water alone for the extraction of anti-malarial activity from Nigerian neem leaves. This activity has been reportedly retained by IRAB (Udeinya et al 2006 and 2008). Its anti-malarial activity has been reported to be superior to chloroquine (Udeinya et al, 2006), gametocytocidal. (Udeinya *et al*, 2006 and 2008) and schizonticidal (Udeinya 2008) against falciparum malaria parasite. Indeed Anyaehie (2009) reported anti-pyrexial activity among Nigerians where malaria remains the commonest cause of Fever. Patients from malaria are also likely to benefit from reported anti-cytoadhesion property of IRAB since adhesion of infected erythrocytes to the endothelium is key factor in pathogenesis of severe falciparum malaria (David *et al*, 1983).

Anti-retroviral:

Udeinya et al (2004) first reported anti-retroviral activity by IRAB on patients with HIV/AIDS in a phase I clinical trial. In another study by Mbah et al (2007) that lasted 12 weeks, IRAB was administered (1g daily) to 60 patients infected with HIV-1 & 11. The results showed a significant increase from the baseline mean CD4⁺ cell count of 266 cells/ul by week 12. Mean body weight and hemoglobin concentration were also significantly increased. Opportunistic infections and other HIV/AIDS related conditions were reportedly completely resolved in most patients by week 12. Also, the erythrocyte sedimentation rate (ESR) was

reported to have been significantly decreased from a baseline mean value of 64mm/hr to 16mm/hr.

Anyaehie (2009) compared the anti-retroviral properties of IRAB with that of highly active anti-retroviral therapy (HAART) and results are consistent with Mbah *et al* (2007) after 16weeks of therapy. However, Anyaehie (2009) documented a more significant increase in CD4⁺ cells and elimination of skin rashes among patients on HAART compared to patients on IRAB. Mbah et al (2007) and Anyaehie (2009) agree that there was a significant improvement in patients' condition with respect to presenting symptoms and physical examination findings. These reports of correction of CD4⁺ cell counts and improvement in patients' clinical profile may indeed relate to corresponding reduction in viral activity and led to a presumptive conclusion that the fractionated neem leaf extract (IRAB) is safe and increases CD4⁺ Cell Levels in HIV/AIDS patients, a conclusion the work of Anyaehie (2008) further supported.

Are there any side effects or interactions?

Neem leaf extracts appear to be very safe at recommended intake levels with no significant reports of problems. Also, use of IRAB has consistently reported no adverse effects either as an anti-malaria (Udeinya *et al*, 2006 and 2008) or an anti-retroviral agent (Mbah *et al*, 2007 and Anyaehie 2009). Water extracts of neem leaf have been shown to decrease blood levels of chloroquine in rabbits (Nwafor *et al*, 2003) but this has not been investigated with IRAB. The use in pregnancy has also not been evaluated and thus is not yet recommended. At the time of writing, there were no well-known drug interactions with IRAB.

Conclusion

Development of modern non-toxic drugs from neem has earlier been suggested (Biswas *et al*, 2002) and IRAB represents such dream. This fractionated acetone/water neem leaf extract is the only drug reported to have activities against Malaria and HIV/AIDS. Recent in-vivo studies have substantiated the earlier in-vitro reports of pharmacological properties. The drug is reportedly safe, and thus further studies both on the extract and/or its chemical constituents are highly suggested to streamline these innovative findings into strategies for achieving the health components of the Millennium Development Goals (MDGs).

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