Natural environment as a source for anti-malarial Annonaceae: relevance, clinical applicability and ethics

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Abstract—Three important anti-malarial plants (Anonidium mannii, Enanthia chlorantha and Polyalthia suaveolens) in the Pygmy culture have been reviewed from an ethnomedical point of view. The relevance of the traditional uses of these species was assessed in the light of the scientific validation of their reported anti-malarial properties. While in vitro analyses show promising anti-protozoal properties for all the species and especially for E. chlorantha, few in vivo and no clinical results are available for any of the plants. Emphasis was placed on the fragility and importance of the Pygmy culture, the indigenous knowledge that may be obtained from it as well as the African rainforest ecosystems that is the source of such novel, but age-old alternatives for anti-malarial treatments.

Keywords—African rainforest, malaria, medicinal plants, Pygmy culture

I. INTRODUCTION

The African rainforest encompasses approximately 10 countries in west and central Africa and is home to one the greatest global diversities of fauna and flora [1]. Unfortunately, the growing populations around the edges of the African rainforest impacts it negatively through prolonged deforestation (logging and indiscriminate burning of vegetation, clearance for agriculture, road construction and plantation establishment) and poaching, with poor implementation of forest and wildlife laws [2]. Results of such irresponsible management ultimately cause alterations in the structure and function of ecosystems, leading to the loss of biodiversity and eventually extinction [3]. Fortunately, a recent cooperative effort amongst 10 involved central African countries, i.e. the Central Africa Forests Commission (COMIFAC), has been initiated and aims to protect the Congo Basin rainforest by implementing improved national forest monitoring systems and boosting regional cooperation [4].

Notably, the countries comprising the African rainforest are amongst those that suffer most under the malaria pandemic. According to the latest WHO reports [5], the DRC and Nigeria are estimated to account for over 40% of the malaria deaths globally (660 000 deaths in 2010, mostly children). When considering the treatment of malaria in Africa, up to 80% of the population uses traditional medicine for primary health care [6] due to the poor economic state of the population resulting in inaccessibility to western medicine, as well as long distances to the nearest medical facility, which in turn may not be adequately equipped [7]. Nevertheless, the use of traditional medicine is discouraged due to doubtful and/or bacteria), and may even result in death [9].

II. LITERATURE REVIEW: PYGMY INDIGENOUS KNOWLEDGE

Approximately 250 000–600 000 Pygmy people are distributed discontinuously across Rwanda, Burundi, Uganda, Zaire, the Central African Republic, Cameroon, Equatorial Guinea, Gabon and the Congo, i.e. the African rainforest. They live in innumerable distinct ethnic groups that are separated by geography, language, customs and technology [10]. While they are hunter-gatherers by nature, they may engage in symbiotic relationships with neighboring farmers affording economic trade and social interaction [11]. These relationships have been threatened by growing populations around the rainforest areas along with severe deforestation, and have led to conflict [12]. Currently, in most central African countries, all land legally belongs to the state and governments have consequently removed many of these forest dwellers to settle in villages and become sedentary farmers, or to work for commercial coffee, rubber or palm plantations or for logging companies [11]. Political conflicts in central Africa have also contributed to a drastic decrease in the size of the Pygmy population. Additionally, the growing demand for food from the surrounding communities, results in pygmies increasingly becoming commercial hunters, selling large
quantities of meat to traders, eventually endangering the forest fauna [13].

Where sickness and health are concerned in the Pygmy culture, the vast majority of diseases are defined in terms of “natural” rather than “supernatural” causation [14], [15]. The most serious and common diseases are malaria and those linked to the stomach and head [14]. The highest-ranking causes for disease are associated with (impure) blood, a dirty body, as well as germs and insects such as mosquitoes. Indigenous knowledge is transferred to all levels of the Pygmy community i.e. the majority of the population is able to prepare and use their own herbal mixtures for basic health care [16]. However, where basic treatments are not effective, a herbalist (e.g. an odunsinni) would be consulted. These herbalists are only able to address ailments that do not have spiritual causes, i.e. nyarewa. If the patient still suffers after treatment by an odunsinni, his/her ailment is considered a disease with supernatural causes (i.e. sunsum yades) and a traditional priest-healer or diviner (i.e. an okomfoo) is consulted [15].

III. ANTI-MALARIAL PLANTS FROM CAMEROON

A. Ethnobotanical study

Dr. Nole Tsabang, an ethnobotanist at the Institute for Medical Research and Medicinal Plants Study, Yaoundé, Cameroon, known and accepted amongst the traditional healers and groups of people from the Bakola pygmy tribe, identified plants used in the treatment of malaria by this tribe by listing the symptoms of malaria [17]. Of the plants that were identified, we studied three species from the Annonaceae family, i.e. Anonidium mannii (Oliv.) Engl. & Diels, Enantia chlorantha Oliv. and Polyalthea suaveolens Engl. & Diels. Table 1 is a summary of ethnobotanical medicinal uses, vernacular (common) names, plant parts used, as well as methods of preparation and application where available.

IV. DISCUSSION

A. Ethnobotanical data scientifically validated

Of the three species discussed in this study, Enantia chlorantha has been studied most extensively, even leading to a commercially marketed product, Hepasor, used for hepatitis virus treatment [18]. E. chlorantha has also been subjected to several in vitro and in vivo tests investigating its anti-parasitic properties. Its extracts seem to be active in vitro (IC₅₀ < 1 μg/mL) [19] and in vivo [20], while its alkaloids have been shown to contribute to this effect in vitro, but had no effect when tested in vivo [21]. In a study comparing the in vitro anti-protozoal activities of aqueous extracts of the three plants discussed in this study [22], it was found that E. chlorantha was most active (IC₅₀ 1.86–10.08 μg/mL) followed by P. suaveolens (IC₅₀ ≥8 μg/mL) and A. mannii (IC₅₀ ≥ 34.8 μg/mL). The methanol extract of P. suaveolens also displayed strong antiproliferative activity against Leishmania infantum and presented high antifungal activity against eight Candida strains and Cryptococcus neoformans (IC₅₀ < 1 mg/ml) [23]. From the available in literature, it is evident that neither A. mannii nor P. suaveolens are as well-studied as E. chlorantha, and that no clinical studies have been conducted for any of these species where malaria is concerned.

Almost all classes of phytochemicals may exhibit anti-malarial activity [24], i.e. some of the best-known anti-malarial agents contain quinine (an alkaloid extracted from Cinchona species [25], or artemisinin (a sesquiterpene from Artemisia annua) [26]. Furthermore, these phytochemicals may be prescribed as single drugs for monotherapy or in combination with other anti-malarials [27]. The use of mixtures is common in Bantu traditional medicine and is based on an expectation that the mixture is more potent than a single ingredient. This phenomenon has been defined as synergism (i.e. a pharmacological interaction in which the effect of two or more extracts or compounds taken simultaneously is greater than the sum of the effects of each on its own [28]).

For the results presented here, it is notable that the three plants described all contain alkaloids [7], [29], [30], that the isolated alkaloids are ineffective when administered in vivo on their own, medium polar extracts (i.e. with methanol) seem to be more potent than aqueous extracts, and that few scientific studies were conducted where these anti-malarial plants were used in combination with other plants, as reported in Table 1. Furthermore, the stem bark or root bark are used preferentially for the three plants (Table 1), but the same or similar compounds may be found in the leaves or fruit. If this is the case, such use should be promoted as excessive harvesting of leaves or fruit is not as detrimental to the survival of the plant.

B. Ethical considerations

The Pygmy culture may be foreign to western civilization, but these people have managed to survive in malaria stricken areas for hundreds of years, and their indigenous knowledge is vital in the discovery of “novel” anti-malarial remedies, bearing in mind that resistance against known anti-malarial drugs are increasing [24]. Furthermore, with (forced) urbanization of Pygmies, the rich heritage contained in their culture will be lost as indigenous knowledge in these ethnic groups is transferred verbally from one generation to the next. For this reason, careful, detailed documentation of their medicinal resources and the use thereof, requires novel means of data collection [31]. However, even with such careful and detailed extraction of indigenous knowledge, the question is always about the ownership and marshaling of this information in and by African societies as well as first world countries participating in the said extraction [16]. In many instances there is no benefit to the people from where the information was obtained. The over-exploitation of these “novel” sources of medicine may lead to extinction of certain species. To this effect, E. chlorantha has now been classified as threatened in Cameroon [32] and as rare species in Nigeria [33].
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<tr>
<th>Common names</th>
<th>Traditional uses</th>
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<tr>
<td><strong>Enantia chlorantha</strong></td>
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<tr>
<td>yellow Moambe</td>
<td>Decoction of 500 g of stem bark removed by scraping with a machete in 3 L of water for 20 min used to treat malaria symptoms, aches, wounds, boils, vomiting, yellow bitter, fever, chills, sore, spleen in children and hepatitis (take 250 mL decoction orally, 3 times daily for 15 days), or Make a decoction of a mixture of 300 g of stem bark of each of <em>E. chlorantha</em>, <em>Rauvolfia vomitoria</em> and <em>Fagara macrophylla</em> and/or <em>Nauclea latifolia</em> in 4 L of water for 20 min (take 250 mL of decoction orally, 3 times a day for 10 days)</td>
<td>[44]</td>
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<tr>
<td>Rodzi konga</td>
<td>Stem bark decoction taken orally for treatment of intestinal worms, intestinal spasms, malaria and sexual asthenia</td>
<td>[49]</td>
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<tr>
<td>Erumeru</td>
<td>Stem bark used to treat malaria</td>
<td>[50]</td>
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<tr>
<td>Oso pupa</td>
<td>Roots used for malaria, jaundice and as antipyretic</td>
<td>[33]</td>
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<td>Awa-opa</td>
<td>Bark used to treat malaria: add several small pieces of bark to ¼ bottle of beer, fill the bottle with “soda pop” to mask the bitter taste, macerate the mixture for 2-3 days, take ½ cup of liquid twice daily for 3 consecutive days</td>
<td>[21]</td>
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<td>Avogba, Dokita igbo</td>
<td>Fever, influenza</td>
<td>[53]</td>
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<tr>
<td>African yellow wood, Osopa, Avopa, Dokita igbo</td>
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<td><strong>Pseudospondias microcarpa</strong></td>
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<tr>
<td>Dried stem bark used to treat malaria, hepatic disorders, tuberculosis, and ulcers</td>
<td>[51]</td>
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<td><strong>Pandanus tectorius</strong></td>
<td>Decoction of 500 g of stem bark from scraping with machete in 3 L of water, evaporating the decoction to 2/3, used for symptoms caused by malaria, childhood illness (diaper rash, measles, diarrhoea, enlarged spleen), fever, amoeba (STD, candidiasis, gonorrhea, etc.) and promotion of breast milk (take 250 ml of decoction 3 times a day for 10 days); vaginitis - use the decoction for the personal hygiene</td>
<td>[44]</td>
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<tr>
<td>Bondéngé</td>
<td>Pieces of bark used as local application on wounds</td>
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<tr>
<td><strong>Pandanus tectorius</strong></td>
<td>Leaf maceration or infusion made from stem bark, trunk and twigs, used as</td>
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<tr>
<td><strong>Pandanus tectorius</strong></td>
<td>Stem bark used to generalised oedema and dysmenorrhoea</td>
<td>[42]</td>
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<tr>
<td><strong>Pandanus tectorius</strong></td>
<td>Bark used to treat kwashiorkor</td>
<td>[43]</td>
</tr>
<tr>
<td>ebo; mpole; wapo; ebome afan</td>
<td>Decoction of 500 g of stem bark from scraping with machete in 3 L of water, evaporating the decoction to 2/3, used for symptoms caused by malaria, childhood illness (diaper rash, measles, diarrhoea, enlarged spleen), fever, amoeba (STD, candidiasis, gonorrhea, etc.) and promotion of breast milk (take 250 ml of decoction 3 times a day for 10 days); vaginitis - use the decoction for the personal hygiene</td>
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<tr>
<td><strong>Pandanus tectorius</strong></td>
<td>Leaf maceration or infusion made from stem bark, trunk and twigs, used as enema</td>
<td>[47]</td>
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<td><strong>Pandanus tectorius</strong></td>
<td>Ash of the bark is applied locally to treat hemorrhoids; Stem bark decoction is drunk against diarrhea and intestinal spasms</td>
<td>[22]</td>
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<tr>
<td><strong>Pandanus tectorius</strong></td>
<td>Bark, fruit sap, seeds and roots used for a range of diseases including gastro-intestinal problems, coughs, rheumatism, wounds, epilepsy, dizziness, caries, angina, haemorrhoids and asthma</td>
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Table 1 (Cont.)

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<th>Common names*</th>
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<tr>
<td>Polyalthia suaveolens</td>
<td>Bark used for dysmenorrhea. Wood is used for construction and illumination as it burns brightly. Bark decoctions are taken to treat stomach-ache and other pains, gonorrhoea and infertility, as diuretic, purgative and aphrodisiac, and to facilitate childbirth. Bark ash is rubbed into scarring on the forehead to treat psychosis. Bark pulp is applied externally against rheumatism, headache, epilepsy and toothache. Bark is applied to scarifications to treat malaria. Bark is used in a mixture with other plants to make arrow poison. Root decoctions are taken to treat liver complaints and headache. Root sap is administered as anthelmintic and aphrodisiac, and to treat oedema and swollen glands. Leaf decoctions or maceration serves to treat hepatitis and pains, and are applied externally to treat rheumatism.</td>
<td>[42]</td>
</tr>
<tr>
<td>Otungui, Ntounqa</td>
<td>To treat malaria symptoms, fever, jaundice, epilepsy, joint pains, headache. Make a decoction of 500 g of stem bark removed by scraping with a machete in 3 L of water for 20 min (drink 250 mL of decoction, 3 times daily for 15 days) or make a decoction of one serrated fruit in 2 L of water for 15 min (drink 250 mL of decoction, 3 times daily for 7 days).</td>
<td>[56]</td>
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<td>Bodzinda</td>
<td>Young leaves are chewed and the juice swallowed to treat gastritis and diarrhea. Pounded inner bark is used locally to treat snakebite. Root bark decoctions are used orally to treat malaria and sexual weakness.</td>
<td>[22]</td>
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V. CONCLUSION

The rich Pigmy culture may present alternatives to current anti-malarial treatments. Careful extraction and documentation of this indigenous knowledge may afford the preservation of the Pygmy culture as well as the fragile ecosystems of the African rainforest.

When studying methods of extraction and administration of proposed medicinal plants, information may be obtained about types of active compounds present as well as possible synergistic interactions between compounds, plant parts or different plants.

ACKNOWLEDGMENT

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REFERENCES


