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Knowledge of traditional medical practitioners in Osun State, Nigeria, about herbal antimalarials: a survey and *in vivo* evaluation of selected plants in mice

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ABSTRACT

Background: Traditional medical practitioners (TMPs) are persons accepted in a community as capable of providing health care using plants, minerals and animal parts. Knowledge of type of herbs and methods of preparation from TMPs, usually passed verbally from one generation to the next, may become lost if not documented.

Objectives: This study investigated the extent of knowledge of TMPs on the use of antimalarial plants and herbal interactions with a view to documenting and investigating their indigenous knowledge.

Methods: One hundred TMPs from Ilesha and Ile-Ife, Osun State, Nigeria, were interviewed using a 26-item, semi-structured questionnaire. Subsequently, leaves of *Ficus exasperata, Alstonia boonei, Azadirachta indica* and *Morinda lucida*, with potentials for herbal interactions, were collected. Ficus was macerated in methanol while decoctions of *Alstonia, Azadirachta* and *Morinda* were freeze-dried. Anti-malarial evaluation was carried out with the chemosuppressive test model: first, Ficus (100, 200 and 400 mg/kg) was orally administered to chloroquine-sensitive *Plasmodium berghei*-infected mice. Then, evaluation of Ficus combined with each of *Alstonia, Azadirachta* and *Morinda* (200 mg/kg each). Chloroquine (10mg/kg) and between 80 (3%) served as positive and negative controls, respectively.

Results: Majority (97%) of the TMPs recommended combination of plants for the treatment of malaria. Many suggested that *Ficus* should not be used with any antimalarial plant. However, the activities of these antimalarial plants were not significantly ($p>0.05$) different from when combined with Ficus.

Conclusion: The study concluded that these TMPs had a good knowledge of herb-herb interaction and *Ficus* had no effect on the antimalarial activities of *Alstonia, Azadirachta* and *Morinda* combinations.

Keywords: Herb-herb interaction, indigenous knowledge, traditional medical practitioners, *Plasmodium berghei*

Connaissance des antipaludiques à base de plantes parmi les médecins traditionnels dans l'État d'Osun, au Nigéria : enquête et évaluation in vivo de certaines plantes chez la souris

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RÉSUMÉ

Contexte : Les tradipraticiens sont des personnes reconnues dans une communauté comme étant capables de prodiguer des soins de santé à l'aide de plantes, de minéraux et de parties d'animaux. La connaissance du type de plantes et des méthodes de préparation des tradipraticiens, généralement transmise verbalement d'une génération à l'autre, peut se perdre si elle n'est pas documentée.

Objectifs : Cette étude a examiné l'étendue des connaissances des tradipraticiens sur l'utilisation des plantes antipaludiques et les interactions avec les plantes en vue de documenter et d'étudier leurs connaissances indigènes.

Méthodes : Cent tradipraticiens d'Ilesha et d'Ile-Ife, dans l'État d'Osun, au Nigéria, ont été interrogés à l'aide d'un questionnaire semi-structuré de 26 éléments. Par la suite, des feuilles de Ficus exasperata, Alstonia boonei, Azadirachta indica et Morinda lucida, avec des potentiels d'interactions avec les plantes, ont été recueillies. Le ficus a été macéré dans du méthanol tandis que les décoctions d'Alstonia, d'Azadirachta et de Morinda ont été lyophilisées. L'évaluation anti-paludisme a été réalisée avec le modèle de test chimio-suppresseur : dans un premier temps, du Ficus (100, 200 et 400 mg/kg) a été administré par voie orale à des souris infectées par Plasmodium berghei sensibles à la chloroquine. Ensuite, évaluation de Ficus combiné avec chacun des produits Alstonia, Azadirachta et Morinda (200 mg/kg chacun). La chloroquine (10 mg/kg) et le tween 80 (3%) ont servi respectivement de contrôles positifs et négatifs.

Résultats : La majorité (97 %) des tradipraticiens ont recommandé une combinaison de plantes pour le traitement du paludisme. Beaucoup ont suggéré que le Ficus ne devrait pas être utilisé avec aucune plante antipaludique. Cependant, les activités de ces plantes antipaludiques n'étaient pas significativement ($p>0,05$) différentes de celles obtenues en combinaison avec Ficus.

Conclusion : L'étude a conclu que ces tradipraticiens avaient une bonne connaissance de l'interaction herbe-herbe et que Ficus n'a eu aucun effet sur les activités antipaludiques des combinaisons Alstonia, Azadirachta et Morinda.

Mots-clés : interaction herbe-herbe, savoir indigène, tradipraticiens, Plasmodium berghei

INTRODUCTION

Traditional medicine includes herbal medicine, which is a significant element in the cultural heritage of the people, and remains the main source of the primary health care of a large majority of people. About 80% of global population use medicinal plants for their primary health care need.[1] Malaria, caused by *Plasmodium falciparum*, is an endemic disease in Africa and a cause of morbidity and mortality. Ethnomedicinally, there are 1,200 plant species of 160 families in Africa for the treatment of malaria.[2] Traditional medical practitioners (TMPs) are persons recognized in the community as competent to provide health care services.[3] They are knowledgeable in the identification, collection and preparation of antimalarial remedies from plants.[4] In many countries in Africa, the ratio of TMPs to the people is much lower than the ratio of orthodox doctors to the people; which reveals the fact that they are the closest health practitioners in any community.[5] In Mali, TMPs demonstrated a low level of knowledge of both herb-herb and herb-conventional drug interactions, but they were willing to acquire more knowledge.[6] However, in Nigeria, there is sparse data on the knowledge of TMPs about herb-herb or herb-conventional drug interactions. With the proximity of TMPs to the people, it is important that the knowledge of drug interactions will guide their prescription and preparation of herbal drugs as well as the treatment of patients.

To investigate the claim in this study by TMPs that *Ficus exasperata* Vahl (Moraceae) should not be used with any antimalarial herb, it was evaluated in combination with common antimalarial herbs such as *Azadirachta indica A. Juss* (Meliaceae), *Alstonia boonei* De Wild (Apocynaceae) and *Morinda lucida Benth* (Rubiaceae). *Ficus exasperata*, with local name of Ewe eepin (common name, sandpaper leaf plant), has antipyretic, anti-inflammatory, hypoglycaemic, anti-ulcer and hypotensive activities.[7] The plant, *A. indica* (local name, Dongoyaro; common name, Neem), has various biological activities attributed to it. Apart from the traditional use for fever, it has antioxidant, anti-inflammatory and antidiabetic activities.[8] Traditionally, the leaf and bark of A. boonei (local name, Ahun; Common name, Stoolwood plant) were used as antimalarial agents and this activity had been scientifically justified.[9,10] The methanol extract of the stem bark was reported to have anti-inflammatory, anti-pyretic and analgesic properties.[11] *Morinda lucida* (local name, Oruwo; Common name, Brimstone tree) is an antimalarial plant which showed seasonal variation in its activity. Ursolic acid, isolated from the petroleum ether extract of the leaf, was implicated as the antimalarial constituent. Apart from its antimalarial activity, *M. lucida* possesses antidiabetic and hypotensive activities as well as activities against trypanosomiasis and onchocerciasis.[12]

Antimalarial remedies are commonly prepared as multi-plant component mixtures. Therefore, the combination of herb-herb or herb-conventional drug may lead to drug interactions which can result in beneficial or harmful outcomes. Therefore, this study was aimed at evaluating the most commonly used or sold antimalarial herbs among the TMPs, assessing the level of knowledge of the TMPs on drug interactions as well as evaluating possible herbal interactions among selected antimalarial plants in mice.

MATERIALS AND METHODS

Description of Study Areas

The ethnobotanical study was conducted from December 2014 to January 2015 in Ife/Ijesa senatorial district of Osun State in Nigeria. The areas comprise two major towns of Ilesa and Ile-Ife, 70N 50E, located in South-Western Nigeria with estimated populations of 212,225 and 355,818, respectively.[13] The people are Yoruba-speaking, with different dialects and are mostly farmers of food and cash crops. The two major seasons are the rainy (April-October) and dry (November-March) seasons with temperature typically varying from 23 to 34 ^{O}C.

Survey of traditional medical practitioners

A total of 100 TMPs in the two towns were interviewed majorly in their places of practice and the sample size was chosen based on the number of registered practitioners. The participants gave their verbal consent and the data were collected using a 26-item semi-structured questionnaire translated to the Yoruba language. Data obtained were collated and analysed using statistical package for social sciences (SPSS version 15.0).

Plant Collection and Authentication

Fresh leaves of the plants with the highest citations: *Ficus exasperata* Vahl (Moraceae), *Azadirachta indica* A. Juss (Meliaceae), *Alstonia boonei* De Wild (Apocynaceae) and *Morinda lucida* Benth (Rubiaceae), were collected on the campus of Obafemi Awolowo University (OAU), Ile Ife, Nigeria in January 2015. They were identified and authenticated by the plant curator of the Faculty of Pharmacy herbarium, OAU, Ile Ife. Voucher specimens of *F. exasperata, A. boonei, A. indica* and *M. lucida*,

deposited in the IFE and Faculty of Pharmacy Herbaria, OAU, were FPI 1940, IFE 16534, IFE 16536 and IFE 16535, respectively.

Preparation of Extracts

The leaves were oven-dried at 40 °C and separately powdered using a grinding machine (Christy Norris, UK). The powdered leaf of *F. exasperata* (100 g) was macerated with methanol (2x0.75 L) and agitated mechanically for 72 h. A re-extraction process was done and the combined filtrates were concentrated *in vacuo* at 40 °C. The extractive yield was 22.5 %. The decoctions of *A. indica, A. boonei and M. lucida* were prepared by boiling each powdered plant material (100 g) in distilled water (1 L) for 1 h, filtered and freeze-dried into dry powders to give extractive yields of 19.4, 34.3, 26.4 %, respectively.

Animal and Parasite

Experimental mice were housed in cages with wood shavings and given feed (TopFeeds, Ibadan, Nigeria) with free access to water in the animal facility of the Department of Pharmacology, Faculty of Pharmacy, OAU. The inoculum of chloroquine-sensitive *Plasmodium berghei* NK 65 was obtained from a donor mouse with rising parasitaemia up to 30%. Each experimental mouse was inoculated intra-peritoneum with dilute blood (200µL) containing $1x10^7$ infected red blood cells.

Evaluation of the early malaria infection (Chemosuppression test)

The chemosuppressive activity was carried out in two phases using the chemosuppression test model.[14] Sixty-five infected albino mice (18-22 g) were randomly divided into thirteen groups of 5 mice per group. Treatment with the extracts started about 4 hours after infection and continued daily for 4 days. On the fifth day, blood samples were collected for thin smears from the tail snip of each mouse. The dried smears were fixed with methanol, stained with giemsa and microscopically assessed under oil immersion (x1000) and average parasitaemia calculated. The animals were humanely handled in line with the ethical guidelines of the Faculty of Pharmacy, Obafemi Awolowo University, Ile-Ife, Nigeria and the "Principles of Laboratory Animal Care" (NIH publication no. 85-23, revised 1985).

In the first phase, five groups of infected mice were orally treated with *F. exasperata* extract at 100, 200 and 400 mg/kg [15] while chloroquine (10 mg/kg) and tween 80 (3%) served as the positive and negative controls, respectively. The median effective dose (ED_{50}) of *F. exasperata* was determined as 200 mg/kg. In the second phase, (assessment of herb-herb interactions), eight groups of parasitized mice were given chloroquine, tween 80, *A. indica, A. boonei* and *M. lucida* (200 mg/kg each) orally and combinations of *F. exasperata* with *A. indica*, *F. exasperata* with *M. lucida* and *F. exasperata* with *A. boonei* at 200 mg/kg each. The antimalarial test model was slightly modified as extracts were administered for 7 days, although chloroquine was given for only 4 days according to the test model. Blood smears were taken on days 5 and 8 which were assessed as previously described.

Determination of temperature and survival rate

The rectal temperature of each mouse was taken daily during the period of treatment using a digital thermometer. The survival time of each group of mice was determined as the ratio of the number of surviving mice to the total number of mice in the group for 28 days post drug administration.

Data analysis

The data representation and statistical analysis were performed with Microsoft ®Office Excel (2010) and Graphpad Instat (2003). Results were expressed as mean ±standard error of the mean. Statistical significance was determined using ANOVA and post-hoc Tukey test. A $p<0.05$ was set as the confidence limit.

RESULTS

Demographics of the traditional medical practitioners

The demographic data revealed that many of the TMPs were between 31-50 years (62%) while 56% of them were female. Majority of them had formal education with about 45% having the basic primary education and quite a large number (36%) had tertiary education. The TMPs cut across different areas of specialization in traditional medicine comprising herb sellers (38 %), psychiatrists (8%), herbalists (36%) and traditional birth attendants (18%). Many (44%) of the respondents have been practicing for between 1 and 10 years and only 36 % of them belong to their professional association (Table 1).

Table 1: Demographics of the traditional medical practitioners

S/No	Parameters		Responses
1.	Age	21-30	6%
		31-40	36%
		41-50	26%
		51-59	19%
		60 and above	13%
2.	Sex	Male	44%
		Female	56%
3.	Level of education	Primary	45%
		Secondary	29%
		Tertiary	26%
4.	Area of Specialisation	Herb sellers	38%
		Herbalists	36%
		Traditional birth attendants	18%
		Psychiatrists	8%
5.	Years of practice	<1	4%
		1-10	44%
		11-20	31%
		21-30	6%
		30-40	6%
		>40	9%
6.	Membership of professional association	Yes	36%
		No	64%

Table 2: Assessment of the knowledge of antimalarial plants among traditional medical practitioners

S/No	Parameters	Responses
1.	Most frequently used antimalarial herbs	*Morinda lucida* (48%), *Azadirachta indica* (35%), *Alstonia boonei* (10%), *Khaya grandifoliola* (7%)
2.	Most frequently sold antimalarial herbs	*M. lucida* (46%), *Azadirachta indica* (28%), *Alstonia boonei* (16%), *Khaya grandifoliola* (10%)
3.	Period of treatment with the herbs	1 day (1%), 2-5 days (61%), 6-10 days (38%)
4.	Herbs used in combination	*Morinda lucida* and *Azadirachta indica* (45%), *Morinda lucida* and *Mangifera indica (*13%*), Morinda lucida* and *Sorghum bicolor* (12%), *Morinda lucida* and *Cymbopogon citratus* (10%), *Azadirachta indica* and *Sorghum bicolor* (7%), *Azadirachta indica* and *Cymbopogon citratus* (6%) *Morinda lucida* and *Khaya grandifoliola* (5%)
5.	Experience with the combination of herbs	Improved treatment (97 %), no effect (3%)
6.	Herbs that should not be taken with any other antimalarial herb	Leaves and bark of *Ficus exasperata* and any other herb (52%), Stem bark of *Erythrophleum suaveolens* and any other herb (14%), Palm kernel tree bark and any other herb (10%)
7.	Knowledge about herb-herb interaction	No (48%), Yes (52%)
8.	Awareness of the use of herbs and conventional drugs	Yes (63%), No (37%)
9.	Most frequently combined herb and conventional drugs	*Azadirachta indica* and chloroquine (58%), *Alstonia boonei* and chloroquine (9%), *Psidium guajava* and chloroquine (11%), *Vernonia amygdalina* and chloroquine (9%)
10.	Reason for encouraging the use of herbs and conventional drugs	For improved treatment (86%), To clear their old herbs by adding them to make the bulk of their preparations (14%)

Knowledge of antimalarial plants and drug interactions

Information obtained from the TMPs revealed that the most commonly-used antimalarial herbs were *M. lucida* (48%), followed by *A. indica* (35%), and usually prescribed for 2-5 days (Table 2).

The following plant combinations were mostly recommended for malaria treatment: *M. lucida* and *A. indica, M. lucida* and *M. indica*, *M. lucida* and *Sorghum bicolor*, *M. lucida* and *Cymbopogon citratus*. About 57% of them recommended a combination of herbs and animal parts to their patients/clients because they believed that combinations of plants resulted in improved treatment. In assessing their knowledge of drug interactions, 45% of the respondents were aware of herbs that should not be taken with any antimalarial herb while more than average (52 %) listed *Ficus exasperata* as an herb that should not be taken in combination with any antimalarial plant. Apart from *Ficus*, the stem bark of E*rythrophyleum suaveolens* and the kernel of *Elaies guineensis* were not recommended to be combined with any antimalarial plant because untoward side-effects have been observed with their use. Furthermore, 48% of respondents stated that they had enough knowledge of herb-herb interactions, while 50% supported having seminars as a means of acquiring more knowledge and 50% suggested in-service training for the TMPs. It is also worthy of mention that 63% of the respondents were aware of and supported the use of combinations of herbs with conventional drugs such as *A. indica* with chloroquine (58%) and *A. boonei* with chloroquine (13%). Some of the respondents (61%) encouraged the use of herbs with conventional drugs with 64 % of these respondents giving improved activity as the reason for the combinations while 36 % indicated such combinations prevented wastages (Table 2).

Evaluation of antimalarial activity

On day 5, the methanol extract of F. exasperata exhibited mean chemosuppression of 48.50±4.89, 44.95±4.62 and 61.56±6.30 % at 100, 200 and 400 mg/kg, respectively, and these were not significantly different ($p>0.05$) from the chemosuppression value of chloroquine (53.76 ± 7.28 %). The extracts (200 mg/kg) of *A. indica*, *A. boonei* and *M. lucida*, with chemosuppression of 58.29±4.73, 45.68±2.52 and 63.95±4.05%, respectively, were not significantly different ($p>0.05$) from activities on day 8 (Table 3). The chemosuppressive antimalarial activities of the combinations of *F. exasperata* with *A. indica, F. exasperata* with *M. lucida* and *F. exasperata* with A. boonei on days 5 and 8 were 51.49.±5.78, 55.85±8.30, 62.32±1.25% and 51.74±8.57, 58.60±6.65, 80.22±9.76%, respectively, which were not significantly different ($p>0.05$) from each other (Table 3).

Survival rate of animals

The mean survival times of mice treated with *F. exasperata* at 100, 200 and 400 mg/kg were 11.00, 16.25 and 23.50 days, respectively, which were significantly ($p<0.05$) higher than that of the negative control-treated mice (5.75 days). Mice treated with the highest dose of *F. exasperata* (400 mg/kg) had survival time that was comparable to chloroquine-treated mice (22.35 days).

Mice treated with *A. indica*, *A. boonei* and *M. lucida* survived for 4.0, 4.7 and 6.2 days, respectively, which were significantly ($p<0.05$) lower than that of chloroquine. Mice treated with the combinations of *F. exasperata* with each of *A. indica*, *A. boonei* and *M. lucida* survived for 10.4, 13.0 and 10.8 days (Table 3).

Table 3: Effects of *F. exasperata* and its combinations with *A. indica, A. boonei* and *M. lucida* on *Plasmodium berghei* in mice using the chemosuppressive model

Plant/Drug (mg/kg)	Day 5		Day 8		
	Mean Para (%±SEM)	Mean Chemo (%±SEM)[b]	Mean Para (%±SEM)	Mean Chemo (%±SEM)[b]	Survival time (Day±SEM)
Ficus (100)	3.55±0.34[a]	48.50±4.89[e]	ND	ND	11.00±1.87[o]
Ficus (200)	3.77±1.00[a]	44.95±4.62[e]	ND	ND	16.25±2.58[o]
Ficus (400)	2.64±1.54[a]	61.56±6.30[f]	ND	ND	23.50±1.65[p]
Tween 80 (3%)	6.86±1.52[b]	0.00±0.00[g]	ND	ND	5.75±1.47[q]
Chloroquine (10)	2.56±0.49[a]	62.55±7.18[f]	ND	ND	22.35±1.25[p]
Azadirachta (200)	1.99±0.27[c]	58.29±4.73[h]	3.31±0.85[k]	72.48±6.96[m]	4.00±1.20[r]
Alstonia (200)	2.36±0.54[c]	45.68±12.52[h]	4.64±2.71[k]	61.27±12.66[m]	7.00±0.40[r]
Morinda (200)	1.56±0.17[c]	63.95±4.05[i]	5.93±1.69[k]	50.54±14.11[m]	6.20±1.45[r]
Ficus (200)+*Azadiracht a* (200)	2.10±0.25[c]	51.49±5.78[h]	5.79±1.02[k]	51.74±8.57[m]	10.40±1.89[s]
Ficus (200)+*Alstonia* (200)	1.63±0.48[c]	62.32±11.25[i]	2.37±1.17[k]	80.22±9.76[m]	13.0±2.05[s]
Ficus (200)+*Morinda* (200)	1.91±0.36[c]	55.85±8.30[h]	4.96±1.21[k]	58.60±6.65[m]	10.80±2.57[s]
Tween 80 (3%)	4.44±0.39[d]	0.00±0.00[j]	11.99±3.28[l]	0.00±0.00[n]	5.75±1.47[t]
Chloroquine (10)	2.15±0.49[c]	53.77±7.28[h]	3.14±2.64[k]	73.81±5.38[m]	22.35±1.25[u]

KEY: Values with the same superscript letters are not significantly different from each other (p>0.05); values with different superscript letters are significantly different from each other (p<0.05); SEM- Standard error of the mean; ND - Not Determined. Mean Para - Mean parasitaemia; Mean Chemo-Mean chemosuppression

Temperature values of animals

The temperature values of mice treated with F. exasperata on each of the four days ranged from 33.77 to 34.22 ^{o}C which were significantly (p<0.05) lower than values for chloroquine -treated mice for the same period (Table 4). The temperatures of mice treated with the combinations of *F. exasperata* with each of A. indica, *A. boonei* and *M. lucida* are presented in Fig. 1. On day 4, the temperature of the mice treated with *F. exasperata* and *A. indica* (39.0 ^{o}C) which was significantly higher than that of chloroquine (35.65 ^{o}C).

Table 4: Mean daily temperature of mice treated with *F. exasperata* using the chemosuppressive test model

Days of drug admin	Temperature (^{o}C)				
	100 (mg/kg) [a]	200 (mg/kg) [a]	400 (mg/kg) [a]	Tween 80 (3%) [a]	Chloroquine (10 mg/kg)
Day 1	33.92±0.33	33.77±0.32	34.22±0.48	34.02±0.39	34.20±0.29 [a]
Day 2	34.02±0.39	34.15±0.56	33.87±0.60	33.20±1.65	35.10±0.51 [b]
Day 3	33.90±0.30	34.07±0.54	34.05±0.45	33.72±0.12	35.59±0.43 [b]
Day 4	33.87±0.44	34.02±0.62	33.80±0.48	33.64±0.27	35.65±0.62 [b]

SEM- Standard error of the mean; Values with the same superscript letters are not significantly different from each other (p>0.05); values with different superscript letters are significantly different from each other (p<0.05); Days of drug admin- Days of drug administration

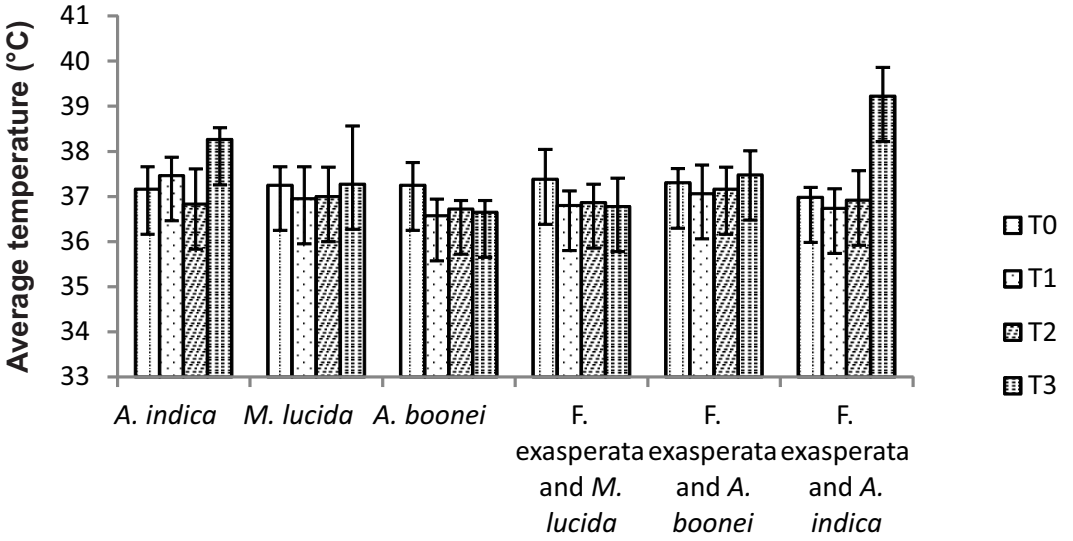

Fig 1: Average Daily Temperature of Mice Treated with *A. indica, A. boonei, M. lucida, F. exasperata* and *A. indica, F. exasperata* and *A. boonei, F. exasperata and M. lucida*

DISCUSSION

This study determined the most commonly-used antimalarial herbs among the TMPs, assessed the level of knowledge of the TMPs on drug interactions as well as evaluated possible interactions among selected antimalarial plants in mice.

Information obtained from the survey showed that a higher number of the TMPs were women. This finding supports previous studies in Nigeria,[16,17] but is in contrast with reports in some other parts of Africa. In the Democratic Republic of Congo, there were more males than females, and the majority of the TMPs interviewed were between 61 and 70 years.[18] Also, in Guinea, the majority of the TMPs were males with those in the age bracket of 41-50 years the most in number.[19] In our communities, the women are recognized as 'Iya elewe omo', 'Iya agbebi' or 'Iya abiye' meaning the "woman that has the remedies for children's ailments", "woman that assists in childbirth" and "woman that helps in bringing forth life", respectively. This buttresses the importance of women as traditional birth attendants or midwives. It is interesting to note that the educational level was very high: all the TMPs were educated, which was quite unusual. This may be due to the fact that the practice is now passed down to younger generations who have basic education. Consequently, they should be able to document their practices and remedies, if prompted. In Guinea, majority (>60%) of TMPs interviewed were not literate; therefore, the documentation of their practice may be impaired.[20] A good number (44 %) of the respondents in this study were relatively new in the practice as they had been practicing for less than 10 years.

Antimalarial plants identified in this study were *Azadirachta indica*, *Morinda lucida*, *Alstonia boonei*, *Mangifera indica*, *Khaya grandifoliola*, *Cymbopogon citratus* and *Sorghum bicolor*. These have been extensively documented as single plants or as combinations of plants, especially in South West Nigeria for the treatment of malaria.[4,9,20] Almost all (97%) of the TMPs claimed that combination of herbs led to improved efficacy. This may be supported by the fact that a combination of *M. lucida*, *A. indica*, *M. indica*, *A. boonei*, produced as *MAMA* Decoction by the Faculty of Pharmacy, OAU, Ile-Ife, as an antimalarial herbal preparation, had been scientifically justified for safety and efficacy with significant results.[9,21]

Furthermore, the TMPs exhibited a good knowledge of both herb-herb and herb-drug interactions. More than half of the respondents (52%) stated that the leaf of *F. exasperata* should not be used with any antimalarial plant as it impaired the antimalarial activities of plants. Other plants that were not advisable to be combined with any other herb were *Erythrophleum suaveolens* and *Elaeis guineensis*. *E. suaveolens*, known to contain diterpenes, alkaloids and toxic saponins, has limited pharmacological use due to its cardiac activity and cytotoxicity[22,23] while E. guineensis - Oil palm- contains fixed oils and is majorly exploited for its food value. *Ficus* leaf possessed flavonoid glycosides, lignans and triterpenoids[24,25] It exhibited hypotensive, anti-ulcerogenic and antioxidant activities[26]. Therefore, *Ficus* was evaluated as a single agent and as a combination with some of the common antimalarial herbs in this study. The herb-drug combinations that were identified were majorly with chloroquine, which was the most commonly-used antimalarial drug before it was withdrawn from the global antimalarial drug list due to decreased sensitivity to the fatal human malaria-causing *Plasmodium falciparum*. The TMPs believed that the combination with chloroquine would result in improved activity.

In the present study, *F. exasperata* exhibited significant antimalarial activity (62 %, 400mg/kg), prolonged the survival of experimental animals but had weak antipyretic activity.[15,27] The median effective antimalarial dose (200 mg/kg) of *Ficus* was combined with the most commonly used antimalarial herbs in order to verify the information obtained from the TMPs. Toxicity studies were not conducted on the plants in this study as they have a long history of human use.[28]

This study revealed there was no significant difference in the antimalarial activities of *Ficus* and its combinations with other antimalarial herbs on both days five and eight. It was thought that increasing the period of administration of extracts may improve efficacy as observed in some orthodox anti-infective drugs which are used for between seven and ten days.

This implies that the leaves of *F. exasperata* can be used with any of *A. indica*, *A. boonei* and *M. lucida* if the need arises in the treatment of malaria and that all the plant extracts used in this study can be used in place of chloroquine. This however, is in contrast to the claims of the TMPs who stated that the leaves of *F. exasperata* should not be used with any antimalarial plant as it will impair their antimalarial activities. Therefore, it can then be inferred that their claims may not have scientific basis. This study lends credence to the documentation of indigenous knowledge and scientific validation of

traditional remedies and practices. Investigation of ethnomedicinal remedies is important so as to give acceptability to traditional methods and remedies which would hopefully gain recognition in the health care of the nation.

CONCLUSION

Azadirachta indica, *Alstonia boonei* and *Morinda lucida* were among the most commonly used antimalarial herbs. The study concluded that TMPs in Ilesa and Ile-Ife had a good knowledge of herbal-drug interaction. It also concluded that the leaf of *F. exasperata*, which many of the TMPs claimed would interact with other herbs, did not influence the antimalarial activities of the locally-identified plants.

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