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COMPARATIVE EFFICACY OF CRUDE AQUEOUS EXTRACT OF *MANGIFEREA INDICA, CARICA PAPAYA* AND SULPHADOXINE PYRIMETHAMINE ON MICE INFESTED WITH MALARIA PARASITE *IN VIVO*

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ABSTRACT

The comparative efficacy of a chemotherapeutic antimalarial drug complex- sulphadoxine-pyrimethamine (maloxine) and two different leaf extracts: *Mangifera indica* (mango) and *Carica papaya* (paw-paw) were investigated on malaria-infested mice using *Plasmodium berghei* - the rodent malaria species. Maloxine had the highest anti-malaria efficacy; reducing the parasite count from average count of 9.4 ±0.04 to 1.4 ± 0.05 after six days of treatment. The paw-paw leaf extract reduced the malaria parasite count from an average of 9.2 ±0.06 to 2.6 ± 0.06; while the mango leaf extract showed a reduction from 9.8 ±0.01 to 3.2 ± 0.03 after six days of treatment. However, a combination of the two leaf extracts (1:1) exhibited a higher anti-malaria efficacy than the separate leaf extracts, reducing the parasite count from 9.4 ± 0.031 to 2.0 ± 0.15. The public health implications of these findings are discussed.

KEY WORDS: Malaria parasites, malaria, antimalaria potency, red blood cells, sulphadoxine pyrimethamine, *Mangifera indica*, *Carica papaya*

INTRODUCTION

Malaria is by far the world's most deadly tropical parasitic disease, and kills more people than any other communicable disease except tuberculosis (*Davey* and *Crewe* 1973). In many developing countries and specially in Africa, malaria exerts an enormous toll on lives, medical costs, and lost labour days (*Edirisinghe* 1988).

The causative agent in humans are four species of *Plasmodium* viz: *Plasmodium falciparum* which causes falciparum (malignant tertian or sub-tertian) malaria which is the most serious form of malaria and can be rapidly fatal in non-immune individuals if not treated promptly. *Plasmodium vivax* which causes vivax (benign tertian) malaria and is widespread but rarely fatal, although symptoms during the primary attack can be severe. *Plasmodium malariae* which causes quartan malaria which is generally mild but can cause fatal nephrosis, and *Plasmodium ovale* which causes ovale (ovale tertian) malaria and is the least common type of malaria, and produces clinical features similar to *Plasmodium vivax (Golgi,* 1989).

Malaria kills one child every 30 seconds. This preventable disease has reached epidemic proportions in many regions of the world, and continues to spread unchecked per day in children under five years of age. It has a death toll that far exceeds the mortality rate from AIDS. African children under five years of age are chronic victims of malaria, suffering an average of six bouts a year. Fatally afflicted children often die less than 72 hours after developing symptoms. In those children who survive, malaria also drains vital nutrients, impairing their physical and intellectual development.

Maloxine is made up of the sulphadoxine-pyrimethamine complex. It is the drug of choice for the treatment of malarial attacks, in case of chloroquine resistance, offering distinct advantages over classical treatment. It is effective against parasites resistant to other common anti-malarials and the risk of the resistance developing is minimal. It has been reported that the sulphadoxine-pyrimethamine complex has effectively displayed its prophylactic and therapeutic properties on all forms of malaria due to *P. falciparum*, *P. vivax*, and *P. malariae*. (Verhoeff *et al* 1997).

The resistance of the plasmodia species especially the *P. falciparum* to several anti-malarial drugs has led more and more people especially in African rural areas to resort to the treatment of malaria with the use of medicinal plants like *Azadiractha indica*, *Carica papaya* and *Mangifera indica*.

Mangifera indica and *Carica papaya* are widely cultivated in different parts of Africa especially Nigeria. *Mangifera indica* leaves, are used medicinally to treat several ailments such as asthma, cough, diarrhoeas, dysenteries, leucorrhoea and malaria; while *Carica papaya* is said to be beneficial in dysenteries, asthma, rheumatism, fever, beriberi, malaria, and as an antihelminthic (*Agoha* 1981).

We thought it necessary to establish the folklore claims that *Mangifera indica* and *Carica papaya* have therapeutic effects on malaria parasites and also to compare the therapeutic effects *in vivo* of their crude aqueous leaf extracts; a combination of the extracts as is often used by some patients, and maloxine (sulphadoxine- pyrimethamine complex) an anti-malarial drug in experimental animals (mice).

MATERIALS AND METHODS

Plant Materials

Both *Mangifera indica* leaves and *Carica papaya* leaves were collected around the campus and were identified at the Botany Department, Abia State University, Uturu.

The leaves were sorted and dried in a carbolite moisture extraction oven at a temperature of 65^{0}C. The dried samples were commuted in an Aurthur Thomas Contact milling machine. The resulting powdered material was used in the extraction process. Extraction was carried out by the method of Harborne (1972) using distilled water as the solvent. One hundred grams (100gm) of the powdered sample was extracted with 200ml of distilled water; and the percentage active ingredient in the samples calculated.

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TABLE 1: Comparative Efficacy of Maloxine and Aqueous extracts of *C.papaya* and *M.Indica* on the treatment of plasmodium parasitaemia in mice

GROUP	CONTROL	MALOXINE TREATED	*CARICA PAPAYA* TREATED	*MANGIFERA INDICA* TREATED	C. *PAPAYA* + M.*INDICA* TREATED
Wt (g)	16.8 ± 0.06	16.1 ± 0.03	17. ± 0.04	18.9 ± 0.05	17.4 ± 0.02
Dose (mg/kg)	---	0.41± 0.0	0.46± 0.03	0.49 ±0.01	0.45 ± 0.06
Parasite count before treatment	8.0 ± 0.05	9.4 ± 0.04	9.2 ± 0.03	9.8 ± 0.01	9.4 ± 0.03
Day 1	8.5 ± 0.02	7.6 ± 0.06	7.9 ± 0.05	8.2 ± 0.06	7.6 ± 0.04
Day 2	9.6 ± 0.01	6.1 ± 0.01	6.5 ± 0.03	6.8 ± 0.02	6.2 ± 0.16
Day 3	10.2 ± 0.04	4.2 ± 0.04	5.4 ± 0.01	6.1 ± 0.01	5.0 ± 0.03
Day 4	11.7 ± 0.02	3.1 ± 0.03	4.3 ± 0.04	4.9 ± 0.05	3.8 ± 0.15
Day 5	13.1 ± 0.03	2.6 ± 0.02	3.4 ± 0.02	3.8 ± 0.04	2.9 ± 0.02
Day 6	14.0 ± 0.01	1.4 ± 0.05	2.6 ± 0.06	3.2 ± 0.03	2.0 ± 0.15

Sulphadoxine-Pyrimethamine

The standard anti-malarial drug, maloxine, is a one-dose treatment drug. The tablets (3) weighed 1.82g. With this as the conventional adult dose, its equivalent in mg/kg was calculated; the average adult body weight was taken to be about 70kg. Thus an average dose of 26mg/kg body weight was administered to the experimental animals.

Experimental Animals

Twenty five (25) mice of the Dumbo rex strain aged between 12 -15 weeks and weighing between 20 -25g were collected from the Departmental animal house. They were separated, 15 males and 10 females and kept in separate cages. They had access to food and water *ad libitum*.

The animals were screened for malarial parasites and were certified to be healthy. They were separated into 5 groups (3 males and 2 females in each group).

Methods of Infection

Blood (3ml) was collected from mice infected with *P. berghei* through its cut tail. Two (2) drops of the freshly collected blood were dropped into 5ml of 0.85% saline solution (physiological saline) and allowed to stand for about half an hour. 1.2-3ml of the blood-saline mixture was injected intraperitoneally into each of the mice through the abdominal wall according to body weight.

RESULTS

After 3 days, the tails of the mice were cut and blood collected for screening to determine its parasitaemia, a process known as test-breeding. Between the 6th and 8th day, parasitaemia approached its peak.

Blood samples for parasitaemia test were collected on the 12th day. The *Plasmodium* species (malaria parasites) entering the body stay latent for some days, four (4) to 8 days (Cook 1990), within which period they replicate into many more parasites.

Screening for Malaria Parasites

Screening for the presence of malaria parasites in the animals was by the method of Davey and Crewe (1973). Thick as well as thin blood films were prepared with the animal's blood on a microscope slide. The thick blood films were stained with Field's stain. Each of the film on the slide was washed and dried and then systematically examined under the microscope using the oil immersion objective.

To avoid recording non-malaria parasites, a certified malaria negative blood sample was used to prepare both thick and thin films, stained accordingly, and examined under the same microscope. The control was therefore necessary to remove errors due to possible pseudoparasites. Results of the screening was expressed in terms of level of parasites observed in the thick films stained with Field's stain. (Ramnik 1990).

Control animals showed increase in plasmodium parasite count from 8.0 ± 0.05 before treatment to 14.0 ± 0.01 after six days of non-administration of drug. The maloxine treated mice had the parasite count reduced from 9.4± 0.04 to 1.4 ± 0.05 after 6 days while the *Carica papaya* and *Mangifera indica* treated animals reduced from 9.2 ± 0.06 to 2.6 ± 0.06 and 9.8 ± 0.001 to 3. 2 ± 0.03 respectively after 6days. But a combination of *Carica papaya* and *Mangifera indica* extract reduced the parasite count of the animals from 9.4 ± 0.031 to 2.0 ± 0.15 after 6 days (Table 1).

DISCUSSION

Results on Table 1 show that maloxine treated mice had their plasmodium parasite count significantly reduced at $p \leq 0.05$ level of significance from 9.4 ± 0.04 to 1.4 ± 0.05 after 6 days of treatment. This observation agrees with those of Verhoeff *et al* (1997) who reported that the anti-parasitic effect of a single dose of maloxine lasts for about 28 days. Maloxine therefore could be said to have a significant anti-malaria potency.

Carica papaya extract treated animals showed reduction of parasite count from 9.2 ± 0.05 to 2.6 ± 0.06 at the sixth day. Agoha (1981) reported that the leaf of *Carica papaya* is used for the treatment of fever and beriberi in Tropical America. The *Carica papaya* leaf extract had significant reduction of parasite count at $p \leq 0.05$ level of significance.

Mangifera indica leaf extract reduced the parasite count from 9.8 ± 0.01 to 3.2 ± 0.03 after 6 days. This reduction is also significant at $p \leq 0.05$ level of significance. Agoha (1981) also reported that the leaf extract of *Mangifera indica* is also effective in the treatment of malaria and is commonly used as anti-malaria drug in Nigeria.

A combination of the two plant leaf extract (1:1) administered to the animals had a significant reduction at $P \leq 0.05$ level of significance on the malaria parasite count from an average count of 9.4 ± 0.03 to 2.0 ± 0.15 after 6 days. This result shows that a combination of the two extracts may have a higher anti-malarial potency than when administered separately. This observation seems to agree with those of Peters *et al* (1986) who reported that a multiple drug therapy could be more effective in reducing parasite count. For effective reduction of parasite count it seems that a combination of the two plant extracts would be recommended. But the standard maloxine drug had a more drastic reduction of parasite count when compared with the leaf extracts singly or in combination; and therefore may be recommended as a better anti-malarial when it could be afforded. It has been reported to be prophylactic and therapeutic on all forms of

malaria due to *Plasmodium falciparum, P. vivax,* and *P. malariae* (Verhoeff *et al* 1997).

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