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EFFICACY OF *MAYTENIUS SENEGALENSIS* (L) EXTRACTS ON RATS EXPERIMENTALLY INFECTED WITH *SCHISTOSOMA MANSONI*

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ABSTRACTS
Maytenius senegalensis extracts was obtained using the solvent polarity technique and were tested on 3-4 weeks rats, infected with Schistosoma mansoni cercariae.Three batches of rats with plant extracts of cold water acetone and methanol were administered orally at 40g/kg body weight. This gave a cure rate ranging from 91.56% to 87.76% in the rats; while praziquantel administered at 60mg/kg body weight gave a cure rate 87.76%.These results are statistically significant (p>0.05).The therapeutic nature of the extracts and praziquantel reduced the pathological conditions of infected animals as evident by mottling of the liver with mean liver mottling score of 4.4 and 4.6 granolumas recorded and the level of damage values of 4.4 and 4.6 in the rats. Using t-test and ANOVA shows that there was no significant difference between therapeutic scores of plant extracts and praziquantel (p>0.05) as shown by the pathological changes observed in the test animals.

Keywords: Efficacy, Maytenius senegalensis, Schistosoma mansoni, Rats, praziquantel.

INTRODUCTION

Schistosomiasis also referred to as Bilharziasis, a parasitic diseases of man and other vertebrate animals,is caused by blood – flukes of the genus Schistosoma.The disease is wide spread in various part of the world. It is a public health problem with considerable magnitude. It is estimated that over 250 million people in 76 countries of the world are infected with the disease with over 600 million others exposed to the risks of the infection (WHO, 1990).

At least 19 species of Schistosoma are recognized through only few are pathogenic to man and domestic animals(Jonson et-al.,1993).The most prevalent species which infect man include *Schistosoma haematobium* found in Africa and the Middle East; *Schistosoma mansonia* which occurs in Africa, the Arabian Peninsula, West Indies and Southern America; *S .japonicum* which is found in Far East and *S. intercalatum* which occurs in Central and West Africa.The first case of *S. intercalatum* infection in man was probably reported in 1914, base on Chesterman's reports from Zaire (now Democratic Republic of Congo (DRC) in 1923, *S. mekongi*, occur in Laos, Thailand (WHO,1990).The geo – epidemiology of infection shows disparity around the globe. Although it infect people of all ages, its more prevalent in children, farmers, and fishermen. The life-cycle of schistosomiasis is complex, involving many hosts. Man and other warm blooded animals being the definitive hosts with fresh water snails (*Biomphalaria spp; Bulinius spp* and *Oncomelinia spp*) as intermediate hosts, while water bodies provide the link between them. Epidemiology of schistosomiasis is characterized by many factors such as level of sanitation, association with water – body and the snail intermediate host among others.

The pathology of schistosomiasis varies among the species and strains. Most infected people do not show any signs or symptoms of the disease. However, the pathology can be subdivided in to the following phases:

-Invasion stage; During the penetration of the cercariae and migration of schistosomula, the clinical signs observed are skin reaction, fever cough and Katamaya syndrome.

- Stage of maturation, characterized by febrile illness.

- Stage of established infection, during which large number of eggs is produced.

In early chronic cases there are haematuria and other intestinal changes with inflammatory reactions, resulting from formation of granuloma.

- Stage of late infection; during which, large number of eggs is produced. In early chronic cases there are haematuria and other intestinal changes with inflammatory reactions, resulting from formation of granuloma.

-Stage of late infection; late chronic infection which may be characterized by corpulmonale, fitula, obstructive uropathy, renal failure, portal hypertension, and abdominal distension (Butterworth *et al.,* 1994). In rare cases elephantiasis may be induced in some individuals (Kela and Bowen, 1995).

Niridazole (Ambilar) that was effective against *S. haematobium* is removed from the marked because of it its carcinogenic effects and cytogenic action on spermatogenesis (WHO 1990) coupled with other side effects such as cramps, dizziness, headache, nausea, vomiting, immune suppression, rash, insomnia, convulsion, haemophilic anaemia in glucose -6-phosphate dehydrogenase (G6PD) deficiency and psychosis among others (Bogitsh and Cheng, 1990).

Oxamniquine, though effective against *S. mansoni* (WHO, 1990), causes rashes , drowsiness, headache, diarrhea, insomnia as well as hepatic enzymes changes (Bogitsh and Cheng, 1990). Praziquantel introduces in the 1970's as a drugs of choice for *S. haematobium, S. mansoni* and *S. japonicum* infections is however costly and not readily available especially in the rural areas where they are most needed (Anthony *et al*, 1994). The present investigation is aimed at test local plant extracts with potent with potent antischistosomal agents .The study was therefore designed to sourcing alternatives which may be easily available and cheap.

MATERIAL AND METHODS

Collection and Processing of Plant Materials

The parts of the plants used were collected at Yankari Game Reserve in Bauchi State of Nigeria, it was dried under shade for two weeks. They were then pulverized in a wooden mortar and pestle, sieved through ordinary four's sieve and the powder stored in labeled polythene bags for use. The extractions of plants materials was done using the solvent polarity technique with three solvents namely; acetone, methanol and water in increasing polarity as described by Moore and Winston (1996).

Collection of Snails

Two well known snail species, intermediate hosts of *Schistosoma mansoni ; Biomphilaria* and *Bulinius species* were collected from the Mayur river in Mubi town, Adamawa State of Nigeria. The snails collected were sorted out and screened for infection according to the method described by the Danish Bilharziasis Laboratory (Madsen, 1985), and finally identified as either *Bulinus physopsis globosus, B. trucatus* or *Biomphilaria pferfferi* using appropriate keys described by Brown and Christensen (1993) and Brown (1994).

Collection and Rearing of Rats

A total of 20 rats purchased from the Animal House University of Jos and the National Institute of Trypanasomiasis Research (NITR), Vom, Plateau State, Nigeria were , they were stabilized and later infected by using paddling method as per Danish Bilharziasis Laboratory (Madsen, 1985) recommendations.

Formulation and Administration of Praziquantel and Plant Extracts

Praziquantel tablets Batch No. DIST 3009 (Shinpoong Pharmaceutical Company, Korea) were purchased and orally given as a suspension of the tablets made of 30% water and 70% glycerin in a single dose of 60mg/kg body weight. Administration of the drugs was done 5-6 weeks post infection with schistosome cercariae as described by Van Lieshout *et al* .(1991). Plant extracts were similarly administered orally as single dose of 40g/kg body weight, dissolved in aqueous suspension of 30% water and 70% glycerin as in case of praziquantel.

Phytochemical screening was carried out, to test the presence of saponins tannins, phenols, flavanoid, alkaloids and volatile oils as described by Sofowora (1984).

RESULTS

Table 1 shows result of phytochemical analysis of the plant extracts.This result shows that *Maytenus senegalensis* apparently lacks tannin and volatile oils, and the water extract does not contain flavanoids. Table 2 shows the liver mottling in rats infected with schistosomes. The acetonic and methanolic extracts of *M. senegalensis* had similar results to that of the praziquantel. The granulomas recorded are shown in table 3. From the table, it was discovered that the number of granulomas recorded in the rats treated with acetonic extracts was significantly lowered than that of praziquantel. Table 4 shows the levels of damage caused by the infection in other viscera. It was also observed that the spleen was apparently normal in all treated batches of animal except that it was darker in all the batches treated with praziquantel. The kidney was not affected by infection while the major pathology observed in lungs was patechial haemorrhage with affected lungs having spots of dark coagulated blood on the surface as shown on the tail. Other pathological changes such as ascites ulcer and perforation of the bowel were also observed on many organs.

Experimental Infection

The result of the experimental infection of mice with cercariae was impressive as shown by the number of worms recovered from animals with an average of 47 worms per rat. As result of this infection, some of the animals infected with *Schistosoma mansoni* cercariae passed out watery stools seven weeks post infection. Furthermore, some infected animals lost their hairs eight weeks post infection. Most of the affected animals that lost their hairs were looking dull, weak, emanciated and anaemic.

Physical Observation After Treatment

Clinically, the worst affected animals were treated with praziquantel and the plant extracts of M. senegalensis. Acetonic and methanolic extracts gave the best result as hair regeneration was achieved within 2- 4 days after oral administration. The water extract gave poor results. Animals treated with paraziquantel recovered their hairs 4 days post treatment. Animals passing watery faces stopped on day 2, when praziquantel and the plant extracts were administered. The water extract of *M.senegalensis* gave positive result by preventing diarrhoea, but failed to regenerate hair. There was also improvement in the general body condition of the animals during treatment, both with praziquantel as well as the plant extracts. Treated animals became active and feeding well.

Table 1: Phytochemical Screening of *M. senegalensis extracts*

	Constituents					
Plant extracts	**Saponins**	**Tannins**	**Phenols**	**Flavanoids**	**Alkaloids**	**Volatile oil**
Acetone	+	-	+	+	+	-
Methanol	+	-	+	+	+	-
Water	+	-	+	+	+	-

Key: + = present, - = absent

Table 2: Liver mottling induced by schistosomes and efficacy of *M. senegalensis* extracts in rats

	Extracts						
Animals	**A_1**	**A_2**	**A_3**	**PZQ**	**$Control_1$**	**$Control_2$**	**Total**
1	5	3	7	4	23	0	42
2	4	5	8	6	20	0	43
3	2	4	9	5	17	0	37
4	6	6	5	4	25	0	46
5	5	5	6	3	19	0	38
Total	**22**	**23**	**35**	**22**	**104**	**0**	**205**

Key: A_1 = *M. senegalensis* acetone extract, A_2 = *M. senegalensis* methanol extract, A_3 = *M. senegalensis* water extract, PZQ = praziquantel, $Control_1$ = Infected but non treated, $Control_2$ =Non Infected

Table 3: Granulosomas recorded in some organs of schistosome infected Rats

	Organs				
Extracta	**Stomach**	**Colon**	**Caecum**	**Intestine**	**Total**
A_1	**0**	**5**	**3**	**5**	**13**
A_2	0	3	5	24	32
A_3	0	5	0	34	39
PZQ	1	8	3	23	35
$Control_1$	4	16	17	94	131
$Control_2$	0	0	0	0	0
Total	**5**	**37**	**28**	**180**	**205**

Key: A_1 = *M. senegalensis* acetone extract, A_2 = *M. senegalensis* methanol extract, A_3 = *M. senegalensis* water extract, PZQ = praziquantel, $Control_1$ = Infected but non treated, $Control_2$ =Non Infected

Table 4: Efficacy of extracts of *M. senegalensis* and praziquantal on schistosomiasis infected Rats

	Viscera							
Extracta	**Spleen**			**Lungs**		**Kidney**		**Total**
	N	**D**	**SM**	**N**	**P.H**	**N**	**AF**	**15**
A_1	5	0	0	4	1	5	0	15
A_2	5	0	0	5	0	5	0	15
A_3	0	5	0	2	3	5	0	15
PZQ	3	0	2	4	1	5	0	15
$Control_1$	5	0	0	5	0	5	0	15
$Control_2$	5	0	0	5	3	5	0	15
Total	**23**	**5**	**2**	**25**	**8**	**30**	**0**	**90**

Key: A_1 = *M. senegalensis* acetone extract, A_2 = *M. senegalensis* methanol extract, A_3 = *M. senegalensis* water extract, PZQ = praziquantel, $Control_1$ = Infected but non treated, $Control_2$ = Non Infected, AF = Affected, N = Normal, D = Darkened, SM = Spleenomegaly, P.H = Partechial haemorrhage

DISCUSSION

The eggs of schistosomes are the main causes of pathology in schistosomiasis infection.The eggs penetrate the blood vessels of the host tissue by secreting proleolytic enzymes (Bogistsh and Chen, 1990).The host reactions to the eggs may vary from granulomatous to intensive fibrosis. As a result of experimental infection in rats with schistosomes, granulomas were observed in all the infected animals, however, with a variable intensity. The stomach was the least affected organs, with only 0.86% of the total granulomas recorded rats. The intestine had the highest concentration of granulomas in contrast to the stomach which had the least concentration. In the control batches of infected but non treated animals, the total score of granulomas was vary high. However, the few granulomas recorded could be attributed to the large quality of eggs as direct consequence of the heavy infection.

There were marked differences in the number of granulomas recorded among the treated rats. The non-treated infected control animal granuloma score were highly significant ($p<0.05$). This could be due to the large number of eggs laid numerous worms recovered. There was significant difference ($p<0.05$), in the number of granulomas in infected rats treated with extracts of *Maytenus senegalensis*. Animals treated with acetone and methanol extracts recorded the lowest number of granulomas along the alimentary canal.

This might be attributed to the antischitosomal potency of the extracts which atleast succeeded in reducing the number of eggs output. With the exception of the water extracts, all the extracts of *M. senegalensis* had flavanoid as the chemical compounds. Water extract had serious side effect on the lungs as observed in table 4.

Flavanoids according to Kumar and Singh (1979) are, not strong therapeutic drugs, but rather toxic to cells of the host organisms. According to the same source, some of the flavanoids are antifungal and antipathogenic agents. The most important substance of pharmacological values are the alkaloids, which were found to be present in all the extracts of *Maytenus senegalensis*. The difference in the potency of the acetone, methanolic and water extracts could be due to solvent polarity extraction technique used which might have removed the active ingredients in the first solvent used. The acetone and methanol as solvents, produced extracts that had better result than the water extracts. The serial extraction might have reduced immensely the therapeutic value of the subsequent extracts by removing some of the potent antischistosomal compounds. There is, however, the need for further analysis of the components of the different extracts to ascertain this claim.

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