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# LACK OF EVIDENCE FOR AN ANTISCHISTOSOMAL ACTIVITY OF MYRRH IN EXPERIMENTAL ANIMALS

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*Abstract.* In a multicenter investigation of the potential antischistosomal activity of myrrh, a resin obtained from an African plant, different derivatives of the resin, including the commercial preparation Mirazid, were tested at different doses in mice and hamsters infected with *Schistosoma mansoni*. In mice infected with the Egyptian (CD) strain of *S. mansoni,* four of six groups treated with Mirazid did not show significant worm reduction, while the remaining groups showed significant but trivial reductions. In mice infected with the Puerto Rican (Mill Hill) strain of *S. mansoni,* a Mirazid solution was toxic for mice at high doses and produced modest or no worm reduction at lower doses. In hamsters and mice infected with Puerto Rican (NMRI) and Brazilian (LE) strains of *S. mansoni* and treated with the crude extract of myrrh in doses ranging from 180 to 10,000 mg/kg, no signs of antibilharzial activity were observed. Total tissue egg load and egg developmental stages were not affected by any of the treatment regimens. These results were in contrast to those obtained in praziquantel-treated animals in which 94% worm reduction and 100% egg reduction was observed. Based on the findings of this work, we cannot recommend the use of Mirazid in human cases of schistosomiasis.

## INTRODUCTION

In the control of schistosomiasis, the use of drugs that are safe and effective will remain the main tool until a successful vaccine is produced. Praziquantel (PZQ) is the only antibilharzial drug effective against all the schistosomes pathogenic to humans.[1] Although PZQ has minimal side effects, its use in the control of schistosomiasis at a population level faces some problems. Reduced cure rates and failure of treatment after PZQ have been reported in Senegalese and Egyptian patients.[2–4] Resistance to PZQ has been recently induced in schistosomes by laboratory selection.[5] For these reasons, a search for new drugs with antischistosomal activity is certainly appropriate.

Mirazid (Pharco Pharmaceuticals, Alexandria, Egypt) is prepared from myrrh (Arabian or Somali),[6] which is an oleo gum resin obtained from the stem of thorny trees (*Commiphora molmol* Engier) and probably other species of the Burseraceae.[7] Myrrh is currently present in the French and British Pharmacopoeias as throat pastilles (lozenges) and cough mixtures and also as suppository for proctitis.[8] It contains the resin myrrhin (23–40%), the volatile oil myrrhol (2–8%), gum (40–60%), and a bitter unidentified component.[9,10] With regard to its potential antischistosomal activity, Sheir and others[11] reported a cure rate of 91.7% after a dose of 10 mg/kg/day for three days in 204 schistosomiasis patients. Badria and others[6] reported significant parasite reductions of 76% and 75% upon treatment of infected mice with 250 mg/kg and 500 mg/kg of myrrh extract twice a day for three days, respectively. These investigators also reported that these treatment regimens induced worm uncoupling and hepatic shift of female worms in a dose-dependent manner. In this report, we provide data from laboratories in Egypt, Italy, the United States, and Brazil that various extracts of myrrh, including the commercial product Mirazid, have no demonstrable antischistosomal activity in infected mice or hamsters. This work was conducted in experimental animals infected with different strains of *Schistosoma mansoni* and treated with myrrh in different doses and formulations. Results were compared with data in infected untreated controls and infected PZQ-treated animals.

## MATERIALS AND METHODS

**Experiments with the Egyptian (CD) strain of *S. mansoni.*** *Acute toxicity.* Adult male CD-1 Swiss albino mice weighing 20 ± 2 grams were used to study acute toxicity of Mirazid. A pilot trial was conducted using a limited number of animals to determine the range of acute oral lethality. According to data of the pilot study, 36 mice were randomly divided into groups of 4–6 animals. These groups received increasing doses of Mirazid from commercial capsules administered orally by gastric intubation from 1,000 mg/kg to 4,500 mg/kg, with 500 mg/kg increments. Animal groups were closely observed after dosing. The 24-hour mortality data were then subjected to computer analysis (PCS Software, Houston, TX) for the determination of the 16% lethal dose ($LD_{16}$), the $LD_{50}$, and the $LD_{84}$.

*Antischistosomal activity.* CD-1 Swiss albino mice were infected with 80 cercariae/mouse of the Egyptian (CD) strain of *S. mansoni* using the body immersion technique.[12] Myrrh was tested in its original form (before preparation by Pharco Pharmaceuticals) as a powder of coarse particles after grinding and resuspension in 2% Cremophor EL (Sigma, St. Louis, MO). The commercially obtained Mirazid was tested using resinous capsules available in the local Egyptian market after resuspension of the content of the capsules in Cremophor EL and also as a suspension provided by Pharco Pharmaceuticals together with the appropriate diluting vehicle. Guided by the $LD_{50}$ estimation, the drug was given orally seven weeks post-infection in two doses of 250 mg/kg and 500 mg/kg for five consecutive days. For comparison to a standard treatment, PZQ (Shin Poong Pharmaceutical Co., Ltd, Kyonggi, South Korea) was given as a freshly prepared suspension in 2% Cremophor EL at a dose of 200 mg/kg for five consecutive days.

*Schistosoma mansoni*–infected mice were divided into eight groups of six mice (except for group 1, which contained eight mice and group 8, which contained seven mice) and treated as follows: group 1: vehicle containing no myrrh; groups 2 and 3: Mirazid from resinous capsules, 250 mg/kg × 5 and 500 mg/kg × 5, respectively; groups 4 and 5: myrrh in its original powder form, 250 mg/kg × 5 and 500 mg/kg × 5, respectively; groups

6 and 7: Mirazid in a suspension, 250 mg/kg × 5 and 500 mg/kg × 5, respectively; and group 8: PZQ: 200 mg/kg × 5.

Animals were killed 14 days post-treatment and the hepatic and portomesenteric vessels were perfused to recover worms. Parts of the liver and small intestine were used to quantitate tissue eggs, while pieces of small intestine were used to study the percentage egg developmental stages (oogram).

**Experiments with the Puerto Rican (Mill Hill) strain of *S. mansoni.*** CB6F1 male mice were infected with 70 cercariae of a *S. mansoni* strain isolated in Puerto Rico and maintained for many years in Mill Hill (United Kingdom) before being established in Rome, Italy. On day 53 after infection, mice were dosed with a Mirazid sample (Pharco Pharmaceuticals) in the form of a red-brown semi-solid resinous material. Since attempts to produce an emulsion in aqueous media were not successful, the material was dissolved in a 2:1 mixture of dimethylsulfoxide (DMSO) and polyethyleneglycol (PEG) 400 (DMSO-PEG 400 2:1), which produced a clear solution. This solution was then administered orally by gastric gavage.

Infected mice were divided into five groups of eight mice (except for group 1, which contained nine mice) and treated as follows: group 1: vehicle (DMSO-PEG 2:1) containing no Mirazid; groups 2–4: Mirazid, 1,000, 300 and 100 mg/kg × 3, respectively; and group 5: PZQ, 100 mg/kg × 3.

Treatment started in the morning of day 53 post-infection, the second dose was given at the end of the same day, while the third and last dose was given in the morning of the following day. Treatment was terminated because three mice of the 300 mg/kg group and six mice of the 1,000 mg/kg Mirazid groups died on the second day. Three days after treatment, three additional mice in the 300 mg/kg group and all mice in the 1,000 mg/kg group died. Twenty-four days after treatment, the remaining mice in all groups were perfused and the number of worms in each animal was recorded.

**Experiments with the Puerto Rican (NMRI) strain of *S. mansoni.*** Sixteen hamsters (Syrian), each infected percutaneously with 130 *S. mansoni* cercariae of the Puerto Rican strain that has been maintained for many years at the Naval Medical Research Institute (Bethesda, MD), were weighed and then dosed with the crude extract of myrrh six weeks post-infection. Myrrh was ground to a wet powder in 75% water, 25% Cremophor EL (BASF, Dusseldorf, Germany) and was administered orally by gastric gavage between 8:00 AM and 11:00 AM on each day of three consecutive days.

*Schistosoma mansoni*–infected hamsters were divided into four groups of four animals and treated as follows: group 1: water and Cremophor EL (vehicle) containing no myrrh; and groups 2–4: myrrh, 60, 180, and 600 mg/kg × 3, respectively.

Sixteen days after the last dose, all hamsters were killed. Autopsies were preformed and the worms in each animal were recovered from the mesenteric and portal veins using an electric pump. Livers were removed and carefully inspected for the presence of any adult worms.

**Experiments with the Brazilian (LE) strain of *S. mansoni.*** Mice were each infected with 100 ± 10 cercariae of the Brazilian *S. mansoni* LE strain. A myrrh extract from Pharco Pharmaceuticals was resuspended in 2.5% Cremophor EL and administered by gavage to infected mice 45 days after infection. Animals were divided into six groups of 10 mice (except for group 1, which contained nine mice and group 6, which contained seven mice) and were treated as follows: group 1: vehicle only (control for groups 2 and 3); group 2: myrrh, 400 mg/kg × 5; groups 3 and 4: myrrh, 1,000 mg/kg × 5; group 5: myrrh, 2,000 mg/kg × 5; and group 6: vehicle only (control for groups 4 and 5).

Animal groups designed to study hepatic shift (groups 1–3) were killed three days after treatment and autopsies were performed. Groups 4–6 were further subdivided into two subgroups according to time of killing post-treatment (either 7 or 15 days). Four animals died after treatment in group 4 and three animals died in group 3. The number of worms recovered in each animal from the mesenteric and portal veins was recorded. Livers were removed and carefully dissected and inspected for the presence of any adult worms.

In accordance with the instructions of Pharco Pharmaceuticals, in all participating laboratories treated animals were deprived from food the night before treatment and were allowed to eat one hour after dosing. The maintenance and care of experimental animals was compliant with the national guidelines of each country for the humane use of laboratory animals.

**Parasitologic methods.** Worm burden, sex, and distribution were determined after perfusion of the hepatoportomesenteric vessels.[13]

*Percentage egg developmental stages (oogram pattern).* After perfusion, the small intestine was separated and transferred to a petri dish. Three fragments (each 1 cm in length) of the small intestine were cut longitudinally, rinsed in saline, slightly dried on filter paper, and then placed between a slide and cover slip. The fragments were examined by low-power microscopy, the stage of each egg was recorded, and the mean number of various stages was calculated for each animal.[14]

*Tissue egg load.* The number of eggs/gram of tissue was determined by weighing a piece of liver or small intestine and digesting it overnight in 5% KOH. The hepatic and intestinal tissue egg loads were determined by multiplying the average number of eggs in each 1-mL sample by the total volume of KOH, then dividing by the weight of sample to yield the number of eggs/gram of tissue.[15]

**Statistical analysis.** Comparisons were made between the treated and untreated groups. The percentage change between the treated group and the infected untreated control was assessed using the formula (mean value of the untreated group - mean value of the treated group) × 100/mean value of the untreated group. Differences were tested for significance using the unpaired, two-tailed Student's *t*-test. The data were considered significant if $P$ values were less than 0.05.

## RESULTS

**Mirazid acute toxicity.** The three values of acute toxicity ($LD_{16}$, $LD_{50}$, and $LD_{84}$) determined were 1,985 mg/kg, 3,139 mg/kg, and 4,964 mg/kg, respectively, in normal CD1 Swiss albino mice. In mice infected with the Puerto Rican (Mill Hill) strain of *S. mansoni*, 100% and 75% mortality was observed 36 hours after dosing with Mirazid solution in DMSO:PEG at doses of 1,000 mg/kg × 3 and 300 mg/kg × 3, respectively.

**Mirazid antischistosomal activity.** Tables 1 and 2 show the effect of myrrh in different formulations in mice infected with the Egyptian (CD) strain of *S. mansoni*. Most of myrrh-treated animal groups, including those treated with the commercial preparation Mirazid, did not show significant worm reduction (mean ± SEM = 18.7 ± 2.2, 18.3 ± 2.0, 23.0 ± 3.5,

TABLE 1

Effect of myrrh derivatives in different formulations and doses in mice infected with the Egyptian (CD) strain of *Schistosoma mansoni* in comparison to praziquantel on worm burden, sex, and distribution

| Animal groups | Dose (mg/kg) | Mean ± SEM number of worms | | | | | |
|---|---|---|---|---|---|---|---|
| | | Hepatic | Porto-mesenteric | Total males | Total females | Total pairs | Total worms |
| Untreated control | 0 | 2.00 ± 0.33 | 20.75 ± 0.86 | 12.37 ± 0.53 | 10.38 ± 0.59 | 9.63 ± 0.70 | 22.75 ± 0.94 |
| Mirazid from resinous capsules | 250 × 5 | 3.17 ± 0.79 | 15.12 ± 1.33 | 10.33 ± 1.02 | 8.00 ± 0.42 | 7.67 ± 0.42 | 18.33* ± 1.02 |
| Mirazid from resinous capsules | 500 × 5 | 2.67 ± 0.76 | 16.00 ± 2.59 | 10.83 ± 0.95 | 7.834 ± 0.95 | 7.76 ± 1.27 | 18.67 ± 2.17 |
| Myrrh powder | 250 × 5 | 1.83 ± 0.60 | 14.67 ± 2.33 | 9.00* ± 1.03 | 7.50 ± 1.35 | 6.67 ± 1.20 | 16.5* ± 2.49 |
| Myrrh powder | 500 × 5 | 0.17 ± 0.17 | 18.17 ± 2.04 | 8.87* ± 1.08 | 9.50 ± 1.02 | 8.00 ± 1.00 | 18.33 ± 2.04 |
| Mirazid suspension | 250 × 5 | 2.14 ± 0.70 | 20.86 ± 3.45 | 13.14 ± 2.48 | 9.86 ± 1.45 | 9.29 ± 1.43 | 23.00 ± 3.46 |
| Mirazid suspension | 500 × 5 | 1.86 ± 0.74 | 17.57 ± 1.78 | 10.86 ± 1.68 | 9.43 ± 0.84 | 6.14 ± 0.91 | 20.29 ± 2.31 |
| Praziquantel | 200 × 5 | 1.14 ± 0.40 | 0.29 ± 0.18 | 0.71† ± 0.18 | 0.71† ± 0.42 | 0.00† ± 0.00 | 1.43† ± 0.53 |

* $P < 0.05$ versus controls.
† $P < 0.001$ versus controls.

and 20.3 ± 2.3 versus 22.8 ± 0.9 worms in the untreated control). A slight (19% and 27%) but significant worm reduction was observed in mice treated with the lowest dose (250 mg/kg × 5) of Mirazid from resinous capsules and myrrh powder. Praziquantel at a dose of 200 mg/kg × 5 produced a highly significant worm reduction (94%). Myrrh and Mirazid did not cause significant reduction in either the hepatic or intestinal tissue egg loads, while PZQ reduced them significantly by 60% and 90%, respectively. Eggs of all developmental stages were observed in the groups treated with all myrrh and Mirazid regimens. In the PZQ-treated group, no immature eggs were found, with marked reduction in mature eggs and a marked increase in dead eggs when compared with parallel values in the untreated control.

In mice infected with the Puerto Rican (Mill Hill) strain of *S. mansoni* killed 24 days after the end of treatment with the Mirazid solution in DMSO:PEG at a dose of 100 mg/kg × 3, a slight but significant reduction (35.9%) in total *S. mansoni* worms was observed. Insignificant worm reduction was observed in animals receiving the Mirazid solution at the dose of 300 mg/kg for three days (Table 3).

In hamsters infected with the Puerto Rican (NMRI) strain of *S. mansoni*, myrrh failed to induce any antibilharzial activity at doses ranging from 60 to 600 mg /kg for three consecutive days (Table 4).

In mice infected with the Brazilian (LE) strain of *S. mansoni* and treated with the myrrh extract in different doses and killed 3, 7, and 15 days after treatment, no schistosomicidal activity was observed, as shown by the insignificant changes in worm distribution, total worm burden, and percentage egg developmental stages (Table 4).

## DISCUSSION

This work showed a striking discrepancy between the antischistosomal activity observed in this study and that reported by previous investigators.[6] We have tested different doses (from 180 mg/kg up to 10,000 mg/kg) of myrrh and Mirazid in mice and hamsters infected with different strains of *S. mansoni* (Egyptian, Puerto Rican [Mill Hill] and [NMRI], and Brazilian [LE]). Animals were treated from the sixth to eighth weeks after infection. Apart from the group killed three days post-treatment to investigate hepatic shift of the worms, the rest of animal groups were killed 7, 15, and 24 days following treatment, which should allow the death of all drug-damaged worms.

In mice infected with the Egyptian (CD) strain of *S mansoni*, a dose (2, 500 mg/kg) approaching the $LD_{50}$ value of the drug (3,138.68 mg/kg) failed to significantly reduce the worm burden. The significant worm reductions of 27% and 19% were recorded in only two of six groups of mice receiving myrrh powder and Mirazid from resinous capsules at the smaller dose tested (1,250 mg/kg).

TABLE 2

Effect of myrrh derivatives in different formulations and doses in mice infected with the Egyptian (CD) strain of *Schistosoma mansoni* in comparison to praziquantel on percentage egg developmental stages and tissue egg load

| Treatment groups | Dose (mg/kg) | Mean ± SEM eggs per gram of tissue × $10^3$ | | Mean ± SEM % egg developmental stages | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Immature | | | | Total immature | Mature | Dead |
| | | Hepatic | Intestinal | 1st | 2nd | 3rd | 4th | | | |
| Untreated control | 0 | 14.8 ± 3.6 | 33.1 ± 6.3 | 8.5 ± 1.3 | 13.4 ± 1.9 | 25.6 ± 3.9 | 6.9 ± 1.9 | 54.4 ± 2.2 | 36.3 ± 3.0 | 9.4 ± 2.2 |
| Mirazid resinous capsules | 250 × 5 | 13.2 ± 4.0 | 32.4 ± 4.9 | 7.5 ± 3.1 | 12.8 ± 3.4 | 30.2 ± 3.0 | 4.2 ± 1.5 | 59.0 ± 5.2 | 34.2 ± 4.6 | 6.8 ± 3.3 |
| Mirazid resinous capsules | 500 × 5 | 16.1 ± 2.6 | 27.1 ± 4.0 | 6.7 ± 1.7 | 19.2 ± 2.4 | 30.0 ± 2.6 | 4.2 ± 1.5 | 60.0 ± 4.1 | 30.0 ± 2.2 | 10.0 ± 2.6 |
| Myrrh powder | 250 × 5 | 14.4 ± 3.3 | 28.4 ± 8.2 | 5.8 ± 1.5 | 22.5 ± 1.7 | 27.5 ± 1.1 | 4.2 ± 1.5 | 60.0 ± 0.0 | 30.5 ± 1.0 | 9.5 ± 1.0 |
| Myrrh powder | 500 × 5 | 14.1 ± 3.3 | 25.1 ± 5.7 | 9.3 ± 6.4 | 20.5 ± 0.3 | 25.8 ± 2.3 | 4.5 ± 1.4 | 60.0 ± 4.2 | 27.5 ± 1.2 | 12.5 ± 2.8 |
| Mirazid suspension | 250 × 5 | 17.7 ± 4.2 | 24.4 ± 5.7 | 4.3 ± 1.7 | 12.1 ± 1.8 | 28.6 ± 2.6 | 5.7 ± 1.3 | 50.7 ± 3.5 | 36.4 ± 2.8 | 12.9 ± 2.6 |
| Mirazid suspension | 500 × 5 | 13.2 ± 3.4 | 20.2 ± 2.8 | 7.9 ± 2.1 | 13.6 ± 1.4 | 32.1 ± 2.1 | 6.4 ± 1.8 | 60.0 ± 3.5 | 30.7 ± 3.8 | 9.3 ± 1.5 |
| Praziquantel | 200 × 5 | 5.9* ± 1.7 | 3.3* ± 1.9 | 0* | 0* | 0* | 0* | 0* | 0.5* ± 0.2 | 99.5* ± 0.2 |

* $P < 0.001$ versus controls.

TABLE 3
Effect of oral Mirazid in mice infected with the Puerto Rican (Mill Hill) strain of *Schistosoma mansoni* in comparison with praziquantel

| *S. mansoni* strain | Animal groups | Dose (mg/kg) | Days after treatment | Total worms* | Total males* | Total females* | Total couples* |
|---|---|---|---|---|---|---|---|
| Puerto-Rican (Mill Hill) | Infected control | – | – | 19.50 ± 1.72 | 11.38 ± 1.29 | 8.13 ± 0.93 | 7.25 ± 0.77 |
| | Mirazid solution | 100 × 3 | 24 | 12.50 ± 0.92† | 6.67 ± 0.67† | 5.83 ± 0.83 | 4.17 ± 0.87‡ |
| | Mirazid solution | 300 × 3 | 24 | 14.0 ± 2.0 | 8.00 ± 1.00 | 10.50 ± 5.50 | 5.50 ± 1.50 |
| | Praziquantel | 100 × 3 | 24 | 1.25 ± 0.77§ | 0.50 ± 0.38§ | 0.88 ± 0.48§ | 0.25 ± 0.25§ |

* Values are the mean ± SEM.
† $P < 0.01$ versus controls.
‡ $P < 0.05$ versus controls.
§ $P < 0.001$ versus controls.

In mice infected with the Puerto Rican (Mill Hill) strain of *S. mansoni* and receiving Mirazid solubilized in DMSO-PEG (2:1) at a dose of 100 mg/kg × 3, a higher but still modest worm reduction (36%) was recorded. The higher percentage of worm reduction observed in this case, compared with the trivial or absent antischistosomal activity in the rest of the myrrh-treated animals, is probably due to the use of Mirazid in a solution, which results in an increase in its bioavailability and thus its toxicity. It should be noted that in those groups receiving Mirazid as a solution at a dose of 300 mg/kg × 3 and 1,000 mg/kg × 3, the death of 75% and 100% of the animals was recorded 36 hours after dosing. It is worth mentioning that in the limited groups of animals infected with the Puerto Rican (Mill Hill) and Egyptian strains of *S. mansoni* showing significant worm reductions, the percentage worm reduction was modest (36%, 27%, and 19%), leaving the treated hosts with 60–80% residual worms.

In hamsters infected with the Puerto Rican (NMRI) strain of *S. mansoni* and treated with the crude extract of myrrh at doses of 60 mg/kg, 180 mg/kg, and 600 mg/kg for three consecutive days, no signs of antischistosomal activity were seen. An absence of antischistosomal activity was also observed in mice infected with the Brazilian (LE) strain of *S. mansoni* and treated with myrrh at doses as high as three times the $LD_{50}$ value (10,000 mg/kg), resulting in death of 40% and 20% of the treated animals assigned to be killed 7 and 15 days post-treatment. In addition, no alterations in either the total number of *S. mansoni* worms or egg developmental stages were observed in these groups. Moreover, myrrh failed to induce any early or late alteration in the oogram pattern when animals were killed 3, 7, or 15 days after treatment.

Our findings are in contrast with those of Badria and others.[6] They reported 76% and 75% worm reduction upon treatment of mice infected with an Egyptian strain of *S. mansoni* with myrrh at doses of 250 mg/kg and 500 mg/kg twice a day for three days. A possible reason for this discrepancy could be related to the somewhat atypical method of worm recovery adopted by Badria and others. They reported that worms in the mesenteric and portal veins were examined *in situ* using a 3× lens and the hepatic worms were counted by crushing the entire liver between glass plates for examination under a dissecting microscope.

In this work, the ratio of paired versus total worms was approximately the same in myrrh- and Mirazid-treated mice as in untreated controls, as opposed to the complete absence of worm couples in mice treated with a full dose of PZQ. In mice infected with the Egyptian strain of *S. mansoni* and treated with myrrh and Mirazid at different doses, no statistically significant reduction in either the hepatic or intestinal tissue egg load was observed. Moreover, eggs in all developmental stages were observed, even in the group showing some reduction in worm burden. Absence of oogram alterations after treatment with myrrh was also observed in mice infected with the Brazilian strain of *S. mansoni.* The percentage of egg developmental stages were comparable to those in untreated animals. Badria and others[6] reported a marked increase (93%) in mature eggs in Mirazid-treated mice with diminution up to complete absence of some of the immature egg stages. They did not report on the percentage of dead eggs, an increase of which can be considered as a hallmark effect for effective antischistosomals. The percentages of dead eggs were 100% in our PZQ-treated animals compared with 9% in

TABLE 4
Effect of oral myrrh suspensions in laboratory animals infected with Brazilian (LE) or Puerto Rican (NMRI) strains of *Schistosoma mansoni*

| *S. mansoni* strain | Animal groups | Myrrh dose (mg/kg) | Days after treatment | Total worms | % Mesenteric worms | % Liver worms | Dead worms | % Oogram alterations |
|---|---|---|---|---|---|---|---|---|
| Brazilian (LE) | Untreated | – | – | 24.90 | 91.10 | 8.90 | 0.00 | 0.00 |
| | Treated | 400 × 5 | 3 | 25.90 | 90.30 | 6.40 | 0.00 | 0.00 |
| | Treated | 1,000 × 5 | 3 | 22.70 | 93.60 | 8.90 | 0.00 | 0.00 |
| | Untreated | – | – | 18.30 | 94.50 | 5.50 | 0.00 | 0.00 |
| | Treated | 1,000 × 5 | 7 | 25.30 | 88.20 | 11.80 | 0.00 | 0.00 |
| | Treated | 2,000 × 5 | 7 | 27.00 | 90.10 | 9.90 | 0.00 | 0.00 |
| | Untreated | – | – | 16.3 | 98.0 | 2.0 | 0.00 | 0.00 |
| | Treated | 1,000 × 5 | 15 | 24.30 | 73.90 | 26.10 | 0.00 | 0.00 |
| | Treated | 2,000 × 5 | 15 | 19.00 | 89.50 | 10.50 | 0.00 | 0.00 |
| Puerto Rican (NMRI) | Untreated | – | – | 26 ± 50 | | | | |
| | Treated | 60 × 3 | 16 | 37 ± 60 | | | | |
| | Treated | 180 × 3 | 16 | 33 ± 30 | | | | |
| | Treated | 600 × 3 | 16 | 30 ± 30 | | | | |

untreated controls and 7–13% in those receiving myrrh or Mirazid.

Although the initial observation concerning the antischistosomal activity of Mirazid appeared promising, we have failed to detect any antischistosomal activity with various preparations and formulations in four different laboratories using two different experimental animal models harboring different strains of *S. mansoni.*

The question of why there is such a significant difference in our results versus those previously reported is difficult to answer. One possibility is that since Mirazid is not a well-defined chemical entity, but simply the extract of a plant, there could be a great deal of variability in the active ingredients of each batch. There are well documented cases demonstrating that "herbal preparations" show a pronounced lack of consistency in their chemical composition. A recent report[16] on dietary and herbal preparations stated that the main problem with dietary supplements and herbal preparations "is that their potency may vary and their purity is suspect." However, the possibility that such variability could be responsible for our results seems remote, since different batches of Mirazid were used in this study.

Based on the findings of this work, we cannot recommend the use of Mirazid in human cases of schistosomiasis for two reasons. First, Mirazid is a very complex mixture of chemicals and a standardization of its components appears unavoidable in view of the variable results obtained so far. In this context, it would be desirable to know the identity of the substance(s) with the hypothetical antischistosomal activity. Second, the use of a medication devoid of proven efficacy would be harmful to the individual patient because it would prevent him from using an effective drug. In addition, it would be harmful to the community because it would undermine the confidence in control measures. The scientific and medical profession should advise against the use of remedies that may sound attractive because of their "natural" name and origin, but that are not based on solid evidence of therapeutic activity.

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