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Treatment of Hookworm Infection with Furfurol

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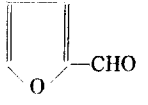
Furfurol was recently found to be effective against hookworm and *Ascaris lumbricoides* infections by various workers in Japan (Tsukamoto et al., 1952: Tanaka et al., 1953: Hoshi, 1956-57: Sato, 1960: Ando et al., 1962). They observed remarkable therapeutic efficacy on hookworm infection in man.

The incidence of hookworm in Korea was reported to be more than 20 percent by Choi et al. (1971). Recently, bephenium hydroxynaphthoate("Alcopar") has been the recommended choice for the oral treatment of hookworm infections.

This study was undertaken to further clarify whether this drug could be applied to cure hookworm diseases in man, and additionally, to compare the therapeutic efficacy between furfurol and bephenium hydroxynaphthoate.

MATERIAL AND METHODS

Furfurol is a furfurylaldehyde. It is marketed in Japan under the trade name of "Furfudol", and consists of 12 gelatin capsules. One gelatin capsule contains 1.3mg of furfurol, 0.5mg of benzyl-alcohol, and 48.2mg of castor oil. The total amount of furfurol in 12 gelatin capsules is calculated to be 15.6mg. The structural formula is as follows:



The majority of the hookworm carriers were selected from the children and teachers of primary school in Taegu. Ages of the carriers ranged from 6 to 46. The test cases were comprised of 7 adults and 21 children. The

Table 1. Results of pre-treatment survey of hookworm infections in 21 children and 7 adults

EPG count	Children		Adults	
	No. of cases	%	No. of cases	%
0— 400	0	0	2	28.6
400— 800	1	4.8	4	57.1
800—1200	7	33.3	1	14.3
1200—1600	5	23.8	0	0
1600—2000	4	19.0	0	0
2000—2400	1	4.8	0	0
2400—2800	2	9.5	0	0
2800—3200	1	4.8	0	0
Total	21	100	7	100

The results of this study were presented at 13th annual meeting of the Korean Society for Parasitology in 1971.

Table 2. Therpeutic efficacy of furfurol against hookworm

Patient	Body weight (kg.)	Dosage(as base)			Total egg count/ml. feces			Patient cured	
		Milli gram	Per diem	No. days	Before therapy	After therapy	Reduction percent	No.	Percent
8	18—27	5.2	1	3	10,600	1,600	84.9	6	75.0
13	22—33	7.8	1	2	20,200	5,000	75.7	6	46.2
7	46—64	15.6	1	1	4,000	1,200	70.0	4	57.1

treatment regimens varied depending on the age of the individual being tested. The regimen for adults consisted of giving 15.6mg of furfurol or 12 gelatin capsules 3 hours after a meal once a day. Children under 8 years old were administered 4 capsules once daily for a period of 3 days. The 9-12 years old were given 6 capsules once daily for 2 days. The side effects were checked by direct questioning of the individuals on successive days.

The worm burden was estimated by the Stoll egg count technique, as shown in table 1. In the post treatment, if no eggs were found in the Stoll count, a Ritche formalin-ether concentration was performed to confirm cure of the infection. Larval cultivation was made by the method devised by Harada and Mori in 1951. Filariform larvae cultivated by Harada and Mori in 1951. Fillariform larvae cultvated for 12 days at 25 degrees C in a B. C. D. incubator were examined to differentiate *Ancylostoma duodenale* from *Necator americanus.*

RESULTS

Twenty-eight carriers, harboring hookworms, were treated with furfurol gelatin capsules from 1 to 3 days (Table 2). Twenty-six (26) of the twenty-eight (28) carriers harbored *Ancylostoma duodenale,* and two (2) harbored *Necator americanus.* Therefore, the therapeutic effect of the drug in this study was directed largely to ancylostomiasis. Furfurol was proven to be considerably effective against hookworm infections. A single dose of 15.6mg(12 capsules) of the drug, given to 7 sdults on 1 day, resulted in an egg count reduction of 70.0 percent. The egg count was reduced slightly and the cure rate was appreciably increased in 13 children, when the adult dosage was divided into 3 portions (i.e. 5.2mg of base or 4 capsules) and administered once daily for 3 days. An egg count reduction of 75.7 percent and a cure rate of 46.2 percent were achieved when half the adult dosage(7.8mg of base or 6 capsules) was given once daily for 2 days.

Table 3. Side effects observed after the administration of furfurol in 21 children and 7 adults

Side effect	Children		Adults	
	No. cases	Precent	No. cases	Percent
Abd. discomfortness	2	9.5	1	14.3
Nausea	0	0	0	0
Vomiting	0	0	0	0
Headache	1	4.8	0	0
Malaise	0	0	0	0
Dizziness	0	0	0	0
Total	3	14.3	1	14.3

Mild side effects were observed in both children and adults(Table 3). A single dose of 15.6mg, administered once a day, caused a mild abdominal discomfort in adults. No ill effects were observed in children 9 to 12 years of age. when half of the adult dosage was given once daily for 2 days. Very mild side effects were observed in 3 cases of the 21 children after administering 5.2mg of the drug once daily for 3 days. Two of the three complained of

mild abdominal discomfort and the third child had a headache. The side effect appeared within 10 minutes after the first administration and continued for a period of 20 minutes. The headache appeared after the third administration of the drug to one of the children. Generally, abdomial discomfort in both children and adults was the only common side effect.

A comparison of the therapeutic effectiveness against hookworm utilizing furfurol and bephenium hydroxynaphthoate are presented in Table 4. The anthelmintic effect against hookworm with a single dose of 15.6mg of furfurol was similar to that of a single dose of 2.5gm of bephenium hydroxynaphthoate. By the t-test, no significant difference was found between these two drugs($p=0.24$).

DISCUSSION

Furfurol is a new anthelmintics. It was first synthesized in Japan for the treatment of hookworm infection and all the trials of the drug were made by Japanese workers, however, the results obtained have not been published yet.

Direct communication with Mishima (Director of Sanko Chemical Company, Japan) revealed that Japanese workers around 1950 found that furfurol showed a satisfactory anthelmintic effect on hookworms and *Ascaris lumbricoides* with little toxic effect on the host. A single dose of 15.6mg of furfurol, without any purge, has been commonly applied by several investigators as the standard dosage for adults.

Table 4. Comparison of therapeutic effects between furfurol and behenium hydroxynaphthoate

Anthelmintics	Dosage (as base)	No. of cases treated	Cases cured	
			No.	%
Furfurol	15.6mg	28	16	57.1
Bephenium hydroxynaphtoate	2.5gm	15	8	53.3

Tsukamoto et al. (1952) observed a 55.9 percent cure rate in 102 Ancylostoma infected patients given a single dose of 15.6mg (base) of the drug. Tanaka et al. (1953) achieved a cure rate of 77.7 percent in 238 patients who harbored hookworms. Furfurol proved to be less effective against *Ascaris lumbricoides* infection showing a cure rate of 70.5 percent. They also observed that there was almost no reactions to the drug. Later, Hoshi et al. (1956-57) observed that furfurol killed an earthworm within 3 minutes and *Ascaris lumbricoides var suum* within 30 minutes after being exposed to the drug. He also stated that the drug appeared active against hookworm infection showing the cure rate of 53.5 percent when given in a single dose of 15.6mg or 12 gelatin capsules. No adverse side effects due to the drug were recognized.

In comparison with other anthelmintics, Ando et al. (1962) stated that furfurol was more effective against hookworms than santonin and santonin-kainic acid mixture. Sato(1960) reached similar conclusions as to the high effectiveness of furfurol against hookworms.

Toxicological studies on mice, rabbits and dogs were performed by Tanaka et al. (1953). He observed no hepatic, renal, or hematological damage when relatively large amounts of furfurol were administered for a week. The LD^{50} dose for mice was 0.088 gm per 10 gm of body weight. The tests also demonstrated no side reactions in adults given a single dose of less than 25gm of the drug. Its metabolites were excreted in the urine of the examined.

As mentioned before, most of the trials have already been conducted by Japanese workers. Therefore, our studies primarily address the therapeutic efficacy of the drug against hookworm.

In the present study, a single dose of 15.6 mg of the drug, given to adults on 1 day, showed an egg count reduction of 70.0 percent and a cure rate of 57.1 percent with a transient side effect of mild abdominal discomfort. In the case of children, the egg count reductions of 75.7 to 84.9 percent and the cure rates of 46.2 to 75.0 percent were achieved. A case of headache in one of the twenty-one children tested was observed after the third administration of the drug. It is of questionable significance because he had caught cold at that time.

There were no significant differences in the therapeutic efficacy of furfurol as compared with bephenium hydroxynaphthoate(Table 4) except in the severeness of the side reactions. Furfurol showed essentially no side effects at therapeutic doses. Abdominal discomfort was the only common side effect and observed less frequently in children after the third administration of the drug. Bephenium hydroxynaphthoate usually revealed some side effects.

On the basis of the results of Tanaka et al. (1953), Hoshi(1956-57), Sato(1960), Ando et al. (1962), and the authors of this paper, it is concluded that furfurol has a remarkable therapeutic effect against hookworms. However, as the majority of the patients were infected with *Ancylostoma duodenale*, we could not demonstrate the anthelmintic effects against a group of Necator infected patients. Therefore, the authors wish to publish the effect of the drug on *Necator americanus* in other reports.

SUMMARY

Furfurol("Furfudol"), a new anthelmintics, was administered to 7 adults and 21 children (6-12 years old) in total amounts of 15.6mg (base) for 1 to 3days. It has proven to be effective against hookworms.

The anthelmintic effect against hookworms with a single dose of 15.6mg of furfurol was similar to that of a single dose of 2.5gm of bephenium hydroxynaphthoate. However, when a total of 15.6mg of the base was given to both children and adults, the side reactions were so mild that the drug can be administered for therapeutic regmens in mass treatment. Minor abdominal discomfort was the only common side effect. This is the primary advantage of furfurol as compared with bephenium hydroxynaphthoate.

These results have indicated that furfurol is safe in therapeutic dosage and is an effective agent to treat patients infected with hookworms.

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=국문초록=

Furfurol에 의한 구충증의 치료

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새로운 구충제인 furfurol는 일본학자들에 의해 구충증 및 회충증에 대하여 현저한 구충효과를 나타냄을 보고한 바가 있다. 저자들은 furfurol 총량 15.6mg를 구충증 성인 7명과 아동 21명(6세에서 12세까지)에 1일 또는 3일간 투약 하였든바 현저한 구충효과를 볼 수 있었다. 구충보충자에 대한 furfurol 1회량 15.6mg의 구충효과는 bephenium hydroxynaphthoate 1회량 2.5gm과 비슷하였다.

구충에 감염된 성인과 아동에게 furfurol 15.6mg를 투여하였을때의 부작용은 대단히 약함으로 집단치료제로 쓰는데 지장이 없겠으며 미약한 복부불쾌감이 유일한 부작용이었다. 이것이 bephenium hydroxynaphthoate에 비해 유리하였다. 이 결과로 미루어 보아 furfurol는 치료량으로 안전하며 구충증치료에 효과적인 약제로 인정된다.