J. Pharm. Pharmacol., 1965, **17**, 239–242 Received January 18, 1965

A comparison of anthelmintic and antibacterial activity of some phloroglucinol derivatives

K. BOWDEN AND W. J. ROSS

Some simple phloroglucinol derivatives previously reported to have anthelmintic properties have been tested for antibacterial action against *Staphylococcus aureus* and *Streptococcus pyogenes*. A comparison is made of the activities of these compounds against *Staph. aureus* and *Hymenolepis nana*.

WE report the antibacterial properties of a series of phloroglucinol compounds previously shown by Bowden, Broadbent & Ross (1965) to have anthelmintic action.

Experimental

PREPARATION OF COMPOUNDS

The synthesis of the phloroglucinol compounds was reported in the paper of Bowden, Broadbent & Ross (1965).

ANTIBACTERIAL TESTING

The compounds were tested for antibacterial activity at Smith Kline and French Laboratories, Welwyn Garden City. We thank Mr. S. G. E. Stevens for permission to publish these results and Mr. B. M. Jones for a description of the method, which is as follows.

A 10% solution or suspension of the substance under test in acetone was diluted with sterile nutrient broth (Oxoid CMI) to give concentrations of 0·01, 0·005 and 0·001%. Samples of each dilution were used in the test; uninoculated controls and nutrient broth blanks were also set up.

Each set of test dilutions was inoculated with 0·05 ml of 24 hr broth cultures of the test organisms and incubated at 37°. The samples were examined at 24 and 48 hr for growth compared with the controls. Samples found to inhibit growth in 48 hr at a concentration of 0·001% were tested at further dilutions, with incubation at 37° for 24 hr, until the minimum inhibitory concentration was reached.

ANTHELMINTIC TESTING

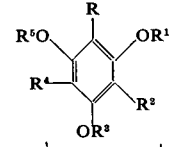
The method of testing for *in vitro* activity against *Hymenolepis nana* was that described by Sen & Hawking (1960). The *in vivo* activity against *H. nana* in mice was determined by the method of Steward (1955) and was based on the effect of a single dose of 400 mg of the substance given orally per kg body weight. The results have been given in detail by Bowden, Broadbent & Ross (1965).

Discussion

Sundman & Sundman (1961) examined the antibacterial properties of a series of phloroglucinol anthelmintics and found some relationship between activity against *Staphylococcus aureus in vitro* and anthelmintic

From the Smith Kline and French Research Institute, Welwyn Garden City, Herts.

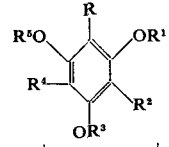
TABLE 1. ANTIBACTERIAL ACTIVITY OF COMPOUNDS

Compounds of the Type 

SK & F No.	R	R^1	R^2	R^3	R^4	R^5	Minimum inhibitory percentage concentration *in vitro* against *Staph. aureus*	Minimum inhibitory percentage concentration *in vitro* against *Str. pyrogenes*
90,525	H	H	Me·CO	H	Me·CO	H	0·0005	0·001
90,533	Me·CO	H	Me·CO	H	Me·CO	H	0·01	>0·01
90,536	Me	H	Me·CO	H	Me·CO	H	0·01	0·0005
90,540	H	H	Pr·CO	H	H	Me	0·005	>0·01
90,547	H	Me	Me·CO	Me	Me·CO	Me	>0·01	0·0005
90,562	H	H	Pr·CO	H	Pr·CO	H	0·00005	0·00005
90,567	H	H	Et·CO	H	Et·CO	H	<0·00001	0·00005
90,569	H	H	$Me_2CH·CO$	H	$Me_2CH·CO$	H	0·00005	0·00005
90,578	Me	H	Et·CO	H	Et·CO	H	0·01	0·005
90,589	Me	H	$Me_2·CH·CO$	H	$Me_2·CH·CO$	H	0·01	0·00001
90,590	H	H	Bu·CO	H	Bu·CO	H	0·00005	0·00001
90,592	Me	H	Bu·CO	H	Bu·CO	H	0·005	0·00005
90,599	H	H	Pr·CO	H	Me·CO	H	0·0005	0·0001
90,616	H	H	$C_5H_{11}·CO$	H	$C_5H_{11}·CO$	H	0·001	0·005
90,617	H	H	Et·CO	H	Me·CO	H	0·005	0·005
90,620	H	H	$C_6H_{13}·CO$	H	$C_6H_{13}·CO$	H	0·001	0·001
90,621	H	H	$Me_2·CH·(CH_2)_2·CO$	H	$Me_2·CH·(CH_2)_2·CO$	H	0·001	0·001

TABLE 1—*continued*

Compounds of the Type



SK & F No.	R	R^1	R^3	R_3	R^4	R^5	Minimum inhibitory percentage concentration *in vitro* against *Staph. aureus*	Minimum inhibitory percentage concentration *in vitro* against *Str. pyrogenes*
90,625	Me	H	C_6H_{11}·CO	H	C_6H_{11}·CO	H	0·01	0·01
90,629	Me	H	C_6H_{13}·CO	H	C_6H_{13}·CO	H	0·01	0·01
90,642	H	H	Ph·CH_2·CO	H	Ph·CH_2·CO	H	0·001	0·0001
90,644	H	H	Bu·CO	H	Me·CO	H	0·005	0·005
90,648	H	H	C_8H_{17}·CO	H	C_8H_{17}·CO	H	0·001	0·005
90,649	Me	H	Me_2·CH·CH_2·CO	H	Me_2·CH·CH_2·CO	H	0·0001	0·00005
90,651	H	Me·CO	Me·CO	Me·CO	Me·CO	Me·CO	0·00001	0·005
90,655	Me	H	C_7H_{15}·CO	H	C_7H_{15}·CO	H	>0·01	0·005
90,656	H	H	C_7H_{15}·CO	H	C_7H_{15}·CO	H	0·005	>0·01
90,657	H	H	Me_2·CH·CH_2·CO	H	Me_2·CH·CH_2·CO	H	0·0001	0·00005
90,681	H	H	Me_2·CH·$(CH_2)_2$·CO	H	H	H	0·005	0·005
90,717	Br	H	Pr·CO	H	Pr·CO	H	0·0001	0·0001

TABLE 2. COMPARISON OF *in vitro* ANTIBACTERIAL ACTIVITY WITH *in vitro* AND *in vivo* ANTHELMINTIC ACTIVITY

SK & F No.	Minimum inhibitory % concentration *in vitro* against *Staph. aureus*	Minimum inhibitory % concentration *in vitro* against *H. nana*	Activity % against *H. nana* in mice
90,547	>0·01	>0·01	0
90,589	,,	0·0002	100
90,625	,,	0·00001	98
90,655	,,	0·00002	94
90,533	0·01	0·01	0
90,536	,,	0·001	61
90,578	,,	0·0002	50
90,629	,,	0·00001	99
90,540	0·005	0·0002	0
90,592	,,	0·00001	99
90,617	,,	0·0002	14
90,644	,,	0·0001	45
90,656	,,	0·0001	92
90,681	,,	0·01	0
90,616	0·001	0·000005	100
90·620	,,	0·00001	74
90,621	,,	0·000005	99
90,642	,,	0·0001	13
90,648	,,	0·0001	90
90·525	,,	0·0002	0
90,599	,,	0·0001	87
90,649	0·0001	0·001	90
90,657	,,	0·00002	83
90,717	,,	0·0002	40
90,562	0·00005	0·0001	89
90,569	,,	0·0001	62
90,590	,,	0·000005	99
90,651	0·00001	0·002	32

activity. They suggested the antibacterial test might be a useful tool in the search for anthelmintic drugs.

In our series of phloroglucinol compounds, comparison of the *in vitro* activities of our phloroglucinol compounds against *Staph. aureus* with the *in vitro* and *in vivo* activities against *H. nana* (Table 2) shows that although antibacterial activity is often accompanied by high *in vitro* anthelmintic activity, this is not always so. An example of this is compound SK & F 90,681. When comparison is made between antibacterial and *in vivo* anthelmintic activity, more exceptions to the suggested general rule appear, for example, SK & F 90,540, 90,642, 90,525 and 90,651. In view of the possible fates of the substances in the host animal it is not surprising that this should be so. The retention of a few compounds with low anthelmintic activity by the antibacterial screening would not be a serious objection to the method but the reverse is not true. If activity against *Staph. aureus* had been used as a screen for potential anthelmintics in the series under consideration, some highly-active anthelmintics, for example SK & F 90,589, 90,625 and 90,655 would have been missed.

References

Bowden, K., Broadbent, J. L. & Ross, W. J. (1965). *Brit J. Pharmacol.* In the press.

Sen, A. B. & Hawking, F. (1960). *Ibid.*, **15**, 436–439.

Steward, J. S. (1955). *Parasitology*, **45**, 255–265.

Sundman, V. & Sundman, J. (1961). *Acta path. microbiol. scand.*, **53**, 345–355.