

BIOCHEMISTRY

Amino acid hydrazides as microbial antagonists

It has been reported¹ that γ -glutamyl hydrazide inhibits the growth of a number of microorganisms. It has been observed² that DL- β -aspartyl hydrazide can act as an inhibitory analogue of aspartic acid. In course of an investigation on amino acid analogues as possible antitumor agents, sixteen amino acid hydrazides (see Table) have been synthesized. Four microorganisms *viz.* *E. coli*, *S. carlsbergensis* (ATCC: 422), *S. faecalis* (ATCC: 8043), and *L. casei* (ATCC: 7469) were found to be inhibited in varying degree when grown in synthetic media, by most of the amino acid hydrazides prepared.

hydrazine hydrate on oil bath (110-115°) under reflux for periods ranging from 15 min. to 6 hr. Excess of hydrazine was removed under vacuum at 40° and the last trace of the hydrazine was eliminated by drying over conc. sulphuric acid under vacuum, and in many cases the products were obtained in crystalline form. Some of the amino acid hydrazides were obtained as oily liquid and they were isolated as crystalline salts of hydrochloric or sulphuric acid. The products were purified by recrystallization from alcohol-water mixture.

For microbiological screening of the amino acid hydrazides, the procedure of Foley³ was adopted using *E. coli*, *S. carlsbergensis*, *S. faecalis* and *L. casei* as test organisms. *E. coli* was grown in inorganic salts glucose medium⁴. Synthetic media published elsewhere were used for *S. carlsbergensis*⁵, *S. faecalis*⁶ and *L. casei*⁷. The

TABLE

Hydrazides	Melting point °C	Inhibition indices for half maximal inhibition†			
		<i>E. coli</i> (μ g/ml)	<i>S. carlsbergensis</i> (μ g/ml)	<i>S. faecalis</i> (μ g/ml)	<i>L. casei</i> (μ g/ml)
1. DL-Aspartic acid—di-	163-64	9.75	63.0	305.0	190.0
2. L-Glutamic acid—di-	137-38	6.00	>1000	57.8	196.0
3. L-Lysine—hydrochlorid	225-28	5.00	68.1	135.0	132.5
4. L-Histidine—sulphate	259-60	17.50	22.5	132.0	112.5
5. L-Arginine—sulphate	240-42	10.05	15.5	192.5	8.5
6. L-Tyrosine—	189-92	**	390.0	555.0	> 1000
7. DL-Phenylalanine—	69-71	**	350.0	500.0	712.0
8. DL-Alanine—hydrochloride	210*	3.13	30.0	>10000	> 1000
9. Glycine—sulphate	240 *	139.0	32.0	> 1000	> 1000
10. DL-Valine—	96-97	91.3	>1000	> 1000	465.0
11. DL-Leucine—hydrochloride	220 *	63.0	>1000	> 1000	> 1000
12. DL-Tryptophan—sulphate	220-25	96.0	50.0	570.0	648.0
13. DL-Methionine—sulphate	212-15	86.3	1000	> 1000	> 1000
14. DL-Serine—hydrochloride	210-15	64.0	290.0	> 1000	> 1000
15. DL-Threonine—sulphate	210 *	154.0	130.0	> 1000	136.0
16. DL-Isoleucine—sulphate	270-75	22.0	71.0	150.0	212.0

*Melts with decomposition

†It is expressed as the concentration in μ g/ml that reduces growth to half of that obtained in the absence of the test compound.

**No inhibition

amino acid hydrazides were prepared by heating ethyl or methyl ester of the corresponding amino acid with 5 molar equivalents of

degree of inhibition caused by the amino acid hydrazides on the growth of these microorganisms were determined by noting the

inhibition indices for half maximal inhibition. The results are shown in the Table. Details of the work will be published elsewhere.

Thanks are due to Sri S. K. Bhattacharya and Sri N. Maitra for technical assistance.

S. B. LODH
P. R. PAL

Department of Biochemistry,
Indian Statistical Institute,
Calcutta-35.
14-6-1968

* American Type Culture Collection.

- ¹ J. A. Paper and H. McIlwain, *Biochem. J.*, **42**, 485, 1948.
- ² M. N. Mickelson and R. S. Flippin, *Arch. Biochem. Biophys.*, **64**, 246, 1956.
- ³ G. E. Foley, R. E. McCarthy, V. M. Binns, E. E. Snell, B. M. Guirard, G. W. Kidder, V. C. Dewey and P. S. Thayer, *Ann. N.Y. Acad. Sci.*, **76**, 413, 1958.
- ⁴ H. J. Kohn and J. S. Harris, *J. Pharmacol. Exptl. Therapy*, **73**, 344, 1941.
- ⁵ L. Atkin, L. W. Williams, A. S. Schultz and C. N. Frey, *Ind. Eng. Chem. Anal. Ed.*, **16**, 67, 1944.
- ⁶ Difco Manual, 1953, 9th Ed. p. 225, (Difco Laboratories, Detroit, Mich., U.S.A.).
- ⁷ *ibid.* p. 215.