Title	Studies on the Antimetabolites of Amino Acids. (IX) : Biological Activity of Aspartic Acid Mono- and Dihydrazide
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Citation	Bulletin of the Institute for Chemical Research, Kyoto University (1958), 36(4): 118-119
Issue Date	1958-07-31
URL	http://hdl.handle.net/2433/75633
Right	
Type	Departmental Bulletin Paper
Textversion	publisher

Studies on the Antimetabolites of Amino Acids. (VIII)

Formation of Arginosuccinic Acid and Canavanosuccinic Acid in Microorganisms

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Journal of the Pharmaceutical Society of Japan (*Yakugaku Zasshi*), **77**, 282 (1957)

Acetone-dried cells of *Escherichia coli* and *Lactobacillus arabinosus* were prepared and the formation of arginosuccinic acid (ASA) and canavanosuccinic acid (CSA) from arginine or canavanine and fumarate was followed by paper electrophoresis and paper chromatography. ASA was found to be formed by the parent strain of *E. coli* but it was not detected with its arginine-requiring mutant (cannot be compensated with ornithine or citrulline). Even with the parent strain, its culture in a medium containing arginine causes disappearance of arginosuccinase activity and ASA formation does not take place. The formation of CSA was identical with the case of ASA. With *Lact. arabinosus* ASA was formed from citrulline and aspartic acid, as well as from arginine and fumarate. CSA itself inhibits proliferation of *Lact. arabinosus* and this inhibition is easily recoverd with arginine. Considerations were made on the action mechanism of canavanine from these experimental results.

Studies on the Antimetabolites of Amino Acids. (IX)

Biological Activity of Aspartic Acid Mono- and Dihydrazide

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Journal of the Pharmaceutical Society of Japan (*Yakugaku Zasshi*), **77**, 1218 (1957)

As partic acid mono- and dihydrazides, and 3-hydroxyaspartic acid were synthesized and their action in inhibiting the growth of *Leuconostoc mesenteroides* P-60 and *Escherichia coli* No. 1 was examined. In the presence of aspartic acid, growth of *Leuc. mesenteroides* was completely inhibited by 100 γ/cc. of monohydrazide, 500 γ/cc. of 3-hydroxyaspartic acid, and 2000 γ/cc. of dihydrazide. So far as *Leuc. mesenteroides* is concened, therefore, the growth-inhibitory action of monohydrazide is stronger than that of dihydrazide. On the contrary, the growth of *E. coli* No. 1, which requires no aspartic acid for growth, was more strongly inhibited by the dihydrazide, the effective concentration for 50 % inhibition being 55 γ/cc. of the monohydrazide and 33 γ/cc. of

the dihydrazide. It was also observed that the dihydrazide had stronger inhibitory action than the monohydrazide upon glutamic acid decarboxylase of *E. coli*. The antagonism of hydrazides to aspartic acid was non-competitive in all the cases but growth inhibition of *E. coli* was more easily recovered by asparagine rather than by aspartic acid. Consideration were made on the biological activity of amino acid hydrazides from foregoing experimental results.

Antagonistic Action of CNS Stimulants against Barbiturates in Mice

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Japanese Journal of Pharmacy and Chemistry
(*Yakugaku Kenkyu*), **29**, 1052 (1957)

After Maloney *et al.* (1931) reported that Picrotoxin reduced anesthesia by barbiturate, antagonistic action of many kinds of CNS stimulants against barbiturates has been observed by various workers. But the comparative evaluation of their actions is not yet sufficient.

In this paper, the comparison was made with antagonistic action of LD 50 CNS stimulant against barbiturate hypnosis and, of 1/2 LD 50 CNS stimulant against Evipan Sodium LD 50. The results obtained are shown in the following table.

CNS stimulant	Antagonistic effect in mice		
	to Veronal hypnosis	to Evipan hypnosis	to Evipan toxicity(LD 50)
Picrotoxine	###	###	###
β-methyl-β- ethyl glutarimide	##	###	###
Metrazol	##	##	###
N,N′-Dibutyl-N.N′-dicarboxy morpholide etheylendiamine	+	+	##
Strychinine	+	−	+
Coffeine sodium benzoate	−	−	±
Methamphetamine	−	−	−

Marked, ## moderate, + slight, ± none, − on the contrary, synergistic.

Pharmacology of Benzhydrol Derivatives

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