The metabolism of γ-aminobutyrylcholine

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KURIAKI *et al.*[1] and Kewitz[2] have indicated isolation of γ-aminobutyrylcholine (GABA-Ch) from extracts of the brains of dogs and swine. Pharmacologic evaluation of this choline ester prompted these investigators to suggest that GABA-Ch may be a transmitter of inhibitory pathways in the nervous system. It seemed of interest, therefore, to investigate the possible routes of metabolism of GABA-Ch. The results of these studies with appropriate substrate comparisons are presented in Table 1. The methods employed have been described.[3]

TABLE 1.

Enzyme	Inhibitor		Substrate
1. Cholinesterase		GABA-Ch*	Butyrylcholine
(a) Human plasma	0	40	385
	P†	3	58
(b) Bovine r.b.c.	0	0	5
(c) Mouse brain	0	0	38
(d) Mouse liver	0	26	359
	P†	1	16
(e) Mouse plasma	0	19	348
(f) Cat plasma	0	0	315
2. Amine Oxidases	GABA-Ch*	Putrescine	5-Hydroxytryptamine
(a) Mono-(g pig liver)	0	—	66
(b) Diamine-(hog kidney)	0	22	—

All results are expressed as microlitres of CO_2 (cholinesterase) evolved or O_2 (oxidase) utilized per 30 min per flask, minus enzyme and substrate blanks. Since the primary amine group of GABA-Ch will influence the evolution of CO_2 in the cholinesterase experiments, the reaction was carried out at pH 7·2 employing the chloride–hydrochloride salt. Though the CO_2 evolution ester hydrolysis relationship is not stoichiometric, the results obtained are indicative of the order of activity of GABA-Ch.

* GABA-Ch (chloride hydrochloride salt) was kindly supplied by Dr. K. Kuriaki.

† P = physostigmine, 10^{-5} M final concentration.

It appears from this preliminary work that few of the enzymes tested were able to catalyse the hydrolysis of the ester. Where hydrolysis was demonstrated, the rate of reaction was small in comparison to the rate of hydrolysis of butyrylcholine. Similar findings have been reported when another naturally-occurring choline ester, imidazole-acrylylcholine,[4, 5] was employed as a cholinesterase substrate.

The catalysed hydrolysis of GABA-Ch by human plasma and mouse liver was inhibited by physostigmine. GABA-Ch did not serve as a substrate for either monoamine or diamine oxidase.

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