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Effect of carbon chain length and amino group position on neutral amino acid transport systems in rat small intestine

The participation of more than one system in the transport of neutral amino acids by different tissues has been discussed recently[1–3]. How many systems there are and whether individual differences exist between different tissues cannot yet be decided from the limited information available. In the rat small intestine two systems are known to be involved in neutral amino acid transfer[4–6], and this report presents further data on their specificity.

These systems can be characterised by using two amino acids, the transfer of one being restricted to one system, and the transfer of the other restricted to the other system. Published data indicate that methionine transfer is transported predominantly by one system in rat intestine[4] whereas the transport of the *N*-methyl substituted amino acid, sarcosine, occurs mainly by a separate system in rat[5] and hamster[7]. On this basis we have examined the effects of several neutral amino acids on the transport of methionine and sarcosine, the object being to determine the influence of chain length and position of the amino group. The inhibitory amino acids can be divided into two groups, (1) straight chain aliphatic α-amino acids with progressively increasing chain length and (2) α-, β- and γ-amino acids.

Experiments were carried out with 17 cm everted sacs of rat jejunum. The sacs contained 1 ml bicarbonate saline (serosal fluid) and were suspended in a mucosal fluid of 25 ml bicarbonate saline containing 28 mM glucose and 1.0 mM L-[*Me*-^{14}C]-methionine or 1.0 mM [*carboxyl*-^{14}C]sarcosine. Other amino acids in a concentration of 10 mM were added to the mucosal fluid as indicated. After gassing with O_2–CO_2 (95:5, v/v) the sacs were incubated at 38° for 30 min, and the amount of methionine or sarcosine present in the gut wall and final serosal fluid was determined using a liquid scintillation counter.

The results in Tables I and II show the amount of methionine or sarcosine transported (μmoles/30 min per 17 cm) and the percentage inhibition of transport caused by addition of other amino acids. Methionine transport is progressively in-

TABLE I

EFFECT OF STRAIGHT CHAIN α-AMINO ACIDS ON METHIONINE AND SARCOSINE TRANSFER BY THE INTESTINE

The methionine and sarcosine were initially present in a concentration of 1.0 mM while other amino acids were present in a concentration of 10 mM. The figures are the means for the number of experiments shown in parentheses with S.E.

Inhibitor	*Methionine*		*Sarcosine*	
	Amount transported (*µmoles*)	*Inhibition* (%)	*Amount transported* (*µmoles*)	*Inhibition* (%)
None	14.59 ± 0.17 (25)	—	5.37 ± 0.14 (23)	—
Glycine	12.44 ± 0.31 (8)	14.7	3.73 ± 0.18 (12)	30.5
L-α-Alanine	9.15 ± 0.27 (18)	37.3	3.78 ± 0.16 (15)	29.6
L-α-Aminobutyric acid	6.27 ± 0.49 (6)	57.0	4.80 ± 0.34 (7)	10.5
L-Norvaline	3.60 ± 0.24 (5)	75.3	4.89 ± 0.29 (10)	8.9
L-Norleucine	3.21 ± 0.38 (5)	77.9	4.69 ± 0.24 (11)	12.6

TABLE II

EFFECT OF α-, β- AND γ-AMINO ACIDS ON METHIONINE AND SARCOSINE TRANSFER BY THE INTESTINE

The methionine and sarcosine were initially present in a concentration of 1 0 mM while other amino acids were present in a concentration of 10 mM. The figures are the means for the number of experiments shown in parentheses with S.E.

Inhibitor	*Methionine*		*Sarcosine*	
	Amount transported (μ*moles*)	*Inhibition* (%)	*Amount transported* (μ*moles*)	*Inhibition* (%)
None	14.59 ± 0.17 (25)	—	5.37 ± 0.14 (23)	—
L-α-Alanine	9.15 ± 0.27 (18)	37 3	3.78 ± 0.16 (15)	29.6
β-Alanine	13.90 ± 0.51 (7)	4 7	3.67 ± 0.06 (10)	31 6
L-α-Aminobutyric acid	6 27 ± 0.49 (6)	57.0	4.80 ± 0.34 (7)	10.5
DL-α-Aminobutyric acid	8 91 ± 0.29 (11)	38.9	4.70 ± 0.20 (13)	12.4
β-Aminobutyric acid	13.96 ± 0.41 (7)	4.3	3.66 ± 0.06 (10)	31.8
γ-Aminobutyric acid	13.95 ± 0.11 (6)	4.5	3.08 ± 0.18 (6)	42 4
α-Aminoisobutyric acid	15.09 ± 0 42 (6)	0	4 49 ± 0 22 (8)	16 4
β-Aminoisobutyric acid	14.37 ± 0.27 (6)	1.5	4.43 ± 0 15 (9)	17 6

hibited with increasing chain length; the longer the carbon chain the greater the inhibition. It is interesting to compare this finding with the results of MATTHEWS AND LASTER[8]. In contrast sarcosine transport is inhibited less with increasing chain length, the short chain glycine and alanine causing more inhibition than the longer α-aminobutyric acid, norvaline and norleucine. It is clear that the order of effectiveness as inhibitors can be reversed depending on which transport system is studied. The effect of a similar sequence of amino acids on histidine transfer was examined and their inhibitory activity paralleled our results with methionine[1].

The methionine system is significantly inhibited only by α-amino acids whereas the sarcosine system is inhibited by α-, β- and γ-amino acids. The importance of the position of the amino group is demonstrated more clearly by extending the carbon chain from amino propionic acid to aminobutyric acid. Methionine transport is strongly inhibited by α-aminobutyric acid but β- and γ-aminobutyric acid have little effect. In contrast, sarcosine transport is little affected by α-aminobutyric acid but β- and γ-aminobutyric acids strongly inhibit. It appears that on increasing the length of carbon chain, separation of the amino and carboxyl groups greatly reduces inhibition of the methionine system but produces more effective inhibition of the sarcosine system. Whether this will hold for still wider separation of amino and carboxyl groups is not known.

The branched chain α- and β-aminoisobutyric acids are not particularly effective inhibitors of either system although sarcosine transfer is clearly more affected than methionine. Straight chain α-amino-*n*-butyric acid causes 57 % inhibition of methionine transfer whereas the branched chain α-aminoisobutyric acid has no effect. It remains to be determined whether this difference is noticeable with further increase in chain length, *i.e.*, are isovaline and isoleucine less effective than norvaline and norleucine, respectively?

This study supports and extends earlier observations which led to the conclusion that two systems are involved in the transport of neutral amino acids by rat small intestine[4]. In general it appears that small water-soluble neutral amino acids are more inhibitory to the sarcosine system whereas the larger, more lipid-soluble neutral amino acids have greater affinity for the methionine system. It is possible that physical factors, *e.g.* pore size and lipid–water partition coefficients determine to some extent the chemical specificity of neutral amino acid transport.

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