

578

EFFECT OF SIDE CHAIN ON TUMOR SPECIFICITY OF ALICYCLIC- α -AMINO ACIDS.

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At the last conference we reported that unnatural amino acids with 8-through 4-membered alicyclic ring systems showed significant tumor specificities. The present work studied the tumor specificities of 6-membered alicyclic- α -amino acid with side chain (methyl group, phenyl group) such as 1-Amino cyclohexane carboxylic acid (ACHC), 1-Amino-2-methyl cyclohexane carboxylic acid (2-MeACHC), 1-Amino-3-methyl cyclohexane carboxylic acid (3-MeACHC), 1-Amino-4-methyl cyclohexane carboxylic acid (4-MeACHC), 1-Amino-4-phenyl cyclohexane carboxylic acid (4-PhACHC). These C-14-labeled amino acids were synthesized by our modified Bücherer synthesis (55%~75% radiochemical yield) and the tissue distributions of C-14-2-MeACHC, C-14-3-MeACHC, C-14-4-MeACHC and C-14-4-PhACHC were compared with that of C-14-ACHC. These studies showed that 3-methyl and 4-methyl alicyclic- α -amino acids such as 3-MeACHC, 4-MeACHC had slightly higher tumor specificity than ACHC. On the other hand, 2-methyl alicyclic- α -amino acid such as 2-MeACHC and 4-phenyl alicyclic- α -amino acid such as 4-PhACHC showed remarkably lower tumor specificity than ACHC.

579

 α -AMINOISOBUTYRICACID ANALOG: 2-AMINO-2-METHYLBUTANOICACID (2-AMB), A POTENTIAL TUMOR-SEEKING AGENT. K.Siba,H.Mori,and K.Hisada.Kanazawa University,Kanazawa.

It has been reported that the unnatural, α -amino acids without α -hydrogen have high tumor specificities.

We prepared a new unnatural α -amino acid without α -hydrogen, C-14-labeled 2-Amino-2-methyl butanoic acid (C-14-2-AMB) and evaluated the potentiality as a tumor-seeking agent.

C-14-2-AMB was synthesized using C-14 potassium cyanide and the corresponding ketone in about 94% yield by our modified Bücherer synthesis.

C-14-2-AMB was intravenously injected through tail vein into separate groups of the mice with Ehrlich Tumor and the tissue distribution of C-14-2-AMB was compared with that of C-14- α -AIB and C-14-ACPC. These studies showed that tumor to tissue concentration ratios of C-14-2-AMB is significantly higher than C-14-ACPC and C-14- α -AIB, while the tumor uptake of C-14-2-AMB is slightly lower than C-14-ACPC and C-14- α -AIB.

These results suggest that 2-AMB may have good potential as a tumor-seeking agent.