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CONCERNING THE MECHANISM OF THE MAMMALIAN CONVERSION OF
TRYPTOPHAN INTO NICOTINIC ACID *

By

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The mechanism of the conversion of tryptophan to nicotinic acid involving kynurenine and 3-hydroxyanthranilic acid as intermediates has been demonstrated in *Neurospora*, (1) and confirmatory feeding experiments in rats have been reported recently. We (2) have shown (3) that tryptophan- β -C¹⁴ is directly converted into kynurenine in the intact mammal, but because the labeled carbon atom was lost, it was necessary (by other means) to establish its further conversion to nicotinic acid.

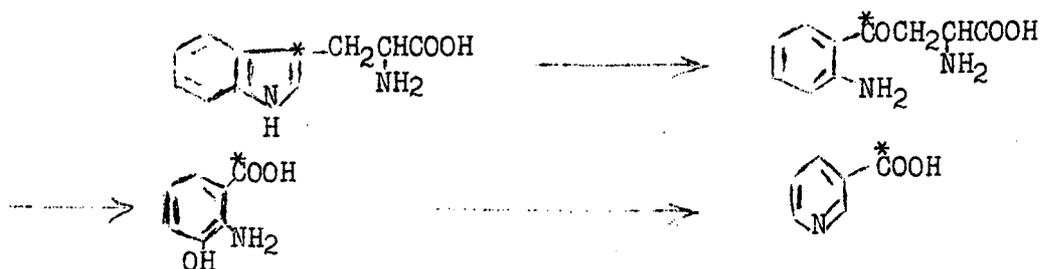
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† On leave from Sir William Dunn School of Pathology, University of Oxford, England.

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We have now synthesized (4) DL-tryptophan-3-C¹⁴ and have shown that the conversion proceeds in the same fashion in the rat as in Neurospora:



The tryptophan (226 mg.) was fed to three rats by stomach tube, and the 24 hour urines were passed through a Permutit column. The N-methylnicotinamide (750 μ g.) was eluted with KCl, (5) 76 mg. of carrier N-methylnicotinamide chloride was added, and the picrate was formed and purified. The amide was freed of picric acid, and converted with HCl in a sealed tube into nicotinic acid which was purified and decarboxylated catalytically. The specific activities are shown in the table. A significant observation is that the carbon atom, which is a precursor to the carboxyl group of the hydroxyanthranilic acid, becomes the carboxyl carbon of nicotinic acid.

| COMPOUND | SPECIFIC ACTIVITY counts/min./mg. |
|--|--------------------------------------|
| Tryptophan (fed) | 2740 |
| N-Methylnicotinamide picrate (carrier) | 0.75 |
| Nicotinic Acid | 2.0 (2.2 calc'd.) |
| Barium Carbonate from decarboxylation | 1.3 (1.2 calc'd.) |

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