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Effect of Ingestion of Various Pyridine Compounds on Excretion of Specific Fluorescent Substances in Urine.*

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In previous publications[1, 2] attention has been called to 2 fluorescent substances in the urine, the concentrations of which appear to depend upon the body stores of nicotinic acid. The composition of these 2 substances which we have designated F_1 and F_2 is as yet unknown. They are characterized by their fluorescence with ultraviolet light, F_1 having an emission spectrum ranging from 4,000 to 4,800 angstrom units with a maximum at 4,350 Å, and F_2 having an emission spectrum ranging from 4,200 to 5,400 Å with a maximum at 4,550 Å. With suitable extraction procedures the excretion of these 2 substances can be measured quantitatively with a fluophotometer. We have found that F_1 is normally present in relatively small quantity in the urine but increases markedly in pellagra. F_2, on the other hand, is present in greater quantity under normal conditions but disappears in pellagra. The administration of nicotinic acid to a pellagrin causes a prompt reduction of F_1 and the reappearance of F_2. Similarly, the administration of nicotinic acid to a normal individual causes F_2 to increase well beyond the normal limits. To explain these facts, we have suggested the hypothesis that F_1 is converted into F_2 through the agency of some nicotinic acid containing enzyme. In nicotinic acid deficiency, failure of such conversion causes F_1 to accumulate and F_2 to disappear, whereas in the presence of this catalyst, F_2 is formed in quantities which bear some relation to the supply of nicotinic acid.

It seemed of interest to ascertain the effect of various pyridine and pyrazine compounds on the excretion of F_2 in human subjects in order to determine if there were any parallelism between this property and the ability to cure pellagra. The compounds chosen for testing were: nicotinic acid, nicotinamide, sodium nicotinate, dinicotinic acid, trigonelline, 2-6 dimethyl nicotinic acid, quinolinic acid, pyrazine monocarboxylic acid, pyrazine, 2,3-dicarboxylic acid, pyridine β-carboxylic acid diethyl amide (coramine) and sulfapyridine. These

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1 Najjar, V. A., and Wood, R. W., PROC. SOC. EXP. BIOL. AND MED., 1940, **44**, 386.

2 Najjar, V. A., and Holt, L. E., Jr., *Science*, 1941, **93**, 20.

TABLE I.
Excretion of F_2 in Urine (Najjar-Wood Units) During a 4-hour Period after Ingestion of Various Pyridine and Pyrazine Compounds.

Compound ingested	Dose, mg	Before treatment	After treatment
Nicotinic acid	100	6	60
Nicotinamide	100	12	87
Pyridine β-carboxylic acid diethyl-amide (coramine)	2500	10	104
Trigonelline	200	15	11
2-6,dimethyl dinicotinic acid K salt	200	10	13
Quinolinic acid	200	4	5
Pyrazine monocarboxylic acid	100	7	2
Pyrazine 2,3-dicarboxylic acid	200	5	4
Dinicotinic acid	200	8	9

compounds were fed to normal male adults, the urine being followed for a period of several hours before and after the test dose. With one exception 3 experiments were carried out with each compound. The analytical procedure used for the determination of F_2 was that described by Najjar and Wood.[1]

Results. It was found that only 4 of the compounds tested: namely, nicotinic acid, nicotinamide, sodium nicotinate and coramine produced a rise in the excretion of F_2 in the urine. The rise was significant in each of the experiments and was of comparable magnitude. With the other compounds no appreciable increase in excretion of F_2 occurred, even with doses many times that required to cause an increase in F_2 with nicotinic acid. Typical protocols obtained in one subject are shown in Table I.

In a few experiments we tested the effect of sodium nicotinate given intravenously. This procedure resulted in an increase of F_2 comparable to that obtained by oral ingestion.

Comment. It is worthy of note that the ability of these pyridine compounds to produce an increased excretion of F_2 in the urine shows a marked parallelism to the efficacy of the compound in the treatment of human pellagra. In the experience of Sydenstricker[3] all 4 of the compounds which in our hands gave rise to increased F_2 excretion have been clinically effective, whereas of the compounds which gave negative results in our tests only one (quinolinic acid) was found by him to be antipellagric for man and that in doses well in excess of those customarily employed. It is possible that if we had used large doses of some of these compounds, as we did in the case of coramine, our results might have been different.†

[3] Sydenstricker, V. P., personal communication.

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