ican Chemical Society, and industrial leaders who are especially interested in the outcome, to read and study carefully the data which the society has assembled on scientific and technological manpower, and having done so to express their views to their Congressmen and to their Senators in order that their representatives may have the reaction of those especially qualified to advise them in this matter. They will read and study your letters especially if you are or are to become a veteran.

Your officials are doing everything in their power to remedy the situation. The public must be aroused. Without the aid of those who will suffer most from the loss of an entire generation of scientists, we are helpless. Please do your duty as you see it.

SPECIAL ARTICLES

GROWTH-RETARDING EFFECT OF CORN IN NICOTINIC ACID-LOW RATIONS AND ITS COUNTERACTION BY TRYPTOPHANE[1]

IN a previous study,[2] it was shown that corn or corn grits exert a pronounced growth-retarding effect in rats on nicotinic acid-low rations and that this untoward effect can be completely counteracted by including 1 mg of nicotinic acid per 100 gm of ration. At the same time, it was reported that raising the level of casein modified the action of corn. This report is an elucidation of that observation.

The basal ration used had the following composition: Labco casein (3 times extracted with 95 per cent. ethanol) 15, sucrose 78, corn oil 3, salts IV[3] 4 and cystine 0.15 parts. Vitamins were incorporated in the ration at the following levels: thiamine 0.2, riboflavin 0.3, pyridoxine 0.25, calcium pantothenate 2.0, choline chloride 100, inositol 10, 2-methyl-naphthaquinone 0.1 and biotin 0.01 mg per 100 gm respectively. Halibut liver oil (diluted 1:2 with corn oil) was fed at a level of 2 drops per week, with α-tocopherol included at 0.5 mg per drop. A norite eluate of solubilized liver extract, prepared so as to contain practically no nicotinic acid, was fed, where indicated, at a level equivalent to 11.5 μg B_c (*S. lactis* assay) per 100 gms of ration. These vitamin levels were maintained both in the basal and corn-supplemented rations and the nicotinic acid content of the basal ration was < 0.01 mg per 100 gm.

The low protein (L.P.) basal ration contained 15 per cent. casein and the high protein (H.P.) 20 per cent. casein. In all cases, corn was incorporated so as to replace 40 per cent. of the entire ration, which reduced the casein levels of the L.P. and H.P. rations to 9 and 12 per cent. respectively. Whole yellow corn meal and corn grits at a level of 40 per cent. added 3.4 and 3.6 per cent. of crude protein (N × 6.25), respectively. Weanling male rats were used throughout and in all cases at least 3 animals were used per group. The growth results obtained on the two rations are shown in Table 1 and demonstrate that casein has a marked protective action.

Since the protective action of casein could not be explained on the basis of its nicotinic acid content, other possible factors were considered. Inasmuch as corn is deficient in the essential amino acids lysine and tryptophane, it seemed logical that the additional casein might be contributing these amino acids in

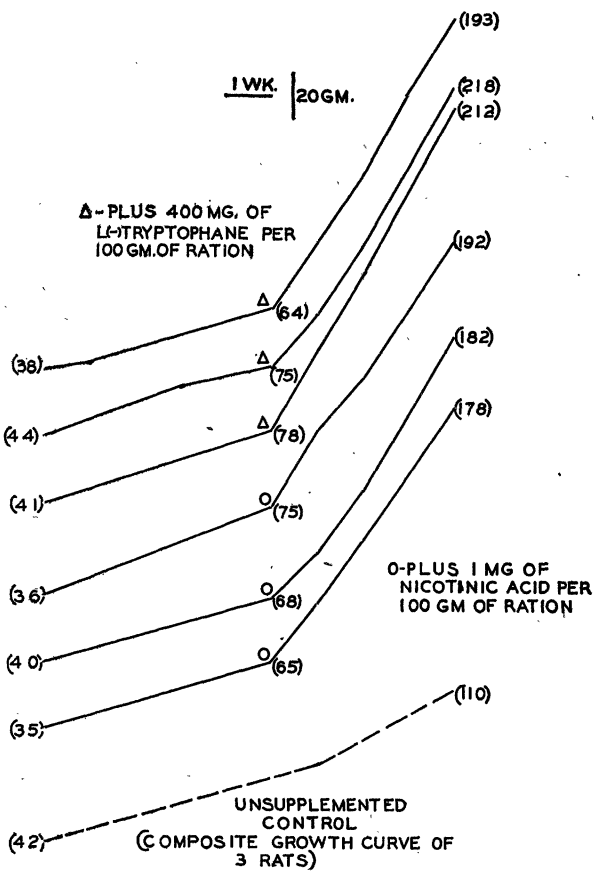

FIG. 1. Growth responses resulting from the addition of l(-)tryptophane or nicotinic acid to the low casein plus corn grits diet and the growth curve of the unsupplemented control. (Figures in parentheses represent rat weights).

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[3] P. H. Phillips and E. B. Hart, *Jour. Biol. Chem.*, 109: 657, 1935.

sufficient quantity to overcome the deficiency caused by corn. It was found that 1(+)lysine included in the ration at a level of 0.5 per cent. did not alleviate the deleterious effect of corn grits. This was not entirely unexpected, since even the low level of casein supplied almost enough lysine to satisfy the requirement indicated by Rose.[4] In concurrent experiments,[5] in which the low level of casein was replaced by purified proteins which contained more tryptophane than casein, corn grits did not produce a growth depression. When l-tryptophane was added at a level of 0.4 per cent. to the low casein diet plus corn grits, there was a dramatic growth response, Fig. 1. When fed from the beginning in this ration, (d,l) tryptophane at levels of 0.5 and 1.0 per cent. was also effective, as was 1(−)tryptophane in amounts as low as 0.05 gm per 100 gm of ration (Table 1). It should be noted, however, that nicotinic acid in much smaller amounts also affords complete protection from the untoward action of corn (Fig. 1).

The extensive use of polished rice prompted us to compare it with corn grits on the same experimental régime. As can be seen in table 1, rice is an excellent supplement even though it contains less nicotinic acid than the whole yellow corn. However, the fact that it contains somewhat more tryptophane than corn may be significant.

Although the efficacy of feeding either nicotinic acid or tryptophane is obvious, the mechanism of their apparent interchangeability remains obscure. It is also difficult to say whether or not the phenomena observed in the rat have a counterpart in human pellagra. The evidence in the literature does attribute a role to protein deficiency in the etiology of pellagra, since Goldberger[6] found rather large amounts of milk and meat proteins to be of value in treating pellagrins. He also observed some beneficial results from tryptophane and cystine.[7] However, in 1925 Goldberger reported[8] that "it is possible that the P-P factor plays the sole essential role in the prevention (and thus the causation) of pellagra." The present report and previous studies show clearly that nicotinic acid is capable of playing "the sole essential role," but it is also shown that protein or tryptophane, particularly, may have a profound effect on the nicotinic acid requirement.

TABLE 1

EFFECT OF NICOTINIC ACID AND TRYPTOPHANE ON THE GROWTH OF RATS ON RATIONS CONTAINING CORN

Ration used	Total protein content (N × 6.25)	Tryptophane content[1]	Nicotinic acid content	Grams gained per week[2] and (range)
	%	*mg%*	*mg%*	*gm/wk*
S–Basal (L.P.)	15.0	180	< 0.01	29 (26–32)
S–Basal (L.P.) + 40% yellow corn	12.4	128	0.92	13 (11–16)
S–Basal (L.P.) + 40% yellow corn + 1 mg% nicotinic acid	12.4	128	1.92	32 (30–34)
S–Basal (H.P.)	20.0	240	< 0.01	32 (31–34)
S–Basal (H.P.) + 40% yellow corn	15.4	164	0.92	30 (22–35)
S–Basal (H.P.) + 40% yellow corn + 1 mg% nicotinic acid	15.4	164	1.92	36 (33–38)
S–Basal (L.P.) + 40% polished rice	12.0	138	0.57	31 (27–34)
S–Basal (L.P.) + 40% corn grits[3]	12.6	118	0.27	7 (5– 8)
S–Basal (L.P.) + 40% corn grits + 0.5 % 1 (+) lysine	12.6	118	0.27	9 (7–14)
S–Basal (L.P.) + 40% corn grits + 0.05% 1 (−) tryptophane[3]	12.6	158	0.27	31 (27–37)
S–Basal (L.P.) + 40% corn grits + 0.1 % 1 (−) tryptophane[3]	12.6	218	0.27	33 (26–35)
S–Basal (L.P.) + 40% corn grits + 1 mg% nicotinic acid[3]	12.6	118	1.27	27 (25–29)
S–Basal (L.P.) + 40% corn grits + 1.5 mg% nicotinic acid[3]	12.6	118	1.77	32 (30–34)

S = Sucrose, L.P. = Low Protein (15 per cent. casein), H.P. = High Protein (20 per cent. casein).
[1] Calculated tryptophane content on the basis of values given by R. J. Block and D. Bolling in "The Amino Acid Composition of Proteins and Foods." Charles C Thomas, publisher, Springfield, Ill.
[2] Five weeks' experiments except for the lysine experiment, which was of two weeks' duration.
[3] Ration contained norite eluate (see text) at a level of 11.5 ug B_c (*S. lactis* assay) per 100 gm of ration.

On the basis of studies with various carbohydrates,[9] and by direct examination of the intestinal flora,[10] strong evidence is at hand to indicate that the observations reported in the present study may be explained at least in part by extensive changes which occur in the intestinal flora.

Summary: Either 50 mg 1(−)tryptophane or 1.0 mg nicotinic acid per 100 gms of ration completely counteracts the growth retardation caused by the inclusion of 40 per cent. corn grits in a low protein ration. A possible explanation of this observation is discussed.

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