Antilipaemic Effect of Nicotinamide

THE antilipaemic effect of nicotinic acid is well known[1] and the clinical value of this compound as an agent for lowering the content of cholesterol has been demonstrated[2,3]. Although many explanations have been offered, the mechanism by which nicotinic acid exerts its antilipaemic effect is not known. It is generally agreed, however, that the effect of decreasing cholesterol is unrelated to this compound's known vitamin role as a precursor of pyridine nucleotides, because nicotinamide, which is more readily incorporated into pyridine nucleotides, has little effect on serum cholesterol concentrations in man[2,3].

I have shown that nicotinamide is as effective as nicotinic acid in decreasing the concentration of cholesterol, triglycerides and free fatty acids in the serum of the rat. I have also shown that both agents are very effective in decreasing the content of serum triglycerides and free fatty acids in the dog. Animals were fasted 16 h before they were given the drug (2 mmoles/kg); blood was sampled at various times. Blood lipid was assayed by standard analytical methods. In the rat, all lipid classes measured were considerably reduced by both agents (Table 1). Similarly, free fatty acids and triglycerides in the serum were reduced in the dog but in these conditions the content of cholesterol was unchanged (Table 2). The time interval between the administration of the drug and the maximal effect on the different lipids varied greatly, and so, for the purpose of this discussion, only the maximal effects and the time at which they occurred are included in Tables 1 and 2.

A maximal decrease in free fatty acids occurred much earlier than the decrease in serum triglycerides which in turn was much earlier than the decrease in serum cholesterol. This temporal relationship has been observed before with nicotinic acid[4,5]. So pronounced is the effect of nicotinic acid on concentration of free fatty acids in serum that it has been suggested that the primary activity of this acid is to inhibit the release of free fatty acids from adipose tissue depots, while the effect on other blood lipid constituents is an indirect consequence of this activity[4,5].

A reduction in cholesterol content caused by nicotinamide and nicotinic acid in rabbits fed cholesterol has been reported by Fontenot[6]. The reduction was paralleled by a corresponding increase in nicotinamide adenine dinucleotide (NAD) in packed erythrocytes. It was suggested that the antilipaemic action of nicotinamide is unique to the rabbit. The experiments reported here indicate that in two other species nicotinamide is as effective as nicotinic acid as an antilipaemic agent.

Ricci and Pallini[7] found an increase in free nicotinic acid in the liver of rats injected with nicotinamide, thus demonstrating the presence of a pathway for conversion of nicotinamide to nicotinic acid. This pathway may also exist in the dog and rabbit, which would be consistent with the *in vitro* data which indicate that the hypolipaemic effect of these substances is a consequence of the presence of free acid[8]. The lack of antilipaemic activity of nicotinamide in man may mean that the conversion pathway does not exist. The demonstration of an antilipaemic action of nicotinamide in some species must be taken into consideration when explaining the mechanisms by which nicotinic acid and related compounds decrease concentrations of cholesterol. A vitamin effect of these substances cannot be disregarded yet.

Table 1. EFFECT OF NICOTINIC ACID AND NICOTINAMIDE ON SERUM LIPID LEVELS IN THE RAT

Compound	FFA (μequiv./l.) ± S.E.*		Triglycerides (mg/100 ml.) ± S.E.*		Total cholesterol (mg/100 ml.) ± S.E.*	
	Control	Treated	Control	Treated	Control	Treated
Nicotinic acid	432 ± 15	103 ± 10†	66 ± 8	8 ± 1†	85 ± 7	47 ± 4†
Nicotinamide	371 ± 14	138 ± 17†	83 ± 9	26 ± 1†	79 ± 4	48 ± 2†

Nicotinic acid and nicotinamide were administered as a single subcutaneous dose of 2 mmoles/kg. There were eight rates in each group.
* Serum free fatty acids (FFA), triglycerides and cholesterol were measured 15 min, 4 h and 24 h, respectively, after the drug had been given.
† Significance of difference from control, < 0·001.

Table 2. EFFECT OF NICOTINIC ACID AND NICOTINAMIDE ON SERUM LIPID LEVELS IN THE DOG

Compound	FFA (μequiv./l.) ± S.E.*		Triglycerides (mg/100 ml.) ± S.E.*		Total cholesterol (mg/100 ml.) ± S.E.	
	Control	Treated	Control	Treated	Control	Treated
Nicotinic acid	300 ± 52	188 ± 49	113 ± 4	75 ± 6†	105 ± 13	114 ± 9
Nicotinamide	344 ± 36	211 ± 21†	163 ± 4	76 ± 6‡	116 ± 16	114 ± 12

Nicotinic acid and nicotinamide were administered as a single subcutaneous dose of 2 mmoles/kg to three dogs.
* Serum FFA, triglycerides and cholesterol were measured 1 h, 6 h and 24 h, respectively, after the drug had been given.
† Significance of difference from control, < 0·05.
‡ Significance of difference from control, < 0·001.

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CYTOLOGY

Structural Basis of Quantitative Variation in Nuclear DNA

RECENT surveys show that variation in the amount of nuclear DNA, quite independently of change in chromosome number, is frequently associated with the divergence and evolution of both plant and animal species[1–10]. The extent of such variation is often very great, particularly among the angiosperms. One of the many problems posed by these findings is the nature of the chromosome structural changes which give rise to the DNA variation. Two proposals have been put forward. The first is a differential polynemy, that is, a difference in the lateral multiplicity of DNA strands between chromosomes of different species[4,9]. While this proposal has many theoretical attractions there is, to date, no direct evidence in its favour. Indeed, Callan[11] has adduced evidence which argues strongly against this view. The second possibility is that the nuclear DNA variation is caused by lengthwise incorporation or loss of chromosome segments such as result from duplication or deletion. Observations in *Lolium*[7] and in *Chironomus*[8] hybrids at pachytene of meiosis and in polytene nuclei, respectively, show that the chromosomes of species with different nuclear DNA contents differ in respect of segmental duplications. There are therefore good grounds for attributing at least part of the DNA variation to such duplications. The following work in *Allium* provides further evidence to support this view. What is more, it shows that segmental duplications can account entirely for the DNA changes observed.

The nuclear DNA content of *Allium cepa* is about 27 per cent greater than that of *A. fistulosum* (Table 1). The *A. cepa* chromosomes, as would be expected[6], are correspond-

Table 1. AMOUNTS OF NUCLEAR DNA IN 2C ROOT TIP INTERPHASE NUCLEI OF *Allium cepa* AND *A. fistulosum*

	DNA (arbitrary units)		
	Replicate 1	Replicate 2	Mean
Allium cepa	33·5	33·5	33·5
Allium fistulosum	27·2	25·6	26·4

Measurements, by Feulgen photometry, from ten cells in each replicate.