According to BRODIE *et al.*[15,16] only Rauwolfia alkaloids with sedative action are able to release 5-hydroxytryptamine and noradrenaline from brain tissue. Isoraunescine in our experiments was practically without sedative action but, nevertheless, able to deplete noradrenaline from the rat heart. However, a higher dose of isoraunescine than raunescine seemed necessary to produce the effect. In the brain, too, 50 mg/kg of isoraunescine lowered the concentration of noradrenaline less than 5 mg/kg of raunescine[17]. The fact that α-yohimbine was ineffective in the experiments reported is in keeping with the finding[18,19] that it does not release noradrenaline from the rat intestine, the tissue most sensitive to depletion of noradrenaline by the reserpine-type Rauwolfia alkaloids.

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Department of Pharmacology, Harvard Medical School, Boston (Mass.), September 11, 1958.

Zusammenfassung

Die chemisch verwandten Rauwolfia-Alkaloide Raunescin, Isoraunescin, Deserpidin, Rescinnamin und Reserpin verursachen einen starken Abfall des Noradrenalingehaltes des Rattenherzens, wenn sie intraperitoneal in einer Dosis von 5 mg/kg gegeben werden. Der Adrenalingehalt wird nicht deutlich oder einheitlich verändert. α-Yohimbin, das chemisch zu einer andern Gruppe gehört, hat keine Wirkung auf den Noradrenalingehalt des Herzens.

[15] B. B. BRODIE, P. A. SHORE, and A. PLETSCHER, Science *123*, 992 (1956).

[16] P. A. SHORE and B. B. BRODIE, in *Psychotropic Drugs* (Ed. by GARATTINI and GHETTI, Elsevier, Amsterdam 1957), p. 442.

[17] M. K. PAASONEN and P. B. DEWS, Brit. J. Pharmacol. *13*, 84 (1958).

[18] M. K. PAASONEN and N. T. KÄRKI, Acta endocr., in press (1958).

[19] N. T. KÄRKI and M. K. PAASONEN, J. Neurochemistry, in press (1958).

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Effects of Different Vegetable Fats on the Cardiac Damage Caused by Pyridoxine Deficiency

Hypertrophy of the heart[1] and a reduction in cardiac transamination[2] are exhibited by animals when vitamin B_6 is lacking from their diet, the former being attributed to hypertension caused by lack of pyridoxine, while the latter is basically due to the vitamin in the form of pyridoxalphosphate being the prosthetic group of transaminases.

Such a picture is remarkably similar to the one observed in human arteriosclerotic forms, whose pathogenesis appears to be heavily affected by vitamin B_6[3] through the relations existing between the latter and lipid metabolism, notably that of the so-called essential fatty acids. It has been established, indeed, that, while a lack of vitamin B_6 tends to increase the severity of the Burr syndrome[4], the administration of non-saturated fatty acids during a diet lacking in pyridoxine will either delay the onset of the hypovitaminosis or mitigate its symptomatology[5].

Table I.—Iodine Values of Fats used (Mean values ± S.E.)

Fat	Iodine Value
Coconut Oil	10·2 ± 0·4
Cocoa Butter	36·5 ± 2·1
Olive Oil	81·9 ± 3·4
Peanut Oil	93·8 ± 6·0
Cottonseed Oil	105·3 ± 8·8
Sesame Oil	107·1 ± 9·2
Corn Oil	123·8 ± 11·5
Wheat Germ Oil	125·2 ± 10·8
Soybean Oil	132·3 ± 12·1
Linseed Oil	177·6 ± 13·4

We were induced by the foregoing considerations to undertake a program aimed to assess the actions exerted by a variety of vegetable fats, all with varying contents of essential fatty acids, upon (1) the size, (2) lipid contents, and (3) pyridoxal phosphate contents of the heart, our experiments being performed on rats submitted to a diet lacking in vitamin B_6.

We used a total of 144 animals averaging in weight from 120 to 150 g, divided into twelve groups of twelve subjects each, on a diet with no vitamin B_6, of known composition to which 25% of a vegetable fat had been added.

The subjects received as much of the above diet as they could eat during a four-week period, at the end of which they were bled to death, their hearts then being removed under aseptic conditions, weighed and tested for total-lipids[6] and pyridoxalphosphate contents. The latter substance was determined by the method developed by BOXER *et al.*[7] using *S. faecalis* as the test germ.

The iodine value of each fat used was determined by the Hanus method as described in U.S.P. XV[8].

Our results are tabulated in Tables I and II.

From the foregoing data it appears that the greatest degree of heart enlargement is obtained from cocoa butter and coconut oil, the slightest from soybean and linseed oils, and that intermediate degrees of hypertrophy are determined by the other fats tested. It may be noted that the order in which the fats are classed according to their iodine values has been maintained, as the lower the iodine value of the fat administered, the greater was the increase in heart weight, and *vice versa*, the only exception being cottonseed oil, whose hypertrophying effect appears to be less than that of corn oil although its iodine value is lower.

Generally, the same considerations apply to the lipid contents of the heart tissue.

On the contrary, the pyridoxalphosphate contents was highest in such subjects as were administered soybean or wheat germ oil and lowest when olive oil was added to the diet. Starting from cottonseed oil, indeed, the effect upon the coenzymic contents of the heart tissue gradually

[1] L. R. C. AGNEW, Proc. Soc. exp. Biol. Med., N. Y. *90*, 452 (1955).

[2] S. R. AMES, P. S. SARMA, and C. A. ELVEHYEM, J. biol. Chem. *167*, 135 (1947).

[3] H. A. SCHROEDER, J. chron. Dis. *2*, 28 (1955).

[4] P. GYORGY and R. E. ECKARDT, Nature *144*, 512 (1939).

[5] T. W. BIRCH and P. GYORGY, J. biol. Chem. *131*, 761 (1939).

[6] W. O. FENN, J. biol. Chem. *128*, 297 (1939).

[7] G. E. BOXER, M. P. PRUSS, and R. S. GOODHART, J. Nutr. *63*, 623 (1957).

[8] U. S. Pharmacopoeia XV (Mack Publ. Co., Easton 1955), p. 896.

Table II.—Variations in Weight, Lipid, and Pyridoxalphosphate Contents in the Heart of Rats (Mean value ± S. E.)

Diet Type	Fat Administered (Diet 'C')	Heart Weight (mg/100 g body weight)	Total Lipids (g%)	Pyridoxalphosphate (μg/100 g)
A	—	324·8 ± 29·5	1·667 ± 0·104	108·6 ± 8·1
B	—	418·5 ± 38·1	2·194 ± 0·178	41·7 ± 3·5
C	Coconut Oil	513·2 ± 42·7	2·838 ± 0·261	16·0 ± 1.3
C	Cocoa Butter	497·5 ± 41·4	2·751 ± 0·246	14·8 ± 1·1
C	Olive Oil	490·8 ± 44.3	2·696 ± 0·225	12·1 ± 0·7
C	Peanut Oil	479·3 ± 38.6	2·655 ± 0·218	14·6 ± 1·2
C	Cottonseed Oil	450·7 ± 36·2	2·618 ± 0·234	24·2 ± 2·2
C	Sesame Oil	461·4 ± 40·7	2·573 ± 0·226	21·5 ± 1·8
C	Corn Oil	454·9 ± 41·5	2·546 ± 0·198	22·9 ± 2·1
C	Wheat Germ Oil	441·6 ± 39.2	2·470 ± 0·183	27·4 ± 2·5
C	Soybean Oil	433·6 ± 41·4	2·484 ± 0·232	29·5 ± 2·7
C	Linseed Oil	428·5 ± 37·4	2·469 ± 0·177	32·2 ± 1·9

Diet 'A' – Devitaminized casein, 16% – Corn Oil, 15% – Vitaminized lactose, 4%* – Salt mixture IV, 4% – sucrose to make 100.

Diet 'B' – Same as 'A' but minus vitamin B_6 in vitaminic supplement.

Diet 'C' – Same as 'B' plus 25% vegetable fat.

* 100 g vitaminized lactose contain: thiamine mononitrate, riboflavine, and pyridoxine hydrochloride, each 12·5 mg – calcium pantothenate, p-aminobenzoic acid, each 50 mg – nicotinamide, 62·5 mg – biothin, folic acid, each 2·5 mg – vitamin A acetate (cryst.), 25000 U. – vitamin D 2, 7500 U. – choline chloride, 5 g – inositol, 2·5 g.

decreases with no evident, direct relationship to the iodine values of the oils used.

To sum up, while heart hypertrophy and lipid contents appear to be evidently related to the non-saturated fatty acid contents of the oils added to the diet, no similar relation exists in respect of pyridoxalphosphate concentration. Consequently, if the effect exerted by alimentary fats upon heart size and lipid contents may be attributed to non-saturated fatty acids being more easily metabolized than saturated ones, the same reasoning does not apply to the action exerted by the very same fats on the coenzyme, whose variations seem to be explainable otherwise.

One of the possible interpretations of the latter phenomenon is related to the oleic acid contents of the fat used, as this acid is known to aggravate the effects of a lack of vitamin B_6[9]. This would account for the severer depletion of pyridoxalphosphate in the heart tissue of such rats as were administered olive oil, wherein oleic acid amounts to 85% of the aggregate fatty acid contents. In addition to this, oleic acid promotes the absorption of alimentary cholesterol by the intestine to a substantial extent[10], thereby further increasing such already heavy cholesterol concentrations as are determined in the blood by lipid diets.

Such a view appears to be supported by the fact that the decrease in pyridoxalphosphate concentrations determined by peanut oil (wherein oleic acid amounts to 57·2% of total fatty acids) is only slightly less than the one determined by olive oil, as well as by the fact that a greater effect is developed by cocoa butter than by coconut oil, the former featuring a higher iodine value but also a greater amount of oleic acid. The same remark applies to cottonseed oil in respect of both sesame and corn oils.

Finally, a considerably important factor appears to be the linoleic contents of the fats used, for the fact should be stressed that linseed oil (highest iodine value among all fats tested) appears to lower the pyridoxalphosphate contents to a greater extent than do cottonseed, wheat germ or soybean oils – all of which have a higher linoleic-acid contents although their iodine values are lower.

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Farmavigor S. p. A. Milano, Research Department, October 9, 1958.

Riassunto

L'effetto di diete contenenti un eccesso di grassi vegetali e carenti di vitamina B_6 è stato studiato dal punto di vista del contenuto di lipidi e di piridossalfosfato nel tessuto cardiaco. Dei dieci grassi vegetali presi in esame il massimo aumento dei lipidi cardiaci si verifica per il burro di cacao e per l'olio di cocco, i più saturi di tutti i grassi usati.

Per quanto riguarda le concentrazioni cardiache di piridossalfosfato la massima diminuzione si registra per l'olio d'oliva, mentre la diminuzione minima si registra per l'olio di germe di grano e per l'olio di soia. Vengono brevemente discusse, dal punto di vista del grado di insaturazione e del contenuto di acidi grassi, le possibili cause di questi risultati.

Appetite Stimulating Effect of Barbiturate-Induced Therapeutic Sleep

In our previous papers[1,2] we gave evidence of an increased food intake as one of the characteristic metabolic peculiarities of therapeutic sleep (T. S.). An attempt at a more detailed analysis of this phenomenon was made in subsequent work by comparing caloric balances in a total of 50 patients (43 with peptic ulceration, 7 with various neurotic states), treated by T. S., induced by barbiturates

[9] P. S. Sarma, E. E. Snell, and C. A. Elvehjem, J. Nutr. *33*, 121 (1947).

[10] A. C. Ivy, T. M. Lin, and E. Karvinen, Amer. J. Physiol. *179*, 646 (1954).

[1] E. Kuhn and J. Mašek, Dtsch. Ges.-Wes. *11*, 577 (1956).

[2] E. Kuhn and J. Mašek, Acta Inst. Aliment. hum. Pragae *1*, 275 (1955).