Rapeseed oil: nutritional aspects and safety considerations

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Original title: Il problema dell'olio di colza: aspetti nutrizionali e di sicurezza


Translated by the Translation Bureau (MG)
Multilingual Services Division
Department of the Secretary of State of Canada

Department of the Environment
Fisheries and Marine Service

Halifax Laboratory
Halifax, N.S.

1976

34 pages typescript
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RAPESEED OIL: NUTRITIONAL ASPECTS AND SAFETY CONSIDERATIONS

S. Scapin, and M.E. Semprini

1. INTRODUCTION

Rape (Brassica Napus L. oleifera) and wild rape (Brassica campestris L. oleifera) are oil-bearing plants belonging to the family Cruciferae, the seeds of which have a high lipid content (varying between 30 and 55%). Oils extracted from the seeds of these varieties are not easily distinguishable.

The generic name of rapeseed oil, therefore, is given to the oil extracted from either variety and also to the oil deriving from a mixture of both types of seeds. The growing of rapeseed, which extends from Canada to the subtropical regions, has been increasing steadily, so that in the last ten years (Table 1) (1) the production has risen from 3.6 million tons yearly to more than 6 million tons.

From an economic point of view its importance has increased mainly in those countries where, due to the scarcity or difficulty of production of other oil-bearing plants, it was deemed advisable to use these seeds to produce a source of vegetable fats for human consumption. If one also considers that rape seeds cost less than peanut, corn or sunflower seeds and that they also give a high yield of oil, it is understandable that their use has steadily increased.

The use of rapeseed oil by man is not recent. In the past, however,
it was used only for lighting and was considered unsuitable as food, mainly because of its unpleasant smell; nowadays, however, modern refining techniques allow the production of an oil free of any peculiar smell or taste.

Even in Italy, a country which by tradition produces and consumes olive oil, statistical data on the production and consumption of oil in the last few years show a progressive shift towards the consumption of seed oils due essentially to a change in economic conditions. For the period 1962-73, in fact, (Table 2) while the per capita availability of olive oil increased to 12.2 Kg. from 9.8 kg per annum, the availability of seed oil increased from 4.8 to 10.4 Kg per annum. The consumption of seed oil, therefore, doubled, while in the same period that of olive oil remained almost unchanged; the availability of animal fats is also practically the same. In addition, if we also consider the data on the production of seed oil in the period 1967-71, we note that while the total production of seed oil is essentially unchanged (4,032,762 q and

Table 1

Growth in world production of rapeseed (1)

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>Prod. (1000t)</td>
<td>% of world prod. (1000t)</td>
<td>% of world prod. (1000t)</td>
<td>% of world prod. (1000t)</td>
<td>% of world prod. (1000t)</td>
</tr>
<tr>
<td>Canada</td>
<td>9</td>
<td>0.3</td>
<td>278</td>
<td>6.5</td>
</tr>
<tr>
<td>India</td>
<td>815</td>
<td>28.9</td>
<td>1,275</td>
<td>29.3</td>
</tr>
<tr>
<td>France</td>
<td>154</td>
<td>5.5</td>
<td>196</td>
<td>4.6</td>
</tr>
<tr>
<td>Germany (Fed. Rep.)</td>
<td>83</td>
<td>2.9</td>
<td>100</td>
<td>2.3</td>
</tr>
<tr>
<td>Low Countries</td>
<td>33</td>
<td>1.2</td>
<td>10</td>
<td>0.2</td>
</tr>
<tr>
<td>Italy</td>
<td>14</td>
<td>0.5</td>
<td>9</td>
<td>0.2</td>
</tr>
<tr>
<td>Belgium</td>
<td>5</td>
<td>0.2</td>
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</tr>
<tr>
<td>China</td>
<td>782</td>
<td>27.8</td>
<td>951</td>
<td>22.2</td>
</tr>
<tr>
<td>Poland</td>
<td>97</td>
<td>3.4</td>
<td>323</td>
<td>7.5</td>
</tr>
<tr>
<td>Germany (Dem. Rep.)</td>
<td>110</td>
<td>3.9</td>
<td>171</td>
<td>4.0</td>
</tr>
</tbody>
</table>

(1) The data reported include the most common varieties.
Table 2

Course of the yearly consumption of oil in Italy (Kg/ per capita) (1)

<table>
<thead>
<tr>
<th>Year</th>
<th>Olive oil</th>
<th>Seed oil (1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1962</td>
<td>9.8</td>
<td>4.8</td>
</tr>
<tr>
<td>1963</td>
<td>9.9</td>
<td>5.6</td>
</tr>
<tr>
<td>1964</td>
<td>10.1</td>
<td>5.5</td>
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<tr>
<td>1965</td>
<td>9.7</td>
<td>6.8</td>
</tr>
<tr>
<td>1966</td>
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<tr>
<td>1967</td>
<td>8.9</td>
<td>9.0</td>
</tr>
<tr>
<td>1968</td>
<td>9.1</td>
<td>9.2</td>
</tr>
<tr>
<td>1969</td>
<td>9.6</td>
<td>10.3</td>
</tr>
<tr>
<td>1970</td>
<td>10.6</td>
<td>10.7</td>
</tr>
<tr>
<td>1971</td>
<td>11.2</td>
<td>10.0</td>
</tr>
<tr>
<td>1972</td>
<td>11.8</td>
<td>10.4</td>
</tr>
<tr>
<td>1973</td>
<td>12.2</td>
<td></td>
</tr>
</tbody>
</table>

(1) Margarine and hydrogenated fats included.

4,415,681 q respectively) the production of rapeseed oil doubled (from 883,133 q in 1967 to 1,441,988 q in 1972). It is therefore clear that in the period observed, of the 10 Kg of seed oil per capita available, yearly for consumption, about 30% is rapeseed oil.

The increased availability of rapeseed oil for consumption is due not only to the lower cost of the oil, but also to the fact that the increased purchasing power in Italy, as in the other industrialized countries, has, in turn, increased the consumption of fats.

However, above and beyond existing restrictions relative to the amount of lipids, which must not exceed certain limits in the diet, in the last few years bibliographic data have been collected which advise caution in the use of rapeseed oil.

At first, in fact, nutritionists approved the use of rapeseed oil because it is rich in unsaturated fatty acids and therefore capable of controlling the endogenous formation of cholesterol. Nowadays, however, they stress the fact that rapeseed oil, precisely because of its content of monounsaturated fatty acids, mainly erucic acid, is an unusual fatty acid for the organism, the metabolism and effects of which are therefore unknown.
For this reason, the constant increase in the use of rapeseed oil as a food has given rise to many studies aimed at clarifying not only its nutritive value, but also the effects of its components and its possible role in the appearance of physiological and pathological alterations some of them rather serious, in experimental animals. From the studies done in this field considered by us, it can be concluded that all laboratory animals do not respond in the same manner to a diet containing rapeseed oil; in fact, not only species differences have been demonstrated but also differences within the same species among various strains. It is, therefore, difficult to correlate experimental results on laboratory animals and human physiology with sufficient certainty.

2. CHEMICAL COMPOSITION

According to the data reported by Griego and Piepoli (2) common rapeseed oil has a peculiar composition characterized by: high content of erucic acid, a mono-unsaturated acid with 22 carbon atoms, which normally constitutes more than 40% of the total fatty acids, and can reach 63%; the presence in moderate amounts of other mono-unsaturated fatty acids like eicosanoic acid (C_{20:1}) (8-13%) and oleic acid (C_{18:1}) (5-30%); the almost constant presence of polyunsaturated acids like linoleic acid (C_{18:2}) (14-18%), linolenic acid (C_{18:3}) (9-12%); small amounts of saturated fatty acids like palmitic acid (C_{16:0}) (2-4%), stearic acid (C_{18:0}) (about 2%), arachidic acid (C_{20:0}) (about 2%) and behenic acid (C_{22:0}) (about 2%). As well, Ackman (3) was able to reveal the presence of many other higher saturated and unsaturated fatty acids.

The main characteristics of rapeseed oil, besides the high amount of erucic acid, are therefore a relatively high amount of essential fatty acids (higher for example, than that of some animal fats, but lower than that of
other vegetable oils) and lastly a scarcity of palmitic acid. Rapeseed oil contains almost no trierucin, but triglycerides are represented by: 54% containing two \( \text{C}_{22} \) unsaturated acids and one \( \text{C}_{18} \) unsaturated acid; 28% with two \( \text{C}_{18} \) unsaturated acids and one \( \text{C}_{22} \); 18% with a saturated acid and a \( \text{C}_{18} \) unsaturated and a \( \text{C}_{22} \) unsaturated acid (3). The monounsaturated fatty acids with longer chains (erucic acid and eicosanoic acid) are also esterified in the 1- and 3- positions of glycerol (4, 5).

Lastly, there are small amounts of phospholipids which are lost mainly during refining processes. During these processes part of the unsaponifiable fraction containing sterols, hydrocarbons and alcohols may also be lost (6). On the other hand, it must be remembered that as early as 1961 Canadian researchers succeeded in selecting and producing a variety of rapeseed oil which was almost free of erucic and gadoleic acid. Recently in other countries some varieties have been selected, the seeds of which produce an oil containing small amounts of or almost no erucic acid. To the oil of the traditional Brassica Napus and Brassica campestris have been added:

- Canbra oil: (extracted from Canadian Brassica);
- Oro oil: (Brassica Napus with 0.6% of erucic acid);
- Zephir oil: (Brassica Napus with 0.4-0.7% of erucic acid);
- Span oil: (Brassica campestris with 2.7% of erucic acid).

A type of oil is also extracted from mustard (Brassica hirta and Juncea) which has characteristics similar to those of rape and wild rape seed oil as regards fatty acids.

3. NUTRITIONAL VALUE

As early as 1941 it was observed by Boer et al. (7) that rats fed a diet containing rapeseed oil showed less growth than rats fed a diet
containing butter. This effect, subsequently confirmed by Von Beznak et al. (8) was attributed to a toxic substance which Thomasson (9, 10) identified as erucic acid, and which is present in high concentrations in rapeseed oil.

Therefore the hypothesis was put forward that the decreased rate of growth observed in the animals fed rapeseed oil was attributable to a decreased consumption of food by the animal (9, 11) rather than to a direct effect of the oil or of the erucic acid. Diets containing rapeseed oil, are in fact, less appetizing than those containing other types of fats. Experiments conducted by Roine et al. (12) and Thomasson et al. (13) with rapeseed oil in "balanced diets" demonstrated however that rats fed this type of oil showed less growth than controls red other types of fats.

Therefore on the basis of the results now available it seems that in rats, a 20% content by weight of rapeseed in the diet significantly inhibits growth. Beare et al. (14), on the other hand, have demonstrated the existence of differences in the response of various strains of the same species to the administration of rapeseed oil. Wistar rats, after a week of rapeseed diet, in fact, grew 35% less than rats kept on a diet containing maize, while for Sprague-Dawley rats the difference was 7%.

The effects on growth following the administration of rapeseed oil with the diet have also been studied in other animal species. In pigs, Crampton et al. (15) found that the administration of a diet containing 20% rapeseed oil significantly reduced growth compared with controls receiving the same amount of butter. Thoron (16) however noticed an apparently identical weight increase in animals fed rapeseed oil and animals fed a mixture of olive and palm oil. However he observed that the nutritional efficiency (gain (g)/ingested food (g) X 100) is lower with rapeseed oil. The effects are less evident in dogs, chickens and ducks; Carroll (17) in fact found normal growth in the first two species following administration
of up to 25% rapeseed oil and Thomasson et al. (13) up to 40% in ducks.

However, according to Joshi et al. (11), there is a significant early slowdown in growth in turkeys; in this species slow growth is already evident in a diet containing 10% by weight of rapeseed oil. An intermediate behaviour is observed in guinea pigs, the growth of which slows down when the level of rapeseed oil administered reaches 20% (Crampton et al.) (15).

It can be concluded, therefore, that as regards growth in general, when the rapeseed oil in the diet does not exceed 10% it behaves like other vegetable oils; when it is higher than 20% negative effects appear which, from a nutritional point of view, put rapeseed oil in an inferior category compared with other fats.

According to other studies, the reduced nutritional efficiency of rapeseed oil could, on the other hand, be attributed to its low digestibility resulting from the composition of the oil. In 1948 Deuel et al. (18) in fact, correlated the reduced rate of growth of rats fed 10% rapeseed oil with its low digestibility, demonstrating that the presence of a considerable amount of monounsaturated fatty acids and above all of erucic acid, compared with other vegetable oils, lowers the digestibility coefficient, which for rats is about 80. Subsequent experiments have shown (19-22) that the low digestibility of rapeseed oil is due to the lower utilization of erucic acid. It has also been demonstrated that more than 75% of the fatty acids present in the stool consist of erucic acid eliminated as such or as mono and diglycerides (20). Rocquelin et al. (23) have also observed that "in vitro" the action of pancreatic lipase on rapeseed oil triglycerides seems to be partially inhibited, at least in the initial phase of hydrolysis. Thomasson (21) demonstrated the existence of a very close correlation between rate of intestinal absorption and growth, due to the high content of erucic
acid which is absorbed less rapidly than other unsaturated fatty acids with a shorter chain length.

As regards the mechanisms which inhibit absorption, Savary et al. (24) have demonstrated that, although erucic acid is well incorporated into the micelles of conjugated bile acids, it is not absorbed as well as oleic acid. Vadovar et al. (25), on the other hand, noted the appearance of numerous lipid droplets in the supranuclear region of the cells of the jejunal mucosa 45 and 60 minutes following the ingestion of rapeseed oil. This accumulation which, on the other hand, occurs under many conditions of altered lipid absorption, is associated with an intranuclear thickening of the mitochondria. These Authors, in the intestinal lumen, also observed a great number of desquamated absorbing cells containing considerable amounts of lipids. The presence of these desquamated cells could be due to a delayed transport of the rapeseed oil fatty acids through the intestinal cell, while the passage from the lumen to the absorbing cell seemed normal. The cause of this altered transport, which results in the accumulation of lipids, desquamation, decreased rate of absorption and decreased digestibility is, however, unexplained.

In order to discover the reasons why erucic acid has a low degree of absorption while its lower homolog, oleic acid, is totally assimilated by the animal organism, Turchetto and Lorusso (26) studied the structure of this acid from a stereochemical point of view. According to these Authors the molecule of erucic acid, which contains four more carbon atoms than oleic acid, could cause more steric hindrance than oleic acid and the longer paraffin chains could be the cause of a different surface-active behaviour. The hydrophobic chains, in fact, would tend to associate, thus minimizing the hydrophilic properties of the polar carboxylic group. This would not
occur with oleic acid which, because of its lower molecular weight, would allow its carboxylic group to increase the surface activity. Besides, the greater distance of the double bond from the carboxylic group would mean a greater tendency of erucic acid to transisomerization and above all to hydrogenation, compared with oleic acid. Animal organisms, in fact, are capable of enzymatically reducing bonds in position 9-10, which is that of oleic acid, but they cannot reduce bonds in position 12-13, which is that found in erucic acid. Erucic acid, therefore, would be less metabolizable and consequently would tend to accumulate in the tissues.

4. EXPERIMENTAL ALTERATIONS

In conditions of experimental feeding involving the administration of diets with high contents of rapeseed oil, physiopathological alterations of various organs and tissues affecting particular functions like reproduction have been demonstrated by many Authors. In spite of contradictions and uncertain interpretations of the data obtained, we are reporting here in detail the alterations observed by various Authors with the functions and the organs affected.

4.1. Effects on the reproductive apparatus.

The administration of rapeseed oil probably has effects on the fertility and reproduction of the animals which receive it in their diet. In 1941 Kennedy and Purves (27) had already observed that female rats fed rapeseed oil matured sexually later than controls and that their ovaries contained a high level of cholesterol. Subsequently Carroll and Noble (28), administering diets containing 25% rapeseed oil to rats observed a slowdown of sexual development, and an increase in the cholesterol content of their ovaries which were smaller than those of the controls. The sexual cycle of the animals did not however undergo any changes.

Noble and Carroll (29, 30) administering 10 to 15% erucic acid in
the diet of male and female rats also observed that in males, there were some alterations of the testicles which caused the total degeneration of the epithelium of the seminiferous tubules; in the female many infertile matings occurred, many litters did not reach the weaning stage or, at that age, they were abnormally small. The mammary glands developed normally during pregnancy, but underwent rapid involution after delivery with consequent diminished lactation.

However, Bourdel and Jacquot (31) recently studying the effect of the administration of 20% rapeseed oil in the diet, on the morphology of the testicles and the dynamics of spermatogenesis in young rats, have concluded that this diet does not have any damaging effect on the reproductive apparatus, either on the development of the testicle, or on the formation of spermatozoa.

In the pig as well, Thoron (32) observed the effect of rapeseed oil on the development of the testicle and of the connected sexual glands; the relative weight of the testicle, of the epididymis and of the Cooper glands was much lower than those of controls fed a mixture of olive and palm oil. From this evidence the Author put forward the hypothesis of a possible interference of erucic acid with the synthesis of androsteroids.

4.2. Effects on the adrenal glands.

The administration of rapeseed seems to cause alterations of the adrenal glands. In rats fed rapeseed oil, Kennedy and Purves (27) had already observed hypertrophy of the cortex of the adrenal gland associated with a considerable accumulation of lipids.

In particular Carroll (28,33), administering 25% rapeseed oil in the diet, found that the marked increase in lipids was due mainly to cholesterol in the esterified form (3-4 times the normal concentration). Also, the
increased cholesterol in the adrenal gland does not seem to be associated with any radical changes in the functionality of said adrenal gland, which, on the contrary, responds normally to stimuli.

Carroll (17) compared the effects on the adrenal glands of various animal species of the administration of rapeseed oil and found significant hypertrophy not only in rats but also in mice; however there were hardly any alterations in rabbits, guinea pigs, chicken and dogs.

Beare et al. (14) demonstrated that analogous differences also exist among different strains of the same species.

According to Budzynska et al (34) in the rat a diet containing 30% rapeseed oil increases the synthesis of adrenocortical hormones; they in fact noticed an increase in the concentration of corticosterone in the adrenal glands and variations in concentrations of the hormone in the urine and the plasma.

Carroll (35), using a chromatographic method, examined the distribution of erucic acid in the various types of lipids present in the adrenal of Sprague-Dawley rats fed 15% erucic acid was found in considerable amounts in the triglycerides, while only small traces were present in the phospholipids.

Abdellatif and Vles (36) in an experiment in which they administered increasing amounts of rapeseed oil (0-16%) in the diet of rats, observed that hypertrophy of the cells of the adrenal cortex became apparent with as little as 5-10%. When the level of rapeseed oil was higher than 16% the hypertrophy was associated with a slight dilation of the renal tubules and interstitial fibrosis. The latter lesions, however, were practically absent in animals receiving rapeseed oil with a low content of erucic acid. On the basis of these observations the Authors suggest that erucic acid is
mainly responsible for the lesions observed, but that undoubtedly other factors, like monounsaturated fatty acids present in the diet, are also involved.

4.3. Effects on the thyroid.

Rapeseed like the seeds of other Cruciferae contain antithyroid principles with goitrogenic effects. It is therefore logical that studies should be undertaken to clarify the effect of rapeseed oil on the thyroid although the problem concerns rapeseed flour and not the oil where the antithyroid principle would be almost completely lost in the extraction and refining processes (37,38).

Carroll (33) noticed however that the administration of diets containing 15% erucic acid caused swelling of the thyroid and consequent weight increase (25 mg compared with a normal weight of 13 mg). The gland which appeared brownish in colour, showed a slight increase in colloid content, but no hyperactivity.

In this respect Niemi and Roine (39) pointed out that the non-saponifiable fraction of rapeseed oil mainly contains an antithyroid principle which is capable of interfering with the gland's ability to take up iodine from plasma, but which does not seem to interfere with organic conversion. Because of this the thyroid comes to lack iodine and cannot synthesize thyroxine, while the hypophysis continues and increases the secretion of thyrotrophic hormone. The result, therefore, is a case of hypothyroidism in spite of an adequate amount of iodine in the diet.

Roine et al. (12) administering 15% rapeseed oil in the diet of pigs, found that generally pigs are more sensitive than rats to this diet;
a histological examination of the thyroid in fact shows well defined alterations which are symptomatic of hyperfunctioning of the gland.

4.4. Effects on the liver.

The effect of the administration of rapeseed oil on the weight and fat composition of the liver has also been studied. Administering diets containing 25% rapeseed oil to rats and guinea pigs, a slight increase in the weight of the liver was observed as well as a marked increase in its cholesterol content and sometimes traces of degeneration in the central part of the lobes (17, 40, 41), while a similar effect was not found in mice, rabbits and dogs (17).

With the use of choline deficient diets, it has also been demonstrated that liver does not accumulate erucic acid even when it is present in the diet in very high amounts; the percentage of erucic acid is much lower in liver than in any other organ examined (42, 43). Analogous results have been obtained with dogs (44).

Studying the effect of erucic acid on the incorporation of acetate into the cholesterol, using thin slices or homogenates of liver, some Authors (45, 46) observed that incorporation was higher in the case of erucic acid and trierucate than with other fatty acids. Subsequent studies have indicated that this is not a specific effect of erucic acid.

Buhak (47) observed that long chain esters of acyl-carnitine increased in the myocardium but not in the liver.

It was also found that rapeseed oil compared with other vegetable oils has no effect on the weight of the liver (22, 48, 49) in most of the species studied (rat, mouse, rabbit, dog, pig) (14, 17, 40, 48, 50, 52); only in the guinea pig and the chicken has a tendency to hypercholesterolemia...
been found.

Linko (53) made an interesting observation in man. He observed a hypocholesterolemic effect of rapeseed oil after the administration of a diet containing butter as the only source of fats.

Interesting observations were made by Gaillard et al. (54) on the activity of microsomal enzymes of the liver responsible for the metabolism of foreign substances, following the administration to rats of oleic acid, erucic acid and their derivatives.

These Authors observed a significant increase in these enzymes following the administration of erucic acid; ethylerucate and triolein have an effect on some enzymes only, while oleic acid, ethyl oleate and trierucin have no effect.

These modifications were also associated with significant variations in the content of DNA, RNA and proteins of the whole liver and of the microsomal fractions. The Authors conclude that erucic acid acts as a strong inductor of detoxicating enzymes as do many food additives, pesticides, drugs and cancerogenous hydrocarbons. In other words, it behaves like a foreign substance in the organism. The same Authors (55) also observed that an intraperitoneal injection of oleic acid or erucic acid or their derivatives causes prolongation of the "sleeping time" and inhibition of some microsomal enzymes of the liver in rats treated with pentobarbital.

Analogous observations in this area were reported by Del Carmine et al. (56). In order to reveal possible functional lesions of the liver following the administration of rapeseed oil, these Authors studied the effect of its administration on hexobarbital oxidation in mice. The oxidation of this drug is in fact dependent on an enzymatic system present only in the liver tissue and it is known that an inverse ratio exists
between "sleeping time" and microsomal oxidase activity on hexobarbital. In mice fed rapeseed oil, the results have shown a significant increase in the "sleeping time" in young animals while this effect was not evident in adult animals. Rapeseed oil, therefore, may have an inhibitory effect on the metabolism of hexobarbital in young animals.

The same Authors have supplemented these indirect methods with a study on direct consumption of hexobarbital by microsomal preparations of liver from young mice fed rapeseed oil; the results previously reported were confirmed.

4.5. Effects on the myocardium.

Particularly interesting are the pathological alterations that various researchers have observed in tissues like the cardiac muscle which, depend on fats for energy. It must in fact be remembered that the myocardium is rich in myoglobin, in the enzymes of the tricarboxylic acid cycle and of the electron transport system, and utilizes mainly aerobic reactions to produce the ATP necessary for its contraction. It takes up relatively small amounts of glucose from the blood and produces the necessary ATP through the oxidation of fatty acids and to a lesser extent through the oxidation of acetoacetic and lactic acid. During exercise, then, when the metabolism of both the skeletal muscle and the cardiac muscle are accelerated, the heart takes up and utilizes the lactic acid produced by the peripheral muscles.

However, rapeseed oil administered in a ratio of 30% to rats, may according to Roine et al. (12) cause inflammatory alterations of the myocardium; in the pig, in addition to interstitial myocarditis, it may be responsible for the onset of inflammatory reactions affecting the gastric mucosa.
Alterations of nutritional etiology following administration of rapeseed oil, have also been described in rats by Raulin et al. (57). These Authors attribute the damage to the non-saponifiable fraction of the oil or to a disequilibrium of the ratio between saturated and unsaturated fatty acids, rather than to erucic acid.

The above findings are also confirmed by other experiments on rats (58) to which two types of rapeseed oil were administered: one with 44% erucic acid and one practically free of the acid. In both cases grave myocarditis sets in. The Authors attributed this type of lesion to the low intake of saturated fatty acids or to the altered ratio of saturated/unsaturated fatty acids present in rapeseed rather than to a specific effect of erucic acid. After three months both types of oil caused an increase in the weight of vital organs, like the heart, liver and kidneys.

In guinea pigs too, the administration of rapeseed oil causes fatty infiltration of the myocardium and in duckling, diets containing 23% rapeseed oil cause hydropericardium and fatty infiltration of the heart (13).

Abdellatif and Vles (59) have observed the appearance of fatty infiltration of the myocardium following administration of high percentages of rapeseed oil in various animal species. This phenomenon, was accompanied particularly in rats, by fatty infiltration of the skeletal muscle and of the adrenal glands. The gravity of these alterations is attenuated if palm oil is added to the rapeseed oil, while it increases if the diet has a low protein content. It is known that a low protein content of the diet causes an alteration of the albumin/globulin ratio, characterized by a decrease in plasma albumin and an increase in globulins. According to these Authors (69), therefore, the altered ability of the liver to synthesize albumin may
be a factor which predisposes those animals fed on rapeseed oil to hydropericardium.

The appearance of cardiac lipidosis with infiltration of mononucleated cells is described by the same Authors (36) for rats in a long term experiment in which 40% of the diet was administered in the form of lipids such as rapeseed with a high content of erucic acid or rapeseed oil with a low erucic acid content.

Bodak and Hatt (61) also report the appearance of lipid droplets in histiocytes and macrophages, as well as of degenerative foci in the subepicardial region as well as an increase in the volume occupied by the mitochondria and the presence of megamitochondria.

From the biochemical point of view, the lipidosis described is characterized by an early accumulation of triglycerides rich in erucic acid and to a lesser extent of free fatty acids. It was also observed that not only the dosages, but also the duration of the experiment and the age of the animal are important factors in the genesis and evolution of these myocardial lesions. In fact, although fatty deposition after three days of rapeseed administration is practically equal both in young (three weeks old) and in adult rats (11 weeks old), after six days it is more serious in the young rats than in the adults, which the more rapid decrease is associated with a higher rate of lysis and cellular proliferation (62).

In young animals fed rapeseed oil it has also been observed that the onset of lipidosis is very early: in males cardiac steatosis begins after 24 hours, reaching a peak within the first week, and remaining constant for many weeks with a tendency to disappear after two months even if administration is not discontinued.

Ziemlanski et al. (63) noticed that just three hours after the
administration of rapeseed oil, lipid droplets appeared in the myocardium and that they began to dissolve after 48 hours compressing and deforming contractile elements and mitochondria.

Vadovar (64) in several short term experiments with rats, observed the appearance of lipid droplets in the cardiac tissue following administration of rapeseed oil. They appeared to be dispersed between mitochondria and in the intermyofibrillar spaces; often too, mitochondria and myofibrils, as well as nuclei, appeared to be deformed by the fat droplets. After seven days of administration this Author also observed the appearance of slight alterations in the structure of the myofibrils and of macrophages loaded with lipids.

In addition, Arrigo et al. (65) conducted a series of short, medium and long term experiments with rats to which rapeseed was administered in the diet. The Authors, in the short term experiments, found lipid infiltration of the heart and muscle which regressed within the second week, while in the medium and long term experiments, they observed an irreversible accumulation of lipids in the same tissues, associated with lipid accumulation and histiocytosis of the lungs, and with degenerative lesions of the liver; however, brain lesions were never observed.

As we have seen, the Authors agree in attributing the lesions of the myocardium to the presence of erucic acid. Many researchers, therefore, have attempted to clarify the effect that rapeseed oil, and in particular erucic acid has on the metabolic processes of the cardiac muscle.

5. POSSIBLE MECHANISMS OF THE OBSERVED ALTERATIONS

As is clearly seen from what we have reported, the Authors mainly describe experimental alterations without formulating hypotheses or showing
the mechanisms which determine the alterations observed.

Some Authors, however, especially as regards the alterations of the cardiac muscle, point out possible action mechanisms.

According to Houtsmuller et al. (66) triglycerides and fatty acids accumulate in the myocardium when this organ takes up more fatty acids than it can oxidize. On the other hand, experiments on isolated mitochondria from the heart of animals which had received erucic acid in the diet, revealed a reduced capacity to oxidize many substrates with resulting fatty infiltration of the myocardium. According to these Authors there is also a linear correlation between erucic acid ingested and reduced synthesis of ATP. The fatty infiltration and the altered functionality of the mitochondria may be attributable to the observed increase in free fatty acids.

Another hypothesis on the causes of reduced formation of ATP was formulated by Maranesi et al (67). These Authors, using gas chromatography, found a change in the fatty acid spectrum of the phospholipids of rat heart. As there is a correlation between the composition of the mitochondrial membrane phospholipids and respiratory activity, which can be traced to the degree of unsaturation of the fatty acids and to the length of their chain, the Authors suggested that the presence of erucic acid and a considerable quantity of highly unsaturated fatty acids are responsible for modifying the optimal degree of fluidity of the apolar part of the membrane phospholipids.

Hornstra (22) feeding rats rapeseed oil in a ratio of 40% of the diet, observed a reduced ability of the animal to use the calories ingested and also a higher consumption of oxygen and a higher elimination of water vapor. The lower efficiency of the diets containing rapeseed oil may, therefore, be attributable to a certain degree of breakdown of the oxidative
phosphorylation and to a consequent higher production of heat.

The fact that the animals who receive rapeseed oil in the diet consumed more oxygen would, according to this Author, indicate that nutritional principles were diverted from the normal synthesis to ATP to the production of heat which is in turn compensated by the increased elimination of water vapor, as the temperature of the animal remains constant.

According to Houtsmuller et al. (68) the equilibrium between uptake and utilization of rapeseed oil is also dependent on the affinity that its fatty acids have for plasma albumins. In the blood, in fact, fatty acids from complexes with albumins. It has been demonstrated that in the case of erucic acid, the affinity of the albumins is lower than that observed for common fatty acids; this could therefore be one of the physiopathogenetic reasons for the uptake by the myocardium.

Another observation which could help in correlating the pathological alterations of the myocardium with erucic acid is that of Christophersen and Bremer (69, 70). They observed an inhibitory effect of erucic acid on other fatty acids in isolated heart mitochondria. It is known in fact that in the metabolism of fatty acids in the mitochondria, three enzymatic systems are involved:

- acyl-CoA synthetase which activates fatty acids;
- carnitine-acyltransferase for transport across the mitochondrial membrane;
- the enzymatic complex of β-oxidation.

Erucyl-carnitine causes a slower uptake of oxygen by isolated mitochondria both of the heart and of the liver compared with palmityl-carnitine, the mitochondrial oxidation of which is also inhibited. Erucyl-carnitine does not undergo the intra-mitochondrial formation of acyl-CoA,
nor the activity of carnitine acyltransferase nor the acylation of glycerol phosphate. It is therefore possible that erucic acid inhibits the oxidation of the other fatty acids, so that the activated fatty acids are accumulated and sent through other metabolic pathways which are not inhibited, or less inhibited by erucic acid, for example towards the synthesis of triglycerides. The fact that heart triglycerides besides erucic acid, also contain other fatty acids in a proportion corresponding to the composition of the diet suggests just such a mechanism.

The tendency of erucic acid to enter into the composition of tissues and to leave them slowly has also been demonstrated by Turchetto et al. (71) in the red blood cells of rats.

Lastly, Slinger et al. (72), observe an increase in cardiac lipids during the first six days of the diet and a subsequent gradual decrease. Simultaneously they also observe a decrease in cardiac glycogen, the concentration of which remains low so long as the rapeseed oil is administered. If administration is interrupted after six days and replaced with wheat oil, there is an increase in the cardiac glycogen; after nine days, however, this change does not occur. These factors indicate that following administration of rapeseed oil with a high content of erucic acid, cardiac metabolism is deeply altered; it seems in fact that the heart can replace fats with glycogen as a source of energy when the β-oxidation of fats is strongly inhibited.

That the whole lipid metabolism is altered by the administration of rapeseed oil seems also to be demonstrated by the observations of Struijk et al. (73) who studied the activity of lipoprotein-lipase stimulated by heparin in rats fed rapeseed oil with a high content of erucic acid. They observed that such a diet increases the activity of the plasma lipoprotein-lipase of a rat by about 45%, and that this increase is a function of time,
being highest between 3-6 days of administration. This increase also coincides with a rapid decrease in the myocardial triglyceride content and would suggest a possible connection with the removal from the heart of the accumulated triglycerides.

Cresteil et al. (74), administering 0.5 and 1 ml of rapeseed oil daily to young rats by gastric tube for three days, also observe that adenylcyclase activity in the cardiac muscle was significantly lower than in controls. They also demonstrated that this decreased activity may be related to a decrease in the number of catalytic units, rather than to inhibition of the enzyme. It is possible therefore that considering the role of cyclic AMP in the regulation of the cardiac metabolism of lipids, rapeseed oil causes an accumulation of lipids by lowering the clearance capacity of the myocardial lipids.

On the other hand, more recent studies have shown that if there are any deficiencies of β-oxidation, the amount of acyl-carnitine esterified with fatty acids should increase; Gumpen (75) and Swarttouw (76) have demonstrated however that following the administration of rapeseed oil, there is no accumulation of long chain esters of carnitine and they have therefore concluded that inhibition of β-oxidation does not occur.

In conclusion, the cause of the limited transport of this acid at the level of the mitochondrial membrane and the consequent accumulation of triglycerides at the level of the myocardium could be attributed to the poor affinity of carnitine-acyl-transferase for erucic acid.

Buhak et al. (47) have analyzed pools of carnitine extracted from male rat hearts following the administration of rapeseed oil, as compared with soya oil. They demonstrated that the presence of erucic acid in the oil ingested increases the level of long chain acyl-carnitine in the heart
and that this effect is significantly increased when more energy is required. This Author, therefore, agrees that lipidosis of the myocardium induced by rapeseed oil is due to the difficulty of oxidation of erucic acid involving its transport, which is carnitine dependent, to the sites where β-oxidation occurs.

This concept also seems to be supported by the observations of Turchetto et al. (77) who found, in two tests of response to stress in rats, that a reduction of muscle efficiency occurred in animals which had received rapeseed oil by the gastric route (1g/100g body wt.) compared with rats which had received olive oil.

Recent observations by electron microscopy on myocardia of rats and pigs fed rapeseed oil for 90 consecutive days showed an excess of neutral lipids in the cells associated with gigantism and degenerative alterations of the mitochondria. At the level of myocardial fibers a localized contraction of the myofibrils and lysis of the myofilaments (78) was observed, by perfusion.

Also, the rat seems to be more sensitive than the pig since, according to Vadovar et al. (64), the number of infiltrated cells is higher in the former species.

5.1. Comparison between rapeseed and Canbra oil.

Most Authors attribute the physiopathological alterations found after the administration of rapeseed oil to its high erucic acid content. Therefore it is worthwhile verifying this hypothesis by comparing the effects of the administration of rapeseed oil high in erucic acid with the effects produced by oils obtained from genetically selected seeds, with a very low erucic acid content.
These oils in fact should show different and possibly more interesting nutritional properties than common rapeseed oils.

Rocquelin and Cluzan (58) compared the effects on rats of rapeseed oil containing 44% erucic acid with those of Canbra oil containing no erucic acid. The two types of oil were administered in a ratio of 15% in the diet. Over six months, canbra oil showed no negative effect on growth, while with rapeseed oil, growth was significantly reduced. With a diet containing canbra oil the animals grew as well as controls fed peanut oil.

Craig and Beare (79) obtained analogous results by administering canbra oil or mixtures of canbra and olive or palm oil in a ratio of 20% by weight of the diet. Growth and consumption of food were normal and mixing various oils did not result in further improvement. It seems therefore that canbra oil, from a nutritional point of view, is very similar to oils deriving from other vegetable sources. This is based on the fact that its digestibility is considerably increased compared to normal rapeseed oil, from 80 to 96% (80).

Abdellatif and Vles (36) administering 40% canbra oil in the diet observed growth and food consumption similar to those of controls receiving sunflower seed oil.

Vles and Houstmuller (81), comparing three types of rapeseed oil: normal, canbra and span (the latter is another variety with low erucic acid content) in the rat, observe a definitely higher growth with canbra and span oil than with normal rapeseed oil. In practice it seems that canbra oil allows a growth performance similar to any other fat and that the effects of the administration of normal rapeseed oil are attributable to its erucic acid content.
Canbra oil has been compared with rapeseed oil as regards the appearance of lesions of the myocardium.

Although pathologic alterations of the myocardium cannot be demonstrated, recent studies on rapeseed oil with a low erucic acid content show the existence of other monoenes which act on ATP synthesis.

According to Vles et al. (81) an inverse ratio between ATP synthesis and levels of canbra and span oil administered with the diet is measurable and reproducible.

Abdellatif and Vles (36) by administering canbra oil to rats for 24 weeks found slight pathological alterations to the myocardium which however, were not attributable to the oil, as they also appeared to some extent in control animals fed sunflower seed oil. These data did not agree with those of Rocquelin and Cluzan (58) and Rocquelin et al. (82) who after administering canbra oil for seven months to rats, found serious myocardial lesions and concluded that the onset of myocarditis is not a specific effect of erucic acid, but is probably related to a lack of balance between saturated and unsaturated fatty acids and to a low content of saturated acids.

More recently Kramer et al. (83) also reported fatty infiltration of the heart of rats fed various types of oil with a low erucic acid content: it was only moderately significant after the administration of span oil (4.3% erucic acid) while it was lower after the administration of oro oil (1.6% erucic acid). After sixteen weeks the heart showed a relatively high incidence of necrotic and fibrotic lesions irregardless of the type of oil administered.

Abdellatif and Vles (36), administering a mixture of rapeseed oil with a low content of erucic acid (4 cal %) and sunflower seed oil, observed slight traces of fatty infiltration of the heart of rats after one week.
After 24 weeks all animals showed cardiac lesions consisting of cardiac lipidosis and fibrosis. Besides, lesions of the renal tubules were also present in some animals. In another experiment the same Authors obtained analogous results by administering small amounts of normal rapeseed oil.

More recently Beare et al. (83 a), experimenting on adult male rats, after 16 weeks, found a high incidence of cardiac lesions following administration of rapeseed oil with both high and low erucic acid contents. However, the appearance of such lesions, after the administration of span, oro or zephyr oil was evident only with higher dosages (15-20% of the diet). In addition, according to the same Authors, refining does not modify the nutritional properties of the oil, while partial hydrogenation would decrease the cardiopathogenetic effects.

These results, together with those obtained by Rocquelin and Cluzan (58, 82), show canbra oil under a new light, because it seems that the negative effects produced by rapeseed oil are not attributable solely to the presence of large amounts of erucic acid, but also to the composition of the oil and in particular to its content of saturated fatty acids. The toxic manifestations found could therefore, be due to the fact that the concentration of fatty acids exceeds the complexing ability to the enzymes.

As a result a certain pathogenicity is attributable to the long chain monoenes, although the cardiac lesions appear later in time and are less frequent and less serious than those observed after the administration of rapeseed oil in which the erucic acid content is also high.

The appearance of such lesions could be due to lack of balance between the ratio of saturated and unsaturated fatty acids and to the low level of palmitic acid which characterizes canbra oil and rapeseed oil in general.
6. OBSERVATIONS ON THE USE OF RAPESEED OIL IN THE HUMAN DIET

The data reported up to now show that the administration of rape-seed oil, as a source of fats in the diet of experimental animals, produces some negative results.

Although as already mentioned, the type and seriousness of the response vary, not only among various species but also among strains, the following effects are however attributable to rapeseed oil:

1) decreased rate of growth;
2) low digestibility coefficient;
3) rapid accumulation of lipids in the myocardium, quickly followed by necrosis, fibrosis and histiocyte infiltration.

Although it has not yet been proven, these effects suggest that man may also respond in similar fashion to the administration of rapeseed oil. Also, the huge increase in the use of this oil over the last few years makes research on the subject mandatory. Such research must deal not only with the nutritional characteristics of the oil in the human diet, to better clarify its nutritional value, but also with its biochemical characteristics to better define the metabolism of erucic acid and of the long chain fatty acids.

At present, however, data on this subject are not very numerous, nor do they clarify the many uncertainties concerning rapeseed oil and above all concerning erucic acid.

One of the first data made available was that of its digestibility coefficient. Deuel et al. (84) found that in man, rapeseed oil shows a high digestibility coefficient (99); in the rat, the same Authors had found much lower values (77 for raw, 82 for refined rapeseed oil). Similar values (variable between 98 and 100) are reported by other Authors (85, 86).
The fact that the human organism is capable of so efficiently utilizing rapeseed oil suggests that in limited amounts the oil would not have negative effects, but the same nutritional value as other vegetable fats. Research on laboratory animals, however, indicated that pathological phenomena start to show up when the levels reach about 9 gr per cent of the diet. This would be about 20% of the total calories, that is, less that the amount of calories contained in the dressing oils in the diet of the average western man. Therefore, the possibility that prolonged administration of this amount of rapeseed oil could cause some negative end effects cannot be ignored, also considering the different response of man compared with rats and other animals.

Another interesting observation on the effects on man of the administration of rapeseed oil has been reported by Linko (53). This Author observed that rapeseed oil administered in a diet containing butter as the only other source of fat, has a hypocholesterolemic effect in humans.

However, we cannot conclude from this observation alone that rapeseed oil is important from a dietetic point of view, as its role or better the role of erucic acid on the metabolism of cholesterol should be clarified.

Recently Tremoliers et al. (87) studied the effect of rapeseed oil administered to normal subjects in a single dose of 0.5 gr/Kg of body weight. Under these conditions the Authors observed that rapeseed oil causes a decrease of RQ, which corresponds to a higher oxidation of fatty acids. They also observed that the ratio between the plasma concentrations of β-hydroxybutyrate and acetoacetate remains unchanged (this indicates a normal capacity of utilization of these substrates), that the intramitochondrial NADH/NAD ratio also remains unchanged (this indicates a normal
functionality of the mitochondria) and, lastly, that it causes an increase in the concentration of all lipid metabolites, but not of cholesterol. The Authors, however, noticed that rapeseed oil, administered in a single dose on an empty stomach causes diarrhea in almost all subjects, while this did not happen to controls to whom peanut oil was administered.

Tremolieres et Carre (88) subsequently confirmed an increase in the oxidation of fatty acids following the administration of rapeseed oil. They observed, at rest, an increase of oxygen consumption of 24%, four hours after administration and suggested the hypothesis that prior to mitochondrial oxidation, erucic acid undergoes oxidation in the microsomes of the liver, but not in the myocardium and skeleton muscles, since these tissues do not have suitable enzymatic systems. They have also suggested that the increase in oxygen consumption could be due to a partial breakdown of oxidative phosphorylation in the mitochondria. This hypothesis seems to be confirmed by the experiments of Houtsmuller (66) on isolated heart mitochondria of rat.

Tremolières et al. (89) also studied the metabolic effects of orally ingested rapeseed oil on human blood. They pointed out that the percentage of erucic acid in the blood rises 4 or 5 times, as the removal of this acid is particularly slow.

Jaillard et al. (90) studied the free erucic acid of plasma extracted from the myocardium, three hours after the administration of rapeseed oil to humans. They conclude that erucic acid is extracted in a manner similar to other fatty acids and that the accumulation of erucic acid observed in the myocardium of various animals is not due to a higher rate of uptake of this acid compared with that of other fatty acids.
Maranesi et al. (91) following administration of rapeseed oil, found some variations in the fatty acid spectrum of plasma lipids, with an increase in palmitoleic acid, coinciding with a reduction in arachidonic acid, and an increase in eicosatrienoic acid: that is of those fatty acids that cause atherosclerosis.

Recently Del Carmine et al. (92) using chromatography studied the composition of the total fatty acids present in the serum of 70 human subjects after fasting for 12 hours, with particular attention to the concentration of erucic acid and of the first product of reduction of erucic acid –behenic acid–. They found normal values as regards the concentration of palmitic, oleic and linoleic acid, but as regards levels of erucic acid, 40 subjects showed a value higher than average. Of these 40 subjects, 11 showed erucic and no behenic acid, while 49 showed both acids. The other 26 subjects showed only behenic and no erucic acid. The Authors concluded that the presence of erucic acid is a direct function of rapeseed oil consumption and that behenic acid is a metabolite of erucic acid.

Lastly Del Carmine et al. (93) studied the composition of total fatty acids in the subcutaneous adipose tissue and in the myocardium of a random sample of the Italian population for the purpose of verifying whether erucic and gadoleic acids are present in human tissues, and in what amount, following a considerable increase in consumption of rapeseed oil. In the adipose tissue of all subjects erucic acid was present in an average percentage of 2.6% of the total fatty acids; gadoleic acid in an average percentage of 2.2%. In the myocardial tissue, however, the percentages of the two acids were lower: the average percentage for erucic acid was 0.7 and for gadoleic acid 0.6%.
By studying fatty acid composition in each subject the Authors observed that with a percentage increase in erucic acid there was a corresponding percentage increase in gadoleic acid; this would suggest that gadoleic acid is an intermediate product of the oxidation of erucic acid. From the examination of the data obtained the Authors advanced the hypothesis that the deposition of erucic and gadoleic acid in the myocardium occurs when a certain threshold is exceeded in the adipose tissue. The threshold would be: for erucic acid 1% in the adipose tissue, 0.2% in the myocardium; for gadoleic acid 1.25% in the adipose tissue, 0.2% in the myocardium.

Therefore, the few data available, do not seem to give sufficient indication that rapeseed oil causes modifications in man similar to those found in experimental animals. Although the epidemiologic investigations do not establish the appearance of any damage in man following the administration of rapeseed oil, there is however the well-found possibility that it could represent a potential risk.

During the IV International Congress on rapeseed oil, held at Gissen in June 1974 in which 350 representatives of 22 countries took part, the most recent advances in the technological production and utilization of this type of rapeseed were presented.

The best varieties of rapeseed selected in the last few years in Europe and in Canada, which have a very low content of erucic acid and therefore are more acceptable from a nutritional point of view, were also indicated.

In that session some guidelines emerged regarding a wider use of rapeseed oil in margarine, in dressing oil and others.
The scientists attending the meeting agreed on the replacement of the old varieties of rapeseed with new varieties.

However, as regards the utilization of rapeseed oil with a low content of erucic acid, the data reported by Rocquelin and Cluzar (58), by Rocquelin et al. (82), by Kramer et al. (83) and Beare-Rogers et al. (83 a) must be verified: these Authors found that serious myocardial lesions accompanied by fatty infiltration also occur following the use of these types of oil.
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RIASSUNTO

IL PROBLEMA DELL'OLIO DI COLZA: ASPETTI NUTRIZIONALI E DI SICUREZZA

In questa breve rassegna vengono esaminati i dati apparati in letteratura riguardanti l'utilizzazione nutrizionale e le alterazioni sperimentali riscontrate in diverse specie animali (topo, ratto, cavia, maiale, anitra, pollo, tacchino) a livello di vari organi e tessuti quali: le gonadi, la corteccia surrenale, la tiroide, il di olie di colza con la dieta.

Vengono infine messi a confronto i risultati ottenuti somministrando olio di colza tradizionale (cioè ad elevato contenuto di acido erucico) con quelli ottenuti impiegando invece olii moderni di tipo Canbra, Span, Oro, Zephir (cioè a basso contenuto di acido erucico). Da tale confronto emerge infatti che l'acido erucico potrebbe essere il maggiore responsabile delle alterazioni riscontrate, ma che anche agli altri monoeni a catena lunga come pure, entro certi limiti, anche all'alterato rapporto tra acidi grassi saturi e monoinsaturi si potrebbe attribuire una certa patogenicità, pur essendo in questo caso le lesioni tardive, meno frequenti e meno gravi.

SUMMARY

RAPESEED OIL: NUTRITIONAL ASPECTS AND SAFETY CONSIDERATIONS

In this review data are reported on the effects of rapeseed oil feeding to several animal species (mice, pigs, rats, guinea pigs, ducklings, chickens, turkeys) with particular regard to its nutritional value as compared to other vegetable fats, and to physiological and pathological modifications on different organs and tissues, namely: gonads, adrenals, thyroid, liver, myocardium.

Finally, the results obtained after administration of regular rapeseed oil (i.e. with high levels of erucic acid) are compared with those obtained using the modern types Canbra, Span, Oro, Zephir (i.e. with low levels of erucic acid). From this comparison it could be inferred that erucic acid could be the major responsible for the observed modifications, but also that other long chain monoenes and the altered ratio between saturated and monoinsaturated fatty acids might have a certain degree of pathogenic effects, although in this case the lesions appear later, are less frequent and less severe.