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Hydrogenation of Edible Oils—Toxicological and Nutritional Implications: A Review

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ABSTRACT

The nutritional, metabolic and pathological implications of hydrogenated oils are considered in relation to their chemical composition.

INTRODUCTION

Partially hydrogenated vegetable and marine oil (consumed as margarines, shortenings, frying and cooking fats) is a major source of dietary fat in many countries. The hydrogenation process results primarily in the reduction of double bonds in the fat, with the concomitant production of isomers. Hydrogenation is used to raise the melting points and plasticities of vegetable oils used for shortenings and margarines, and to improve their flavour and odour stability.

Commercial hydrogenation of oils results in their saturation and the production of a complexity of isomer fatty acid mixtures e.g. *cis*- and *trans*-monoenes and *cis, trans* nonconjugated dienes, as in soybean oil (Applewhite, 1981). Isomerization of *cis* double bonds to the *trans* configuration results in greatly improved functional properties of hydrogenated oils. *trans* Fatty acids (*t*-FAs) possess at least one *trans* double bond and therefore have a higher melting point than the corresponding *cis* fatty acid, a feature which allows a dietary oil to acquire a harder consistency. Margarine manufacture usually involves the use of hydrogenated oils to achieve the desired texture and oxidative stability.

Since the early 1950s there has been a continuous increase in the worldwide consumption of margarines, e.g. in the US (US Bureau of Census, 1980) and Canada (Fig. 1) (Al-Zand & Hassan, 1977). This dietary change has generated interest in the health implications of increased consumption of the resultant *t*-FAs.

Sahasrabudhe & Kurian (1979) compiled data on the component fatty acids of margarines manufactured in Canada. Of a total of 95 samples, 35 contained less than 15% *trans*-monoenes while 45 samples contained

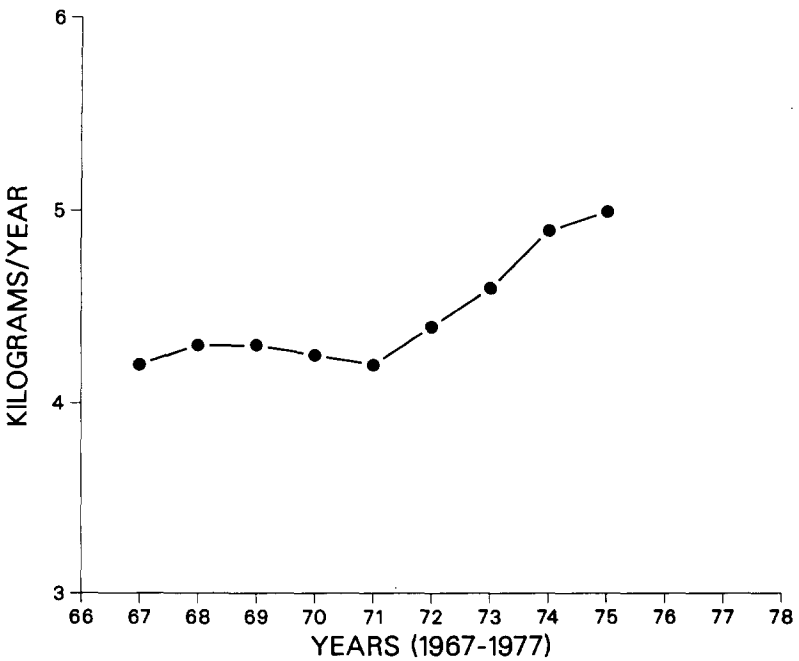

Fig. 1. Per capita consumption of margarines in Canada.

27·2–32·8%. Traces of up to 0·1% *trans*-dienes were found in 40 of the margarine samples (this was reported to be of some concern). The frequency of samples containing various levels of *trans* unsaturated acids comprising of *t*-18:1, *t,t*-18:2 is shown in Fig. 2.

t-FA's are found in all fat-containing products derived from ruminants, particularly products derived from cow's milk fat. Unlike monogastrics, ruminants are able to produce *t*-FAs by means of the rumen flora. These products can contain 1–9% *t*-FAs depending on their diet. However, it appears that the most important source of *t*-FA in the human diet is often partially hydrogenated vegetable oil.

Total daily intake of *t*-FAs, based on food consumption data of

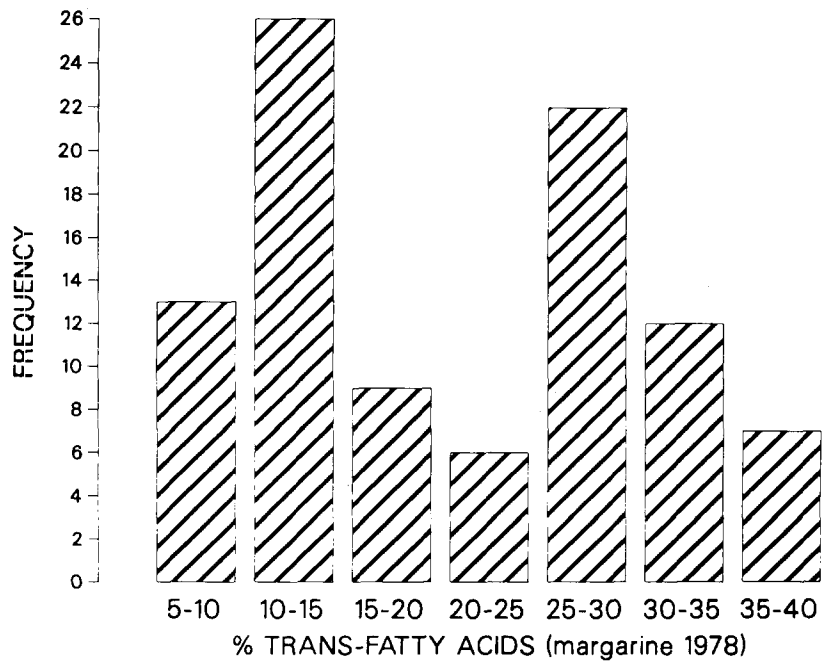

Fig. 2. Frequency of samples containing various levels of *trans*-unsaturated fatty acids.

20–39 year old males, has been estimated to be 11–12 g per person per day in both Canada (Expert Committee on Human Nutrition, 1979) and the US (Rizek *et al.*, 1974). The recommended maximum level for saturated and *t*-unsaturated FAs together is 40% (FAO, 1975). In the Canadian study mentioned earlier, 50 samples were above this limit.

ABSORPTION AND TRANSPORT

Partially hydrogenated fats have digestibilities in the range of 79–98%. Fully saturated fats, however, such as tristearin are poorly absorbed (Emken, 1980). In long-term multigeneration studies (over 30 years), Alfin-Slater & Aftergood (1979), in their review, reported that rats fed margarine containing 35% *t*-FAs as the sole dietary fat, experienced no problems in growth (Table 1), reproduction or survival.

Moore *et al.* (1980), after 3 months of feeding a 15% fat diet to rats, found *trans*-octadecenoate primarily in the phosphoglycerides and triacylglycerides of plasma, liver, kidney, heart, adipose tissue, and red blood cells. Eight weeks after the withdrawal of dietary *t*-FAs, only negligible amounts were left in the tissues.

TABLE 1
Growth of Rats of Representative Generations in a Multigeneration Experiment fed Dietary Fat containing 35% *trans*-Fatty Acids

Fat level (%)	*Generation*	*Weight at 90 days (g)*[a]	
		Males	*Females*
11·2	40	290	200
	75	310	212
16·0	5	283	219
	25	278	209
Purina Chow		280	210

[a] Twelve males and 24 females/group, from Alfin-Slater & Aftergood (1979).

Radioactive elaidic acid injected into developing rats either intracerebrally or intragastrically became incorporated into brain tissue (Cook, 1978). When the dose was administered by the intracerebral route, the rate and extent of total label uptake into the complex lipids was similar for *cis* and *trans* fatty acids.

Dietary *trans* isomers of linoleic acids are reported to aggravate the symptoms of essential fatty acid deficiency and alter lipid metabolism (Privett *et al.*, 1977). Administration of *trans,trans*-linoleate to rats reduced the concentration of arachidonic acid, apparently by inhibiting the enzyme converting *cis*-linoleate to dihomolinoleate (Selinger & Holman, 1965). Partially hydrogenated fats that contain large amounts of *t*-FAs can have deleterious effects in rats, promoting degeneration of the testes in animals deficient in essential fatty acids (Jensen, 1976). However, it was recently observed that if diets containing partially hydrogenated oils, and which were supplemented with an adequate amount of linoleic acid, were fed to rats, no essential fatty acid deficiency was observed (Svensson, 1983).

Islam *et al.* (1983) reported that if rats were fed *t*-FAs as a high proportion of the total fatty acid content of the diet, protein efficiency ratio (PER) could be adversely affected. However, with the diets in which *t*-FA-containing hydrogenated soybean oil were fed, at levels of 7·8% and 20·1%, PER values were no different from those obtained with an all *cis* fatty acid soybean diet. These authors thereby concluded that normal dietary levels of *t*-FAs have no adverse effect on protein utilization.

As far as humans are concerned, it is well established that isomeric fatty acids formed during hydrogenation can be deposited in human tissue. Fatty acids in adipose tissue from 24 subjects contained 2·4–12·2% *t*-FAs

(Johnston *et al.*, 1957), but those in the myocardium and aorta contained levels of less than 1% (Heckers *et al.*, 1977).

ACYLTRANSFERASES AND DESATURASES

These enzymes are important for the elongation and transformation of fatty acids and their metabolism.

Acyltransferases

In studies involving ethyl elaidate and linoelaidate Takatori *et al.* (1976) reported that, in groups of rats fed linoelaidate, enzyme activity increased initially, but was suppressed as the animals became older. Changes in tissue lipid fatty acid composition as well as reduced growth were observed, chracteristic of an essential fatty acid deficiency. If linoleic acid was present in the system, different results would have been obtained. Lands (1979) described the 'retailoring' of the phospholipid by the acyltransferase for position 2 which tends to bind fatty acids with double bonds in positions 5, 9 and 12 without regard to configuration.

Desaturases

Desaturation of palmitic acid to palmitoleic acid (9-desaturase) by rat liver microsomes was inhibited by *trans*-3-, -5-, -7-, -10-, -12-, -13-, or -16-octadecenoic acid when the inhibitor to substrate ratio was 3:1 (Mahfouz *et al.*, 1980). In diets containing partially hydrogenated oils supplemented with linoleic acid, Svensson (1983) observed that the sum of contents of 20:2ω6 and 20:3ω9 was low. The author concluded that dietary partially hydrogenated oils supplied with an adequate amount of linoleic acid could affect the metabolism of linoleic acid in rat liver microsomes.

PROSTAGLANDIN (PG) SYNTHESIS

trans, trans-Octadecadienoic acid was found to depress the serum levels of prostaglandins in rats (Hwang & Kinsella, 1979). The syntheses of both PGE_1 from 20:3(*n*-6) and PGE_2 from 20:4(*n*-6) were reduced, presumably because linoleic acid could not be converted to long chain polyenoic acids in the presence of a large influx of the *trans, trans*-isomer.

Eicosatrienoic acid (20:3), a derivative of linoleic acid, appears to be less

readily formed in the presence of the *trans, trans*-isomer. Its influence on prostaglandin synthesis therefore appeared to be exerted at an early stage in the elongation and desaturation steps of polyenoic fatty acid conversion.

ENERGY PRODUCTION

For β-oxidation to proceed, a fatty acid must first be activated by acyl-CoA synthetase. The activity of the enzyme with various *trans*-octadecenoates as substrates was reported to be lowest with the 9-isomer and to increase as the double bond moved to either end of the molecule (Lippel *et al.*, 1973). Such results from microsomal preparations are not in agreement with later findings indicating that acyl-CoA synthesis was unaffected by the configuration or position of the double bond in the octadecenoic acid (Norman *et al.*, 1981).

The most efficient oxidation of fatty acids occurs in the mitochondria. It was reported by Anderson & Coots (1967) that *cis*- and *trans*-isomers of octadecenoic acid were similarly degraded to carbon dioxide in adult male rats. Ono & Fredrickson (1964) similarly found that *trans, trans*-octadecadienoic acid was normally oxidized.

Some fatty acids may be at least partly oxidized by an extramitochondrial system, such as the peroxisomes. β-oxidation in the peroxisomes differs from that in the mitochondria in several aspects. Carnithine is not involved, oxygen is required, and potassium cyanide has no effect (Cooper & Beevers, 1969).

The feeding of partially hydrogenated marine oil (*t*-FAs content unspecified) as 30% of the dietary energy for 3 weeks caused proliferation of peroxisomes in isolated rat hepatocytes and enhanced chain shortening of docosenoic acid (Christiansen *et al.*, 1979). These investigators also observed that rapeseed oil and partially hydrogenated marine oil, both having 11·5% docosenoic acid, had unequal effects on peroxisomal induction.

In determining substrate specificity for peroxisomal oxidation in the liver, Neat *et al.* (1981) found that *trans*-monoenoic acids of different chain lengths were oxidized at faster or similar rates to those of the corresponding *cis*-isomers. Information is lacking on the effect of chain length of *t*-FAs on the induction of peroxisomal β-oxidation (Beare-Rogers, 1983).

In addition to the studies already mentioned, there are many publications, particularly in the last decade, that deal with other aspects of the health implications of hydrogenated oil with considerable attention to the *trans*-isomers in model systems. It is beyond the scope of this paper to consider all of these implications, whether they are real or artifacts that may be drawn from these model studies.

Two aspects of both animal and human nutrition as related to partially hydrogenated oils, which have received increased attention recently, are those concerned with coronary heart disease and cancer.

CORONARY HEART DISEASE (CHD)

The possibility of an association beteen *t*-FAs and serum cholesterol has been a matter of some concern. The effects of elaidic acid and trielaidin on atherosclerosis in cholesterol-fed rabbits were studied many years ago by Weigensberg & McMillan (1964) who found that these fatty acids were more hypercholesterolemic but not more atherogenic. Jackson *et al.* (1977) have found that *t*-FAs are not inordinately atherogenic in swine.

In the more recent experiments by Kritchevsky (1982) and Ruttenberg *et al.* (1983), diets which were semipurified and cholesterol-free, containing either 3·2% or 6·0% *t*-FAs, when fed to rabbits, were found to be slightly hyperlipidemic, but no more atherogenic than the control diet. The activities of five hepatic enzymes (glucose-6-phosphatase, fatty acid synthetase, malate dehydrogenase, hydroxybutyrate dehydrogenase, and monoamine oxidase) were examined. It was found that there were no significant differences in activities of these enzymes, with the exception of the activity of monoamine oxidase, which was lower in the rabbits fed 6·0% *t*-FAs. The authors thereby concluded that *t*-FAs appear to exert a hypercholesterolemic effect but do not influence aortic atherosclerosis in rabbits or in vervet monkeys.

One can summarize the human studies to date in much the same fashion as the animal studies discussed earlier. In carefully controlled and designed human experiments, it is not apparent that any '*trans*-effect' exists (Applewhite, 1981).

Hydrogenated fats have been the subject of many epidemiological studies. The use of hydrogenated fat is increasing in almost every part of the world; therefore it is often tempting and easy to find a statistically valid association between consumption of hydrogenated fat and heart disease.

Kummerow's discussion in 1979, though lacking data, claims a 'correlation' has been developed from existing data on hydrogenated fat consumption and CHD deaths in many countries. It further points to 'differences' in the level of blood cell lipids as support for correlation. However, statistical validity was not shown and the number of samples was undefined.

Kummerow's discussion is part of a larger review dealing with '...angiotoxins' as dietary risk factors in coronary heart disease (Kummerow, 1979) where, in addition to epidemiological 'evidence', he mentioned earlier studies

with essential fatty acid-deficient swine as supportive of the idea that *trans*-isomers are 'angiotoxins'. Based on present knowledge, it seems unlikely that angiotoxic agents are either the cause of atherosclerosis or the key to curing or preventing this disease in our society (Levy, 1979).

CANCER

Interrelationships between fat and cancer have been the subject of experimental studies for over 40 years. Mortality from cancer of the colon and cancer of the breast shows a strong positive correlation with the corresponding consumption of fat per capita (Carroll, 1975). Two studies in Canada (Miller *et al.*, 1978; Lubin *et al.*, 1981) found that, compared with control patients, those with breast cancer reported eating more fat, whereas an American case-control study (Graham *et al.*, 1982) found no correlation.

Enig *et al.* (1978) presented (a) positive correlations between processed vegetable fats, especially *trans*-isomers, and total cancer mortality, especially of the colon and breast, (b) negative correlations with the same death cause, and total animal fat from selected data from various US governmental publications. These studies were criticized by a number of authors; for example, by Hunter (1983), as erroneous and simplistic approaches to very complex problems. Enig *et al.* (1979) corrected several errors in her original publication, but insisted on the use of only selected data, both as to fat consumption and cancer mortality, in order to justify the associative relationship they perceive between hydrogenated fats and cancer.

Proof of a causal relationship between cancer and hydrogenated fat has not been developed to date, even though Enig. *et al.* (1978) speculated that results of very early work in this field by Tannenbaum (1942) could be accounted for by assuming that hydrogenated fat was a factor rather than only fat level, as suggested.

Carroll & Hopkins (1979) have clearly shown that, if a minimum essential fatty acid level is provided, then tumorigenesis is related to dietary fat level and not to fat type. Subsequently, Brown (1979) reported that, under the conditions employed in their study, there was no apparent *trans*-effect noted earlier in chemically-induced or spontaneous tumours.

Hopkins & West (1976) have suggested that fats may be involved in carcinogenesis by altering the membrane permeability to carcinogens. Evidence that *t*-FAs affect the function of cellular membranes is indicated by Hsu & Kummerow (1977), who have shown altered mitochondrial enzyme function in tissues from animals fed hydrogenated vegetable fat. This resulted due to the significant incorporation of *t*-FAs into the membrane phospholipids.

CONCLUSION

Most of the evidence outlined here does not show that partially hydrogenated vegetable oils and the *trans*-isomers therein are implicated as lacking nutritional qualities. Also it is not demonstrated that they contribute to CHD or cancer, nor are they capable, under normal essential fatty acid conditions, of causing perturbations of cell enzymes or membranes.

The idea that *trans*-isomers are 'unnatural' as reported by Awad (1981), and of recent occurrence in the food chain is false. Furthermore, it is not evident from the results to date that the *trans*-isomers of processed vegetable oils possess any unique, negative biological qualities in humans and animals when adequate essential fatty acid levels are present in the diet.

However, certain researchers such as Heckers & Melcher (1978) with a West German study and Sahasrabudhe & Kurian (1979) with a Canadian study proposed the idea that it would be of advantage to eliminate *t*-FAs as much as possible from hydrogenated products. This could be achieved by using the process of rearrangement of completely hydrogenated vegetable oils with unhydrogenated oil, and even better would be the process of transesterification of hardened fats. Results by Heckers & Melcher (1978) have demonstrated that, in West Germany, many commercially available margarines, shortenings, frying and cooking fats are manufactured in accordance with this demand, being essentially free of *t*-FAs.

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