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REVISIÓN

Trans fatty acid isomers from hydrogenated fats: The controversy about health implications

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RESUMEN

Acidos grasos con isomería *trans* a partir de grasas hidrogenadas: Controversia sobre sus implicaciones en la salud.

Toda vez que exista un doble enlace en un ácido graso, existe la posibilidad de formación de estructuras isómeras. La hidrogenación parcial de los dobles enlaces de los triglicéridos que forman un aceite puede cambiar la isomería de estos enlaces desde la configuración *cis* a la configuración *trans,* por lo cual aquellos productos derivados de la hidrogenación de aceites, tales como las margarinas, las mantecas y otras grasas industriales, presentarán altos contenidos de ácidos grasos con isomería *trans.* Las implicaciones para la salud derivadas del consumo de ácidos grasos *trans* en la dieta, son en la actualidad motivo de muchas controversias, ya que se ha demostrado que los ácidos grasos *trans* se comportan biológicamente como ácidos grasos saturados. Los ácidos grasos *trans* aumentan el colesterol-LDL y disminuyen simultáneamente el colesterol-HDL, siendo consideradas ambas situaciones como aterogénicas. La industria oleoquímica ha desarrollado diferentes estrategias para reducir el contenido de ácidos grasos *trans* en los aceites hidrogenados, y en la actualidad es posible disponer de margarinas y de otros productos hidrogenados con bajas cantidades de ácidos grasos *trans.*

PALABRAS-CLAVE: Grasa hidrogenada — Grasa saturada — Isómero trans — Revisión (artículo) — Salud.

SUMMARY

***Trans* fatty acid isomers from hydrogenated fats: The controversy about health implications.**

Wherever there is a double bond in a fatty acid, there is also a possibility for isomerization. Under partial hydrogenation triacylglycerols composing oils'double bonds may change from *cis* to *trans* configuration, therefore products derived from hydrogenated oils such as margarines, shortenings and other industrial fats show high content of *trans* fatty acid isomers. The health implications of *trans* fatty acids in our diet is now a concern of controversy, because it has been demonstrated that its metabolic behaviour is as saturated fats. *Trans* fatty acids increase LDL-cholesterol and simultaneously decrease HDL-cholesterol, being considered both parameters as atherogenics. The oleochemical industry has developed several strategies to reduce the *trans* fatty acid content of hydrogenated oils, and now margarines and other hydrogenated derived products with low *trans* fatty acids content can be obtained from the retail market.

KEY-WORDS: Health — Hydrogenated fat — Review (paper) — Saturated fat — Trans isomer.

1. INTRODUCTION

Many traditional fat products require a solid or semisolid consistency in order to fulfill their functions. In modern industrial practice these fats are often produced by blending oils and fats from different sources. The solid content of these fats may be obtained by different procedures, being the partial or the total hydrogenation of some of the components a frequently applied alternative. Hydrogenation produces a series of chemically complex reactions leading to the formation of very complex mixtures of isomers, being *trans* fatty acid isomers the most relevant. Nowadays, *trans* fatty acids constitute a variable but significant proportion of the diet in the western countries, with the exception of some european countries such as Spain and Portugal (Wolff, 1995). These fatty acids are predominantly derived from hydrogenated vegetable and marine oils. In the last several years major changes in the *trans* fatty acid intake have ocurred. Cooking oils were no longer partially hydrogenated after about 1985, and the major fast food chains switched from beef tallow to heavily hydrogenated oils çontaining 25% to 40% *trans* fatty acids for deep frying (Dupont et al., 1991). The *trans* fatty acid question is one of the biggest issues which the margarine and shortening industry are facing in recent times, because there are some concerns about the health effects of these products (Willett & Ascherio, 1994). The present review is not comprehensive but will discuss the presence of *trans* fatty acids in our diet, the chemical characteristics of these fatty acids, and the effect of *trans* fatty acids in human health.

2. *TRANS* FATTY ACIDS IN OUR DIET

The health implications derived from the ingestion of *trans* fatty acids in our diet, has became an issue of controversy for scientists and food technologists (Gurr, 1983; Emkem, 1984). *Trans* fatty acids are unsaturated fatty acids with at least one double bond in the *trans* configuration (Figure 1).

The most common *trans* fatty acids are monounsaturated, but various diunsaturated *cis-trans,* and *trans-cis* isomers occur frequently in some products such as margarines or shortenings prepared from hydrogenated marine oils. *Trans* fatty acids are originated primarily from the catalytic hydrogenation of vegetable or animal (e.g fish) oils (Applewhite, 1981). Hydrogenation in the liquid phase of vegetable oil, which has been practiced since the discovery by Wilhelm Normann in 1903, has become an extremely important process because it is the most practical way to impart the desired stability and other functional properties in many food applications. This process which is extensively applied to harden liquid oils to improve their functionality and stability to oxidation, leads to the obtention of solid or semi-solid products which are used in the food industry as a base for the manufacture of margarines, solid cooking fats, shortenings, crackers, breads, pastries, french potatoes, and many other different food products. Hydrogenation increases also the length of time that cooking oils can be used in deep-fat-frying operations. The percentage of isomers in hydrogenated vegetable oils varies widely with hydrogenation conditions, but typical hydrogenated soybean oil products contain about 12% *trans* 18:1, 4% *cis* 18:1, and 9% 18:2 and 18:3 positional and geometrical isomers (Carpenter et al., 1976).

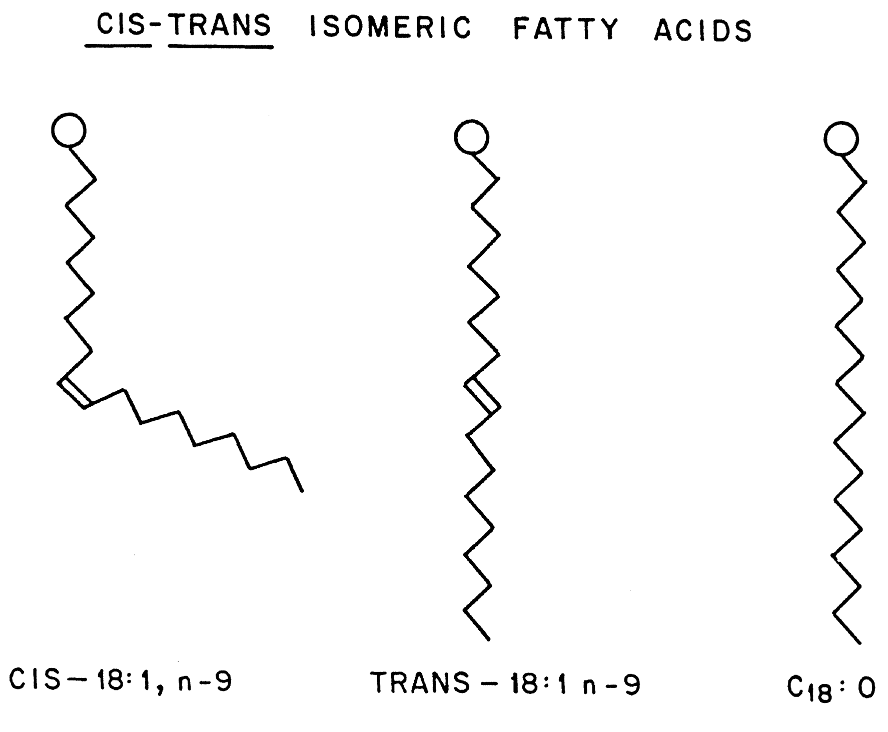

Fig. 1

Natural fatty acids are mostly in the *cis* form in the foods which constitute the bulk of our dietary intake (Beare-Rogers, 1988). *Trans* fatty acids present in hydrogenated oils have been referred to as "unnatural" but this is not strictly true since these fatty acids do occur in nature but not with the same overall concentration or the variety of isomers found in the processed fats. Some foods, such as meats from beef or from other ruminants, milk and milk-derived products (such as butter and cheese), and tallow, contain variable smaller amounts of *trans* fatty acids or mixtures of *trans* and *cis-trans* fatty acids. In milk, the *trans* monounsaturated fatty acids are quantitatively the most important and may constitute up to 21% of the total monounsatured acids (Hay & Morrison, 1970). These isomeric forms are formed as a result of microorganism activity in the ruminants forestomach which by hydrogenation reduce the mono and polyunsaturated fatty acids present in the foods eaten by these animals (Parodi, 1976). Milk fat has from 2 to 5% total *trans* fatty acid isomers, depending on the ruminant diet and how long it remains in the forestomach. For example, spring-summer butter has a higher percentage of *trans* isomers than autumn-winter butter, because of the higher percentage of roughage in the summer diet (Parodi, 1976; Wolff, 1994). Nevertheless, the fatty acid composition of products from cows and sheeps provide approximately 5% of the *trans* fatty acids in our diet. Industrial hydrogenated oils provide up to 80% of the *trans* fatty acids in our diet, being margarines and shortenings the most common sources of isomeric *trans* fatty acids (Slover et al., 1985).

Historically, the comsumption of *trans* fatty acids has increased steadily since the 1920's, in parallel with the increasing commercial production of margarines, a product invented in 1869, and shortenings (Booyens & Louwrens, 1986). Consumption of *trans* fatty acids within a given population will differ greatly depending on the lifestyle and socioeconomic status. The average dietary intake of *trans* fatty acids in western industrialized countries is estimated in 6-8 grams/day, providing 1,5-3% of the calories in the diet (Hunter & Applewhite, 1991). Althought this is a rather low percentage compared to 30-37% of dietary calories provided by total fat intake (12-14% from saturated fats), concerns about the safety for the *trans* fatty acid intake have been aroused since the 1950s.

3. INDUSTRIAL HYDROGENATION, THE MOST IMPORTANT SOURCE FOR *TRANS* FATTY ACIDS.

The object of hydrogenation, which is probably the margarine manufacturer 's most important tool, is to reduce the degree of unsaturation, thereby raising the melting point of the oil. By careful choice of the catalyst and temperature, the oil can be selectively hydrogenated so as to achieve a product with precisely the desired characteristics. Hydrogenation of vegetable oils under usual conditions leads to mixture of *cis* and *trans* monoenes plus some lower levels of *cis-trans* and *trans-cis* dienes, mostly 9, 12-octadecadienoic acid. The process is seldom taken to completion, since completely saturated fats would have melting points that were too high and without the desired plasticity characteristics (Gurr & James, 1980).

Hydrogenation is carried out in enclosed tanks in the presence of 0.05%-0.20% of a finely powdered catalyst at temperatures up to 180°C, with hydrogen gas pressure ranging from 0.5 to 4 atmospheres, and after which all traces of catalyst are removed by filtration. Nickel is used almost exclusively as selective catalyst. In the course of hydrogenation some of the double bonds are eliminated, while a significant proportion of the *cis* double bond of the natural oils are isomerized through *cis-trans* conversion and positional shift along the chain. Therefore, whereas a natural fat contains a high proportion of double bonds at position 9, the product of partial hydrogenation contains double bonds that are randomly distributed (Carpenter & Slover, 1973). The variety of isomers formed depends largely on the starting oil with the greatest assortment coming from highly unsaturated fatty acids as those present in fish oil. Selective hydrogenation is characterized by high *trans* unsaturation development with minimum iodine value drops (Windermann, 1978). In principle, there is little difference between the chemically-catalyzed reduction of double bonds employed by the food industry and the enzymatically catalyzed reduction of double bonds by the anaerobic fermentation of microorganisms in ruminant animals. The main difference is that the more drastic and less controlled industrial process produces a wide variety of isomers and in some products a higher concentration of isomers than the biological process. *Trans* fatty acids occurring in manufactured fats cannot be said to be unnatural in the sense that they occur in nature, but they may well occur in unnaturally high concentrations. Figure 2 outlines the main stages of a hydrogenation process (modified from Fitch-Haumann, 1994).

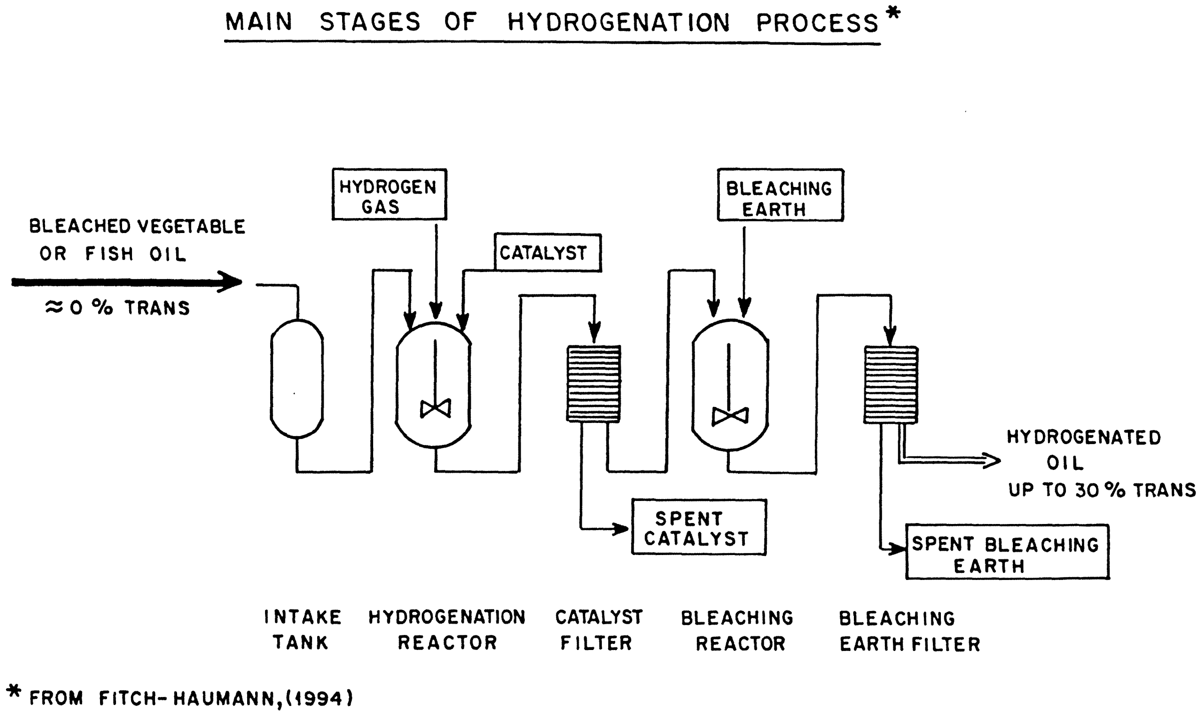

Fig. 2

4. CHEMICAL AND PHYSICAL CHARACTERISTICS OF *TRANS* FATTY ACIDS AND METHODS FOR IT ASSESSMENT.

Trans fatty acids differ markedly from their respective *cis* isomers in tertiary structure, melting points, interaction with enzymes and metabolism. The *trans* double bond creates a linear carbon chain compared with the kinked chain of the *cis* acids. Thus, *trans* fatty acid molecules can pack together in a crystalline array and their melting points are correspondingly higher than those of corresponding *cis* acids (Gurr & James, 1980) (Table I). The position of the double bond in *trans* monounsaturated fatty acids from partially hydrogenated vegetable oils, tended to be normally distributed around the position of the original *cis* double bond. *Trans* isomers contribute to the hardness of the products, the carbon moieties on the two sides of a double bond provides a straight, packed configuration, whereas the *cis* isomers found in vegetable oils have a bent configuration. Thus, *trans* fatty acids most closely resemble saturated fatty acids in their structural and physical characteristics (Emken, 1983).

Table I
Boiling point of different isomeric *cis, trans* fatty acids

ISOMERIC FATTY ACID	BOILING POINT (°C)
12:0	44.2
16:0	62.7
18:0	69.6
c- 18:1	13.2
t-18:1	44.0
c,c -18:2	-5.0
t,t-18:2	28.5
c,c,c - 18:3	-11.0
t,t,t- 18:3	-29.5

Currently, there are three methods officially accepted by the AOCS for the assessment of the *trans* fatty acid content of food products (Steiner, 1993). One is only applicable to margarines and two work with most vegetable fats and oils, these are the following: a) *Trans* insaturation in margarines by gas-chromatography (method Cd 17-85). b) Isolated *trans* isomers infrared-spectrophotometric method (method Cd 14-61). c) Fatty acid *cis* and *cis-trans* isomers by gas-chromatography (method Ce 1c-89).

Method Cd 17-85 determines the *trans* unsaturation in margarine by packed gas-chromatography column. This method uses the analyses of a mixture of methyl elaidate and methyl oleate as reference material. Retention times of known esters an peaks can be measured and used to identify peaks in the samples. Total *trans* content is obtained by addition of all *trans* isomers. Results agree well with those from the infrared method.

Method Cd 14-61, which is suitable for most vegetable fats and oils, is based on the fact that long chain fatty acids, esters and triacylglycerols may be measured by an infrared-spectrophotometer. The samples as free fatty acid, the methyl ester derivative or the triacylglycerol as such is dissolved in carbon disulfide and the absorption band of the sample at 10.3 nm is measured. The transmittance or absorbance of the sample is compared against a corresponding solution of elaidic acid, methyl elaidate or trielaidine. The method, which is frecuently used shows, however, some limitations e.g: inaccurate determinations when *trans* content is <15%, it is applicable only to isolated *trans* double bonds, and only the total *trans* content can be obtained.

Method Ce 1c-89; fatty acid composition by gas-chromatography, evaluates the fatty profile, the level of *trans* unsaturation, and *cis-cis* methylene-interrupted unsaturation in vegetable oils. In this method, esters are prepared from triacylglycerols and injected into the gas-chromatograph. Reasonable separation is achieved when a polar stationary phase and columns of proper length are selected. A concern with this method is that it understimates the 18:1 *trans* values, a substantial margin in favor of the *cis* isomers because of a *cis/trans* 18:1 overlap. At low *trans* levels (<15%), accurate determinations become difficult.

5. BIOLOGICAL EFFECTS OF *TRANS* FATTY ACIDS

The overall physiological implications of consuming *trans* fatty acids remain unclear. Dietary *trans* fatty acids are readily absorbed and incorporated into most mammalian tissues, including human tissues, at concentrations which apparently reflect their content in the diet (Senti, 1985). Monoenes *trans* fatty acids seem to have properties and enzyme selectivities between saturated and *cis* monoenes and are not equivalent to the correspondent saturated fatty acid. The extent of incorporation of individual positional *cis* and *trans* isomers into tissue lipids is different for specific tissues and between the neutral triacylglycerols and phospholipids in the same tissue (Beare-Rogers, 1988). However, it appears that most isomeric *trans* fatty acids can be located in membrane phospholipids at sites frequently occupied by saturated fatty acids (i.e. sn-1 and sn-3 positions). The brain and placenta apparently discriminates more readily against isomer inclusion compared to heart, liver and adipose tissue (Ohlrogge et al., 1982). The *trans* content of phospholipids is generally lower than of triacylglycerols (Senti, 1985). The level of dietary polyunsaturated *cis* fatty acids influence *trans* isomer incorporation into tissue lipids; inadequate intakes allowing greater *trans* isomer incorporation (Beare-Rogers, 1988).

Trans fatty acids have been implicated in the etiology of various metabolic and functional disorders. They increase erythrocyte fragility (Decker & Mertz, 1967), produce mitochondrial swelling reducing its oxygen consumption and ATP synthesis (Zevenbergen et al., 1988), and enhance the arrhytmogenicity of cardiac miocytes in experimental animals, probably by modulating or by diminishing membrane fluidity (Wenzel & Kloepell, 1980). Because of the effects of *trans* fatty acids on the metabolism of gamma-linolenic and arachidonic acid (Kinsella et al., 1981), ingestion of *trans* fatty acids can affect the metabolism of prostaglandins and other eicosanoids and may alter platelet aggregation and vascular function (Asherio et al., 1994). *Trans* fatty acids also show competitive interactions with essential fatty acid metabolism (EFA) by inhibition of it incorporation into membrane phospholipids and by reduction of the conversion of EFA to eicosanoids in different animal cells (Peacock & Wahle, 1989). *Trans* isomers ingestion results in essential fatty acids deficiency which may be prevented by increasing EFA availability (Kinsella et al., 1981; Zevenbergen & Haddeman, 1989). In addition, incorporation of *trans* fatty acids into membrane phospholipids may influence the physical properties of the membrane as well as the activities of the membrane-associated enzymes (Holman et al., 1991). *Trans* isomers have a weaker inhibitory effect on collagen-induced platelet aggregation than do *cis*-isomers (Peacock & Wahle, 1988). Further support for a specific effect of isomeric fatty acids derives from evidence that dietary *trans* fatty acids inhibit the activities of membrane-bound enzymes like Na+/K+ATPase and adenylate cyclase, and reduce the density of beta-adrenergic receptors in the plasma membrane of heart tissue taken from animals which were not deficient in EFA (Alam et al., 1989). However, *trans* fatty acids do not appear to have significant effect on reproduction, longevity, or the incidence of cancer (Senti, 1985).

Perhaps the main concerns about the health effects of *trans* fatty acids have arised because these isomers are structurally similar to saturated fats, they lack the essential metabolic functions of their parent polyunsaturated fats and compete with EFA in many complex metabolic pathways (Mann, 1994).

Recently, important new data on the health effects of *trans* fatty acid have become available. It has been demonstrated that *trans* fatty acid ingestion increase low-density lipoprotein (LDL) cholesterol to a similar degree as do saturated fats (Mensink & Katan, 1990). In contrast to other forms of fats, *trans* isomers decrease high-density lipoproteins (HDL) cholesterol. Thus the increase in the ratio of LDL cholesterol to HDL cholesterol for *trans* fatty acids is approximately double that for saturated fatty acids (Mensink & Katan, 1990). Thus, the effect of *trans* fatty acids on the serum lipoprotein profile is at least as unfavourable as that of the cholesterol-raising saturated fatty acids, because they not only raise LDL-cholesterol levels but also lower HDL-cholesterol levels. Similar adverse effects were confirmed in other studies. Willet et. Al., (1993) after a eight years long study including 85,000 nurses concluded that the intake of *trans* fatty acids, mainly from margarines, increases risk of coronary heart disease. Unlike other fats, *trans* fatty acids were found to increase lipoprotein(a), another risk factor for coronary heart disease (Mensink et. al., 1992).

Partially hydrogenated marine oils, which are extensively used in the manufacture of cheaper margarines, may contain up to 50% *trans* bonds and quite high amounts of 20 and 22 monoenes isomers.

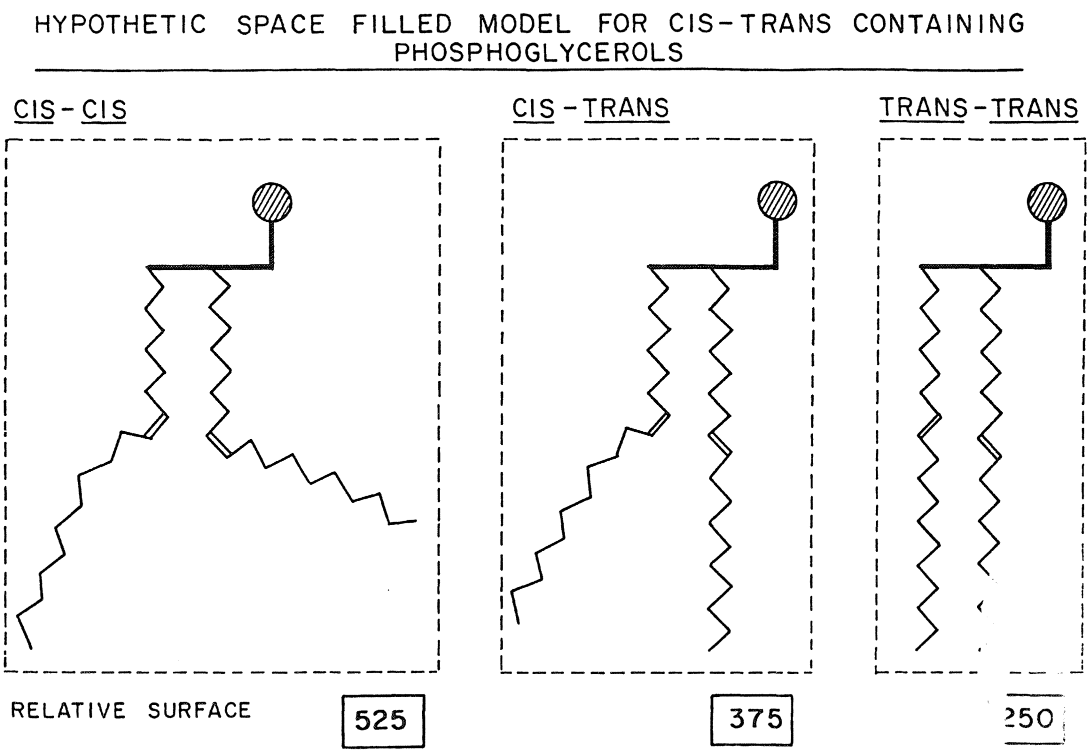

Fig. 3

These isomers, whose tissue distribution is quite different from those found in natural fats, are not incorporated into the membrane phospholipids, but induce peroxisome proliferation and are beta-oxidized to chain lengths of 18 and 16 carbons in the peroxisomes (Hoy, 1991). The marine oils hydrogenated fatty acids *trans* isomers interfere with delta-5 desaturases in the liver (Rosenthal and Doloresco, 1984) resulting in an accumulation of 18:2 n-6 and 20:3 n-6, and reduction of 20:4 n-6 fatty acids (Hoy, 1991). Figure 3 shows a hypothetic space filled model for *trans*-containing phosphoglycerols.

6. EFFORTS TO REDUCE THE *TRANS* FATTY ACID CONTENT OF FOODS

In response to the controversy, some companies are taking steps to develop products with lower or no *trans* fatty acid content. As margarines are the main target of criticisms referred to the *trans* fatty acid concern, the oleochemical industry has focused their effort to reduce or eliminate the *trans* content of these products. One strategy has been the blending of fully hydrogenated oils, containing no *trans* isomers, with unhydrogenated liquid oils naturally having no *trans* isomers. The hardness and the spreadability of the product must be adjusted by varying the proportion of the solid and the liquid portion of the blend. By means of these procedures it has been possible to reduce the *trans* fatty acid of stick and tub margarines from 50% to 10% content or less. Low fat content margarines, "diet margarines", containing below 40% fat, have *trans* content ranging from 10% to 7%.

Another strategy which is not yet full developed consist in the interesterification of highly hydrogenated fats with liquid oils by means of chemical or enzimatic-drive procedures. Unlike hydrogenation, interesterification neither affects the degree of saturation nor causes isomerization of the fatty acid double bond. Thus, it does not change the fatty acid profile of the starting material. Instead, it rearranges the fatty acids on the glycerol molecule. Random interesterification changes the crystal form of an oil or blend to produce desired solid fat content curves or to produce blends with high levels of polyunsaturated fatty acids. By this mixed procedure, hydrogenation-interesterification, it will be possible to obtain margarines with virtually zero *trans* content. However to achieve improved results it is necessary further developments (Fitch-Haumann, 1994).

GFA Brands, New Jersey (USA) is expending Smart Beat, a margarine which has zero saturated fats, zero *trans* fatty acids and only 2 grams of fat per one-tablespoon serving. This product first was sold under the name Heart Beat, but after pressure of FDA about the reference to "heart" the company changed the name to Smart Beat. The product is produced using high internal phase-ratio emulsion technology, which creates a water-in-vegetable-oil emulsion. However due to the low-fat nature of the margarine, it is not recommended for baking or cooking but only as a spread (Anonymous, 1994). The latest development in Europe has been the introduction of a fish oil spread manufactured by FDB Viby Fabrikker of Denmark. The spread consists of 20-25% highly deodorized liquid fish oil and 75-80% of highly hydrogenated vegetable fat. The product called Tobis has *trans* isomer contents lower than 15%, it contains no water, has a slightly yellow colour, and it is stable to oxidation (Anonymous, 1990). A product with different characteristics was developed by Unilever NV of The Netherlands. This is a blend of unhydrogenated marine oil with vegetable oil with a ratio of marine to vegetable oil below 1:3. This product which has non-trans isomers can be used for frying, baking and for making margarines and soft spreads (Anonymous, 1990). As another approach, non-caloric or hypocaloric fat substitutes are now used to develop non-*trans* and non-cholesterol butter and margarines (Singhal et al., 1991).

7. FUTURE PROSPECTS FOR *TRANS* FATTY ACIDS

The food industry could voluntarily phase out the production of *trans* fatty acids, but at present producers are resisting even the acknowledgment that their products have adverse effects. Thus a voluntary phase out is unlikely, although some largest producers have publicly committed themselves to reducing the *trans* isomer content of their products. An alternative is the development of policies regulating the *trans* fatty acids in foods by labeling its content. Some have suggested that *trans* fatty acids be included with the saturated fat on the label, but this must be accompained by education efforts directed to the consumers concerning the significance of *trans* fatty acids and the potential risks of their consumption from hydrogenated fats. Today such warning labels are applied to alcoholic beverages and cigarettes, being more justifiable to apply to partially hydrogenated fats because the nature of the product is invisible to the consumer.

As a matter of fact, some conclusion may be drawn from the actual information which may be summarized as follows:

- Intake of *trans* fatty acids cannot be avoided when the diet includes milk fat, ruminant fat and/or hydrogenated fats in margarines and shortenings.
- Much of the success of *trans* fatty acid-containing products is due to the economic appeal of their longer shelf life and decreased expense compared with other fat products such as butter.
- The average dietary intake of *trans* fatty acids will tend to decline, due to general reduced fat content in foods.
- Nutritionally, *trans* fatty acids should be of secondary priority, compared to saturated fatty acids. However, high intakes may have adverse effects on the plasma LDL/HDL, cholesterol ratio.
- There appear to be many ways to avoid *trans* fatty acids, but the healthiest would require some individual changes in eating style.

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